Iowa Newborn Screening Follow Up Program

Annual Report
January 1, 2011 through December 31, 2011

Iowa Newborn Screening Program Report for Calendar Year 2011
Short Term and Long Term Follow Up Report

The following report describes the purpose, processes and activities of the short term and long term follow up program component of the Iowa Newborn Screening Program. Definitions of terms used in this report can be found in Appendix A. Program staff members are willing to answer any questions the reader might have. Contact information is provided at the end of the report.

What is the purpose of newborn screening?

The National Institute of Child Health and Human Development defines the purpose of newborn screening as this: "The intent of newborn screening is to detect potentially fatal or disabling conditions in newborns. Identifying infants early on provides a window of opportunity for treatment, often before the infant displays any signs or symptoms of a disease or condition. Such early detection and treatment can have a profound impact on the severity of the condition in the child. The consequences of many of the screened for conditions, if left undiagnosed and untreated, can be dire, often causing irreversible neurological damage; intellectual, developmental, and physical disabilities; and even death."

The Iowa Newborn Screening Program pamphlet states, "All parents want a healthy baby. Screening helps assure that your baby will be as healthy as possible. Babies can look very healthy at birth and still have one of these disorders. If a condition is not found early, poor physical and mental development, and even death, may occur. To make sure these disorders are found quickly, Iowa law requires that all babies be screened. If found early, most babies with these conditions can be treated and live health lives."

The *Saving Babies Through Screening Foundation* slogan puts it even more simply, "Newborn Screening Saves Lives – One Foot at a Time".

It is important to remember that newborn screening is exactly that – a *screening* test. *It is not a diagnostic test and should not be considered the final step in testing a baby for any disorder.*

An Overview of the Laboratory and Clinical Process of Newborn Screening in Iowa

Local Hospital - At 24-48 hours of age, a few drops of blood are taken from a baby's heel to perform the newborn screening test. These drops are placed on a card that contains information about the baby, the mother, and the blood sample. This is called the dried blood spot card.

Courier - The card is picked up at the local hospital by a courier service and is driven to our newborn screening laboratory in Ankeny. Cards from throughout the state arrive in the laboratory around 9:00 pm seven days a week.

Newborn Screening Laboratory - Once the card arrives in the lab, quality checks are performed and the data from the card is entered into a database. Laboratory staff begin the testing process within one hour of receiving the card. A laboratory staff member calls and emails the short term follow up staff with any abnormal endocrine or metabolic results so that immediate (and sometimes life-saving) action can occur. These results, along with testing results of other screened disorders, are entered into a database.

Short Term Follow Up/Medical Consultant – Short term follow up staff are informed of abnormal testing results. This is called a "presumptive positive" or a "borderline" result. Presumptive positive or borderline means that the screening test for the disorder is abnormal and requires further action. It does not always mean that the baby has that disorder. That is why the short term follow up component of the newborn screening program is crucial/ Follow up staff help local care providers through the process of determining if a screening result is real (ie a "true positive") or a "false positive" (baby is not affected with a disorder/disease). Follow up staff inform the local hospital (if baby is still an inpatient) or local provider (if baby has gone home) of the abnormal results. Recommendations are provided to the local entity verbally and then followed by a fax and/or email with the same information as was given verbally. Education about the disorder that screened positive is also provided. A medical consultant (a MD with particular expertise in a certain area) will also review abnormal results and assist staff and local providers when necessary. Sometimes it is recommended to repeat the newborn screen and/or to get additional specialized testing. The follow up staff review the tests recommended with local providers (and sometimes local laboratories too) and follow up to make sure that these tests are obtained. Once the tests are obtained, follow up staff remain in communication with the local hospital or provider to obtain the results of further testing. Once these results are in, follow up staff review the results with the medical consultant to see if further action is necessary. Sometimes no further action is necessary and the case is closed as a "false positive" indicating that the baby does not have the disorder. If the specialized testing is reviewed and does not appear to be normal, then a referral is made to a specialist so the baby can be further evaluated. This is called long term follow up.

Long Term Follow Up – Long term follow up staff/physicians provide guidance to short term follow up staff during the positive screen process. The long term follow up staff/physicians often talk to local health care providers and/or parents to provide guidance and/or education about specific disorders. Referrals are made to specialized physicians and allied health care providers when a newborn screen is abnormal and/or confirmed. Long term follow up staff provide clinical care for a diagnosed disorder. For instance, if a baby is determined to have congenital adrenal hyperplasia, the newborn screening program makes a referral to a pediatric endocrinologist in the state. Often, babies referred to specialists for disorders identified through newborn screening are followed by the specialist for the lifespan.

Of note - Iowa is the only newborn screening program (laboratory and short term follow up) in the nation that runs 365 days per year. The Iowa Newborn Screening Laboratory and Short Term Follow Up Staff also provide newborn screening services to North Dakota and South Dakota.

