GENETIC INVESTIGATION OF HEALTHY SUBJECTS-REPORT ON PRESYMPTOMATIC GENE DIAGNOSIS OF AUGUST, 2000

Introduction

Here the Council of Ethics outlines the background to its review of presymptomatic genetic testing.

Presymptomatic genetic testing is an investigation of people at risk of genetically conditioned disease or predisposed to a disease,[1] undertaken before that disease has presented with symptoms. Presymptomatic genetic testing is a relatively new phenomenon in the health service. Until the beginning of the 1970s it was the case that the only way to predict or prevent a hereditary disorder in a person was to have a geneticist try and evaluate the risk to the person in question. But the early 1970s saw the emergence of biochemical genetics, in which studies of enzymes[2] and other proteins could in certain cases be used to diagnose a gene defect in a person. To all intents and purposes, however, the studies were only of use for congenital hereditary disorders or diseases with early onset in childhood. Only when the gene for the nervous disorder Huntington's (degenerative chorea)[3] was localized in 1983 did the opportunity for presymptomatic genetic testing present itself–that is to say, the possibility of determining with certainty whether a healthy person is carrying a gene that will produce a severe late-onset disorder.

This possibility triggered international debate on the use of presymptomatic diagnostics. Out of fear for the psychological and social consequences that a presymptomatic examination might conceivably involve (for instance, suicide), the research team that held the key to performing the examination refused to hand it over before clarification had been obtained on the ethical consequences of testing for the disorder without being able to treat it. Other researchers criticized the team for this decision. Amongst other things, they felt that it was wrong to deprive those interested of the possibility of having presymptomatic genetic testing carried out.

Since 1983 it has increasingly become possible to perform presymptomatic genetic testing for similarly severe late-onset disorders such as hereditary breast and intestinal cancer. All these conditions are relatively rare, but the mapping of the human genome,[4] which is expected to be complete by 2003 at the latest, will presumably also enable presymptomatic investigations to be conducted for hereditary forms of prevalent di-

1 See glossary at the end of this chapter.
2 *Idem*.
3 *Idem*.
4 *Idem*.

seases such as mental illness and cardiovascular disease. These disorders are multifactorial (that is to say that any outbreak of the disorder will depend on a number of different factors, not solely on the person's genetic status), so that it will be possible to predict whether a person has a substantial risk of contracting such a disease at some point during his or her life.

In the process, the target group for presymptomatic genetic testing is being expanded so as potentially to include all of us; and the ethical issues of personal relevance to a limited number of people in 1983 will be issues that concern us all.

The Danish Council of Ethics therefore feels that it is time even now to debate the ethical consequences of presymptomatic genetic testing for the individual, for his/her relatives and for society. With this report, then, the Council hopes to encourage broader public debate and contribute to our obtaining "Ethics in Time". What is meant by this is that the ethical implication of new techniques and procedures within the health service needs to be discussed while a technique is at the research and development level, not just once it is ready for use and groups of patients and carers have acquired an interest in it.

The Council has elected to focus on four main topics in the discussion of presymptomatic genetic testing and for each of these four topics to formulate a number of recommendations. These main topics are:

1) *The right to know and the right not to know about one's genetic status.*[5] Unlike other health data (that a person might have about him/herself), genetic information does not include information solely about the actual person but also information about the person's relatives. The question that presents itself, therefore, is whether a person who has been given such knowledge should pass it on to his or her relatives? Do relatives have a right to knowledge? And/or do they have a right to non-knowledge? How can the pros and cons be weighed up out of consideration for the individual person, his/her relatives and society?

2) *Presymptomatic Genetic Testing of Minors.* Should presymptomatic genetic testing of minors be conducted? Including for late-onset diseases? How old must the children be before they can make up their own minds about having such an examination performed? Can parents of a minor make a decision about testing? Does testing constitute a violation of the child's right not to know? Or is non-testing disregard for the child's right to know and the parents' right to know with regard to their care of the child?

3) *Social and Psychological Effects of Presymptomatic Genetic Testing.* Presymptomatic genetic testing has both social and psychological consequences. The psychological consequences pertain to the person who has had or is contemplating having presymptomatic genetic testing done, as well as his/her relatives and other family, for example spouses. The social consequences bear upon the same group of people-amongst other things when applying for insurance and adoption. But the social

[5] *Idem*.

consequences also relate to society as a whole, since the use of presymptomatic genetic testing is instrumental in shaping a society's concepts of, say, disease and health.

4) *Prioritization of Presymptomatic Genetic Testing.* What priority should the use of presymptomatic genetic testing have in the health system? Does society have a duty to offer presymptomatic genetic testing for those diseases it is possible to test for? If so: How is the target group for such testing to be defined? Or, put another way: How is society to control the use of presymptomatic genetic testing? What requirements should be met before presymptomatic genetic testing is implemented if at all?

Most recently in a debate outline from 1998, the Danish Council of Ethics treated the ethical issues associated with the use of fetal diagnostics. It will only be reviewed in this context, therefore, to the extent that it relates to presymptomatic diagnostics for late-onset diseases. The ethical problems with pre-implantation diagnostics[6] (egg sorting), which bears some relation to presymptomatic diagnostics, will be particularly affected, however, as these problems have not previously been dealt with.

In this context, moreover, the Council has chosen not to treat questions relating to genetic carrier diagnostics. A genetic carrier is usually taken to mean a person carrying a gene that does not give rise to disease in the actual person (but possibly in that person's children if the partner also has the relevant diathesis). A genetic carrier test is not a presymptomatic genetic test, however, because no risk of disease is revealed in the person being tested, who —as mentioned— will not him/herself become ill as a result of carrying the offending gene. Questions relating to genetic carrier diagnostics will not be a subject of debate in this report, therefore. This report deals only with examinations of healthy subjects for genetic traits with varying probabilities of resulting in severe illness.

The Human Genome Project and Presymptomatic Genetic Testing

This chapter discusses some aspects of the fact that the human genome[7] will soon have been mapped, answering the questions of what presymptomatic genetic testing is, what are the most common reasons for a person wanting to have presymptomatic genetic testing and what types of result can be the outcome of a test.

What is the Human Genome Project?

The Human Genome Project is an international research project initiated in 1990 for the purpose of mapping man's genetic make-up the human genome. The aim of mapping human genes is to obtain knowledge about the function of the genes in order to enable methods (and medicines) to be developed to treat genetically conditioned disorders. Before that stage is reached, though, the knowledge of the genes will provide scope for presymptomatic

6 *Idem*.
7 *Idem*.

genetic testing, *i. e.* an opportunity to test a person who is healthy, or at any rate free of the symptoms of disease, thereby giving the person a knowledge of whether he or she will contract a disease that may or may not be treatable.

Mapping the genome involves not merely charting man's 100,000-140, 000 genes[8] but also mapping the sequence of approximately three billion nucleotides[9] along the DNA thread, the so-called base pairs.[10] Were it to be written down in letters, the information on the sequence of the nucleotides would fill 200 telephone directories, each containing 1,000 pages. Or, to put it another way: if a person wished to read the sequence of his/her base pairs aloud, it would take that person 91 2 years non-stop.[11]

Today, some 10 percent of the genes and 32 percent of the DNA base pairs have been mapped. Amongst other things, the chart of the entire large chromosome 22 has been mapped – a milestone in the Human Genome Project. The entire genome is expected to have been mapped by about 2003, which is 50 years after James Watson and Francis Crick discovered the genetic code in DNA.

James Watson, who sponsored the Human Genome Project, said of it that one of the purposes is to figure out what it means to be a human being.[12] With such a formulation in mind, it is scarcely possible to imagine anything in biological research more ambitious than the Human Genome Project. And needless to say, great hopes and aspirations attach to the use of the knowledge being uncovered by the genome project.

As shown by the examples below, however, there is no consensus among researchers as to how quickly this knowledge can be translated into practice. The futurologist Joseph Coates thinks that with the mapping of the genome we will soon be capable of manipulating human beings. Not only will we be able to prevent or cure diseases, we will also be able to enhance memory, learning, physical ability, social skills and a person's psyche–adjust temperament and humour, for instance. Granted, there are different time-frames for the various technologies, but the projections form part of an article in which Coates describes technological developments in the 25 years ahead.[13]

8 *Idem*.

9 *Idem*.

10 *Idem.*

11 The Human Genome Project's homepage.

12 Haarr, Lars and Dag E. Helland (eds), *Genteknologi og det menneskelige* [Genetic Engineering and the Human Aspect], Alma Mater Forlag, Bergen, 1998:81.

13 Coates, Joseph, "The Next Twenty-five Years of Technology: Opportunities and Risks," *21st Century Technologies. Promises and Perils of a Dynamic Future*, OECD 1998: 36. See also the Council of Ethics' English-language homepage, where it is possible to read a presentation given by Coates at the Council of Ethics' conference Humans and Genetic Engineering in the New Millennium. The Internet address is: *www.etistkaad.dk/publikationer/genethics/kap01.htm*.

The Danish professor of human genetics, Lars Bolund, on the other hand, feels that there are longer-term prospects until the mapping of the genome in its entirety can be translated into practice, because familiarity with the gene map does not provide a knowledge of gene function. He illustrates his view of this gap in our knowledge with the image of a six-year-old boy put in an ordinary aeroplane with a manual (here, then, the image of the mapped genome) and given instructions to convert the aircraft into a supersonic plane. The boy has only just learned to read, and if he is going to be able to do anything at all in the plane, it will be to repair a hole in a table with a piece of chewing gum at most, says Bolund.[14]

If there is doubt about the time-frame, conversely there is no doubt that the mapping of the genome will assume gargantuan importance for our understanding of both the normal and the abnormal biological processes in man, and hence for the prevention and treatment of disease. The mapping will not only result in our acquiring tremendous information about mankind as a species, but also in the possibility of knowledge and insight into the individual person.

So the mapping is a minefield, both politically and ethically, which raises —and has raised— ethical and philosophical questions of a highly fundamental nature, such as: What is a human being? Can a human being be explained? Is mankind really nothing other and more than the sum of his genes? What is normal and abnormal? What is health and sickness? And how can people relate to predictive knowledge, knowledge of what the future will bring (or may possibly bring) for each individual?

It is some of these questions —and particularly the latter— that the Danish Council of Ethics intends to deal with in this report.

What is Presymptomatic Genetic Testing?

Presymptomatic genetic testing means to examine a person for any genetic disorder or predisposition to disease before that disease has presented with symptoms.

In principle, with the methods currently available, it is possible to examine everyone for genetic make-up[15] that predisposes them to disease, *i. e.* to screen[16] the entire population. But since, for the time being, it is only possible to undertake presymptomatic genetic testing for relatively rare disorders, which only a comparatively small number of people have, screening proper is not being done as it is, for example, in the organized screening for cancer of the cervix among women in certain age groups.

Usually, therefore, the target group for presymptomatic genetic testing will be individuals in whose family there is

14 Lars Bolund, during a presentation at the Council of Ethics' debate day The Man-made Person—The Future with GenEthics and Cloning, 25 march 1999. The presentation can be read on the Council of Ethics' homepage, as it forms part of a publication by the same name as the conference.

15 See glossary at the end of this chapter.

16 *Idem*.

genetic disease and who therefore have a known, high risk of the disease concerned. For instance, grown-up children one of whose parents have a dominant hereditary disorder and who would therefore like to know whether they have inherited the pathogenic gene.[17] As already mentioned, however, it is certainly possible to imagine the target group for presymptomatic genetic testing being able to be extended to include the whole population when the mapping of the human genome provides opportunities for examining widespread diseases such as cancer, mental illnesses and cardiovascular disease.

Why Carry Out Presymptomatic Genetic Testing?

The most common reasons for a person wishing to have presymptomatic genetic testing are:[18]

— A desire for the potential to initiate treatment early on when symptoms arise (in the case of hereditary breast cancer, for instance).

— A desire for the possibility to prevent the disease breaking out (in the case of hereditary intestinal cancer and hereditary breast cancer, for example, the intestine and breasts can be removed before the disease erupts).

— The need for knowledge when making a decision as to whether it is wished to have children - or to refrain from having children in order not to transfer predisposition to a disease to the children; or the need for knowledge with a view to taking a position on fetal examination and possibly also abortion.

— The need for knowledge in connection with life planning-for example, choice of education/training or decision about major financial considerations.

— The mental strain caused by the uncertainty of being an at-risk individual and the need to have certainty ("Will I or will I not contract the disease myself?").

What Results Can be Given After a Genetic Test?

Following presymptomatic genetic testing, a number of results are possible:

Certainty of Disease. The testee can be given the result that he or she is the carrier of a gene known with certainty to lead to disease and able to be transmitted to the testee's children. It might be the gene for Huntington's, for instance, a disease for which no treatment is available, or it might be the gene for familial adenomatous polyposis (FAP), for which preventive treatment does exist on the other hand.

Certainty of not Contracting Disease. The testee can be given the result that he or she is not the carrier of the gene for the disease being tested for. That means that the testee will not contract the disease, nor can he or she transmit the gene to his or her children.

Increased Risk of Disease. The testee can receive the result that he or

17 *Idem*.

18 The following five points are based on a personal communication from Dr. Sven Asger Sørensen, MD, associate professor, Department of Medical Genetics, Panum Institute, University of Copenhagen.

she is the carrier of a gene that may possibly confer the disease tested for. In the case of women, for instance, it might be the gene for hereditary breast cancer, which will lead with about 50 percent probability to breast cancer before the woman is 50, and with 85 percent probability to breast cancer before she has turned 70. But the gene test, then, cannot provide definite information as to whether the woman will contract breast cancer because other, provisionally unknown factors also play a part. This might be both the presence of other genes and environmental factors such as work environment and lifestyle.

Risk of Disease on a Par with that of the Normal Population. When performing presymptomatic genetic testing, it is subsequently possible to pronounce only on the disease due to the gene tested for. In the event of a negative result (information that the testee is not the carrier of the gene in question), therefore, there is no ruling out that the testee can contract other diseases, of course. Similarly, if the subject being tested for a cancerous disease, say, is notified that he or she is not the carrier of the gene for a particular cancerous disease, it does not rule out the possibility that the person in question can contract cancer. Genetic mutations[19] other than the one that has been tested for can confer the same disease; and finally, like everyone else, the testee is at risk of contracting the disease, which can occur sporadically.[20] Even with a negative gene test[21] in hand, then, the testee is not precluded from contracting the particular disease.

In other cases a testee will be able to be told with certainty about the importance of having or not having a specific gene. It was mentioned above, for example, that a person who has tested negative for the Huntington's gene (*i. e.* does not have the gene for the disease) will certainly not contract Huntington's; and conversely, that a person who has tested positive for the Huntington's gene (*i. e.* does have the gene for the disease) will certainly succumb to Huntington's. But in the majority of cases it is not possible to say anything about when the disease will break out or how it will run its course. A positive presymptomatic test is a gene diagnosis, not a disease diagnosis.

Certain Result Uncertain Interpretation

By way of summary, the methods for gene testing can be said to be reliable, but the expressivity of a test may involve some uncertainty in instances when it is not possible to say exactly what is involved in having a gene that deviates from the norm.

There is a great difference, therefore, between being diagnosed with the gene for Huntington's, say, which will definitely erupt and can neither be cured nor alleviated, and being diagnosed with the gene for HNPCC (hereditary non-polyposis colorectal cancer), which will certainly erupt but

19 See glossary at the end of this chapter.
20 *Idem*.
21 *Idem*.

can often be prevented, and finally being diagnosed with the gene for hereditary breast cancer, which will only possibly erupt and is linked to certain available treatments.

Equally, there is certainly a difference in testing negative (which is to say that the gene for the disease is not detected) for Huntington's, and thus being spared any further deliberations, and testing negative for hereditary breast cancer, which merely means being acquitted of those mutations that have been tested for, and thus at most reduces the person's risk to that of the normal population, which —as known— is very great.

What of the Future?

As already mentioned, there are doubts about the speed with which the facilities for presymptomatic genetic testing and subsequent treatment will develop. But there is no doubt that such facilities make demands in terms of ethical reflection. The instant we know the genetic source of the great popular diseases and the target group for presymptomatic genetic testing is thus expanded to include all of us potentially, we shall have taken a quantum leap in our perception of disease and health. The Danish Council of Ethics therefore feels that now is already the time to debate the ethical consequences of presymptomatic genetic testing for the individual, for his/her next-of-kin and for society.

The following chapter (Chapter 3) will contain a factual description of four diseases for which presymptomatic genetic testing is currently being carried out and will shed light on some of the ethical problems to which presymptomatic genetic testing can give rise. On the basis of this, Chapter 4 will contain a compilation of the main ethical topics which the Council of Ethics has discussed in relation to presymptomatic genetic testing.

Main topics in the Council of Ethics' discussion of presymptomatic genetic testing

In this chapter the Council of Ethics will focus on four main topics in its discussion of presymptomatic genetic testing, formulating a number of recommendations for each one.

The Four Main Topics Are:

— The right to know and the right not to know about one's genetic status.

— Presymptomatic genetic testing of under-age children.

— Social and psychological effects of presymptomatic genetic testning.

— Prioritization of presymptomatic genetic testing.

In overall terms, of course, it is debatable whether it is even ethically defensible to perform presymptomatic genetic testing and hence place the testee in the dilemmas raised by a positive result—that is to say, the result that the testee is a carrier of a pathogenic gene. Without this necessarily reflecting the individual council member's stance on such a discussion, for purely practical reasons it has nonetheless been chosen to base considerations on the assumption that testing does actually take place. In section 4.4, however, the Council will discuss which criteria should form the basis of any offer of presymptomatic genetic testing.

The Right to Know and the Right not to Know about One's Genetic Status

The right to know versus the right not to know is a topic that quickly raises its head in the discussion on presymptomatic genetic testing. The reason is that genetic information belongs to the group of health data that does not include information solely about the person him/herself but also about the person's relatives —about parents, children, siblings, uncles, aunts and cousins. That means that as soon as a person is made aware of his or her genetic profile,[22] he or she simultaneously has a knowledge about others—- and a knowledge that may be relevant to them. The question immediately presents itself, therefore, of whether a person who has received such knowledge should pass it on to the next-of-kin. Is he or she entitled to do so? Or perhaps even obligated to do so if that knowledge can be of importance to the next-of-kin's lives? Is the person violating the next-of-kin's right to information about their health by not saying anything? Or, conversely, is the person in question, by coming forward with his or her knowledge, violating the next-of-kin's right not to know— *i. e.*, their right to be protected from receiving unwanted information?

