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OREGON DEPARTMENT OF HUMAN SERVICES

SCREENING OREGON NEWBORNS FOR CYSTIC FIBROSIS

While lancing a baby's heel isn't the most hospitable way to welcome new Oregonians into the world, we do it to all Oregon newborns for a good reason: to screen for more than 30 metabolic, endocrine, and hemoglobin disorders. Screening works; for every thousand or so babies tested we detect one of these disorders. Screening requires two blood samples collected on filter paper—the first within 48 hours after birth and the second 10–14 days later.*

Cystic fibrosis (CF) is the most common lethal genetic disease among Caucasians. On November 1, Oregon joined 16 other states in heeding national recommendations¹⁻³ by implementing universal CF newborn screening. This change was also endorsed by the Oregon CF Newborn Screening Task Force in 2005. This issue of the *CD Summary* describes the reasons behind the implementation of this new screening test, and provides information about resources in Oregon that can help you care for your patients with CF.

INHERITANCE AND INCIDENCE

CF occurs in one of every 3,700 births in the U.S., and we estimate that approximately 15 Oregon infants are born each year with CF. It is caused by a defect in the normally occurring cystic fibrosis transmembrane regulator (*CFTR*) gene, which encodes a protein that regulates the transport of salts across cellular membranes. This defect leads to excessively viscous secretions that cause blocked glands, chronic respiratory obstruction, and infection.

Although there are over 1,000 different mutations of the *CFTR* gene, at least 70% of CF cases in the US are caused by one specific mutation ($\Delta F508$). Another 25% of cases result from one of about 40 other mutations, and the remaining 5% result from any of 1,000+ other mutations.⁷

CF shows automal recessive inheritance; for a child to have CF, the child must inherit a CF mutation from each parent. One in 32 people carries one *CFTR* gene with a CF mutation plus one normal *CFTR* gene. These "carriers" do not have CF. One in 3,700 newborns has two *CFTR* genes with mutations, and therefore has CF. The frequency of CF varies by race and ethnicity (see Table):

Group	CF Cases/Live Births
Caucasian	1 in 2,500–3,000
Hispanic	1 in 4,000–10,000
African American	1 in 15,000–20,000
Asian	1 in 30,000

Although CF is the most common lethal genetic disease of Caucasians, it can occur in any racial or ethnic group. In 2004, 95.3% of U.S. CF cases occurred in Caucasians, 6.7% in Hispanics, and 4.0% in African Americans (total >100% due to multiple race or ethnicity).⁴

CF DIAGNOSIS AND TREATMENT

CF diagnosis is suggested by symptoms, family history, or abnormally high levels of immunoreactive trypsinogen (IRT) in blood; confirmation of CF requires sweat chloride or genetic testing.

Early diagnosis and treatment

of CF are crucially important in improving the quality and length of life because early treatment can minimize the long-term consequences of lung involvement and malnutrition. However, the non-specificity of CF symptoms in young children (e.g., recurrent cough, wheezing, abdominal pain, loose stools, and failure to thrive) may delay diagnosis.

Newborn screening has the potential to help identify children with CF, facilitating early treatment including chest physiotherapy and inhaled medications to improve lung function and combat infection, oral pancreatic enzymes, oral or tube feedings with high-caloric supplements, and repletion of essential vitamins. Therapies that target the underlying mechanism of CF by improving salt transport across membranes are under investigation.

THE IMPORTANCE OF EARLY TREATMENT

Without newborn screening, a very small percentage of infants with CF are diagnosed *in utero* by prenatal testing, and another 15–20% are diagnosed soon after birth when they suffer complete intestinal obstruction. The remaining 80–85% go undiagnosed for months or years. In the US, the median age at clinical diagnosis of CF is 14½ months; with newborn screening the median age at diagnosis is 2 weeks. Babies diagnosed based on clinical symptoms, as opposed to newborn screening, are significantly more likely to suffer from malnutrition and vitamin deficiencies, which can harm future cognitive function.^{4,5} The frequent, severe respiratory infections in

* For additional information about newborn screening and specific disorders, go to <http://www.oregon.gov/DHS/ph/nbs/index.shtml> and click on the Practitioner's Manual.



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undiagnosed children correlate with more rapid progression of lung disease.

With better understanding of the disease and improved treatment in recent decades, the median predicted age of survival for CF patients in the U.S. has risen from 14 to 33 years.¹ Recent data demonstrate that newborn screening for CF can improve child survival.⁶

SCREENING METHODS AND DIAGNOSTIC TESTING

Newborn screening for CF is performed by the Oregon State Public Health Laboratory, using the same dried blood samples collected for other newborn screening tests. Samples are tested for IRT, an indication of pancreatic obstruction that is present at birth in almost all newborns with CF. When an increased IRT level is detected the lab promptly notifies the physicians of these infants. Although an elevated IRT level on both of two newborn screens indicates a greatly increased risk of CF, in itself it is not diagnostic; a positive screening test should be followed up by sweat chloride testing by a nationally standardized method adopted by the Clinical and Laboratory Standards Institute.⁸ Eight Oregon laboratories offer sweat chloride testing (<http://oregon.gov/DHS/ph/nbs/docs/cflabs.pdf>). Approximately one-third of newborns with two elevated IRT results will

have a positive sweat chloride test, which does indicate CF. OSPHL will not test for specific CF mutations in the infant's DNA as part of the screening process; however, such testing is available from a number of reference laboratories.

CF CARE CENTERS

Oregon's has two CF Care Centers, both located in Portland, that offer multidisciplinary care consistent with the clinical practice guidelines of the national Cystic Fibrosis Foundation: the Pediatric Cystic Fibrosis Center at Oregon Health & Science University (Michael A. Wall, MD, Director, wallm@ohsu.edu, 503/494-8023) and the Affiliate Cystic Fibrosis Center at Kaiser-Permanente (Richard Cohen, MD, Director, richard.cohen@kp.org, 503/652-2880). The OHSU Center is fully accredited by the Foundation, and the center at Kaiser Permanente is accredited as an Affiliate Center. These centers provide comprehensive outpatient management of CF, including respiratory therapy, nutritional counseling, laboratory services, social work evaluations, and hospital inpatient care. Twenty-four-hour physician and staff coverage is available. Center professionals also provide consultation to the patient's primary-care and other service providers.

ADDITIONAL RESOURCES

For more detailed information about CF newborn screening, contact the Oregon State Public Health Laboratory (503/229-5882) or visit <http://oregon.gov/DHS/ph/nbs/cf.shtml>.

To request an in-service or grand rounds presentation about CF or any other aspect of newborn screening, please contact Judi Tuerck, RN, MS, Education Coordinator at 503/494-2776 or tuerckj@ohsu.edu.

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