

Timeline:

The following is a historical background of how newborn screening started and how it has progressed:

- **1934: The discovery of PKU...** Dr. Asbjorn Folling of Norway discovered that some of his mentally ill patients had high levels of phenylpyruvic acid in their urine, which showed a deficiency in an important enzyme needed to break down the amino acid phenylalanine. This deficiency is now known as Phenylketonuria (PKU).
- **1951: Discovery of Treatment for PKU...** A German physician, Dr. Horst Bickel, discovered a treatment for PKU. He proved that a low phenylalanine diet could control the intellectual and developmental damage caused by PKU.
- **1960: Dr. Robert Guthrie Invents a Test for PKU...** Dr. Guthrie, an American cancer researcher who had a niece with PKU, developed a simple and inexpensive bacterial inhibition assay which utilized a dried filter paper blood spot sample from a heel stick and could be used to screen for PKU in newborns and infants. Untreated PKU results in severe brain disability and the need for lifelong care of the child. For this achievement, Dr. Guthrie has been deemed the "Father of Newborn Screening".
- **1963: Newborn Screening Begins...** After Dr. Guthrie published his findings regarding his very effective test and the benefits that early treatment can provide, Massachusetts passed the first NBS law to screen for PKU. Other states soon followed suit throughout the coming years.
- **1965: Missouri passes its first NBS law...** A few large hospitals in Missouri began conducting PKU testing on their newborns. Since PKU was so rare, individual hospitals were unable to maintain proficiency in its detection. Many babies from smaller hospitals were not even screened.
- **1967: Missouri State Public Health Laboratory begins PKU screening...** A law was passed to require that all PKU testing was to be conducted by the Missouri State Public Health Laboratory (MSPHL) for all babies born in Missouri, and so statewide PKU screening on all newborns was implemented at the MSPHL. PKU has an incidence of around 1 in 15,000 infants.
- **1979: Congenital Hypothyroidism Screening Begins...** Treatment for Congenital Hypothyroidism (CH) is easy and inexpensive, and saves the affected newborns from severe brain damage and developmental disabilities. The screening methods for this disorder have improved tremendously over the years, and the positive predictive value of the screen has improved from 5% in the beginning to around 75% today. CH has an incidence of around 1 in 1,600 infants and is currently the most common disorder detected in the NBS laboratory. It is the only disorder on the NBS panel that is not genetically inherited.
- **1985: Galactosemia Screening Begins...** Galactosemia is a disorder resulting from the inability to breakdown galactose in milk and milk products. Although classical galactosemia only has an incidence of 1 in 41,000, without treatment the disease is fatal within a few days or weeks after birth. Also in 1985, **the Missouri Genetics Disease Advisory Committee was formed**. Legislation required this committee to advise DHSS regarding the NBS program's policies and panel of disorders.
- **1989: Sickle Cell Disease Screening Begins...** Screening for sickle cell disease and other hemoglobinopathies was implemented as it was determined that prophylactic treatment with penicillin highly reduced the mortality rate in affected infants. These disorders have a combined incidence of 1 in 1,700 in Missouri. The testing method used also detects carriers of abnormal hemoglobins.
- **2001: Hearing Deficiency Screening Begins...** Screening for hearing deficiency was added to the required NBS tests, however, this screen is conducted at the hospital with special hearing sensitivity equipment designed for babies. This is by far the most common newborn disorder, with an incidence of up to 1 in 300 infants. Early detection allows special measures to be taken to keep children from falling behind in early developmental milestones, and also later on in school. This same year, **the expanded newborn screening law passed** and was signed by the Governor directing the department to add many other disorders to the NBS panel; in particular,

amino acid, fatty acid, and organic acid disorders, along with congenital adrenal hyperplasia, cystic fibrosis, biotinidase deficiency, and G-6-PD deficiency. The testing would require two tandem mass spectrometers and several additional scientists, and could not begin until funding became available.

- **2002: Congenital Adrenal Hyperplasia Screening Begins...** Screening for CAH was implemented at the direction of the Genetics Disease Advisory Committee and by the previously stated expanded screening law. CAH is a defect in the pathway leading to the biosynthesis of cortisol, and can result in ambiguous genitalia in females and salt-losing crisis in either males or females. Early detection and treatment is essential to prevent death in infants with salt-losing CAH. It has an incidence of about 1 in 13,000.
- **2005: Expanded Screening for Amino, Organic and Fatty Acid Disorder Screening Begins...** With the addition of the Tandem Mass Spectrometry multiplex testing method to the NBS laboratory, an additional 41 metabolic disorders were added all at once, including the PKU testing that was currently conducted as a stand-alone fluorometric assay. The combined incidence of these disorders is around 1 in 2,000. Also during this year, **the nationally Recommended Uniform Screening Panel (RUSP) was created** by the American College of Medical Genetics (ACMG) and was endorsed by the March of Dimes.
- **2007: Cystic Fibrosis Screening Begins...** Shortly before the move into the new State Public Health Laboratory, Missouri added Cystic Fibrosis (CF) screening to the NBS panel with the direction of the expanded screening law and the RUSP. CF is a genetic disorder characterized by severe lung damage and nutritional deficiencies. Early treatment can improve growth, improve lung function, reduce hospital stays and add years to life. CF has an incidence of around 1 in 3,000.
- **2008: Biotinidase Deficiency Screening Begins...** Biotinidase deficiency (BIOT) is a genetic disorder of impaired Biotin (vitamin B complex) usage and recycling. Children with profound BIOT, the more severe form of the condition, often have seizures, weak muscle tone (hypotonia), breathing problems, and delayed development. Treatment for this disorder merely requires biotin supplementation, and is easy and inexpensive. The incidence for profound BIOT is around 1 in 40,000 however several milder forms of the disorder are picked up through routine NBS.
- **2012: Lysosomal Storage Disorder Screening Begins...** Screening for Krabbe Disease began in August of 2012 in response to the Brady Alan Cunningham Act. The testing is temporarily being contracted to the New York State NBS Laboratory, which is the only other State laboratory in the U.S. currently screening for Krabbe. Missouri began the full population implementation phase for four other Lysosomal Storage Disorders (LSDs); Pompe, Gaucher, Fabry and Hurler Diseases in January of 2013. Missouri is the first state in the country to provide statewide screening and follow-up for these four LSDs, which are proving to have a combined incidence of greater than 1 in 2,000.
- **2013: Critical Congenital Heart Defect Screening Begins...** Screening for Critical Congenital Heart Defects (CCHD) was added to the required NBS tests in January 2013. However, similar to the hearing screen, this test is conducted at the hospital before discharge of the newborn. A routine and non-invasive testing method called Pulse Oximetry measures the oxygen saturation in the baby's blood from a finger or toe and can uncover heart defects that are not otherwise easily detected. Early intervention can prevent serious harm to the infant.