**Tales from the Crib**

The Texas Newborn Screening Program

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**Newborn Screening: Tales from the Crib**

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Debra Freedenberg MD, Ph.D.
Medical Director Texas Newborn Screening Program

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**BASICS: PURPOSE OF NEWBORN SCREENING**

- Program to screen for 30 congenital and heritable disorders.
- Disorders may cause severe intellectual disability, chronic illness, or death with no clinical symptoms.
- Early detection and treatment leads to dramatic positive outcomes for most affected babies.
- Typically treatment through diet control, hormone replacement, and medical supervision.

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**BASICS: TIMING IS EVERYTHING**

- Many disorders may cause irreparable damage in the first days of life.
- Changes in diet and/or other simple interventions can prevent lifelong consequences.
- If an abnormal result occurs, prompt follow-up is critical.
- Accuracy in testing and correct demographic information are essential.
Disorders Screened in Texas

As of December 2012, Texas screens for 30 disorders:
- 29 rare disorders: Newborn Screening blood spot specimen.
- Congenital hearing loss is considered another Newborn Screen.

Newborn Screening Advisory Committee

Purpose of Advisory Committee:
To advise DSHS on strategic planning, policy, rules and services related to newborn screening tests.
- 9 member committee formed in May 2010
- 2 additional members to be added 2014

Last meeting June 20, 2014

TEXAS EARLY HEARING DETECTION AND INTERVENTION

TEHDI
TEXAS NEWBORN HEARING SCREENING

Hearing screening by one of two tests:

- Otoacoustic Emissions (OAE).
- Automated Auditory Brainstem Response (AABR).

Critical Congenital Heart Disease

- 20-30% of all congenital heart defects
- 2/1000 potentially lethal - “critical”
  - Requiring expert cardiac care and intervention in the immediate NB period or early infancy
- In the US, about 4800 babies are born each year with CRITICAL CHD
- One of the leading causes of death in infants < 1 year old
**CCHD Screening**

- US Health and Human Services (HHS) Secretary’s Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC)
  - In 2010, recommended that CCHD be added to the newborn uniform screening panel to identify newborns with structural heart defects associated with hypoxia that could have significant morbidity or mortality early in life with closing of the patent ductus arteriosus or other physiologic changes
  - 2011, Endorsed by Secretary of HHS Kathleen Sibelius
  - 2013 Texas HB 740 added CCHD to core panel in 83(R) session

**CCHD 7**

The seven defects classified as CCHD are:

1. Hypoplastic Left Heart Syndrome (HLHS)
2. Pulmonary Atresia with intact septum (PA/IVS)
3. Tetralogy of Fallot (TOF)
4. Total Anomalous Pulmonary Venous Return (TAPVR)
5. Transposition of the Great Arteries (TGA)
6. Tricuspid Atresia (TA)
7. Truncus Arteriosus communis (TAC)
How is it done?

Critical Congenital Heart Disease
Newborn Screening Algorithm

1. Pulse ox on right hand and foot after 24 hours
2. >95% in right hand and foot
3. >90% in right hand and foot
4. >90% in right hand and foot
5. Repeat screen in 1 hour
6. Notify referral

NEWBORN BLOOD SPOT SCREEN
Disorders fall into the following categories:

- Organic acid disorders.
- Fatty acid oxidation disorders.
- Amino acid disorders.
- Hemoglobinopathies.
- Endocrine disorders.
- Other disorders.

THE 29 RARE DISORDERS

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>IV (isovaleric acidemia)</td>
<td>MSUD (methylsuccinyluria)</td>
</tr>
<tr>
<td>MSUD (3-hydroxyisovaleric acidemia)</td>
<td>MEUD (methylcitryl-L-threonine dehydrogenase deficiency)</td>
</tr>
<tr>
<td>NDC (N-acylglycine dehydrogenase deficiency)</td>
<td>NET (neuronal transporter deficiency)</td>
</tr>
<tr>
<td>PRPP (propionyl-CoA carboxylase deficiency)</td>
<td>SS (Sickle cell anemia)</td>
</tr>
</tbody>
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CYSTIC FIBROSIS

- 297 cases confirmed as of July 15, 2014.
Severe Combined Immunodeficiency

Storage and Use of Residual Dried Blood Spots

HB 411  82nd Legislature

New Requirements Regarding the Storage and Use of Dried Blood Spots after Completion of Newborn Screening
House Bill 411

- Strengthens DSHS management review and approval processes of proposed uses of dried blood spots after screening is completed

- Effective June 1, 2012 - Requires parental consent for:
  - External public health research uses
  - Storage longer than 2 years

- New “Decision” Form

Specimen Collection Kit

USE AND STORAGE OF NEWBORN SCREENING BLOOD SPOT CARDS (PAGE 2)

House Bill 411 (2011) includes requirements for healthcare providers for the distribution of forms to parents regarding the storage and use of dried blood spots cards after completion of the newborn screen.

