Newborn Screening

Not just PKU anymore!
PKU was the beginning

Dr. Robert Guthrie (1916 – 1995) developed a bacterial inhibition test for PKU and other disorders from dried bloodspots
Automation was needed to use dried bloodspots in widespread screening programs

Robert E. Phillips (1921-2010) invented the punch index machine that automated the Guthrie test
Automated Punch Machine
THEN

• Best time for a test was at 72 hours of age, after full feeding – antibiotics interfered
• For PKU, phenylalanine would continue to rise so delay in testing would not result in a false negative result
• Disorder didn’t show symptoms immediately (although elevated phe does damage before symptoms appear)
• Newborn screening panels varied by state
NOW

- Multiplex testing platform – tandem mass spectrometry (MS/MS) for most disorders
- Panel now includes disorders that are life-threatening within the first week of life
- FAODs can be missed if testing is delayed
- Best screening window is much earlier (close to 24 hours of age)
- National panel of disorders recommended
Tandem Mass Spectrometer
National effort to standardize screening

- ACMG surveyed the newborn screening and genetics community and developed a recommended panel of 29 core disorders (and 25 secondary disorders) for inclusion in all state newborn screening panels
- The HHS Secretary’s Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC) recommended this panel in 2005
Uniform Screening Panel

- HHS Secretary has accepted and endorsed the original Uniform Screening Panel that was proposed by ACMG and recommended by ACHDNC
- SCID and related T-cell lymphocyte deficiencies were added to the panel in May, 2010 (Although AZ has not adopted them yet)
Original Uniform Screening Panel – 29 core disorders

- **Endocrine disorders** (2)
  - Hypothyroidism, CAH
- **Hemoglobinopathies** (3)
  - Sickle cell anemia, sickle beta thalassemia, sickle C disease
- **Other enzyme deficiencies** (2)
  - Biotinidase deficiency, galactosemia
- **Amino acid disorders** (6)
  - PKU, MSUD, HCY, CIT, ASA, TYR 1
- **Fatty acid oxidation disorders** (5)
  - CUD, MCAD, VLCAD, LCHAD, TFP
- **Organic acid disorders** (9)
  - IVA, GA-1, HMG, 3MCC, MCD, MMAs, PA, BKT
- **Cystic Fibrosis** (1)
- **Hearing Loss** (1)
Most screened disorders are inherited in an autosomal recessive pattern (except hypothyroidism and hearing loss)
Add disorder to the panel if:

- Disorder is relatively common, harmful if undetected
- Disorder is identifiable by screening prior to appearance of clinical symptoms
- Test is available with appropriate sensitivity (few false negatives) and specificity (few false positives)
- Test is adaptable to a mass screening program (DBS or simple in-nursery method) – high throughput, reasonable cost: *technically feasible and financially possible*
- There are demonstrated benefits of early detection and timely intervention – effective treatment: *medically necessary*
- Benefits of early identification outweigh any adverse consequences (including cost-benefit)
ACHDNC reviews applications for new disorders for the panel

- Severe Combined Immunodeficiency (SCID) was the first core disorder added to the original Uniform Screening Panel
- Disorders considered but not added to the panel include: Pompe disease, Krabbe disease and Hemoglobin H disease
- Currently under consideration: critical congenital cyanotic heart disease (CCCHD) and hyperbilirubinemia
Provider Responsibilities

1. Inform parents about NBS
2. Collect acceptable bloodspot specimens
3. Ensure timely collection of specimens
4. Transport specimens promptly to the State Lab
5. Document NBS results in the medical record
6. Follow-up on any abnormal results
7. Perform and report hearing screening
1. Inform Parents about NBS

• Convey the importance of newborn screening and consequences of delayed identification of affected infants
  – there is no way of predicting affected babies
  – most are identified with no family history
  – most affected babies look normal at birth
  – permanent damage can be done before symptoms appear and some babies can die
  – risk of a disorder is much more likely than winning the lottery
Inform parents (cont.)

• Provide educational materials to parents of any baby who has a bloodspot test ordered
  – NBS brochure
• Carriers for CF, hemoglobinopathies and some other disorders are identified
Newborn Screening
A Guide for Parents

What is Newborn Screening?
Babies born in Arizona have a few drops of blood taken from their heels to test for certain medical disorders. They also have their hearing tested.

Why are babies tested?
- The blood tests could save your baby's life.
- Most babies are healthy when they are born. A few babies look healthy but have a rare health problem.
- If the problem is found early, we can help prevent serious results like mental retardation or death.
- Finding hearing loss will help your child learn speech and language.

When are babies tested?
- The hospital will do the first blood spot test and the hearing test.
- Your baby's doctor will order the second blood spot test at your first visit.

For what disorders are babies tested?
- The 29 core disorders including hearing loss on the Recommended Uniform Screening Panel from the U.S. Department of Health and Human Services (HHS)
- This panel is also endorsed by the American Academy of Pediatrics and the March of Dimes.

How will I know the results?
Blood spot results:
- Ask your baby's doctor for the results of both the first and second tests.
- Give the hospital and the baby's doctor your correct address and phone number.

Hearing results:
- The hospital will write the results on the back of the immunization record. Bring the blue shot card to your baby's doctor.
- A second test may need to be done.

What if my baby's results are abnormal?
- You will get a call from your baby's doctor asking you to get more testing done immediately.
- An abnormal second blood spot or hearing test may not mean your baby has a problem. Your baby may be referred to a specialist for diagnostic testing and treatment. If needed, the Arizona program will help you get special services for your baby.

