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ORIGINAL RESEARCH

Long-term Evaluation of Genetic Counseling Following False-Positive Newborn Screen for Cystic Fibrosis

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Abstract This cross-sectional mixed method study was a long-term follow-up evaluation of families who participated in an earlier survey of their understanding of cystic fibrosis (CF) genetics and their infants' false-positive CF newborn screening (NBS) results. Thirty-seven of the original 138 parents participated in the follow-up telephone survey. Results showed parents who received genetic counseling at the time of their infants' diagnostic sweat tests had significantly higher long-term retention of genetic knowledge than those without genetic counseling. However, both groups still had misconceptions and lacked accurate information about the actual risk associated with being a CF carrier. Most parents either had already informed (65%) or planned to inform (19%) their children about the child's carrier status. Mean child age at the time of disclosure was 9.2 years. Situational prompts were the most common reasons for informing their children. Neither parental knowledge, medical literacy, nor parental education predicted whether parents informed their children about their carrier status. False-positive NBS results for CF were not associated with parental perceptions of child vulnerability 11–14 years after the testing. Although the sample from this study was small, these findings underscore the benefits of genetic counseling at the time of the diagnostic sweat test and offer information that can assist parents in talking with their children about the implications of having one CFTR mutation.

Keywords Cystic fibrosis · False-positive · Genetic counseling · Newborn screening · Psychosocial

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Introduction

Overview of Cystic Fibrosis

Cystic Fibrosis (CF) is a potentially life-shortening autosomal recessive genetic condition affecting approximately one in 3,500 live births in the United States (US). Mutations in the CF transmembrane conductance regulator (CFTR) gene produce an abnormal protein that causes a functional defect in the chloride channel. Over 1,600 mutations have been found in the CFTR allele (Moskowitz et al. 2008). Although the phenotypic presentation can be influenced by a combination of genetic and environmental factors, patients with CF typically have chronic pancreatic insufficiency and recurrent exacerbations of pulmonary bacterial infections that lead to serious morbidity and mortality (Moskowitz et al. 2008). Although medical advances have significantly improved the longevity of patients with CF, the diagnosis is still associated with a limited life span of about 37 years (Cystic Fibrosis Foundation [CFF] 2008).

CF Newborn Screening and Diagnosis

With mounting evidence of health benefits associated with newborn screening (NBS) and diagnosis of CF (Farrell et

al. 2001a, b, 2005; Collins et al. 2008), in 1991 Wisconsin became the first state to include DNA testing in NBS for CF. The initial program, conducted on a research basis, became standard practice in 1994 and it has served as a model for CF NBS nationally and internationally. As of January 2010, all 50 states and the District of Columbia include CF on NBS panels (National Newborn Screening and Genetics Resource Center [NNSGRC] 2009). While NBS algorithms vary by state, in Wisconsin where the current study was conducted, the two-tiered screening procedure begins with a measurement of immunoreactive trypsinogen (IRT) in a blood sample obtained from a heel prick during the newborn's first days of life. IRT levels falling in the highest 4% of each day are entered into the second tier which involves genetic testing. This method adjusts for seasonal fluctuations of IRT levels and the 96th percentile optimizes the ratio of true to false-positive results (Kloosterboer et al. 2009; Rock et al. 2005). The DNA analysis in Wisconsin currently identifies 23 of the most common CFTR mutations, which account for about 88% of cases (Amos et al. 2006). If one or two mutations are found, the primary care provider is notified and s/he contacts the parents to recommend a sweat test, the gold standard CF diagnostic test. For infants less than 6 months (Farrell et al. 2008), a sweat chloride level ≥60 mmol/L is diagnostic of CF. When levels fall in the intermediate range of 30 to 59 mmol/L, either the sweat test is repeated or additional genetic testing is performed. CF is unlikely in infants with sweat chloride levels <30 mmol/L, which is considered to be the normal range. The presence of one CFTR mutation identified through NBS plus a negative sweat test, referred to as a false-positive NBS, indicates the infant is a CF carrier and does not have the illness. Although the rate of false-positive results can vary by population and screening method, the majority (about 91% of all positive NBS results; 97% of NBS results that identify one CFTR mutation) prove to be false-positive (Rock et al. 2005).

Genetic Counseling

Since the introduction of DNA analysis into NBS for CF and resulting incidental detection of infants who are heterozygote carriers of one CFTR mutation, providing genetic counseling to families at the time of the sweat test has become standard practice. This counseling includes an explanation of NBS procedures, meaning of test results, genetics of CF, and the reproductive implications of being a CF carrier (Wheeler et al. 2001). A survey of CF Centers across the US found 76% of NBS programs reportedly provided counseling services to families with positive NBS results (Farrell et al. 2001a). Although the American Academy of Pediatrics (2001) recommends communicating the incidental carrier status of minors to the parents, it does not state who or how such results should be shared with the children. In a review of 14 guidelines for carrier testing in minors derived from 24 groups internationally, Borry et al. (2006) noted that the French National Consultative Ethics Committee for Health and Life Science, the Canadian Paediatric Society and the German Society of Human Genetics explicitly confer parents with the responsibility for informing their children about their carrier status. Until now, there have been no long-term studies documenting whether parents follow through on this recommendation and, if so, how parents make decisions about the best time and approach to convey this information.

