

Newborn Screening in Arkansas SFY10

Report of Results from July 1, 2009 - June 30, 2010

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

December 2010

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 last year's report, "Newborn Screening in Arkansas SFY09."

Changes During the Year

With respect to overall program operation, few significant changes occurred in SFY10 compared to SFY09. 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 through the Child and Adolescent Health Section. Partnerships among ADH, the University of Arkansas for Medical Sciences (Department of Pediatrics), and Arkansas Children's Hospital remained very strong and vital to programmatic success.

As a dynamic and progressive program, a few notable changes did occur during SFY10. Cutoff values for the analytes for certain amino acid and fatty acid oxidation defects were adjusted in order to improve specificity, i.e. minimize false positives. Cutoffs were also adjusted for the congenital adrenal hyperplasia analyte in response to changes in the kit supplied by the laboratory vendor. In an effort to reduce false positive results, the cutoffs for congenital hypothyroidism (CH) were made dependent on the age of the baby at time of specimen collection. Additionally, the requested follow-up for "borderline" CH results changed from a repeat filter paper sample to serum TSH and free T4. Finally, notification letters and interpretation sheets sent to physicians, along with fact sheets intended for parents, were all thoroughly reviewed and revised in a joint effort with UAMS Department of Pediatrics medical staff. These revisions went into effect in January 2010. As always, smaller scale revisions to notification materials occurred as needed at other times.

List of Disorders Screened for in SFY10

The following list encompasses all disorders screened for in SFY10. 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

No significant changes in methodology occurred during SFY10. 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 – Colorimetric/qualitative 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, 37,989 births occurred within Arkansas's borders, of which a matching newborn screening record was found for 37,465. These figures imply that 98.6% of infants born in the state had a newborn screening specimen submitted.

Unsatisfactory specimens. A total of 186 newborn screening specimens were rejected by the ADH Public Health laboratory in SFY10 because they were unsuitable for testing. This total represents less than 0.5% of all specimens submitted (both initial and repeat).

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, 2009, and June 30, 2010.

Note: All of the following “% of total” figures are based on a total of 37,465 initial screens.

Congenital Hypothyroidism

Initial positives (% of total)	1,523 (4.0)
Confirmatory/repeat test normal	1,481
Lost to follow-up, before confirmatory/repeat test	10
Parental refusal/non-compliance	2
Confirmatory/repeat test pending	11
Confirmed cases	19
Confirmed cases who received treatment (%)	19 (100)
Confirmed cases lost to follow-up (%)	0 (0)

Sickle Hemoglobin Diseases

Sickle Cell Anemia, Sickle- β^0 -Thalassemia (FS results)

Initial positives (% of total)	14 (0.04)
Confirmatory test normal	0
Lost to follow-up, before confirmatory test	0
Confirmed cases	14
Confirmed cases who received treatment (%)	13 (92.9)
Confirmed cases lost to follow-up (%)	1 (7.1)

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)	2 (0.005)
Confirmatory test normal	0
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)

Galactosemia

Initial positives (% of total)	72 (0.2)
Confirmatory test normal	52
Lost to follow-up, before confirmatory test	0
Physician inaction	2
Parental refusal	4
Confirmed cases – classic galactosemia	1
Confirmed cases – variant galactosemia	13
Confirmed cases who received treatment (%)	14 (100)
Confirmed cases lost to follow-up (%)	0 (0)

Cystic Fibrosis

Initial positives - first tier screening (% of total)	803 (2.1)
Positive mutation analyses - second tier screening (% of total)	73 (0.2)
Confirmatory (sweat) test not indicated	2
Confirmatory (sweat) test normal	56
Lost to follow-up, before confirmatory test	1
Sweat test still pending	2
Confirmed cases	12
Confirmed cases who received treatment (%)	12 (100)
Confirmed cases lost to follow-up (%)	0 (0)

Congenital Adrenal Hyperplasia

Initial positives - first tier screening (% of total)	583 (1.6)
Positive steroid profiles - second tier testing (% of total)	2(0.005)
Confirmatory test normal	0
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)	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)

Amino Acid Disorders

Initial positives* (% of total)	484 (1.3)
Confirmatory/repeat test normal	475
Lost to follow-up, before confirmatory test	7
Confirmed cases**	2
Confirmed cases who received treatment (%)	2 (100)
Confirmed cases lost to follow-up (%)	0 (0)

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

**1 case of Phenylketonuria, 1 case of Citrullinemia

Fatty Acid Oxidation Defects

Initial positives* (% of total)	56 (0.15)
Confirmatory/repeat test normal	53
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)

* 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)	260 (0.7)
Confirmatory/repeat test normal	250
Lost to follow-up, before confirmatory test	5
Parental refusal	4
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

** One case of Isovaleric Acidemia

Discussion of Results/Trends

As in SFY09, numbers of confirmed cases found were approximately as expected for the various disorders screened for. Overall, the program successfully detected 75 infants with significant conditions, including the first case of an organic acidemia since expanded screening began in July 2008. Save for one infant with sickle cell disease (who moved out of state and could not be located), all children with confirmed disorders received initial treatment. Likewise, numbers and proportions of infants with positive screens who were lost to follow-up prior to confirmatory testing were very small for all categories of conditions screened (Chart 1).

