Newborn Genetic Screening: A Proposal of New Ethical Guidelines

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“Our scientists were so preoccupied with whether or not they could, they didn’t stop to think if they should.” - Ian Malcolm, Jurassic Park by Michael Crichton

The Dilemma in Genetic Testing

The World Health Organization and the Institute of Medicine deem newborn genetic screening appropriate only, “if the genetic disorder is serious, the test is accurate, and a therapy or intervention is available.” In other words, newborn screening should be an “intervention in order to protect a child from imminent harm.” However, these guidelines are filled with uncertain terms. As an increasing number of genetic disorders become identifiable through newborn genetic screening, the ambiguous guidelines will become much more difficult, if not impossible, to impose. The medical community is in need of a new, more explicit set of guidelines in order to ensure the ethical use of newborn genetic screening now and in the future.

Princiaplism is an ethical theory that has been popular in medical ethics since the mid-1970s and provides a useful framework for the current genetic screening dilemma. The four components of the theory are, 1) beneficence, or contributing to the general welfare of people 2) Non-malfeasance, which is the obligation to not intentionally or negligently inflict harm 3) Justice, referring to the fair and equal treatment that is owed to an individual, and 4) autonomy, the freedom of will and actions. Each of these components relates to a specific aspect of newborn genetic screening and that will be used to develop a set of ethical guidelines.

Newborn Genetic Screening

A brief background in genetic testing is constructive in understanding its uses and consequences. Newborn screening is a health program that uses genetic testing to diagnose diseases and disorders in newborn infants. Genetic screening began after the discovery of the DNA double helix structure by James Watson, Francis Crick, Rosalind Franklin, and Maurice Wilkins on April 25, 1953. This discovery of the DNA structure paved the way for genetic research. In the 1960s, information gathered from the DNA of infants was used to identify rare genetic conditions. Today, state public health programs in all 50 states screen an estimated 4.1 million infants annually for genetic and metabolic disorders.

Since the 1960s, the emergence of technological advancements has opened the door to a new wealth of knowledge regarding genetic research. April 25, 2003 not only marked the 50th anniversary of the discovery of the DNA structure, but this date also
marked the completion of a project that redefined the capabilities of genetic screening. The Human Genome Project (HGP) began in 1990 with the intent to uncover new and improved ways to detect and treat genetic diseases. With this purpose in sight, the HGP had established goals to:

- Identify all of the approximately 20,000-25,000 genes in human DNA
- Determine the sequences of the 3 billion chemical base pairs that make up human DNA
- Store this information in databases
- Improve tools for data analysis
- Transfer related technologies to the private sector.  

There is no doubt that the completion of the HGP has catapulted genetic research into a new era with astounding possibilities for diagnosis and treatment of newborns. However, recent developments have come at such a rapid pace that our society is not yet prepared to handle the ethical implications of tests with less immediate and less clear benefits.

Technology now affords us the ability to test for over 1,300 genetic diseases and disorders including myotonic dystrophy, Duchenne muscular dystrophy, hemochromatosis, polycystic kidney disease, and Huntington’s disease to name a few. Capabilities also exist to determine the probability of common disorders such as coronary artery disease, diabetes, stroke, hypertension, Alzheimer’s disease, some forms of colon and breast cancer, and several psychiatric conditions. Each of these disorders comes with a unique set of causes, symptoms, and implications. The seriousness of a disease is largely subjective, and the accuracy of tests is frequently changing, as are the intervention possibilities. Therefore, to justify use of a genetic test based only on these three broad guidelines has become an outdated method for the complexity of the various aforementioned disorders. Using the framework of Principlism and its four components will allow us to develop a more useful set of ethical guidelines.

**Beneficence**

In general, beneficence is defined as the doing good, and in regards to genetic screening it refers to a procedure that will contribute to the welfare of an individual. There are two components of newborn tests that determine beneficence. The first is the seriousness of the disease and the second involves the ability to intervene in order to achieve an improved outcome. The latter will be dealt with first.

