

## **Lifesaving clues found in drop of baby's blood: Expanded testing of infants pays off**

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Had Noah O'Connell been born four months earlier, his brain probably would have begun to disintegrate from a genetic defect that turned food into poisonous wastes.

But he was spared mental retardation and possibly early death because of Illinois' recently expanded newborn screening program that picked up his disorder in time for him to be put on a brain-saving diet.

Noah is among a growing number of children with a variety of severe, inherited metabolic disorders who are now being diagnosed at the surprising rate of about one a week in Illinois.

Noah is one of the first infants in Illinois to be diagnosed under the revamped statewide newborn-screening program. Initiated 17 months ago, the expanded program more than quintupled the number of diagnosable genetic disorders for which all newborns are routinely tested.

State law requires screening for potentially devastating genetic disorders, although parents can refuse the tests by signing a waiver. Previous screening included tests for only six disorders.

But new technology, called tandem mass spectrometry, greatly increased the number of disorders that can easily be detected. The new system enabled Illinois to add 27 metabolic disorders to the newborn screening program.

The technology breaks a dried drop of blood into millions of molecules that are analyzed to identify abnormal body chemistry caused by malfunctioning genes that can derail development and mental function.

The single drop of blood taken from Noah's heel-stick immediately after birth was quickly tested for 33 genetic disorders. A preliminary diagnosis was made in two weeks and subsequent tests to verify the errant ASA enzyme defect were made a week later. It changed Noah's future.

"He's right on target for normal development," said Noah's mother, Cris O'Connell, 29, of Elmhurst. Noah even seems to like the special formula that substitutes safe nutrients for potentially deadly ones.

O'Connell knows Noah had a close call, especially after she had a frightening glimpse of the future that might have been his.

Frantically searching for information about her son's genetic mishap, O'Connell began contacting the few mothers around the country whose children had been diagnosed with the same problem. She was stunned.

"It was really scary," she said. "It was something I had never heard of. When I went on the Internet to reach out to other parents to see how their kids were doing, I found most of their stories were so crippling. The children were developmentally delayed. A lot of them are brain damaged and many of them have died."

### **Diagnosis too late**

It was too late for those children. They had been diagnosed after their metabolic disorder had time to take hold. They were born with an enzyme deficiency called argininosuccinic aciduria, which prevents food from being properly metabolized, thereby allowing deadly ammonia to build up in their brains.

They had not been screened at birth. Although they started life seemingly robust and healthy, they rapidly deteriorated before their parents' eyes, the promise and brightness of infancy dimming more and more as irreversible brain damage set in.

"We're literally taking on average a kid a week who would have had a very dim future, if it wasn't for newborn screening, and allowing that kid in many instances to grow up happy and healthy--to have a chance at a relatively normal life," said Mark Schmidt, chief of the Illinois State Department of Public Health's division of Children's Health and Safety, which oversees newborn screening.

Of the 186,000 infants born annually in Illinois, the expanded newborn screening program diagnoses one metabolic disorder for roughly every 3,500 births.

"Historically we talked about these disorders as being rare, but now we are finding that collectively they're fairly common," said Noah's physician, Dr. George Hoganson, chief of clinical genetics and director of the biochemical genetics laboratory at the University of Illinois at Chicago.

"I'm in a very unique position to be involved with families early in an infant's life to diagnose medical problems that would result in mental retardation or other serious problems, and to prevent them," said Hoganson, chairman of Illinois' Newborn Screening Advisory Committee.

The nation's first newborn screening started in 1962 when researchers discovered that phenylketonuria, a brain destroying metabolic error, could be

prevented by a strict diet eliminating such common foods as milk and meat that contain the amino acid phenylalanine.

Most metabolic genetic errors that threaten newborns involve deficiencies in enzymes that are designed to break down food into nutrients the body can use. Instead, waste products build up in cells, especially in the brain. Cells become clogged, their function grinds to a halt, and they die off.

Because infants on PKU diets develop normally into adulthood, scientists believe that children with other genetic errors who stick to restricted diets all their lives will do the same.

### **Not all tests mandated**

Every state soon adopted PKU screening. More tests were gradually added but critics maintain that many states are failing to mandate all the tests that are currently available.

"It really troubles and angers me that the means to detect these disorders already exist, the treatments for them already exist, and people are ignoring them," said Jana Monaco, 38 of Lake Ridge, Va.

Two and a half years ago Monaco's 6-year-old son developed a serious upset stomach that triggered a dormant metabolic disorder. The disorder, isovaleric acidemia, left Stephen severely brain damaged.

During her next pregnancy Monaco had prenatal genetic testing done. The fetus carried the same defective gene as Stephen. Immediately after birth Caroline was put on a diet that strictly limited her intake of proteins containing the amino acid leucine.

Now 14 months old, Caroline is "happy, bright and normal. She won't share Stephen's fate," Monaco said. "He was a normal child running around, playing with his big brothers. Now here he is, he's legally blind and he doesn't talk. It didn't have to be this way."

### **Most states do fewer tests**

A survey of state newborn screening programs as of December 2002, conducted by the U.S. General Accounting Office, found that the number of tests included in screening range from four to 36 with most states doing eight or less. In Virginia newborn screening covers eight disorders. An estimated 4 million infants are born each year in the U.S.