The rate of positive screens for some disorders increased somewhat during SFY10 as compared to SFY09. In particular, positive results for tandem mass spectrometry (MS/MS)-detectable disorders (amino acidopathies, fatty acid oxidation defects, organic acidemias) rose about 50% overall (Chart 2). A marked rise in MS/MS positive results first noted in mid-SFY09, especially for amino acids, persisted through the first part of SFY10, after which a reduction was noted (Chart 3). Changes in cutoff values implemented in mid-SFY10 aimed at curtailing false positives may have helped slow the trend. Still, continued close monitoring of these results is required to assess the need for further adjustments.

The rate of positives for congenital hypothyroidism (CH) screening also increased, from 2.6% in SFY09 to 4.0% in SFY10 (Chart 4). A change to cutoffs that are dependent on age at specimen collection was implemented in late SFY10. Based on early data from SFY11, this change should result in a marked reduction in false positives for CH screening.

The number of rejected specimens in SFY10 (186) was substantially reduced compared to SFY09 (356; Chart 5). 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.

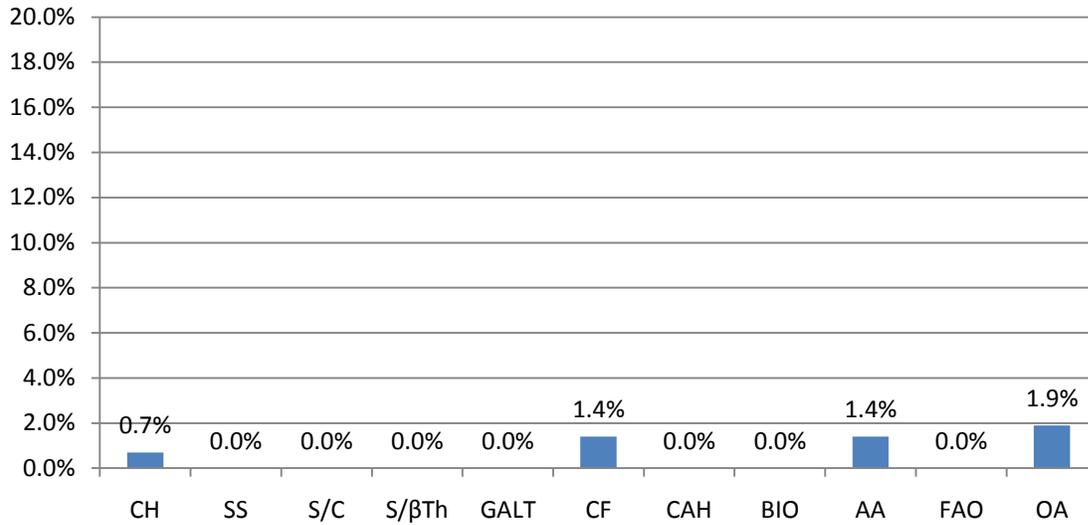
Future Plans

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 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. This recommendation 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 confirmatory testing, by NBS disorder,* Arkansas SFY2010



*See page 2 for disorder abbreviations key.

Chart 2. Number of positive results by category of MS/MS-detectable disorder, Arkansas SFY09 and SFY10

