ETHICAL, LEGAL AND SOCIAL ISSUES IN NEWBORN SCREENING IN THE UNITED STATES

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Abstract. Four million babies are born annually in the US. There are 51 separate laws mandating universal screening and each has its own restrictions. Forty-nine programs allow the parents to "opt out" of testing (dissent), and 2 programs allow the parents to "opt in" (consent). The extent to which these decisions are "informed" varies and in most cases, no information exists as to whether the parents knew or understood what the newborn screening program entailed. Most programs have educational material available describing the state program but whether this information is the information needed (in terms of literacy level and content) to provide a sufficient understanding of the program is not generally known. In most programs, testing is automatic and the program information is contained in the hospital materials given to the mother upon entry or exit from the birthing facility. All newborn screening programs are administered by the state public health agency and ultimately the state legislatures are responsible for creating the laws governing newborn screening. Financing mechanisms are complex with fees varying from $0 - $60 and not directly related to the number of disorders screened, although system components such as education, methods of sample collection, sample submission, laboratory testing, follow-up, confirmation, diagnosis, treatment, outcome and quality assurance are considered in most fee setting processes.

The standards for programs have developed over the years at least partly as a result of medical-legal confrontations. During the past several years there has been a notable increase in program expansions including expanded biochemical testing and screening for hearing loss. In 1999, the Maternal and Child Health Bureau funded a newborn screening task force to review the issues facing state newborn screening systems and to make recommendations for improvements and/or changes in these systems. Two primary issues of ethical, legal and social consequence were considered: (1) the inclusion of diverse groups (including consumers) in newborn screening decision making, and (2) existence of adequate policies regarding privacy, consent, and research ethics. Following extended review and discussion, the Task Force recommended greater emphasis on parent education, permission for testing, and prenatal education. It was also recognized that studies should be carried out to improve parental understanding of newborn screening and the informed permission process, and to improve the public's overall understanding of the screening process.

INTRODUCTION

The population of newborn babies each year in the United Sates is approximately 4 million. A national newborn screening program does not exist, however each state and territory has a legally mandated program. Because the laws governing US territories and protectorates are less well known than those of the states, it is usual to discuss only the situation in the 50 US states and the District of Columbia (DC), which is the area surrounding the US capital. Therefore, whenever 'state' screening programs are mentioned, the term 'state' also includes the DC program (this designation is in no way intended to minimize the newborn screening programs that exist in Puerto Rico, the Virgin Islands, Guam, Saipan or other US jurisdictions). While individual state laws mandate screening each of the 51 programs, in 2 states (Maryland and Wyoming) the mandate extends only to offering the screening tests.

In 47 US state screening programs, therefore, parents may "opt out" of testing (dissent – usually for religious reasons), while in 2 programs they may "opt in" (consent), and in 2 mandated programs there is no "opt out" provision. In the case of some pilot programs, there is also an "opt in" or "opt out" provision. In all cases, the extent to which decisions about testing are "informed" varies and in most cases, no information exists as to the whether the parents knew and understood what the newborn screening program entailed. Most state screening programs have information available outlining the state requirements but whether the information included is appropriate information for providing sufficient understanding of the dissent or consent option (in terms of literacy level and content) has not been validated. Thus, in most programs, testing is automatic and newborn screening information is contained within the hospital materials given to the mother upon entry or exit from the birthing facility. The actual extent of the distribution or impact of state provided screening information is not known with any certainty.

Each of the 51 state programs has its own testing panel, which varies from 3 to 30 different disorders. While there are traditional ideas and guidelines concerning the addition of screening tests that have existed for over 30 years (Wilson and Jungner, 1968), their interpretation and validity are meeting more and more scrutiny as testing technology improves and genetic knowledge increases (Therrell, 1999; 2001). All state testing panels currently include phenylketonuria (PKU) and congenital hypothyroidism (CH), and inclusion of galactosemia (GAL) screening is expected to be a part of all programs by 2003, however inclusion of other disorders varies widely among the states (see Fig 1). Most state programs have a newborn screening advisory committee, or a subcommittee of a larger genetics advisory committee, that is responsible for making recommendations concerning testing disorders and for reviewing other technical issues within the program. In some cases these committees have official status, while in others the committee may be ad hoc or informal. Despite a recommendation from the Council of Regional Networks for Genetic Services (CORN) (Therrell *et al*, 1992) and from the American Academy of Pediatrics Task Force on Newborn Screening (American Academy of Pediatrics, 2000) that all programs have a well-informed multi-disciplinary group of advisors who can also act as program advocates, some programs do not currently have such a committee. In some state programs, the law provides a mechanism for adding or subtracting screening disorders that does not require input from a multi-disciplinary 'expert' committee, and in some cases disorders are specified within a screening law. In any case, each US newborn screening program has its own procedure for adding or deleting disorders from the screening panel, and this has led to wide variations in the disorders included (Stoddard and Farrell,