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Disorders Screened for in Iowa

AMINO ACIDEMIAS AND UREA CYCLE DISORDERS

- (ASA) Argininosuccinic aciduria*
- (CIT) Citrullinemia, type 1 or ASA Synthetase Deficiency*
- (HCY) Homocystinuria (cystathionine beta synthetase)*
- (MSUD) Maple Syrup Urine Disease*
- (PKU) Classic Phenylketonuria*
- (TYR-1) Tyrosinemia, type I*
- (ARG) Argininemia**
- (BIOPT-BS) Defects of biopterin cofactor biosynthesis**
- (CIT-II) Citrullinemia, type II**
- (BIOPT-REG) Defects of biopterin cofactor regeneration**
- (H-PHE) Benign hyperphenylalaninemia**
- (MET) Hypermethioninemia**
- (TYR II) Tyrosinemia, type II**
- (TYR III) Tyrosinemia, type III**

ORGANIC ACIDEMIAS

- (GA-1) Glutaric acidemia type I*
- (HMG) 3-Hydroxy 3-methylglutaric aciduria *
- (IVA) Isovaleric acidemia*
- (3-MCC) 3-Methylcrotonyl-CoA carboxylase*
- (Cbl-A,B) Methylmalonic acidemia (cobalamin disorders, vitamin B12 disorders)*
- (βKT) βeta-Ketothiolase*
- (MUT) Methylmalonic Acidemia (methylmalonyl-CoA mutase)*
- (PROP) Propionic acidemia*
- (MCD) Holocarboxylase synthase*
- (2M3HBA) 2-Methyl-3-hydroxybutyric aciduria**
- (2MBG) 2-Methylbutyrylglycinuria**
- (3MGA) 3-Methylglutaconic aciduria**
- (Cbl-C, D) Methylmalonic acidemia with homocystinuria**
- (MAL) Malonic acidemia**

FATTY ACID OXIDATION DISORDERS

- (CUD) Carnitine uptake defect (Carnitine transport defect)*
- (LCHAD) Long-chain L-3 hydroxyacyl-CoA dehydrogenase*
- (MCAD) Medium chain acyl-CoA dehydrogenase*
- (TFP) Trifunctional protein deficiency*
- (VLCAD) Very long-chain acyl-CoA dehydrogenase*
- (CACT) Carnitine acylcarnitine translocase**
- (CPT-Ia) Carnitine palmitoyltransferase type I**
- (CPT-II) Carnitine palmitoyltransferase type II**
- (GA2) Glutaric acidemia type II**

- (MCAT) Medium-chain ketoacyl-CoA thiolase**
- (M/SCHAD) Medium/Short chain L-3-hydroxyacyl-CoA dehydrogenase**

ENDOCRINE

- (CAH) Congenital adrenal hyperplasia *
- (CH) Primary Congenital hypothyroidism *

HEMOGLOBINOPATHIES

- (Hb SS) S,S Disease (Sickle Cell Anemia)*
- (Hb S/C) S,C Disease*
- (HB S/βTh) S, βeta-thalassemia*
- (Var Hb) Variant hemoglobinopathies **

OTHER

- (BIOT) Biotinidase deficiency *
- (CF) Cystic Fibrosis *
- (GALT) Classic Galactosemia *
- (GALE) Galactoepimerase deficiency **
- (HEAR) Hearing loss*

* Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC) Recommended Uniform Screening Panel - Core Panel

** SACHDNC Recommended Uniform Screening Panel - Secondary Targets - Screening for the Core Panel of disorders may show information about secondary conditions (by-products of mandatory screening)

Disorders on the SACHDNC recommended panel that we do not screen for:

(SCID) Severe Combined Immunodeficiency* (plan to screen for in 2012); (CCHD) Critical Congenital Heart Disease*; (DE-RED) 2,4 Dienoyl-CoA reductase deficiency**;(GALK) Galactokinase deficiency**; (SCAD) Short-chain acyl-CoA dehydrogenase**; (IBG) Isobutyrylglycinuria**

Screens Submitted

There were 39,466 newborn screening cards submitted to the newborn screening laboratory for testing. This number includes more than one screen on some babies (repeat screens that the program asked for). The number of births would be slightly less than the number of screens submitted.

Presumptive Positive Screens

To reiterate, "presumptive positive" is a term used by the laboratory and follow up personnel to identify a screen that was positive. The term "presumptive" is used because until further testing is done, the result is considered positive until the disorder is either confirmed or determined to be a false positive (ie no diagnosis is made).

Disorder	Number of Presumptive Positives	Borderline Cases*	Comments
Biotinidase	26		
Congenital Adrenal Hyperplasia	14	191	
Congenital Hypothyroidism	26	303	
Cystic Fibrosis (CF)	49		43 that required 2nd tier testing in the lab; 6 that were definite on first screen
Galactosemia	0		
Hemoglobinopathies	147		12 disease; 135 traits
Metabolic Disorders	422		

All presumptive positive screens are reported to the short term follow up staff to inform the local provider, make recommendations, and follow up on confirmatory testing results. A portion of the presumptive positive cases do not detect true disease, but identify babies who are carriers for a disease or have disease "traits". *Endocrine disorders are slightly different than other disorders. There are reference ranges for borderline results as well as presumptive positive reference ranges. Borderline cases are not as likely as presumptive positive cases to be confirmed as a disease, but need the same follow up completed as a presumptive positive case. As you can tell by the number of cases, a significant amount of case management occurs with these borderline endocrine cases.

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Confirmed Cases for 2011

Confirmed cases are counted in the year that they were confirmed, not necessarily the year the baby was born.