An example may serve as an illustration. We shall use hereditary breast cancer as an example here, as this disease lends visibility to many of the ethical deliberations raised with presymptomatic genetic testing. Hereditary breast cancer is a disease that can be attempted to be prevented by removing breasts and ovaries, so the example is apt for such conditions, above all, and less so for disorders in which there is no scope for intervention.

Seen from the Individual's Point of View

The main character in the example is a daughter whose mother, (maternal) aunt and (maternal) grandmother died of breast cancer at an early age. The daughter is worried whether it may be a case of hereditary breast cancer in the family; needless to say, she is afraid of contracting the disease and is tiresomely alert to any change in her breasts. She therefore decides to eliminate the uncertainty by having a presymptomatic genetic test done. The grandmother's records are obtained for precise information as to her medical history. At the hospital where the mother died, a sample is available of the mother's tumor,[23] which the

22 *Idem*.

23 The Council of Ethics has previously dealt with the ethical problems connected with the use of so-called biobanks where, for example, samples of scirrhi can be preserved. See *Sundhedsvidenskabelige informationsbanker – biobanker* [Health Science Information Banks-Biobanks], published in 1996 by the Danish Medical Research Council, the Danish Central Scientific Ethical Committee and the Danish Council of Ethics (available on request from the Council of Ethics). In this context, therefore, the Council will not go into more detail about this area, merely mentioning that the preservation of biomaterial gives cause for deliberation, one consideration being the balancing of regard for the person submitting biomaterial and regard for the documentation needed by the health service (or health science researchers, respectively) for diagnostic and research purposes.

daughter arranges to have genetically examined. This is done to identify the inherited mutation, in order to know exactly what to look for when testing the daughter for genetic mutation. Against this background, it proves to be perfectly correct that the women of the family are at increased risk of developing genetically conditioned breast cancer.

That gives the daughter certain possible courses of action of her own accord. She can choose to attend mammographic examinations more often than is usual, with a view to finding any tumor early on; she can choose to have preventive removal of breasts and ovaries undertaken; and she can choose not to bring children into the world because she does not wish to expose them to the life she herself will live, *i. e.* a life with the awareness of an increased risk of disease.

But that awareness of belonging to a high-risk family[24] has also provided the daughter with knowledge about her sisters, her aunt and her aunt's daughters, *i. e.* the daughter's cousins. Each of these women individually will be at risk of having inherited the mutated gene. This opens up the way for the questions that were outlined above: Should the daughter allow her relatives to share in the new knowledge, or should she keep it to herself?

Power can engender impotence. In the situation outlined by the example, the daughter must consider whether the knowledge she possesses will give her sisters and cousins possible options or a feeling of powerlessness. The daughter must attempt to weigh up the merits and demerits of making the women of the family aware that they are at high risk of contracting breast cancer. This weighing-up process incorporates concepts like self-determination, autonomy,[25] solidarity and privacy.

For the sake of good order, it should be mentioned that, as also shown by the section on hereditary breast cancer in Chapter 3, Danish practice says that the at-risk person herself (that is to say the daughter here) is the one responsible for contacting her relatives - or not contacting them. In other words, it is not customary for the at-risk person's doctor to contact known relatives to inform them about genetic knowledge. Similarly, it should be mentioned that the daughter does not have any legal obligation to pass on private health information—regardless of its relevance to others. That is why this example has been crafted as it has.

Arguments for Disclosing Genetic Knowledge

In favour of passing on the information is the fact that it gives the women the same options as the daughter herself has, *i. e.* possibilities for seeking to prevent breast cancer or to discover any breast cancer early on after the outbreak; and possibly to make the decision not to bring children into the world themselves or decide about any fetal examination that may be relevant during pregnancy.

24 See glossary at the end of this chapter.
25 *Idem*.

The daughter may therefore be of the conviction that she should not withhold from her relatives information that may be of essential importance to themselves and their children. To put it another way: that her relatives' right to know weighs more heavily than their right not to know.

She may even feel that she not only has a right to pass on the information, but actually has a duty to do so and that, were she to fail in that duty, she would bear part of the responsibility if a sister or cousin were later to die of breast cancer who could possibly have been cured if there had been a greater awareness of the risk of breast cancer. In this case she might feel that her duty to inform should weigh more heavily than her relatives' right to privacy.

"What you don't Know Can't Hurt You". Arguments against Passing on Genetic Knowledge

Against the daughter passing on the information to her relatives is the regard for their privacy, their right to have no one interfere in their lives and place them in dilemmas they themselves have not asked to be placed in.

The daughter, for instance, may feel that she does not have the right to saddle them with knowledge that can cause them worry and anxiety – regardless of the fact that it has given her herself peace of mind in a life where the uncertainty was worse than the certainty. She may feel that she is not entitled to make her sisters and cousins aware that they are at-risk individuals, and hence potentially alter their conception of healthiness, until the opposite has been proved. Even if her relatives were to choose to say that they do not want presymptomatic genetic testing, and therefore do not obtain a knowledge of their genetic status, they can still be said to have lost their right not to know. The mere fact that the daughter has approached them gives them a knowledge of a possible risk which it is subsequently impossible to be ignorant of. The daughter may feel, then, that the relatives' self-determination and integrity[26] will be violated as a result of such an approach and that this is more essential than any possible right to know.

The daughter may also feel that she should not contact her relatives about the risk of a disease that will not definitely erupt, as she will thus be inflicting altogether undue alarm on an unknown number of her relatives in the process. Conveying and understanding risk assessments[27] is normally perceived as being difficult, and the daughter may judge that her knowledge is not sufficiently compelling to be passed on, viewed in relation to the anxiety and fear it must be presumed to be going to cause.

Finally, the daughter may also feel that she should not approach her relatives with information that gives them less than ideal courses of action. She may feel that the duty or right to approach them is closely linked with the options opened up by such an approach; that the right or duty would have been far more compelling if she had been able to announce that her relatives were suffering from a disease

26 *Idem*.
27 *Idem*.

or were at high risk of contracting a disease that could be cured and prevented, simply and without side-effects. The options open to a woman at high risk of hereditary breast cancer are not without their problems: preventive removal of the breasts is a very drastic measure, and mammographic examination involves a number of known problems indeed, particularly so for younger women, in that it is difficult to obtain informative images of the breast in younger women, who often make up the very target group for hereditary breast cancer examinations.

The daughter may therefore feel that the options generated by a knowledge of a possible increased risk of breast cancer are not good enough to set aside her relatives' right not to know. In other words: that in this case, knowledge does not generate possible courses of action with any certainty but could just as conceivably induce powerlessness.

Seen from the Relatives' Point of View

It must be assumed that among relatives there will be advocates of both wishing to know and not wishing to know depending on what each individual considers to weigh heaviest in the given situation: the right of self-determination or the right to privacy the right to know or the right not to know. Realistically speaking, however, it is certainly the case that unless there is a hereditary disorder in the family, and a person him/herself is thus living with the awareness of being at risk of the particular disease, only very few will have taken a prior position on the problem. Usually, a position will only be taken on the question the moment one has been made aware that there is actually something to know. It is an ethical dilemma that even by this stage there has been a partial violation of the right not to know.

In purely legal terms, relatives do not have a claim to know. It is only fair to mention, however, that a doctor may judge that they have such an essential interest in gaining access to knowledge that the doctor can choose to break his or her duty of confidentiality and contact them against the wishes of the testee. The doctor can also choose to break his or her duty of confidentiality after being contacted by the next-of-kin the initiative need not necessarily come from the doctor.[28] In this, genetic information is no different from any other health information. Similar situations are known from, say, the field of infectious medicine, where a doctor can choose to break his or her duty of confidentiality in a case where, for example, an HIV-infected person refuses to tell a partner about his or her HIV status, and the doctor thus has grounds to suppose that the partner will be expo-

[28] In the Danish Act on the Legal Status of Patients, for example, it says the following in Part 5, Section 26, subs. 2, subpara. 2: "Disclosure of… information can take place without the consent of the patient when… disclosure is necessary for the justifiable safeguarding of a patently general interest or is essential for the sake of the patient, healthcare professional or others".

Very similar formulations are seen in the following legislation: Danish Penal Code, Section 152e, letter 2; Danish Practice of Medicine Act, Part 2, Section 9; Danish Public Administration Act, Part 8, Section 28, subs. 2, subpara. 3.

sed to the HIV infection, which the person in question can be protected against by being told the status of the HIV-infected person.

In the example with breast cancer, it is not certain that the daughter's doctor will consider her relatives' interest so urgent that it can override the daughter's right of self-determination and the doctor's duty of confidentiality. But there are currently no guidelines that take a position on these issues for each individual disorder. It is thus down to the judgement of the individual doctor whether there is or is not sufficient reason to break the duty of confidentiality.

The Danish Council of Ethics has discussed the extent to which there is a need for such overall guidelines, describing for each single genetic disease what is considered to be the good, professional standard in force within the field. Such guidelines might describe what information should be given to anyone wishing to have presymptomatic genetic testing for the disorder concerned; and the guidelines could also take a stance on the question of the terms governing the disclosure of genetic information to a third party.

It might be felt that general guidelines are an aid to any doctor who is to conduct genetic counselling and who may not have experience of either the relevant disease or genetics more generally, and that such guidelines would therefore increase the certainty of the patient receiving sufficient and sufficiently correct information to make a decision on an informed basis. It might be said that, at any rate, the experienced doctor will not be any the less prepared for having a set of guidelines available, whereas an inexperienced one will certainly benefit from having them.

But it might also be claimed that written guidelines for genetic counselling, including guidelines for divulging information to another party, come hand in hand with a risk that they will be used as a checklist, that is run through slavishly with no eye for the peculiarities of each individual counsellee's situation, thus making overall guidelines of more harm than good.

Whose Wishes are to be Accommodated?

A particular problem in terms of relatives' right to know/right not to know is linked to presymptomatic genetic testing of people at a 25 percent risk. A person with a 25 percent risk of testing positive (*i. e.* proving to be a gene carrier) as a result of presymptomatic genetic testing will be the child of a person with a 50 percent risk, *i. e.* a person whose parent has tested positive for a dominant hereditary disorder, such as Huntington's. A grandparent may conceivably have died from Huntington's. The latter's child has a 50 percent risk of being a gene carrier; and his or her child (the grandchild of the Huntington's patient) consequently has a 25 percent risk.

If the grandchild wanted to have presymptomatic genetic testing carried out, an examination showing the grandchild to be a gene carrier would simultaneously provide information about the person's parent, even though the latter might not wish to be told whether he or she was the carrier of the pathogenic gene. If the genetic examination shows that the grandchild is a

gene carrier, this will necessarily be the case for the parent too. If the examination reveals that the grandchild is not a gene carrier, the parent of the person concerned may well still be so the risk is (as, of course, it has been the whole time) 50 percent.

Here a conflict of interests can arise between parent and child. The parent will be in a situation where he/she does not intend to have more children, has completed an education and is in work, has no financial considerations such as buying a house and therefore sees no point in being tested. This will only trigger concern. The converse of this is that the child's situation may be that he/she may need to take a decision on the choice of a shorter or longer-cycle education, on the issue of children including fetal examination and possible abortion and possibly on financial decisions. The child may have an interest in knowing its genetic status before decisions are made on such matters that will be crucial to his/her future life.

Who is to be accommodated? The parent or the child? The dilemma is that it is not possible to accommodate both the person with the 25 percent risk's right to make his or her own decision about genetic examination and the person with the 50 percent risk's right to the same; or, you might put it this way: that one at-risk individual's right to know will presuppose overriding another at-risk individual's right not to know. If it is felt that the child's interest may take priority over that of the parent, then in order to accommodate the parent testing could be made conditional on the child not informing the parent about the result. Is it an ethically acceptable solution and is it feasible and practicable?

In cases where the gene for a disease is not known but its position on a chromosome is, a presymptomatic test can be carried out with the aid of markers.[29] This does presuppose, however, that both parents' markers have been determined. In other words, it means that the test on the child can only be performed if the at-risk parent consents. In such cases the parent will be placed in a situation where he/she has to choose between his/her own wish not to know and the regard for the child's wish for knowledge.

A similar ethical dilemma in relation to the right to know versus the right not to know can arise in the situation where an at-risk person is a parent-to-be and would like to have fetal diagnostics carried out to clarify whether the fetus has inherited the gene for the disease at issue, yet does not wish to know about his or her own genetic status.[30] It is possible to envisage the parent-to-be as the child of a patient with Huntington's. As Huntington's is a dominant hereditary disorder, the parent-to-be will have a 50 percent risk of having inherited the disease gene from his or her parent. And if the parent-to-be has inherited the gene from his or her parent, the

29 See glossary at the end of this chapter.

30 The example is taken from the following article: Sørensen, Sven Asger, "Etiske aspekter ved diagnostik af arvelige sygdomme, specielt med henblik på Huntingtons chorea" ["Ethical Aspects of the Diagnosis of Hereditary Disorders, with Special Reference to Huntington's Disease"], *Nordisk Medicin*, vol. 105, 1/1990:2-4.

child expected also has a 50 percent risk of inheriting the gene for its part. In order to be able to distinguish with great certainty whether or not the child expected has inherited the disease gene, it is necessary to examine the one parent who is the at-risk person. But diagnosing the gene in the fetus, of course, will also have diagnosed it in the one parent who is the at-risk person - and who does not wish to know his or her genetic status. A fetal examination can therefore be conducted that does not determine the at-risk parent, but rather the latter's affected parent (the grandparent of the child expected). The examination, then, checks whether or not the child expected has inherited a chromosome 4 (since the gene for Huntington's is located on chromosome 4) from its affected grandparent. If this is the case, the child's risk of having the gene for Huntington's will be roughly 50 percent. If, on the other hand, the child expected has not inherited chromosome 4 from its affected grandparent, its risk of having the gene for Huntington's will be just a few percent.

This method (indirect testing) has the advantage that the at-risk parent is not examined, thereby preserving his or her right not to know. Conversely, however, the method has the drawback that in cases where a termination is performed, a healthy fetus will be aborted in half of all cases. The method results in the abortion of either a fetus with no predisposition to the disease or a fetus which, if allowed to live, will not develop symptoms until about 40 years later. By using indirect testing, the interest of the at-risk parent is thus allowed to take precedence over that of the fetus.

Illustration of Indirect Testing

The illustration shows a man (I:1) who has a hereditary disorder that erupts during adulthood. The daughter (II:1), who is pregnant, has a 50 percent risk of having inherited the predisposition from her father but does not wish to know whether she has this diathesis. Her father (I:1) has two different markers, A and B, which are inherited together with, respectively, the gene that results in disease and the gene that is normal. But we do not know whether A or B is inherited together with the disease gene. The pregnant mother (I:2), who has no disease gene, has marker C on both of her chromosomes, which is also the case for the woman's husband (II:2). The woman's markers are not determined. During fetal examination the fetus's markers are determined. It must have a C from the father. From the pregnant woman the fetus has received either A, B or C, which comes from the paternal grandparents. If it has received a C, then it has nothing from the affected maternal grandfather and will therefore not have the disease gene either. If it has A or B, there is a 50 percent risk that it will have inherited the disease gene, as we do not know whether this gene is located together with A or B.

Is There a Duty to Know?

It might be said that these examples bring us up against the limit for an individual's right not to know; or to phrase it the other way around, that in some situations there must be a duty to know rather than a right to know/right not to know. With refe-

rence to the examples above one might take the view that parents ought not to be able to assert their right not to know if done at the cost of the younger generation's right to know. It might be argued that there are duties associated with parenting, including a duty to know about one's genetic status when this is essential to a child.

Similarly, it might be stated that it is unethical if a parent-to-be insists on not knowing on their own behalf yet insists on knowing the genetic status of their child-to-be, thus allowing their own interest to take priority over that of the child-to-be. This prioritization involves a relatively great risk of aborting a healthy fetus, which would not be the case if the parent-to-be underwent testing themselves before having the fetus tested in the possible event of a positive outcome. In this situation too, therefore, it might be thought that there ought to be a duty to know about one's genetic status, in as much as asserting the right not to know has great consequences for another person, here the fetus.

Pre-implantation examination might be cited as another example that raises the question of the limit on the right not to know and, carrying on from that, of whether, under certain conditions, there should be a duty to know about one's genetic status. In the case of pre-implantation examination (the examination of fertilized eggs before they are placed in a woman's womb) it is possible to examine fertilized eggs from couples where one party is an at-risk individual but does not wish to know his or her genetic status. Any eggs that turn out to contain the gene for the disease being examined for will be destroyed, and a healthy egg will be implanted in the womb. The person examining the eggs will thus find out whether the at-risk person is the gene carrier or whether the at-risk person is healthy. But since the at-risk person wishes to preserve his or her right not to know, the obvious implication is that this knowledge cannot be disclosed, not even if it should transpire that the at-risk person probably has no predisposition to the disease[31] and that pre-implantation diagnostics (which is both physically stressful and financially costly) is a completely unnecessary procedure. To this end, it might be asked whether the right not to know weighs so heavily that it gives the parent-to-be the right to insist on a potentially unnecessary use of pre-implantation diagnostics, or should there be a duty to know in this situation, so that only the parent-to-be, who has previously had presymptomatic genetic testing carried out with a positive outcome and can therefore document that the use of pre-implantation diagnostics is indicated, is entitled to have the diagnostics performed?

One might wonder, then, whether it makes any difference to attitudes towards this service, which of the parents-to-be is the at-risk individual?

When the mother-to-be is the at-risk individual wishing to have pre-implantation diagnostics done in order to preserve the right not to know about her own genetic status, the decision involves no major inconvenience to her husband that might cause her right of self-determination to be set aside.

31 See glossary at the end of this chapter.

According to legislation the woman is at liberty to make an independent decision concerning her body/the fetus. And her wish to have pre-implantation diagnostics performed and in this connection to undergo hormone treatment in order to mature a sufficient number of eggs for diagnosis entails no violation of the husband's rights and physical integrity.