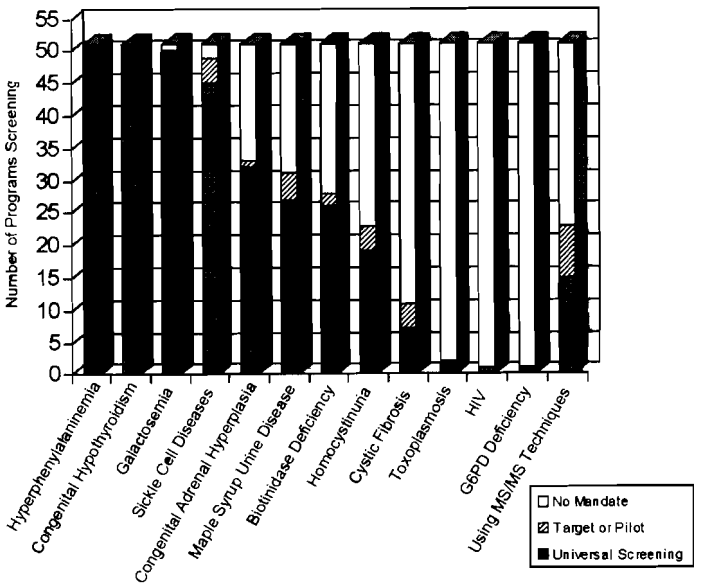

Fig 1. Disorders included in US newborn screening programs including programs utilizing MS/MS as a testing technique regardless of disorders being reported – September 2002.

1997). In addition to testing for inborn errors of metabolism, congenital hypothyroidism and hemoglobinopathies, some state programs test for infectious diseases including HIV and toxoplasmosis. Thus, from the early concept of newborn screening to prevent mental retardation, programs now include conditions of a much broader variety, with much more catastrophic consequences in some cases (i.e. death in the case of patients with CAH, galactosemia, or certain other metabolic disorders).

The decision by most states not to include cystic fibrosis (CF) screening is primarily due to the lack of a definitive cure for the disease and a shortened life expectancy (Centers for Disease Control, 1997). However, increasing attention has been given to the development of pilot projects to more broadly document the effects of newborn screening and early diagnosis in improving health outcomes, and to identify the mutations present in the racially and ethnically varied state populations. In the last 2 years, new technology (tandem mass spectrometry, MS/MS) has also resulted in several states adding screening for other rare metabolic conditions to their programs. MS/MS testing allows for simultaneous multi-disorder screening from a single sample aliquot, however the complex results that occur and the disorders detected have created new challenges for screening programs (Levy, 1998; Therrell, 2001). One issue not yet resolved concerns the ability of the technology to detect disorders that may not have a definitive cure, similar in some respects to the arguments raised by some regarding testing for CF.

At least part of the pressure to expand newborn screening to more and rarer disorders, whether or not there are demonstrated cures or cost benefits, is coming from active parent support groups who have been made aware of the possibilities of such screening by private testing laboratories. These laboratories offer supplemental newborn laboratory testing to maternity hospitals and physicians apart from the newborn population screening mandated in the states. Sometimes the private testing programs lack the follow-up capabilities necessary to resolve presumptive positive or unusual testing results that are usually provided in state screening programs. Thus, follow-up of abnormal or unusual screening results, of necessity, reverts back to the state newborn screening system in place for the state-mandated conditions. State programs are then faced with providing expanded follow-up services for the supplemental testing without funding. The extent to which state governments should provide expanded testing and/or follow-up is a dilemma currently under debate in many different venues in the US.

DNA testing is also a part of some newborn screening programs. Multiple mutation analysis for approximately 25 of the more commonly occurring mutations has become a routine second tier test in many programs performing newborn screening for cystic fibrosis. Several screening laboratories also use DNA techniques to confirm sickle cell anemia and some related hemoglobinopathies as a second tier newborn screening test. In this case, the DNA test results are used to confirm the presence or absence of clinically significant conditions within the first days of life in order to more quickly initiate antibiotic prophylaxis and prevent morbidity and mortality from unnecessary infections (Zhang *et al*, 1994). In the usual case, without such testing, confirmation of sickle cell anemia cannot occur until approximately 2-3 months due to a high percentage of fetal hemoglobin that complicates the analytical testing results.