The literature showed mixed results regarding parents' understanding and recall of genetic information received at the time of the sweat testing. Lewis et al. (2006) evaluated the effectiveness of the genetic counseling provided to parents whose infants were found to be heterozygote carriers of one CFTR mutation through NBS in Victoria, Australia. The results of questionnaires completed by the parents showed that only 60% of participants correctly identified the one in four chance of having a child with CF when both parents are carriers. Ciske et al. (2001) conducted a similar survey in Wisconsin, United States. In that investigation, parents were asked questions assessing their knowledge of the genetics of CF as well as their understanding of their child's carrier status. They found 88.3% of parents understood their child was a carrier, 12.4% of parents were unsure that at least one of them was a carrier of the CF mutation, and only 57% of parents knew that their child had a one in four chance of having a child with CF if the other parent also carried a CF mutation. This study also noted significantly higher knowledge scores on the portion of the questionnaire related to CF genetics and inheritance in parents who received genetic counseling at the time of the sweat test as compared with those who did not. Although genetic counseling has been associated with improving parental knowledge shortly after the diagnostic sweat test, it is not known how well parents retain this information more than a decade after testing, when the information is most relevant to their children. Parsons and colleagues (2003) found that parents appreciated having the information about their children's carrier status because it offered them an opportunity to inform other family members about genetic risk as well as their children in the future. However, there is no empirical evidence documenting whether and how such communication with their children took place.

Informing Children About Genetic Conditions

The study of genetic risk communication with children or adolescents is very limited. Gallo et al. (2005) interviewed

139 parents of children between 3.7 and 15.9 years diagnosed with inherited diseases to learn if and how they informed their children about their genetic conditions. Almost half of the parents reportedly informed their children about the condition and its inheritance. Parents explained that their decisions to do so were based on their appraisal of the child's maturity and capacity to comprehend the information. When talking with their children, parents selectively chose aspects of the conditions that would not frighten the child. The main reason for not sharing details was the belief that the child was "too young" or immature to understand the information. The authors noted that health professionals failed to provide the majority of parents (80%) with support or strategies about how to inform their children about these genetic conditions. Metcalfe et al. (2008) conducted a meta analysis of what parents tell their children about inherited genetic risk, why parents shared the information, and the children's understanding. Many parents waited until their children initiated the discussion about genetic issues or the conversation was prompted by a specific life event, such as marriage or first sexual experience. Other parents reported that they started introducing some facts about the genetic condition during the preschool years. To gain a better understanding of children's knowledge about CF and their opinions about carrier testing, Cobb et al. (1991) surveyed a randomly selected group of high school students aged 14–16. Eighty-six percent of the respondents believed that carrier detection should be offered routinely to future parents. These studies suggest that parents want to share genetic information with their children and adolescents possess sufficient cognitive development to understand CF genetics and the psychological maturity to appreciate the implications of being a carrier.

Vulnerable Child Syndrome

The "vulnerable child syndrome" (VCS) was first described by Green and Solnit (1964) who found that parents of children who had a life threatening episode viewed their children as susceptible to illness or harm. Consequently, these parents reported "overprotective" behaviors, such as checking their children in the middle of the night and interpreting minor symptoms as signs of serious illness. Forsyth and Canny (1991) surveyed mothers who had a child with feeding and crying problems in early infancy. They found that about 3 years later, 20% of the mothers still perceived the children as vulnerable. They also found a significant relationship between vulnerable child syndrome and childhood behavior problems. Characteristics of the VCS also have been associated with false-positive results from NBS for hearing impairment (Poulakis et al. 2003) and metabolic disorders (Waisbren et al. 2003; Gurian et al. 2006), as well as genetic risk for type 1 diabetes (Kerruish et al. 2007). The current report addresses the question about whether there is long-term risk of parental perceptions of child vulnerability following false-positive NBS for CF.

Family Development Theory

Family development theory offers a conceptual framework to understand how parents might decide when to inform their children about their CF carrier status (Fiedman et al. 2003). As children approach adolescence they enter a stage of formal cognitive operations that offer them the capacity to grasp abstract concepts, such as recessive genetics, and the ability to comprehend the implications. During adolescence they become physiologically able to reproduce and socially interested in seeking life partners. Thus, their genetic risk for having a child with CF becomes increasingly salient. (Cole and Cole 2001). The recognition of their child's emerging maturity combined with anticipation of the developmental tasks of adolescence might prompt parents to inform their children about their CF carrier status.

