Storage, Retention, and Use of Residual Dried Blood Spots

Harry Hannon, PhD and Brad Therrell, PhD

Centers for Disease Control and Prevention
Atlanta, Georgia
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Austin, Texas

Storage, Retention, and Use of Residual Dried Blood Spots

Overview

- Storage of residual DBS by screening labs
- Retention times for residual DBSs
- Use of residual DBSs and the restrictions
- Policies impacting dried-blood spot (DBS) use
- Controversy: media, and parents
- National DBS repository: actual BDS or virtual?

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Guidelines for the Retention, Storage, and Use of Residual Dried Blood Spot Samples after Newborn Screening Analysis: Statement of the Council of Regional Networks for Genetic Services.

Therrell, Hannon, et al., Biochem Molec Med 1996;57:116-24.

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Guidelines for the Retention, Storage, and Use of Residual Dried Blood Spot Samples after Newborn Screening Analysis: Statement of the Council of Regional Networks for Genetic Services

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These guidelines provide scientific information for policy development by state health departments considering appropriate use of newborn screening specimens after screening tests are finished. Information was collected, debated, and formulated into a policy statement by the Newborn Screening Committee of the Council of Regional Networks for Genetic Services (CORN), a federally funded national consortium of representatives from 10 regional genetics networks. Newborn screening programs vary widely in approaches and policies concerning residual dried blood spot samples (DBS) collected for newborn screening. Recognition of the epidemiological utility of DBS samples for HIV seroprevalence surveys and a growing interest in DBSs for DNA analysis has intensified consideration of issues regarding retention, storage, and use of residual DBS samples. Potentially these samples provide a genetic material "bank" for all newborns nationwide. Their value as a resource for other uses has already been recognized by scientists, administrators, and judicial officials. Programs should promulgate rules for retention and use of residual newborn screening DBS samples based on scientifically valid information. Banking of newborn samples as sources of genetic material should be considered in light of potential benefit or harm to society.

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BACKGROUND

The Council of Regional Networks for Genetic Services (CORN) is a federally funded project to improve the quantity, quality, and availability of cost-effective genetic services in the United States. CORN was developed in 1985 in response to the need for an organization that could coordinate activities among federally funded genetic service networks encompassing the entire United States and could implement programs of national significance that emerge from regional initiatives in priority areas such as quality assurance, data collection, and education. Two delegates from each of the 10 defined networks serve on the CORN steering committee with additional representation from the Alliance for Genetic Support Groups, national sickle cell disease programs, and certain other organizations involved in genetic services. CORN members constitute a unique organization of genetic service providers, public health personnel, and consumers. In its goals

Guidelines for the Retention, Storage, and Use of Residual Dried Blood Spot Samples after Newborn Screening Analysis: Statement of the Council of Regional Networks for Genetic Services.

"Whole blood absorbed into filter paper and then dried offers an excellent means for creating a repository (bank) of samples for DNA investigations."

"Ideally, residual DBSs should be stored frozen (preferably at −20°C) in sealed bags with low gas permeability containing a desiccant and a humidity indicator."

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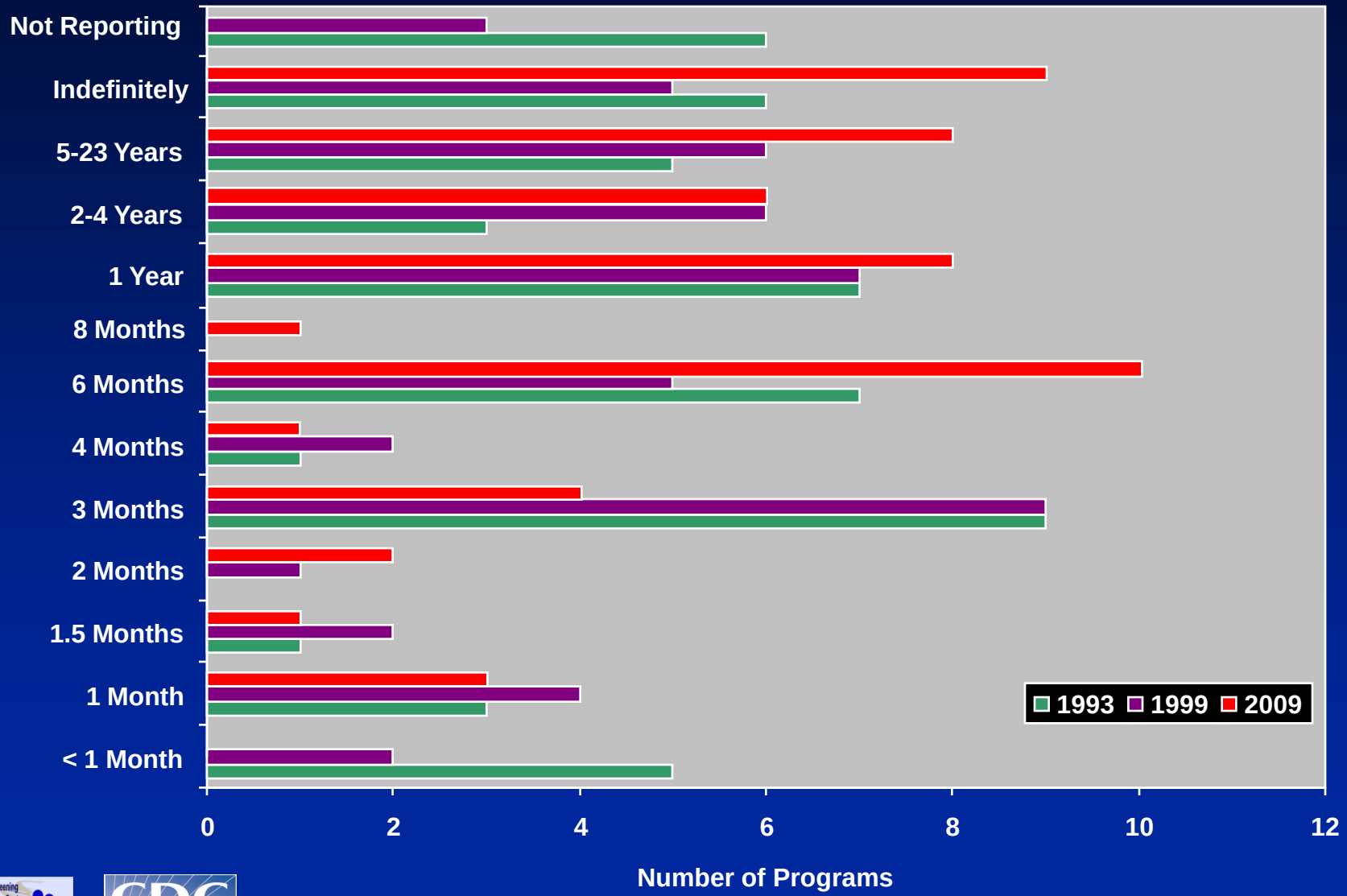
U.S. Newborn Screening Data

