

A Project Report of the Michigan Newborn Screening Program A pilot project to explore additional data sources for identification of false-negative cases of CH and CAH

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The Endocrine project of the Region 4 Genetics Collaborative conducted a meeting of endocrinologists and state newborn screening laboratory and program personnel in May 2007. At the meeting, attendees discussed the difficulty of identifying false negatives for the newborn screening endocrine disorders, Congenital Hypothyroidism (CH) and Congenital Adrenal Hyperplasia (CAH). When Newborn Screening Programs (NBS) modify their screening algorithms to decrease the rate of false-positives and increase positive-predictive-value the program's ability to accurately determine the false-negative rate increases in importance.

Much of the current awareness of false-negative cases is a result of physician reports of late diagnosed cases of CH or CAH to the NBS program. Other attendees knew of national efforts to identify possible false-negative cases by surveying endocrinologists and asking for information regarding cases that were detected outside of the NBS process. Attendees felt that there might be other useful databases that would assist in identifying false-negative cases.

The Michigan Newborn Screening Program screens approximately 125,000 babies per year and for the endocrine tests uses:

1. For CAH, evaluates 17-OHP and incorporates as a second tier a steroid profile conducted at the Mayo's Biochemical Genetics Laboratory in Rochester, MN; and
2. For CH, uses a primary TSH screen but does not evaluate T4 as a component of the initial screen.

After the meeting, Michigan NBS program staff identified several possible useful data sources that might contain information that would identify false-negatives. One such source was Michigan's Children's Special Health Care Services Program (CSHCS). CSHCS provides funding and case management for approximately 35,000 children enrolled in the program.

The CSHCS linked files for 2005 and 2006 were searched and 8 CAH cases and 33 CH cases were identified. These cases were then matched to the newborn screening database.

All 8 CAH cases were previously screened and diagnosed by the newborn screening program.

Of the 33 CH cases found in the CSHCS linked files, 31 were in the NBS database and 2 were not. CSHCS case reviews found that the 2 cases not in the NBS database were born out-of-state.

Of the 31 CH cases in the NBS database, 22 had abnormal CH screens and were diagnosed with CH. The remaining 9 had normal initial CH screens. A review of the 9 cases found that 8 of the 9

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were in the NICU and 1 was a home birth. Of the 8 NICU cases, 2 had evidence of Down Syndrome, 1 had neurosurgery shortly after birth, and one died at approximately 7 months of non-CH related conditions.

This review of a significant cross section of Michigan's children with disabilities, suggests that most cases of CH missed by NBS (false negatives) are associated with NICU births and two had Down Syndrome. This is not surprising in view of the known association between both prematurity and Down Syndrome and delayed TSH rise in cases of CH. It is significant that, with the exception of the home birth, none of the missed cases were non-NICU newborns. These observations also confirm the need for Michigan's recently implemented program of repeat screening of newborns in the NICU at 14 and 30 days. Since the start of NICU re-screening, 16 cases of CH have been diagnosed in the NICU based on an abnormal re-screen following an initial normal screen (as of 5/1/2008).

A rough estimate of the resources required to conduct this activity is as follows:

Newborn quality assurance coordinator	4 hours
CSHCS epidemiologist	4 hours
Medically trained epidemiologist	4 hours
Newborn screening program manager	1 hour

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