A commentary on the President's Council on Bioethics report: the changing moral focus of newborn screening

Alan R. Fleischman, MD[1,2], Bruce K. Lin, MPH[1], and Jennifer L. Howse, PhD[1]

BACKGROUND: NEWBORN SCREENING IN THE UNITED STATES

Newborn screening is a public health program that provides early identification of rare genetic, metabolic, hormonal, and functional disorders among infants, and follow-up care for those affected. Without treatment, the screened-for disorders can result in devastating health consequences, and in some cases, death. What began in the mid-1960s as an activity to identify a single rare but serious metabolic disease that occurred in about 1 in 25,000 newborns, phenylketonuria, has now dramatically expanded. This increase in recent years is due to a much better understanding of these rare conditions and the advent of new technology to reliably identify such rare disorders. These advances resulted in a 2005 report by the American College of Medical Genetics (ACMG), commissioned by the U.S. Health Resources and Services Administration that recommended mandatory newborn screening for a core panel of 29 disorders.[1] The ACMG report, which was enthusiastically endorsed by the Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children, the American Academy of Pediatrics and the March of Dimes, was an attempt to move the nation toward a uniform newborn screening panel for serious disorders for which effective preventive interventions and treatments exist.

From the time ACMG released its report in 2005, through February 4, 2009, 25 states and the District of Columbia, have fully implemented state laws or regulations that mandate newborn screening for the 29 core conditions. In addition, two states have set in motion the requirement for screening of all 29 core conditions, but have yet to fully implement the program; 10 states require screening for 28 core conditions and universally offer, but do not require screening for the 29th condition; and 17 states require screening for 28 of the core conditions. At present, nearly 97% of America's newborns live in states that require screening for 21 or more of the core conditions.[2] In most cases, adoption of the new panel of tests followed intense debate by state newborn screening advisory committees, which provided yet another layer of review.

PRESIDENT'S COUNCIL ON BIOETHICS REPORT

In December 2008, The President's Council on Bioethics released a report on newborn screening entitled, "*The Changing Moral Focus of Newborn Screening*."[3] This is one in a series of monographs and reports developed by this Council that was created in 1995 to advise the President on ethical issues related to advances in biomedical science and technology.

The aim of the current report is to: "foster public awareness of the practice of newborn screening, the ethical principles that have guided it until now and the ethical problems posed by its current and future expansion." As the Council notes in the introduction, the report is written to answer the question, "What ethical principles should guide the practice of newborn screening in the United States?" The report consists of four chapters. Chapter 1 describes newborn screening practice and policy as it exists in the United States. Chapter 2 presents the classic principled justification for mandatory newborn screening and argues that present newborn screening programs have shifted from those principles in recent years. In Chapter 3, the report discusses the possible future of newborn screening in the context of the genomic era, and finally, in Chapter 4, the report delves into the mandatory nature of newborn screening and questions the justification for the present newborn screening program without informed parental consent. On the basis of this analysis, the Council concludes with seven elements that should be part of "an ethically sound approach to public policy in newborn screening:

1. Reaffirm the essential validity and continuing relevance of the classical Wilson-Junger screening criteria.
2. Insist that mandatory newborn screening be recommended to the states only for those disorders that clearly meet the classical criteria.
3. Endorse the view that screening for other conditions that fail to meet the classical criteria may be offered by the states to parents on a voluntary basis under a research paradigm.
4. Affirm that when differential diagnosis of some targeted disorders entails detection of other poorly understood conditions that would not otherwise be suitable candidates for newborn screening such results need not be transmitted to the child's physician and parents.
5. Encourage the states to reach a consensus on a uniform panel of conditions clearly meriting mandatory screening.
6. Urge a thorough and continuing re-evaluation of the disorders now recommended for inclusion in the mandatory screening panel, to ascertain whether they genuinely meet the classical criteria that would justify mandatory screening of all newborns, or whether they instead are suitable candidates for pilot screening studies.
7. Reject any simple application of the 'technological imperative,' i.e., the view that screening for a disorder is justified by the mere fact that it is detectable via multiplex assay, even if the disorder is poorly understood and has no established treatment."