Comparison of Retained Residual Samples - 1993 vs.1999 vs. 2009



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Informed/Consent Issues

NOTICE OF INFORMATION PRACTICES AND PRIVACY POLICY – Effective 01/24/01

THIS NOTICE DESCRIBES HOW YOUR NEWBORN'S MEDICAL INFORMATION MAY BE USED AND DISCLOSED AND HOW YOU CAN GET ACCESS TO THIS INFORMATION. PLEASE REVIEW IT CAREFULLY.

The California Department of Health Services is authorized to collect information requested by Health and Safety Code Sections 125000, 125025, and 125030. This information is used to identify newborns with inherited or congenital disorders in order to expedite prevention or treatment of the disorder. Provision of this information is required by law (17CCR 6500 through 6510) and if not provided could result in the death or permanent handicaps for affected newborns.

Uses and Disclosures of Health Information: The California Department of Health Services uses health information about your newborn for screening, to provide health care service, to obtain payment for screening, for administrative purposes, and to evaluate the quality of care that you receive.

We may use the information and specimens obtained by participation in the program for medical research without identification of the person from which they were obtained unless you specifically request in writing they not be used by contacting the person listed below.

資訊使用通知2001年1月24日生效

本通知闡述了新生兒醫療資訊的使用和披露方法以及獲取該資訊的方法。請認真閱讀。

加州健康服務部享有授權收集「健康與安全法」125000、125025和125030所規定的資訊。該資訊用於發現新生兒先天性或遺傳性紊亂症，以便盡快採取預防或治療措施。法律（17CCR 6500至6510）規定必須提供該資訊，不提供該資訊可能導致患病的新生兒永久性殘障。

健康資訊使用與披露： 加州健康服務部把關於新生兒健康的資訊用於篩選檢查、提供健康護理服務、收取檢查費、行政管理和評估護理品質。

我們可能把參加計劃者的資訊和樣本用於醫學研究，而不披露研究對象的身份，除非您向下文指定之人士提出特別書面請求，要求不要使用該資訊和樣本。

Some reasons for retaining residual DBSs

- Legal accountability (e.g., number of punches taken for analysis, the existence of a sample and its adequate collection)
- Future DNA testing
- Reconfirmation of newborn screening analytical results
- New method evaluations and comparisons
- Epidemiological or other public health surveys
- Special health related studies for patient or family
- Forensic studies

From: Guidelines for the Retention, Storage, and Use of Residual Dried Blood Spot Samples after Newborn Screening Analysis: Statement of the Council of Regional Networks for Genetic Services. Biochem Molec Med 1996;57:116-24.

Some reasons for retaining residual DBSs

- Confirmatory diagnosis (reconfirm false negative or false positive finding)
- Quality assurance and public health needs (method development, epidemiological studies)
- Research uses (DNA extraction – understanding disease history; gene-environment interactions)
- Clinical testing – post mortem i.d. of disease cause
- Non-medical use – kidnapped children i.d., deceased persons i.d., paternity (subpoena), criminal i.d.

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Kharaboyan L et al. Storing Newborn Blood Spots, J Law Med Ethics, Winter 2004.

Examples of Previous Use of Residual NBS Specimens

- HIV Seroprevalence
- Diabetes type 1 risk and autoimmune disease onset
- Searching for new early markers of diseases
- Surveillance for environmental factors, infections, and genomic health issues, e.g., autism, cerebral palsy
- Determining allele frequencies for public health assessments
- Understanding hearing loss causes -- CMV association
- Searching for frequency of deaths caused by SCID
- Environmental exposures: e.g., polyfluoroalkyl chemicals, perchlorate, lead
- Quality assurance – case specimen exchange among labs

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National Report on Genomics and Health

Need for population-based data

- Population-based data on gene variants
  - Prevalence of gene variants
  - Association with risk of disease, death
  - Gene-environment and gene-gene interactions
- Genetic test evaluation(validity, utility)
- Development of public health interventions, e.g., newborn screening expansion
- Currently, minimal population-based data on gene variants to guide screening or interventions

Policy Statements
Residual Newborn Dried Blood Spots

- AAP Task Force 2000 [Pediatrics 2000; 106 (suppl)]
  - Develop policies for unlinked/linked residual samples in research/surveillance
  - Organize collaborative efforts to develop minimum standards for storage of residual samples at state level
  - Consider creating national or multi-state population-based specimen resource for research

APHL Position / Policy Statement -- 2005

Residual Newborn Screening (NBS) Specimens

A statement of position:

"There may be other reasons (*other than QA*) to save DBS specimens, including test development, research, and forensic identification. To retain DBSs for such purposes requires clear guidelines that are incorporated into national consensus policies that state health departments follow in carrying out their authorized NBS programs."