If, on the other hand, it is the father-to-be who is the at-risk individual and wishes to have pre-implantation diagnostics performed in order to preserve the right not to know about his own genetic status, one might ask whether it is reasonable for him to dictate in this way that the mother-to-be has to undergo the stressful hormone treatment needed to conduct pre-implantation diagnostics. Is it reasonable that his interest can override the woman's interests? Even if the woman consents to undergo the hormone treatment (because she sees it as the only way of having a child with her husband or because she does not envisage any problems with the hormone treatment), could there be any question that the health service in this situation ought to refuse to carry out pre-implantation diagnostics with reference, for example, to the fact that it is not wished to provide hormone treatment without a sure knowledge that such therapy is indicated? In this context, reference might be made to Section 6 of the Danish Practice of Medicine Act on the doctor's duty to exercise care and conscientiousness, maintaining that it would be counter to this duty to subject a person to stressful treatment unless indicated.

It can be averred, therefore, that in certain situations there is a duty to know rather than a right to know/right not to know. Opponents of such a duty, however, will object that it is difficult to see this duty as anything other than a moral duty. It can hardly be a case of a legal duty with the resultant presymptomatic genetic testing being forced upon people not wishing to have such testing performed. Yet even the moral duty can lead to examinations that bear the mark of coercion for example, if a pre-implantation examination is done independently of the fact that the parents-to-be have been tested and the at-risk parent can thus be "pressured" into being tested. Apart from this being problematic per se, any positive outcome to the examination of a person who did not wish for the examination may turn out to create great problems. It is fair to assume that a parent who is examined because his or her child wishes to know about its genetic status will have a hard time accepting a positive outcome to the examination and the question is whether the ensuing problems associated with testing outweigh the advantages:

If an altruistic parent who really does not wish to be tested is tested, depression or suicide following on from a gene-positive diagnosis can be just as harmful or more so for the family than living with the doubt and the hope.[32]

32 Wexler, Nancy S. "The Tiresias Complex: Huntington's Disease as a Paradigm of Testing for Late-Onset Disorders", *FASEB Journal*, vol. 6, july, 1992:2822 (Council of Ethics' translation).

The same concern could be asserted for the parent-to-be tested out of a sense of duty towards their child-to-be.

Opponents of a duty to know might therefore adduce the argument that a duty to know creates unmanageable psychological and social problems; and, furthermore, that asserting a duty to know about one's genetic status must mean simultaneously being prepared to clearly define the situations in which that duty is to be asserted, and the diseases for which it is to hold good; and that is far from being as simple as it might sound, based on the examples above:

Should there be a duty to know about one's genetic status for diseases that will not erupt with certainty? If so, how great must the probability be of such a duty being involved? Can, for example, a mother's right to make her own decision not to wish to know whether she is the carrier of the gene for hereditary breast cancer be overridden by the daughter's wish to know, if a positive outcome fails to provide an exact answer to whether the disease will erupt, but merely provides information about the increased risk? Is the daughter's wish for such knowledge sufficiently compelling to disregard the mother's right not to know? Can the duty to know be said to increase with the penetrance of a disease? If so, this would mean that the duty to know about one's genetic status would apply at the very least to the dominant diseases, such as Huntington's. Or, conversely, can it be said that precisely in the case of the dominant diseases, disregarding a person's right not to know has such far-reaching consequences that the duty to know should not be asserted?

Is it possible to talk about the severity of a hereditary disorder, having to be crucial to whether there should be a duty to know? If so, how is the severity of a disease to be defined? And should the duty to know increase with the severity of a disease or, conversely, should severity be an argument that militates against the duty to know?

Is it the scope for prevention, treatment and alleviation of the disease that should be decisive? And, if so, how good must such scope be?

Or, finally, is it the evaluation of the social and psychological consequences of presymptomatic genetic testing with a positive outcome that must determine whether the right to know and the right not to know can be overridden by a duty to know?

Seen from Society's Point of View

Some will claim that society has an interest in eradicating or reducing the incidence of hereditary disorders and hence an interest in knowing about people suffering from or being at increased risk of a hereditary disorder. Such an interest could be rooted in health-economics considerations *i. e.* the view that diseases are expensive for society and that resources would be freed up to fight other illnesses if hereditary disorders were eradicated. Apart from arguing from a health-economics perspective, one could also argue from a eugenic[33] perspective that is to say that society's interest in

33 See glossary at the end of this chapter.

eradicating hereditary disorders could be rooted in the view that hereditary disorders curb the national state of health and inhibit the overall development of society.

This knowledge can be used in a number of ways. Previously, when the possibility of gene diagnostics[34] was nonexistent, such knowledge lay at the root of sterilizing people with hereditary disorders, the spread of which society considered it expedient to prevent. Today one could envisage people with particular hereditary disorders having fetal diagnostics imposed on them during pregnancy with a view to the compulsory abortion of any fetuses proving to have inherited a predisposition to that specific disease. Thus, for example, in the case of fetal examination and subsequent termination it would be possible to eradicate Huntington's at the expense of just a single generation, namely those parents told about their genetic status contrary to their wishes. This use of coercion, however, is regarded as a serious violation of the individual's autonomy and is therefore not ethically acceptable.

Instead, perhaps, society's possible interest in eradicating certain hereditary disorders could be envisaged as encouraging unsolicited approaches to relatives to be arranged, offering presymptomatic genetic testing. That would mean ring-fencing or completely waiving the testee's right to anonymity. The daughter in the example, for instance, would thus have to inform a register of her genetic status, and her right of self-determination would therefore be superseded by a duty to inform.

This gives rise to the same question as outlined above: Under what circumstances is it permissible for the principles of self-determination, autonomy and the right to privacy to yield to a principle of solidarity based on a collective mentality, allowing the individual's right to be overridden for the benefit of "the common good of society" however that is to be understood?

Should such a consideration be linked to the pathogenic gene? Could one, for example, specify the incidence a pathogenic gene needs to have in order for the health authorities to be able to take the liberty of approaching a citizen unsolicited?

Should such a consideration be linked to the therapeutic scope of the disease? Could one, for example, envisage the health authorities being able to contact a citizen unsolicited if and only if the disease to which the approach relates could be prevented or successfully treated in accordance with criteria to be specified? Would it, in that case, be acceptable to approach sisters and cousins of the daughter in the example if the therapeutic option entailed preventive removal of the breasts?

Or should the consideration be linked in other ways to the severity of the disease, the time of outbreak (early or late on in life) or questions of the social and mental stresses-including the risk of stigmatization-presumed to follow on from a positive presymptomatic genetic test?

In this connection it may be mentioned that different registers handle the question of approaching another

34 *Idem*.

person differently. As mentioned in the section on the two types of intestinal cancer, FAP and HNPCC (Chapter 3), the Danish Ministry of Health's registers have been directed to inform first-degree relatives (*i. e.* parents, siblings and children) of gene carriers that they have a 50 percent risk of being predisposed to the disease. This decision is based partly on a statement from the Danish Central Scientific Ethical Committee, which has signalled that it would be unethical not to inform at-risk people of the possibility of preventive examinations.[35]

In the register for Huntington's no approach is made to the at-risk people listed in the records. During genetic counselling of an at-risk individual it is mentioned that other relatives may be at-risk individuals, but the task of informing relatives is left to the actual person receiving the counselling. The rationale for this is partly that there is no effective treatment for Huntington's.

The register for alpha-1-antitrypsin deficiency[36] adopts a practice that can be said to be midway between the two just mentioned. The register asks the person who has tested positive[37] for alpha-1-antitrypsin deficiency whether he or she wishes to tell family members about the illness and, if necessary, give the register the necessary particulars about the family members whom the proband (the first person in a family to be investigated) thinks would like to be examined for alpha-1-antitrypsin deficiency. The information involved concerns the proband's parents, children, brothers and sisters, their children, uncles/aunts and cousins, and children of cousins. For smaller children, this may additionally involve grandparents, their brothers and sisters, and their children and grandchildren. The risk of contracting pulmonary disease among siblings is 25 percent, whereas the risk to the other relatives is between 1 2 percent and 21 2 percent. The register will then approach those family members who may have the altered gene for alpha-1-antitrypsin with information and an offer of presymptomatic examination. After one year first- degree relatives are reminded of the need to reply to the enquiry.

Whatever the registers' practice, it will entail violating either the right to know or the right not to know. The intestinal cancer registers and alpha-1-antitrypsin register can violate some individuals' right not to know and may be reproached for having allowed this to impair the quality of life of these people. Others will appreciate the enquiry from the registers, because it gives them a possibility to prevent disease.

The Huntington's register, on the other hand, can violate people's right to know and will thus be open to re-

35 Wexler, Nancy S., "The Tiresias Complex: Huntington's Disease as a Paradigm of Testing for Late-Onset Disorders, *FASEB Journal*, vol. 6, july, 1992, 2822 (Council of Ethics' translation).
Letter of 15 january 1996 from the Danish Central Scientific Ethical Committee to the Danish Ministry of Health.

36 See glossary at the end of this chapter.

37 *Idem*.

proach on the part of some of these people that this lack of knowledge has precluded them from promptly making important decisions about education and children (possible fetal examination and termination, respectively). A person who has not been informed by the register about being an at-risk individual may feel, then, that his or her quality of life has deteriorated, partly owing to the risk of that person's children having inherited a predisposition to the disease.

Moreover, it might be felt that the practice of leaving it to the testee him/herself to approach family members to inform them of their risk status is not an optimal solution, either, on the grounds that it places the testee in a dilemma that should be shouldered by the doctor or the genetic counsellor. Is there, in reality, some unethical blurring of the lines of responsibility when the latter are unwilling to assume the job of informing at-risk people but, on the contrary, impose this burden on the testee?

One way of solving this problem and safeguarding citizens' right to receive information about whether they are at-risk individuals on a voluntary basis might be to collect the genetic registers at a central institution (along the lines of the Danish Cancer Registry), where the GP can enquire at a person's request whether that person is registered as an at-risk individual. If that is the case, the person can then decide him/herself whether or not to have additional information. Such centralization would have the added advantage of making the authorities' task of checking that there is no abuse of register data easier than when such information is spread across an array of more or less private registers. Conversely, it could also be claimed that a concentrated accumulation of highly sensitive and potentially stigmatizing information harbours a risk of abuse. For example, centralizing information would increase the state's scope for merging data. Such register merges are familiar from the social field and are often the target of criticism from citizens who feel they are being monitored and "smeared" by "Big Brother".

The arguments for society's interest in eradicating hereditary disorders were mentioned above: a social-economics argument and a eugenic argument. It should also be mentioned that, conversely, arguments can be made against society's interest in eradicating hereditary disorders. One might hold the conviction that the problem is beyond the remit of what society is entitled to interfere with: that government meddling in citizens' private matters, including pregnancy and birth, should take place to the least possible extent. One might also hold the conviction that attempting to eradicate hereditary disorders violates the principle that all people (irrespective of abilities, health and so on) have the same human dignity, and it is thus an expression of social brutalization. And, as an extension of this, it might be said to be unethical to attempt to eradicate hereditary disorders and thus reduce the multiplicity of life and the inviolable amenity value that is connected precisely with that diversity. Finally, a slippery slope argument might be adduced to the effect that once society is accepted as having an interest in eradicating hereditary disorders (or possibly just hereditary disorders previously defined

as "serious" according to specific criteria), it will lead on to a slippery slope, and less severe diseases will gradually also be included in a raft of diseases or disorders justifying a greater or lesser degree of government intervention or inducement with a view to eradicating these.

The Council of Ethics' Recommendation on the Right to Know versus the Right not to Know

Central to the Danish Council of Ethics' discussions on the right to know/the right not to know were possible ways of weighing up regard for the individual person, his/her relatives and society.

Danish legislation (the Act on the Legal Status of Patients and the legislative rules concerning the protection of sensitive personal data) attaches importance to protecting personal integrity.[38] In this context, that means a taste's right to make his or her own decision concerning the disclosure of genetic information. Thus, in the legislation, the individual's rights generally enjoy privileged *status vis-à-vis* relatives' and society's right to information.

The Danish Council of Ethics believes that the disclosure of genetic information to another person is best done by having the decision about the approach made by the testee, who can fairly be presumed to be the person best able to evaluate whether another particular individual wishes to possess that knowledge. The Council of Ethics concurrently acknowledges that entrusting the decision to inform another person to the testee places that person in a dilemma that some people would feel should be shouldered by the doctor or genetic counsellor.

In relation to instances where a testee does not wish to take charge of disclosing information to another person, the Council of Ethics would state the following:

The Council of Ethics recommends that for groups of diseases presenting the same hereditary succession and ethical problems, descriptions be formulated of the practice considered to be the good, professional standard in force, and that these overall guidelines accommodate a stance on the question of the conditions governing the disclosure of genetic information to another person. It is the Council's opinion that such guidelines must be drawn up for these groups of diseases, since the risk, prevention and therapy potentials vary greatly for the individual groups of diseases.

The Council of Ethics wishes to signal that the guidelines must make it clear that they may not be used by the genetic counsellor as a checklist that is run through slavishly with no eye for the peculiarities of the individual counsellee's situation.

The legal rights of the person who has had presymptomatic genetic testing undertaken are not sufficiently well safeguarded today, since the definition of "the special case", which can justify breaking the duty of confidentiality, is based exclusively on the judgement of the individual doctor.

Another question that could be accommodated in such guidelines is the right to information claimed by the party wishing for presymptomatic ge-

38 *Idem.*

netic testing (see also Appendix 1 to this report on "Information and consent").

The Council of Ethics recommends that the Danish Ministry of Health/National Board of Health, Denmark outline, in the form of an instructive guide, overall guidelines for the dissemination of information, setting out inter alia the conditions governing when a doctor can make contact with another person. One condition of such an approach might thus be that there is essentially the possibility of preventing or delaying the outbreak of a severe disease, provided that another person is advised of his or her genetic predisposition to the disease on the basis of the information. Since the Council of Ethics' point of view is that it is the medical experts providing the genetic counselling and examination in practice that must devise more precise criteria for disseminating information within the individual disease groups, the Council recommends that more precise supplementary criteria for each individual disease group be drawn up by the medical companies/geneticists' professional organization.

The Council of Ethics recommends that, apart from that, there be no legislative changes in the rights of a person who has had presymptomatic genetic testing carried out. The Council emphasizes that the legislation should primarily ensure regard for the testee's judgement and right to privacy, and thus considers it essential to protect the testees' scope for themselves exercising what they perceive to be an obligation in terms of close, genetically linked relatives.

The Council considers that, subject to the implementation of the above recommendation to formulate a guideline, the legislation fulfils this, while at the same time accommodating any third person by giving health-care workers the possibility of disclosing information in special cases.

The Council of Ethics recognizes that a conflict may arise between a person's right to know and another's right not to know. The legislation gives the individual the right to determine him/herself whether or not he or she wishes to know. This right of self-determination does not give the individual the right to control other people's choice. In practice, however, the legislation cannot prevent a person invalidating another person's, *e. g.* a relative's, freedom of choice, *e. g.* by passing on unwanted information to that person.

In cases where a person has unknowingly been registered as a carrier of a hereditary disorder and no presymptomatic genetic testing has otherwise been undertaken in the family, the Council pronounces as follows:

The Council of Ethics recommends that it be permitted to address an enquiry with information about genetic status and an offer of genetic investigation and, where appropriate, presymptomatic genetic testing to the person in question in accordance with the above guidelines and, more particularly and essentially, that there must be scope for preventing a severe disease or delaying its outbreak.

The Council of Ethics recommends that citizens be informed that they can contact registers themselves about hereditary disorders with a view to clarifying whether they are registered as being predisposed to a particular di-

sease. In this connection it is recommended that the Danish Data Surveillance Authority's list of registers be designed in such a way as to include all registers in Denmark.

The Council of Ethics is aware that there are situations in which the regard for another person's right not to know could cause the testee's right of self-determination to be overridden.

The Council of Ethics has Discussed Two Situations in Particular:

1. One is the situation in which an at-risk individual's wish to have presymptomatic genetic testing carried out is conditional on a corresponding genetic examination of one of the parents, who nevertheless wishes not to receive the attendant knowledge and is therefore unwilling to undergo an examination.

The Council of Ethics wishes to signal that in such a situation there is no sense in talking of a right to know or a right to autonomously make a decision about genetic examination, in that such a right provides no basis for compelling another person to undergo an examination unless there are altogether extraordinary circumstances regarding crucial societal or individual interests that can justify such coercion. That is not considered to be the case in this situation. The Council of Ethics is thus of the opinion that situations do exist in which the regard for another person's right not to know means that presymptomatic genetic testing cannot be carried out.

Where it is possible to carry out genetic examination of an at-risk individual without involving the parent of the person concerned, the Council of Ethics feels that the examination should be conducted despite the parent not wishing to know his or her genetic status, as the at-risk individual's right to know is accorded greater weight than the parent's right not to know.

2. The other situation is the one in which there are conflicting desires on the part of a couple as to whether fetal examination should be performed. A distinction can be made here between cases in which it is the husband or the woman, respectively, who is the at-risk person and does not wish to know whether he/she has a predisposition to the disease.

Thus, it may be a case of a woman being pregnant by an at-risk person and of her wishing to have a fetal examination conducted with a view to establishing whether the child is a carrier of the disease gene. If the examination is carried out, and if it shows that the child is a carrier of the gene, it will simultaneously have demonstrated that the husband is the genetic carrier and he will thus have received a piece of information at odds with his wish not to know.

Conversely, it may be a case of the pregnant woman being the at-risk person, but not wishing to know whether or not she actually is the genetic carrier. If the husband in this situation wants fetal examination performed, and if it is carried out and yields the result that the child is the carrier of the disease gene, it will simultaneously have been demonstrated that the woman is the genetic carrier and –contrary to her desire not to know– she will have been given information about her status.

The Council of Ethics wishes to stress the equal nature-in-principle of motherhood and fatherhood, and the importance of securing for parents-to-be the best conditions imaginable for a forum enabling them to arrive at a solution to any mutual disagreement on the possible performance of a fetal examination through dialogue.

The situation in which two parents-to-be disagree as to whether fetal diagnostics should be performed is rare, though nonetheless unfortunate in each individual case. Where the couple in question ends up being unable to resolve the conflict themselves, there is a need to clarify how society, represented in the form of the executive staff, should act in a situation that involves the right to know, as acknowledged by the legislation and as supported in ethical terms, being at crucial variance with the right not to know, as also acknowledged by the legislation and also supported in ethical terms.

By way of introduction it needs to be highlighted that, faced with this dilemma, a fetal examination cannot be performed without performing an intervention on the woman's body. Such an intervention undertaken without the woman's informed consent would entail setting aside the ethical requirement of respect for a person's integrity and dignity. Very generally speaking, this ethical requirement means that interventions in the form of forced examination and treatment can only be considered in special situations where there are essential societal or private interests at stake. This ethical requirement is expressed in the legislation, which permits forced examination and treatment of citizens only in altogether unique situations. The Danish Council of Ethics does not feel that the nature of the situation mentioned, in which a husband wishes to know about his child-to-be's genetic status, is such that it can override the ethically determined requirement that examinations calling for an intervention on a person's body cannot be undertaken without the informed consent of that person.