Many of the disorders for which screening exists do not currently have a known cure or prevention treatment available. However, the rate of scientific advancement and the resulting growth of the biotechnology markets are at an all time peak and only continue to increase. According to Forbes Magazine, a biotechnology company called ImClone Systems is the second fastest growing technology company nationwide, trailing only behind Google, with 163% growth over the past five years. An additional five other biotechnology firms also made the list for the 25 Fastest-Growing Technology Companies in 2006. Such a rate of increase makes it illegitimate to discredit a particular test simply because there is currently no treatment. It discounts the idea that newborns should not be screened for diseases and disorders that do not reduce morbidity and mortality through interventions initiated in childhood. It is probable that treatment may become available within that person’s lifetime, if not within the next few years, and in
those cases, it is both beneficial and necessary for an individual to be informed of their disorder.

Because arguing treatment options is not legitimate, we must focus on the seriousness of the disease in order to determine beneficence. There is great discrepancy among people in their view of disability and what constitutes a “serious” disorder. It is very difficult to determine which tests should be administered to newborns as more diseases that may not be classified as serious become testable. Many diseases that become identifiable show that a newborn has a high susceptibility to symptoms, but even with a high probability to develop the disease it is not a certainty. Inevitably there are problems determining how high the probability of contracting a disease must be in order for the newborn to qualify for treatment.

It is important to develop a clear definition of what constitutes a serious disease and in order to do this we can look at the notion of health. The definition of health has transformed over time from an emphasis on survival to a multifaceted perspective that includes "an emphasis on the individual's ability to perform daily activities, and ... an emphasis on positive themes of happiness, social and emotional well-being, and quality of life." Similarly, the World Health Organization claims that, "for people to reach a state of complete physical, mental, and social well-being, an individual or group must be able to identify and realize aspirations, to satisfy needs, and to change or cope with the environment." Based on these definitions we have developed a multidimensional definition of a serious disease:

* A serious disease is an incorrectly functioning organ, part, or system of the body, which perceptibly hinders the ability of the individual to perform normal daily activities and/or impairs quality of life in regards to emotional and social well-being.*

The following are examples of diseases with varying degrees of seriousness for which screening is very common.

**Phenylketonuria (PKU)**

Phenylketonuria (PKU) is a genetic disorder that is characterized by an inability of the body to utilize the essential amino acid, phenylalanine, which if left untreated can cause progressive and severe mental retardation. Newborns have been screened for this disease since the 1960s and once diagnosed, simple dietary changes can be made to prevent symptoms from surfacing. Using the above definition we can determine that PKU is indeed a serious disease because the accompanying mental retardation would both affect the ability to perform daily activities and quality of life. PKU is a simple case, but there are more complex diseases that are not quite as cut and dry.

**Diabetes**

Currently, there is an ensuing debate occurring over predictive diabetes screening. Type I Diabetes Mellitus is the most common metabolic disease seen among children and currently two states offer voluntary newborn screening in conjunction with other metabolic screening to identify children with a genetic predisposition to it. The reality that exists with Type I Diabetes screening is that it reveals predisposition, not a certain diagnosis. This is a prime example of a much more complex disorder where the effects on a particular individual are unknown. However, we can still attempt to determine the seriousness of the disease based upon the probability associated with predisposition. The onset of Type I Diabetes does produce symptoms requiring extensive treatment that would be classified as serious under the definition. Diabetes also drastically affects the
way an individual performs daily activities, especially with regards to diet and exercise. Therefore, while revealing predisposition to the disease does not constitute it being a serious condition, the probability of the onset does.

**Non-Serious Conditions**

The 1997 film, *Gattaca*, provides insight as to the risks of testing for non-serious conditions. Although this drastic scenario is not necessarily occurring, it is foreseeable. The film portrays a future where society analyzes DNA and determines where each person belongs in life. Things such as life expectancy, aptitude, and likelihood of certain physical features are ascertained and determine whether, for example, a person should go to military school, into the low-labor workforce, or to a prestigious university, completely based on the results of genetic tests obtained at birth. The main character Vincent was born with a congenital heart condition and due to die at the age of 30, which cast him immediately out of a chance to achieve his aspiration of space travel. He in turn is forced to assume the identity of an athlete whose genes would allow him to realize his dream. Professor Alan B. Wood of Northern Arizona University also foresees this scenario as a “not-too-distant future world in which genetic research and engineering has fulfilled its wildest dreams,” and claims that a “human being cannot be defined and delimited by genetic possibility.”