Disorder	Number Confirmed Cases	Incidence Rate/Comments
Amino Acid Disorders		
Citrullinemia	1	1 in every 57,000 births
PKU	2	1 in every 12,000 births
HyperPhe	1	Not true disease but are sometimes followed clinically
Biotinidase Deficiency	3	1 in every 137,401 for profound biotinidase deficiency; 1 in every 109,921 for partial biotinidase deficiency; and 1 in every 61,067 combined rate for both profound and partial
Congenital Adrenal Hyperplasia	1	1 in every 16,000 births
Congenital Hypothyroidism	15	1 in every 3,000 births
Cystic Fibrosis		Approximately 1,000 new cases are diagnosed in the US each year. Approximately 30,000 children and adults have CF in the US. Data suggests that 2-5% of the US population are carriers for CF
Disease	5	
CRMS	7	
Carriers	27	
Fatty Acid Oxidation Disorders		
Carnitine Uptake Deficiency	2	MCAD deficiency is the most common of the disorders with an incidence of 1 in every 6,000 to 1 in every 10,000 births. Deficiency of VLCAD, LCAD, and SCAD is rare compared to MCAD. We removed SCAD from our panel but it is still diagnosed when other confirmatory tests are performed
Glutaric Acidemia Type II	1	
IBDH	1	
MCAD	4	
SCAD	4	
VLCAD	2	
Carriers	4	
Galactosemia		People with Duarte galactosemia have a less severe form of the disease and may or may not have any symptoms and may or may not need any dietary restrictions/treatment. One in every 70,000 babies born will have galactosemia
Classic	0	
Duarte	1	

Hemoglobinopathies Beta Thalassemia Major Hemoglobin E Disease Hemoglobin H Disease Sickle Cell Disease	 2 2 2 4	Beta Thal Major – 1 in every 114,000 births; Hemoglobin E Disease – varies widely based on ethnicity; Hemoglobin H Disease – 1 in every 15,000 births. Approximately 90,000-100,000 residents in the US have sickle cell disease. One in every 500 blacks/African Americans have disease. One in every 36,000 Hispanics have sickle cell disease. One in every 12 blacks/African American's have sickle cell trait.
Organic Acidemia Glutaric Acidemia Type I	 1	Overall incidence rate for all organic acidemias is 1 in every 20,000 births

False Negative Case Reported

On November 7, 2011, Dr. Norris (endocrine medical consultant) reported a possible false negative case to the coordinator. The infant was born November 11, 2009. She was born premature (31 weeks and 1850 grams) and had an initial CAH screen of "borderline". Repeat screen was collected on day of life 9 and called normal so no further workup was performed. She presented to a pediatric endocrinology in Des Moines with progressive symptoms of non-salt wasting CAH. Though she does not have salt-wasting, the significant evaluation of her 17-hydroxy-progesterone suggests that she was almost severe enough to have salt-wasting (the most severe form of CAH). Dr. Norris and his colleagues are reassessing how to interpret repeat screens and normative data for CAH and hypothyroidism as well.

Newborn Screening Stories

Story #1 - Baby Brody was diagnosed with profound biotinidase deficiency this year. His parents were very grateful that newborn screening found this disorder in their son. They cannot imagine what his life would have been like if this disorder was not found. They have become vocal advocates for newborn screening and have told their story to the media and given us permission to tell their story to anyone who will listen. Stories about Brody have been posted on national websites, Facebook, Pinterest, and have been published in local newspapers. At the time of this writing, Brody was picked as one of the national faces of newborn screening and will be featured in many media campaigns celebrating the 50th anniversary of newborn screening in the United States. Brody's mother is now a member of our Congenital and Inherited Disorders Advisory Committee that helps oversee the newborn screening program and other programs at the Iowa Department of Public Health. This story represents the positive impact of newborn screening from a parent's perspective.

Story #2 - The newborn screening laboratory called the short term follow up case manager on call on a Sunday with a presumptive positive citrullinemia case. The test result above the alert

value. Alert values are considered a medical emergency. The case manager tried multiple times to contact the physician of record on the newborn screening card. She tried calling the phone number of the practice, paging the physician, and calling the local hospital to try to locate the physician. She was not able to reach the physician. After a period of time, the case manager was able to talk to a nurse affiliated with this physician's practice who was staffing an urgent care clinic. The nurse got the physician that was staffing the urgent care clinic to help. The baby was sent to the local hospital to be assessed and to have some recommended lab testing done to determine how sick the baby might be. Ultimately, the baby was transferred to University of Iowa Children's Hospital later that night due to the abnormal results of the tests performed locally and the potential critical nature of the disorder. Ultimately, this was a success story. The baby received appropriate medical care, was diagnosed, and is being followed by our long term follow up metabolic team for her metabolic disorder and doing well. However, it does point out the odyssey of what can happen in the short term follow up arena. One case can take hours, one case can take 30 minutes. In this situation, the case manager worked on this case from 7:30 am till about 9:00 pm that night. The physician never contacted the program about this baby. This case illustrates some of the problems case managers have when dealing with local physicians or health care providers. However, this is an extreme example. Most physicians respond quickly to newborn screening staff when called. Although we still don't know why this physician never called back, you could speculate that this physician needed further education about the importance of newborn screening and timely response and/or didn't know or understand that the program will report abnormal results 7 days a week. This illustrates the need for additional and continued education of local health care providers regarding newborn screening.

