

Newborn Screening in Arkansas SFY12

Report of Results from July 1, 2011 - June 30, 2012

**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

With respect to overall program operation, few significant changes occurred in SFY12 compared to SFY11. 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.

As a dynamic and progressive program, a few notable changes did occur during SFY12. ADH continues to send selected specimens to ACH for "second tier" steroid profile testing. The test 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. As experience with this methodology unfolded, however, concerns emerged. While the second tier screen as applied probably did detect most cases of salt-wasting CAH, it appeared inadequate to pick up all cases of simple virilizing CAH. Because of these concerns, changes were made to the laboratory's reporting system for the 17-OHP results, with changes in cutoff values for babies above and below 2500 grams. Once implemented in early SFY12, there was less reliance on the second tier steroid profile ratio to exclude disease and more reliance on the 17-OHP newborn screen to help ensure all forms of the disorder are detected. This has been successful in continued early identification of infants with potential CAH. Follow-up protocols for CAH were updated to reflect the changes and there were no problems with implementation.

Other 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.

A program self-assessment was accomplished through the Program Evaluation and Assessment Scheme (PEAS) developed for newborn screening programs by HRSA and the National Newborn Screening and Genetics Resource Center. Results informed the decision 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.

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.

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). Sample delivery times continued to be monitored and only 9.7% arrived 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.

The ADH local health unit courier system had not been used to pick up and deliver newborn screens. In the fall of 2011, we worked with the local health units and hospitals to set up a system where hospitals could drop their samples off at their local health units to be picked up by the ADH daily courier, and be delivered the same day to the PHL at no cost to the hospital. By January of 2012, about half of the hospitals were using the service and we were seeing improvements in sample delivery times. This will continue to be monitored.

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. 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.

Results

- Surveys were sent via Survey Monkey to all 43 hospitals that perform newborn screening in Arkansas. Thirty nursery managers representing 29 hospitals responded to all the questions (67% of hospitals responded to all 12 questions).
- Overall nursery managers thought some type of web-based training would be very helpful or helpful (87%). They prefer email as the best way to get information to them (70%) and most of the written comments included online learning as the easiest and most efficient way to improve our technical assistance and service to them, although they still would like routine site visits, and 70% found site visits very helpful or helpful.
- 80% found the current CLSI (Clinical and Laboratory Standards Institute) NBS blood spot training DVD to be very helpful or helpful, and 87% thought that a state-specific DVD for NBS and Infant Hearing would be very helpful or helpful. 67% said that annual conferences or workshops would be very helpful or helpful.
- Respondents described their learning needs as primarily related to blood spot specimen collection technique. The vast majority (87%) would like to obtain CEUs through NBS education programs. 83% said a standardized newborn screening orientation tool/procedure check list would be helpful or very helpful.

The next phase of the project will be carried out in SFY 2013 to develop an education program founded on the results of the needs assessment.

The NBS parent brochure (provided at every birthing hospital) was completely revised to reflect HRSA and American Academy of Pediatrics recommended parent education topics for NBS. The brochures were also simplified to 5th grade reading level, available in Spanish, and now contain culturally relevant pictures. These parent education topics were also updated on the NBS website. Brochures are mailed annually to each hospital and available for download on our website.

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 development of the nursery education program and parent brochures.

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 SFY12

The following list encompasses all disorders screened for in SFY12. 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 SFY12. 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, 37,545 births occurred within Arkansas's borders, of which a matching newborn screening record was found for 37,013. These figures imply that 98.58% of infants born in the state had a newborn screening specimen submitted.

Unsatisfactory specimens. A total of 79 newborn screening specimens were rejected by the ADH Public Health laboratory in SFY12 because they were unsuitable for testing. This total represents 0.2% 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, 2011, and June 30, 2012.

Note: All of the following “% of total” figures are based on a total of 37,013 initial screens.

Congenital Hypothyroidism

Initial positives (% of total)	664 (1.7)
Lost to follow-up, before confirmatory/repeat test	0
Confirmed cases	28
Confirmed cases who received treatment (%)	28 (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 (0.04)
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)	6 (0.02)
Confirmatory test normal	0

Lost to follow-up, before confirmatory test	0
Confirmed cases	6
Confirmed cases who received treatment (%)	5 (83.0)
Confirmed cases lost to follow-up (%)	1 (17.0)

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 (%)	3 (100)
Confirmed cases lost to follow-up (%)	0 (0)

Galactosemia

Initial positives (% of total)	12 (0.032)
Lost to follow-up, before confirmatory test	0
Confirmed cases – classic galactosemia	2
Confirmed cases – variant galactosemia	4
Confirmed cases who received treatment (%)	6 (100)
Confirmed cases lost to follow-up (%)	0 (0)