Purpose and Hypotheses

The first cohort of children to be screened for CF using DNA analysis through the Wisconsin NBS program have reached adolescence and young adulthood, a time when parents may choose to inform their children of their carrier status. This study was designed to determine whether and how parents make use of genetic information about CF that they received more than a decade earlier. This study answered the research questions: Do parents inform their children about their carrier status? If so, when, how, and what do they convey to their children? What are the consequences of informing children? If not, what are the reasons? We also hypothesized the following: H_1 parental medical literacy, education, and the presence of genetic counseling at the time of the sweat test would be positively associated with parental knowledge of CF genetics, H_2 parents with greater knowledge of CF genetics would be more likely to have already informed their children about their child's carrier status at the time of data collection, and H_3 parents with greater knowledge scores would perceive their child to be less vulnerable than parents with lower knowledge.

Methods

Design

This cross-sectional mixed method study was designed as a long-term follow-up evaluation for an earlier study of

genetic counseling (Ciske et al. 2001). In the original study, 138 families were surveyed regarding their understanding of CF genetics and their infants' false-positive CF NBS results. The University of Wisconsin-Madison Health Sciences Institutional Review Board approved the original and current protocol.

Recruitment

In the original study (Ciske et al. 2001), parents of children identified as CF carriers through the NBS for CF in Wisconsin between July 1994 and December 1997 were recruited through the Wisconsin State Laboratory of Hygiene. A letter describing the study along with an opt-in card was mailed to potential participants requesting their permission for the researchers to send parents the study questionnaire. Those parents, who returned the card indicating that they would be willing to participate in the study, received the survey to complete and return by mail. Participants in the original study received genetic counseling if their infants had their diagnostic sweat tests performed at one of two certified CF Centers.

At the conclusion of the earlier study in 1999, the researchers mailed each family a letter asking them to contact the researchers by mail or telephone if they wanted no future contact with the research team. Since none of the parents replied to this request, all families from the original study were considered potential participants. Parents who did not participate in the original study or did not speak English were excluded from the study. One of the investigators for this study was the principal investigator for the original study and, therefore, provided access to participant information from the earlier study. Current family contact information (e.g. telephone number) was obtained through internet searches on White Pages. We found contact information for 94 (68%) parents from the original study. Attempts to reach each parent were made three times, unless the first attempt revealed a wrong or disconnected number. One parent of each child was contacted for this survey. Two genetic counseling graduate students, who conducted the telephone interviews, were able to reach 40 (29%) parents. At the beginning of the interview, a script was used to explain the study's purpose, potential risks, benefits, and voluntary nature of participation. The caller answered parents' questions and invited them to participate. Upon receipt of verbal consent, the parents were asked to state their child's date of birth to verify the accuracy of the contact. With verification completed, data collection continued. Three parents declined to participate. Thus, the final sample included 37 (27%) of the 138 participants in the original study. Table 1 details participant demographics.

Sample

All 37 participants self-identified as Caucasian, were mostly female, and were highly educated. Participant ages ranged from 30 to 55 years, with a mean age of 43.9. The ages of children identified as carriers ranged from 11 to 14 years with a mean age of 12.5 years and were almost equal distributed among gender, 20 (54%) females and 17 males (46%). As illustrated in Table 1, this sample was representative of the 138 families surveyed in original study. The length of time between the NBS and contact for this study ranged from 11 to 14 years.

Procedure and Materials

Several instruments were combined to form a 67-item interview that lasted about 15 min. The interviewer manually recorded parental responses to close-ended and multiple choice questions whereas responses to the semi-structured items were audio-taped. Demographic information included parent's age, gender, education, and racial/ethnic background. An 18-item *Knowledge Questionnaire* was adapted from instruments used in previous studies (Ciske et al. 2001; Tluczek et al. 1992) and modified for this study. It consisted of 18 multiple choice and yes/no/unsure questions regarding the genetics of CF (e.g. If your child has a baby with another person who is a CF carrier, what are the chances the baby will have CF?) and their child's sweat test results. Four of the knowledge items were excluded because they were not applicable to this cohort (e.g. Both of us, parents, might be carriers of the CFTR mutation). *Medical literacy* was measured by two questions adapted from previous studies (Chew et al. 2004; Morris et al. 2006). Items were rated with a Likert scales: (a) How comfortable are you filling out medical forms by yourself? Response options included 1 = not comfortable at all, 2 = somewhat comfortable, 3 = very comfortable and (b) How often do you find written information from doctor's offices difficult to understand? Response options included 1 = always, 2 = often, 3 = sometimes, 4 = rarely, 5 = never. A higher score signified greater medical literacy. The *Child Vulnerability Scale (CVS)* was incorporated into the survey to measure parents' perceptions about their children's susceptibility to illness (e.g. My child gets more colds than other children I know). The CVS consisted of 9 items, 8 of which were scored on a scale from 0 to 3 (0 = strongly disagree, 3 = strongly agree). A higher score signified increased parental perception of child vulnerability (Forsyth et al. 1996). The ninth item inquired about the child's history of having a life-threatening health problem. The literature (Forsyth et al. 1996) suggests that scores above 10 are associated with high parental concern about child's vulnerability to health problems. We added the question,