Story #3 - On a Friday, the case manager received a phone call from the newborn screening laboratory with a possible MCAD case. MCAD is considered a medical emergency. When a presumptive positive screen is considered an emergency (based on lab values and the type of disorder), case managers ask to speak to the physician directly. The case manager called the local care provider and talked with a nurse because the physician was not available to come to the phone. The tone of the conversation with the nurse didn't go well. The case manager was not convinced the person understood the critical nature of the disorder nor was she sure that the parents would be called to inform them of the results and to give them care instructions. Babies with MCAD – a fatty acid oxidation disorder – cannot fast and need to eat every 2-3 hours to avoid serious side effects and/or death. There were also other confirmatory tests that were recommended to be done that day. Because of her concerns, the case manager called back and talked to this nurse twice (the first time she called back nothing had been done) to make sure this baby was being taken care of and to offer her help to them. Later this same day, a phone call was transferred to the case manager from the UIHC call center. It was the father of this baby with possible MCAD. The father reported to the case manager that the doctor's office had called and told them, paraphrasing, "make sure your baby eats every 2-3 hours. She might have this disorder called MCAD. It might cause her to have seizures, go into a coma and die. But, we're too busy to call Iowa City and get you an appointment". The case manager could hear the mother crying in the background. The case manager was able to explain what MCAD was, go over the feeding precautions, offer reassurance, and to talk with the long term

follow up metabolic staff to get this family an appointment with the metabolic team on Monday. The long term follow up staff saw this family on Monday. The baby was examined by a metabolic geneticist and further testing was ordered to determine if the baby had MCAD or not. Education about the disorder was provided to the family that included the special feeding requirements and instructions to take the baby/child to an ER if they developed the flu or some other sickness that prevented them from eating (these patients have to eat on a routine basis or they could become critically ill). An emergency room protocol was provided to the family. Many metabolic patients have a letter that outlines what special things need to be done in the ER if they get sick because of their metabolic disorder (such as starting an IV). Genetic counseling was provided. Not only was this family upset about their new baby having MCAD, but were now worried that their older child might have MCAD. Ultimately, this baby was diagnosed with MCAD and continues to be followed in the metabolic clinic. This story highlights the work that's done by the program's long and short term follow up staff as well as the genetic counselor. The lesson learned from this story is that (some) local care providers and allied help staff need further education about the newborn screening process and about the disorders screened for. I believe that education is key and would improve interactions and communications between newborn screening staff and the provider and the care provider and the parents.

Newborn Screening Conundrums

There was a case reported to the program that illustrates that screening can be affected by things out of our control. The mother had a genetic mutation for CF that apparently interfered with the testing done on the baby. Because both parents were known to be carriers of CF with different genetic mutations, mutation analysis was done on the baby even though his IRT newborn screen was normal. Mutation analysis showed that he had two mutations and was therefore positive for CF, even though the baby's newborn screen and two sweat tests were normal. He was found to have pseudomonas, a common infection in patients with CF. For program metrics and quality control, do you call this a false negative when the newborn screen and sweat tests were negative? This situation also points out once again that this is a screening test, not a diagnostic test.

Quality Improvement Activities

Tri-State Quality Improvement Committee

The Tri-State Quality Improvement Committee is comprised of representatives from the laboratory, short term follow up, long term follow up, physicians, coordinators, and department of health representatives from Iowa, North Dakota and South Dakota. The committee meets on a regular basis throughout the year. The regional coordinator is in charge of setting the agenda and compiles quality assurance data. The purpose of this committee is to address quality control/improvement issues that arise and to plan and execute quality improvement activities.

Tri State Team Meeting

The Tri-State Team Meeting is comprised of program staff from the laboratory, short term follow up, long term follow up, physicians, coordinators, administrators, and department of health representatives from Iowa, North Dakota and South Dakota. The committee meets on a regular basis throughout the year. The regional coordinator is in charge of setting the agenda. Anyone from the entities named above can attend this meeting. Each entity is called on to report during this meeting and an update of the QI committee activities is also shared. The main purpose of this meeting is to facilitate communication amongst all parts of the newborn screening program and to promote team building.

Tri-State Metabolic Case Review

The metabolic medical consultants from Iowa, North Dakota and South Dakota (Drs. Copeland, Serrano-Russi and Shchelochkov from Iowa; Dr. Kenien from North Dakota; and Dr. Davis-Keppen from South Dakota) along with short term follow up staff, coordinators, and genetic counselors from all three states meet via conference call approximately every 4-6 weeks to discuss all ongoing presumptive positive metabolic cases. Quality assurance and improvement activities take place during this call (making sure that babies are receiving the best care possible) as well as clinical decision making and education. The physicians report this is invaluable to them in their newborn screening practice.

Genetics Conference

Genetics Conference is a weekly conference in the Division of Medical Genetics/Department of Pediatrics at the University of Iowa Children's Hospital and is attended by all employees in the division. This includes metabolic medical consultants, long term follow up staff, and the short term follow up staff. Metabolic and newborn screening cases are reviewed and participants can offer additional suggestions for care of these patients. It also serves as a communication tool for on call staff to know what newborn screening cases they might encounter and need to take care of while on call.