8½X11 versions of form are available at:
http://www.dshs.state.tx.us/lab/nbsbloodspots.htm
Form **MUST** be distributed to parents upon collection of all Newborn Screening specimens.

Parents may choose:

- Specimens stored for up to 25 years and made available for possible public health research uses outside of DSHS.
- Specimens destroyed within 2 years and not allowed for research uses outside of DSHS.

**FINAL STEPS**

Parents may:

- Complete the decision form and return to the healthcare provider to be shipped with any regular newborn screening specimen shipment; OR
- Mail in at a later date.

Healthcare providers must:

- Check the box on the patient demographic form to indicate that the Decision form has been distributed.

**IMPORTANT:**

- The Use and Storage forms DO NOT allow the parent to decline NBS screening.
- The only legal reason a parent can decline the screen is for religious tenets or practices per Texas Health & Safety Code Sec. 33.012.
TIMING

- 1st blood sample is collected at 24 – 48 hours after birth or before transfusion or discharge, regardless of weight or feeding status.
- 2nd sample is recommended to be collected at 7 – 14 days of age.
- The later a specimen is drawn outside this timeframe, the greater the chance the screen may not identify a disorder.

WHY TWO SCREENING TESTS?

1st Screen
- The tests for certain disorders pick up abnormal levels produced by the stress of birth.
- Abnormal levels for some disorders may normalize by the second screen.
- Early testing may mean the difference between life and death for a patient.

2nd Screen
- Some disorders may be missed on the 1st screen due to infant physiology.
- The second screen is necessary to capture some disorders not picked up on the first screen.
- The CF testing protocol requires two screens.
IT TAKES A TEAM

• NBS Laboratory Services.
• NBS Clinical Care Coordination.
• Medical Providers/Medical Facilities.
• Parents and/or Caregivers.

NBS LABORATORY SERVICES

DSHS NEWBORN SCREENING LABORATORY

• Operates 6 Days a week
• Testing processes begin on all specimens within 1 business day of receipt
• Initial (critical) results available in as little as 24 hours
• All results reported within 4-5 business days
LAB TESTING THE BLOOD SPOTS

• Approximately 380,000 infants born in Texas each year.
• Approximately 750,000 newborn screens per year.
• Approximately 2,500 specimens received each day.

RESULT REPORTING

• Mailed Result Reports
• Web Application (Neometrics)
• HL7 Messaging

http://www.dshs.state.tx.us/lab/nbsRemoteDataServices.shtm

Remote Services

Web-Based System
• Available to any healthcare provider
• Username & password required
• Features:
  - Remote demographic entry/orders
  - Online access to patient results
  - Report cards to be available online soon

Goal – for all submitters to have access to the online system

HL7 File transfer capabilities
• Direct transfer of demographics and results between computer systems
  - 3 large hospital systems fully implemented (~10% of all specimens)
  - Several facilities waiting to start implementation
WEB APPLICATION (NEOMETRICS)

Sign Up in 3 Easy Steps

1. Download forms from:
   http://www.dshs.state.tx.us/lab/nbsRDSforms.shtm

2. Complete
   A. Security/Confidentiality Agreement (1 per facility)
   AND
   B. Web User Agreements (1 for each user)

3. Submit the completed forms:
   Fax to: 512-458-7452 ATTN: DSHS Laboratory Services;
   L457.1 Web Services
   Or e-mail to: remotelabsupport@dshs.state.tx.us

NORMAL SCREEN REPORT

ABNORMAL SCREEN REPORT
TEXAS NEWBORN SCREENING
CLINICAL CARE COORDINATION

CLINICAL CARE COORDINATION TEAM

• Medical Director.
• Registered Nurses.
• Public Health and Prevention Specialist (PHPS).
  – Nurses and PHPS are assigned to specific disorders.
  – Nurses and PHPS are cross-trained for full coverage Monday–Saturday.
• Educators.
• Ombudsman.