APHL ASSOCIATION OF PUBLIC HEALTH LABORATORIES

APHL Position/Policy Statement

Residual Newborn Screening (NBS) Specimens

A. Statement of Position

APHL supports the development of national consensus policies, procedures, and standards for retaining residual dried blood spot (DBS) specimens following NBS analysis. These policies and procedures must recognize existing federal regulations for clinical testing, state laws, professional guidelines, and ethical and legal precedents. The policies should also allow for introduction of new analytes and techniques into the NBS laboratory arena. To meet recognized laboratory quality assurance practices, DBS specimens must be retained for a time period and under conditions that permits analytical validation [1]. There may be other reasons to save DBS specimens, including test development, research, and forensic identification. To retain DBSs for such purposes requires clear guidelines that are incorporated into national consensus policies that state public health departments can follow in carrying out their authorized NBS programs.

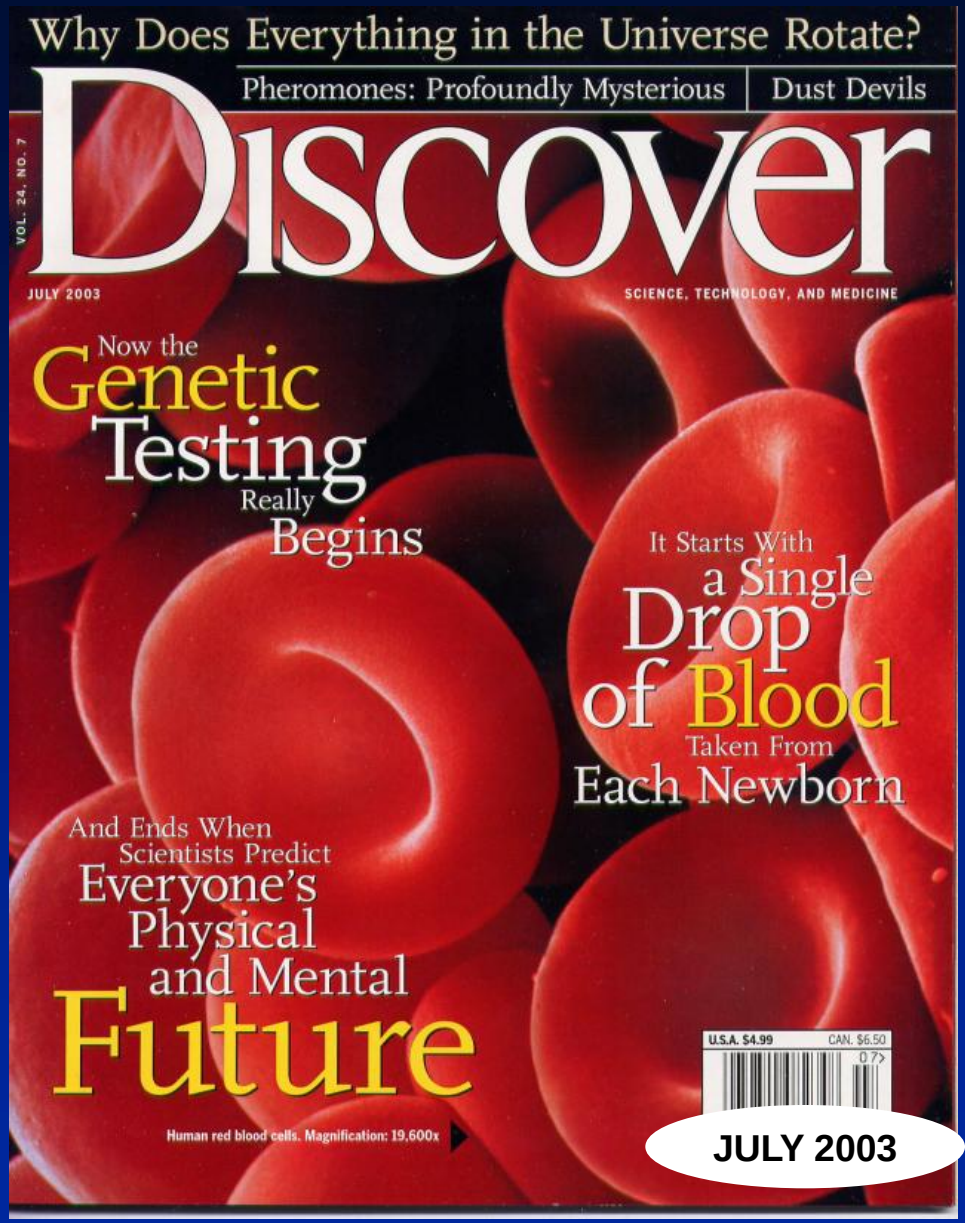
B. Background

A survey of state NBS programs found large variations in policies regarding retention of specimens, extending from a few weeks to 21 years or longer [2]. In 1996, the Council of Regional Networks for Genetic Services (CORN) issued guidelines for the retention, storage, and use of DBSs following NBS analysis [3]. As this report noted, the length or retention of residual DBS specimens should be made on the basis of the stability of the analytes of interest, the potential use of the DBS specimens, and technical issues concerning proper storage and ease of retrieval. While methods for analyzing DNA from DBSs continue to improve and provide a mechanism for performing multiple molecular techniques from a single DBS, additional issues are raised concerning the availability of genetic information from these potential DNA banks.