Databases

The Iowa Newborn Screening Program has its own database that is used to communicate and document information about each screen. In addition, there are two national databases where confirmed cases are entered into a repository. The "Region 4" database is used to document confirmed metabolic cases, including values for all of the analytes tested. The long term goal of the Region 4 database is to help newborn screening programs determine the probability of a presumptive positive screen being real. It might also be used to help newborn screening programs set more appropriate cut off values to reduce the number of presumptive positive screens. The NNSIS is another database where confirmed cases are documented. All confirmed newborn screening disorders are entered into this database. The purpose of this database is to

provide prospective information on the disorders screened for and to determine the efficacy of newborn screening.

Educational Activities

Presentations Given by Program Staff

Name	Title	Date/Location	Audience
Kim Turner	Newborn Screening in the Older Child and Sibling	January 2011	Genetics Faculty and Staff, UIHC
Judy Miller	The clinical manifestation of MCAD deficiency: challenges towards adulthood in the screened population.	March 1, 2011	Genetics Journal Club, UIHC
Oleg Shchelochkov	Linking Chromosome Abnormality and Copy Number Variation	March 8, 2011	Genetics Journal Club, UIHC
Jenny Marcy	Segregation of mtDNA Throughout Human Embryofetal Development: m.3243A> G as a Model System	March 8, 2011	Genetics Journal Club, UIHC
Leslie Thomas	NBS Orientation for NICU Nurses	March 23, 2011	NICU, UIHC
Deborah Chalupa Kim Turner	Heartland Regional Meeting	April 6-8, 2011	Kansas City, MO
Jenny Marcy	Increased Prevalence of False Positive Hemoglobinopathy Newborn Screening in Premature Infants	July 12, 2011	Genetics Journal Club, UIHC
Judy Miller	The adult galactosemic phenotype.	July 26, 2011	Genetics Journal Club, UIHC

Oleg Shchelochkov	The interplay between genotype, metabolic state, and cofactor treatment governs phenylalanine hydroxylase function and drug response	July 26, 2011	Genetics Journal Club, UIHC
Jenny Marcy	Hemoglobinopathies and Cystic Fibrosis in NBS	September 2, 2011	Genetics and Maternal Fetal Medicine Fellows; Pathology and Pediatric Residents, UIHC
Judy Miller	NBS Beyond the Bloodspot	September 14, 2011	Dietetic Interns, Dietetic Program, UIHC
Alvaro Serrano-Russi	Vaccination in Children with Urea Cycle defects	October 4, 2011	Genetics Journal Club, UIHC
Judy Miller	Hepatocytes from wild-type or heterozygous donors are equally effective in achieving successful therapeutic liver repopulation in murine phenylketonuria (PKU).	November 1, 2011	Genetics Journal Club, UIHC

Meetings and Presentations Attended by Program Staff

Oleg Shchelochkov	Society for Inherited Metabolic Disorders	February 27-March 2, 2011	Pacific Grove, CA
Kim Turner	Heartland Regional Meeting	April 6-8, 2011	Kansas City, MO
Carol Johnson Kim Turner	Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC)	May 5-6, 2011	Washington, DC
Cheryl Stimson	Abbott Metabolic Nutrition Meeting	June 2-4, 2011	Chicago, IL

Oleg Shchelochkov	Urea Cycle Disorders Consortium Annual Meeting	July 8-9, 2011	Denver, CO
Jenny Marcy	Camp Sunshiny Day (Sickle Cell Camp)	August 2-4, 2011	Waubeek, IA
Carol Johnson Kim Piper Barb Schweitzer Leslie Thomas	Heartland Collaborative NBS and Genetics Conference	August 24-27, 2011	Bismarck, ND
Carol Johnson	Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC)	September 22-23, 2011	Washington, DC
Jenny Marcy	Preaching Beyond the Choir: How to Prove the Value of Genetics	September 28, 2011	Webinar
Jenny Marcy	National Society of Genetic Counselors, 30th Annual Meeting	October 27 – 30, 2011	San Diego, CA
Pam DeBoer Carol Johnson Kim Piper Alvaro Serrano-Russi	APHL Symposium on Newborn Screening and Genetic Testing	November 7-10, 2011	San Diego, CA

Committee Activites (external from Iowa/Tri-State Committees)

Carol Johnson – Heartland Regional Collaborative – Clinical Workgroup
Kim Turner – Heartland Regional Collaborative – Newborn Screening Committee

Program Personnel – Follow Up Services

Name	Title	Disorder	Location
Deborah Chalupa	Case Manager, Short Term Follow Up	Early Collection, Hemoglobinopathies, Poor Quality, Transfused	University of Iowa Children's Hospital, Iowa City, IA
Pamela DeBoer	Case Manager, Short Term Follow Up; then Long Term Follow Up – Metabolic Disorders	Metabolic Disorders, others as assigned	University of Iowa Children's Hospital, Iowa City, IA

