

Newborn Screening in Arkansas SFY11

Report of Results from July 1, 2010 - June 30, 2011

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

October, 2012

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 SFY11 compared to SFY10. Filter paper blood samples continued to be collected at local hospitals and sent to the Newborn Screening Laboratory 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 SFY11. 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 being planned 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 will be 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.

The follow-up protocols used by ADH Newborn Screening 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.

Newborn Screening Annual Report SFY11

The Newborn Screening Nurse Educator continued to make annual site visits to the 42 birthing hospitals across the state for technical assistance, training, and collaboration. This year additional tools and resources were provided to the hospitals, including newborn screening training DVDs, posters, 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 rejected in 2007 to 0.1% in 2011.

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.

Updates of parent resources were accomplished through revisions to the Newborn Screening website. New links were added and the site was made more user-friendly and culturally relevant.

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 Newborn Screening Program nurses at the Arkansas Department of Health continued to work daily with the Newborn Screening 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 SFY11

The following list encompasses all disorders screened for in SFY11. 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/βTh)

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

The only significant change in screening methodology during SFY11 involved the assay for biotinidase deficiency. In July 2010, the method changed from qualitative colorimetric analysis to a quantitative assay developed by Perkin Elmer. In addition to the advantages afforded by a quantitative analysis, the newer method yielded results much faster than the old (4 hours vs. 24 hours).

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, 37,188 births occurred within Arkansas’s borders, of which a matching newborn screening record was found for 36,645. These figures imply that 98.5% of infants born in the state had a newborn screening specimen submitted.

Unsatisfactory specimens. A total of 48 newborn screening specimens were rejected by the ADH Public Health laboratory in SFY11 because they were unsuitable for testing. This total represents 0.1% of all specimens submitted (both initial and repeat). (Chart 4).

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 Public Health Laboratory between July 1, 2010, and June 30, 2011.

Note: All of the following “% of total” figures are based on a total of 36,645 initial screens.

Congenital Hypothyroidism

Initial positives (% of total)	741 (2.0)
Confirmatory/repeat test normal	714
Lost to follow-up, before confirmatory/repeat test	2
Parental refusal/non-compliance	0
Confirmatory/repeat test pending	2
Confirmed cases	23
Confirmed cases who received treatment (%)	23 (100)
Confirmed cases lost to follow-up (%)	0 (0)

Sickle Hemoglobin Diseases

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

Initial positives (% of total)	20 (0.05)
Confirmatory test normal	0
Lost to follow-up, before confirmatory test	0
Confirmed cases	
Confirmed cases who received treatment (%)	20 (100)
Confirmed cases lost to follow-up (%)	0 (0)

Sickle-Hemoglobin C Disease (FSC, FCS results)

Initial positives (% of total)	10 (0.03)
Confirmatory test normal	0
Lost to follow-up, before confirmatory test	0
Confirmed cases	10
Confirmed cases who received treatment (%)	10 (100)
Confirmed cases lost to follow-up (%)	0 (0)

Sickle-β⁺-thalassemia (FSA results)

Initial positives (% of total)	1 (0.003)
Confirmatory test normal	0
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)

Galactosemia

Initial positives (% of total)	19 (0.05)
Confirmatory test normal	13
Repeat NBS normal	2
Lost to follow-up, before confirmatory test	0
Confirmed cases – classic galactosemia	1
Confirmed cases – variant galactosemia	3
Confirmed cases who received treatment (%)	4 (100)
Confirmed cases lost to follow-up (%)	0 (0)

Cystic Fibrosis

Initial positives - first tier screening (% of total)	713 (1.9)
Positive mutation analyses - second tier screening (% of total)	67 (0.2)
Confirmatory (sweat) performed	67
Confirmatory (sweat) test not indicated	0
Confirmatory (sweat) test normal	62
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)	556 (1.5)
Positive steroid profiles (% of total)	1 (0.003)
Very high 17-OHP notifications	6 (0.02)
Confirmatory test normal	5
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)

Note: the one case detected had notification based on a very high 17-OHP screening result and also had a positive steroid profile.

