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Cystic Fibrosis Research News

Title: Children with Non CF Causing Mutations detected by Newborn Screening are Healthy

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What was your research question?

The Clinical and Functional TRanslation of CFTR project (CFTR2) classified some cystic fibrosis gene mutations as non-disease causing. Our research question was: do children identified by newborn screening carrying one CF-causing mutation and one non CF-causing mutation show CF-like signs and symptoms?

Why is this important?

Some but not all mutations in the CF gene cause CF. The CFTR2 is an ambitious worldwide project with a mission to classify which of nearly 2,000 CF mutations so far identified are CF-causing, non CF-causing, or varying in disease severity. The CFTR2 uses clinical data from CF patients, genetic information from fathers of CF cases, and data on how mutated CF cells function to make this classification. It is important to determine whether the classification of non CF-causing mutation is accurate, so that clinicians can be certain that infants detected with these mutations through newborn screening can be counseled and discharged, instead of followed unnecessarily.

What did you do?

We studied the California CF Newborn Screening database looking at all children born from July 2007 to July 2011 with a positive CF screening test and followed by all 17 CF centers for at least 2 years. We compared and selected between children with two CF-causing mutations (CF-C group) and those with one CF-causing and one or more non CF-causing mutations (N-CF group), looking for various signs and symptoms usually seen in CF.

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What did you find?

There were 226 newborns identified by screening with two CF-causing mutations (CF-C group) and 57 with one CF-causing and one or more non CF-causing mutations (N-CF group). Children in the N-CF group were healthier compared to those in the CF-C group, based on: sweat chloride levels (measure of the concentration of salt in the sweat), fecal elastase (measure of digestive enzyme production), and persistent *Pseudomonas aeruginosa* infection (a common bacteria in CF). Differences between the groups were also seen for birth weight and growth. No child in the N-CF group was diagnosed with CF.

What does this mean and reasons for caution?

These findings among children 6 years and under are consistent with the CFTR2 classifications of CF causing and non CF-causing mutations, confirming that children with N-CF mutations do not have disease. These results help inform families, CF Care Centers, and the screening program about how to best refer and care for children with a positive CF newborn screening. In an effort to ease parents concern, new methods have been adopted for referral of newborns having one CF-causing mutation and one or more non CF-causing mutation, which involves a visit with a genetic counselor at a CF center and discharge from care. This measure avoids unnecessary visits and procedures to these children.

What's next?

This study evaluated seven different mutations as non CF-causing; however, there will be more mutations that CFTR2 will determine to be non CF-causing. Development of new techniques to measure each individual's *CFTR* function accurately would be valuable in better understanding non CF-causing and other mutations, and predicting future health outcomes.

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