Even though there are 51 state newborn screening programs, there are not 51 state newborn screening laboratories. In some instances, smaller population states have formed coalitions to benefit from economies of scale, in some there are one or more contracted laboratories, and in most, the state public health laboratory performs the newborn screening testing. When states contract out the testing or form coalitions (see Fig 2), it is sometimes the case that the tests performed in the outside laboratory may directly impact which disorders are screened in a program. Note that while it is most common to use a public health laboratory for newborn screening laboratory analyses, other alternatives exist including private laboratories and university medical center laboratories. Also consider that performing laboratory testing outside of the public health system presents special public sector/ private sector partnership challenges for follow-up coordination and residual specimen handling.

All newborn screening programs are administered by the state public health agency, but ultimately all respond to state legislatures that are responsible for creating the laws governing newborn screening. In many states, the responsibility for developing and administering the rules and regulations regarding screening has been delegated by the legislature to the state health agency. The standards for program operation including sample collection, sample submission, laboratory testing, follow-up, confirmation, diagnosis, treatment, outcome and quality assurance have developed over the years at least partly as a result of medical-legal confrontations.

An effective and efficient newborn screening system must have sufficient funding if it is to survive. While ultimately the state legislatures control the manner in

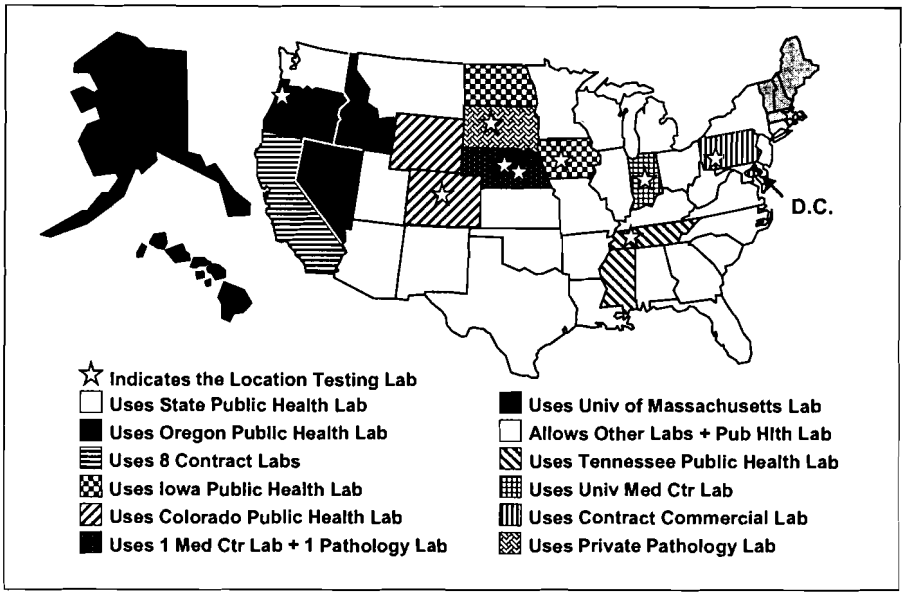

Fig 2. Newborn Screening Laboratories in the US – June 2002.

which newborn screening programs are financed, the exact mechanisms for financing usually reside with the state health departments. The financing mechanisms are complex and usually include a mixture of public and private funding, although a limited number of state programs (currently 9) rely solely on public funding from state tax revenues, federal Maternal and Child Health (MCH) block grant funds, and/or other federal funding for operational support. (Note that in the US, large grants of money are allocated by the federal government to each state to use for maternal and child health programs according to established guidelines. This funding mechanism allows for leeway in determining actual percentages and amounts of federal funding for various programs. These allocations are known as "block grants.") In the states that charge a fee for the newborn screening program, the fee amounts vary from US$5 - US$60 and the manner in which fees are collected and the program services they support also varies. The fees charged do not directly relate to the number of disorders included in screening nor do they relate directly to the follow-up services provided, although in most cases, these system components are considered in the fee setting process.

During the past several years there has been a notable increase in newborn screening program expansions including not only expanded biochemical testing, but also expanded screening of newborns for health problems that can be diagnosed with other procedures including hearing loss. Now, the majority of states include newborn hearing screening as a required procedure soon after birth, although some states limit the requirement to newborns falling into certain high-risk categories (American Academy of Pediatrics, 2000). Newborn hearing screening usually occurs at the hospital before the baby goes home just as with dried blood spot screening. Hearing test results require action within a relatively short time period after birth in order to initiate effective intervention by six months of age, similar to dried blood spot screening but slightly slower. Because both hearing and dried blood spot testing occur in the hospital, essentially all patient demographic information required for follow-up in either program is the same. Thus, many programs are now considering how best to integrate the data into one easily accessible warehouse of patient information. The considerations of such programs are presented elsewhere in this journal (Therrell, 2003).

