Pediatricians' Knowledge of and Attitudes Toward Fragile X Syndrome Screening

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Background.—Fragile X syndrome (FXS) screening exemplifies the challenges of screening for rare genetic conditions, including the potential to detect carriers and the lack of evidence regarding the benefit of early intervention.

Objectives.—The aim of this study was to evaluate knowledge, experience, and attitudes of pediatricians toward FXS screening, either as part of newborn screening or at the 12-month well-child visit.

Methods.—Responses to survey mailings to 400 general pediatricians were analyzed.

Results.—The response rate was 47%. Although most (98%) reported knowing that FXS causes intellectual disability, only half (53%) knew that females could be affected and 28% knew that carriers can have health problems as adults. Only 39% reported knowing enough about FXS to discuss the condition with the family of a child who might have the condition. Most respondents (78%) believed that newborn screening for FXS would be beneficial for children and families. About half (55%) believed that parents should be offered FXS screening as part of well-child care. Few (8%) reported that they would not support FXS newborn screening or screening during well-child care because of carrier detection.

Conclusions.—Among respondents there is good support for FXS newborn screening and some support for FXS screening as part of well-child care. Prior to implementing screening, efforts are needed to educate pediatricians and assess their ability to inform parents about the implications of testing and provide care after the identification of FXS or carriers. These activities can serve as a model for how to introduce other genomic tests into the primary care setting.

KEY WORDS: fragile X syndrome; genetic screening; neonatal screening; preventive health services

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Screening is a core component of pediatric preventive care.[1] Screening must be part of a larger coordinated system because identified children and their families must receive appropriate follow-up. The number of conditions for which screening is recommended is increasing (eg, newborn screening expansion,[2] autism spectrum disorder screening at 18 and 24 months of age[3]) and the timeline between the development and availability of screening tests is shrinking. Such advances are creating a complex and rapidly changing environment for pediatricians, as exemplified by the case of fragile X syndrome (FXS), a condition for which screening tests are in development.[4] For FXS screening to be beneficial, affected individuals and their families would require coordinated medical, psychosocial, and educational interventions.[5–7] This poses a challenge because studies of presymptomatic FXS interventions have not been conducted. Other challenges include variations in the expression of FXS, late-onset medical problems (eg, tremor/ataxia, ovarian insufficiency), the possibility that screening would detect carriers, and the need to offer testing or counseling to extended family members.[8] Despite these concerns, parents are supportive of FXS newborn screening.[9] A survey conducted in 2004 of fellows of the American Academy of Pediatrics, primarily selected from subspecialty sections (pulmonology, neurology, endocrinology, and genetics), found that 32% supported newborn screening for FXS and 28% supported screening infants at a later time.[10] This study did not evaluate the challenges of incorporating FXS screening into clinical care (eg, carrier detection, care coordination). Another study found that pregnant women endorsed prenatal FXS screening. However, these women had little knowledge about FXS screening even after an intervention to improve understanding about FXS.[11]

Historically, the viewpoint of general pediatricians is not considered when developing and evaluating new screening tests. We believe that it is important to consider the reality of primary care in parallel with the development of new screening tests. The purpose of this study was to evaluate primary care pediatricians' knowledge, experience, and attitudes about FXS screening as part of a larger ongoing effort to incorporate genomic medicine[12] into primary care.

METHODS

Survey Instrument Development

We developed an instrument to assess knowledge, practice, and experience with FXS and attitudes toward FXS screening. We considered 2 scenarios: FXS screening could be incorporated into the newborn screening or be offered at the 12-month routine preventive visit. Because our primary goal was to evaluate attitudes toward FXS

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screening, we provided basic information about FXS (Table 1) to ensure that respondents were knowledgeable enough to make judgments about the value of screening. Although FXS knowledge assessment was not a primary goal, we did ask respondents whether they were aware of this information prior to the survey. Because screening tests for FXS are under development, we could not provide information about test sensitivity or specificity. Therefore, we asked respondents to assume a test that is "highly accurate" with a "negligible false-positive rate," that would detect carriers. To provide a context to interpret attitudes toward FXS screening, we asked about the degree to which screening is conducted for other conditions as part of routine preventive care (eg, hematocrit testing for 1-year-olds, standardized developmental screening for 18-month-olds). Finally, we collected information about practice demographics. Year of medical school graduation was available from the address data source.

The instrument was pilot tested by a convenience sample of FXS experts and general pediatricians and revised to ensure clarity. The instrument consisted of 25 questions, which were primarily of multiple choice or Likert scales of agreement and took 10 minutes to complete. The final survey instrument is available upon request.