Currently, the Genetic Services Branch of the Maternal and Child Health Bureau, Health Resources and Services Administration, Department of Health and Human Services, in addition to supporting the National Newborn Screening and Genetics Resource Center, has funded two contracts to develop model policies and procedures for NBS programs (American College of Medical Genetics, UCLA Center for Society, the Individual and Genetics). Both organizations held conferences on these topics in late 2002 to consider the feasibility of establishing a multi-state or central DBS bank for the purpose of providing a resource for obtaining population-based data on prevalence of gene variants of public health significance, and the association of gene variants with disease and risk factors. At the meetings, consensus was not reached on these complex ethical, public education, and scientific issues.

Professional societies have also examined these issues [4]. Until such time that recognized national policies and procedures are in place, individual states will have to address a number of technical, legal, and ethical issues regarding retention of DBSs and other specimens for potential genetic, epidemiologic, research, test development, liability, or forensic purposes. As noted in the CORN report [2], these include: 1) the stability of analytes; 2) the length of time that specimens should be retained and for what purposes; 3) the requirement of legal consent; 4) a Human Subjects Review process; 5) the removal of identifiers; and 6) the ownership of the specimens.

News Media & Public Perceptions



JULY 2003

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Med-Tech : Genetics

Newborn-Blood Storage Law Stirs Fears of DNA Warehouse

By Alexis Madrigal 05.21.08 | 12:00 AM

An obscure bill that sailed through Congress and was signed into law last month is stoking fears of a nationwide DNA warehouse potentially open to abuse by law enforcement agencies or health insurance companies.

But proponents say the law is a much-needed rationalization of the way the government stores and tests blood from newborns.

The Newborn Screening Saves Lives Act of 2007 (S.1858/H.R.3825), signed into law on April 24, empowers a committee to provide guidelines to all states on how -- and for how long -- they should store blood. At present, all states store blood from all newborns, and some, like California, store it indefinitely. Eight of the committee's nine members are medical researchers, who almost universally favor longer storage times, so critics fear that the national guidelines will lead to more storage of samples, which contain recoverable DNA.

"What we are doing is taking an individual genetic code and saying it's the government's," said Twila Brase, of the Minnesota activist group Citizens' Council on Health Care. "And once we do that, it's available for whatever a legislature wants to do in 20 years. The fact of the matter is that we don't know what they could or would do."

States have been storing blood samples from newborns since blood screening for genetic defects and diseases began in the 1960s. The samples can help detect and treat a wide range of diseases, but in the age of the genome, the issue of storing samples has taken on unprecedented importance. Blood samples contain DNA that can be unambiguously linked to individuals, which may in the future present tempting data to governments, businesses and health providers.

Currently, each state has its own policy about storing newborn blood samples. California has screened and stored more than 12 million newborn babies' blood spots since 1980, while Texas disposes of them within months.

Brase's group wants to see all so-called biobanks destroyed.

"You're building an entire DNA warehouse for the public without the public's consent," Brase said. "Who will own the DNA of the citizens and what is that going to mean? And what we're doing is pushing an entire genetic research program on the population without the consent of the population."

Proponents, however, say the scientific and medical value of the blood samples far outweigh the privacy risks of storing biological material from every newborn.

"They are extremely valuable when they are anonymized for research when looking at new technologies," said Edward Howell, chairman of the committee referred to in the bill, the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children to the Health Resources and Services Administration. "Those conspiracy theories are very popular on the blogs, but ... the states have been very careful in dealing with [blood spots]."

Howell says law enforcement agencies have asked states for blood samples and been turned down.

"The bottom line is that many states have kept these for a very long time and I am unaware of anything that has been done with them that would concern even a very conservative person," Howell said.

Edward McCabe, co-director of the UCLA Center for Society and Genetics and co-author of *DNA: Promise and Peril*, agreed that so far, states have been trustworthy guardians of their biobanks.

McCabe said that even in the case of the identification of a missing child, California's health regulators still turned down a law enforcement request to use a blood spot.

He applauded that decision and others like it that establish a clear policy for dealing with the samples and limiting their use.

"We actually think there ought to be a firewall between forensic and medical uses," McCabe said.

And he argued that -- from a health care perspective -- the samples are extremely and uniquely useful.

"It's one of the most unbiased cross sections of the newborn population of a state," McCabe said.

Donna Levin, who as general counsel for the Massachusetts Department of Public Health works in the trenches with the issue, said she believed her state's policy had the right ethical safeguards in place.

"Parents are told prior to screening that the residual specimen is kept for at least 10 years," she wrote in an e-mail.

She also noted that all research conducted on residual specimens has to be approved by an Institutional Review Board, which set ethical guidelines for human experiments. The state also requires that research on identified specimens only be conducted with the informed consent of the subject of the specimen, or a parent/guardian.

Those are the types of checks-and-balances that the newly empowered committee could take up during their next meeting this September, when they will begin drafting the state guidelines.

One thing is for sure: As scientists and law enforcement officials continue to learn more about how to use the DNA in each of our cells, the way biological samples are handled by the government seems certain to receive more scrutiny.

