

## Newborn Metabolic Screening

### History & Overview

Oregon's newborn metabolic screening program has been in existence since 1962 and is one of the oldest in the country. The program began with the detection of phenylketonuria (PKU), a disorder resulting from the absence of an enzyme needed to metabolize the amino acid, phenylalanine. By identifying children in the newborn period and placing them on a protein-restricted diet, children were able to experience normal growth and development. Prior to this newborn screening, untreated PKU was a major cause of mental retardation.

The Newborn Screening Program resides within the Oregon State Public Health Laboratory (OSPHL), an office of the Oregon Department of Human Services/Health Services (formerly known as the Oregon Health Division). Over the years, several other states have joined Oregon to create the Northwest Regional Newborn Screening Program. Current members include Oregon, Hawaii, Alaska, Idaho, and Nevada. In addition to PKU, Oregon's newborn screening panel includes maple syrup urine disease, galactosemia, congenital hypothyroidism, biotinidase deficiency, and hemoglobinopathies (e.g., sickle cell anemia). In October 2002 the Oregon Newborn Screening Program incorporated tandem mass spectrometry (MS/MS) technology which adds 20+ metabolic conditions to the newborn screening panel, including Medium Chain Acyl CoA-Dehydrogenase Deficiency (MCAD) and other fatty acid and organic acid disorders. The program plans to add congenital adrenal hyperplasia (CAH) to Oregon's screening panel early in 2003. Idaho, Alaska, Hawaii, and Nevada also participate in the regional screening program, but each state is able to select its own panel of tests.

Infants in Oregon are required to have two screens, one at 24-48 hours of life and the second at approximately two weeks of age, to assure that all infants are screened and that all conditions are detected. All test results are mailed to the submitting birthing center and the physician of record. All urgent results are phoned to the submitting hospital or practitioner with recommendations for further action. Although responsibility for follow-up remains with the physician of record until another practitioner actively accepts responsibility, a newborn screening follow-up coordinator housed at the OSPHL confirms or facilitates appropriate follow-up. The OSPHL also contracts with medical metabolic physicians, a pediatric hematologist, and a pediatric endocrinologist to provide consultation to the newborn screening program and to the infant's primary care provider.

Newborn screening is mandatory in Oregon; however, parents have the option to opt-out for religious or philosophical reasons and must sign a waiver to that effect. No infant is refused screening because of a family's inability to pay the fee.

## Program Data

Based on the number of blood spot specimens received and the birth cohort, it appears that close to 100% of newborns born in Oregon are screened each year, but there is currently no statewide system to verify this. Documented parent refusals account for less than 0.1% of the total number of samples received. From 1996-2000, 190,814 Oregon newborns were screened for the panel of six disorders. During this time period, twenty-one children were identified with classical phenylketonuria (OR incidence 1:9,100; US incidence 1:15,900), two children with maple syrup urine disease (OR incidence 1:95,400; US incidence 1:150,000), six children with biotinidase deficiency (OR incidence 1:31,800; US incidence 1:60,000), two children with galactosemia (OR incidence 1:95,400; US incidence 1:60,000), eighty-eight children with primary hypothyroidism (OR incidence 1:2,200; US incidence 1:4,485), and ten children with sickle cell disease (OR incidence 1:19,100; US incidence 1:15,000).<sup>1</sup> Long-term information on the health status of these children is not available, though reduced morbidity and mortality associated with early identification of these conditions are believed to be significant.

## Policy Development

OSPHL is responsible for developing policy related to the newborn screening program including decisions as to which disorders to include in screening panels. The lab relies on expert advice from a newborn screening advisory committee made up of laboratory personnel, follow-up staff, and Oregon Health & Science University pediatric metabolic, endocrine, and hematology physicians. In addition the lab holds regular meetings with representatives from all programs participating in the Northwest regional program.

Recent policy decisions for Oregon have included:

- Implementing MS/MS for urea cycle, amino, fatty, and organic acid disorders
- Opting to screen for a comprehensive panel of disorders using a vendor's kit format, rather than select disorders individually
- Updating endocrine testing equipment and protocols and adding CAH to the testing panel
- Requiring all states that want to participate in the regional screening program to adopt expanded screening using MS/MS by mid-2003 (old technology will be maintained until that point)

In addition, the lab has considered adding cystic fibrosis screening in the future, although this would require entirely different testing protocols (DNA-based

---

<sup>1</sup> **Program data derived from information submitted to the National Newborn Screening and Genetics Resource Center from the OSPHL. Oregon incidence rates calculated using number of cases identified/number of children screened in a 5-year period from 1996-2000. US incidence rates obtained from NNSGRC.**

testing) and long-term risks and benefits are still controversial. Future program plans also include expanding the program advisory panel to include additional outside expertise including primary care providers, consumers, and advocacy groups.

## **Laws/Legislation**

A number of statutes related to Oregon's newborn screening program are currently in place.

*Oregon Revised Statute (ORS) 433.285* requires testing of infants in Oregon for metabolic conditions as specified by Department of Human Services/Health Services (DHS/HS), unless parents decline due to religious reasons. It also gives DHS/HS authority to determine testing and follow-up protocol.

