

Newborn Screening in Arkansas SFY13

Report of Results from July 1, 2012 - June 30, 2013

**Child and Adolescent Health Section
Family Health Branch
Arkansas Department of Health**

Introduction

Newborn screening for inborn conditions has been mandatory in Arkansas since Act 192 of 1967 stipulated screening of all newborns for phenylketonuria. Since that time, the number of conditions screened for has grown substantially. The largest single increase occurred in July 2008, when 22 conditions were added to the screening panel, bringing the total number of conditions screened for to 28. These latest changes to the program were documented in some detail in the 2009 report, "Newborn Screening in Arkansas SFY09."

Changes during the Year

The "second tier" steroid profile testing is intended to differentiate infants with congenital adrenal hyperplasia (CAH) caused by 21-hydroxylase deficiency from those who merely have false positive 17-OHP screening results. In 2012, the program reduced reliance on the steroid profile ratio to exclude disease and updated 17-OHP cut-offs and follow-up protocols in order to initiate earlier evaluation when there was an elevated 17-OHP. This resulted in more rapid assessment of infants with potentially true positive results instead of waiting for the steroid profile results. In 2013, the cut-off for the steroid profile testing was changed to a lower value. Experience with the steroid profile through the years showed that a few infants with values under the cut off still had disease. This has ensured more rapid evaluation and that all forms of the disorder are detected early.

With respect to overall program operation, few significant changes occurred in SFY13 compared to SFY12. Filter paper blood samples continued to be collected at local hospitals and sent to the Public Health Laboratory (PHL) at the Arkansas Department of Health (ADH). Screening laboratory methods remained very similar, as did follow-up procedures carried out by nurses in the Child and Adolescent Health Section. Partnerships among ADH, the University of Arkansas for Medical Sciences (Department of Pediatrics), and Arkansas Children's Hospital (ACH) remained very strong and vital to programmatic success. In particular, Dr. Bradley Schaefer, Director of Genetics at ACH/UAMS, has served as interim NBS Medical Director for ADH in the absence of a pediatrician for the Section starting January, 2013.

Follow-up protocols used by ADH Newborn Screening (NBS) nurses were reviewed and updated with minor revisions that reflected programmatic changes and improvements in clarity. Notification letters and interpretation sheets sent to physicians, along with fact sheets intended for parents, were all reviewed and required very few minor revisions since they had been reviewed and revised with UAMS Department of Pediatrics medical staff in 2009.

Program improvement strategies continued to focus primarily in on improving the pre-analytic phase of the program (sample collection and delivery), since those were most critical for timely diagnosis.

Specimen rejection rates have dropped significantly since hiring a Nurse Educator in 2008; from 1.2% of samples in 2007 to 0.1% in 2011. In 2012, the rate went up to 0.2% (79/39,304 samples). In 2013 the specimen rejection rate went up further to 0.3% (126/39,186 samples); the majority being due to insufficient blood or sample was too old to test. 95 of these tests were repeated.

Sample delivery times continued to be monitored and improved from 9.7% in SFY2012 to 12% in SFY13 arriving at the PHL within the recommended 48 hour time frame from collection. The nurse educator and NBS lab supervisor continued to work with hospitals in improving sample collection and delivery through site visits and phone contacts. More than half of the rural hospital continued to use the ADH local health unit daily courier as a way to ensure timely sample pick-up and delivery.

The NBS Nurse Educator continued to make annual site visits to the 42 birthing hospitals across the state for technical assistance, training, and collaboration. Additional tools and resources were provided to the hospitals, including NBS training DVDs, posters demonstrating correct sample collection, and a list of recommended activities to improve specimen collection, and delivery.

