POLICY

Research Results: Preserving Newborn Blood Samples

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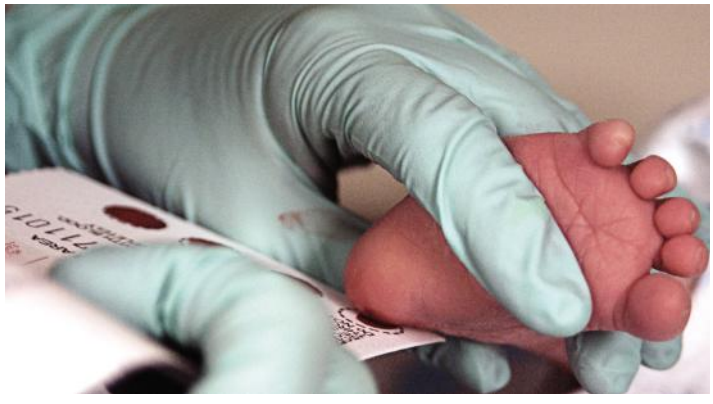
Retention and use, without explicit parental permission, of residual dried blood samples from newborn screening has generated public controversy over concerns about violations of family privacy rights and loss of parental autonomy. The public debate about this issue has included little discussion about the destruction of a potentially valuable public resource that can be used for research that may yield improvements in public health. The research community must advocate for policies and infrastructure that promote retention of residual dried blood samples and their use in biomedical research.

Millions of residual dried blood samples (DBSs) left over from newborn screening have been destroyed because of controversy surrounding their retention and secondary use in biomedical research without explicit parental permission. Last year, the Texas Department of State Health Services destroyed 5.3 million DBSs (*1*), and more recently, the Minnesota Department of Health announced plans to begin destroying DBSs as soon as screening of a newborn has been completed (*2*). Earlier this year, the Irish Minister of Health announced plans to destroy 1.5 million archived DBSs (*3*). The controversy over DBSs has generated public debate about the privacy rights of newborns and the autonomy rights of parents to decide whether or not their child's DBS should be retained and used in future research.

Largely absent from the debate, however, is discussion of these DBSs as a valuable public resource that could be used in biomedical research for the improvement of public health or of the detrimental effect that the destruction of these diverse sample sets may have on the advancement of biomedical science. If the DBSs are to be preserved as a resource for biomedical research, it is incumbent on scientists to offer evidence of potential public health benefits that may be garnered from the use of these samples and to advocate on behalf of policies that support their ethical use in research.



Precious mettle. The research community must commit to developing newborn screening dried-blood samples as a resource for human health research.

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PUBLIC HEALTH PROGRAM

Newborn screening has been hailed as one of the most successful public health programs of the 21st century (*4*). Shortly after birth, almost all of the 4 million babies born each year in the United States undergo mandatory newborn screening to detect certain heritable disorders that can cause irreversible, devastating effects if the conditions remain undetected before the onset of symptoms. For some of these conditions, presymptomatic treatment can reduce the associated morbidity and mortality.

When newborn screening has been completed, a small amount of residual blood remains. Historically, these residual DBSs have been used to conduct quality assurance (QA) activities that help to maintain a state's ability to provide high-quality newborn screening services. For example, DBSs can be used to ensure that the state laboratory equipment is calibrated properly. However, DBSs are also valuable resources for other types of public health and biomedical research.

For example, DBSs have been used to detect environmental toxins (*5*), conduct public health surveillance activities such as the detection of HIV seroprevalence rates (*6*), and carry out post mortem metabolic or genetic testing on children who die unexpectedly (*7*). Research with DBSs has contributed much to our current understanding about the mechanistic bases and timing of the origin of childhood leukemia, a heterogeneous cancer characterized by genetic modifications in white blood cells. Until recently, it was unknown when in the disease process genetic modification occurs. Research using DBSs has shown that in certain types of childhood leukemia, the genetic modification occurs in utero. By sequencing genomic DNA from patients at the time of diagnosis and then backtracking to test for the presence of the patient-specific gene sequence on the patient's DBS, researchers were able to demonstrate the in utero origins of specific chromosomal translocations (*8*).

Although the extent to which DBSs currently are used for biomedical research has not been fully documented, the potential impact of such research is far-reaching. First, because many states retain DBSs for at least some period of time after newborn screening has been completed (*5*), over time DBSs collectively could be used to develop a population-wide genomic database (*9*). Genomic information from these samples could be linked to databases with clinical information collected throughout life, which provides unprecedented opportunities to learn about health and disease physiology from the early stages of life. Second, as demonstrated by the research on childhood leukemia, DBSs are an exceptional source of epigenetic information that can be used to study in utero exposure genomics and the effects of both in utero and ex utero exposures to chemicals and infectious agents (*10*). This information can

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be used to distinguish causal from consequential epigenetic variation. Last, newborn screening occurs at the early stages of life, when the potential impact of interventions based on actionable research results could have tremendous health benefits.

At this time, we cannot predict with any certainty exactly what the benefits of research using DBSs might be, and it may take decades before the impact of this research is fully realized. However, if these samples are destroyed we will never define the benefits that can arise from making these rare collections of biological materials available to scientists.

CONTROVERSIAL CONDUCT

Controversy surrounding DBSs jeopardizes both internal QA activities and external biomedical and public health research. The retention and secondary use of DBSs without explicit parental permission has driven litigation in Texas and Minnesota. A class action lawsuit against the Texas Department of State Health Services that was ultimately settled alleged that the state's practice of retaining DBSs and using them for biomedical research without explicit parental permission violated privacy rights guaranteed by the U.S. Constitution (*11*). As part of the negotiated settlement, the state agreed to destroy more than 5 million archived DBSs (*12*). Beginning this past June, Texas now requires informed consent from parents to retain DBSs and use them for secondary research (*13*). Similarly, the Minnesota Supreme Court recently ruled that because DBSs contain genetic information, the state's Genetic Privacy Act requires that informed consent be obtained to retain DBSs and use them for secondary research (*14*).