Biotinidase Deficiency

Initial positives (% of total)	20(0.05)
Confirmatory test normal	15
Lost to follow-up, before confirmatory test	0
Confirmed cases – partial deficiency	5
Confirmed cases – complete deficiency	0
Confirmed cases who received treatment (%)	5 (100)
Confirmed cases lost to follow-up (%)	0 (0)

Tandem Mass Spectrometry (MSMS) Disorders

Amino Acid Disorders

Initial positives* (% of total)	344 (0.9)
Confirmatory/repeat test normal	318
Lost to follow-up, before repeat/confirmatory test	0
Expired prior to repeat/confirmatory test	22
Confirmed cases**	4
Confirmed cases who received treatment (%)	4 (100)
Confirmed cases lost to follow-up (%)	0 (0)

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

** 2 cases of Phenylketonuria, 1 case of hypermethioninemia, 1 mild hyperphenylalaninemia

Fatty Acid Oxidation Defects

Initial positives* (% of total)	88 (0.2)
Confirmatory/repeat test normal	84
Lost to follow-up, before repeat/confirmatory test	0
Expired prior to repeat/confirmatory test	1
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)	201 (0.5)
Confirmatory/repeat test normal	192
Lost to follow-up, before repeat/confirmatory test	1
Parent refusal/noncompliance with confirmatory testing	1
Expired prior to repeat/confirmatory test	7
Confirmed cases**	0
Confirmed cases who received treatment (%)	0 (0)
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

For all MSMS disorders:

Total initial positives	633
Total confirmed cases	7
Confirmatory/repeat test normal	600
Lost to follow-up, before repeat/confirmatory test*	1
Expired before getting repeat test**	24
Parent refusal/noncompliance***	1

* Borderline C3 (organic acidemia) needing repeat sample

** Several infants who expired had abnormalities in multiple MSMS screening categories

*** Abnormal C5OH (organic acidemia) needing confirmatory testing

Total number of disorders detected:

Congenital Hypothyroidism	23
Sickle Hemoglobin Disorders	31
Galactosemia	4 (1 Classic, 3 Variant)
Cystic Fibrosis	5
Congenital Adrenal Hyperplasia	2
Biotinidase Deficiency	5
Amino Acid Disorders	4 (2 PKU, 1 hypermethioninemia, 1 hyperphe)
Fatty Acid Oxidation Defects	3 (3 MCAD)
Organic Acidemias	0
Total	77

Discussion of Results/Trends

As in SFY10, numbers of confirmed cases found were approximately as expected for the various disorders screened for. Overall, the program successfully detected 77 infants with significant conditions. All children with confirmed disorders received timely initial treatment. Only three infants were lost to follow-up prior to confirmatory or repeat testing. One had a borderline C3 (organic acidemia screening) that needed a repeat specimen, and the other two had mildly elevated TSH levels (congenital hypothyroidism screening) (Chart 1). There was also one case of parent refusal of confirmatory testing for abnormal C5OH (organic acidemia screening). These phenomenally low levels of lost-to-follow-up reflect the extreme conscientiousness and persistence on the part of the newborn screening follow-up staff.

In mid-SFY10, cutoff values for analytes used in screening for amino acid (AA) disorders, organic acidemias (OA), and fatty acid oxidation (FAO) disorders were re-evaluated due to rising positive screen rates observed that year. Changes to these cutoffs were implemented in late SFY10. These changes may be responsible for the decreases in positive rates observed in SFY11 for AA and OA disorders (Chart 2). However, the rate of positive screens for FAO disorders increased slightly in SFY11.