Cystic Fibrosis

Initial positives (IRT) - first tier screening (% of total)	717 (2.0)
Positive mutation analyses - second tier screening (% of total)	59 (0.16)
One mutation detected	45
Two mutations detected	14
Confirmatory (sweat) performed	54
Lost to follow-up, before confirmatory test	0
Sweat test still pending	0
Confirmed cases	6
Confirmed cases who received treatment (%)	6 (100)
Confirmed cases lost to follow-up (%)	0 (0)

Congenital Adrenal Hyperplasia

Initial positives - first tier screening (% of total)	434 (1.2)
Positive steroid profiles (% of total)	4 (0.01)
Lost to follow-up, before confirmatory test	0
Confirmed cases	1
Confirmed cases who received treatment (%)	1 (100)
Confirmed cases lost to follow-up (%)	0 (0)

Biotinidase Deficiency

Initial positives (% of total)	33 (0.09)
Lost to follow-up, before confirmatory test	0
Confirmed cases**	7
Confirmed cases who received treatment (%)	7 (100)
Confirmed cases lost to follow-up (%)	0 (0)

** 5 partial, 2 deficiency

Tandem Mass Spectrometry (MSMS) Disorders

Amino Acid Disorders

Initial positives* (% of total)	268 (0.7)
Lost to follow-up before repeat/confirmatory test	0
Parent refused repeat/confirmatory test	1
Expired before repeat/confirmatory test**	12
Confirmed cases***	8
Confirmed cases who received treatment (%)	8 (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, 1 mild hyperphenylalaninemia, 3 cases of citrullinemia, 1 case of argininosuccinic acidemia

Fatty Acid Oxidation Defects

Initial positives* (% of total)	36 (0.1)
Lost to follow-up, before repeat/confirmatory test	0

Confirmed cases**	3
Confirmed cases who received treatment (%)	3 (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

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

Organic Acidemias

Initial positives* (% of total)	286 (0.8)
Lost to follow-up, before repeat/confirmatory test	0
Parent refused repeat/confirmatory test	5
Confirmatory tests not all completed	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

**Glutaric acidemia

Total number of disorders detected:

Congenital Hypothyroidism	28
Sickle Hemoglobin Disorders	24
Galactosemia	6 (2 Classic, 4 Variant)
Cystic Fibrosis	6
Congenital Adrenal Hyperplasia	1
Biotinidase Deficiency	7 (5 partial, 2 def.)
Amino Acid Disorders	8 (3 PKU, 1 hyperphe, 3 CIT, 1 ASA)
Fatty Acid Oxidation Defects	3 (3 MCAD)
Organic Acidemias	1 (GA 1)
Total	84

Discussion of Results/Trends

As in SFY11, numbers of confirmed cases found were approximately as expected for the various disorders screened for. Overall, the program successfully detected 84 infants with significant conditions. All children with confirmed disorders received timely initial treatment save for one with Sickle Hemoglobin C Disease (FSC) who moved out of state. This baby was seen by a physician in Arkansas, missed the Sickle Cell clinic appointment, not started on Pen VK, and recommended to follow-up in the new state. The family could not be located after the move. No infants were lost to follow-up following initial positive results. 6 parents refused a repeat newborn screen for borderline results (1 AA and 5 OA); and one infant did not receive all the recommended confirmatory tests and the parent refused further testing. 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. It is likely that both these recommended screenings will be proposed in bills in the 2013 Arkansas legislative session.

Charts

*See page 4 for disorder abbreviations key.

Chart 1. Number of positive results by category of MS/MS-detectable disorder, Arkansas SFY09 - SFY12

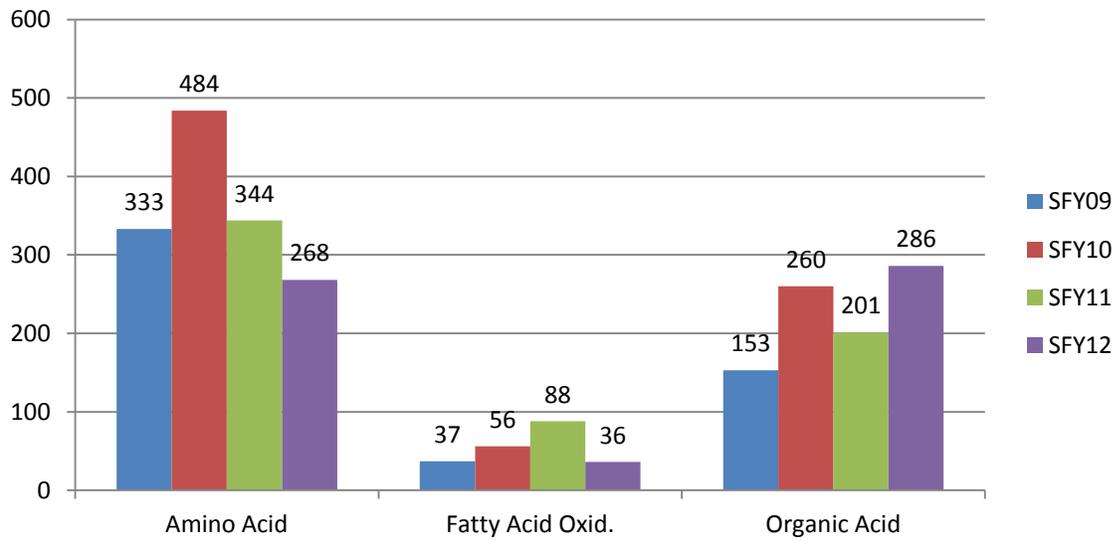


Chart 2. Summary of congenital hypothyroidism newborn screening results Arkansas SFY09 - SFY12