SHORT TERM FOLLOW UP

Overview
• A case is opened for each screen positive result.
• Cases are monitored until an infant is cleared or diagnosis is determined.
NBS CLINICAL CARE COORDINATION

- In Fiscal Year 2013, the DSHS laboratory screened approximately 745,000 specimens for metabolic, endocrine, and hematological disorders
- Of those screens approximately 16,000 were abnormal screens that required follow-up by Clinical Care Coordination
- There were approximately 750 diagnosed cases in Fiscal Year 2013

FINDING THE MEDICAL PROVIDER

- Find the Medical Provider responsible for the medical care of the baby.
  - Determine if the baby is in the hospital.
- If a Medical Provider can be located:
  - Provide results.
  - Provide guidance for recommended actions.

FINDING THE FAMILY

If a Medical Provider cannot be located:
- Contact parents to obtain Primary Care Provider (PCP) information.
- If a PCP is not identified:
  - Provide results to family.
    - Direct family to an Emergency Department (ED) if necessary.
    - Clinical Care Nurse will coordinate with ED staff if family directed to ED.
WHEN ALL ELSE FAILS

If baby cannot be located:
• Utilize DSHS Regional Social Workers to assist with:
  • Locating the baby,
  • Connecting baby with health-care providers and services.
• Involve other agencies, including law enforcement and/or CPS if necessary.

RESOURCES DISTRIBUTED

Screen Positive NBS
• Information mailed to parent.
• NBS letter
• General NBS Brochures

SHORT TERM FOLLOW UP

POSITIVE SCREEN WITH VERY ELEVATED LEVELS: MEDICAL EMERGENCY
• Reported immediately to nurses in NBS Clinical Care Coordination.
• Nurse will notify PCP by phone and fax the same day the laboratory results reports are received from the DSHS lab.
• If no PCP is on record for the newborn or cannot be located, the nurse will notify the parents directly.
RESOURCES DISTRIBUTED FOR A NEWBORN REQUIRING URGENT FOLLOW UP

Fax to Medical Provider
• NBIS letter with:
  - NBIS disorder-specific lab results.
  - Contact information for the NBIS Nurse responsible for the NBIS case.
  - Disorder-specific ACT/FACT Sheet.
• List of regional subspecialist consultants.

ACT (ACTION) SHEETS FOR PROVIDERS
• Adapted from the American College of Medical Genetics (ACMG).
• Designed for the medical provider.
• Contain the following:
  - Differential Diagnosis.
  - Condition Description.
  - For medical emergencies, follow the instructions in the black outlined box.
• Available on the NBIS Clinical Care Coordination website.

FACT SHEETS FOR PARENTS
• Each disorder has a FACT sheet that is modeled from the ACMG Fact Sheet.
• Designed for the PCP to share with the family.
• Information for the parents about symptoms, treatment, and things to remember for the specific disorder.
• Available on the NBIS Clinical Care Coordination website.
• Available in English and Spanish.
PRIMARY CARE PROVIDER AND FACILITY RESPONSIBILITIES

Birth Hospital:
• Assist with locating baby if needed.
• Identify PCP for infant.

PCP:
• Agree to follow-up with newborn/family.
• Agree to accept patient into practice.
• Refer to subspecialists as appropriate.
**PARENTAL RESPONSIBILITIES**

- Parent provides PCP information to Clinical Coordination Staff.
- If the newborn does not have a PCP:
  - Parent is asked to identify a PCP.
  - Take infant to ED if necessary.
- Parent must follow-up to ensure newborn:
  - Attends appointments.
  - Receives treatment and care if diagnosed.

**LONG TERM FOLLOW UP**

Goal: To ensure the best possible outcome for individuals with disorders identified through newborn screening.

Components:
1. Care coordination through a medical home.
2. Evidence-based treatment.
3. Continuous quality improvement.

**LONG TERM FOLLOW UP**

What is Involved?
- Continuing PCP/specialist visits.
- Continuing documentation of treatment.
- Parental involvement.
- Physician/specialist participation.

How long is a child in long term follow-up?
- Begins when an infant receives a confirmatory diagnosis.
- Continues until child is 4-21 years old, depending on the disorder.
LONG TERM FOLLOW UP

Why Track Long Term?

- Evaluate effectiveness of the NBS Program.
- Develop evidence-based treatment.
- Improve treatment of affected individuals.
- Provide continuous quality improvement.

NBS BENEFITS PROGRAM

WHAT IS THE NBS BENEFITS PROGRAM?

- Redesigned in 2007 to account for the expansion of NBS disorders screened.
- Targets families without Medicaid or private insurance.
WHO IS ELIGIBLE FOR NBS BENEFITS?