Elizabeth Dowd	ARNP, Long Term Follow Up	Cystic Fibrosis	University of Iowa Children's Hospital, Iowa City, IA
Ayman El-Sheikh	MD Medical Consultant	Hemoglobinopathies (Sickle Cell Disease/Trait; Thalassemia's, etc.)	University of Iowa Children's Hospital, Iowa City, IA
Endocrinologist On Call – Vanessa Curtis, Katie Larsen Ode, Andrew Norris, Liuska Pesce, Michael Tansey, Eva Tsalikian	MD Medical Consultants	Endocrine Disorders (Congenital Adrenal Hyperplasia; Congenital Hypothyroidism)	University of Iowa Children's Hospital, Iowa City, IA
Carol Foster	Program Support		University of Iowa Children's Hospital, Iowa City, IA
Tammy Hatland	Case Manager, Short Term Follow Up	Endocrine and Metabolic Disorders, others as assigned	University of Iowa Children's Hospital, Iowa City, IA
Myrl Holida	PA, Long Term Follow Up	Hemoglobinopathies	University of Iowa Children's Hospital, Iowa City, IA
Carol Johnson	Program Administrator, Coordinator from 9/2011		University of Iowa Children's Hospital, Iowa City, IA
Jennifer Marcy	Genetic Counselor, Short Term and Long Term Follow Up	Counselor for all disorders; Short Term Follow Up for Cystic Fibrosis and Hemoglobinopathies; Long Term Follow Up for Metabolic Disorders	University of Iowa Children's Hospital, Iowa City, IA
Judy Miller	ARNP, Long Term Follow Up	Metabolic Disorders	University of Iowa Children's Hospital, Iowa City, IA
Lisa Neff-Letts	Program Administration and Support		University of Iowa Children's Hospital, Iowa City, IA
Andrew Norris	MD Lead Medical Consultant	Endocrine Disorders (Congenital Adrenal Hyperplasia; Congenital Hypothyroidism)	University of Iowa Children's Hospital, Iowa City, IA
Kimberly Noble Piper	State Genetics Coordinator		Iowa Department of Public Health, Des Moines, IA

Mavis Rike	Long Term Follow Up	Endocrine Disorders	University of Iowa Children's Hospital, Iowa City, IA
Barbara Schweitzer	Regional Coordinator	Iowa, North Dakota, South Dakota	North Dakota Department of Health, Bismarck, ND
Alvaro Serrano-Russi	Co-Lead MD Medical Consultant	Metabolic Disorders	University of Iowa Children's Hospital, Iowa City, IA
Oleg Shchelochkov	Co-Lead MD Medical Consultant	Metabolic Disorders	University of Iowa Children's Hospital, Iowa City, IA
Val Sheffield	Medical Director		University of Iowa Children's Hospital, Iowa City, IA
Cheryl Stimson	Dietitian, Long Term Follow Up	Metabolic Disorders	University of Iowa Children's Hospital, Iowa City, IA
Leslie Thomas	Case Manager, Short Term Follow Up	North Dakota, others as assigned	University of Iowa Children's Hospital, Iowa City, IA
Pamela Trapane	MD Medical Consultant	Metabolic Disorders	University of Iowa Children's Hospital, Iowa City, IA
Kimberley Turner	Coordinator		University of Iowa Children's Hospital, Iowa City, IA
Miles Weinberger	MD Medical Consultant	Cystic Fibrosis	University of Iowa Children's Hospital, Iowa City, IA

A couple of personnel changes occurred in 2011. Pam DeBoer was moved to long term follow up for metabolic conditions and Tammy Hatland took over the case management for metabolic disorders in Iowa in addition to her other assignments. In September 2011, Kim Turner was not able to work for a period of time and Carol Johnson was appointed as interim coordinator for the program. In November 2011, it was determined that Kim would not be returning to her position as coordinator, and Carol Johnson was assigned to be the coordinator permanently.

Summary

Thank you for reading this report. Please feel free to contact the Iowa Newborn Screening Program at 866-890-5965 or email me at carol-johnson@uiowa.edu if you have any questions.

In addition, you may contact Kimberly Piper, State Genetics Coordinator at the Iowa Department of Public Health at 515-570-4952 or kimberly.piper@idph.iowa.gov.

Appendix A

Terms and Definitions Used in Newborn Screening and in this Report

Alert Value – a test result that is very high and considered a medical emergency. For metabolic disorders, the laboratory and the metabolic medical consultant have established a reference ranges for what is considered a normal result, a result that is considered abnormal (cut off value) and needs evaluation, and a result that is not only abnormal, but needs immediate attention.

Amino Acid Disorders – Babies born with one of these disorders cannot process certain amino acids in their body. The amino acids, along with other toxic substances, build up in the body and cause serious effects on health, growth and learning. Treatment may include a special diet for life, close monitoring and/or vitamin and amino acid supplements. An example of an amino acid disorder is phenylketonuria (PKU). Babies with PKU cannot process a substance called phenylalanine. Left untreated, phenylalanine builds up in the bloodstream and causes brain damage, intellectual disability, depression, and other problems. If PKU is detected early and the special diet is started by Day 10 of life, these problems can be greatly reduced or prevented. PKU occurs in about 1 in every 12,000 births.

