Overview of Newborn Screening, Potential Uses of Residual Dried Blood Spots, and Protection of Privacy

Alan R. Fleischman, M.D.
Senior Vice President and Medical Director

Chair, Federal Advisory Committee, National Children’s Study
National Institute of Child Health and Human Development/NIH

and

Clinical Professor of Pediatrics
Clinical Professor of Epidemiology and Population Health
Albert Einstein College of Medicine
Newborn Screening:
A Public Health Program

Newborn screening is a public health program that identifies rare genetic, metabolic, hormonal, and functional disorders in infants right after birth and assures early management and comprehensive follow-up care for those affected.
Newborn Screening Programs

- Sample collection and submission to the laboratory
- Laboratory testing
- Reporting of results
- Diagnostic confirmation
- Referral for treatment
- Long term support of patients and families
- Program evaluation
Dr. Robert Guthrie

1959-Test for PKU

1963-MA Tests all Babies
Newborn Screening: Sample Collection
American College of Medical Genetics
Newborn Screening Report (2005)
29 recommended conditions

<table>
<thead>
<tr>
<th>Five fatty acid disorders</th>
<th>Nine organic acid disorders</th>
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<tr>
<td>• Carnitine uptake defect (CUD)</td>
<td>• 3-Methylcrotonyl-CoA carboxylase deficiency (3MCC)</td>
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<td>• Long-chain 3-OH acyl-CoA dehydrogenase deficiency (LCHAD)</td>
<td>• Beta-ketothiolase deficiency (BKT)</td>
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<td>• Medium-chain acyl-CoA dehydrogenase deficiency (MCAD)</td>
<td>• Glutaric acidemia type 1 (GAI)</td>
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<td>• Trifunctional protein deficiency (TFP)</td>
<td>• Hydroxymethylglutaric aciduria (HMG)</td>
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<td>• Very long-chain acyl-CoA dehydrogenase deficiency (VLCAD)</td>
<td>• Isovaleric acidemia (IVA)</td>
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<td>• Methylmalonic acidemia cbIA and cbIB forms (CBLAB)</td>
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<td></td>
<td>• Methylmalonic acidemia due to mutase deficiency (MUT)</td>
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<td></td>
<td>• Multiple carboxylase deficiency (MCD)</td>
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<td></td>
<td>• Propionic acidemia (PROP)</td>
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<tr>
<th>Six amino acid disorders</th>
<th>Six conditions classified as ‘Other’</th>
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<tr>
<td>• Argininosuccinic acidemia (ASA)</td>
<td>• Biotinidase deficiency (BIOT)</td>
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<td>• Citrullinemia (CIT)</td>
<td>• Classical galactosemia (GALT)</td>
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<td>• Homocystinuria (HCY)</td>
<td>• Congenital adrenal hyperplasia (CAH)</td>
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<tr>
<td>• Maple syrup urine disease (MSUD)</td>
<td>• Congenital hypothyroidism (CH)</td>
</tr>
<tr>
<td>• Phenylketonuria (PKU)</td>
<td>• Cystic fibrosis (CF)</td>
</tr>
<tr>
<td>• Tyrosinemia type 1 (TYR-1)</td>
<td>• Hearing loss (HEAR)</td>
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<th>Three hemoglobinopathies</th>
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<tr>
<td>• Sickle cell anemia (HbSS)</td>
<td></td>
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<tr>
<td>• Hb S/Beta-thalassemia (HbSA)</td>
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<tr>
<td>• Hb S/C disease (HbSC)</td>
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</tbody>
</table>
Newborn Screening Tests by U.S. State 2004

March of Dimes
Saving babies, together

9 tests
6 - 8 tests
5 or fewer tests
Newborn Screening Tests

Source: March of Dimes. Data reported from NNSGRC.
Newborn Screening Tests

In September, 2009:
42 States + DC screen for all 29 disorders;
and All States screen for 23 or more disorders.
Newborn Screening Saves Lives Act (P.L. 110-204), 2008

Purpose

• To facilitate creation of national guidelines;
• To assist State newborn screening programs in meeting Federal guidelines;
• To improve education, outreach and coordinated follow-up care;
• To improve laboratory quality; and
• To reauthorize the Secretary’s Advisory Committee.
Residual Blood Spots from Newborn Screening

- Newborn Screening programs require very little blood for testing--resulting in residual blood spots available for other uses.