**Recommendation**

According to the first component of beneficence, each disease must be looked at individually to determine the seriousness of that condition. The following recommendation for a new guideline is based on this principle:
- The introduction of new newborn screening tests should be subjected to carefully monitored research procedures, which will determine if the tested disease qualifies as being serious or not.

**Non-Malfeasance**

Non-maleficent actions are those, which are not intentionally evil in nature. In the medical realm, it is unlikely to find a test that would intentionally harm an individual; however, malfeasance encompasses negligent actions that cause harm as well. This is much more common, and there are many examples of maleficent actions that occur with newborn screening simply due to negligence including relying on false test results, underestimating psychological implications, and inadequate interpretation of results.

A particular study on Tandem Mass Spectrometry, a type of screening used for metabolic disorders, showed that the screening produced test results at a 90 percent false-positive rate. This means that only 10 percent of the patients diagnosed with a metabolic disorder through screening actually had the disorder. The implications of such false-positive results are immense including psychological, emotional, and social anxiety and risks. With increasing pressure in hospitals to release newborns earlier, the false-negative problem only becomes exasperated due to abnormal blood levels common within the first few days of birth.

False-positive results can leave families with a feeling of unnecessary anxiety. For example, in a 1991 study only 6.1 percent of infants with positive first tests were ultimately found to have cystic fibrosis, however, one-fifth of the parents of false-positive babies had lingering anxiety about their child’s health. Although they were told their child was not actually affected by the disease, they could not seem to escape from the
idea that their child would be ill or disabled. In fact, in a cystic fibrosis study done in Wisconsin, 5 percent of the parents who were told that their newborn was healthy after a false-positive result still believed one year later that their child had the disease, negatively impacting the parent-child relationship. In addition, the same study showed that 8 percent of families receiving false-positive results still changed their future reproductive plans, and an astonishing 22 percent were considering changing their plans despite perfectly healthy first children.

As pediatric testing is a complex process, results are not always accurate. However, the results depend not only on reliable laboratory procedures but also on accurate interpretation of results. According to the Lawrence Berkeley National Lab (LBNL) report among a group of one million children receiving genetic screening, there will be at least 500 false-negatives, who remain unaware of their diseases and 10,000 false-positives. Advancements in technology will allow for improvements in these numbers, however, being able to analyze and convey the results of genetic tests to affected individuals and their families requires a very specialized set of skills and training that many physicians do not yet possess.

There are a very limited number of genetic screening experts and counselors to manage genetic screening results, laboratories and technologies. Being totally dependent on a relatively small, specialized workforce and providing proper education and training has proved to be difficult. These limited specialists generally do not have enough time and resources to explain the importance, appropriateness, and risks of genetic screening to parents. Under-qualified physicians are instead often relied upon for explanation.

**Recommendation**

The negligence in these cases occurred because the test results were never validated or the interpretation of the results was not given a high enough duty of care. The negative resulting consequences are an example of how this negligence can lead to harm. The following recommendation is based upon this evidence in conjunction with the principle of non-malfeasance:

- Until proper training can be administered, pediatricians and other physicians need to be assisted in managing many of the complex issues involved in genetic testing by collaborating with geneticists, genetic counselors, and other subject-matter experts.

**Justice**

The notion of justice refers to the fair and equal treatment that is owed to an individual. There are many fairness issues that need to be considered with newborn genetic testing. Mismangement of genetic test results presents the risk of personal genetic information falling into the hands of employers or insurers, which may lead to discrimination. Also, some tests may be viewed as discriminatory in and of themselves to certain groups of people or within families. Another concern is that because genetics generally have familial implications, results may be interpreted (or misinterpreted) to assume the parents or other members of the family possess the same genetic abnormalities causing a premium increase or denial to the entire family. Finally, it is also common that misunderstanding of carrier status may lead to the erroneous belief that a carrier is affected with the disease.
According to the National Council on Disability, a 1996 survey of 917 individuals at risk of developing a genetic condition and parents of children with specific genetic conditions indicated more than 200 instances of genetic discrimination. Employers, insurers, and other organizations practiced the discrimination. Another survey of genetic counselors, primary care physicians, and patients identified 550 individuals who were denied employment or insurance based on genetic information. Science magazine reported that in a study of 332 individuals with one or more family members with a genetic disorder who are affiliated with genetic support groups, 40 percent of the respondents recalled being specifically asked about genetic diseases or disabilities on their applications for health insurance. Twenty-two percent of the respondents said they or a family member were refused health insurance as a result of the genetic condition in the family. Fifteen percent of the respondents reported that they or affected family members had been asked questions about genetic diseases or disabilities on employment applications. Thirteen percent reported that they or a family member had been denied a job or fired from a job because of a genetic condition in the family, and 21 percent reported being denied a job or fired due to their own genetic disorder.

