

Guidelines for genetic testing of healthy children



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Recent international efforts to sequence the human genome have greatly enhanced our ability to test definitively for many genetic conditions. For many, this has been welcome, allowing the diagnosis of disorders that have been previously only suspected. This has also led to the advent of the 'unpatient' (1), where there is an increasing ability to test healthy individuals for genetic conditions that they will get (presymptomatic or predictive testing), conditions that they may get (susceptibility testing), and conditions that their children may get (carrier status). In response to concerns with genetic testing in general, professional and governing bodies from several nations worldwide have developed statements to deal with societal concerns (2). As part of this, genetic testing of healthy children has received due attention (3-6). For example, the 1998 World Health Organization's *Proposed International Guidelines on Ethical Issues in Medical Genetics and the Provision of Genetic Services* (7) recommends that:

Every genetic test should be offered in such a way that individuals and families are free to refuse or accept according to their wishes and moral beliefs. All testing should be preceded by adequate information about the purpose and possible outcomes of the test and potential choices that might arise. Children should only be tested when it is for the purpose of better medical care.

Thus, genetic testing to confirm a medical diagnosis in a symptomatic infant or child is appropriate as part of medical care. As well, genetic testing for the purpose of enhancing medical monitoring, prophylaxis or treatment in a healthy (asymptomatic) child at risk for a genetic condition may also be in the best interest of the child (such as for familial hyperlipidemia, hereditary hemochromatosis or multiple endocrine neoplasia). The present statement explores the ethical issues posed by the ability to test healthy children when there is no foreseeable timely medical benefit. Although the ethical issues may be similar, the present document does not explore newborn genetic screening issues, which deserve special attention.

BACKGROUND

Although it is well established that it is a competent individual's own decision whether one should be tested for

genetic status, children may undergo testing, requested by parents and health care providers, before they are able to consent to the testing themselves. A 1993 survey in the United Kingdom of 49 geneticists and 209 paediatricians revealed that the majority of paediatricians would test healthy children for 11 of 12 conditions listed, including Huntington disease (8-9). Although guidelines informing health care providers about the concerns with genetic testing have been well distributed since then, a more recent (1999), much larger survey in the United Kingdom (692 responses) suggests that testing children for adult onset disorders and carrier status is still not an uncommon practice. That is, 165 professionals had tested 955 children for conditions with adult onset and 178 respondents had tested 3319 children for carrier status (10). Furthermore, in a survey of 105 Canadian and American laboratories carrying out genetic testing, the majority have received and responded to requests to test healthy children for genetic disease or carrier status (11).

The willingness, however, for asymptomatic adults to have genetic testing for conditions they are at risk for varies from individual to individual. For example, less than 20% (12) of all those at risk for Huntington disease, an incurable degenerative neuropsychiatric disorder, have come forth for predictive testing, although linkage and direct DNA tests have been available for more than a decade. However, for conditions where preventive measures may be taken, there seems to be a higher preference to be tested, such as for hereditary cancer (13). For carrier status of autosomal recessive conditions, where the implications are for the next generation, uptake is variable even when the condition is present in the family, suggesting that this information may be desirable for some, but others prefer not to have the information (14). Thus, for a child it is difficult to predict whether testing in childhood will be beneficial to that individual in adulthood. Some advocate genetic testing in childhood for conditions such as adult onset blindness, where anticipatory training is possible and may potentially alter positively the affected individual's quality of life. Research exploring the potential benefits of presymptomatic testing to guide such nonmedical intervention will be important as an increasing number of genetic tests become available.

Some suggest that the issue of whether to test healthy children may be overemphasized. There is concern that

insufficient emphasis has been placed on the merits of open discussion in the context of familial genetic risk and appropriate counselling, which is likely to be more helpful than the testing itself (15).

SOCIAL CONCERNS

Genetic information is considered to be 'private' information because there is significant societal concern that stigmatization followed by discrimination may occur against individuals and groups on the basis of genetic status (2). There is particular concern about the availability of the information to third parties such as insurers and employers (16). Indeed, there are sufficient historical data to substantiate the concern when African Americans were compelled in some American states to undergo testing for sickle cell disease in the 1970s, and were subsequently discriminated against on the basis of carrier status (17). Therefore, beyond the basic right for an individual to decide whether one wants genetic testing that will reveal genetic information, he or she should also have the right to control the information by deciding whether third parties should have access (16). Although the concept of an individual right to decide about testing and control of information may be challenged when considering the duties and responsibilities one may have to family members, to have testing imposed on an individual without consent would be unacceptable, even in the context of a family situation.