The only thing that remains to be considered, then, is the situation in which the woman wishes to have a fetal examination performed based on her right to know about the genetic make-up of the fetus, while the husband opposes the performance of the examination with reference to his right not to know.

The legislation in force gives a pregnant woman the right to have fetal examinations performed on the child being expected, on request, where medically indicated and assuming that other conditions have also been met. Although giving ethical consideration to whether the husband's consent should also be obtained cannot be dismissed in principle, there is currently no requirement to do so under the legislation. The question is, then, whether the fact that a fetal examination with the nature of presymptomatic genetic testing can provide knowledge about not only the child but also the husband, can constitute ethical grounds for introducing demands for a change in the law, under which he too must grant his consent for the performance of the examination.

Suffice it to mention here that introducing a requirement that the at-risk

person must grant consent for a fetal examination of the nature of presymptomatic genetic testing furnishes no solution to the dilemma described, to wit in the event of the two parties not reaching agreement on the question, with the at-risk person saying no and the other party saying yes to a fetal examination.

At all events, therefore, one may be left with the dilemma and forced to contemplate whose right is to take priority over that of the other person, even if the two sets of rights were to be considered of equal value in principle.

The Members of the Danish Council of Ethics Have Various Ethical Assessments of the View Society Should Adopt in Such a Situation:

A. All members of the Council of Ethics save for Sven Asger Sorensen and Lene Gammelgaard recommend here that fetal examinations with an eye to diagnosing a gene may continue to be conducted, despite opposition to the examination by the father of the child-to-be. However, those members who endorse this recommendation do not agree on the rationale for such.

A.1. Some members (Ragnhild Riis, Mette Hartlev, Ole Hartling, Karen Schousboe, Ellen Thuesen, Pelse Helms Kaae, Asger Dirksen and Nikolaj Henningsen) justify the recommendation on the grounds that the deleterious effects for the woman, if not given an opportunity to have a fetal examination performed, are greater than the harm sustained by the husband in being saddled with knowledge he does not want. In this connection these members refer to the fact that although no intervention on the physical integrity of the woman is imposed, on the face of it, she loses the opportunity to make an informed decision on what her body is to be subjected to. At all events, she will have to make a choice: *i. e.* the choice between completing or terminating the pregnancy. Regardless of whether she chooses one or the other, the choice will have consequences for her physical and mental integrity. An abortion is an intervention that can have both harmful physical and mental effects. These harmful effects can be compounded when the decision about abortion is made on an insufficiently informed basis, thereby leaving some uncertainty as to whether the decision to terminate the pregnancy was right. Similarly, if the woman opts to see the pregnancy through, it can also have an adverse mental and physical impact on her. As is the case with the abortion choice, these potentially harmful effects can be envisaged as being greater when the decision to complete the pregnancy is made on an informative basis which the woman herself considers inadequate. For the woman, the consequences of being deprived of the opportunity to make an informed choice thus concern not only her need for knowledge but also her psychological and physical integrity. Although it is difficult to balance the woman's and the husband's ethically justified rights, these members deem that the potential harm to which the woman is exposed weighs so heavily that her right to secure an informed decision-making basis must take priority over the husband's right not to know. The fact that a female and a male

at-risk person are thus placed on different footings needs to be seen in the context of the fundamental difference in their plights.

A.1.a. Amongst these members, Karen Schousboe, Ellen Thuesen and Pelse Helms Kaae wish to supplement this reasoning with the view that, by virtue of her special emotional relationship with the child-to-be, the woman is the weak party: she unlike the father-to-be cannot merely "opt out" of pregnancy and raising a child. Historical experience bears out the woman's weakness: down through the ages, women have been abandoned by the father of their child-to-be, cornered into abortion etc. The legislation currently in existence in the field is a basic reflection of the protection afforded the weak party's interests: the woman's. These members wish to preserve the legal status quo, because setting aside the woman's unconditional right to make a decision about fetal diagnostics in favour of the father-to-be's right not to know would reflect an unacceptable restriction on the protection of the woman as the weak party.

A.2. Other members (John Steen Johansen, Naser Khader, Frederik Christensen, Lisbeth Due Madsen, Peter Ohrstrom and Erling Tiedemann) did not consider that more fundamental ethical principles had been highlighted above, which in the event of disagreement between the two parents can solve the dilemma at issue; and in the context they do not consider any clear-cut comparison of alternative harmful effects possible but, on the contrary, prone to the significant risk that any prejudice in either direction may ultimately have a watershed influence on the outcome. In so doing, they refer to the quotation on page 74, which mentions depression or suicide as a possible consequence of gene-positive diagnosis, pointing out that such an outcome would invariably guide the calculation and comparison of harmful effects to a completely different conclusion.

These members further find that said comparison between harmful effects easily ends up taking the form of a paradigm for a line of argument that aims at extensive ethical legitimation of abortion, which they do not endorse.

On first thoughts, these members are sympathetic to Sven Asger Sorensen's suggestion in as far as this points towards acknowledging both parents' equal status in respect of both rights and obligations towards the joint child-to-be. However, they feel that the parents' equal rights and obligations should only be viewed in the context of the child's rights, as well as finding it inadvisable only to attach certain indeed, limited recognition of such rights to the rather unique situation under review, in which the father of a child is the person at risk. In the view of these members, therefore, the Council of Ethics should undertake an investigative project at some point on the ethical values and requirements associated with the mother, father and child triad.

On the basis currently available, John Steen Johansen, Naser Khader, Frederik Christensen, Lisbeth Due Madsen, Peter Ohrstrom and Erling Tiedemann have therefore concurred that fetal examinations with an eye to diagnosing a gene may still be con-

ducted, despite opposition to the examination on the part of the child-to-be's father. This endorsement needs to be seen as a provisional and more pragmatic solution to the dilemma described. They rationalise this endorsement on the grounds that there is no obvious reason for the Council of Ethics to propose any legislative amendment regarding consent to the performance of fetal examinations until such time as an ethical rationale for such a change in the law can be demonstrated as the result of more complete fact-finding work.

B. A minority on the Danish Council of Ethics (Sven Asger Sorensen and Lene Gammelgaard) recommend introducing a rule into the legislation to the effect that fetal examination for a severe, late-onset disease based on one of the parents being at substantial risk of carrying a predisposition to the disease, which may have been passed on to the fetus, may only be carried out if the parent who is the possible genetic carrier consents to the examination.

To exemplify this, a possible scenario is that one half of the parenting couple him/herself has a parent with Huntington's but does not wish to know whether he/she is him/herself a carrier of the predisposition to this disease. If fetal examination is performed and it evinces the result that the fetus is predisposed to the disease, the process will lead to the at-risk parent being made aware —contrary to his or her wish— that he or she is also predisposed. Knowing that one is going to develop a severe disorder can bring with it major adverse psychological effects and impaired quality of life which, taken to the extreme, can lead to harmful physical effects, *e. g.* suicide.

For the partner it means that he/she is given the knowledge that both the spouse (the cohabitee) and the expected child are predisposed to the disease.

If a decision is taken to abort the child, the result is that the at-risk parent —contrary to his or her wish— is made aware that he or she will contract a severe disease and the wished-for child will be aborted. For the partner it means being told that the spouse (the cohabitee) is predisposed to the disease and at the same time will be exposed to the psychological pressure induced as a result of terminating a wished-for child.

Fetal examinations for late-onset diseases, in which the at-risk parent does not know his/her genetic status, can thus assume far-reaching negative consequences for the person at risk, the spouse and the fetus alike. This will particularly be the case if the examination is undertaken against the wishes of the at-risk parent, violating the right of self-determination and running counter to the intent of the legislation, which usually confers upon the individual privileged status with regard to relatives' right to information.

By introducing a rule that requires the at-risk parent's consent to fetal examination, the consequence may be that a pregnancy is brought to term with the birth of a child predisposed to the disease, or that a fetus is terminated that may not have the predisposition.

The minority feel that this is far less interventive than the harmful effects that may be triggered by fetal examination in this situation. This judgement allows for the fact that these are late-onset diseases which are not usually developed until many

years after the birth of the child, providing hope that effective treatment will be available if the child is born with the predisposition to the disease. Such hope will presumably mean that only few women will choose abortion if they do not have the chance to have a fetal examination conducted.

In the legislation currently in force it is the woman who holds the absolute power to decide about fetal examination and abortion. Yet this legal position was instigated at a time when fetal examinations for late-onset diseases were not relevant, and the problems discussed here were not relevant either, therefore. The minority's proposal implies that, in these altogether unique situations, a man who is at risk and does not wish to know his genetic status is given the chance to prevent fetal examination being performed The proposal thus entails no form of intervention on the woman's body but merely results in the woman's right to determine whether fetal examination should be performed being restricted in rare cases. Such restrictions on women's right of self-determination are found, for instance, in society's ban on abortion after the 12th week of pregnancy.

Presymptomatic Genetic Testing of Minors[39]

Should the parents of a minor (a child under the age of 18) possibly carrying or predisposed to a late-onset genetic disease have the right to know that is to say, to have presymptomatic genetic testing of the child undertaken? Or should that right cede to the child's right not to know and the right of self-determination? And, if so: at what age should a minor be independently able to make a decision for or against presymptomatic genetic testing?

Assuming the parents' right to know is acknowledged, should they then have a moral duty to tell the child the results of the genetic examination? Or should they have a right to withhold that knowledge?

These questions have been central to the Danish Council of Ethics' discussion of the ethical problems connected with presymptomatic genetic testing of minors.

In Denmark, presymptomatic genetic testing of minors is carried out for late-onset diseases. Testing is done for two types of colonic cancer and for alpha-1-antitrypsin deficiency, which was described in Chapter 3. In addition, presymptomatic genetic testing is performed for "familial hypercholesterolaemia", a condition with a severely increased level of cholesterol in the blood and a resultant increased risk of early cardiovascular disease. No presymptomatic testing of minors has been done for Huntington's or hereditary breast cancer, but testing of minors for hereditary breast cancer is known to have taken place in other countries including Sweden. In principle, there is nothing to stop such tests being able to take place in Denmark, since there is no legislation in existence regulating the use of presymptomatic genetic testing of minors

[39] This section was inspired chiefly by articles in the following publication: Clarke, Angus (ed.), *The Genetic Testing of Children*, Oxford, BIOS Scientific Publishers Ltd, 1998.

for late-onset diseases. Present-day practice has thus evolved as a result of what is regarded as good clinical practice by the geneticists and other physicians involved.

However, the Council of Ethics wished to investigate whether there is a need for better legal controls in the field and has therefore discussed what criteria need to be met in order to make it ethically defensible to perform presymptomatic genetic testing of minors for late-onset diseases.

Clarifying the questions of parents' right, if any, to subject their child to presymptomatic genetic testing vis-B-vis the child's right, if any, not to know and its right of self-determination has necessitated taking up a position on a number of additional questions, including the significance of the following:

To what extent a knowledge of the child's genetic status is important to its health: Whether positive knowledge, in other words, can lead to prevention, alleviation or cure, or whether such knowledge will have no therapeutic consequences.

The anticipated outbreak time for the disease in relation to the time of the genetic examination.

The severity and penetrance of the disease (*i. e.* its clout).

The risk of unwanted social and psychological consequences.

The child's maturity and own ability to make a decision.

Criteria for the Presymptomatic Genetic Testing of Children

Options

Presymptomatic genetic testing of minors could be made dependent on whether a positive examination result (*i. e.* detection of the gene being examined for) provides scope for action that will benefit the child. It might be medical treatment that prevents, postpones or alleviates the outbreak of the disease or the sequelae following the outbreak of the disease. An obvious example (as already mentioned in Chapter 3) is that a minor diagnosed as a carrier of the gene for hereditary colonic cancer will be offered regular laparoscopic examinations of the intestine with a view to diagnosing polyps or cancer proper and subsequently removing the intestine in an operation.

Other options might be social or psychological measures aimed at preparing the child and/or family for a future with illness or increased risk of illness. That might entail planning an education or childhood and adolescence in which the parents place greater emphasis on arming the child psychologically for a life of illness (and possible discrimination) than they would have done without a knowledge of the child's genetic status.

In families with illness (genetic as well as other disease), incidentally, it is known from experience how difficult it is to keep such knowledge secret from the children, who sense that there is something wrong and can therefore be troubled by uncertainty and fear. Although the knowledge that a child is carrying the gene for a late-onset disease does not provide specific options, clarifying the question can therefore provide such great emotional relief as to warrant testing per se.

Finally, it might be stated that presymptomatic genetic testing of minors also provides increased scope for action in cases where the examination

disconfirms a suspicion that the child is carrying a pathogenic gene. If an examination gives the child a "clean bill of health", the child can avoid any preventive examinations required (such as the laparoscopic examinations mentioned), saving both the child and the rest of the family the concern.

Conversely, one's conviction might be that the options must be very favourable indeed to be able to justify presymptomatic genetic testing of minors for late-onset diseases—and the violation of the children's right of self-determination this entails. According to this conviction the possibility of social and psychological measures will not be sufficiently compelling arguments for disregarding the child's rights, not least because such social and psychological measures cannot be said to be unequivocally beneficial to the child. Clarification of genetic status can give emotional relief, but can equally well turn out to be a great emotional strain. And, despite the best of intentions, childhood and adolescence that aim to equip the child for a life of illness can result in the child feeling pathologized and stigmatized in relation to other children, particularly brothers and sisters who are not carriers of the gene in question. Similarly, the child can perceive social measures aimed at guiding it towards, say, specific occupational choices as severely restrictive, engendering in the child a feeling of having no influence over its own life.

This attitude is supported by the fact that there is only a minimum of documented knowledge about the importance for children of having presymptomatic genetic testing carried out. Socially and psychologically; and in the short and long term.[40] It might be argued that as long as this knowledge is lacking, great reticence should be exercised in carrying out presymptomatic genetic testing of minors for late-onset diseases.

Time of the Outbreak of the Disease

One of the factors that should be taken on board when adopting a position for or against presymptomatic genetic testing of a minor is the time of the outbreak of the disease for which any presymptomatic genetic testing has to be performed.

One may be of the belief that presymptomatic examination should not be carried out for a disease whose outbreak lies way off in the future in relation to the time of the examination. One example might be testing for the hereditary form of Alzheimer's, which does not break out until the child is no longer a child but on the contrary is around 60 years old. Since there is no preventive treatment for hereditary Alzheimer's, such testing can be deferred to adulthood without any problems, when the person concerned can decide the pros and cons of testing him/herself. Where there is no medical determination to say that the presymptomatic examination must be conducted during childhood, the examination should be postponed, therefore, so that the child's right of self-determination is not violated.

40 Cohen, Cynthia B. "Moving Away from the Huntington's Disease Paradigm in the Predictive Genetic Testing of Children". In Clarke, Angus (ed.), *op. cit*., note 39.

Another conviction might be that it is lacking in subtlety merely to say that it ought not to be possible to conduct presymptomatic genetic testing of minors for late-onset diseases. For what may seem obvious in the case with hereditary Alzheimer's is far less obvious in connection with diseases that can break out earlier on in a person's prime working age. Alpha-1-antitrypsin deficiency might be an example of a condition where the parents of an at-risk child might feel that knowing the child's genetic status would give them options for example, along the lines of protecting the child from tobacco smoke. According to this conviction, therefore, stressing the time of the outbreak has no meaning. On the contrary, the criterion for whether or not to carry out presymptomatic genetic testing should be linked to whether a positive examination result yields constructive courses of action, as is actually the case on detecting a predisposition to pulmonary disease.

Severity and Penetrance

How the severity of a disease is perceived varies from one person to another. Owing to these differences in the perception of what is a severe disease, it is not possible to say anything clear-cut about the influence that the severity of a genetic disease should have on the decision whether to conduct presymptomatic genetic testing of a minor.

It might be claimed that the more severe the disease is deemed to be, the more powerful the arguments in favour of presymptomatic genetic testing need to be. The rationale might be that testing for a very severe illness has correspondingly more serious implications for the testee, and that based on a regard for protection, therefore, such testing should be deferred pending the time when the person in question can make his or her own decision for or against testing.

But the contrary might equally well be claimed: that the more serious a disease is judged to be, the more powerful the arguments against presymptomatic genetic testing have to be. The argument here might be that precisely because the disease is a severe one, it is all the more important to be able to take early precautions or make mental preparations for any constraints that might be imposed by the disease.

One possibility is that the degree of severity could be viewed in the context of the degree of penetrance, *i. e.* the likelihood of the disease breaking out. In this regard it could be said that a slim likelihood of the specific disease breaking out does not warrant the performance of presymptomatic genetic testing, which creates undue worry and concern on the part of many of those tested. Once again, however, one finds oneself in a situation where it is seldom possible to gauge what is a slight and what is a great probability, respectively. For example, an examination is conducted for alpha-1-antitrypsin deficiency on minors with 1 2 percent risk of being predisposed to pulmonary disorders (male and female cousins of a patient with alpha-1-antitrypsin deficiency). Any gene carriers are at increased risk of developing alpha-1-antitrypsin deficiency, but even for smokers the probability of the disease breaking through is not 100 percent, but rather

85 percent or so. This procedure could be said to reflect the great willingness to test combined with the slight probability of disease. In contrast to this is the fact that in Denmark presymptomatic genetic testing for Huntington's is not carried out on minors, and generally only on people at 50 or 25 percent risk of being gene carriers (that is, children and grandchildren of a patient with the disease). Gene carriers will develop the disease with certainty. This procedure might be said to reflect greater reticence about testing combined with relatively great likelihood of the disease. These procedural disparities reflect differences in the perception of severity and the importance of penetrance and in the subsequent evaluation of when it is ethically defensible to carry out presymptomatic genetic testing of minors.

Social and Psychological Consequences

Presymptomatic genetic testing of minors could be made conditional on an evaluation of the social and psychological consequences of testing. As mentioned below, however, only scantily documented knowledge of such factors exists. Nevertheless, there is some experience to indicate that the psychological consequences are considerable compare the section on screening of children for alpha-1-antitrypsin deficiency, which was halted prematurely on account of the undesirable social and psychological consequences for the children and their parents (the parents were very concerned about the children; and the children, for example, more fussed over than non-tested peer-group children).