There are several individual cases of employment discrimination that support the aforementioned statistics. During the early 1970s, employers used genetic screening to identify and exclude African Americans carrying a gene mutation for sickle cell anemia. Many of those who were not hired turned out to be completely healthy and never developed the disease. On May 6, 2002 the Equal Employment Opportunity Commission (EEOC) settled a case against Burlington Northern Santa Fe Railway concerning the conducting of undisclosed genetic testing on employees. The company was receiving complaints from workers with Carpal Tunnel Syndrome who claimed their condition stemmed from workplace activities. Burlington proceeded to secretly screen employees for an existing predisposition to the condition.

Discriminatory practices have been proven to exist in conjunction with genetic screening of adults in the workplace. Today, results of newborn genetic screening tests are recorded into medical databases that make it much easier for insurance companies and employers to access personal genetic information. Increased access to this information may or may not necessarily lead to an increase in employment and insurance discrimination but will, however, encourage those companies who already engage in this practice.

A much more obscure social consequence of genetic screening lies in the fact that genetic diseases affect people of different races or ethnic backgrounds differentially. Minority groups who have been historically discriminated against may feel that screening targets disorders that occur entirely or mostly within their race. The resulting abstention from reproduction caused by positive test results can be viewed as a form of genocide. Similarly, people currently living with a particular genetic disorder may view mandatory screening for that disorder as an effort to eradicate their kind.

The risk of discrimination can also occur within a family, specifically affecting the parent-child relationship. Sherlock and Morrey make the claim that parents may
actually treat their child differently pending abnormal test results stating that they may stigmatize or reject children with the abnormal genes, or may be less willing to devote financial resources, education or other benefits for such children. In fact, in Denmark, screening for a disorder called alpha 1 amitrypsin deficiency was terminated after it was determined that the long-term effects on the mother-child relationship were negative and detrimental.

Recommendations

Without a guideline to ensure justice it is easy to see how increasing use of genetic screening can lead to various forms of discrimination, which threatens the fairness and equal treatment that is owed to all people. The following recommendations are based on the principle of justice:

- Current and future newborn screening tests that are administered should be administered equally to all races and sexes.
- Insurance companies and employers should not have access to genetic information. In light of the ever-changing technology, current and future tests should be periodically assessed to eliminate tests that have become discriminatory and do not provide a benefit.

Autonomy

Autonomy refers to an individual’s freedom of choice. Two conditions are essential for autonomy: (1) liberty, which is independence from controlling influences, and (2) a capacity for intentional action. There is much discrepancy across the country on genetic screening policy. In some places, autonomy is being respected, and in others it is being rejected. It is important to look at the varying domestic policy to determine what will provide autonomy in regards to genetic testing.

Currently, the scientific community, in discussions of whether genetic screening should be mandated, is comparing the method to a paradigm of clinical testing for infectious diseases. In applying the public health model to genetic testing, there lies the question of where individual rights and decisions end, and group responsibility begins. The logic states that society has a duty to intervene in order to provide good to the public, for example, the mandating of certain vaccines and educational campaigns against such risks as smoking. However, due to many discrepancies between clinical and genetic testing, the public health model approach to genetics does not hold water.

The main disparity between genetic and clinical testing is that infectious diseases pose a direct and immediate threat to society, whereas genetic abnormalities pose a potential risk to individual or even future generations. More importantly, the goal with diagnosis of infectious disease is to provide some form of treatment or cure to prevent dissemination. However, the concept of prevention or cure does not fundamentally fit this model because most genetic defects, unlike most infectious diseases, generally cannot now be fixed. A different approach must be taken with genetic screening.