The Council neither endorses nor rejects the list of recommended core conditions. However, the report rejects the notion that additional test results that reveal a child has a

From the [1]March of Dimes Foundation, White Plains, New York; [2]Departments of Pediatrics and Epidemiology and Population Health, Albert Einstein School of Medicine, Bronx, New York.

Alan R. Fleischman, MD, 1275 Mamaroneck Avenue, White Plains, NY 10605. E-mail: afleischman@marchofdimes.com.

Disclosure: The authors declare no conflict of interest.

Submitted for publication April 13, 2009.

Accepted for publication April 13, 2009.

Published online ahead of print May 27, 2009.

DOI: 10.1097/GIM.0b013e3181a9d66c

disorder not presently amenable to treatment, found during the course of screening for the core conditions, should be revealed to families.

Comments and clarifications

1. Reaffirm the essential validity and continuing relevance of the classical Wilson-Junger screening criteria.

The classic Wilson-Junger principle referenced by the Council report that justifies mandatory newborn screening can be summarized by the phrase "screen only if you can effectively treat." The ACMG criteria for including a disorder in the recommended core screening list were identification of the disorder before symptoms occur through a sensitive, specific test performed shortly after birth; and demonstrated benefit of early detection, timely intervention, and efficacious treatment.[1] The March of Dimes supports universal, mandatory newborn screening for the recommended panel of core conditions and believes these disorders meet the following criteria: (1) There is documented medical benefit to the affected infant from early detection, and treatment; (2) There is a reliable screening test for the disorder; and (3) Early detection can be made from newborn blood spots, or other specific means.[4] These ACMG and March of Dimes criteria for disorders included in the recommended list of core conditions are wholly consistent with the Wilson-Junger principle and the view of the Council.

2. Insist that mandatory newborn screening be recommended to the states only for those disorders that clearly meet the classical criteria.

Mandatory newborn screening is only recommended for the 29 core conditions that do meet the criteria. A clear distinction needs to be made between these core conditions recommended for mandatory screening and the "secondary" conditions that are identified as a result of the use of tandem mass spectrometry as the laboratory approach to newborn screening. Tandem mass spectrometry testing is used to measure 20 of the core conditions. This approach inevitably reveals results for several other conditions not in the core panel. These additional conditions are revealed as incidental findings of the testing procedure or as a consequence of clarifying the differential diagnosis of a core panel condition.

3. Endorse the view that screening for other conditions that fail to meet the classical criteria may be offered by the states to parents on a voluntary basis under a research paradigm.

Some states do screen for conditions not recommended in the core panel and not revealed incidentally by the testing procedures as secondary conditions.[5] This has generally been the result of local efforts by affected families and others who convince state legislatures to mandate testing for a rare and serious disorder for which effective treatment is not yet available. Well-intentioned legislatures have justified these laws to include other disorders in the mandatory panel of tests without invoking a research paradigm. We do not object to individual states providing screening tests in addition to those recommended in the core panel or revealed as secondary conditions after due consideration by that state's advisory panel on newborn screening and approved through a legislative or regulatory process. There is also a role for research within newborn screening programs to enhance screening techniques and study other disorders that may be candidates to join the recommended core panel. Such research should be subject to federal and state research regulation and reviewed by an appropriate institutional review board for research involving human participants.

4. Affirm that when differential diagnosis of some targeted disorders entails detection of other poorly understood conditions that would not otherwise be suitable candidates for newborn screening such results need not be transmitted to the child's physician and parents.

The Council concludes that each state should formulate rules governing whether and when to disclose incidental findings to families, and argues that states have no ethical obligation to reveal to a family that their child has tested positively for a known, rare, and serious disorder for which treatment is not presently available. The report argues that the potential harm done by revealing an incidental finding to a family without the availability of treatment is so great as to mandate that states either suppress the information, not revealing it to families, or develop an informed consent that is administered at the time of obtaining the blood sample shortly after birth, allowing families to opt out of learning about positive test results.