- Those with a presumed positive screen or a confirmed diagnosis of a disorder screened for in the Texas Newborn Screening Program.
- An income at or below 350% of the federal poverty income level (FPL).
- Texas resident

WHAT ARE THE NBS BENEFITS FOR PATIENTS?

- Confirmatory testing.
- Dietary supplements.
- Metabolic foods.
- Low-protein foods.
- Medications.
- Vitamins.
- Follow-up care.

What's Next: Secondary Conditions on RUSP Panel

24 additional Secondary Conditions

- Secondary conditions are believed to be clinically significant, but some may have an unclear natural history or lack appropriate medical therapy that affects long-term outcome.
- Detected during screening for core conditions.
- The additional conditions will be detected through the same newborn screen specimen collected from a heel stick and tested at the Texas Department of State Health Services Laboratory.
- No additional blood spots will need to be collected.
- No additional fee is anticipated at this time*

*As cost estimate of the whole newborn screening panel is expected in 2015
<table>
<thead>
<tr>
<th>Secondary Conditions</th>
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<tbody>
<tr>
<td><strong>CblC,D (Methylmalonic acidemia with homocystinuria)</strong></td>
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<tr>
<td><strong>MAL (Malonic academia)</strong></td>
</tr>
<tr>
<td><strong>IBG (Isobutyrylglycinuria)</strong></td>
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<tr>
<td><strong>2MBG (2-Methylbutyrylglycinuria)</strong></td>
</tr>
<tr>
<td><strong>3MGA (3-Methylglutaconic aciduria)</strong></td>
</tr>
<tr>
<td><strong>2M3HBA (2-Methyl-3-hydroxybutyric aciduria)</strong></td>
</tr>
<tr>
<td><strong>SCAD (Short-chain acyl-CoA dehydrogenase deficiency)</strong></td>
</tr>
<tr>
<td><strong>M/SCHAD (Medium/short-chain L-3-hydroxyacyl-CoA dehydrogenase deficiency)</strong></td>
</tr>
<tr>
<td><strong>GA2 (Glutaric acidemia type II)</strong></td>
</tr>
<tr>
<td><strong>MCAT (Medium-chain ketoacyl-CoA thiolase deficiency)</strong></td>
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<tr>
<td><strong>DE RED (2,4 Dienenoyl-CoA reductase deficiency)</strong></td>
</tr>
<tr>
<td><strong>CPT IA (Carnitine palmitoyltransferase type I deficiency)</strong></td>
</tr>
<tr>
<td><strong>CPT II (Carnitine palmitoyltransferase type II deficiency)</strong></td>
</tr>
<tr>
<td><strong>CACT (Carnitine acylcarnitine translocase deficiency)</strong></td>
</tr>
<tr>
<td><strong>ARG (Argininemia)</strong></td>
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<tr>
<td><strong>CIT II (Citrullinemia, type II)</strong></td>
</tr>
<tr>
<td><strong>MET (Hypermethioninemia)</strong></td>
</tr>
<tr>
<td><strong>H-PHE (Benign hyperphenylalaninemia)</strong></td>
</tr>
<tr>
<td><strong>BIOPT (BS) (Biopterin defect in cofactor biosynthesis)</strong></td>
</tr>
<tr>
<td><strong>BIOPT (REG) (Biopterin defect in cofactor regeneration)</strong></td>
</tr>
<tr>
<td><strong>TYR II (Tyrosinemia, type II)</strong></td>
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<tr>
<td><strong>TYR III (Tyrosinemia, type III)</strong></td>
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<tr>
<td><strong>Var Hb (Various other hemoglobinopathies)</strong></td>
</tr>
<tr>
<td>*<strong>GALE (Galactoepimerase deficiency)</strong></td>
</tr>
<tr>
<td>*<strong>GALK (Galactokinase deficiency)</strong></td>
</tr>
<tr>
<td><strong>T-cell related lymphocyte deficiencies</strong></td>
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* At this time NBS is not testing.