The program was awarded a performance improvement project grant from the ADH Office of Performance Improvement Management (OPIM) through CDC funds aimed at improving health departments' capacity for performance/quality improvement in preparation for the Public Health Accreditation process. The NBS project focused on improving outreach, training, and technical assistance to birthing hospitals in order to improve screening competencies of Arkansas nursery personnel. The first phase of the project was implemented in 2012 and included an assessment of training needs through stakeholder interviews and a survey of nursery managers. The second phase was implemented in 2013 and included developing an education program founded on the results of the needs assessment. Outcome measures include sample delivery time and sample rejection rates; along with reported satisfaction of the education program.

The education program included developing a state-specific video that will be available on the ADH NBS website and a DVD to be delivered to every birthing hospital at site visits. A tool-kit with resources and information was also being developed in SFY13 and will be provided to every birthing hospital at site visits and on the ADH website; all of which will be provided as an online (A-TRAIN) nursing education package offering continuing education units.

Also in 2013, our NBS Advisory Committee made recommendations to improve sample delivery time in addition to the nursery education performance improvement project and courier. These were implemented and included:

- Quarterly newsletters to hospitals and stakeholders
- Quarterly certificates of improvement to the hospital with the most improved sample delivery time, signed by the ADH director and ADH NBS lab and nursing supervisors.
- Email blasts to nursery and lab managers prior to every holiday reminding them to use same day or overnight delivery services to transport samples to the PHL.
- Presentations about newborn screening at pediatric workshops.

Outcomes (sample delivery times and rejection rates) will continue to be monitored quarterly.

The Arkansas Genetic Health Committee met three times during the past year. The Newborn Screening Subcommittee of the Arkansas Genetic Health Committee met quarterly with discussions about additional future test inclusion, e.g. Severe Combined Immunodeficiency (SCID) and Critical Congenital Heart Disease (CCHD), and ideas for improvement in newborn screening protocols/practices, including the development of the nursery education program.

Children diagnosed with a condition identified through newborn screening continued to be followed annually until 5 years of age to determine health and developmental outcomes. Also, through a grant from the state Medicaid office, Dr. Bradley Schaefer and other staff within the University of Arkansas for Medical Sciences Department of Pediatrics continued work on a database for long-term follow-up of cases detected through newborn screening. This project will include long-term data on cases never collected before in Arkansas, or in virtually any other state. ADH will collaborate with the project through requesting consent from parents of known cases to participate in project activities. Plans are to follow children with NBS-detected disorders up to 21 years of age.

The NBS nurses at the Arkansas Department of Health continued to work daily with the NBS Coordinator at Arkansas Children's Hospital to coordinate follow-up care for babies with abnormal newborn screening results and those requiring second tier testing.

List of Disorders Screened for in SFY13

The following list encompasses all disorders screened for in SFY13. Clinical features of these disorders were described in some detail in the SFY09 report.

Congenital hypothyroidism (CH)
Galactosemia (GALT)
Sickle cell disease (SS)
Sickle – hemoglobin C disease (S/C)
Sickle–beta–thalassemia (S/ β Th)
Biotinidase deficiency (BIO)
Congenital adrenal hyperplasia (CAH)
Cystic fibrosis (CF)

Amino Acid Disorders (AA)

Phenylketonuria (PKU)
Maple syrup urine disease (MSUD)
Homocystinuria (HCY)
Citrullinemia (CIT)
Argininosuccinic acidemia (ASA)
Tyrosinemia, Type 1 (TYR-1)

Fatty Acid Oxidation Defects (FAO)

Medium chain acyl CoA dehydrogenase deficiency (MCAD)
Very long chain acyl CoA dehydrogenase deficiency (VLCAD)
Long chain hydroxyacyl CoA dehydrogenase deficiency (LCHAD)
Trifunctional protein deficiency (TFP)
Carnitine uptake deficiency (CUD)

Organic Acidemias (OA)

Glutaric acidemia, Type I (GA I)
3-hydroxy-3-methyl glutaric acidemia (HMG)
3-methylcrotonyl CoA carboxylase deficiency (3MCC)
Beta-ketothiolase deficiency (BKT)
Multiple carboxylase deficiency (MCD)
Propionic acidemia (PROP)
Methylmalonic acidemia due to mutase deficiency (MUT)
Methylmalonic acidemia due to cobalamin A,B defect (Cbl A,B)
Isovaleric acidemia (IVA)