The rate of positives for congenital hypothyroidism (CH) screening decreased substantially in SFY 11, from 4.0% in SFY10 to 2.0% in SFY11 (Chart 3). This drop in the percentage of positives is attributable to a change in TSH cutoffs that was implemented in late SFY10. With this change, TSH cutoffs became dependent on age at specimen collection, reflecting normal physiologic changes in TSH levels in the first few days of life.

There were decreases in initial positives and confirmed cases of variant galactosemia in SFY11 compared to SFY10. In SFY10 there were 72 (0.2%) initial positive screens and 13 confirmed variant cases. In SFY11 there were 19 (0.05%) initial positive screens and 3 confirmed variant cases. In each of those years, there was 1 confirmed case of classic galactosemia. The reason for the reduced number of positives in SFY11 is unknown.

The number of rejected specimens in SFY11 (48) was substantially reduced compared to SFY10 (186) (Chart 4). The Newborn Screening Laboratory Manager at ADH made multiple phone calls to submitting hospitals upon receipt of an unsatisfactory specimen to explain the problem with the specimen and how it could be avoided. Meanwhile, the Newborn Screening Outreach Nurse continued to make visits to each birthing hospital in the state to work with nursery and other hospital staff to improve collection technique and submission procedures. Collectively, these efforts appear to have been helpful in reducing the volume of rejected specimens.

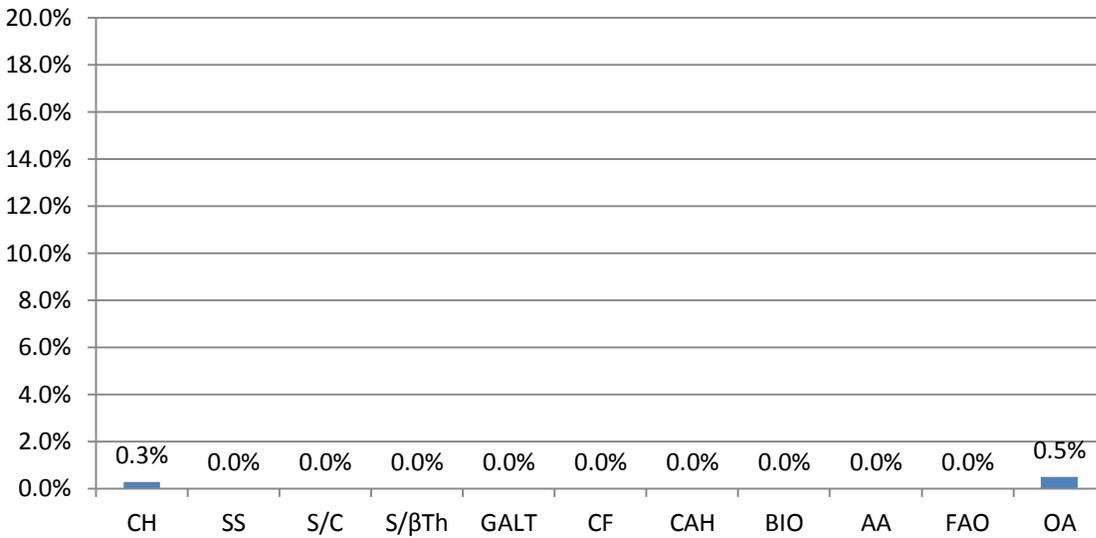
Future Plans

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 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.

Charts

Chart 1. Percentage of positive screens lost to follow-up prior to repeat/confirmatory testing, by NBS disorder,* Arkansas SFY2011



*See page 4 for disorder abbreviations key.