"The whole confidentiality issue is certainly a huge issue in the age of genomics," McCabe said.

May 2008

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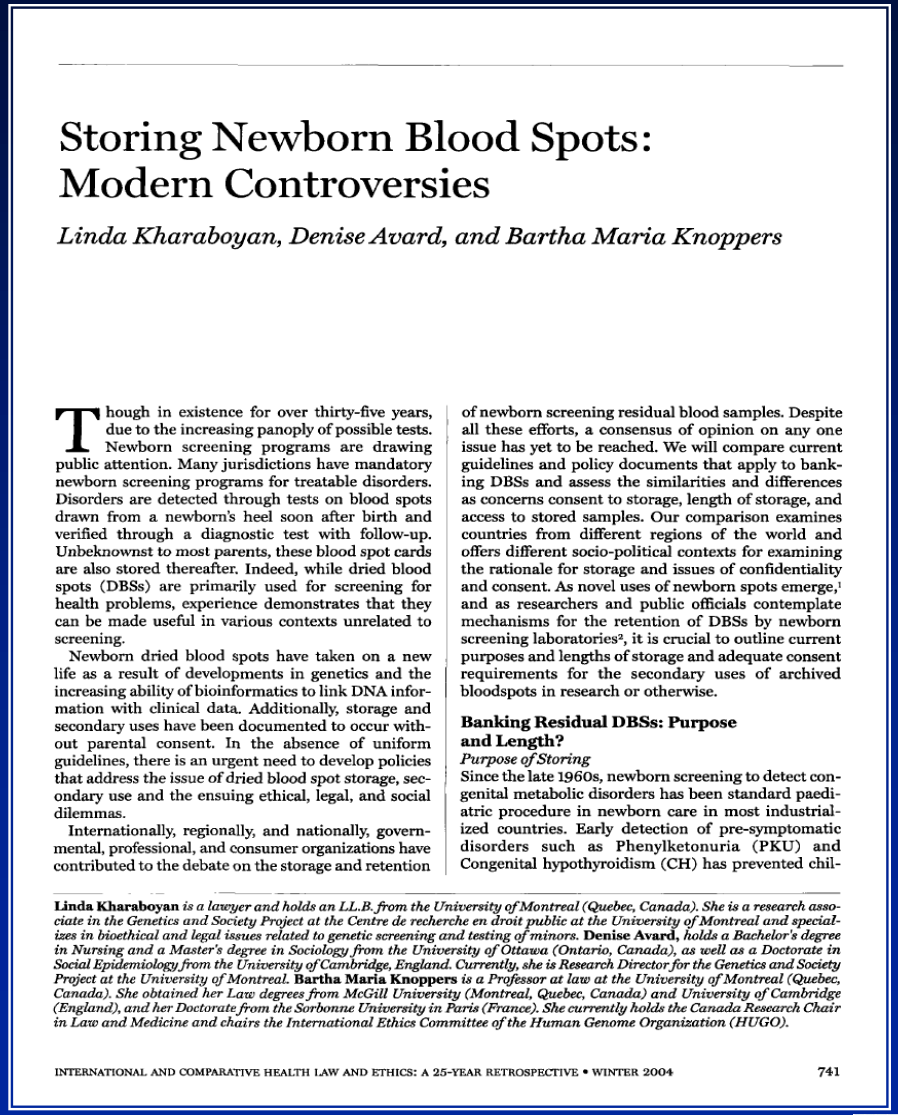
Storage Newborn Blood Spots: Modern Controversies (2004)

"Additionally ,storage and secondary uses have been documented to occur without parental consent."

"In the absence of uniform guidelines there is an urgent need to develop policies that address the issues of DBS storage and their secondary uses, and the ensuing ethical, legal, and social dilemmas."



Storing Newborn Blood Spots: Modern Controversies

Linda Kharaboyan, Denise Avard, and Bartha Maria Knoppers

Though in existence for over thirty-five years, due to the increasing panoply of possible tests. Newborn screening programs are drawing public attention. Many jurisdictions have mandatory newborn screening programs for treatable disorders. Disorders are detected through tests on blood spots drawn from a newborn's heel soon after birth and verified through a diagnostic test with follow-up. Unbeknownst to most parents, these blood spot cards are also stored thereafter. Indeed, while dried blood spots (DBSs) are primarily used for screening for health problems, experience demonstrates that they can be made useful in various contexts unrelated to screening.

Newborn dried blood spots have taken on a new life as a result of developments in genetics and the increasing ability of bioinformatics to link DNA information with clinical data. Additionally, storage and secondary uses have been documented to occur without parental consent. In the absence of uniform guidelines, there is an urgent need to develop policies that address the issue of dried blood spot storage, secondary use and the ensuing ethical, legal, and social dilemmas.

Internationally, regionally, and nationally, governmental, professional, and consumer organizations have contributed to the debate on the storage and retention of newborn screening residual blood samples. Despite all these efforts, a consensus of opinion on any one issue has yet to be reached. We will compare current guidelines and policy documents that apply to banking DBSs and assess the similarities and differences as concerns consent to storage, length of storage, and access to stored samples. Our comparison examines countries from different regions of the world and offers different socio-political contexts for examining the rationale for storage and issues of confidentiality and consent. As novel uses of newborn spots emerge,[1] and as researchers and public officials contemplate mechanisms for the retention of DBSs by newborn screening laboratories[2], it is crucial to outline current purposes and lengths of storage and adequate consent requirements for the secondary uses of archived bloodspots in research or otherwise.

Banking Residual DBSs: Purpose and Length?