Laboratory Screening Methods

There were no changes in screening methodology during SFY13. A summary of screening strategies and methods employed for each disorder/group of disorders follows:

Congenital hypothyroidism – TSH as primary screen; thyroxine (total T4) run on top 10% of the day's run (both by fluorometric immunoassay)

Sickle hemoglobin diseases – High phase liquid chromatography; isoelectric focusing as a secondary method

Galactosemia – Quantitative (fluorometric) measurement of galactose-1-phosphate uridyl transferase enzyme activity

Cystic Fibrosis – First tier: quantitative measurement of immunoreactive trypsinogen (IRT); second tier: top 2% of week's IRT values received CF gene mutation analysis

Congenital Adrenal Hyperplasia – First tier: quantitative measurement of 17-hydroxyprogesterone (fluorometric immunoassay); second tier: specimens exceeding cutoff received steroid profile testing (liquid chromatography-tandem mass spectrometry).

Biotinidase deficiency – Quantitative enzyme assay

Amino Acid Disorders (including PKU) – tandem mass spectrometry

Fatty Acid Oxidation Defects – tandem mass spectrometry

Organic Acidemias – tandem mass spectrometry

Results

Completeness of screening. A data matching program to link birth records with newborn screening results was continued through the ADH Center for Health Statistics. For the reporting year, 36,869 births occurred within Arkansas's borders, of which a matching newborn screening record was found for 36,216. These figures imply that 98.22% of infants born in the state had a newborn screening specimen submitted.

Unsatisfactory specimens. A total of 126 newborn screening specimens were rejected by the ADH Public Health laboratory in SFY13 because they were unsuitable for testing. This total represents 0.3% of all specimens submitted (both initial and repeat). (Chart 3).

Results by disorder/category. A summary of screening results for each disorder or category of disorder follows. These results pertain to specimens received in the ADH PHL between July 1, 2012, and June 30, 2013.

Note: All of the following “% of total” figures are based on a total of 36,216 initial screens.

Congenital Hypothyroidism

Initial positives (% of total)	783 (2.16)
Lost to follow-up, before confirmatory/repeat test	0
Confirmed cases	29
Confirmed cases who received treatment (%)	29 (100)
Confirmed cases lost to follow-up (%)	0 (0)

Sickle Hemoglobin Diseases

Sickle Cell Anemia, Sickle-β⁰-Thalassemia (FS results)

Initial positives (% of total)	15 (0.4)
Confirmatory test normal	0
Lost to follow-up, before confirmatory test	0
Confirmed cases	
Confirmed cases who received treatment (%)	15 (100)
Confirmed cases lost to follow-up (%)	0 (0)

Sickle-Hemoglobin C Disease (FSC, FCS results)

Initial positives (% of total)	5 (0.01)
Confirmatory test normal	0
Lost to follow-up, before confirmatory test	0
Confirmed cases	5
Confirmed cases who received treatment (%)	5 (100)
Confirmed cases lost to follow-up (%)	0 (0)

Sickle-β⁺-thalassemia (FSA results)

Initial positives (% of total)	3 (0.008)
Confirmatory test normal	0
Lost to follow-up, before confirmatory test	0
Confirmed cases	3
Confirmed cases who received treatment (%)	2 (100)

Confirmed cases lost to follow-up (%) 0 (0)

Galactosemia

Initial positives (% of total) 7 (0.019)

Lost to follow-up, before confirmatory test 0

Confirmed cases – classic galactosemia 1

Confirmed cases – variant galactosemia 4

Confirmed cases who received treatment (%) 5 (100)

Confirmed cases lost to follow-up (%) 0 (0)

Cystic Fibrosis

Initial positives (IRT) - first tier screening (% of total) 495 (1.36)

Positive mutation analyses - second tier screening (% of total) 55 (0.15)