Sampling Frame

A random sample of 400 general pediatricians was drawn from the American Medical Association Masterfile, a database of all licensed physicians in the United States. The sampling frame included physicians in office-based, direct patient care whose board certification and self-described primary specialty was primary care pediatrics from 17 states (Connecticut, Delaware, Georgia, Florida, Maine, Maryland, Massachusetts, New Hampshire, New Jersey, New York, North Carolina, Pennsylvania, Rhode Island, South Carolina, Vermont, Virginia, and West Virginia) and the District of Columbia. These locations were chosen to group attitudes toward FXS newborn screening by different state-level newborn screening program characteristics. We excluded physicians-in-training and those who practice at military or federal facilities. On the basis of survey response, we also excluded physicians who reported that they did not provide well-child care for children aged 5 years and younger.

Table 1. Fragile X Syndrome Information Provided With the Survey

- FXS* is the most common inherited form of intellectual impairment.
- FXS affects 1 in 4000 males and 1 in 8000 females. Carriers are about 10 times more common.
- Affected males have moderate-to-severe intellectual impairment, and social and behavioral difficulties. One third have autism. Affected females can vary from having a mild learning disability to having a severe intellectual impairment.
- Carriers are at risk for primary ovarian insufficiency and tremor, ataxia, dementia, and Parkinsonism as adults.
- Most with FXS are diagnosed around 3 years of age, although most develop symptoms around 1 year of age.
- No large-scale study has evaluated treatment for FXS prior to the development of symptoms. Some parents might benefit from early diagnosis to help with coping, planning for the child, and family planning.

*FXS indicates fragile X syndrome.

Survey Administration

The first survey mailing, accompanied by a cover letter, an inexpensive incentive gift, and a reply envelope, was sent during April 2008. Two subsequent mailings to nonrespondents were sent at 3-week intervals.

Data Analysis

Pearson χ^2 tests of independence were used to test for associations among the categorical variables. The Wilcoxon signed rank test was used to evaluate differences in the distribution of medical school graduation year between respondents and nonrespondents to the survey and among selected categorical variables. To further evaluate the association between medical school graduation year and selected categorical variables, we categorized graduation year into before or after the lowest quartile. All analyses were performed with Stata 10.0 software (StataCorp LP, College Station, Tex). We considered $P < .05$ to be statistically significant. The Duke University Health System Institutional Review Board approved this confidential survey.

RESULTS

Response Rate and Demographic Characteristics

Of the 400 physicians in the sample, 38 did not provide well-child care for children aged ≤5 years, and 12 had undeliverable addresses. The response rate was 47% (165 eligible surveys). The likelihood of responding did not vary by state ($P = .26$) or median year of medical school graduation (1987 respondents vs 1984 nonrespondents; $P = .33$). Respondent characteristics are listed in Table 2.

Anemia and Developmental Screening Practices

Most respondents (81%) reported that they always (>95% of the time) screen for anemia at the 1-year well-child visit. Eleven percent usually (60%–90% of the time) and only 6% rarely (<20% of the time) do so. Most also reported that they always (55%) or usually (22%) conduct standardized developmental screening for 18-month-olds. Sixteen percent rarely conduct developmental screening.

Knowledge and Experience With FXS

Most respondents (98%) reported knowing that FXS causes intellectual disability and that diagnosis is often delayed (87%). Only half (53%) knew that females could be affected, and 28% knew that carriers can have FXS-related health problems as adults.

Table 2. Practice Characteristics of Respondents (N = 165)

Characteristic	Percentage (No.)*
Average number of well-child visits for children aged ≤ 2 years per month	
<10	4% (7)
10–30	22% (37)
>30	73% (121)
No. of providers, including nurse practitioners and physician assistants	
1	13% (22)
2–5	45% (74)
>5	42% (69)
Patients aged ≤ 2 years covered by Medicaid, %	
<10	32% (52)
10–50	42% (70)
>50	26% (43)
Practice affiliation	
Private	68% (113)
Medical center or university health system	23% (38)
Practice network	2% (4)
Public clinic	5% (9)
Other	1% (1)
Practice Setting	
Urban	29% (48)
Suburban	59% (98)
Rural	10% (17)
Missing	1% (2)

*Categories may not add to 100% due to rounding.

In the past 5 years, 46% reported referring a child for suspicion of FXS and 40% tested a child for FXS. However, only 10 respondents (6%) diagnosed a child with FXS. Overall, 32% of the respondents neither referred nor tested a child for FXS.