When the Commissioner of the Minnesota Department of Health announced plans to begin destroying DBSs, he acknowledged that the destruction would have a direct, negative effect on the state's ability to assure the quality and accuracy of the newborn screening program, but he said he felt that it was "necessary to take this step in order to comply with the Supreme Court's decision" (*2*).

Similarly, the destruction of more than 5 million DBSs in Texas was a devastating blow to researchers who were developing projects that would have used the samples as part of their research protocols. For example, one of the authors (M.E.S.), a pediatric cancer epidemiologist, had applied for funding to use DBSs to conduct genome-wide association studies of rare pediatric brain tumors. When plans were announced to destroy the DBSs, he and his research team petitioned the Texas Department of State Health Services to allow the researchers to obtain consent from parents of affected children for the continued use of their samples, but the request was denied. The project was no longer feasible and had to be abandoned until alternative sources of DBSs could be located. Anecdotal evidence suggests that similar research studies were affected at other institutions throughout Texas. However, the full extent of the destruction's impact on research is unknown.

PROTESTING POLICY

In response to the Irish Minister of Health's announced plans to destroy 1.5 million archived DBSs, members of the scientific community in Ireland, who represent a wide range of specialties such as genetics, cardiology, pulmonology, and gastroenterology, have denounced these plans as "appalling" and called for greater public debate about this issue. One suggestion is that the public be informed about the existence of the archived DBSs and that individuals be offered the opportunity to have their specific samples destroyed. If no request is received from an individual, that individual's DBS may be used for secondary research (*15*).

In the United States, the controversy surrounding the retention and use of DBSs may cause state officials to be reluctant to pursue the development of policies that permit the retention and use of DBSs for biomedical research. There is concern that greater transparency and public dialogue about the potential benefits, to public health, of research using DBSs may lead to increased refusals for newborn screening and imperil the health of newborns. These concerns are valid and point to a need for greater public education on these issues, but they do not justify the wholesale destruction of DBSs.

This controversy and the resulting litigation also may have implications for biomedical research beyond the retention and use of DBSs. The Minnesota ruling, in particular, may affect the conduct of research with other types of archived biological samples that have been retained and used without informed consent, even if the samples were deidentified.

The research and bioethics communities have framed the debate about the use of DBSs around the question of whether or not the samples remain identifiable when they are released for research. For parents, however, the major concern has not been whether the samples of their children remain identifiable. Instead, they have objected in principle to the fact that their children's blood samples have been stored and made available to researchers without their knowledge or consent. These privacy concerns are of course legitimate, but the larger issue is the erosion of trust in the research enterprise caused by the violation of basic ethical principle of respect for persons, as perceived by the parents.

VARIATIONS IN STATE LAW

In the United States, the extent to which state newborn screening statutes and regulations address the retention and use of DBSs and related information varies widely. A review of state newborn screening laws from 2008–2009 revealed that the retention or use of DBSs had not been addressed in 18 states, and that parental consent was required under certain circumstances to release DBSs for research in only six states (*16*). A recent study by the Children's Oncology Group assessed the feasibility of obtaining DBSs for pediatric cancer patients from state newborn screening programs and concluded that state policies limit the number of DBSs available for this type of research. For example, six states reported that they do not allow the release of identifiable DBSs for research even if parental consent has been obtained, and 10 states reported storing DBSs for less than 1 year (*17*). In addition, the Minnesota Supreme Court decision illustrates that other types of state laws, in addition to ones that regulate newborn screening, may affect the ability of a state to store residual DBSs for secondary research purposes.

POLITICAL SCIENTISTS

DBSs possess value beyond their use for newborn screening. If the research community wishes to take advantage of these resources, it must advocate for policies that support the development of an infrastructure to promote the retention and use of DBSs for biomedical research. At the same time, the public health mission of state newborn screening programs must not be jeopardized. Accordingly, greater transparency is needed on the part of state departments of health regarding their policies related to the retention and use of DBSs. In addition, the privacy and autonomy rights of parents should be recognized and respected. Although it may be ethically appropriate to inform parents about the retention and secondary research use of their chil-

dren's DBSs and afford them the opportunity to refuse (or opt out), given the controversy surrounding this issue, it may be wiser from a public policy standpoint to require explicit parental permission to retain the DBSs and use them for research. Moreover, as suggested by the Irish scientific community, additional public debate should be encouraged about the disposition of archived DBSs that were retained without explicit consent, particularly because the resolution of this issue may have broader implications for the research use of other types of retained samples.

In addition, the research community should support the development of policies that promote partnerships among researchers, the public, and state departments of health. Education should be the cornerstone of these policies so that the public can learn about and better understand the potential benefit of research using DBSs. Research currently is underway to explore innovative methods to educate parents about these issues. Privacy concerns should be addressed by the establishment of strong mechanisms to prevent misuse of DBSs and their related information. These mechanisms should include: (i) criteria for secure storage and for specifying who may have access to DBSs and under what circumstances, and (ii) the development of transparent policies regarding who may have access to DBSs for research and for what purposes. In this way, loss of this valuable resource can be prevented, and public trust in the research enterprise can be restored.

The research community should not squander the opportunity to conduct additional potentially life-saving research with these samples. We should be the generation that recognizes the potential value of these samples and commits to developing them as a resource to promote public and individual health. The scientific community has a responsibility to the nation and its citizens to use these resources responsibly but also to use them to the fullest extent possible to improve the health of our citizenry.

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