One mutation detected 39

Two mutations detected 16

Confirmatory (sweat) performed 34

Lost to follow-up, before confirmatory test 0

Sweat test still pending 0

Confirmed cases 5

Confirmed cases who received treatment (%) 5 (100)

Confirmed cases lost to follow-up (%) 0 (0)

Congenital Adrenal Hyperplasia

Initial positives - first tier screening (% of total) 503(1.38)

Positive steroid profiles (% of total) 21 (0.06)

Lost to follow-up, before confirmatory test 0

Confirmed cases 2

Confirmed cases who received treatment (%) 2 (100)

Confirmed cases lost to follow-up (%) 0 (0)

Biotinidase Deficiency

Initial positives (% of total) 23 (0.06)

Lost to follow-up, before confirmatory test 0

Confirmed cases** 8

Confirmed cases who received treatment (%)	8 (100)
Confirmed cases lost to follow-up (%)	0 (0)

** 2 partial, 6 deficiency

Tandem Mass Spectrometry (MSMS) Disorders

Amino Acid Disorders

Initial positives* (% of total)	370 (1.0)
Lost to follow-up before repeat/confirmatory test	0
Parent refused repeat/confirmatory test	0
Expired before repeat/confirmatory test **	12
Confirmed cases***	6
Confirmed cases who received treatment (%)	6 (100)
Confirmed cases lost to follow-up (%)	0 (0)

*Specimens displaying more than one amino acid abnormality were counted as a single positive result.

** Sick, premature infants on TPN

*** 3 cases of phenylketonuria, 3 cases of citrullinemia

Fatty Acid Oxidation Defects

Initial positives* (% of total)	90 (0.2)
Lost to follow-up, before repeat/confirmatory test	0
Parent refused repeat/confirmatory test	0
Expired before repeat/confirmatory test**	1
Confirmed cases***	2
Confirmed cases who received treatment (%)	2 (100)
Confirmed cases lost to follow-up (%)	0 (0)

* Specimens displaying more than one screening abnormality suggestive of fatty acid oxidation defect were counted as a single positive result.

** Sick, premature infants on TPN

***2 cases of Medium chain Acyl-CoA Dehydrogenase Deficiency

Organic Acidemias

Initial positives* (% of total)	300 (0.8)
Lost to follow-up, before repeat/confirmatory test	0

Parent refused repeat/confirmatory test	1	
Expired before repeat/confirmatory test**		1
Confirmed cases***	1	
Confirmed cases who received treatment (%)	1 (100)	
Confirmed cases lost to follow-up (%)	0 (0)	

* Specimens displaying more than one screening abnormality suggestive of organic acidemia were counted as a single positive result

** Sick, premature infants on TPN

***3-methylcrotonyl CoA carboxylase deficiency (3MCC)

Total number of disorders detected:

Congenital Hypothyroidism	29
Sickle Hemoglobin Disorders	22
Galactosemia	5 (1 Classic, 4 Variant)
Cystic Fibrosis	5
Congenital Adrenal Hyperplasia	2
Biotinidase Deficiency	8 (2 partial, 6 def.)
Amino Acid Disorders	6 (3 PKU, 3 CIT)
Fatty Acid Oxidation Defects	2 (2 MCAD)
Organic Acidemias	1 (3-MCC)
Total	80

Discussion of Results/Trends

As in SFY12, numbers of confirmed cases found were approximately as expected for the various disorders screened for. Overall, the program successfully detected 80 infants with significant conditions. All children with confirmed disorders received timely initial treatment. No infants were lost to follow-up following initial positive results. One parents refused a repeat newborn screen for borderline results (OA). These phenomenally low levels of lost-to-follow-up reflect the extreme conscientiousness and persistence on the part of the newborn screening follow-up nurses.