- Newborn screening specimens are unique -
  - representing a sample from every baby born in the U.S.
  - potentially a very valuable resource to improve the health of all children and families.
Potential Uses of Residual Blood Spots from Newborn Screening

- Program quality assurance and test validation
- Develop new screening methods
- Parental requests for additional testing (particularly in cases of an infant death)
- Public health research--populations
  - Prevalence of disease
  - Identify new infectious agents, toxins, bioterrorism, etc.
- Health related research--individuals
  - Identify affected children
  - Assess long term health status
Residual Blood Spots from Newborn Screening

Stakeholders

Scientists and Clinicians

Child

Family

Government and Public Health Departments
Research with Residual Blood Spots from Newborn Screening

In the interests of all children there are two critical questions:
1-Can residual blood spots be stored for future research without jeopardizing the important public health goals of newborn screening programs?
2-Should any uses of residual blood spots other than the actual screening tests be permitted without permission?
Research with Residual Blood Spots from Newborn Screening

- **Anonymous**
  - Samples separated from all possible identifiers
  - Cannot be re-linked to individual

- **De-Identified** (sample coded and separated from all identifiers)
  - Cannot be linked to specific individuals by investigator
  - Data access agreements—investigator will make no attempts to re-identify samples to subject
  - Possible to re-link to individual if finding critical to health (honest broker)
Research with Residual Blood Spots from Newborn Screening

• Is the study “Research”?
  - 45 CFR §46.102: Research means a systematic investigation...designed to develop or contribute to generalizable knowledge.
    • Quality Improvement?
    • New laboratory methods?

• Does the study involve “Human subjects”?
  - 45 CFR §46.102: Human Subject means a living individual about whom an investigator conducting research obtains:
    • Data through intervention or interaction with the individual, or
    • Identifiable private information
Can the study be done with fully de-identified data?

“OHRP considers private information or specimens not to be individually identifiable when they cannot be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems. For example, OHRP does not consider research involving only coded private information or specimens to involve human subjects as defined under 45 CFR 46.102(f) if the following conditions are both met:
(1) the private information or specimens were not collected specifically for the currently proposed research project through an interaction or intervention with living individuals; and
(2) the investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain”
Research with Residual Blood Spots from Newborn Screening

• Does the study require review by an Institutional Review Board for Research with Human Subjects?

45 CFR§46.101 Studies Exempt from Review

(b)4. “Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.”
Research with Residual Blood Spots from Newborn Screening

- Health related research on Individuals
  - Requires Identifiers
  - Requires Institutional Review
  - Generally requires full informed consent

- Families may be approached for willingness to participate after Newborn Screening testing has been completed
Research with Residual Blood Spots from Newborn Screening

• Does the study require informed consent? May informed consent be waived entirely? May written informed consent be waived and oral consent suffice?

45 CFR§46.116 Waiver of Informed Consent
(d) “An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that: (1) The research involves no more than minimal risk to the subjects; (2) The waiver or alteration will not adversely affect the rights and welfare of the subjects; (3) The research could not practicably be carried out without the waiver or alteration; and (4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.”
State Approaches to Research with Residual Blood Spots
State Approaches to Research with Residual Blood Spots

South Carolina

Parents receive educational materials at time of Newborn Screening:

“What happens to my baby’s blood sample after the lab tests? -- You decide....”
State Approaches to Research with Residual Blood Spots

**Michigan**

Parents receive educational pamphlet at time of Newborn Screening...

“What happens to my baby’s blood specimen after testing?”
Residual Blood Spots from Newborn Screening

- Newborn Screening is a highly successful public health program
- Residual blood spots are a unique resource
- Residual blood spots can be stored while assuring confidentiality and privacy of the individual child and family
- There are many important uses of anonymized or de-identified residual blood spots that do not require prior informed consent
- Institutional Review Boards for research with human subjects should assure compliance with all federal regulations for informed consent when individual subjects can be identified.
Residual Blood Spots from Newborn Screening

- All families receiving prenatal care, and all new parents, should be educated about newborn screening programs, including the potential uses of residual blood spots;
- Health professionals who serve families receiving prenatal care, and new parents, should be knowledgeable about newborn screening programs, including the potential uses of residual blood spots;
- The public must be educated about newborn screening programs and reassured that research utilizing residual blood spots can enhance health and be performed with respect for and protection of privacy and confidentiality.
Thank You