Beta Thalassemia – *Beta thalassemia major* usually causes severe anemia that can occur within months after birth. If left untreated, severe anemia can result in insufficient growth and development, as well as other common physical complications that can lead to a dramatically decreased life-expectancy. Fortunately, in developed countries beta thalassemia is usually identified by screening in the newborn period, before symptoms have developed. Children who are identified early can be started on ongoing blood transfusion therapy as needed. Although transfusion therapy prevents many of the complications of severe anemia, the body is unable to eliminate the excess iron contained in the transfused blood. Over time, the excess iron deposits in tissues and organs, resulting in damage and organ failure. Another medication must be administered to help the body eliminate the excess iron and prevent iron-over-load complications. *Beta thalassemia intermedia* describes the disease in individuals who have moderate anemia that only requires blood transfusions intermittently, if at all

Biotinidase Deficiency – Babies with biotinidase deficiency cannot reuse the vitamin biotin. Biotin helps maintain the normal body functioning. Without treatment, this disorder can lead to seizures, developmental delay, eczema and hearing loss. Biotin has to be added to the diet for treatment of this disorder. This disorder occurs in about 1 in every 60,000 births.

Card – a card/form that contains circles with filter paper to deposit the blood from the baby's heel on. This card also contains demographic information regarding the baby, mother, and sample information. Also called the "dried blood spot card".

Carrier – a person that has inherited a genetic trait or mutation but has no symptoms of the disease

Confirmatory/Second Tier Testing – specific testing that is recommended and performed post newborn screening to determine if a baby has a specific disorder or not, e.g. a sweat test for cystic fibrosis.

Confirmed – used to convey that the newborn screen and/or confirmatory testing determined that a baby had a disorder.

Congenital – a condition or problem present at birth.

Congenital Adrenal Hyperplasia – Babies born with this disorder have adrenal glands that cannot make enough of the hormone cortisol, and sometimes not enough of the hormone aldosterone. Sometimes this disorder affects the development of the genitals. You treat this disorder by taking medication that replaces the hormones that are deficient or eliminating the source of excess hormones. Without treatment, severe cases of this disorder can cause death. This disorder occurs in about 1 in every 16,000 births.

Congenital Hypothyroidism – Babies with this disorder are born with a thyroid gland that does not make enough thyroid hormone. This can lead to poor growth and abnormal brain development. If it is detected in time, a baby can be treated with medication. This disorder occurs in about 1 in every 4,000 births

Courier – the contractual entity that travels to Iowa birthing facilities on a daily basis to pick up newborn screening cards and delivers them to the newborn screening laboratory.

CRMS - When a person has a sweat test that gives an intermediate (borderline) result or a genetic test that shows only one CF gene, he or she is said to have CFTR-related metabolic syndrome (CRMS). People with CRMS can be at a higher risk of having problems in the airways and sinuses; the intestines and pancreas; or the reproductive tract.

Cut-Off Value - a test result that is abnormal and needs further evaluation – a "presumptive positive" case. For metabolic disorders, the laboratory and the metabolic medical consultant have established a reference ranges for what is considered a normal result, a result that is considered abnormal (cut off value) and needs evaluation, and a result that is not only abnormal, but needs immediate attention.

Cystic Fibrosis – Cystic fibrosis (CF) is the most common inherited (genetic) disorder, affecting about 30,000 children and adults in the US. A defective gene causes lung infections and digestive problems with malnutrition. CF can be life-shortening[5]. It's important to diagnose CF early, so that CF health care providers can help parents learn ways to keep their child as healthy as possible and delay problems related to CF. Research shows that children who receive CF care

early in life have better nutrition and are healthier than those who are diagnosed later. Good nutrition in CF is important for overall health and well-being.

Early Collection – the newborn screen was obtained prior to 24 hours of age. The newborn screen is not valid if collected before 24 hours of age. A repeat screen will be requested on the baby by program staff.

False Negative – a term used when the newborn screen was negative, but a baby is found to have a disorder that we are screening for. As stated above, the newborn screen is a screening test, not a diagnostic test. Every attempt is made to reduce the number of false negatives, but it is understood that some cases will be missed. It is an inherent part of newborn screening.

False Positive – the newborn screen was positive for a particular disorder, but further testing was negative for the disorder.

Fatty Acid Oxidation Disorders – Babies with fatty acid disorders are unable to breakdown stored fats for energy. People who have this disorder cannot fast, and need prompt medical intervention when they have the stomach flu, fevers, etc. One example of a fatty acid disorder is Medium Chain acyl-CoA Dehydrogenase Deficiency (MCAD). Babies born with MCAD cannot break down fat into energy because an enzyme is missing or does not work correctly. People with MCAD should not fast (go without food) for very long or they can experience low blood sugar, seizures, coma and even death. MCAD occurs in about 1 in every 12,000 births.

Galactosemia – Babies with this disorder cannot convert galactose, a sugar present in milk, into glucose, a sugar the body uses as an energy source. Galactosemia can cause death in infancy, or blindness and intellectual disability. A baby will this disorder is not able to drink milk and/or eat other dairy products. They have to drink special formula and follow a special diet for their lifetime. This disorder occurs in about 1 in every 70,000 births.

Hemoglobin E Disease - is an inherited blood disorder characterized by an abnormal form of hemoglobin, called hemoglobin E. People with this condition have red blood cells that are smaller than normal and have an irregular shape. It is thought to be a benign condition. The mutation that causes hemoglobin E disease has the highest frequency among people of Southeast Asian heritage (Cambodian, Laotian, Vietnamese and Thai). However, it is also found in people of Chinese, Filipino, Asiatic Indian, and Turkish descent.