Purpose of Storing

Since the late 1960s, newborn screening to detect congenital metabolic disorders has been standard paediatric procedure in newborn care in most industrialized countries. Early detection of pre-symptomatic disorders such as Phenylketonuria (PKU) and Congenital hypothyroidism (CH) has prevented chil-

Linda Kharaboyan *is a lawyer and holds an LL.B. from the University of Montreal (Quebec, Canada). She is a research associate in the Genetics and Society Project at the Centre de recherche en droit public at the University of Montreal and specializes in bioethical and legal issues related to genetic screening and testing of minors.* **Denise Avard,** *holds a Bachelor's degree in Nursing and a Master's degree in Sociology from the University of Ottawa (Ontario, Canada), as well as a Doctorate in Social Epidemiology from the University of Cambridge, England. Currently, she is Research Director for the Genetics and Society Project at the University of Montreal.* **Bartha Maria Knoppers** *is a Professor at law at the University of Montreal (Quebec, Canada). She obtained her Law degrees from McGill University (Montreal, Quebec, Canada) and University of Cambridge (England), and her Doctorate from the Sorbonne University in Paris (France). She currently holds the Canada Research Chair in Law and Medicine and chairs the International Ethics Committee of the Human Genome Organization (HUGO).*

Kharaboyan L et al. Storing Newborn Blood Spots, J Law Med Ethics, Winter 2004.

Jay Janner
AMERICAN-STATESMAN

(enlarge photo)

Texas law does not require parental consent to take blood from newborns for birth defect screening or other uses. Medical technologist Isaac Pan tests samples at a state laboratory.

Jay Janner
AMERICAN-STATESMAN

(enlarge photo)

Blood spots taken from Texas newborns are stored on cards identified by numbers. Names matching those codes are not released to researchers without parental consent, the state says.

Texans unknowingly donate children's blood to research

Medical privacy advocates, ethicists say parents should be asked for consent before newborns' screening samples are kept.

By Mary Ann Roser
AMERICAN-STATESMAN STAFF

Sunday, February 22, 2009

For almost seven years, the state has been indefinitely storing blood from nearly all newborns in Texas without their parents' consent for possible use in medical research.

The blood is collected as part of a 44-year-old state-mandated newborn screening program in which hospitals, birthing centers and midwives draw blood from a baby's heel — parental consent isn't required for that, either — so the state can test for a host of birth defects. The state either discarded the blood after six months or, more recently, stored it for three years before destroying it.

But starting in 2002, the state health department began collecting and keeping blood indefinitely for current or future medical research, a practice that has been the subject of a legal challenge in Minnesota.

Five dots of blood are collected on paper for the screening and then stored.

Under the health department's policy, the samples can be used by the medical community for things like cancer research, birth defects studies and calibration of lab equipment, said Doug McBride, spokesman for the Department of State Health Services.