The issue of whether physicians and researchers should reveal incidental findings to patients or research participants is not new.[6] In the context of newborn screening, many families report wanting to know such information to best prepare for when the child begins to have symptoms and to obviate the need for what has been called the "diagnostic odyssey," an experience that families embark on when their child begins to have nonspecific symptoms for which physicians seek to unravel the cause.[7,8] Because the diseases are rare and the symptoms are not specific, this process can often be protracted and expensive as symptoms worsen. In addition, another pregnancy may ensue without proper preconception testing of the parents that might reveal important information about their reproductive choices and could ensure that the next child is not affected by the same disorder. Many parents of affected children, whether treatment is available or not, would have wished to know about the diagnosis before initiation of symptoms in infancy.[9] For these reasons, we support revealing incidental test results of these secondary conditions to families accompanied by the provision of counseling and support services. This approach will also allow families to decide if they wish to enroll their child in clinical research studies that might be available to explore new treatments for that child's disease.

The report does not advocate informed consent for the core tests, and we agree that informed consent should not be part of newborn screening. An informed consent process designed solely to highlight the potential to learn about incidental test results would be confusing to families at best and potentially harmful to the child and possibly to future siblings. Even though we do not believe informed consent is required for the present newborn screening program, we encourage education of families and professionals so that that they are knowledgeable about newborn screening. It is important to inform all prospective and new parents about newborn screening, its purpose, and the potential for some children to need confirmatory testing if results are positive.

5. Encourage the states to reach a consensus on a uniform panel of conditions clearly meriting mandatory screening.

We agree that there should be a uniform panel of core conditions that all states adopt. The geographic location in which a child is born in the United States should not determine whether one of these rare, serious, and treatable disorders is diagnosed and treatment initiated before irreversible harm occurs. It is the

responsibility of the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children that was chartered in 2003 to advise the Secretary "regarding the most appropriate application of universal newborn screening tests, technologies, policies, guidelines, and standards for effectively reducing morbidity and mortality in newborns and children having, or at risk for, heritable disorders." This committee has recommended that the 29 core conditions proposed in the ACMG report be adopted by state newborn screening programs, and has transmitted this recommendation to the Secretary. In addition, the committee has created a systematic methodology for the evaluation of any other disorder proposed to be included in the mandatory screening panel including a formal evidence-based assessment of what is known about the disease, the proposed test, and the available treatments. A national review process is needed because no individual state has the expertise alone to evaluate all these conditions.

6. Urge a thorough and continuing re-evaluation of the disorders now recommended for inclusion in the mandatory screening panel, to ascertain whether they genuinely meet the classical criteria that would justify mandatory screening of all newborns, or whether they instead are suitable candidates for pilot screening studies.

A recent report from the Centers for Disease Control and Prevention estimates that close to 6500 infants per year would be identified with a metabolic, hematologic, or hormonal disorder through newborn screening if all the states adopted the ACMG recommended panel of core conditions.[10] In addition, universal hearing screening is estimated to identify 12,000 infants per year who have impairment.[11] Continual evaluation of the national newborn screening program to assure clinical effectiveness of these public health efforts is certainly warranted. Not only should data be collected on the effectiveness of treatment for the indicated disorders but also on the effectiveness of state programs for referral and provision of services for the affected children and families.

7. Reject any simple application of the "technological imperative," i.e., the view that screening for a disorder is justified by the mere fact that it is detectable via multiplex assay, even if the disorder is poorly understood and has no established treatment.