Table 1 Comparison of Parent Gender and Education between Original and Follow-up Study

Variable	Original study N=138 (%)	Follow-up study N=37 (%)	Chi-square value (df)	Exact alpha error
Gender				
Mothers	N=120 (87.6)	N=32 (86.5)	0.0327 (1)	0.8651
Fathers	N=8 (5.8)	N=5 (13.5)		
Both	N=9 (6.6)	0		
Parent education				
Some high school	N=3 (2.2)	N=1 (2.7)	3.05 (3)	0.3714
High school graduate	N=21 (15.4)	N=4 (10.8)		
Some college or vocational training	N=33 (23.5)	N=14 (37.8)		
College graduate	N=81 (58.8)	N=17 (48.6)		
Post-graduate training		N=1 (2.7)		

"Do you think that being a CF carrier has affected your child's health in any way?" Response options included yes, no, or unsure. We also developed 28 semi-structured questions to investigate *whether and how parents informed their children* about their carrier status. This portion of the interview was audio taped to accurately document participant responses.

The research team conducted directed, summative content analyses (Krippendorff 2004) of transcribed interviews to identify and quantify themes within a priori domains of when, how, and what parents communicated to their children regarding their genetic status, the consequences of informing children, and parents' plans for informing their children if they had not done so. The resulting categories and quantifiable themes were mutually exclusive and no data were excluded. After identifying and defining thematic codes, a minimum of 90% inter-rater agreement was established by the highly experienced principal investigator (PI) and the two coders who were genetic counseling graduate students. The PI also conducted random reliability checks for slippage in agreement. Documentation of whether or not the parent received *genetic counseling* at the sweat test appointment was based on self-report.

Results

Quantitative Results

Correlational analyses along with simple descriptive statistics were used to assess the hypotheses in this study. H_1 predicted that parental medical literacy, education, and the presence of genetic counseling would be positively associated with parental knowledge of CF genetics. The point-biserial correlation showed parents who received genetic counseling had statistically significantly higher knowledge scores than those who did not receive genetic counseling (r=−0.53, 95% CI=−0.73 to −0.24; Fig. 1). Table 2 shows the mean responses to individual items based on presence or absence of genetic counseling. Seventy percent of parents reported that they received genetic counseling at the time of the sweat test. Based on parent self-reports, genetic counseling was provided by certified genetic counselors (n=16, 61.5%), physicians (n=2, 7.7%), and a nurse (n=1, 3.8%). Seven parents (n=7, 27%) could not remember who provided the genetic counseling. The Pearson correlation analysis showed no statistical significance between medical literacy and parental knowledge (r=−0.05, 95% CI=−0.36 to 0.27). Although the Pearson tests suggested some association between demographic factors (parental gender, parental level of education, and religious beliefs), none reached statistical significance (Table 3). Therefore, H_1 was only partially supported because only the presence of genetic counseling was significantly correlated with parental knowledge of CF genetics.

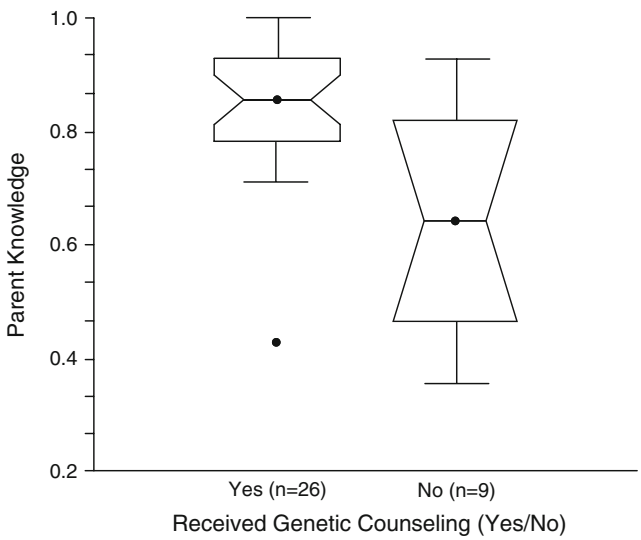

Fig. 1 Parents' Genetic Knowledge and Genetic Counseling.

