Newborn Screening and Timely Diagnosis of Cystic Fibrosis in Montana

The goal of newborn screening is to identify infants who would benefit from early diagnostic testing and treatment to improve infants’ health outcomes. The screening tests performed with blood spots from newborn heels do not confirm diagnoses but do identify infants at high risk for whom a diagnosis should be ruled-in or ruled-out. This process and achieving this goal is illustrated by newborn screening for cystic fibrosis. Randomized trial data demonstrate improved nutritional outcomes in cystic fibrosis infants identified early through newborn screening and diagnosis rather than diagnosed clinically later in childhood. The extent to which outcome advantages from early diagnosis continue into adolescence, especially health-related quality of life, is the subject of ongoing research. This issue of Montana Public Health describes newborn screening for cystic fibrosis (CF) and provides information about resources available in Montana to help clinicians care for patients with CF.

Incidence and genetics. In Caucasians CF occurs in one of every 2500 births. It is caused by a mutation in the cystic fibrosis transmembrane regulator (CFTR) gene which is located on chromosome 7. This gene encodes a protein that regulates the transport of salts across cell membranes. The defect leads to excessively viscous secretions that cause blocked glands, chronic respiratory obstruction, and infection.

More than 1000 different mutations of the CFTR gene have been identified, but approximately 70% of CF cases in the US are caused by one specific mutation (ΔF 508). Another 25% of cases result from one of about 40 other mutations. A specific CFTR mutation that affects Hutterite persons has also been identified. Because CF shows autosomal recessive inheritance, a child with CF inherits a CF mutation from each parent. About one in 32 Caucasians are carriers of mutated CFTR gene, but these carriers do not have CF.

Screening for CF. Newborn screening for CF has been performed at the Montana Public Health Laboratory since 1991. Dried blood on a filter paper is tested for immunoreactive trypsinogen (IRT); an elevated IRT level is an indication of pancreatic obstruction that is present at birth in almost all newborns with CF. The normal IRT level decreases as infants get older. (Table) When an elevated IRT level is found the laboratory notifies the newborn’s physician and requests a second blood spot so that a second IRT test can be performed. If both the initial and second IRT levels are elevated these results indicate a greatly increased risk of CF. However, these screening tests are not diagnostic and must be followed by sweat chloride testing by a standardized method to rule-in the diagnosis. Also, no screening test is perfect. Infants with symptoms consistent with CF should be considered for diagnostic testing regardless of newborn screening IRT results.

<table>
<thead>
<tr>
<th>Age</th>
<th>Normal value (ng/ml)</th>
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<tbody>
<tr>
<td>7 days or less</td>
<td>&lt;= 100</td>
</tr>
<tr>
<td>8-21 days</td>
<td>&lt;= 80</td>
</tr>
<tr>
<td>More than 21 days</td>
<td>&lt;= 70</td>
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Testing for specific CFTR mutations is not done routinely by the Montana Newborn Screening (NBS) Program, although this testing is available at reference laboratories. Because sweat chloride testing is difficult to administer to low birth weight (less than 1500 grams) babies, when these newborns have two elevated IRT results the MT NBS Program does provide for a CF DNA mutation panel test.

During 2008-2010 the MT NBS Program identified 11 newborns with two elevated IRT results, and 9 of these were subsequently diagnosed with CF.

Consultation and support for diagnosis and treatment. Treatment for babies and children with CF can be quite complex and early initiation of this treatment can greatly improve both the quality and length of life. Among the major goals are to minimize long-term consequences of lung involvement and malnutrition. Early treatment includes chest physiotherapy and inhaled medications (to improve lung function and prevent infections), oral pancreatic enzymes and oral or tube feedings with high-caloric supplements and essential vitamins (to assure adequate nutrition). Because these early treatments have been so successful and life expectancy for persons with CF has increased dramatically, treatment and support for adolescents and adults with CF has become another challenge for which expert clinicians can provide essential consultation and support.

In order to assure the availability of expert consultation regarding diagnosis and treatment for CF, DPHHS has
contracted with Jerimiah Lysinger, MD, Director of the CF Center at Billings Clinic. (see Recommendations box, below, for contact information).

**Interdisciplinary CF Clinics** The DPHHS Children’s Special Health Services (CSHS) Program supports regional CF clinics in Missoula, Great Falls, and Billings. These clinics are available regardless of patient’s ability to pay; limited financial assistance for medical care is available through CSHS.

**Genetic counseling for CF.** Many important questions need to be addressed with parents advised by their baby’s physician that their baby has elevated IRT screening results. Answers to questions about the genetics can be complex and parents benefit from thorough, unhurried answers to their questions. Most babies with elevated initial and second IRT levels will either be affected with CF or will be unaffected carriers of the CF trait. Genetic counseling is essential to help parents understand the meaning of both screening and diagnostic test results. Achieving these parental communication goals requires expertise.

In order to assure the availability of expert genetic counseling for parents and timely consultation for clinicians, DPHHS has contracted with Shodair Children’s Hospital Genetic Services (See Recommendations box, below, for contact information).

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### Recommendations for health care providers

- Screen all newborns for CF and the other required NBS conditions.
- If you are not certain that a newborn screening bloodspot was submitted by the nursery for your patient call the Montana Public Health Laboratory (800-821-7284) to confirm, or simply submit another specimen.
- If a second specimen is requested, please have the specimen submitted in a timely manner.
- If questions about diagnosis or treatment, clinicians are encouraged to contact Jerimiah Lysinger, MD or Rosalie Bush, RN, MSN at 406-235-5137.
- If consultation desired for genetic counseling, clinicians are encouraged to contact Shodair Children’s Hospital Genetic Services at 800-447-6614.

For more information, contact the Montana Newborn Screening Program, 800-821-7284, or the CSHS Program, 800-762-9891.

### References:


2,275 copies of this public document were published at an estimated cost of $0.67 per copy, for a total cost of $1524.25, which includes $518.49 for printing and $1005.76 for distribution.