Hemoglobin H Disease - Hemoglobin H disease is a relatively mild form of thalassemia that may go unrecognized. It is not generally considered a condition that will reduce one's life expectancy. Transfusions are rarely needed in this disorder, except in a variant of this disorder called constant Spring. Occasionally additional medication is required for treatment.

Hemoglobinopathies – Hemoglobinopathies are inherited red blood cell disorders. Hemoglobin is the protein in the blood that carries oxygen from the lungs to the body. The most common

hemoglobin disorder is sickle cell disease. When sickle cell shaped cells block small blood vessels, less blood can reach that part of the body. Sickle cell anemia occurs in about 1 in every 375 African Americans.

Iowa Department of Public Health – state agency that administers and oversees newborn screening processes in Iowa.

Long Term Follow Up - fundamentally, long-term follow-up comprises the assurance and provision of quality chronic disease management, condition-specific treatment, and age-appropriate preventive care throughout the lifespan of individuals identified with a condition included in newborn screening. Integral to assuring appropriate long-term follow-up are activities related to improving care delivery, including engagement of affected individuals and their families as effective partners in care management, continuous quality improvement through the medical home, research into pathophysiology and treatment options, and active surveillance and evaluation of data related to care and outcomes.

Medical Consultant – A physician who makes medical recommendations for a specific disorder to the newborn screening program, state health department, and health care providers throughout the state. They may also assist with development of protocols and provide education.

Newborn Screening Laboratory - The newborn screening laboratory is part of the State Hygienic Laboratory at the University of Iowa (Ankeny campus). This is the laboratory where the testing is performed.

Organic Acidemia – Babies born with organic acid disorders have a chemical imbalance in their bodies which can be toxic. Organic acids play an important role in the breakdown of fats, sugars and protein for the body's use and storage. Muscle wasting, seizures, developmental delays and even death can occur if untreated. Treatment may include a special diet, monitoring and medications.

Outcome – the final determination of a newborn screen, such as "confirmed, false positive, false negative, etc.

Poor Quality – a term used to describe that the sample was not able to be tested. A sample is called "poor quality" when the blood does not soak through the filter paper layers, when the sample is clotted, when too much blood is placed on the card, etc. A repeat screen will be requested by program staff.

Presumptive Positive – a term used by the laboratory and follow up personnel to identify a screen that was positive. The term "presumptive" is used because until further testing is done, the result is considered positive until the disorder is confirmed or determined to be a false positive.

Primary Care Provider/Local Care Provider – also known as "PCP". The physician who is taking care of the baby, or is listed as the baby's physician.

Reference Range – in laboratory testing, there is often a range of answers – or values – that are considered normal if they are within a certain number. For instance, a reference range could be determined to be between 10-20. If the test result is lower or higher than this reference range, it is considered abnormal.

Rejected Sample – similar to early collection and poor quality determinations. This term is usually used in association with a screen that was submitted after the 30 day cut off time frame. It is also used when the screening card does not have enough information recorded on it to determine who the baby really was.

Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC) - The committee advises the Secretary, U.S. Department of Health and Human Services on the most appropriate application of universal newborn screening tests, technologies, policies, guidelines and standards. Specifically, the committee provides to the Secretary, the following: Advice and recommendations concerning grants and projects authorized under the Heritable Disorders Program administered by the Health Resources and Services Administration; technical information to develop Heritable Disorders Program policies and priorities will enhance the ability of the state and local health agencies to provide screening, counseling and health care services for newborns and children who have or are at risk for heritable disorders; and recommendations, advice and information to enhance, expand or improve the ability of the Secretary to reduce mortality and morbidity from heritable disorders in newborns and children. The committee was chartered in February 2003.

Short Term Follow Up - refers to the process of ensuring that all newborns are screened, that an appropriate caregiver is informed of results, that repeat testing on a new specimen or confirmatory testing has been completed, and that the infant has received a diagnosis and, if necessary, treatment.

Sickle Cell Disease/Trait – Sickle cell anemia is caused by an abnormal type of hemoglobin called hemoglobin S. Hemoglobin is a protein inside red blood cells that carries oxygen. Hemoglobin S changes the shape of red blood cells. The red blood cells become shaped like crescents or sickles.The fragile, sickle-shaped cells deliver less oxygen to the body's tissues. They can also get stuck more easily in small blood vessels, as well as break into pieces that can interrupt healthy blood flow. These problems decrease the amount of oxygen flowing to body tissues even more. Sickle cell anemia is inherited from both parents. If you inherit the sickle cell gene from only one parent, you will have sickle cell trait. People with sickle cell trait do not have the symptoms of sickle cell anemia. Sickle cell disease is much more common in people of African and Mediterranean descent. It is also seen in people from South and Central America, the Caribbean, and the Middle East. About 90,000-100,000 residents of the US have sickle cell disease. One in every 500 blacks/African American's have disease. One in every 36,000 Hispanics have sickle cell disease. One in every 12 blacks/African American's have sickle cell trait.

Trait – a distinct, observable change in a person that might be inherited, such as sickle cell trait which can possibly be determined by newborn screening. It is not true sickle cell disease.

Unsatisfactory Specimen – a term used to state that there was not enough blood placed on the card to perform the newborn screen.