Table 2 Knowledge and Genetic Counseling (GC)

	Mean (%) correct	
Item	GC Group N=26	No GC Group N=9
1. Your child had a positive CF screening blood test when he/she was a newborn and then a follow-up sweat test a few weeks later. What was the result of the sweat test? Correct: normal	23 (88)	6 (67)
2. Which of the following statements best describes your child's condition? Correct: S/he definitely does not have the disease	26 (100)	9 (100)
3. If your child has a baby with another person who is a CF carrier, what are the chances that the baby will have CF? Correct: 1 in 4	12 (46)	3 (33)
4. If both you and your partner are carriers of the CF gene, what are the chances that a future child of yours would have CF? Correct: 1 in 4	13 (50)	3 (33)
5. If only you or your partner is a carrier of the CF gene, what is the chance that a future child would have CF? Correct: zero	17 (65)	2 (22)
6. Which of the following is true of parents of a child with CF? Correct: It is due to both the father's and the mother's genes	25 (96)	7 (78)
7. A child can get CF when only one parent has the gene for it. Correct: false	23 (88)	3 (33)
8. CF does not run in families since it is not a genetic disease. Correct: false	25 (96)	6 (67)
9. If a couple has a child with CF, then both of them must have the CF gene. Correct: true	24 (92)	5 (56)
10. If a couple has no relatives with CF, they cannot have a child with CF. Correct: false	15 (58)	6 (67)
11. Our child might have cystic fibrosis. Correct: false	26 (100)	9 (100)
12. Our child is a carrier of the CF gene. Correct: true	25 (96)	8 (89)
13. Being a CF carrier may cause illness. Correct: false	23 (88)	5 (56)
14. Our child may develop CF when he/she is older. Correct: false	26 (100)	8 (89)

Two parents could not remember whether or not they had genetic counseling and were not included in this table

H_2 predicted that parents with high knowledge scores would be more likely to inform their children about the child's carrier status than those with low knowledge scores. The point-biserial test showed no relationship between CF knowledge and parent disclosure of a child's carrier status (r= −.02, 95% CI=−.35 to .30). These results did not support H_2.

H_3 predicted an inverse relationship between parental knowledge and perceived child vulnerability. The Pearson test revealed a very small positive, but not significant correlation (r=.11, 95% CI=−.22 to .41; Fig. 2). The average CVS score was 2.35. Four participants with high CVS scores (9, 10, 14, 11) were outliers from the majority of the participants. We decided to see if there was a unifying characteristic that might explain the higher scores. A closer examination of the data, ruled out a knowledge deficit because three of these participants had over 80% correct on the CF knowledge questionnaire, which was above the groups mean score (71.4%). However, all four of these participants reported a time when they feared for their

Table 3 Relationship Between Parent Demographics and CF Knowledge Performance

Demographic factor	Correlation	95% Confidence interval
Parent gender	0.26	−0.06, 0.54
Education level	0.22	−0.11, 0.50
Parent age	0.16	−0.16, 0.46
Racial/ethnic background	0.00	NA
Religious influence	−0.24	−0.52, 0.08
Presence at sweat test	0.01	−0.31, 0.33

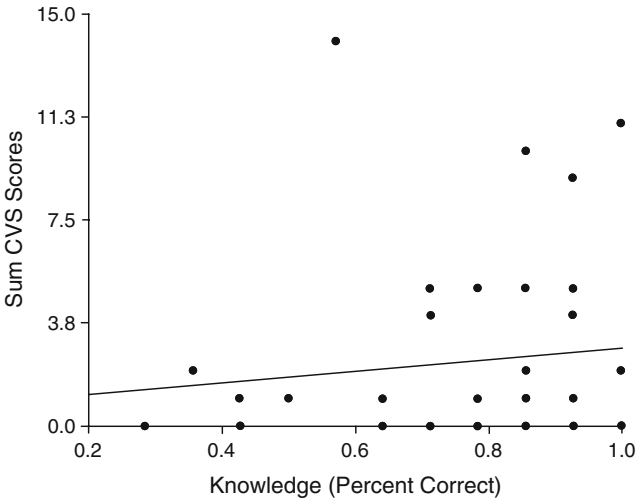

Fig. 2 Child Vulnerability Scale (CVS) and Parents' Genetic Knowledge.

children's lives, e.g. high fevers, kidney infections, and seizures. Perceptions about child vulnerability appeared to be associated with health concerns unrelated to their child's carrier status or their knowledge about CF genetics. Therefore, H_3 was not supported.

Qualitative Results

When Parents Informed Children The mean age at which children in this study were told about their carrier status was 9.2 years. Parents identified three criteria for determining the most appropriate time to inform children about their carrier status. First, parents (n=11) stated that children should be told when they are mature enough to understand the genetic information, particularly the meaning of being a carrier. The actual reported ages ranged from 8 years through the mid-adolescence. Second, parents (n=5) believed that their children needed this information before they become sexually active. Third, one parent (n=1) recognized the importance of considering the child's emotional readiness to hear this information. Three parents explained that they informed their children very early in life. For example, the newborn screening experience had been incorporated into the story about the child's birth; thus, each child knew his/her genetic status for his/her "whole life." The remaining parents (n=4) had no response.

> I believe you have to know how mature your child is.
>
> Probably mid to late adolescence...they have to understand. When they start to contemplate their future, they ought to start thinking about it.
>
> Well definitely before they become sexually active... because she has a 1 in 4 chance of having a child with cystic fibrosis if her, if whoever she's with happens to carry the gene.