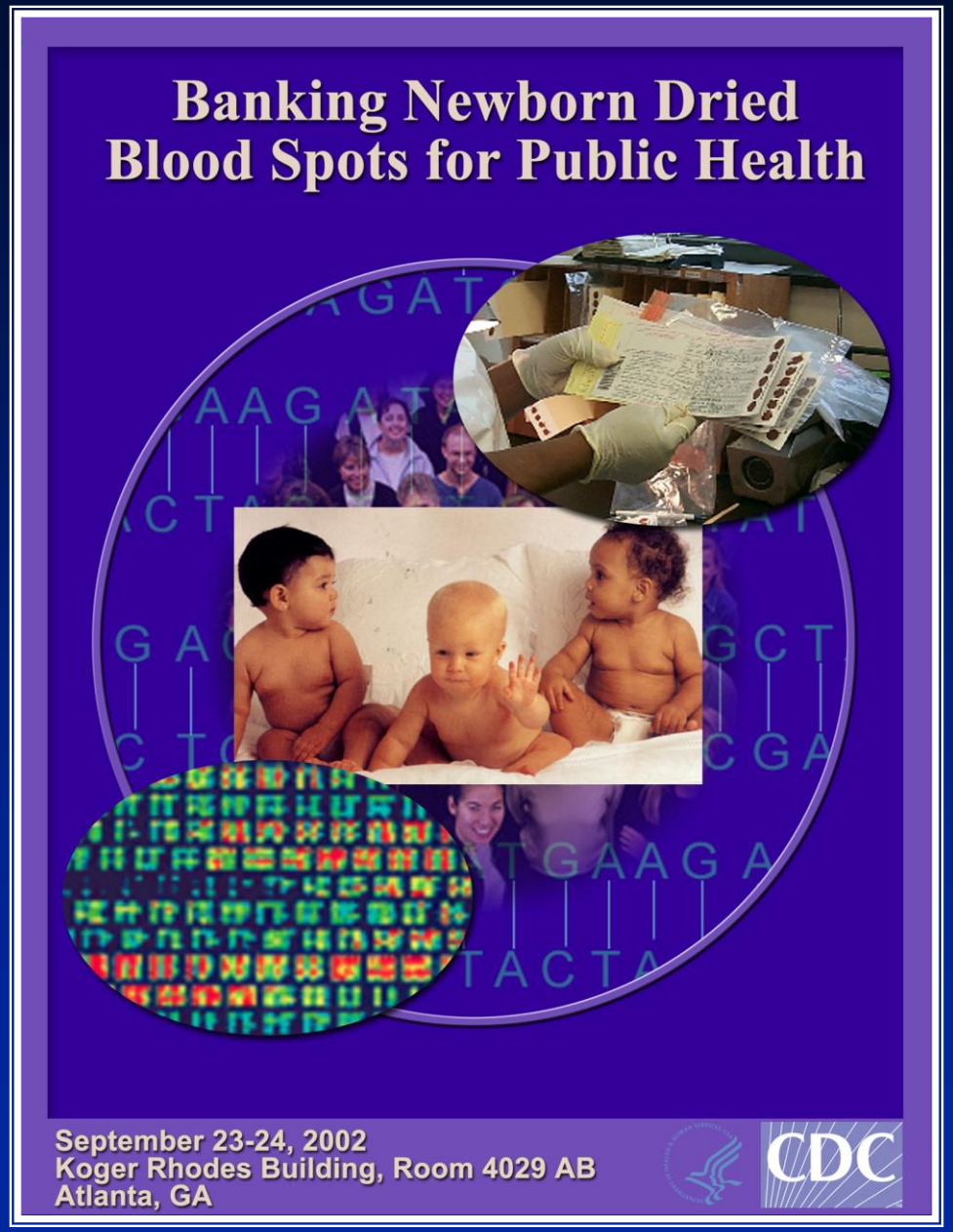
February 22, 2009

Austin American Statesman

"… without the parents' consent for possible use in medical research."

Purpose: To Develop a Strategic Plan to Assess the Feasibility, Utility, and Practical Implementation of Establishing a National/Multi-state Bank of Residual Newborn DBS

Host: Mary Lou Lindegren, MD
Centers for Disease Control and Prevention



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Objectives of the Meeting

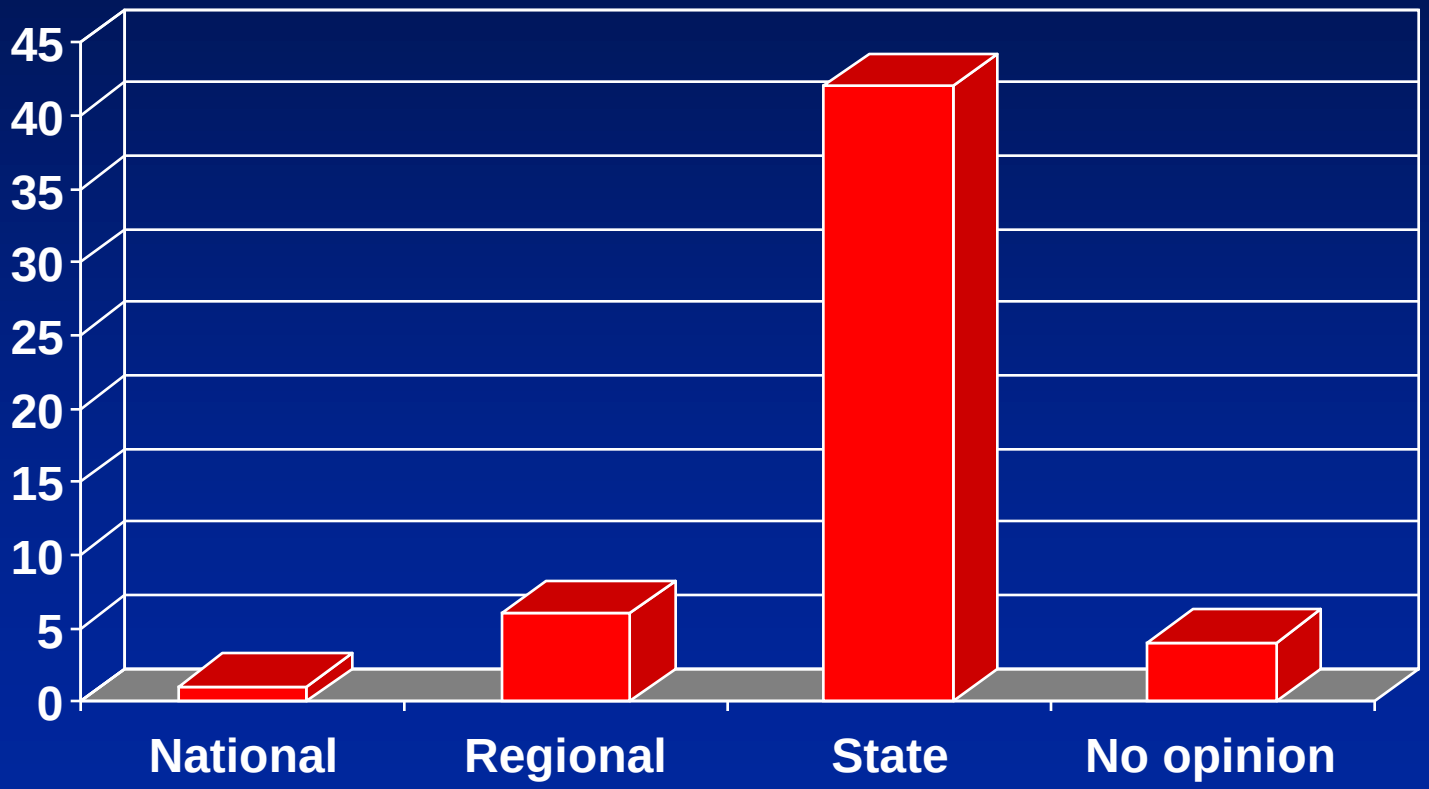
- Outline potential uses of banks for public health
- Review experiences using state-based spot banks for public health applications
- Assess storage, laboratory, and database issues
- Propose multi-state models for the future
- Review feasibility issues-challenges + barriers
- Update status of state storage and use policies for leftover specimens
- Design strategic plan for banking implementation