The 33 tests now offered in Illinois' newborn screening program resulted in the diagnosis of 344 genetic disorders in the first full year of the expanded program,

a rate of 1 disorder for every 541 births. Of these, 44 cases plus nine probable ones were metabolic errors. Older tests such as those for PKU, sickle cell disease, hypothyroidism and galactosemia picked up the rest.

"A lot of the diseases we're detecting could prove very damaging," said Schmidt. "We're talking about severe developmental delays, mental retardation and even death if undiagnosed. But if diagnosed, many are manageable medically by changes in diet, food supplements and other treatments."

The state charges hospitals a fee of \$47 to perform screening on every newborn. Private health insurance or Medicaid usually pays the fee. In addition to covering the cost of screening, the money pays for a staff that monitors the progress of infants diagnosed with genetic disorders and for special formulas many of them require.

Annually, \$7.5 million is spent on newborn screening in Illinois, a bargain in terms of future medical savings, Schmidt said.

No one can measure the value to an individual who has been spared a damaged brain or other severe disability. But researchers are trying to figure the costs of such programs versus their benefits.

An early study in Illinois found PKU testing and treatment saves the state \$75,000 a year for each child who otherwise would need expensive custodial care. Another early study by the Centers for Disease Control and Prevention concluded that every \$1 spent on newborn screening saves \$8.90 in health costs that otherwise would have been needed.

The newest study, reported last month in the Journal of the American Medical Association, found that expanded newborn screening is a lifesaver for children with metabolic errors.

"The study shows that newborn screening prevents the severe consequences of these disorders," said Dr. Susan E. Waisbren of Harvard and Children's Hospital Boston, lead author.

"There are fewer hospitalizations in children identified by newborn screening, their parents have less stress and they report fewer effects on their daily life," she said.

### **Early screening pays off**

The study compared 50 infants identified with genetic disorders by newborn screening with 33 infants who were not screened but who were diagnosed later after symptoms appeared. At the age of 6 months, only 1 infant (2 percent) in the newborn screening group suffered mental retardation, but 8 children (24 percent)

in the late diagnosis group were retarded.

Ninety-four other screened infants in the study had false-positive results, which means that on subsequent follow-up tests no genetic disorder was found.

While false-positive findings may increase stress levels in parents, that stress was alleviated in couples who received clear explanations from knowledgeable people that their children did not have a disease, Waisbren said.

Because the lack of newborn screening had such a devastating effect on Stephen, Monaco now gives a special gift at baby showers for friends and relatives in other states that require fewer tests--a \$25 screening kit that is used when a newborn has a needle stick for PKU. The blood sample is sent to a laboratory for analysis and the results returned to parents.

### **Newborn screening in Illinois**

Illinois requires all newborns to be screened for nine types of disorders before they leave the hospital. Three of those types, which includes 27 disorders, were added last year due to a new technology called tandem mass spectrometry that allows for easy detection. The technology analyzes a dried drop of blood to identify abnormal body chemistry.

Approximate number screened in Illinois annually: 186,000

**NEWLY ADDED CATEGORIES Effective July 1, 2002**

**DISORDER: Amino acid (6 disorders):** Class of disorders that are caused by the inability to process amino acids, the building blocks of proteins. Can lead to brain damage or death.

2003 CASES: 5

INCIDENCE RATES: 1 in 150,000 births

**DISORDER: Fatty acid oxidation (11 disorders):** Inability to produce specific enzymes that burn fat for energy.

2003 CASES: 14

INCIDENCE RATES: Up to 1 in 10,000

**DISORDER: Organic acid (10 disorders):** Inability to produce enzyme that removes certain waste products from blood.

2003 CASES: 25

INCIDENCE RATES: Up to 1 in 100,000

#### EXISTING CATEGORIES

DISORDER: Biotinidase deficiency: Born without enzyme that recycles a vitamin called biotin that assists in nerve functions. Can lead to neurological problems.

2003 CASES: 1

INCIDENCE RATES: 1 in 150,000

DISORDER: Congenital adrenal hyperplasia: Inability to produce certain hormones, which regulate the body's response to stress and fluid balance.

2003 CASES: 10

INCIDENCE RATES: 1 in 15,000

DISORDER: Galactosemia: Lack of a liver enzyme causes inability to process a certain part of milk sugar called galactose. Can lead to death, liver damage or cataract.

2003 CASES: 30

INCIDENCE RATES: 1 in 60,000

DISORDER: Hypothyroidism: Underproduction or lack of thyroid hormone, which is important for brain growth.

2003 CASES: 94

INCIDENCE RATES: 1 in 3,500

DISORDER: Phenylketonuria: Lack of an enzyme required to digest an amino acid called phenylalanine. Can cause severe mental retardation.

2003 CASES: 23

INCIDENCE RATES: 1 in 12,000

DISORDER: Sickle cell disease: Malformation of red blood cells causing a severe form of anemia. Most prevalent in African-Americans.

Can lead to strokes and other life-threatening diseases.

2003 CASES: 142

INCIDENCE RATES: 1 in 375\*

\*For African-American babies, who are most often affected.

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