Future Plans

The program will continue to make adjustments as needed to assure the proper balance between sensitivity (detection of all cases of disease) and specificity (minimization of false positive results). Quality improvements of interest will focus on improved collection technique, promptness of specimen submission, analysis, and follow-up. The program will also cooperate with efforts underway through the UAMS Department of Pediatrics to develop a system of long-term follow-up for infants diagnosed through the newborn screening process.

In May 2010, the Secretary of the US Department of Health and Human Services (HHS) formally endorsed a recommendation by the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children to add screening for Severe Combined Immunodeficiency (SCID) to the "core panel" of conditions for which universal newborn screening is strongly recommended. In 2011, Congenital Critical Heart Disease (CCHD) was also added to the Recommended Uniform Screening Panel. These recommendations will be studied by ADH and others in Arkansas with respect to feasibility of implementation within the next few years. In the 2013 legislative session, a bill mandating CCHD screening was passed (Act 768). A bill also passed (Act 428) that broadened the range of disorders that could be added to the Arkansas newborn screening panel as approved by the Arkansas Board of Health. Language was changed to delete the word "metabolism" so that non-metabolic genetic disorders could be added. This was specifically aimed at adding SCID, but will be useful in adding other disorders without resorting to a disorder-by-disorder change in the law. In FY 13, the Newborn Screening program worked with pediatric specialists from Arkansas Children's Hospital and other agencies to plan for adding these 2 new disorders.

Charts

*See pages 3 & 4 for disorder abbreviations key.

Chart 1. Number of positive results by category of MS/MS-detectable disorder, Arkansas SFY09 - SFY13

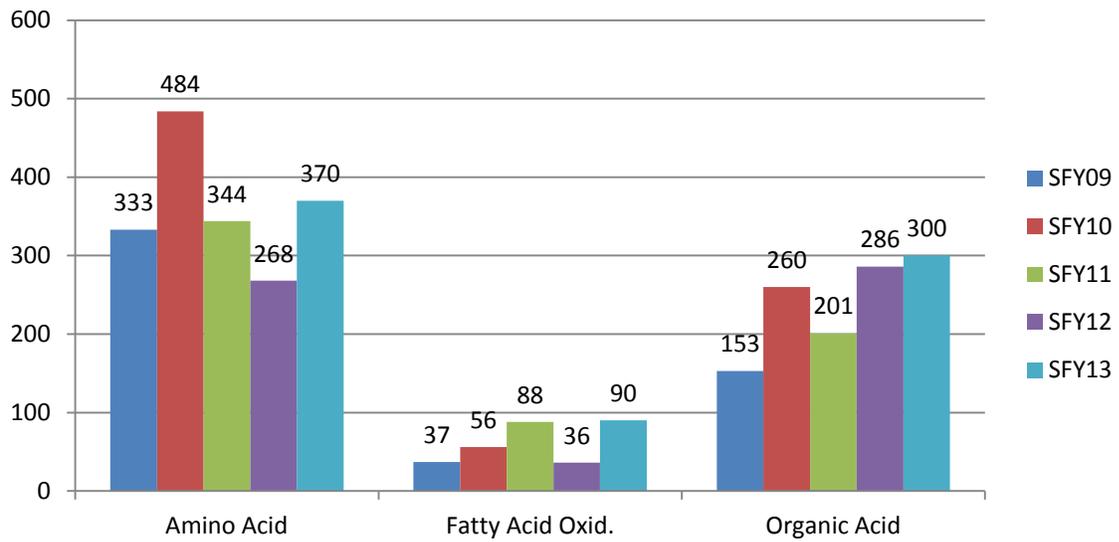


Chart 2. Summary of congenital hypothyroidism newborn screening results Arkansas SFY09 - SFY13