PSYCHOLOGICAL CONCERNS

The potential psychological impact of the knowledge that one has (or has not) inherited a gene conferring risk has been extensively considered (13). Studies of those at risk for Huntington disease demonstrate that a positive result in a well-prepared individual may not be as devastating as one might predict; however, the knowledge that one is not at risk has unexpectedly been shown to increase psychological stress in some cases (18,19). As well, there may be an advantage to not knowing one's carrier status. For example, relational bonds that develop for those at risk for a familial condition may be shattered when true at-risk status is known. Family dynamics in general may be affected by testing (8,14). Testing may confer a psychological impact not only on the child being tested, but on the parents who may feel a sense of guilt or responsibility if a child tests positive. Codori et al (20) evaluated 41 children ages six to 16 years for short term psychological effects of predictive testing for familial adenomatous polyposis. Although depression and anxiety scores remained outside those which would be considered clinically significant, children who were mutation positive with affected mothers had significantly higher depression scores. Interestingly, children of affected mothers, regardless of mutation status, had significantly higher anxiety scores after testing. Also important was the effect on parents (unaffected and affected) who had higher depression scores at follow-up when their children tested positive for mutation.

Testing healthy individuals for carrier status for X-linked or autosomal recessive conditions is often considered to be of minimal risk when comparing with testing those who are at risk for adult onset disorders. That is, generally, carriers are unaffected and remain unaffected. The knowledge, however, that one is a carrier for a genetic condition that may affect one's offspring may have a negative impact. For example, a study of women tested for Fragile X carrier status demonstrated that five months after testing, carriers were found to have situational specific changes in feelings about themselves that were predominantly due to concerns about the implications of being a carrier (21). As well, the abstract notion of genetic carrier status may be open to misunderstanding. In a study of 84 adults with a sibling or spouse's sibling affected with cystic fibrosis, one-third had significant misunderstandings about their genetic risks. In some cases, the misunderstandings affected reproductive decision making adversely (15,22). In contrast, an eight-year follow-up questionnaire of adolescents screened for carrier status for Tay Sachs disease in a high school screening program were predominantly in favour of having been screened (23). Although 46% of carriers were "worried" after receiving results, the majority were "indifferent" eight years later to the knowledge of being a carrier.

CONSENT ISSUES

Because of the highly sensitive nature of genetic testing and historical concerns of societal oppression (24), the right to autonomy and self-determination is the principle underlying the emphasis on informed consent, and is the basis for international statements on the personal nature of genetic testing. However, autonomy as a concept is not independent, but rather influenced by relational forces. Individuals make health care decisions based on responsibilities to others (25). In general, the interests of the family and the child are intricately related and difficult to separate. Indeed, appropriate information and counselling about testing issues are essential to the decision making process of the family. The best interests of the child are paramount, however, and the perceived benefits and risks of testing must be carefully weighed. The practitioner needs to distinguish the need for a parent to know whether his or her child has inherited the disease-causing gene from the need for the child to know. Ideally, the decision to test should be made with the child, when the child is competent to make the decision.

Consent must be informed, voluntary without coercion, and the consenting individual must be competent. Thus, the ability to provide consent is, in part, developmentally determined. As early as four years old, children understand some concepts of inheritance. Early concepts of disease may be overshadowed with feelings of guilt and responsibility. Illness may be perceived as punishment. Indeed, the concept of a family member's illness may be fraught with self-blame (15). Concrete concepts of health-related procedures are generally developing by age seven years, correlating with the acceptance of 'assent', which implies a crude

understanding of medical concepts, and an ability to decline elective medical procedures, such as research participation. A full understanding of the nature and consequences of agreeing to or refusing medical management does not occur until early adolescence, and maybe later. The ability to understand the abstract concepts of social risk, including loss of privacy, social stigmatization and potential employment or insurance discrimination, may require even more sophistication. Concepts of probability that are often the basis of genetic risk may be difficult for some adults to understand (26,27). It does not seem justified, however, to refuse testing to a fully informed, competent adolescent who is requesting it (28). In response to international guidelines restricting testing for Huntington disease to those 18 years of age and over, it has been argued that imposing such restriction may be an infringement on individual rights and may be a threat to reproductive autonomy (29).