It might be said that a lack of knowledge about the social and psychological consequences calls for reticence in testing minors. But conversely, it could be maintained that studies into the social and psychological consequences of presymptomatic genetic testing (and resultant testing guidelines) will generalize to the detriment of the single individual. It is therefore preferable to have the decision for or against taken by the family contemplating testing, in consultation with a genetic counsellor. Only in this way will sufficient emphasis be assigned to the regard for each individual family's special conditions.

The Maturity of the Child

Danish legislation on patients' legal status gives a child the right to grant its consent for medical treatment from the time the child turns 15. From this age on, then, a child is judged mature enough to make a decision concerning disease and treatment. As stated, in Denmark no presymptomatic genetic testing of children under 18 is carried out for Huntington's. This policy is a result of what the geneticists regard as good clinical practice. But there is probably no authority in law for preventing the examination of a child over 15 who him/herself insists on having an examination conducted which there can be said to be a medical basis for performing. The same applies to the examination of an under-15 whose parents insist on such an examination. The same applies, of course, to genetic diseases for which presymptomatic genetic testing of minors is already being conducted now. The fact that the gene-

ticists have no authority in law to prevent such examinations, then, merely means that other factors, for example the perception of good clinical practice, form the basis for the decision.

There is no clear-cut knowledge of how old a child needs to be before the individual in question can be referred to as sufficiently mature to understand both the genetic facts and the emotional and social consequences of presymptomatic genetic testing for a late-onset disease and hence when the child is old enough to be competent to grant informed consent for testing. The age limit is defined differently by different specialists for different diseases, the only legal guideline being the 15-year-old limit in the Danish Act on the Legal Status of Patients.

Even among researchers there is no consensus as to how to define "being competent". For some, competence is associated with a child's ability for abstract thought, for instance, while others maintain that even without the capacity for abstract thought children can have the competence to make concrete decisions in a social setting.

Furthermore, there is a lack of knowledge about the way in which parents' pressure on children may possibly affect the children's' self-determination and their genuine ability to give non-directed informed consent.[41]

As also stated above under the section on "Social and psychological consequences", the lack of knowledge about these aspects might dictate reticence in performing presymptomatic genetic testing of minors for late-onset diseases.

As long as we have no knowledge of when a child, in real terms, can take a stand on the performance of presymptomatic genetic examination, testing of children under 18 should be limited wherever possible.

Conversely, it might be stated that there are such great individual differences between children and between families that it makes absolutely no sense to have a precise age limit on when presymptomatic genetic testing can be conducted. It must be assessed from situation to situation, so as to give consideration for the individual family the greatest possible weight and bring it into line with the phrasing of the UN Convention on the Rights of the Child: "States Parties shall assure to the child who is capable of forming his or her own views the right to express those views freely in all matters affecting the child, the views of the child being given due weight in accordance with the age and maturity of the child." (article 12, para. 1.).

The Council of Ethics' Recommendation on Presymptomatic Genetic Testing of Minors for Late-onset Diseases

Central to the Danish Council of Ethics' discussions on presymptomatic genetic testing of minors were the following general questions: Should parents of a minor who may possibly be carrying or predisposed to a la-

41 Source of three sections above: Marteau, Theresa M. and Susan Michie. "Predictive Genetic Testing in Children: the Need for Psychological Research". In Clarke, Angus (ed.), *op. cit.*, note 39.

te-onset genetic disease have the right to know that is, the right to have presymptomatic genetic testing of the child conducted? Or should that right cede to the child's right not to know and the child's right of self-determination? And, if so: at what age should a minor independently be able to make a decision for or against presymptomatic genetic testing?

Acknowledging the parents' right to know, should they then have a moral duty to tell the child the results of the genetic examination? Or should they have a right to withhold this knowledge?

The Council of Ethics is of the view that presymptomatic genetic testing of minors should take place on the basis of the overriding principle that the minor's right not to know and his/her right of self-determination should be allocated sufficient weight so that presymptomatic genetic testing of minors should not be carried out for diseases onsetting after the age of 18, when the child —having come of age— can adopt its own position pro or contra genetic testing.

The Council of Ethics does feel, however, that this overriding principle can be departed from in cases where a positive genetic examination result (that is, detection of the gene being examined for) provides scope for treatment which to any essential degree prevents, defers or alleviates the outbreak of disease or the consequences of the outbreak of disease.

In relation to cases where the overriding principle can be departed from because, for example, preventive options exist and presymptomatic genetic testing of children under 18 can therefore be conducted, the Council of Ethics pronounces as follows:

The Council of Ethics recommends, in respect of minors under the age of 15, that the parent holding custody be the one with the competence to make the decision concerning the performance of presymptomatic genetic testing. However, it is essential to ensure that an under-age child's own views are made an increasingly decisive factor, the older and more mature the child becomes.

The Council further recommends that presymptomatic genetic testing of a child under 15 should generate a moral obligation on the part of the child's parents to notify the child, together with a genetic counsellor, about the examination in order to protect the child's right to express its views in that regard. If the child so wishes, he or she must be notified of the results of the genetic examination and its consequences. This should be done at a time when the child is thought to be capable of understanding the information and by the time the child turns 15 at the latest.

With the above recommendation the Council of Ethics wishes to protect the minor from making decisions whose scope he or she does not have the maturity to understand while at the same time accommodating the minor's own views in step with his or her increasing age and maturity.

The recommendation is in accordance with the Council of Europe's Convention on Human Rights and Biomedicine, article 6, which states that the views of a child are to be taken into consideration as an increasingly determining factor in proportion to his or her age and degree of maturity. Similarly, the recommenda-

tion is in keeping with the UN Convention on the Rights of the Child, article 12, which states that the child's views are to be given due weight in accordance with its age and maturity.

The Council of Ethics recommends, in respect of minors between 15 and 18 that a child between these ages should itself determine whether it wishes to have presymptomatic genetic testing undertaken. This means that parents need not assent to, say, the wish of a 16 year-old child to have presymptomatic genetic testing performed, nor can they prevent the 16 year-old from realizing his or her wish.

This recommendation is in line with the Danish Act on the Legal Status of Patients, which states that an individual must have turned 15 in order to give informed consent for treatment in person.

The Council of Ethics recommends that, in the event of fundamental disagreement between parents and child, there must be an opportunity for the mature child, doctor and/or parents to obtain advice and counselling and expert child guidance. This offer should also include children between the ages of 15 and 18.

The Council of Ethics recommends that offers of presymptomatic genetic testing for minors always be given to the children and their parents together with an offer of qualified counselling. The consequence of this recommendation is that the priority assigned to training and further training of counsellors should be upgraded, so as to ensure that:

Counselling is based on documented knowledge of children's emotional and intellectual development,

Counselling is based on documented knowledge of the psychological and social consequences of presymptomatic genetic testing of minors, and

Counselling is geared to the child's age and maturity on a case-by-case basis.

The Council of Ethics Recommends that its recommendation above be translated into a set of general guidelines, *e. g.* in the form of a guideline from the Danish Ministry of Health/ National Board of Health or, if necessary, by amending the law.

Social and Psychological Effects of Presymptomatic Genetic Testing

It is obvious that presymptomatic genetic testing has both social and psychological consequences, the dimension of which makes it necessary to adopt a stance on them. The psychological consequences pertain to the person who is considering having or who has had presymptomatic genetic testing performed, as well as his or her relatives and other family, *e. g.* spouse. The social consequences pertain to the same group of people, as presymptomatic genetic testing can also have an impact within a family for example, when the conditions shared by the family prior to presymptomatic genetic testing are altered by the division brought about by a genetic examination of family members into gene carriers and non-gene carriers. In addition, the social consequences of presymptomatic genetic testing pertain to society as a whole, as the use of this testing is instrumental in shaping society's concepts of, say, disease and health.

Psychological Effects of Presymptomatic Genetic Testing

As presymptomatic genetic testing is a comparatively new phenomenon, there is no record of the long-term psychological consequences the examinations entail for both those who test positive (individuals who prove to be carriers of the gene being examined for) and those who test negative (individuals who prove not to be carriers of the gene in question).

The short-term psychological reactions to presymptomatic genetic testing are better researched. Not surprisingly, the literature in the field evidences reactions of a highly varied nature. The following formulations about possible psychological responses are consonant with the literature in the field, but a conscious choice has been made to present these possible reactions in highly succinct form:

Psychological reactions on the part of people in whom the gene has been detected can range from relief and clear-headedness to disappointment, uncertainty about the disease process, fear, hopelessness, despair, an altered sense of identity, grief and depression.

Correspondingly, the psychological reactions on the part of people in whom the gene has not been detected can range from a feeling of relief and joy to a sense of guilt and sorrow on behalf of, for example, siblings who did not have such a "lucky escape".

The response to genetic examination will vary, of course, not only from one person to the next but also from one disease to the next. There is a great difference between being diagnosed with the gene for *e. g.* Huntington's, which will certainly erupt and is neither curable nor relievable, being diagnosed with the gene for HNPCC (intestinal cancer), which will certainly erupt but can often be prevented, and finally being diagnosed with the gene for hereditary breast cancer, which may only possibly erupt and goes hand in hand with certain therapeutic offers.

Equally, there is certainly a difference between testing negative for Huntington's (that is to say that the gene for the disease was not detected), thus being spared any further deliberations, and testing negative for hereditary breast cancer, which means being cleared solely of the mutations tested for, and thus at most reduces the risk for the person involved to that of the normal population which, as known, is very great.

Social Effects of Presymptomatic Genetic Testing

The social effects of presymptomatic genetic testing can pertain partly to the testee, his/her relations and the rest of the family, and partly to society as a whole.

Social Effects for the Testee

For the testee, it is the risk of stigmatization and discrimination in particular that are the subject of discussion.

The risk of stigmatization is understood to mean that the person who has had presymptomatic genetic testing carried out (and has been diagnosed with the gene), can feel branded and hence at risk of discrimination. This risk of stigmatization alone could warrant a certain amount of caution,

initially in encouraging people to undergo presymptomatic genetic testing whether such encouragement takes the form of an overall call by the health authorities making test facilities available, or a more direct call from a health professional to the person contemplating having presymptomatic genetic testing carried out. Moreover, the risk of stigmatization might warrant trying to minimize this by incorporating it into the design of presymptomatic genetic testing controls, as reflected in the legislation, protocols and reference programmes.[42]

As already mentioned under the social effects for the testee, the impact that presymptomatic genetic testing can have on the internal dynamic of a family must also be included. For example, a family's communality can be altered if a genetic examination splits the family into gene carriers and non-gene carriers.

The Labour Market

The Danish Act on the Use of Health Data etcetera. on the Labour Market seeks to prevent discrimination. The purpose of the Act is to ensure that health data are not used unfairly to restrict wage-earners' chances of obtaining or retaining employment. This applies irrespective of whether the information stems from genetic data, routine check-ups or other sources. For example, it is stated that "when appointing or employing a wage-earner, an employer may not request, obtain or receive and make use of health data for the purpose of elucidating the wage-earner's risk of developing or contracting diseases".[43] In special cases, however, the Act opens the way for offering the employee presymptomatic genetic testing, though the employer may not be given the results.

Insurance and Pensions

Danish insurance and pension legislation has a similar aim, as this legislation forbids private insurance companies and pension funds asking (potential) customers to have a genetic test done and forbids requesting access to inspect a test result already available. According to the way the Act is worded, both insurance companies and pension funds may not "request, obtain or receive and use information that may shed light on a person's genetic make-up and the risk of developing or contracting diseases, which includes demanding examinations necessary to generate such information".[44]

The explanatory notes to the Act state that its purpose is to counter a trend in which people are being discriminated against on the basis of their own or relatives' genetic make-up in a manner that poses a threat to their personal integrity.

However, there are other factors at play when a person applies to the public authorities for, say, early retire-

42 See glossary at the end of this chapter.

43 Danish Act on the Use of Health Data etcetera. on the Labour Market, Part 2, Section 2, subs. 3. Enacted by parliament on 26 april 1996.

44 Danish Insurance Contracts Act and Act on the Supervision of Company Pension Funds, Part 1, Sections 3a and 9a. Passed in parliament on 29 may,1997.

ment as a result of presymptomatic genetic testing. The Danish Ministry of Justice and the Danish Medical Association have ruled that the applicant and the geneticist are obliged to provide the public sector with information that can verify the applicant's genetic profile. This, then, is in contrast to an application for a pension from a private pension fund, where the pension fund may not obtain, receive or use information about a person's genetic profile because the private pension fund can use that information to exclude the person from a pension.

Adoption

The possibility of adoption is another area where presymptomatic genetic testing can assume social consequences. A woman whose family history gives her reason to suppose that she is at increased risk of developing hereditary breast cancer or Huntington's, for instance, might wish to adopt a child rather than giving birth to one herself and thus running the risk of transmitting the disease gene. However, the adoption authorities may ask the woman to have a presymptomatic genetic test done. If this test is positive (that is, the pathogenic gene is detected), she will be unable to adopt, by all accounts. If the test is negative (that is, the pathogenic gene is not detected), the woman will probably prefer to become pregnant herself. Thus the adopter's right not to know is nonexistent in real terms, and the adopter is not covered by the protection against discrimination on the basis of genetic make-up embodied in the Danish Act on Private Insurance Companies and Pension Funds.

In order to prevent an adopter being asked to have presymptomatic genetic testing done in which case the adopter will only be given serious consideration as an adoptive parent if the outcome is negative a choice could be made to blankly deny adoption beforehand to people suffering from or at increased risk of a hereditary disorder. This approach might also be said to offer some protection of the adopted child's interests. Given that the number of adopted children is so much lower than the number of potential adoptive parents, it could be said to be advantageous for the child to be protected from adoption by a family suffering from or at increased risk of a hereditary disorder. In the process, the child would be protected from growing up in a family with the strains and stresses that might follow from an increased risk of disease and possibly even the premature death of a parent. The child would also be protected from growing up in a family where, despite the desire to adopt, the parents might anyway give birth to a child of their own that is sick and requires extraordinary care and attention.

Conversely, such an approach could be said to overemphasize the significance of a hereditary "taint" on the part of potential adoptive parents at the expense of any qualities the couple might otherwise have that should be taken on board in the overall evaluation of their parenting abilities.

In addition, it might be said to be counter-productive in stigmatizing people suffering from or at increased risk of genetic disease. A person found to be carrying a pathogenic gene by presymptomatic genetic testing is, as

already mentioned, no more ill than before the test was conducted, and may never become so (depending on the disease examined for). The point of the examination is gene diagnosis, not disease diagnosis.

Social Effects for Society

In conjunction with the use of presymptomatic genetic testing it has often been adduced that the target group for such testing can now be assumed to have expanded to include us all. At the same time, it is said that with this expansion of the target group for genetic testing follows the risk of our developing a "worry culture" or a risk-focused testing society. The bugbear of such a culture is the image of every newborn citizen equipped with a complete chart of his or her genome and later being summoned to regular examinations for any genetically conditioned disease(s) the person might be predisposed to develop.

Presymptomatic genetic testing can thus dramatically alter our understanding of what disease is, increase our sense of illness and contribute to a society of pathologized and anxietized pre-patients, *i. e.* people who are healthy but may become ill.

But presymptomatic genetic testing can also improve our lives by offering us certainty and possible courses of action in a society with conscious citizens or consumers who exert pressure on the health system. Testing can give us the possibility of changing lifestyle or obtaining medical treatment to prevent, postpone or alleviate a genetic disorder, and hence presymptomatic genetic testing can also conceivably reduce the sense of illness in the individual as well as society as a whole.

Doctor Thorvald Sirnes of the Department of Administration and Organization Theory at the University of Bergen in Norway has articulated the potential problem of genetic testing thus:

The problem is not what effect gene tests will have in today's society, but what society and what culture they are instrumental in creating.[45]

Thorvald Sirnes goes on to say that one of the key questions is the significance that genetic testing will assume for the dividing line between the notions of sick and healthy. Given that everyone, as mentioned, has several genetic "flaws", everyone will be capable of being labelled as sick. The concept of sickness will therefore be extendable so far as to make it difficult to draw the line between sick and healthy with immense priority-setting problems as a result. Widespread use of genetic testing can thus render the notion of sickness just as fuzzy and difficult to define as the notion of health, and result in the notion of sickness becoming unusable as a criterion and control instrument. And in that case, what are we going to put in its stead, asks Sirnes?

Similarly, the social effects of presymptomatic genetic testing can be

45 Sirnes, Thorvald, "Sociale konsekvensar av genetisk testning" [Social Consequences of Genetic Testing]. In: Gentestning–nye muligheter, nye dilemmaer [Gene Testing–New Opportunities, New Dilemmas]. Norwegian Biotechnology Advisory Board, 1998. Available for reading on: Above quotation stems from page 1 of the Internet article and was translated from the New Norwegian by the Danish Council of Ethics.

imagined within people's self-knowledge and lifestyle. People are known to find it hard to comprehend and relate to risk assessments: for instance, being notified of having a 50 percent risk of developing a particular disease before a certain age, and an 80 percent risk of developing it before a more advanced age; and possibly also being at some increased risk of developing an entirely different disease.

The widespread use of presymptomatic genetic testing and accompanying risk assessments can thus assume importance for the way in which people organize their lives. On the one hand, one can imagine a disease-determinism or fatalism that might justify taking no action to possibly prevent the outbreak of an illness "since there's nothing to be done about it anyway".

On the other hand, one can envisage risk assessments becoming a major determinant in the planning of our existence so that lifestyles, for example, were arranged with a view to obviating the disease which the individual experiences as being the most threatening.

Sirnes interprets both these possibilities (the fatalism and the individualized lifestyle arrangement) as problematic.

Both these scenarios will involve lifestyles becoming medicalized, or controlled by the risk of genetic disease. That can create a one-dimensional society in which medicine and disease are assigned far too much space in relation to other aspects of life.[46]

The Council of Ethics' Recommendation on Psychological Effects of Presymptomatic Genetic Testing

The Danish Council of Ethics recommends generating knowledge about the psychological long-term effects of presymptomatic genetic testing both for those who have been diagnosed with a pathogenic gene and for those whose test failed to detect the gene in question.

Such knowledge, which might take the form of interdisciplinary examinations, should at the latest be generated in time to take it on board together with knowledge of the short-term psychological effects when considering whether or not to offer presymptomatic genetic testing for widespread national diseases, thereby effecting a marked extension of the target group for genetic testing.