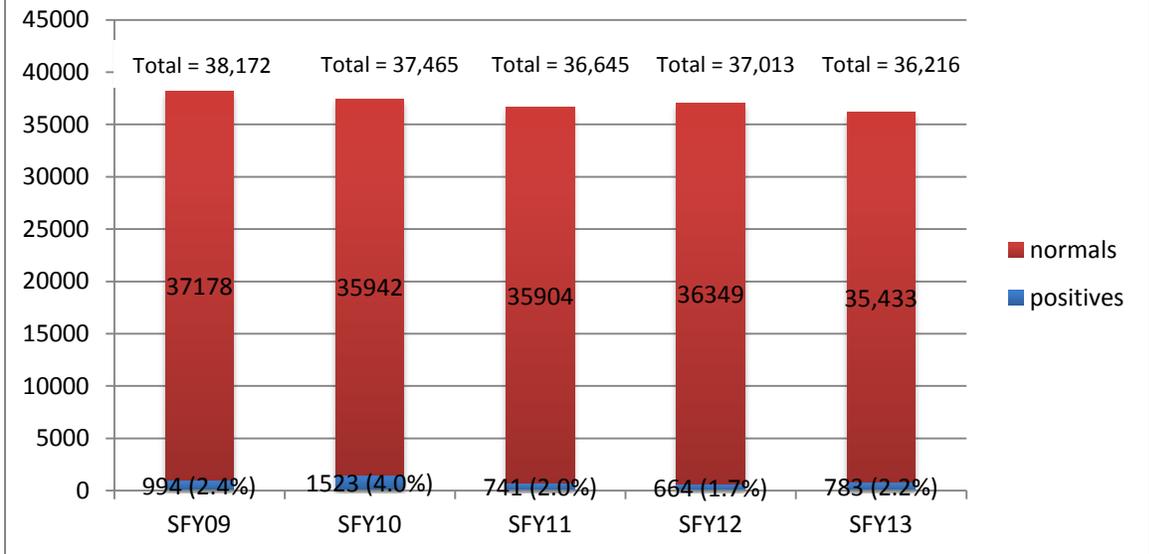
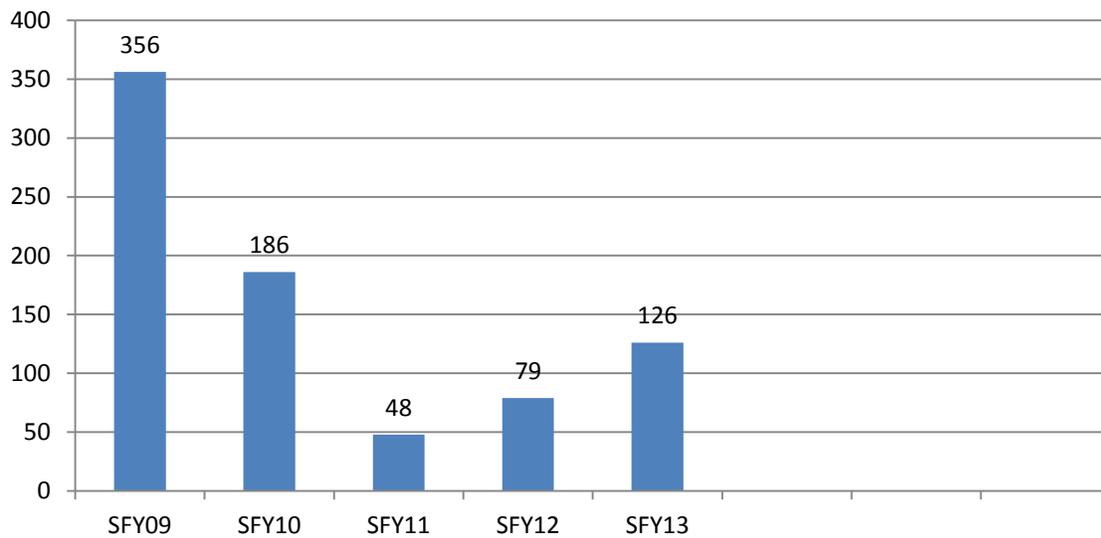


Chart 3. Number of rejected newborn screening specimens SFY09-SFY13



**Chart 4. NBS sample arrival to Public Health Laboratory: days from collection to arrival
SFY09-SFY13
(percent arriving within 2 days)**