**What's Next:**

**Pompe**
- DCHDNC recommended adding May 2013
- HHS Secretary Sebelius requested the ICC review Pompe NBS with recommendation by July 31, 2014

**MPS1, X-ALD**
- DCHDNC sent to formal evidence review, which is the next step in moving condition forward for consideration

**Case 1 Hypothyroidism**

BG D was the 3.4 Kg product of an uncomplicated term gestation

- DOL 2 - 1st NBS collected
- DOL 8 - Received by DSHS Lab, no PCP listed.
- DOL 11 - Results to CCC. Hospital contacted, provided PCP name. PCP notified of abnormal screen and guidance provided, parent letter mailed
- DOL 30 family cell-changing PCP, but no new PCP identified
- DOL 32 family phone not answered. Certified letter sent to home
- DOL 35 Regional SW to home, appointment made with new PCP
- DOL 38 PCP office noted baby scheduled for lab draw
- DOL 40 PCP office noted baby scheduled for lab draw
- DOL 43 - 1 Year Child could not be located. At 1 year of age, admitted to PICU with severe developmental delay and malnutrition.
Case 2 PKU

Baby Girl J was the 2.5 KG product of a 36 week uncomplicated gestation

DOL 2 - 1st NBS obtained

DOL 3 - Received by NBS Lab

DOL 4 - Elevated phenylalanine and elevated phenylalanine/tyrosine ratio. PCP notified, requested repeat NBS obtained same day. Referred to metabolic MD by PCP.

DOL 6 - Evaluated by metabolic MD, confirmatory testing obtained

DOL 8 - 2nd NBS obtained, phenylalanine remained elevated

DOL 9 - Diagnosis of classical PKU confirmed

Case 3 CAH

Baby Boy T, 3.2Kg product of uncomplicated term pregnancy

- DOL 2 NBS obtained, DOL 6 Sample received at lab
- DOL 7 Preliminary result very elevated 17-OHP
  - Birth Hospital contacted, child already discharged - newborn PCP listed as PCP, but when contacted stated not accepting new Medicaid patients
  - Family contacted-No PCP identified
  - Child referred to ED of local hospital, guidance given to ED
  - ED obtained electrolytes but refused to obtain 17-OHP, Na 133, K 4.9
  - Education provided to ED, stated no Pedi Endocrine in area. Transfer to tertiary center arranged
  - Tertiary center requested 17-OHP be obtained prior to transfer, 17-OHP obtained three hours later at local ED
- DOL 8 Final 17-OHP very elevated
- DOL 10 regional social worker contacted to help find PCP
- DOL 11 Family directed back to ED for additional lytes by social worker. Still no PCP
- DOL 17 17-OHP level returned. Still no PCP. Child obtained appropriate care

Case 4 CF Twins

- Baby Boy’s Smith were the 1.2kg and 1.8kg products of a 31 week monozygotic twin gestation born to a 29 G1P0 female by primary C section. Pregnancy was complicated by a maternal, unrepaired meningo(myel)ocoele with associated sequelae.
- Limited prenatal care was obtained in Mexico but concern was noted of a possible twin-twin transfusion. Maternal history notes the use of oral steroids due to “maternal short stature” 3 weeks prior to delivery.
Case 4 CF TWINS

Twin A

- Indication at time of presentation twin A was noted to have fetal ascites, polyhydramnious, hydrops, and no end diastolic blood flow.
- At time of attempted placement of an umbilical line twin A had significant bleeding and the decision to transfuse before obtaining NBS was based on clinical status.
- During the first day of life child received FFP, packed irradiated RBC, and required RBC, FFP, cryoprecipitate, and platelets over the next few days.
- Child was noted to have in utero bowel rupture.
- First NBS collected at 48 hours of life. Child received a total of 220ml pRBC (183ml/kg), 125ml FFP (104ml/kg), and 20ml cryoprecipitate prior to NBS being obtained.

Twin B

- Child had initially appeared stable but was noted to have scrotal discoloration.
- During w/u for scrotal discoloration fecal contents were noted in scrotum.
- Further work up noted bowel perforation.
- NBS was obtained prior to transfusion with packed irradiated RBC and FFP.

Case 4 CF Twins

Twin B (1.8kg)

**First Screen:**
- Collected DOL 2
- Received DOL 5
- Reported DOL 9
- Elevated IRT

**Second Screen:**
- Collected on DOL 10
- Received DOL 13
- Reported DOL 20
- Elevated IRT

**DNA:**
- Homozygous F508 Deletion

**Third Screen:**
- at our request
- Elevated IRT DOL 28

**Elevated IRT DOL 28**
Case 4 CF Twins

NBS on Twin A

First Screen:
- Collected DOL 2
- Received DOL 5
- Reported DOL 7
- IRT not out of range

Second Screen:
- Collected DOL 10
- Received DOL 14
- Reported DOL 17
- IRT not out of range

Third Screen:
- at our request
- Elevated IRT DOL 28
- IRT not out of range

DNA Studies:
- (obtained due to twin’s NBS results)
- Homozygous F508 deletion

Newborn Screening Program

Newborn Screening System
Questions?