How Parents Informed Children Twenty-four (65%) parents reportedly informed their children about the child's carrier status. All used a discussion format and one parent included the "diagram and literature" given to them at the time of the child's sweat test appointment. When asked "how" they told their children, parents typically described the circumstances prompting the disclosure. Four mutually exclusive themes emerged: situational prompts, spontaneous telling, normalized telling, and developmental prompts. Many parents (n=9) described some situation that prompted them to inform their children. For example, when their children were studying genetics and/or the reproductive system in health class, parents decided that it was a good opportunity to share the information. Other situational prompts included the telephone survey for this study, the child having other genetic problems, having a family member with CF, or an older sibling who was considering genetic testing.

> She was starting health class. She was starting to understand about the reproductive system...and so when she got into the health class, we talked to her about it a lot more.

Some parents (n=6) described more spontaneous conditions with no particular event that prompted them, e.g. "it just comes up in conversation." Several parents (n=3) viewed their child's carrier status as just a normal part of the child's identify. For example, they normalized the information by including it in the story of their child's birth and therefore informed their children very early in life. An important contextual factor for two of these parents was their prolonged wait for the diagnostic sweat test.

> And here you are a new mom with your first baby going my child could have this disease. It changes everything about how you feel and your baby could cry all night as long as it's ok. And it was always part of it because you can't have that test for so long between the time they told us and the time [of the sweat test]...we had to wait like 8 weeks. And it was always just a part of his story. So he knew...we have always told him you don't have this disease but you do have a gene.

The child's age and onset of pubescence motivated parents to discuss the genetics of CF and the child's carrier status (n=3). These parents wanted to make sure their children were aware of their genetic risk before they became intimately involved with someone of the opposite sex. Finally, three parents described how they informed their children but not the circumstances that prompted them to do so.

> He's a pre-teen and I want him to know before he gets involved in a private matter that there's that probability.

What Parents Convey to Children Parents were fairly consistent about the content of their conversations with their children. Most (n=16) discussed the child's carrier status and one in four risk of conceiving a child with CF if their partner also is a CF carrier. These parents advised their children to ask potential partners to have carrier testing. Some parents (n=2) included a description of the CF symptoms in the discussion. Other parents told their child about their experience with the NBS process. Parents chose different strategies to convey the information about being a carrier to their children. For example, some (n=2) consulted with the child's pediatrician and/or used the internet to access information in preparation for talking with their child. Several (n=3) reassured their children that being a

CF carrier would not affect their health. Some (n=4) normalized being a CF carrier by explaining that everyone possesses disease-causing genes or by explaining that one of the parents is also a CF carrier.

> I just told her that if she happens to meet a man and decide that they want to get married that maybe they should get tested before they have kids to see if he's carrying the gene and then pass it on to the baby.

> I told him that we had quite a scare when he was first born and that the hospital called and told me about the test results,... and explained how they did the [sweat] test and [we were] amazed by how little drops of sweat could tell that.

> Just told her that I carry the gene and she got it from me and that it could impact her sometime in the future, but not to worry about it.

Consequences of Informing Children Participants reported no negative consequences resulting from telling their children about their carrier status. Parents appraised their children's initial understanding of the genetic information to be marginal, however, over time and with further discussion they believed that their children's understanding improved. The child's increasing maturity combined with multiple exposures to information from multiple sources, e.g. parents and school, could have enhanced the children's comprehension. Parents based their assessments on the child's intelligence and the content of their conversations. Interestingly, some parents interpreted the absence of questions as a sign that the child clearly understood, while others equated asking questions with comprehension. Reasons cited for children not fully grasping the information included the child's limited knowledge of human reproduction and not yet contemplating parenthood.

> Because she asked some questions. I don't remember exactly what they were, but she asked questions... and I even think she shared with her class that she is a carrier of it.

> He's still young; he doesn't understand much about sexual information, just what they learned in school.

Parents Who Had Not Informed Their Children Some parents (n=13, 35%) reported that they had not informed their children of their carrier status. About half of these parents (n=7) planned to do so when their children were older or planning to marry. Reasons for not telling their children included having forgotten about it, lacking knowledge about CF genetics, or believing the child was not old enough. One parent stated that she had not told their child because there was no reason to do so. Most of the parents in this group were unable to describe the content of the conversation that they might have with their children. One parent stated that she planned to discuss the reproductive implications of being a CF carrier. Another parent planned to include the NBS process as the context for knowing the child's carrier status.

> Yes... when she's a little bit older we'll inform her that before having kids she should have a screening of her mate.

> No... I haven't really thought about it. We really were told there was no reason to really tell him about it. The chances of him meeting up with someone that would also be a carrier were slim to none. That's what we were explained.

> I haven't given that much thought. I guess, no.