*ORS 433.290* requires DHS/HS to conduct educational programs regarding metabolic diseases to physicians, hospitals, public health nurses, parents of newborn children, and the public.

*ORS 433.295* requires all cases of PKU to be reported to DHS/HS on forms supplied by DHS/HS.

*ORS 192.537* allows the lab to store newborn screening samples for up to one year for quality control purposes. The OSPHL is licensed as a clinical laboratory under Oregon law (ORS 438), holds a federal CLIA certificate, and is accredited by the College of American Pathologists (CAP).

*House Bill 2268* (passed in 2001) amended ORS 431.310 to allow DHS/HS to increase the fee cap on newborn screening from \$16 to \$30 per specimen to cover the implementation of CAH and MS/MS for an additional 20+ disorders.

In addition to laws mandating screening and defining the DHS/HS role, statutes also include mandatory insurance reimbursement for clinical services and medical foods related to inborn errors of metabolism, including those identified through newborn screening (ORS 743.726).

## **Data Collection, Analysis, and Utilization**

OSPHL uses Neometrics software for screening data collection and analysis. Recent efforts have included making screening data available online to hospitals and practitioners through a secure *WebRad* system. As of August 2002, this system is operational in a testing mode.

Abnormal metabolic screening results are followed in an Oracle-based database, referred to as the *Case Management System*. This is largely a short-term follow-up system to ensure that children are connected with appropriate medical

services according to established protocols. At this time, the lab does not have long-term follow-up capacity but has expressed interest in acquiring this capacity.

In early 2002 the Oregon Newborn Screening Program began participating in a DHS/HS pilot study to link several strands of newborn data including electronic birth certificates, newborn hearing screening, and metabolic screening information, using the screening number from the metabolic kits as the unique identifier. Three private hospitals were recruited for participation and have been working closely with DHS/HS staff on data-sharing mechanisms. One hospital is sending newborn hearing screening information to the OSPHL via metabolic screening cards for entry into the Neometrics data system; two hospitals are reporting hearing screening to DHS/HS electronically. Newborn record linking can help to ensure that no child is missed in the metabolic or hearing screening process. Eventually record linking may also reduce redundant data collection at the hospital and program level. The initial goal of the pilot study, however, is to determine if it is possible to accurately link the various strands of information. If the pilot study is successful, plans will be developed to extend data linking to other hospitals and to implement appropriate systems for follow-up of children who are in need of screening services.

### **Quality Assurance**

The newborn screening program maintains a comprehensive quality assurance and control program. In addition to meeting CAP accreditation and CLIA certification standards for participating in analytical proficiency testing, the lab monitors the quality of pre-analytical screening practices such as timing of sample collection, completeness of patient data, adequacy of sample, and transit time. The lab provides monthly practice profiles to hospitals and other birthing facilities. These profiles include information about number of specimens submitted, number submitted without error, and number/type of error. This feedback is critical to decrease the rate of errors and missed children. The lab also follows up with hospitals when a specimen is sent in as a “second specimen” and no first specimen was recorded. In addition to the facility profiles and feedback, the lab creates a monthly state-level report for feedback to each of the states in the regional program.

In addition, the newborn screening program maintains step-by-step follow-up algorithms for all the disorders for which it screens. The lab tracks all children with abnormal results until a diagnosis is made and the child is connected to medical services.

Newborn screening blood spot samples are stored for one year for quality control purposes.

## Public and Health Care Provider Education

Oregon's newborn screening program distributes a variety of written educational materials for parents, including:

- *Testing Your New Baby for Hidden Birth Defects* (The Northwest Regional Newborn Screening Program), English and Spanish
- *Technique for Neonatal Blood Sample Collection* (OSPHL), English
- *All You Need to Know About Sickle Cell Trait* (Northern California Comprehensive Sickle Cell Center-NCCSCC), English and Spanish
- *Alpha Thalassemia* (NCCSCC), English and Chinese
- *Hemoglobin E* (NCCSCC)
- *Hemoglobin C* (NCCSCC)
- *Newborn Screening* page in the "Newborn Handbook" (DHS/HS), distributed to all new parents at birth via birthing hospitals, English and Spanish

In addition, the newborn screening program maintains a *Practitioner's Manual* ([www.ohd.hr.state.or.us/nbs/nbspract/index.cfm](http://www.ohd.hr.state.or.us/nbs/nbspract/index.cfm)) and provides a variety of educational programs and information to health professionals. Materials are currently being revised/updated to include information about new disorders and MS/MS technology (e.g., *CD Summary* article on implementation of MS/MS screening sent to all licensed practitioners in August 2002, lectures at pediatric meetings and genetics meetings, etc.). In addition, representatives from Oregon's newborn screening program and state genetics program are participating in a Health Resources and Services Administration funded multi-state Maternal and Child Health Improvement Project that focuses on conducting research, identifying strategies, and developing materials which address ethical, legal, social, and financial issues surrounding the use of MS/MS for newborn screening of a culturally and ethnically diverse population.