Summary of State Policy Data – CDC 2003

- State-to-state variability in residual blood spot storage duration and adherence to suggested storage guidelines
- 45% of states had written guidelines concerning the uses of their residual samples
- 16% informed parents DBSs retained
- Nearly 80% of states favored future storage of identifiable samples at state level

Olney RS, Moore CA, Ojodu JA, Lindegren ML, Hannon WH. Storage and use of residual dried blood spots from state newborn screening programs. J Pediatr 2006:148;618-22

Assuming funding is available, in which type of facility would you prefer to store residual NBS specimens? (2000 data)



Challenges

- Resources
- Data sharing issues
- Confidentiality, security, privacy issues
- IRB (ethical reviews)
- Legal, ethical, social issues
- Informed consent issues
- Education efforts for parents and others
- Maintain primary functions of NBS program

Outcome – Develop a Strategic Plan for a Virtual Database of Available Specimens for Research Use

- Create a working group to develop and publish a strategic plan for implementation
- Establish a central gatekeeper
- Establish criteria for inclusion, access and use
- Develop consensus standards for storage, QA, and cataloging/retrieval, data elements, linkages
- Plan Pilot Studies to demonstrate usefulness
- Address gaps + feasibility issues
- Larger stakeholders meeting for buy in

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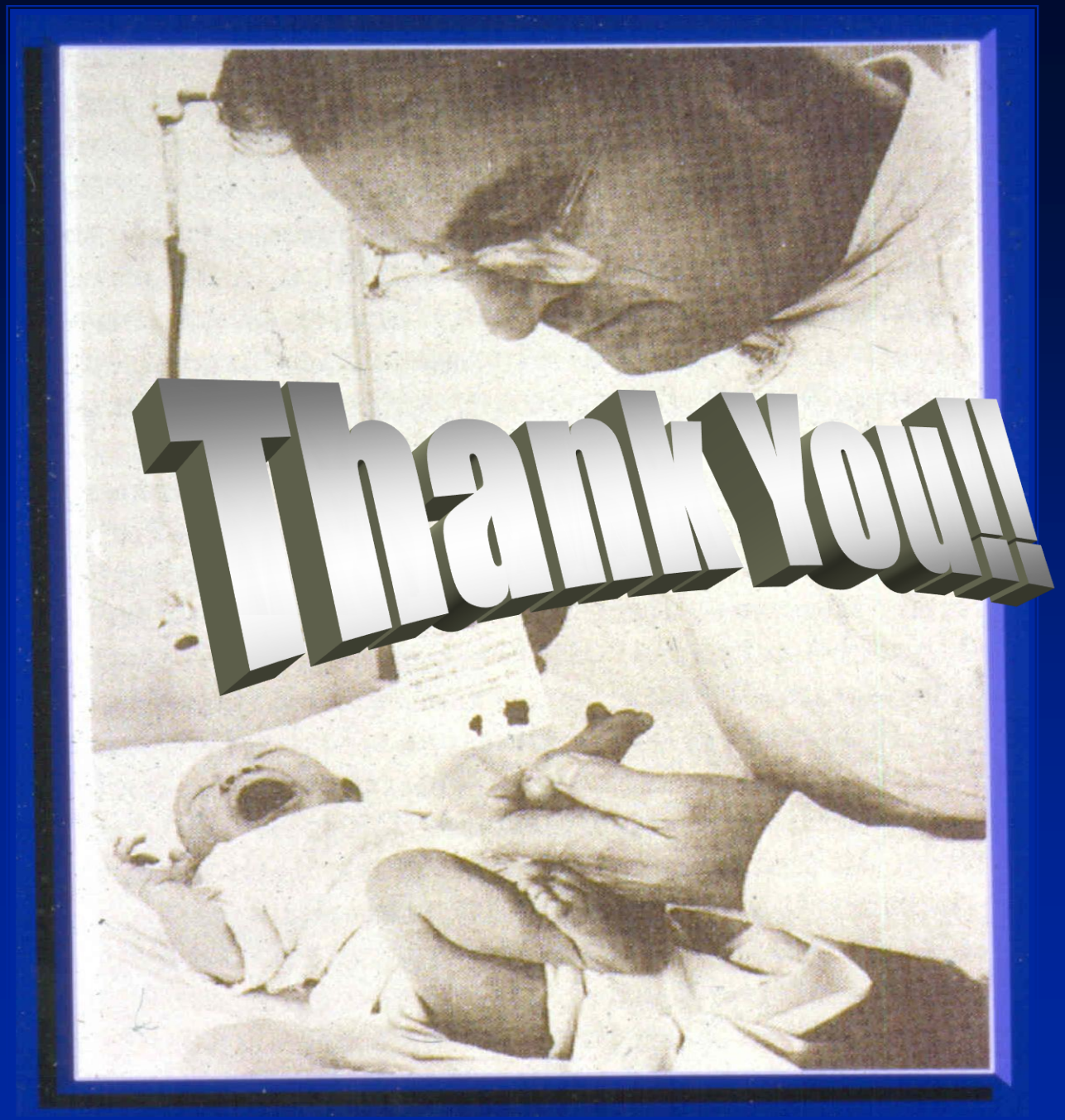
Current Thinking

- Still need to develop state policies on retention, storage, and use.
- NIH funding long-term outcome database for rare conditions diagnosed through newborn screening.
- Virtual specimen database for use in conjunction with the long-term outcomes database is possible.
- States appear interested in collaborating.
- Tendency towards referring to residual spots as patient “record” for policy implementation.


ThankYou!!