We agree that it is unwise to simply adopt a technological imperative in planning the expansion of the newborn screening program. Rather, as laboratory technology evolves in the genomic era with DNA-based testing replacing tandem mass spectrometry, we will need to carefully reassess the criteria for mandatory newborn screening. It is likely that in the future, the public will be more knowledgeable about the importance of genetic information, better able to balance the risks and benefits of knowing such intensely personal information about themselves, their children and their family, and will be more accepting of the benefits and limitations of such information.[12,13] In addition, new laws and regulations seem to be helping to decrease fears about genetic discrimination and stigmatization.[14]

CONCLUSION

Newborn screening is an established and effective public health program to identify children with rare diseases and refer them for needed treatment. The President's Bioethics Council report recognizes the positive impact of this program and aims to foster public awareness of the practice of newborn screening and the ethical principles that have guided it. The recently enacted federal legislation, *Newborn Screening Saves Lives Act,*[15] which authorizes funding for grants to help states expand and improve their newborn screening programs, educate parents, and health care providers about newborn screening, and improve comprehensive follow-up care for infants with an illness detected through newborn screening, could go a long way to fulfilling those laudable aims if the law is fully funded and implemented.

The Council report also cautions that there could be ethical problems posed by the current and future expansion of newborn screening. We do not believe that the present newborn screening program is ethically problematic. We support the Secretary's Advisory Committee in its role to create the recommended list of disorders that should be universally screened and believe all states should adopt that list. We urge states to reveal to families the results of those secondary conditions that are incidental findings from the laboratory testing for core disorders. We believe this is ethically justifiable and should not require prior informed consent.

We agree that a technological imperative should not drive the future expansion of newborn screening programs, but we are more optimistic than the Council that thoughtful review of planned changes in the program can be accomplished as new technologies for testing become available. Most importantly, present and future newborn screening programs should focus on identifying infants with serious disorders and assure referral for needed services for the affected child and family to optimize the child's health and well-being.

REFERENCES

1. Newborn screening: toward a uniform screening panel and system. *Genet Med* 2006;8(suppl 1):1S–252S.
2. March of Dimes Foundation, 2009. Available at: http://www.marchofdimes.com/aboutus/22684_51920.asp. Accessed March 23, 2009.
3. The President's Council on Bioethics, 2008. Available at: http://www.bioethics.gov/reports/newborn_screening/index.html. Accessed February 18, 2009.
4. Howse JL, Weiss M, Green NS. Critical role of the March of Dimes in the expansion of newborn screening. *Ment Retard Dev Disabil Res Rev* 2006; 12:280–287.
5. Wadsworth Center–New York State Department of Health, 2005. Available at: http://www.wadsworth.org/newborn/babhealth.htm#listing. Accessed February 16, 2009.
6. Illes J, Kirschen MP, Edwards E, et al. Ethics: incidental findings in brain imaging research. *Science* 2006;311:783–784.
7. Skinner D, Sparkman KL, Bailey DB Jr. Screening for Fragile X syndrome: parent attitudes and perspectives. *Genet Med* 2003;5:378–384.
8. Centers for Disease Control and Prevention, 2004. Available at: http://www.cdc.gov/ncbddd/Duchenne/documents/NBS_Lay_Report.pdf. Accessed February 18, 2009.
9. Alexander D, Van Dyck PC. Neonatal screening: old dogma or sound principle? (in reply) *Pediatrics* 2007;119:407.
10. Centers for Disease Control and Prevention (CDC). Impact of expanded newborn screening—United States, 2006. *MMWR Morb Mortal Wkly Rep* 2008;57:1012–1015.
11. National Center for Hearing Assessment & Management, Early Hearing Detection and Intervention, 2008. Available at: http://www.infanthearing.org/resources/fact.pdf. Accessed March 23, 2009.
12. Collins FS, Green ED, Guttmacher AE, Guyer MS. A vision for the future of genomics research. *Nature* 2003;422:835–847.
13. Discretionary Grant Information System, Consumer Initiatives for Genetics Resources and Services. Rockville, US Department of Health and Human Services, Maternal Child Health Bureau, 2004. Available at: https://perfdata.hrsa.gov/mchb/DGISReports/default.aspx. Accessed February 16, 2009.
14. Hudson KL, Holohan MK, Collins FS. Keeping pace with the times—the Genetic Information Nondiscrimination Act of 2008. *N Engl J Med* 2008; 358:2661–2663.
15. Thomas database—Newborn Screening Saves Lives Act. Washington DC: Library of Congress, 1995. Available at: http://thomas.loc.gov/. Accessed February 16, 2009.