

Genetic testing in asymptomatic minors

Proposed recommendations of the European Society of Human Genetics

Introductory considerations

Since their introduction, genetic tests and their widespread application have been considered carefully, with special attention to the release of information about the test and test results, the confidentiality of genetic information, the voluntariness of the request, the responsibility towards blood relatives and the psychological impact of the test. When for example a genetic disorder is diagnosed in an index-patient, other family members might also be at risk of developing the disease or passing it to their offspring. For competent adults, it has been agreed upon that the provision of genetic services should be based on respect for the principle of self-determination of the persons concerned. For this reason, any genetic testing, even when offered systematically (e.g. in screening), should be subject to their express, free and informed consent. In this set of recommendations genetic *screening* of asymptomatic minors is not considered, except for the possibility of incidental discovery of carrier status. The recommendations concern genetic testing of asymptomatic minors in a clinical context (testing upon request of the parents or the minors themselves).

Careful consideration is needed when family members at risk are asymptomatic children or adolescents. Cautious reflection is needed whether and under which conditions genetic testing might be performed on asymptomatic minors. With these recommendations the European Society of Human Genetics wants to address in a thorough way the issue of genetic testing in asymptomatic minors. Hereby we want to stress that predictive genetic testing of asymptomatic minors should only be considered after detection of the mutation in the family. Of course, diagnostic testing of minors can follow clinical assessment to confirm a diagnosis.

First, these recommendations will advance some general considerations regarding the treatment of minors and the process of genetic counselling. Second, recommendations regarding predictive genetic testing in minors, incidental and intentional carrier testing are formulated. It should be noted that the term *presymptomatic diagnosis* is only used for those situations where an abnormal test result will almost inevitably lead to development of the disease at some point in later life, whereas the term *predictive testing* covers a broader range of situations, namely also situations in which an abnormal test result implies a substantial risk but no certainty to get the disease later in life. In addition it is essential to distinguish between predictive testing for monogenic diseases and susceptibility genetic testing for multifactorial diseases. Susceptibility testing will not be considered in these recommendations, due to their limited clinical validity and utility. *Carrier tests* are performed to determine whether an asymptomatic male or female carries a mutation relevant for an autosomal recessive disorder or whether an asymptomatic female carries a mutation relevant for an X-linked disorder or whether an asymptomatic person has a balanced chromosomal rearrangement. *Minors* are defined as all human beings who have not reached the age of legal majority in health decisions. The *onset of a*

condition is defined as the time of appearance of the first clinical symptoms of this condition or its first manifestations detected by laboratory tests, radiological results or other technical examinations. These recommendations do not address the issue of neonatal screening, except for the situation of incidental discovery of carrier status.

To discuss these issues and produce recommendations from the professional point of view, a draft background document and recommendations were prepared by Pascal Borry and Kris Dierickx, who had been involved in a EUROAGENTEST¹ workpackage on testing in minors. These documents were discussed in a workshop with an ad-hoc committee of the Public and Professional Policy Committee (PPPC) of the European Society of Human Genetics (ESHG) at a workshop in November 2007 in Leuven, Belgium. Revised versions were discussed at the PPPC meetings in April 2008 in Amsterdam and in June 2008 in Barcelona.

Recommendations

General considerations

- (1) The primary reason to carry out a genetic test on a person who does not have the capacity to consent should be his or her direct benefit.
- (2) The opinion of the minor shall be taken into consideration as an increasingly determining factor in proportion to his or her age and degree of maturity. Decision-making involving the health care of a minor should include, to the greatest extent feasible, his or her consent or assent.
- (3) The parents (or legal guardians) should participate as much as possible in the decision-making process regarding the health care of their children. If the decision of the minor's parents or legal guardians is not in the direct benefit of the minor, health care professionals have the responsibility to defend the interests of the minor.
- (4) Although parental support is recommended, asymptomatic minors with a genetic risk who are well-informed, who have an adequate understanding of a test and its potential implications, who have the capacity to make this decision, who are not exposed to external pressure and who received appropriate counselling, should be considered competent to undergo genetic testing.
- (5) Parents are responsible to inform their children about their genetic risk whereby the information is tailored to their age related capacities. Genetic services should take up a supportive role in this process
- (6) Genetic counselling is always required when considering genetic testing in asymptomatic minors.

Predictive genetic testing

- (7) Predictive testing of minors for conditions with adult-onset is only recommended if preventive actions (e.g. preventive surgery or early detection aimed at therapeutic interventions) can be initiated before adulthood. Otherwise predictive genetic testing in minors for adult-onset disorders should be deferred until the person is old enough to make this decision with a free and informed consent.
- (8) Predictive genetic testing for conditions with childhood onset should only be available at the age that is considered adequate for initiating preventive actions. Genetic testing should, in general, not be performed earlier than the age of the first possible onset of disease or the earliest age when preventive measures are considered useful.
- (9) With unpreventable and untreatable genetic diseases with likely childhood-onset, there are both benefits and risks to predictive genetic testing, and usually neither the benefits or risks completely outweigh the other. Genetic testing could be considered if this would be in the psychological or social benefit of the child and his family. As in the case of preventable or treatable diseases, genetic testing should, in general, not be performed before the age of the earliest possible onset of disease.

Intentional carrier testing

- (10) Testing for carrier status should be discouraged until the minor is able to consent to be tested.
- (11) Carrier testing of children might be considered if another child within the same family has the disorder AND if refusing to comply with a parental request for carrier testing is expected to harm the child.

Incidental discovery of carrier status

- (12) The possibility of incidental discovery of carrier status should be discussed during the pre-test counselling. Parents should decide before the test whether they would like to receive such a result or not.
- (13) Carrier status results that are obtained incidentally should be provided to the parents, unless parents did decide otherwise during the counselling.
- (14) Intentional carrier testing of children might be considered in families where other children within the family have been identified incidentally as a carrier or have been identified as having the disorder

1. www.eurogentest.org

The members of the Public and Professional Policy Committee (PPPC) of ESHG were in 2007-2008:

Martina Cornel (chair, Amsterdam, The Netherlands), Gerry Evers-Kiebooms (Leuven, Belgium), Ségolène Aymé (Paris, France), Suzanne Braga (Bern, Switzerland), Franca Dagna Bricarelli (Genoa, Italy), Shirley Hodgson (London, UK), Gyorgy Kosztolany (Pécs, Hungary), Ulf Kristoffersson (Lund, Sweden), Jan Lubinski, (Szczecin, Poland), Meral Özgüc (Ankara, Turkey), Christine Patch (London, UK), Jorge Sequeiros (Porto, Portugal), Lisbeth Tranebjaerg (Copenhagen, Denmark), Veronica van Heyningen (Edinburgh, UK).

The workshop participants were Pascal Borry, Kris Dierickx, Gerry Evers-Kiebooms (all three from Leuven, Belgium), Martina Cornel (Amsterdam, The Netherlands) and Angus Clarke (Cardiff, UK).