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Review

Carrier testing in children and adolescents

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ABSTRACT

Many international guidelines recommend that carrier testing in minors should be postponed either until the age of majority or until the child can be actively involved in the decision making process. Although a number of high school programs exist which provide carrier screening to adolescents in at-risk populations, recent guidelines published by the American Society of Human Genetics do not advocate this testing. Despite this, there are some circumstances in which carrier testing does occur in minors. This testing might be intentional, in which identification of carrier status is the goal of the test, or unintentional, where carrier status is identified as a by-product of testing. In this review we outline the situations in which carriers may be identified in childhood and the positions of professional guidelines that address carrier testing in children. We then review the arguments for and against carrier testing presented in the literature and compare this to the empirical evidence in this field.

Contents

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1. Introduction

Genetic carrier testing for both autosomal recessive and X-linked conditions is performed primarily to provide information to individuals to enable future reproductive planning and informed choices. This is in contrast to testing to determine whether one is a 'carrier' of an autosomal dominant condition, where the purpose is to identify their risk of developing a genetic condition themselves. Results from this predictive or presymptomatic testing incur different psychological impacts that are beyond the scope of this review. There is a general acceptance that the best time to learn of one's carrier status is before, rather than during, pregnancy (British Medical Association Ethics Department, 2012). Although preconception carrier testing is strongly encouraged in adulthood, both with and without the presence of a family history of a genetic condition, population-based carrier screening is not widely available apart from in some specific communities, such as the Ashkenazi Jews, and certain regions, for instance Cyprus and Sardinia (Borry et al., 2011). Yet carrier testing in childhood is usually considered inappropriate (Borry et al., 2006). Although many international guidelines recommend testing should be postponed until age of majority, most commonly 18 years of age (Borry et al., 2006), consideration may be given to 'mature minors' who are less than 18 years but considered capable of making informed decisions about having genetic testing (Duncan and Delatycki, 2006).

Despite this, there are some circumstances in which carrier testing does occur in individuals who are less than 18 years of age. This testing might be intentional, in which carrier status is identified deliberately and is the goal of the test, or unintentional, where carrier status is identified as a by-product of testing that has been performed for other purposes. In this review we outline the situations in which carriers may be identified in childhood and the positions of professional guidelines that address carrier testing in children. We then review the arguments for and against carrier testing presented in the literature and compare this to the empirical evidence in this field.

2. Intentional carrier testing in children

2.1. Cascade carrier testing

There are two main situations when intentional carrier testing may occur. The first is in the context of a family history of a genetic condition, such as following the diagnosis of a child in the family. In this context, the parents and other adult family members are usually offered cascade testing to determine their carrier status. Although carrier testing is generally not recommended in any unaffected siblings of the affected child, technically this could also occur. The literature indicates that, depending on the genetic condition, a large proportion of parents want to know the carrier status of their other unaffected children (Balfour-Lynn et al., 1995; Barnes, 1998; Brunger et al., 2000; Fanos and Mackintosh, 1999). In a study of 114 parents of children with cystic fibrosis (CF) in the UK, 90% wanted testing performed in their other children who did not have CF and 91% felt they had a right to the information (Balfour-Lynn et al., 1995). Likewise, in parents of children with ataxia telangiectasia in the USA, a high proportion of parents (42/68; 84%) stated they would test for carrier status in their other children prior to 18 years of age (Fanos and Mackintosh, 1999). However, carrier testing was less strongly desired in a US-based study of parents who have children with deafness with only 31/70 (44%) wanting genetic testing performed in their other hearing children (Brunger et al., 2000). In addition, although a proportion of parents of children with unbalanced chromosomal translocations had already had their unaffected children karyotyped, of those remaining, 39/72 (54.2%) had considered testing (Barnes, 1998).

Not only do parents want to know their child's carrier status, the literature confirms that, in practice, some parents receive carrier results for their other unaffected children following the diagnosis of their child with a genetic condition (Balfour-Lynn et al., 1995; Borry et al., 2007; Fryer, 2000; Lavery, 1998; McConkie-Rosell et al., 1999; Meldrum et al., 2007; Multhaupt-Buell et al., 2007; Vears et al., 2015). In Finland in the 1980s, carrier testing in siblings of affected children was standard procedure for some conditions including Duchenne muscular dystrophy (DMD), haemophilia and aspartylglucosaminuria (Järvinen et al., 1999a, 2000a, 2000d). Since then, five investigations of healthcare providers' practices undertaken in the UK, Europe, USA and Australia, have provided insights into genetic testing practices in children (Borry et al., 2007; Fryer, 2000; Multhaupt-Buell et al., 2007; Noke et al., 2015; Vears et al., 2015).

In the European study, 3–36% of clinical geneticists had performed carrier testing in a minor, depending on the condition (Borry et al., 2007). Similarly, in one UK study, 178 of their 692 respondents (25.7%), had performed carrier testing in children for autosomal recessive conditions and balanced translocations (Fryer, 2000). Of the 83% of respondents in the US study who had received requests from adolescents, 84% had tested an adolescent in the last year (Multhaupt-Buell et al., 2007). A recent study in the UK identified that 16/25 professionals interviewed (64%) advise parents to have carrier testing for sickle cell disease performed in their children (Noke et al., 2015). These professionals were generally focused on the clinical and reproductive relevance of the testing and the rights of the parents to make these decisions. In contrast, in an Australian study of key informant genetic counsellors and clinical geneticists, all 17 participants indicated that they initially discourage or recommend against carrier testing in children following parental requests (Vears et al., 2015). However, the genetic health professionals reported different responses if parents persist with their request. While some indicated they continue to refuse testing, others may facilitate testing for the family, taking into account factors such as the maturity of the minor, parental anxiety, and the health and reproductive implications for the child depending on the genetic condition in the family (Vears et al., 2015).

Research with parents of children with genetic conditions also suggests that some carrier testing does take place in siblings of children with fragile X syndrome, CF, spinal muscular atrophy and muccopolysaccharidosis (Balfour-Lynn et al., 1995; Lavery, 1998; McConkie-Rosell et al., 1999; Meldrum et al., 2007). All of these studies suggest that health professionals do undertake carrier testing in childhood, but their willingness to test is dependent on the genetic condition under consideration, with CF, DMD, fragile X syndrome, balanced translocations, β-thalassemia and sickle cell often listed as the most commonly tested conditions (Borry et al., 2007; Fryer, 2000; Multhaupt-Buell et al., 2007; Vears et al., 2015).

2.2. Population or targeted high school carrier screening

The second situation when carriers might be identified intentionally in childhood is through population-based carrier screening in which testing takes place in specific groups who have a higher carrier frequency or prevalence of the genetic condition in question, rather than prompted by a positive family history. A classic example of carrier screening is the measurement of serum hexosaminidase A to test for carriers of Tay-Sachs disease in adolescents of Ashkenazi Jewish descent through high school programs which commenced in Montreal in the early 1970s (Clow and Scriver, 1977). Screening spread to Israel in 1986 and then began in Australia a decade later (Barlow-Stewart et al., 2003; Gason et al., 2003). These programs now use DNA-based testing and involve a number of