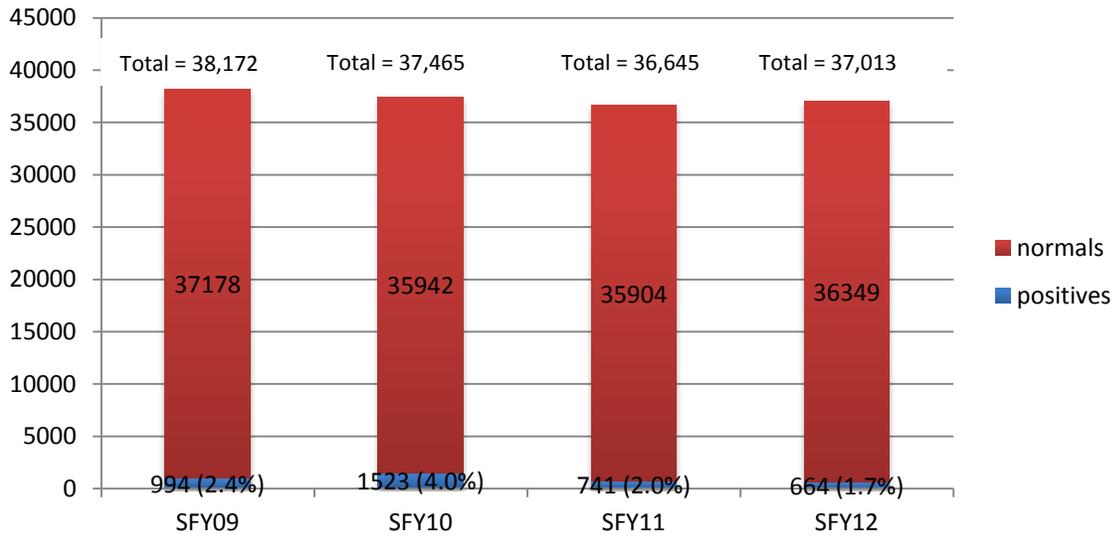
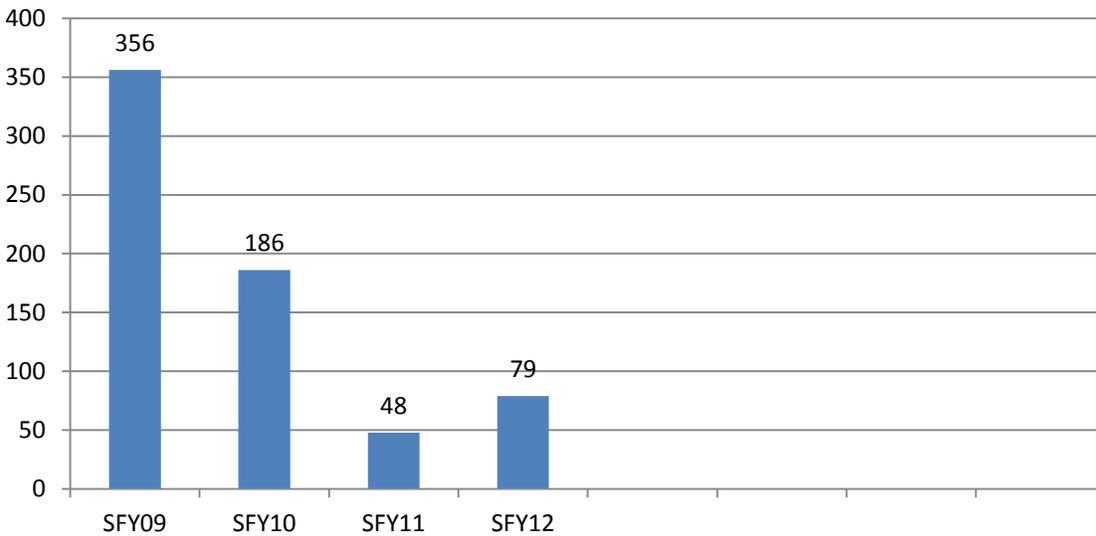


Chart 3. Number of rejected newborn screening specimens SFY09-SFY12



**Chart 4. NBS sample arrival to Public Health Laboratory: days from collection to arrival
SFY09-SFY12
(percent arriving within 2 days)**