The Council considers that there is a basis for a research project on the psychosocial consequences both for the individual and for the family that becomes involved in presymptomatic genetic testing.

The Council of Ethics' Recommendation on Social Effects for the Individual of Presymptomatic Genetic Testing

The Danish Council of Ethics recommends that the same rules apply for pension applications to the public sector as to a private pension fund. That means that in connection with pensions cases, the public sector may not request, obtain or receive and use

46 *Ibidem*, p. 3 of the article.

information that can shed light on a person's genetic make-up.

One result of this is that it will not be possible to qualify for a pension on the basis of a positive presymptomatic genetic test. This, of course, may be felt to mark a deterioration in the terms for the individual applicant. The Council of Ethics' reasoning behind this recommendation, however, is that such rules safeguard against gene-based discrimination, maintaining that genetic carrier diagnosis is not disease diagnosis: that a person who has been diagnosed with a pathogenic gene by presymptomatic genetic testing is healthy and not entitled to a pension solely on the basis of that gene test.

The Council of Ethics likewise recommends that adoption authorities not be allowed to request, obtain or receive and use information that can shed light on the genetic make-up of an adopting party.

The background to this recommendation is a wish to guarantee an adopter's right not to know and to counter a trend in which people are being discriminated against on the grounds of their own or relatives' genetic make-up.

The Council of Ethics' Recommendation on Social Effects for Society of Presymptomatic Genetic Testing

The Council of Ethics is aware that the widespread use of presymptomatic genetic testing that can be expected to follow in the wake of the mapping of the human genome can assume negative social consequences. The Council fears that this expansion of the target group for genetic testing will be accompanied by the risk of a "worry culture" or risk-focused testing society developing.

Such a testing society can cause general pathologization and anxietization of the population, which can produce a marked change in healthy people's self-knowledge and choice of lifestyle.

In addition, there may be an undesirable slide in our understanding of sickness and health, making it even more difficult to define the notion of sickness and hence define how health service resources should be prioritized.

The Council of Ethics recommends that examinations be put in place to shed light on the possible social consequences for society of presymptomatic genetic testing as well as the possibilities for controlling these.

The Council regards such knowledge as necessary to the quality of the debate on the possible introduction of the widespread use of presymptomatic genetic testing.

Priority-setting and Genetic Counselling in Connection with Presymptomatic Genetic Testing

Any examination or treatment within the health service is a piece in the greater jigsaw puzzle of making resources go far enough. Priorities must be set, because there are insufficient resources to offer all patients or potential patients the examinations, treatments or care which are called for and would benefit them.

Presymptomatic genetic testing too, of course, is included in this prioritization of resources, and in this context the Danish Council of Ethics has discussed the following issues:

1. Which patient groups should the health service prioritize first the sick or the possibly sick?

2. Does society have a duty to offer presymptomatic genetic testing for diseases it is possible to test for?

3. If so, how is the target group for such testing to be defined? Put another way: how can society control the use of presymptomatic genetic testing?

4. What demands need to be met before any relevant presymptomatic genetic testing can be implemented?

The Sick or the Possibly Sick?

1. Which patient groups should the health service prioritize first the sick or the possibly sick?

There Must Be No "Taking from the Poorly" to Give to the Healthy

When there are limited resources at the disposal of the health service, it may be felt that these should at least be spent on the sick not on the healthy or possibly sick. Consequently, it might be felt that presymptomatic genetic testing should not be a publicly funded service, as the people targeted by the service are healthy or at any rate free of symptoms. If the health service is going to expend resources on testing healthy people for possible diseases, resourcing will necessarily be taken from the sick in far more pressing need of examinations, treatment and care. This is not solidarity, it might be thought, but rather a reverse Robin Hood scenario: taking from the poorly to give to the healthy.

Prevention and Alleviation Are Also Worthwhile

Nonetheless, it might equally well be thought of as just that solidarity: that the offer of presymptomatic genetic testing reflects a recognition that the need for health services is generated not just by broken arms and infections but also by genuine fears about one's future health. It might be felt that for a woman who is at increased risk of hereditary breast cancer or Huntington's, the desire for alleviation is at least equally as legitimate as the wish, for example, that gives women the option of mammographic screening or screening for cervical cancer. As an extension of this, offering presymptomatic genetic testing might not be felt to constitute a failure to care if such testing were able to help an at-risk person prevent the disease, defer or alleviate symptoms by taking early action, or merely help the at-risk person plan their existence better. This view is in harmony with a widely accepted formulation of the objectives of the Danish health service, which includes not only health promotion but also disease prevention and the control and alleviation of health-related suffering.[47]

[47] See, for example, this formulation of the overriding objective for the health service in the Danish Council of Ethics' report Priority-setting in the Health Service, 1996:71: "Furthering health and preventing disease, fighting and relieving suffering related to health with the aim of ensuring the opportunity for self-expression for all, irrespective of their social background and economic ability".

To the argument that presymptomatic genetic testing takes from the poorly to give to the healthy, it might be said that this is a short-term point of view: this is only so at the outset, whereas preventing sickness will be a boon for society in the long term.

Duty to offer presymptomatic genetic testing?

2. Does society have a duty to offer presymptomatic genetic testing for diseases it is possible to test for?

Testing Should not Be Done Merely Because it is Possible

The answer to the question about society's duty will depend, in turn, on how one views the objectives of the Danish health service and thus how it is wished to prioritize resources. There may be a feeling that no such duty exists: that presymptomatic genetic testing is beyond the confines of the core services that should be given the greatest priority in the health service and that widespread testing would constitute an unethical disregard for the obligation to help where need and distress are greatest. It may be felt that simply being able to do so is not a compelling argument in favour of also having to actually do so. New technical possibilities should not be translated into practice at the drop of a hat, but should be subjected to an evaluation of the technical and ethical problems associated with the specific technology. Failing that, there is always the fear that the new technical possibilities will set the agenda for controlling the health service and, more specifically, for example, that the presumably rapid increase in scope for carrying out presymptomatic genetic testing will end up defining what is regarded as a severe disorder, with corresponding demands for services from the health sector.

Research Results are in the Public Domain

Conversely, it may be considered unethical not to make a given test available to those whom it has been developed to help particularly if the test has been developed against the background of publicly funded research and can thus be said to belong to "society". It may be perceived as guardianship and disregard for the individual's right of self-determination if the decision for or against testing is made by a public authority on behalf of the at-risk person to whom the test relates. So it may be felt that the priority-setting discussion should be included at a much earlier juncture in order to ensure that the public can gain influence over the technological development process by means of open debate. Once a test has been fully developed, and patients and health-care staff have begun to call for it, it is too late to bring in deliberations on priority-setting. Where this belief is held, it would be unethical not to make the test available at this point. But of course, how the target group for a given test should be defined is debatable.

How Should the Target Group be Defined?

3. How is the target group for presymptomatic genetic testing to be

defined? Or, put another way: how should society control the use of presymptomatic genetic testing?

Again, hereditary breast cancer makes a good example to illustrate the problem issue. Hereditary breast cancer is one of the world's commonest genetic diseases.[48] That means that with the possibility of genetic testing for hereditary breast cancer we have taken the first step towards a situation in which genetic diagnosis is not limited to the rare hereditary disorders but it is possible to test for national-level diseases a situation that will presumably become commonplace once mapping of the human genome has been completed and the potential target group for presymptomatic genetic testing can thus be extended to include the entire population. As a result, the offer of presymptomatic genetic testing will no longer be directed at the few who have a known, high risk of a hereditary disorder, but at the many.

But who is to be offered testing for hereditary breast cancer? A genetic test is required to differentiate between hereditary and sporadic (*i. e.* randomly occurring) forms of breast cancer; hence the whole of the female population become potential end-users of the test, which can at best sort high-risk groups from the average-risk group.[49]

This will necessarily assume consequences for the distribution of health service resources if there has been no prior discussion to clarify which considerations or criteria are going to regulate the use of presymptomatic genetic testing.

Restricted Access

One approach might be that presymptomatic genetic testing should only be made available to people who are at risk of genetic diseases on a special positive list[50] according to specific criteria for the severity of a disease. Such a positive list would act as a means of control, ensuring that health service resources are spent on those initiatives deemed of greatest importance.

Another view might be that presymptomatic genetic testing should only be made available to a person who has previously sought genetic counselling. The genetic counsellor's task would then be to draw up a genealogical tree of the person's family and the family's clinical picture and, on the basis of this, to assess whether there is any basis for regarding the counsellee as a high-risk person (and hence offer a genetic test) or whether it is merely a case of random accumulation in her family. In order to decide the issue of gene carrier status, however, information from family members is required, and that opens up a can of worms regarding the ethics of approaching and informing relatives, as discussed above under the section

48 Caskey, C. Thomas and Belinda J. F., Rossiter, "Presymptomatic Testing for Genetic Diseases of Later Life. Pharmacoepidemiological Consideration", *Drugs and Aging* 7 (2),124, 1995.

49 Koch, Lene, *Etiske aspekter ved genetisk testning og rådgivning for arvelig cancer* [*Ethical Aspects of Genetic Testing and Counselling for Hereditary Cancer*], Ugeskrift for Læger 160/12, 16 march, 1998, 1839.

50 See glossary at the end of this chapter.

on "The right to know and the right not to know".[51]

Carrying on from there, an additional argument in favour of restricting access to presymptomatic genetic testing is that very widespread use of genetic testing increases the risk of compromising the quality of the attendant genetic counselling, in that it cannot to the same extent be guaranteed to be provided by skilled geneticists but will be passed on to, say, GPs.

By the same token, it might be felt that unlimited access to presymptomatic genetic testing will have unwanted social and psychological consequences along the lines of pathologization and anxietization. As previously mentioned, this may lead to a plunge in our understanding of sickness and health, making it difficult to define the notion of sickness and hence to define how the health service should prioritize its resources. Unlimited access to presymptomatic genetic testing, then, can assume undesirable consequences for the distribution of resources in the health service.

Finally, unrestricted access to presymptomatic genetic testing could have the consequence of making it difficult to adhere to a necessary ban on the testing of minors.

Access for Everyone

Another view might be that access to a test cannot be restricted, as it would not be possible to adopt ethically defensible criteria for such a restriction. By very definition, criteria laid down by a public authority will be unable to take sufficient individual account and will thus deprive the individual of his or her right to make autonomous decisions, based on the very individual peculiarities that apply to the life of the person concerned. With what right can certain people be barred from the benefit of acquainting themselves with their genetic profile?

The same objection might be raised to the proposal to restrict access to testing with the aid of positive lists. A further argument against the use of positive lists —and an argument in favour of unlimited access to testing— is that experience shows there is no need for such controls. The people concerned are able to take a stand for or against testing by themselves, and this makes for sensible self-regulation in the field. By way of example, in several countries there have been studies into attitudes towards presymptomatic genetic testing among people at risk of Huntington's before it was offered. Between 80 and 90 percent indicated that they would avail themselves of the facility. Later, however, when the test became a reality, it turned out that only between 10 and 15 percent chose to have presymptomatic genetic testing undertaken.[52]

The argument that unrestricted access to presymptomatic genetic testing will open the way for overwhelming ethical problems in relation to relatives' right to know/right not to know is not a sufficiently compelling argument for restricting access to knowledge for people who consider themselves to be at-risk individuals in need of the clarification that presymptomatic genetic testing can bring.

51 See *op. cit.*, note 49.

52 Clarke, Angus (ed., *op. cit.*, note 39, appendix 1. p. 291.

Another argument in favour of unrestricted access to presymptomatic genetic testing is that there is reason to surmise that such testing will become a commercial offer, functioning in parallel with the public service. Even now, in countries including the USA it is possible to buy hereditary breast cancer tests. If there is limited access to presymptomatic genetic testing in the publicly funded hospital service, people wishing to have such an examination will be thrown back on the commercial market. That may mean a deterioration in the quality of information and counselling before and after testing, which in such a situation is no longer being performed by specially trained geneticists and is generally working on market conditions of supply and demand. If it is wished to ensure that access to presymptomatic genetic testing is controlled by professional medical evaluations and the provision of optimal information and counselling for the person wishing to have the examination, and conversely to safeguard against access being controlled purely by supply and demand, it is thus necessary for the public sector not to restrict access to these examinations.

Requirements of Presymptomatic Genetic Testing

4. What requirements need to be met before any relevant presymptomatic genetic testing is implemented?

In answering this question, a number of criteria can be posited and an attempt made to fulfil them, individually or collectively. In brief, these include four criteria that often crop up in discussions about priority-setting within the health service generally and the discussion about upgrading the priority assigned to presymptomatic genetic testing specifically.

Cost-effectiveness and Public Utility Requirements

The implementation of presymptomatic genetic testing could be made dependent on whether such early diagnosis is worthwhile from a purely economic point of view, whether it has a positive impact on the national state of health and whether it can thus be regarded as being of public utility.

Adherents of such a requirement might state that these considerations are necessary in order to ensure well-documented prioritization of resourcing rather than the kind of prioritization that comes from a deficient knowledge basis, coincidences in the decision-making process, and the ability of powerful and visible patient groups to accentuate their own needs at the cost of weaker patient groups.

By contrast, sceptics might state that, firstly, it is extremely difficult to perform those kinds of calculations, one reason being that they are based on estimates of the population's willingness to accept the particular offer. There is experience to show that it is difficult to make such an estimate with the requisite accuracy (*cfr*. above on the mismatch between the proportion of people at risk of Huntington's indicating their willingness to take advantage of presymptomatic genetic testing and the proportion of at-risk individuals actually choosing to have the examination performed). Secondly, it would invariably create un-

wanted consequences if health-economics analyses in no way geared to taking on board the "soft" aspects of priority-setting were to be ranked higher than consideration for the individual. How, for example, would analyses of importance for national health that gauge success by the number of life-years gained be able to allow for the value of the security that presymptomatic genetic testing can give an at-risk individual?

Treatment Requirements

The implementation of presymptomatic genetic testing could be made dependent on the quality of the treatment that can be offered to people diagnosed with a pathogenic gene, and on a knowledge of whether the chances of treatment and cure are substantially better for diagnosed gene carriers[53] than for non-diagnosed gene carriers.

As above, adherents of this requirement could state that without such documentation for the quality of treatment, priority-setting would not be done on a sufficiently informed basis.

The sceptics, on the other hand, could state that it is a condition within the health service that nothing precise can be stated about such conditions until, in this instance, the offer of presymptomatic genetic testing has been in use for some time; and even then it would be difficult to satisfy the quality of the treatment requirement when part of the "treatment" can be said to consist of providing those who want a test performed with knowledge and options (compare Chapter 2 on the most common reasons for people wishing to have presymptomatic genetic testing carried out).

Gene Incidence and Penetrance Requirement

The implementation of presymptomatic genetic testing could be made dependent on the pathogenic gene's incidence and penetrance. For each individual disease one could evaluate whether the magnitude of the risk can justify healthy people being offered a genetic test and relatives being traced.

Adherents of this might state that such an evaluation of the disease gene's incidence and penetrance is an altogether necessary control instrument. If genetic diseases with a relatively low penetrance are prioritized on a par with high-penetrance diseases, it will generate a disproportionately large number of ethical problems as well as sending the consumption of resources out of control. The ethical problems, for example, would be the altogether undue pathologization and anxietization of a large number of people who are contacted with a view to being tested for a genetic disease that only very few will develop. By way of extension, problems will arise related to the violation of the right not to know or the violation of the individual's autonomy, as discussed earlier on in this report.

Sceptics, on the other hand, might state that the question of penetrance is a medical distinction, which has no relevance for the individual in real terms. Any person who feels at increased risk of developing, say, alp-

53 See glossary at the end of this chapter.

ha-1-antitrypsin deficiency, will not feel reassured by the statistical observation that the probability is only about 2.5%, for example. Any requirement concerning a given magnitude of penetrance, therefore, could produce the tendency to which health-economics analyses might also be prone the tendency to understress consideration for the individual.

Severity of Disease Requirement

The implementation of presymptomatic genetic testing could be made dependent on predetermined criteria governing the severity of a disease, including the time of outbreak, and the social and mental strains expected to follow on from the disease.

Adherents of such a requirement could state, in turn, that such positive lists are a necessary control instrument for distinguishing between severe and less severe genetic diseases, in order to ensure that resources are used where the need is genuinely greatest and not to open up a Pandora's box of ethical problems.

The sceptics, on the other hand, might say that it is ethically indefensible to prioritize on the basis of requirements concerning the severity of a disease, since genetic diseases (like all other diseases) pan out differently in different people. It is seldom possible, therefore, to say anything unequivocal about the severity of a disease. To this must be added that the severity of the disease is experienced differently by different patients. Hypercholesterolaemia, for example, can be perceived by one patient as a very severe and a socially and mentally stressful condition, whereas another patient with an equally severe clinical picture in objective terms may have managed to arrange his or her life in such a way that the disease is perceived as being far less severe and onerous. Nor, then, will it be possible to isolate the social and mental strains that are expected to follow from the disease with such precision that these statements can form the basis for prioritizing the offer of presymptomatic genetic testing.

The Council of Ethics' Recommendation on Prioritizing Presymptomatic Genetic Testing

The prerequisite for the Danish Council of Ethics' recommendation on the prioritization of presymptomatic genetic testing is an acknowledgement and acceptance of the fact that presymptomatic genetic testing is —and will also be in future— part of the health service's activity.

At the same time, the Council wishes to point out that, in future, presymptomatic genetic testing will also become a commercial offer controlled by supply and demand. The Council harbours some concern about the consequences this might have for the quality of the information and counselling that are necessary, both before and after the performance of presymptomatic genetic testing. Consequently, the Council finds it necessary to make both publicly available genetic examinations and those on offer from the private market subject to politically stipulated and binding standards.

The Council is further worried that commercial companies can obtain a patent on the examination of genes for special mutations. The company holding the patent rights can demand

that the examinations be carried out exclusively at the company's laboratories. This involves a risk of genetic examinations being monopolized and, with it, the risk of abuse of information, for example, mapping the large volumes of genetic material without the originators' consent and knowledge.

Such monopolization further entails the risk of a price-fixing policy, restricting access to presymptomatic genetic testing. The Council of Ethics consequently recommends that a political stance be taken on how to minimize the risks that may follow from the monopolization of genetic examinations.

The Danish Council of Ethics recommends initiatives for a broad-based popular debate on the use of presymptomatic genetic testing on a par with the initiatives previously mounted by Danish parliament and the Ministry of Health in connection with the Minister for Health's report to parliament on genetic engineering and medical treatment of human subjects.