The major question is whether genetic screening should be mandated or whether explicit parental consent should be required, and what effect this has on autonomy. An approach requiring explicit consent necessitates an informed decision by parents about
newborn screening. Mandatory screening typically requires an explicit refusal of screening by parents, although many parents are unaware of this option.

There currently exists a wide spectrum of policies on newborn screening across the United States. The District of Columbia and Maryland are the only two jurisdictions that clearly state that screening is voluntary. On the contrary, South Dakota does not even permit parental refusal of newborn screening even for religious or personal reasons. In addition, Missouri and South Carolina have criminal penalties for parents who refuse newborn screening. The principal ethical justification presented for mandatory screening is the claim that society has an obligation to promote welfare of the nation’s children through early detection and treatment of particular disorders. This obligation surpasses parental rights to refuse this simple medical intervention. The opposing argument states the claim that parents typically have broad discretion for making health care decisions for their own children. Although parents do not possess the right to refuse effective treatments for life-threatening conditions, they generally have the option to pursue a variety of alternatives in less threatening circumstances, including decisions that medical professionals would not recommend.

The core rule at stake is autonomy, which, if used as a guiding principle, says that people should be allowed to make informed, intentional decisions. Evidence shows that the majority of parents will continue to be supportive of newborn screening once they are informed of the risks and benefits anyway. In a study of newborn screening in Maryland involving informed consent, the informed refusal rate was only 5 per 1000 infants. In general, mothers preferred and appreciated being informed. In this particular study, it was reported that the consent process typically took 5 minutes or less of staff time and placing minimal burden on both hospital staff and parents.

Recommendation

Principlism asserts autonomy to be a guiding standard and an informed consent approach for genetic screening will allow the programs to continue while enhancing the quality and maintaining respect for traditional parental prerogatives to be informed participants in health care decisions for their children. The following recommendation is based on autonomy:

- There is a need for uniform policy among states requiring a voluntary informed consent method for implementing the tests. Because genetic screening and testing is not well understood, there is a need to provide parents the necessary information and counseling about the limits and flaws of genetic knowledge, treatment capabilities (should they exist), and the potential harm that may be done by gaining certain genetic information.

Conclusion

It is recognized that genetic screening in the age of the human genome project has provided the medical community with information that can be very beneficial. However, the problem lies within the fact that these technologies are being produced at a far faster rate than society can ethically manage them. The current ethical guidelines are insufficient for the complexities that exist in genetic screening today.

Principlism provides a very useful framework for addressing this issue guided by the four standards of beneficence, non-malefeasance, justice, and autonomy. Based upon
these components, we have developed a more useful set of ethical guidelines that will allow
the scientific and medical community to better analyze very complex disorders and
situations that have arisen due to sweeping technological advancements. The following is a
recap of our recommendations for new guidelines.

- The introduction of new newborn screening tests will be subjected to
carefully monitored research procedures, which will determine whether or not
the disease for which it is testing qualifies as being serious according to a
universal definition.
- Until proper training can be administered, pediatricians and other physicians
need to be assisted in managing many of the complex issues involved in
genetic testing by collaborating with geneticists, genetic counselors, and other
subject-matter experts.
- Current and future newborn screening tests that are administered should be
administered equally to all races, ethnicities, and sexes, and insurance
companies and employers should not have access to the results.
- In light of the ever-changing technology, current and future tests should be
periodically assessed to eliminate tests that have become discriminatory and do
not provide a benefit.
- There is a need for uniform policy among states requiring a voluntary or
explicit and informed consent method for implementing the tests. Because
genetic screening and testing is not well understood there is a need to provide
parents the necessary information and counseling about the limits and flaws
of genetic knowledge, treatment capabilities (should they exist), and the
potential harm that may be done by gaining certain genetic information.

Newfound possibilities for newborn genetic screening present risks that demand
greater ethical consideration than what is currently being recognized by the scientific and
medical communities. Only by adhering to a defined set of well-framed guidelines can the
ethical use of genetic tests be ensured now and in the future.

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