Discussion

We surveyed 37 parents whose children were identified as CF carriers through NBS between July 1994 and December 1997 and who participated in a previous study examining parental knowledge following false-positive NBS for CF (Ciske et al. 2001). Twenty-four parents informed their children about their carrier status while 13 had not. Situational prompts were the most common reasons for parents initiating a conversation with their children. Although 13 families had not yet informed their children, about half of these parents had plans to do so. Regardless of whether parents had already informed their children or they had plans to do so, they wanted their children to be aware of the reproductive risk associated with being a CF carrier and to learn about this risk before becoming sexually active. The mean child age at the time of telling was 9.2 years which is about the age when children are typically studying genetics and reproduction in school. Middle school age is well suited for disclosing such information because at this developmental stage children are fond of figuring out how things work, they have the capacity to comprehend abstractions, and they are approaching their reproductive years.

The significantly higher knowledge of CF genetics among parents who received genetic counseling at the time of the sweat test, compared with that of parents who did not receive genetic counseling, underscores the value of this intervention. However, even with counseling, about half of these parents, and only one third of those with no counseling knew the one in four risk of two carriers conceiving a child with CF. Although most respondents had high levels of education and medical literacy, only 65% of

those who received counseling and 22% of those without counseling knew that there is no chance of having a child with CF if only one parent is a CF carrier. Additionally, three parents were found to have misconceptions. One parent mislabeled the abnormal newborn screen as being for a congenital condition that was not part of the NBS panel. Another parent believed the genetic mutation found in her child's NBS resulted from one of the parents being exposure to toxins while deployed abroad in the military. A third parent thought that the CF mutation was responsible for the child having chronic nasal congestion. The first parent did not receive genetic counseling but the latter two parents had. These findings raise questions about how much genetic information parents in these circumstances really need to know. It is clearly essential that parents understand what the child was tested for and the meaning of test results but is it really necessary for parents of children who are CF carriers to know the one in four risk or is being aware that there is some risk sufficient? One could argue that if parents have limited information, there is a high probability that they will share incorrect information with their children. Thus, these young people may be entering their reproductive years with the knowledge that they are CF carriers, but whether they appreciate the true implications of this information remains questionable. On the other hand, if parents accurately understand the presence of some risk and recognize the limitations of their own knowledge, perhaps, they will be more likely to encourage their children to seek genetic counseling when planning a family. Additional research is needed to provide an empirically-based answer to this question.

The information about how and when parents talk with their children about the NBS results and the child's genetic status may be useful to clinicians who counsel other parents about this process. Since children with false-positive CF NBS results typically receive their health care from primary care providers (PCP), not specialists, PCPs are central to supporting parents' efforts to disclose genetic information to their children. However, knowledge of the ever increasing complexity of genetics may exceed the scope of the PCP's expertise; therefore, referral to a genetic counselor may be preferable. In an era of genetic preventive health programs, such as NBS, primary care providers might consider incorporating genetic counseling services into their settings to accommodate growing numbers of individuals, such as heterozygote CF carriers, identified by population screening initiatives. A genetic counselor can meet with the parents and/or child to assess the accuracy of their genetic information and offer anticipatory guidance about appraising the child's readiness to receive the information, introducing the subject, choosing developmentally appropriate content, assessing the child's understanding, encouraging discussion, and helping the child cope with emotional responses.

Overall, parents did not perceive their children as particularly vulnerable to health problems. No parents identified the false-positive NBS as a life-threatening event in their children's lives. The four parents with high CVS scores cited reasons other than the abnormal NBS for CF as life-threatening events. Because the identification of infants as CF carriers in infancy offers no health benefits, the main concern has been whether parents might misinterpret the results to suggest that the child is susceptible to illness or that the child might develop a mild form of the condition later in life. The findings from this study were encouraging because they suggested that the latter scenarios may not be the case. Although not all of the parents in this study had an accurate understanding of CF genetics, they seemed to have effectively absorbed information about the most important outcome of the NBS process—their child's test results.

The limitations for this study included a relatively small sample size and homogeneity of the sample regarding gender and racial/ethnic background, which reflects the demographics of populations with the highest prevalence of CFTR mutations. Given the length of time between the child's NBS results and the data collection, recall bias may also have been present. Finally ascertainment bias was a limitation because all of the participants in our study were recruited from a previous study. Parents who were motivated enough to participate in two related studies could be more knowledgeable and likely to tell their children about their carrier status than those who declined to participate. Despite these potential limitations, this study was, to our knowledge, the first documentation of the long-term effects of genetic counseling received at the time of the diagnostic testing related to NBS for CF.

The results of this study are similar to those of Ciske et al. (2001) in documenting that parents who received genetic counseling are more likely to acquire and retain genetic knowledge than those who do not receive counseling. Both studies also show that parents remain confused about the actual risk associated with being a CF carrier. These collective findings call for additional investigation of risk communication to identify the most effective methods for helping parents understand and retain genetic facts. Given parents' dubious recall of information, further study of their children's knowledge is also warranted.