RECENT GOVERNMENT ACTIVITIES

In 1999, the Maternal and Child Health Bureau (MCHB) of the Health Resources and Services Administration (HRSA) or the US Department of Health and Human Services (HHS), funded a Newborn Screening Task Force of the American Academy of Pediatrics (AAP) to review the issues facing state newborn screening systems and to make recommendations for improvements and/or changes in these systems. As noted in its final published report (American Academy of Pediatrics, 2000), the AAP Task Force established five working

groups of invited experts to consider the topics of: (1) newborn screening and its role in public health; (2) the medical home and systems of care; (3) economics of screening; (4) ethical, legal and social issues; and (5) research, surveillance and assessment. In order to more clearly focus their attention, the AAP Task Force agreed upon the basic principles and assumptions concerning newborn screening listed below:

(1) Infants should benefit from and be protected by newborn screening systems.
(2) Using previously defined (WHO) criteria for inclusion of a screening test, not all conditions are good candidates for newborn screening.
(3) Newborn screening is a system and every newborn should receive appropriate and timely services.
(4) Newborn screening is an essential public health prevention activity requiring service integration for affected newborns.
(5) State public health agencies have responsibility for assessment, assurance, and policy development.
(6) The newborn screening system must be clinically, socially, and ethically acceptable to the public and health professionals.
(7) Every newborn should have a medical home.
(8) All newborns should have access to screening according to nationally accepted criteria regardless of their location.
(9) Parents have a right to information about newborn screening, the right to refuse testing, and the right to privacy protection.
(10) Increased newborn screening program coordination and uniformity will benefit families, healthcare professionals, and public health agencies.
(11) Parents and consumers must be involved in policymaking and program implementation. (American Academy of Pediatrics, 2000)

The final Task Force report included recommendations in 4 major categories: (1) public health infrastructure; (2) public and professional involvement; (3) surveillance and research; and (4) financing. Of major importance in their conclusions was the fact that newborn screening services are unequal from state to state and there is a need for increased emphasis on national policies and funding in order to provide more uniformity across the state systems. The Task Force proposed an agenda for action that defined the need for a partnership among the public health system(s), health professionals, and consumers to continue a process that:

(1) Defines responsibilities – federal and state.
(2) Models regulations for newborn screening systems.
(3) Defines minimum standards for newborn screening systems.
(4) Models guidelines and protocols for professionals.
(5) Models systems of care from infancy to adulthood.
(6) Designs strategies to inform and involve families and the general public.
(7) Funds demonstration projects to evaluate technology, quality assurance, and health outcomes. (American Academy of Pediatrics, 2000)

ELSI ISSUES

Of the many issues on which the Task Force commented, two dealt specifically with issues of ethical, legal and social consequence: (1) the inclusion of diverse groups (including consumers) in newborn screening decision making, and (2) existence of adequate policies regarding privacy, consent, and research ethics. As previously noted, one of the working groups from whom advice was sought by the Task Force was specifically concerned with these ethical, social and legal issues. This group included well-known legal experts, consumers, and program administrators.

In examining ELSI challenges to newborn screening systems, the ELSI Working Group proposed that, "...given the imperatives of new science, newborn screening programs must decide on some basic questions: (1) how to evaluate new tests; (2) how long to store left-over blood samples; (3) what research uses of left-over samples are appropriate; and (4) how to ensure the role of parents in decision-making." In this regard, the group made two key recommendations: "(1) states should comply with existing national standards wherever they exist; and (2) each state should establish and adequately fund a commission or similar entity to conduct oversight of the newborn screening program." In further elaboration, the group recommended that the oversight commission (or advisory committee) should not only exist, but also it "...should have the authority to, and should: (1) review new tests under consideration by the program; and (2) develop pilot programs to investigate potential outcomes of new techniques and technologies. This oversight commission should have the authority to assess data from testing, follow-up, and treatment efforts, minimize the impact to families of receiving a false positive screening result, and monitor the program's process for handling consumer input, including grievances." Membership on

the oversight committee was suggested to include health professionals, other relevant professionals, families affected by screening, and members of the broader public with the goal of 'meaningful' (as opposed to 'token') representation from each of these groups. In addition to creating an oversight commission, it was suggested that each state should create mechanisms for obtaining direct input from parents of children affected with condition(s) in question in addition to parent(s) of newborns who might have received false positive results.

