Cystic fibrosis screening

Cystic fibrosis newborn screening and detection of carriers

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Detection of carriers can be managed

A decision to introduce nationwide cystic fibrosis (CF) newborn screening in the United Kingdom has now been taken, although the exact procedure is still being determined, except in Scotland where screening began in February 2003. In Scotland, as well as in a number of regions in England and Wales where ad hoc newborn screening was started some time ago, an immune reactive trypsin (IRT)/DNA system of newborn screening is used, DNA analysis being undertaken on those above a cut off point of IRT. The multiplex DNA arm covers about 86% of the most common mutations in the native UK population. There is evidence that the more severe mutations of the cystic fibrosis transmembrane regulator (CFTR) gene are the ones most likely to cause an increase in IRT.3

There are a number of advantages of IRT/DNA programmes: earlier full diagnosis within the first few weeks of life becomes possible for those in whom both mutations are found; there is a reduction in sweat testing and in the uncertainty that may follow inadequate sweat collection; also many fewer couples need to be faced with the worry that their baby might have CF than when IRT is used alone.4 In those from ethnic minorities where the mutation spectrum is largely unknown, one has no choice other than to proceed to sweat test in those with a persistently raised IRT.

The disadvantage of the IRT/DNA method is that the genetic analysis step results in the discovery of some healthy carrier infants, with the spectre of CF raised for the parents before the situation is resolved by negative sweat test. Two or three carrier newborns are discovered for each child diagnosed with CF.4

One issue that has concerned some is that one might discover non-paternity in the DNA arm of the test, when one tests the parents. Experience from our CF cascade programme5 is that, although we have discovered non-paternity of grandparents, none was found among the parents. This may indicate self selection in those parents who refuse tests. As long as no pressure is exerted on the parents to have themselves tested, those geneticists who participated in an email debate on this topic organised by Professor Rodney Pollitt in 2002 did not see discovery of non-paternity as a major problem.

Having discovered a carrier, what does one do with the information? There can be no argument that the parents must be informed of the result. For one thing, a sweat test is being organised on their infant to cover the possibility of CF with the second mutation not covered by the screening method; for another, both parents might be carriers with a risk of CF in future or existing children.

How much distress does the finding of a carrier newborn cause? Parsons and colleagues3 sought to answer this specifically in a small questionnaire study based on newborn screening in Wales. Attitudes and feelings of parents were compared with those of a control group of mothers. The authors report their results with particular reference to the implications when the infant was found to be a carrier under the headings: attitude to newborn screening, infant carrier identification, adult carrier identification, the newborn screening protocol, and the family dimension. All carrier families were in favour of screening, and no evidence was found that the mother/baby relationship had been affected by carrier identification. None regarded their baby as ill, and most regarded the information that their baby was a carrier as useful and of relevance, and that one might discover non-paternity. Parents saw an inconsistency in this. One of the authors (Angus Clarke) chaired a working party for the Clinical Genetics Society on genetic testing in children.6 The tone of the report was generally against such testing, suggesting that children should make their own decisions on whether to be tested when of an age to do so. It is refreshing to note that the authors are prepared to question their current practice in response to strongly expressed wishes of parents. The Genetic Interest Group (GIG) have long campaigned on behalf of parents in this respect, adopting the attitude expressed by many of their members, “Parents generally make decisions for the benefit of their families and children.”

The other negative aspect that parents found most difficult was the suggestion that they contact their relatives to inform them of their potential carrier status. The authors suggest that their reluctance to do so signified dysfunctional family relationships. I disagree with them on this and find the parents’ behaviour understandable. They are in a state of grace after the birth of their healthy baby and are understandably

Abbreviations: CF, cystic fibrosis; IRT, immune reactive trypsin; CFTR, cystic fibrosis transmembrane regulator

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their parents when one CF mutation in an IRT/DNA screening programme in Massachusetts. The parents were counselled in the genetics department on the same day as the sweat test, in the hour before the result became known. As there was a low chance that the child would have CF, discussion of the disease was brief and more for the purposes of explaining why carrier testing was being offered to the parents. In their study, most parents gave the chance that they might both be carriers as their reason for opting to have themselves tested. Although it would require some organisation, this is an approach in which clinical genetics and IRT/DNA screening units could fruitfully cooperate in the United Kingdom. Again it would be useful to have written national protocols to follow.

The advantages of including DNA analysis in newborn CF screening outweigh the disadvantages, but special care must be taken in managing the parents of neonates discovered to be carriers.

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