Conclusions

Parents who received genetic counseling at the time of their infants' diagnostic sweat test had significantly higher long-term retention of genetic information than those who received no genetic counseling. However, both groups still had misconceptions and lacked accurate information about the actual risk associated with being a CF carrier. Most

parents either had already informed their children or planned to inform their children about the child's carrier status. Parental knowledge, medical literacy, and parental education level did not predict whether parents had informed their children about their carrier status. False-positive NBS results for CF were not associated with parental perceptions of children being especially vulnerable to health problems. Although the sample from this study was small (n=37) and ascertainment bias was a limitation, these findings highlight the benefits of genetic counseling at the time of the diagnostic sweat test and offer information that can assist parents in talking with their children about the implications of having one CFTR mutation. Additional research is needed to explicate the perspectives of young adults who had false-positive NBS for CF and their understanding about the implications of being a heterozygote carrier of one CFTR mutation.

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Questions for Continuing Education Credit

1. Which statement is **not true** about the Ciske et al (2001) study which this project was a follow-up to?
   a. The parents were asked about the genetics of CF and about their understanding of their child's carrier status.
   b. The participants were parents of children identified as carriers of CF through the Wisconsin NBS between July 1994 and December 1997.
   c. Five parents out of the 138 participants contacted the researchers because they wanted no more future contact from the research team.
   d. The study found significantly higher knowledge scores on the portion of the questionnaire related to CF genetics and inheritance in parents who received genetic counseling at the time of the sweat test as compared with those who did not.
   e. The majority of parents understood that their child was carrier, but only 57% of parents knew that two carriers have a 1 in 4 chance of having a child with CF with each pregnancy.
2. The two-tiered newborn screening algorithm for CF that was developed in Wisconsin and adopted by other newborn screening programs includes:
   a. Measurement of immunoreactive trypsinogen (IRT) followed by DNA analysis if the IRT is elevated and referral for sweat test if 1 or 2 CFTR mutations are found
   b. Measurement of IRT followed by a sweat test if the IRT is elevated
   c. DNA analysis followed by measurement of IRT if 1 or 2 CFTR mutations are found and referral for sweat test
   d. Measurement of IRT plus DNA analysis regardless of IRT level
   e. Measurement of IRT followed by complete DNA sequencing of the CFTR gene if the IRT level is elevated
3. An assessment of parental knowledge of CF genetics conducted 11-14 years after the child's false-positive newborn screening showed that:
   a. Parents in both genetic counseling and non-genetic counseling groups had high knowledge scores.
   b. Parents in both genetic counseling and non-genetic counseling groups had low knowledge scores.
   c. Parents in the genetic counseling group had significantly higher knowledge scores than those in the non-genetic counseling group.
   d. Parents in the non-genetic counseling group had significantly higher knowledge scores than those in the genetic counseling group.
   e. No significant differences between genetic counseling and non genetic counseling groups.
4. Which factor(s) most influenced parents' decisions to inform their children about the child's carrier status?
   a. Child's maturity and emotional readiness.
   b. Child's age and curiosity.
   c. Pediatrician encouraged parental disclosure.
   d. Parental readiness to give information.
   e. Parental education level.
5. The child vulnerability scale revealed that:
   a. Parents whose children were identified as CF carriers through newborn screening perceived their children as highly vulnerable.
   b. Parents with higher knowledge scores perceived their children as highly vulnerable.
   c. Parents' with lower knowledge scores perceived their children as highly vulnerable.
   d. Parental knowledge level was not associated with parental perception of child vulnerability.
   e. Several parents identified the abnormal newborn screen for CF as an event causing them to fear for their children's lives.
6. Parents' conversations with their children reportedly included all of the following except:
   a. Discussion of the reproductive risks associated with that being a CF carrier.

b. The impact the NBS results had on parental reproductive decisions.
c. Symptoms of CF.
d. Parents' experience with the NBS process.
e. The importance of genetic testing for future partners.

7. Limitations of this study include all except:
   a. small sample study
   b. recall bias because of the length of time between the child's NBS results and the data collection
   c. ascertainment bias because all of the participants in our study were recruited from a previous study
   d. homogeneity of the sample
   e. no intra-rater agreement established
8. The implications of this study include all except:
   a. When counseling parents about newborn screening results, counselors can share the information about how and when other parents made decisions to inform their children about the child's CF carrier status
   b. Significantly higher knowledge of CF genetics found among parents who received genetic counseling as compared with those who received no genetic counseling illustrates the value of offering parents genetic counseling services at the time of the infant's diagnostic sweat test
   c. The misconceptions among parents who received genetic counseling suggest that further research is needed to identify the most effective genetic counseling approach in the context of abnormal newborn screening results.
   d. Healthcare providers should be aware that parents continued to perceive the need for a sweat test as a life-threatening event in their child's medical history
   e. Children identified as CF carriers through newborn screening and their families might benefit from genetic counseling when the children enter their reproductive years

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