The Council of Ethics wishes to have the discussion about the way in which presymptomatic genetic testing is to be prioritized within the health service initiated at a juncture that will ensure the public is given influence over this discussion by means of open debate.

The Council of Ethics recommends that new initiatives for presymptomatic genetic testing not be initiated before the requisite financial resources for testing and qualified genetic and psychological counselling are in place, and before the source of the financial resources for implementing such initiatives is clarified.

The Council of Ethics recommends intensifying and qualifying the requirements governing the decision-making basis for introducing any additional offers of presymptomatic genetic testing.

By way of example, as part of the decision-making basis, an inventory should be drawn up detailing the scope of the benefit available from implementing the offer as compared to not doing so. It should show how great a drop in morbidity can be expected as a result of implementing the offer. It should show whether treatment results and the chances of a cure are improved for diagnosed gene carriers in relation to non-diagnosed gene carriers. Studies should be done into the social and psychological consequences of implementing the offer of genetic testing, evaluated in relation to a situation where no such offer exists. Finally, deliberations about a given disease's incidence, penetrance and severity should form part of the overall evaluation of whether or not to implement an offer of presymptomatic genetic testing.

For the Danish Council of Ethics it is essential that the priority-setting decision be made on the basis of a balanced consideration of these many relevant aspects: regard for the individual, regard for his or her family, and regard for society collectively must, then, form part of the discussion as to whether an offer of presymptomatic genetic testing should be implemented.

Summary of the Council of Ethics' Recommendations

In the preceding chapters the Danish Council of Ethics discussed the ethical problems connected with presymptomatic genetic testing. The discussion revolved around four main topics in

particular, and for each main topic a number of recommendations were formulated. For the sake of clarity, these recommendations have been summarized in the last chapter.

Ethics in Time

The Council of Ethics views with some concern the fact that new techniques and procedures within the health service are often introduced without the ethical consequences having been made the subject of prior public debate. Such debate should take place even as a given technique is at the research and development stage, without waiting until the technique is ready for use and groups of patients and carers have acquired an interest in it.

There is reason to assume that the target group for presymptomatic genetic testing will be extended to include the entire population when the mapping of the human genome provides increased scope for studying popular diseases such as cancer, psychogenic diseases and cardiovascular disorders. Carrying on from the above, therefore, the Danish Council of Ethics considers it essential even at this stage to add impetus to the debate on the ethical issues associated with the use of presymptomatic genetic testing. With this report and the recommendations below, the Council thus hopes to contribute to "Ethics in Time".

The Council of Ethics' Recommendation on Social Effects for Society of Presymptomatic Genetic Testing

The Council of Ethics is aware that the widespread use of presymptomatic genetic testing that can be expected to follow in the wake of the mapping of the human genome can assume negative social consequences. The Council fears that this expansion of the target group for genetic testing will be accompanied by the risk of a "worry culture" or risk-focused testing society developing.

Such a testing society can cause general pathologization and anxietization of the population, which can produce a marked change in healthy people's self-knowledge and choice of lifestyle.

In addition, there may be an undesirable slide in our understanding of sickness and health, making it even more difficult to define the notion of sickness and hence define how health service resources should be prioritized.

The Council of Ethics recommends

That examinations be put in place to shed light on the possible social consequences for society of presymptomatic genetic testing as well as the possibilities for controlling these.

The Council regards such knowledge as necessary to the quality of the debate on the possible introduction of the widespread use of presymptomatic genetic testing.

The Council of Ethics' Recommendation on the Right to Know versus the Right not to Know

Central to the Danish Council of Ethics' discussions on the right to know/the right not to know were possible ways of weighing up regard for the individual person, his/her relatives and society.

Danish legislation (the Act on the Legal Status of Patients and the legis-

lative rules concerning the protection of sensitive personal data) attaches importance to protecting personal integrity.[54] In this context, that means a testee's right to make his or her own decision concerning the disclosure of genetic information. Thus, in the legislation, the individual's rights generally enjoy privileged status vis-B-vis relatives' and society's right to information.

The Danish Council of Ethics believes that the disclosure of genetic information to another person is best done by having the decision about the approach made by the testee, who can fairly be presumed to be the person best able to evaluate whether another particular individual wishes to possess that knowledge. The Council of Ethics concurrently acknowledges that entrusting the decision to inform another person to the testee places that person in a dilemma that some people would feel should be shouldered by the doctor or genetic counsellor.

In relation to instances where a testee does not wish to take charge of disclosing information to another person, the Council of Ethics would state the following:

The Council of Ethics recommends that for groups of diseases presenting the same hereditary succession and ethical problems, descriptions be formulated of the practice considered to be the good, professional standard in force, and that these overall guidelines accommodate a stance on the question of the conditions governing the disclosure of genetic information to another person. It is the Council's opinion that such guidelines must be drawn up for these groups of diseases, since the risk, prevention and therapy potentials vary greatly for the individual groups of diseases.

The Council of Ethics wishes to signal that the guidelines must make it clear that they may not be used by the genetic counsellor as a checklist that is run through slavishly with no eye for the peculiarities of the individual counsellee's situation.

The legal rights of the person who has had presymptomatic genetic testing undertaken are not sufficiently well safeguarded today, since the definition of "the special case", which can justify breaking the duty of confidentiality, is based exclusively on the judgement of the individual doctor.

Another question that could be accommodated in such guidelines is the right to information claimed by the party wishing for presymptomatic genetic testing (see also Appendix 1 to this report on "Information and consent").

The Council of Ethics recommends that the Danish Ministry of Health/ National Board of Health, Denmark outline, in the form of an instructive guide, overall guidelines for the dissemination of information, setting out *inter alia* the conditions governing when a doctor can make contact with another person. One condition of such an approach might thus be that there is essentially the possibility of preventing or delaying the outbreak of a severe disease, provided that another person is advised of his or her genetic predisposition to the disease on the basis of the information. Since the

54 *Idem*.

Council of Ethics' point of view is that it is the medical experts providing the genetic counselling and examination in practice that must devise more precise criteria for disseminating information within the individual disease groups, the Council recommends that more precise supplementary criteria for each individual disease group be drawn up by the medical companies/geneticists' professional organization.

The Council of Ethics recommends that, apart from that, there be no legislative changes in the rights of a person who has had presymptomatic genetic testing carried out. The Council emphasizes that the legislation should primarily ensure regard for the testee's judgement and right to privacy, and thus considers it essential to protect the testees' scope for themselves exercising what they perceive to be an obligation in terms of close, genetically linked relatives.

The Council considers that, subject to the implementation of the above recommendation to formulate a guideline, the legislation fulfils this, while at the same time accommodating any third person by giving health-care workers the possibility of disclosing information in special cases.

The Council of Ethics recognizes that a conflict may arise between a person's right to know and another's right not to know. The legislation gives the individual the right to determine him/herself whether or not he or she wishes to know. This right of self-determination does not give the individual the right to control other people's choice. In practice, however, the legislation cannot prevent a person invalidating another person's, *e. g.* a relative's, freedom of choice, *e. g.* by passing on unwanted information to that person.

In cases where a person has unknowingly been registered as a carrier of a hereditary disorder and no presymptomatic genetic testing has otherwise been undertaken in the family, the Council pronounces as follows:

The Council of Ethics recommends that it be permitted to address an enquiry with information about genetic status and an offer of genetic investigation and, where appropriate, presymptomatic genetic testing to the person in question in accordance with the above guidelines and, more particularly and essentially, that there must be scope for preventing a severe disease or delaying its outbreak.

The Council of Ethics recommends that citizens be informed that they can contact registers themselves about hereditary disorders with a view to clarifying whether they are registered as being predisposed to a particular disease. In this connection it is recommended that the Danish Data Surveillance Authority's list of registers be designed in such a way as to include all registers in Denmark.

The Council of Ethics is aware that there are situations in which the regard for another person's right not to know could cause the testee's right of self-determination to be overridden.

The Council of Ethics has discussed two situations in particular:

1. One is the situation in which an at-risk individual's wish to have presymptomatic genetic testing carried out is conditional on a corresponding

genetic examination of one of the parents, who nevertheless wishes not to receive the attendant knowledge and is therefore unwilling to undergo an examination.

The Council of Ethics wishes to signal that in such a situation there is no sense in talking of a right to know or a right to autonomously make a decision about genetic examination, in that such a right provides no basis for compelling another person to undergo an examination unless there are altogether extraordinary circumstances regarding crucial societal or individual interests that can justify such coercion. That is not considered to be the case in this situation. The Council of Ethics is thus of the opinion that situations do exist in which the regard for another person's right not to know means that presymptomatic genetic testing cannot be carried out.

Where it is possible to carry out genetic examination of an at-risk individual without involving the parent of the person concerned, the Council of Ethics feels that the examination should be conducted despite the parent not wishing to know his or her genetic status, as the at-risk individual's right to know is accorded greater weight than the parent's right not to know.

2. The other situation is the one in which there are conflicting desires on the part of a couple as to whether fetal examination should be performed. A distinction can be made here between cases in which it is the husband or the woman, respectively, who is the at-risk person and does not wish to know whether he/she has a predisposition to the disease.

Thus, it may be a case of a woman being pregnant by an at-risk person and of her wishing to have a fetal examination conducted with a view to establishing whether the child is a carrier of the disease gene. If the examination is carried out, and if it shows that the child is a carrier of the gene, it will simultaneously have demonstrated that the husband is the genetic carrier and he will thus have received a piece of information at odds with his wish not to know.

Conversely, it may be a case of the pregnant woman being the at-risk person, but not wishing to know whether or not she actually is the genetic carrier. If the husband in this situation wants fetal examination performed, and if it is carried out and yields the result that the child is the carrier of the disease gene, it will simultaneously have been demonstrated that the woman is the genetic carrier and —contrary to her desire not to know— she will have been given information about her status.

The Council of Ethics wishes to stress the equal nature-in-principle of motherhood and fatherhood, and the importance of securing for parents-to-be the best conditions imaginable for a forum enabling them to arrive at a solution to any mutual disagreement on the possible performance of a fetal examination through dialogue.

The situation in which two parents-to-be disagree as to whether fetal diagnostics should be performed is rare, though nonetheless unfortunate in each individual case. Where the couple in question ends up being unable to resolve the conflict themselves, there is a need to clarify how society, represented in the form of the executive staff, should act in a situation that

involves the right to know, as acknowledged by the legislation and as supported in ethical terms, being at crucial variance with the right not to know, as also acknowledged by the legislation and also supported in ethical terms.

By way of introduction it needs to be highlighted that, faced with this dilemma, a fetal examination cannot be performed without performing an intervention on the woman's body. Such an intervention undertaken without the woman's informed consent would entail setting aside the ethical requirement of respect for a person's integrity and dignity. Very generally speaking, this ethical requirement means that interventions in the form of forced examination and treatment can only be considered in special situations where there are essential societal or private interests at stake. This ethical requirement is expressed in the legislation, which permits forced examination and treatment of citizens only in altogether unique situations. The Danish Council of Ethics does not feel that the nature of the situation mentioned, in which a husband wishes to know about his child-to-be's genetic status, is such that it can override the ethically determined requirement that examinations calling for an intervention on a person's body cannot be undertaken without the informed consent of that person.

The only thing that remains to be considered, then, is the situation in which the woman wishes to have a fetal examination performed based on her right to know about the genetic make-up of the fetus, while the husband opposes the performance of the examination with reference to his right not to know.

The legislation in force gives a pregnant woman the right to have fetal examinations performed on the child being expected, on request, where medically indicated and assuming that other conditions have also been met. Although giving ethical consideration to whether the husband's consent should also be obtained cannot be dismissed in principle, there is currently no requirement to do so under the legislation. The question is, then, whether the fact that a fetal examination with the nature of presymptomatic genetic testing can provide knowledge about not only the child but also the husband, can constitute ethical grounds for introducing demands for a change in the law, under which he too must grant his consent for the performance of the examination.

Suffice it to mention here that introducing a requirement that the at-risk person must grant consent for a fetal examination of the nature of presymptomatic genetic testing furnishes no solution to the dilemma described, to wit in the event of the two parties not reaching agreement on the question, with the at-risk person saying no and the other party saying yes to a fetal examination.

At all events, therefore, one may be left with the dilemma and forced to contemplate whose right is to take priority over that of the other person, even if the two sets of rights were to be considered of equal value in principle.

The Members of the Danish Council of Ethics Have Various Ethical Assessments of the View Society Should Adopt in Such a Situation:

A. All members of the Council of Ethics save for Sven Asger Sorensen

and Lene Gammelgaard recommend here that fetal examinations with an eye to diagnosing a gene may continue to be conducted, despite opposition to the examination by the father of the child-to-be. However, those members who endorse this recommendation do not agree on the rationale for such.

A.1. Some members (Ragnhild Riis, Mette Hartlev, Ole Hartling, Karen Schousboe, Ellen Thuesen, Pelse Helms Kaae, Asger Dirksen and Nikolaj Henningsen) justify the recommendation on the grounds that the deleterious effects for the woman, if not given an opportunity to have a fetal examination performed, are greater than the harm sustained by the husband in being saddled with knowledge he does not want. In this connection these members refer to the fact that although no intervention on the physical integrity of the woman is imposed, on the face of it, she loses the opportunity to make an informed decision on what her body is to be subjected to. At all events, she will have to make a choice: *i. e.* the choice between completing or terminating the pregnancy. Regardless of whether she chooses one or the other, the choice will have consequences for her physical and mental integrity. An abortion is an intervention that can have both harmful physical and mental effects. These harmful effects can be compounded when the decision about abortion is made on an insufficiently informed basis, thereby leaving some uncertainty as to whether the decision to terminate the pregnancy was right. Similarly, if the woman opts to see the pregnancy through, it can also have an adverse mental and physical impact on her. As is the case with the abortion choice, these potentially harmful effects can be envisaged as being greater when the decision to complete the pregnancy is made on an informative basis which the woman herself considers inadequate. For the woman, the consequences of being deprived of the opportunity to make an informed choice thus concern not only her need for knowledge but also her psychological and physical integrity. Although it is difficult to balance the woman's and the husband's ethically justified rights, these members deem that the potential harm to which the woman is exposed weighs so heavily that her right to secure an informed decision-making basis must take priority over the husband's right not to know. The fact that a female and a male at-risk person are thus placed on different footings needs to be seen in the context of the fundamental difference in their plights.

A.1.a. Amongst these members, Karen Schousboe, Ellen Thuesen and Pelse Helms Kaae wish to supplement this reasoning with the view that, by virtue of her special emotional relationship with the child-to-be, the woman is the weak party: she unlike the father-to-be cannot merely "opt out" of pregnancy and raising a child. Historical experience bears out the woman's weakness: down through the ages, women have been abandoned by the father of their child-to-be, cornered into abortion etc. The legislation currently in existence in the field is a basic reflection of the protection afforded the weak party's interests: the woman's. These members wish to preserve the legal status quo, because setting aside the woman's unconditio-

nal right to make a decision about fetal diagnostics in favour of the father-to-be's right not to know would reflect an unacceptable restriction on the protection of the woman as the weak party.

A.2. Other members (John Steen Johansen, Naser Khader, Frederik Christensen, Lisbeth Due Madsen, Peter qhrstrrm and Erling Tiedemann) did not consider that more fundamental ethical principles had been highlighted above, which in the event of disagreement between the two parents can solve the dilemma at issue; and in the context they do not consider any clear-cut comparison of alternative harmful effects possible but, on the contrary, prone to the significant risk that any prejudice in either direction may ultimately have a watershed influence on the outcome. In so doing, they refer to the quotation on page 74, which mentions depression or suicide as a possible consequence of gene-positive diagnosis, pointing out that such an outcome would invariably guide the calculation and comparison of harmful effects to a completely different conclusion.

These members further find that said comparison between harmful effects easily ends up taking the form of a paradigm for a line of argument that aims at extensive ethical legitimation of abortion, which they do not endorse.

On first thoughts, these members are sympathetic to Sven Asger Srrensen's suggestion in as far as this points towards acknowledging both parents' equal status in respect of both rights and obligations towards the joint child-to-be. However, they feel that the parents' equal rights and obligations should only be viewed in the context of the child's rights, as well as finding it inadvisable only to attach certain —indeed, limited— recognition of such rights to the rather unique situation under review, in which the father of a child is the person at risk. In the view of these members, therefore, the Council of Ethics should undertake an investigative project at some point on the ethical values and requirements associated with the mother, father and child triad.

On the basis currently available, John Steen Johansen, Naser Khader, Frederik Christensen, Lisbeth Due Madsen, Peter Ohrstrom and Erling Tiedemann have therefore concurred that fetal examinations with an eye to diagnosing a gene may still be conducted, despite opposition to the examination on the part of the child-to-be's father. This endorsement needs to be seen as a provisional and more pragmatic solution to the dilemma described. They rationalize this endorsement on the grounds that there is no obvious reason for the Council of Ethics to propose any legislative amendment regarding consent to the performance of fetal examinations until such time as an ethical rationale for such a change in the law can be demonstrated as the result of more complete fact-finding work.

B. A minority on the Danish Council of Ethics (Sven Asger Srrensen and Lene Gammelgaard) recommend introducing a rule into the legislation to the effect that fetal examination for a severe, late-onset disease based on one of the parents being at substantial risk of carrying a predisposition to the disease, which may have been passed

on to the fetus, may only be carried out if the parent who is the possible genetic carrier consents to the examination.

To exemplify this, a possible scenario is that one half of the parenting couple him/herself has a parent with Huntington's but does not wish to know whether he/she is him/herself a carrier of the predisposition to this disease. If fetal examination is performed and it evinces the result that the fetus is predisposed to the disease, the process will lead to the at-risk parent being made aware contrary to his or her wish that he or she is also predisposed. Knowing that one is going to develop a severe disorder can bring with it major adverse psychological effects and impaired quality of life which, taken to the extreme, can lead to harmful physical effects, *e. g.* suicide.

For the partner it means that he/she is given the knowledge that both the spouse (the cohabitee) and the expected child are predisposed to the disease.

If a decision is taken to abort the child, the result is that the at-risk parent —contrary to his or her wish— is made aware that he or she will contract a severe disease and the wished-for child will be aborted. For the partner it means being told that the spouse (the cohabitee) is predisposed to the disease and at the same time will be exposed to the psychological pressure induced as a result of terminating a wished-for child.