Concerning decisions about new tests, the ELSI Working Group recommended that states should use an evidence-based approach for decisions about adding and discontinuing new tests. Further, they suggested that the earlier reports of the National Research Council (National Research Council, 1975), the Institute of Medicine (Institute of Medicine, 1988) and the Ethical Legal and Social Issues Task Force established in conjunction with the Human Genome Project should provide guidance. It was suggested that states should require empirical evidence of the benefit or harm resulting from serious disorders that can be effectively ameliorated only if treatment is started in the newborn period prior to the appearance of symptoms in order to add such testing to their screening program.

On the issue of retention and use of dried blood samples that might exist following their use for newborn screening, the working group recognized that limited storage of leftover newborn screening blood samples (residual samples) might be useful for quality control and for some limited research (Therrell *et al*, 1996). At the same time, they noted that recognition should be given to the concerns that have been voiced by racial, ethnic and other diverse communities concerning storage and research. Likewise, security issues and problems related to commercialization of samples and the resulting information obtained were identified as other issues of concern. In summary, the ELSI Working Group called for a cautious approach to using samples for research, with protections for privacy and safety, and sample storage for no more than two calendar years, whether for programmatic or individual legal purposes. If residual dried blood spots are considered for research, it was suggested that investigators should be required to demonstrate why newborn blood spots are the optimal tissue source for the project. In particular, it was noted that if other samples are available from adults, preferably from individuals who have already consented to research, those samples should be used. Additionally, research involving the use of newborn screening samples should concentrate on the health concerns of children. If residual samples are to be used in research, it was recommended that they should be unidentified unless there is compelling evidence for the need for access to medical records. In cases where linkages are retained, specific requirements for usage were recommended that include: (1) institutional review board (IRB) approval; (2) informed permission; (3) encrypted sample identifiers; and (4) identification of an intermediary so that any further required medical information could be retrieved. It was strongly suggested that consideration be given to creating a population-based tissue resource for research in which consent is obtained from the individuals from whom the tissue is obtained.

In summary, it was recommended that states should place greater emphasis on parent education and permission (the parental equivalent of informed consent), and that prospective parents should be educated about newborn screening during the prenatal period. Additionally, it was suggested that permission for screening should be sought. It was also recognized that studies should be carried out to improve parental understanding of newborn screening and the informed permission process, and to improve the public's overall understanding about the effectiveness of the screening process.

CURRENT GOVERNMENT ACTIVITIES

Responding to the AAP Task Force Report, the US federal government has begun funding initiatives in line with the published recommendations. Thus, a number of federal grants have been issued to state health department programs working to develop more integrated newborn screening data systems as a part of more comprehensive infant health services planning. Continuing funding has also been made available for a National Newborn Screening and Genetics Resource Center to serve as a focal point for information on newborn screening and genetics and to provide technical assistance to improve ongoing programs. HRSA has established a contract with the American College of Medical Genetics to develop national policy guidance aimed at providing more uniformity of newborn screening services across the country. In particular, this contract focuses on developing a national testing panel along with procedures for deciding on additional disorders that may be considered specific to individual or regional state populations. Other contracts funded by HRSA include research into the fairness of distribution of costs in newborn screening and issues about consent in newborn screening, with particular emphasis on utilization of residual blood spot material remaining after the newborn screening process.

Quality assurance of newborn screening laboratories has also been addressed through continued funding of the

Centers for Disease Control and Prevention (CDC) Newborn Screening Branch activities in providing a national laboratory quality assurance program. Additionally, the CDC has received funding for a new Center for Birth Defects and Developmental Disabilities that includes a yet to be defined newborn screening component. The National Institutes of Health has also indicated that newborn screening is an important part of its research agenda.

The US Congress has passed the Child Health Act of 2000 (Public Law 106-310, 2000), which provides for funds to be used in support of newborn screening activities, but the funding has not yet been finalized. As part of this Act, a national newborn screening oversight committee will be established to provide guidance to state and federal screening initiatives. There is also Congressional interest by Senators from Ohio and Connecticut, who together are sponsoring additional legislation to provide expanded funding for newborn screening educational and research efforts. As part of this effort, the US Government Accounting Office is reviewing the operation of all state newborn screening programs.

It seems fair to say that the increased political and consumer interest in newborn screening activities will lead to more expansion in the future. With continuing research efforts and expanding information arising from the Human Genome Project, it would appear that genetic testing and newborn screening have a dynamic future. It will be incumbent on the screening community to carefully work through the ethical, legal and social issues to the benefit of the newborns, their families and society if we are to succeed in maintaining valid newborn screening programs.

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