Only 39% reported that they know enough about FXS to discuss it with a family of a delayed child who might have FXS. Many (62%) would refer to a specialist instead of directly ordering a diagnostic laboratory test if they were concerned that a child has FXS. However, most (77%) reported that their practice can coordinate the care for a child with FXS. There was no statistical association among the overall distribution of year of medical school graduation and knowing enough to discuss FXS ($P = .08$), likelihood of referring to a specialist instead of testing ($P = .08$), or being able to coordinate the care for a child with FXS ($P = .60$). However, respondents who graduated earlier (ie, the first quartile) were more likely to report knowing enough to discuss FXS with a family of a delayed child (53% vs 34%; $P = .03$). There was no statistical association between earlier graduation and ability to coordinate care ($P = .48$).

Among the respondents, most knew a genetic counselor (75%) or behavioral specialist (69%) in their community to whom they could refer patients with FXS. Respondents in rural settings were less likely to know of a genetic counselor (29% vs 79%; $P < .01$) or behavioral specialist (41% vs 72%; $P = .01$) than those in urban or suburban settings.

Newborn Screening

Most respondents believed that newborn screening would be beneficial for both children (78%) and parents (78%). More than half (58%) did not believe that the stress to families by the diagnosis of FXS in their newborns or identification of carriers would outweigh the benefits of early detection; 27% were unsure, and 16% believed that family stress would outweigh benefit. Overall, few (8%) would not support newborn FXS screening that identified carriers. However, 27% were unsure.

Only 33% reported that they knew enough about FXS to counsel parents considering an optional newborn screening test that would identify both FXS and carriers. About an equal number (35%) were unsure. There was no association between the ability to counsel families considering screening and the belief that it is beneficial for either the child ($P = .33$) or the family ($P = .82$). Because of the low response rate, we chose not to evaluate support for newborn FXS screening based on location.

Screening as Part of Well-Child Care

About half (55%) believed that all parents should be given the option of FXS and carrier screening at the 12-month well-child care visit, 25% were unsure, and 20% disagreed. Most (74%) reported that they would only suggest screening for children who were delayed if there was a family history of FXS or if the family had concerns. Some (12%) reported that FXS is too rare to worry about for normal children. About one third (34%) believed that routine preventive visits are too busy to add FXS and carrier screening. However, compared with those who did not believe that routine preventive care is too busy, those who believed that routine preventive care is too busy were less likely to believe that parents should be given the option of screening (35% vs 66%; $P < .001$) and more likely believe that screening should be risk based (93% vs 64%; $P < .001$). There was no association between the belief that preventive care visits were too busy to add FXS and carrier screening and whether screening was usually or always conducted for anemia ($P = .59$) or development ($P = .97$), the number of well-child visits per month ($P = .27$), the number of providers in the practice ($P = .09$), affiliation of the practice ($P = .63$), proportion of Medicaid-enrolled patients ($P = .12$), practice setting ($P = .94$), or year of medical school graduation ($P = .34$).

Few (8%) would not use an FXS screening test as part of well-child care because they believed that it is not appropriate to identify carriers, and 38% were unsure. Among the 54% who would support an FXS screening during well-child care despite carrier detection, most (84%) would also support FXS newborn screening despite carrier detection.

DISCUSSION

Adding FXS to newborn screening would ensure high rates of testing and linkage to the public health system. However, such screening could increase parental stress during a vulnerable time. In contrast, incorporating FXS screening into well-child care would allow families to make informed decisions about whether such testing is desired, but it could lead to fragmentation of care and could

delay intervention, and some parents would have additional children without knowing reproductive risk. These concerns combined with the challenges of carrier detection and questions about the effectiveness of early intervention make FXS a good model for the challenges of implementing genomic medicine in pediatric primary care. Many pediatricians are not prepared for the complexity of genetic testing (eg, genotype-phenotype variation), which is further complicated by the lack of geneticists.

Conclusion

We believe the response rate to this survey was lower then others we have conducted because of the difficulty of the questions (eg, attitude toward carrier detection) and perhaps less interest in FXS among nonrespondents. However, among the respondents, many do not feel sufficiently knowledgeable to discuss the condition with the family of a child with developmental delays who might have FXS. Also, we found good support for FXS newborn screening among the respondents and some support for FXS as part of routine preventive care. Carrier detection was not a significant barrier to the support of FXS screening. This may reflect the desire to have the public health system be responsible for FXS screening. These findings highlight the need prior to the implementation of any recommendation for FXS screening to educate pediatricians and assess their ability to inform parents about the implications of testing and coordinate the care needed after the identification of FXS or carriers.

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