Fetal examinations for late-onset diseases, in which the at-risk parent does not know his/her genetic status, can thus assume far-reaching negative consequences for the person at risk, the spouse and the fetus alike. This will particularly be the case if the examination is undertaken against the wishes of the at-risk parent, violating the right of self-determination and running counter to the intent of the legislation, which usually confers upon the individual privileged status with regard to relatives' right to information.

By introducing a rule that requires the at-risk parent's consent to fetal examination, the consequence may be that a pregnancy is brought to term with the birth of a child predisposed to the disease, or that a fetus is terminated that may not have the predisposition.

The minority feel that this is far less interventive than the harmful effects that may be triggered by fetal examination in this situation. This judgement allows for the fact that these are late-onset diseases which are not usually developed until many years after the birth of the child, providing hope that effective treatment will be available if the child is born with the predisposition to the disease. Such hope will presumably mean that only few women will choose abortion if they do not have the chance to have a fetal examination conducted.

In the legislation currently in force it is the woman who holds the absolute power to decide about fetal examination and abortion. Yet this legal position was instigated at a time when fetal examinations for late-onset diseases were not relevant, and the problems discussed here were not relevant either, therefore. The minority's proposal implies that, in these altogether unique situations, a man who is at risk and does not wish to know his genetic status is given the chance to prevent fetal examination being per-

formed The proposal thus entails no form of intervention on the woman's body but merely results in the woman's right to determine whether fetal examination should be performed being restricted in rare cases. Such restrictions on women's right of self-determination are found, for instance, in society's ban on abortion after the 12th week of pregnancy.

The Council of Ethics' Recommendation on Presymptomatic Genetic Testing of Minors for Late-onset Diseases

Central to the Danish Council of Ethics' discussions on presymptomatic genetic testing of minors were the following general questions: Should parents of a minor who may possibly be carrying or predisposed to a late-onset genetic disease have the right to know that is, the right to have presymptomatic genetic testing of the child conducted? Or should that right cede to the child's right not to know and the child's right of self-determination? And, if so: at what age should a minor independently be able to make a decision for or against presymptomatic genetic testing?

Acknowledging the parents' right to know, should they then have a moral duty to tell the child the results of the genetic examination? Or should they have a right to withhold this knowledge?

The Council of Ethics is of the view that presymptomatic genetic testing of minors should take place on the basis of the overriding principle that the minor's right not to know and his/her right of self-determination should be allocated sufficient weight so that presymptomatic genetic testing of minors should not be carried out for diseases onsetting after the age of 18, when the child (having come of age) can adopt its own position pro or contra genetic testing.

The Council of Ethics does feel, however, that this overriding principle can be departed from in cases where a positive genetic examination result (that is, detection of the gene being examined for) provides scope for treatment which to any essential degree prevents, defers or alleviates the outbreak of disease or the consequences of the outbreak of disease.

In relation to cases where the overriding principle can be departed from because, for example, preventive options exist and presymptomatic genetic testing of children under 18 can therefore be conducted, the Council of Ethics pronounces as follows:

The Council of Ethics recommends, in respect of minors under the age of 15, that the parent holding custody be the one with the competence to make the decision concerning the performance of presymptomatic genetic testing. However, it is essential to ensure that an under-age child's own views are made an increasingly decisive factor, the older and more mature the child becomes.

The Council further recommends that presymptomatic genetic testing of a child under 15 should generate a moral obligation on the part of the child's parents to notify the child, together with a genetic counsellor, about the examination in order to protect the child's right to express its views in that regard. If the child so wishes, he or she must be notified of the results of the genetic examination and its

consequences. This should be done at a time when the child is thought to be capable of understanding the information and by the time the child turns 15 at the latest.

With the above recommendation the Council of Ethics wishes to protect the minor from making decisions whose scope he or she does not have the maturity to understand while at the same time accommodating the minor's own views in step with his or her increasing age and maturity.

The recommendation is in accordance with the Council of Europe's Convention on Human Rights and Biomedicine, article 6, which states that the views of a child are to be taken into consideration as an increasingly determining factor in proportion to his or her age and degree of maturity. Similarly, the recommendation is in keeping with the UN Convention on the Rights of the Child, article 12, which states that the child's views are to be given due weight in accordance with its age and maturity.

The Council of Ethics recommends, in respect of minors between 15 and 18 that a child between these ages should itself determine whether it wishes to have presymptomatic genetic testing undertaken. This means that parents need not assent to, say, the wish of a 16 year-old child to have presymptomatic genetic testing performed, nor can they prevent the 16 year-old from realizing his or her wish.

This recommendation is in line with the Danish Act on the Legal Status of Patients, which states that an individual must have turned 15 in order to give informed consent for treatment in person.

The Council of Ethics recommends that, in the event of fundamental disagreement between parents and child, there must be an opportunity for the mature child, doctor and/or parents to obtain advice and counselling and expert child guidance. This offer should also include children between the ages of 15 and 18.

The Council of Ethics recommends that offers of presymptomatic genetic testing for minors always be given to the children and their parents together with an offer of qualified counselling. The consequence of this recommendation is that the priority assigned to training and further training of counsellors should be upgraded, so as to ensure that:

Counselling is based on documented knowledge of children's emotional and intellectual development.

Counselling is based on documented knowledge of the psychological and social consequences of presymptomatic genetic testing of minors, and

Counselling is geared to the child's age and maturity on a case-by-case basis.

The Council of Ethics recommends that its recommendation above be translated into a set of general guidelines, *e. g.* in the form of a guideline from the Danish Ministry of Health/ National Board of Health or, if necessary, by amending the law.

The Council of Ethics' Recommendation on Psychological Effects of Presymptomatic Genetic Testing

The Danish Council of Ethics recommends generating knowledge about the psychological long-term effects of presymptomatic genetic testing both

for those who have been diagnosed with a pathogenic gene and for those whose test failed to detect the gene in question.

Such knowledge, which might take the form of interdisciplinary examinations, should at the latest be generated in time to take it on board together with knowledge of the short-term psychological effects when considering whether or not to offer presymptomatic genetic testing for widespread national diseases, thereby effecting a marked extension of the target group for genetic testing.

The Council considers that there is a basis for a research project on the psychosocial consequences both for the individual and for the family that becomes involved in presymptomatic genetic testing.

The Council of Ethics' Recommendation on Social Effects for the Individual of Presymptomatic Genetic Testing

The Danish Council of Ethics recommends that the same rules apply for pension applications to the public sector as to a private pension fund. That means that in connection with pensions cases, the public sector may not request, obtain or receive and use information that can shed light on a person's genetic make-up.

One result of this is that it will not be possible to qualify for a pension on the basis of a positive presymptomatic genetic test. This, of course, may be felt to mark a deterioration in the terms for the individual applicant. The Council of Ethics' reasoning behind this recommendation, however, is that such rules safeguard against gene-based discrimination, maintaining that genetic carrier diagnosis is not disease diagnosis: that a person who has been diagnosed with a pathogenic gene by presymptomatic genetic testing is healthy and not entitled to a pension solely on the basis of that gene test.

The Council of Ethics likewise recommends that adoption authorities not be allowed to request, obtain or receive and use information that can shed light on the genetic make-up of an adopting party.

The background to this recommendation is a wish to guarantee an adopter's right not to know and to counter a trend in which people are being discriminated against on the grounds of their own or relatives' genetic make-up.

The Council of Ethics' Recommendation on Prioritizing Presymptomatic Genetic Testing

The prerequisite for the Danish Council of Ethics' recommendation on the prioritization of presymptomatic genetic testing is an acknowledgement and acceptance of the fact that presymptomatic genetic testing is —and will also be in future— part of the health service's activity.

At the same time, the Council wishes to point out that, in future, presymptomatic genetic testing will also become a commercial offer controlled by supply and demand. The Council harbours some concern about the consequences this might have for the quality of the information and counselling that are necessary, both before and after the performance of presymptomatic genetic testing. Conse-

quently, the Council finds it necessary to make both publicly available genetic examinations and those on offer from the private market subject to politically stipulated and binding standards.

The Council is further worried that commercial companies can obtain a patent on the examination of genes for special mutations. The company holding the patent rights can demand that the examinations be carried out exclusively at the company's laboratories. This involves a risk of genetic examinations being monopolized and, with it, the risk of abuse of information for example, mapping the large volumes of genetic material without the originators' consent and knowledge.

Such monopolization further entails the risk of a price-fixing policy, restricting access to presymptomatic genetic testing. The Council of Ethics consequently recommends that a political stance be taken on how to minimize the risks that may follow from the monopolization of genetic examinations.

The Danish Council of Ethics recommends initiatives for a broad-based popular debate on the use of presymptomatic genetic testing on a par with the initiatives previously mounted by Danish parliament and the Ministry of Health in connection with the minister for Health's report to parliament on genetic engineering and medical treatment of human subjects.

The Council of Ethics wishes to have the discussion about the way in which presymptomatic genetic testing is to be prioritized within the health service initiated at a juncture that will ensure the public is given influence over this discussion by means of open debate.

The Council of Ethics recommends that new initiatives for presymptomatic genetic testing not be initiated before the requisite financial resources for testing and qualified genetic and psychological counselling are in place, and before the source of the financial resources for implementing such initiatives is clarified.

The Council of Ethics recommends intensifying and qualifying the requirements governing the decision-making basis for introducing any additional offers of presymptomatic genetic testing.

By way of example, as part of the decision-making basis, an inventory should be drawn up detailing the scope of the benefit available from implementing the offer as compared to not doing so. It should show how great a drop in morbidity can be expected as a result of implementing the offer. It should show whether treatment results and the chances of a cure are improved for diagnosed gene carriers in relation to non-diagnosed gene carriers. Studies should be done into the social and psychological consequences of implementing the offer of genetic testing, evaluated in relation to a situation where no such offer exists. Finally, deliberations about a given disease's incidence, penetrance and severity should form part of the overall evaluation of whether or not to implement an offer of presymptomatic genetic testing.

For the Danish Council of Ethics it is essential that the priority-setting decision be made on the basis of a balanced consideration of these many

relevant aspects: regard for the individual, regard for his or her family, and regard for society collectively must, then, form part of the discussion as to whether an offer of presymptomatic genetic testing should be implemented.

Glossary

Affected parent. A parent of a person wishing to have presymptomatic genetic testing undertaken and presenting symptoms of the disorder to be examined for is termed an affected parent.

Alpha-1-antitrypsin deficiency. Genetically caused condition that creates an increased risk of pulmonary disease. See section 3.3 of report.

Genetic carrier. A genetic carrier is a person carrying a gene that does not give rise to sickness in the actual person.

Genetic make-up. See gene.

Gene (genetic) stock. A person's gene stock is understood to mean the person's total DNA, which is unique to every single individual. The human gene stock (or genome) is understood to mean that which is characteristic of human beings, in particular with regard to the positioning of genes in the chromosomes and the base sequence in the DNA.

Autonomy. The word autonomy is used in many senses. In this report it can usually be thought of as equivalent to "self-determination".

Autosomal. Connected to the autosomes, *i. e.* the chromosomes that are not sex chromosomes.

Base pair. The individual genes are determined by the sequence of the base pairs.

Bilateral breast cancer. Double-sided cancer in both breasts.

Danish Central Scientific Ethical Committee. A committee partly mandated to assess whether concrete research projects expose the trial subjects who are going to be involved in them to unacceptable risk or whether they can give cause for other ethical problems.

Personal integrity. In this report the word is usually used in the sense of "a wholeness which must not be violated".

Human Genome Project. An international research project, the purpose of which is to map man's gene stock the human genome.

Diagnosed gene carrier. A person who has had presymptomatic genetic testing carried out and been diagnosed with the gene for the disease examined for as a result is a diagnosed gene carrier; in contrast to a non-diagnosed gene carrier, who carries the gene but has not had this established during a genetic examination.

Predisposition. If a person is carrying one or more genes that can result in a particular disease, that person is said to have a particular predisposition.

DNA. An abbreviation of the chemical substance genes consist of (deoxyribonucleic acid).

Dominant hereditary disease. A dominant hereditary disease manifests itself despite the person also having a normal gene for the disease in question. See illustration on p. xx. If a disease is dominant hereditary, it means there will be a 50 percent risk of a patient's children having inherited the mutated gene.

Enzymes. See protein.

Eugenics. The branch of "science" that works to improve inherited human characteristics (formerly known as "racial hygiene"). Its purpose is to explore the nature, succession and spread of hereditary attributes with a view to restricting them.

Family mutation. The change to a gene that exists in a specific family with a particular genetic disease.

Fetal diagnostics. Examination of a fetus, for example by means of placental sampling (chorionic villus biopsy/CVB) or amniocentesis.

First-degree relative. A person's first-degree relatives are his or her parents, children or brothers and sisters (siblings).

Gene. A unit of hereditary material. A gene consists of DNA. The genes determine the make-up of the body's proteins and thus its biological characteristics.

Gene carrier. Being a gene carrier means having the gene examined for, say, by means of presymptomatic genetic testing.

Gene-diagnostic examination. Examination to see whether a healthy or sick person has a gene mutation.

Genetic profile. The sum total of a person's genes draw his or her genetic profile.

Genetic counselling. Genetic counselling is a process of communication that deals with the problems associated with the origins of a genetically conditioned disease in a family. It endeavours to help the individual (family) understand the underlying biomedical factors, to understand the risk present, to understand what options or courses of action are available, and to make the choice most appropriate for the person (family) in the situation at hand and act accordingly.

Genetic investigation. If a geneticist, for instance, is going to work out whether there is any basis for carrying out presymptomatic genetic testing of a person, the geneticist will often start with a genetic investigation into the person's family. That is to say that particulars are obtained about the family's illnesses and the likelihood, if any, evaluated of there being genetically conditioned disease in the family.

Gene mutation. A gene mutation is the term for a gene that has mutated, *i. e.* altered.

Genome. Gene stock. See Human Genome Project.

Genetic status. Knowledge of whether a person does or does not have a disease gene.

Huntington's (disease/chorea) Dominant hereditary disorder. See section 3.2 of the report.

High-risk family. Genetic investigation and examination can often clarify whether a family is at particular risk of contracting a certain disease —*e. g.* hereditary breast cancer— in which case it is said to be a high-risk family.

Clinical examination. The examination a patient is given by a doctor, as opposed to a laboratory analysis or an X-ray examination.

Clinical symptoms. The presence of symptoms indicating disease.

Linkage analysis. Examination to see whether a person has a marker located very close to a disease gene.

Mammographic examination. An X-ray examination of a woman's breasts.

Marker. A sequence in the DNA whose chromosome location is known

and which varies from one person to another.

Molecular-genetic examination. Examination of a gene.

Multicentric breast cancer. Occurrence of multiple scirrhi (cancerous lumps).

Multifactorial. Many genetically conditioned diseases are thought to be multifactorial, *i. e.* the cause of the disease is an interaction of several genes and environmental factors.

Mutation. A change in a gene is called a mutation. The gene is then described as "mutated". Used most often in connection with changes that can result in disease or malformations.

Negative (adverse) test result / negative test / to test negative. A variety of terms, all meaning that presymptomatic genetic testing has not detected the pathogenic gene examined for.

Neurodegenerative diseases. Diseases in which cells in the central nervous system die.

Nucleotides. Molecules (bases) linking the two DNA strands. There are some three billion nucleotides, the sequence of which will be mapped by the Human Genome Project.

Penetrance. Some pathogenic genes do not always erupt. There is no certainty, therefore, that a person will contract the relevant disease, despite having the gene for it. What is meant when speaking of a gene's penetrance is the probability of it erupting and causing illness.

Polyposis. Hereditary intestinal cancer with polyps in the bowels. See section 3.1 of the report.

Positive list. A list enumerating diseases that trigger *e. g.* different rights or options. One example might be a positive list of diseases for which society makes available presymptomatic genetic testing or fetal examination facilities.

Positive test result / positive test / to test positive. A variety of terms denoting that presymptomatic genetic testing has detected the pathogenic gene examined for.

Primary cancer. The original cancerous lump as opposed to metastases.

Proband. The first person to be examined in a family is called the proband or propositus.

Proteins. Albumens. Enzymes and some hormones, such as insulin, are proteins. These also form part of the structure of cells.

Protocol. Description of the way an experiment, trial or examination is to be run.

Pre-implantation diagnostics, *Egg sorting*. Sorting of fertilized eggs with a view to ensuring that only eggs without a particular disease gene are placed (implanted) in the woman's uterus (womb).

Prenatal examination. See Fetal examination. *Presymptomatic genetic testing*. Examination to see whether a healthy person has a disease-causing gene before that disease has manifested with symptoms.

Prevalence. The spread of a disease among the population.

Recessive hereditary disease. Recessive inheritance. A recessive disease occurs only when a person has two disease genes: one from the father, the other from the mother. Most frequently, the parents will be gene carriers, *i. e.* they will each have a normal gene and a disease gene and will not therefore contract the disease.

Reference programme. Description of practices considered to offer a good professional standard – for example, in connection with presymptomatic genetic testing for a particular disease.

Risk analysis. Use of examination methods to evaluate the probability of disease.

At-risk person. A person at increased risk of, say, a genetically conditioned disease. Most often used of the children of a person with a dominant hereditary disease.

Risk status. The risk a person has of contracting a disease, depending partly on whether he/she is tested. For instance, the risk of Huntington's is 50% if the person has a parent with the disease. If the person is tested, the risk is 0 or 100%, depending whether he/she has the gene.

Risk assessment. Evaluation of the probability of disease.

Screening. To screen means to examine a segment of the population that feels healthy – or at any rate has no inkling of being ill with the particular disease targeted by the screening programme. The screening programme can either take in the whole population or a selected part of the population – for example, women or men of a certain age.

Sporadic cancer. Randomly occurring cancer, unlike cancer occurring as a result of a genetic predisposition to the disease.

Stigmatized. Branded a person, who stands out from the crowd by virtue of having, say, a disease that brings out other people's anxieties or prejudices, can feel stigmatized or branded.

Predisposition to disease. In this report, being predisposed or prone to a disease means being a carrier of a pathogenic gene. A person is predisposed to a disease if he/she has one or more genes that will or may result in disease.

Pathogenic gene. Term for a gene that provokes a particular disease or yields an increased risk of that disease.

Pathologization. When healthy subjects are examined with a view to detecting disease, there is a risk of those people feeling pathologized, *i. e.* regarded as sick until the opposite has been proved, rather than being regarded as healthy until the opposite has been proved.

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