REPRODUCTIVE PRIVACY CONCERNS

Although carrier testing for the purpose of future reproductive decision making may be perceived to be of low risk because the carrier will not manifest the condition, the child's right to future reproductive privacy is an important consideration. Because there is great variability in the uptake of carrier testing by adults of reproductive age, it is difficult to predict whether carrier testing for the purpose of future reproductive decision making of any individual child is in his or her best interest. In an ethical exploration of carrier testing of children for Tay Sachs disease, Dena Davis explains (30):

Children will grow up to be adults. Respecting them as potential adults means respecting their right and ability when they reach that state, to have autonomy over information personal to them.

Thus, if an infant or child is tested for carrier status, and the result is known to parents and possibly other family members, the right to autonomy over information personal to them has been removed. Some assert, however, that parents are in the best position to decide when and how such information should be revealed to their children (31,32). Although this may be true with appropriate counselling and involvement of the child, genetic testing of a healthy child is definitive and cannot be reversed. Interestingly, in a study of Fragile X carriers, the average age at which parents thought their daughters should be tested for Fragile X carrier status (10 years) was significantly younger than the age they felt the information was ideal for themselves (15 years) (33).

PARENTAL REQUESTS FOR GENETIC TESTING

It is essential that the parent and health care provider who request testing have a good understanding of the ethical and social implications of genetic testing. In the rare circumstance that genetic testing of a healthy child is insisted upon after the parents are fully informed of the ethical and

social concerns, the best interests of the child within the family context should be considered. The benefits of testing for the child should be weighed against the potential harms. If the testing is felt to have potential for undue harm, the health care provider should not feel obligated to participate in the testing. Although parents are the decision makers for their children's therapeutic treatment, they do not have authority over nontherapeutic interventions, including genetic testing (27,34). Exceptional circumstances may arise, however, when not testing may create more harm than testing. These cases should be decided upon with the support of ethics and/or legal counsel.

ADOPTION

As in all circumstances, the best interest of the child needs to direct genetic testing. This remains true for children who will be candidates for adoption. Adoption agencies are obligated to seek and disclose medical history information to potential adoptive families (including genetic information), however, they are under no obligation to request genetic testing of biological families or of children who are candidates for adoption. They are obligated to protect the child's best interests. Although it may seem to be in the child's best interest to increase their chance for adoption with a negative result, consider the circumstance where a positive result may not only decrease the chance of adoption, but also potentially affect the child negatively in other ways. The American Society of Human Genetics and the American College of Medical Genetics (2000) joint statement recommends that genetic testing guidelines in place for children should be followed (35). That is, that timely medical benefit should guide genetic testing. Furthermore, the guidelines state:

In the adoption process, newborns and children should not be tested for the purpose of detecting genetic variations of, or predisposition to physical, mental, or behavioral traits within the normal range.

RECOMMENDATIONS

- In all situations where genetic testing of healthy children is considered, parents should be informed of potential psychological and social risks associated with testing. Open discussion regarding familial genetic risk, in an age-appropriate manner, should be encouraged within the context of the family unit. The best interests of the child should be the primary consideration when contemplating testing. Appropriate counselling and genetic service involvement should be instituted.
- Timely medical benefit to the child should guide genetic testing. That is, genetic testing to confirm a diagnosis in a symptomatic child, to allow for adequate medical monitoring, prophylaxis or treatment in a child at risk for a genetic condition that will occur in childhood is appropriate.

- For genetic conditions that will not present until adulthood (susceptibility or predictive testing), testing should be deferred until the child is competent to decide whether they want the information.
- For carrier status for conditions that will be important only in reproductive decision making, testing of children should be discouraged until the child is able to participate fully in the decision to be tested.
- A request for genetic testing by a competent, well-informed adolescent for the purpose of reproductive decision making should be considered, accompanied by appropriate counselling. The decision to include his or her family in the decision making should be made by the adolescent.
- In exceptional circumstances where parents insist that

genetic testing of healthy children be carried out where there is no medical or other benefit to the child, the physician is not obligated to carry out testing that is not in the best interests of the child. In exceptional circumstances, not testing may create more harm than testing. In these cases, a referral for ethics or legal opinion may be appropriate.

- Infants and children being considered for adoption should not be subjected to genetic testing where there is no timely medical benefit.

ACKNOWLEDGEMENTS: Tim Caufield of the University of Alberta reviewed and gave helpful comments, as did several general paediatricians and members of the Canadian College of Medical Geneticists (CCMG). The Board of Directors of the CCMG reviewed and approved the statement.

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The recommendations in this statement do not indicate an exclusive course of treatment or procedure to be followed. Variations, taking into account individual circumstances, may be appropriate.