Chart 2. Number of positive results by category of MS/MS-detectable disorder, Arkansas SFY09 - SFY11

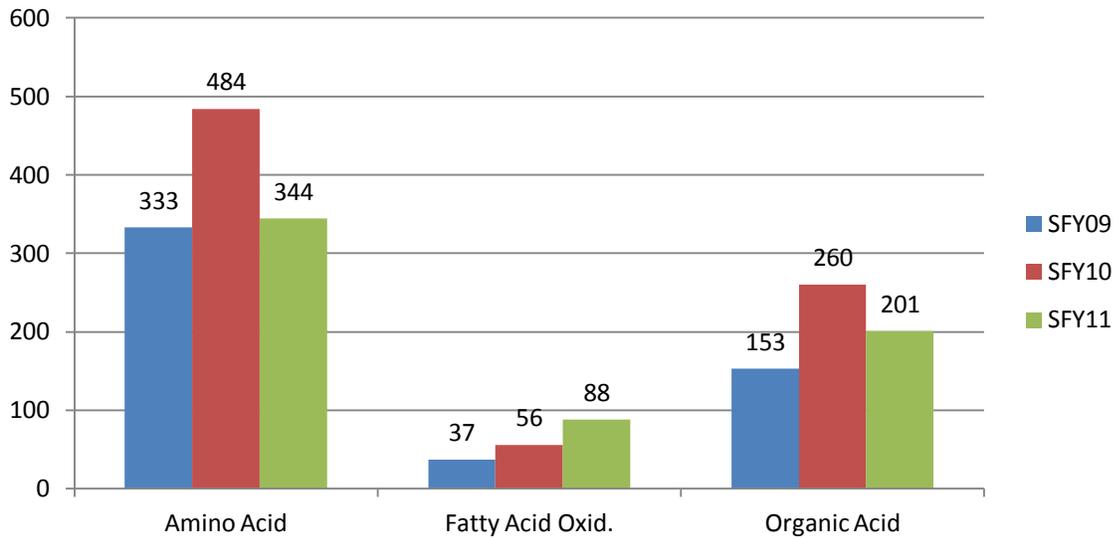
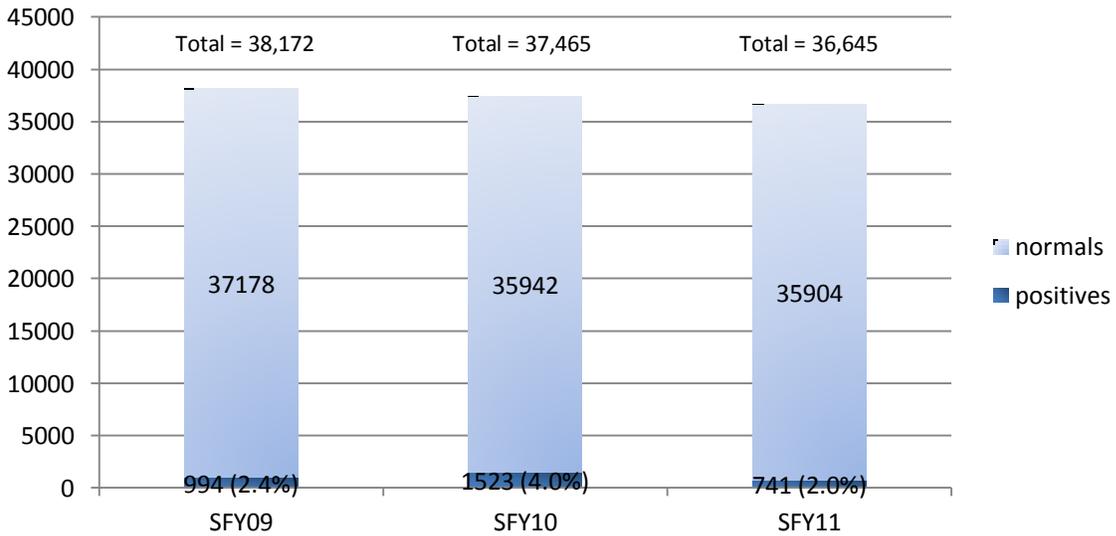


Chart 3. Summary of congenital hypothyroidism newborn screening results, Arkansas SFY09 - SFY11



**Chart 4. Number of rejected newborn screening specimens
SFY09-SFY11**