Where can I get more information?
- Ask your baby's doctor
- Call the Newborn Screening Program at 602-364-1409 (1-800-548-8381 outside the Phoenix metropolitan area)
- Visit our website at: www.aznewborn.com

Arizona Department of Health Services
Bureau of State Laboratory Services
Newborn Screening Program
250 N. 17th Ave., 1st Floor
Phoenix, Arizona 85007-3231
Phone: 602-364-1409
Outside the Phoenix metropolitan area:
1-800-548-8381
Deaf and Hard of Hearing call 711 for AZ Relay Service

Permission to quote from or reproduce materials from this publication is granted when due acknowledgment is made.
2. Collect acceptable bloodspot specimens

- One large drop of blood per circle
  - yields a uniform amount of blood in each punch for testing
- Mother’s name and DOB included
  - needed for matching specimens
- Accurate contact information for mother
  - needed for notification of abnormal results
Specimen Rejection Reasons

• Insufficient specimen
• Multiple specimen applications
• Incomplete or uneven saturation
• Torn or scratched
• Serum or tissue fluid separation
• Clotted or caked blood
• Contaminated specimen
• Expired card
• Specimen too old (received more than 14 days after collection)
• Specimen detached from form
• Infant too old (more than one year old)
• No identifying information
Multiple Specimen Applications
Incomplete saturation – insufficient specimen
3. Ensure timely collection of specimens (for well babies)

- Ideal collection time for first screens is at 24 – 36 hours of age
- Collect prior to factors that influence results
  - Transfusions, ECMO, therapies, parenteral feeding
- Collect prior to transfer to another hospital or discharge
- Medical home will collect second screen at the first outpatient visit or 5 – 10 days of age, whichever comes first
3. Ensure timely collection of specimens (for NICU babies)

- Ideal collection time for first screens is at 24 – 36 hours of age.
- Collect prior to factors that influence results even if earlier than 24 hours of age:
  - Transfusions, ECMO, therapies, parenteral feeding.
- Collect prior to transfer to another hospital.
- If in hospital at 5 days of age, collect second screen at 5 – 10 days of age or before discharge.
4. Transport specimens promptly to the State Lab

- Each specimen sent **no more than 24 hours after collection** or on the next business day (by hospital courier or free ADHS - provided FedEx)
- Package sent each weekday (5 per week)
- Friday package especially important for delivery on Monday so that no more than the weekend delays testing
5. Document NBS results in the medical record

- Note results in the discharge summary sent to the medical home

- To obtain NBS results, call 602-364-1409 or fax a request to 602-542-4099 for any missing reports
6. Follow-up on any abnormal results or unsatisfactory specimens

- Phone call, fax or letter from NBS Follow-up
- Obtain further testing
- Consult with specialist, if needed
- Obtain diagnosis or normal results
- If disorders confirmed, refer to CRS or specialty care
- Send copies of test results from other labs to NBS Program
7. Perform and report hearing screening

• Hearing loss – most common congenital condition in the US
• Every day, 33 infants in the US are born with some degree of hearing loss
• All infants should be screened no later than one month of age
7. Perform and report hearing screening

- Hearing screening prior to discharge
- Repeat screening as outpatient, if a “refer”
  - Unless high risk – they go direct to a diagnostic test with an audiologist
- Report all testing weekly to NBS Program
- Include identifying information (mother’s name and DOB to help match results and avoid duplicates in database)
Hearing Screening - NICU

• Increased risk of neural hearing loss compared with healthy term infants.

• NICU infants that fail a hearing screen should not be rescreened but referred for a diagnostic hearing test.

• NICU infants with a greater than 5 day stay (or treated with any of the following, regardless of length of stay) is at higher risk for late onset/progressive hearing loss:
  – Assisted ventilation
  – Ototoxic medications (gentamycin, tobramycin, loop diuretics)
  – Hyperbilirubinemia requiring exchange transfusion
  – ECMO

*See JCIH 2007 Position Statement for other risk factors
Bloodspot screening - NICU

• NICU babies are just as likely to have a bloodspot disorder as well babies
• Prematurity, therapies, feeding and transfusion confound NBS results
• 1st specimen should be collected between 24 and 36 hours or before transfusion, TPN, etc.
• Heelstick not required – blood can come from venous or arterial blood draw
Arizona Newborn Screening Program Responsibilities

- Bloodspot specimen testing
- Reporting of bloodspot results
- Follow-up on abnormal bloodspot results and unsatisfactory specimens
- Follow-up on hearing screening results
- Proposing the disorders for the screening panel
- Selecting testing methodology and adjusting cutoffs for bloodspot screening
Challenges for the Arizona NBS Program

- Prompt testing and reporting of results
- Shortening transport time
- Reducing the unsat rate (goal of <1%)
- Reducing loss to follow-up for hearing loss
- Funding for current program and expansion
What we need from you for successful Newborn Screening

• For Bloodspot Screening
  – Collect acceptable specimens
  – Ensure timely collection
  – Send specimens promptly to the State Lab

• For Hearing Screening
  – Screen all babies before discharge
  – Don’t rescreen high risk babies - send them for diagnostic testing
  – Mandatory weekly reporting of hearing results
NBS Resources

• 2010 Revised Program Guidelines (available as a download from our website)
• www.AZNewborn.com with links to other resources
• Bloodspot collection video from CLSI available for loan
• Hearing Screening-Loss and Found DVD (free)
• Educator/Quality Improvement available for training/technical assistance: Sondi Aponte, 602-364-1642, sondi.aponte@azdhs.gov
• Follow up Coordinator for hearing screening and bloodspot questions: Brigitte Dufour, 602-364-1406 brigitte.dufour@azdhs.gov
Arizona Department of Health Services
Newborn Screening Program
(602) 364-1409

www.AZNewborn.com