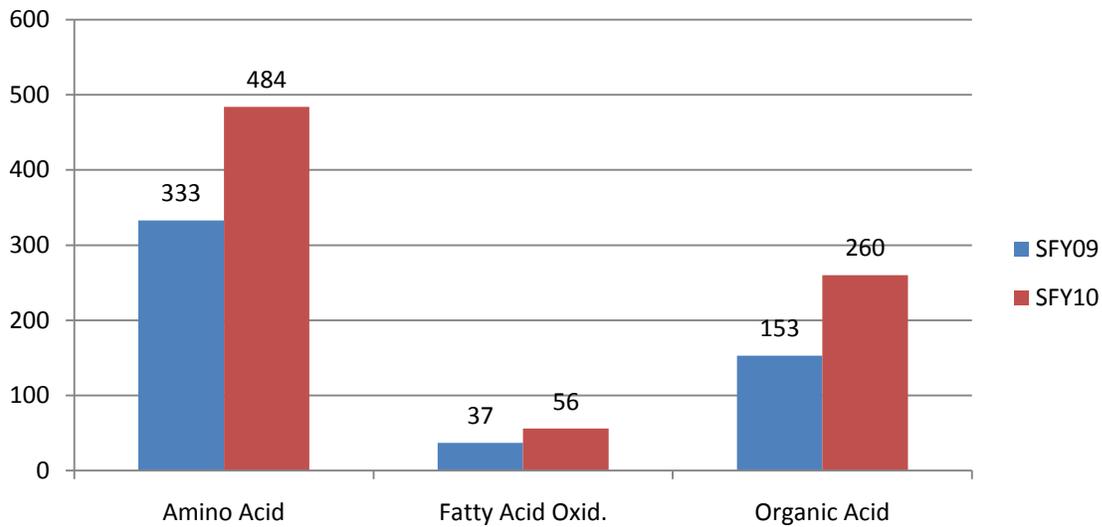


Chart 3. Number of positive results for amino acid disorders by quarter, Arkansas SFY09 - SFY10

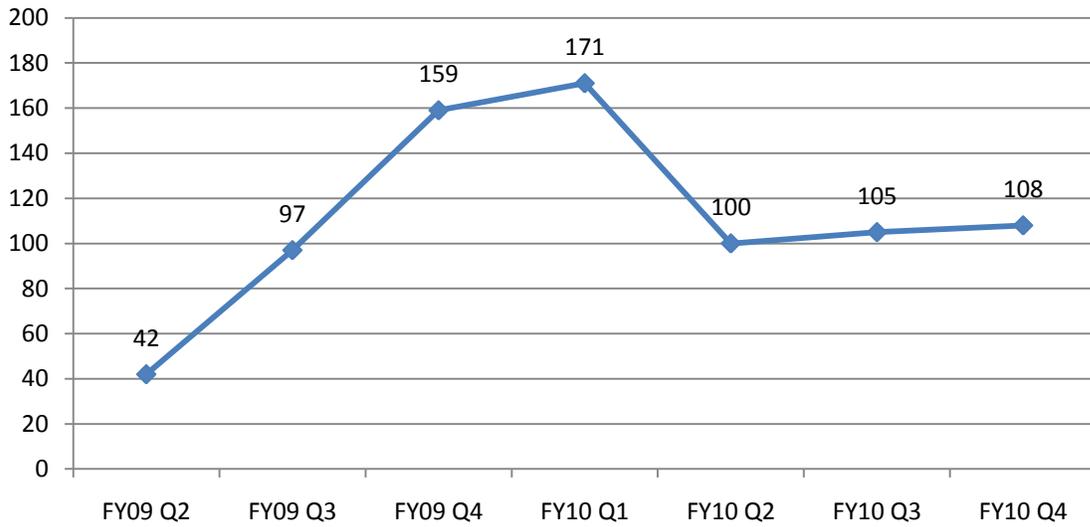


Chart 4. Summary of congenital hypothyroidism newborn screening results, Arkansas SFY09 and SFY10

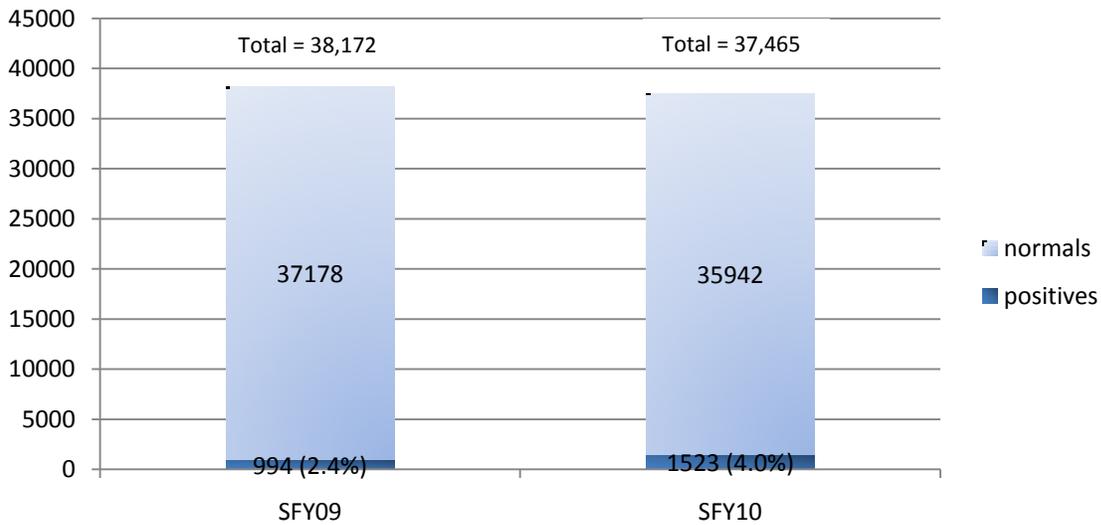


Chart 5. Number of rejected newborn screening specimens by quarter, Arkansas SFY09-SFY10

