Prenatal Diagnosis for Late-Onset Single-Gene Disorders and for Susceptibility Genes

The ability to identify genes through the use of DNA technology is increasing rapidly, and with it the need to assess its implications and consequences to ensure that any uses are ethical and beneficial. Evident in the testimony the Commission heard from Canadians were concerns that new capacities with regard to genetic identification held the potential for misuse and that rapid evolution of the field is making social oversight difficult. The fact that there are vulnerable interests to be protected — for example, against discriminatory uses of the technology by employers and insurers — makes this a matter for all of society to deal with.

DNA testing raises important social issues, and it is clear that public policy will be needed in a range of settings, but many of these applications are outside our mandate. In this chapter we consider DNA testing as it relates to reproduction and prenatal diagnosis for late-onset single-gene disorders and for susceptibility genes. We consider other uses relating to reproduction elsewhere. We evaluate current and potential prenatal uses of DNA testing and make recommendations about these uses in light of our ethic of care and guiding principles. Our goal is to ensure that uses of this technology will be principled and beneficial, and not driven by commercial goals or the mere existence of the technology.

We discussed the use of prenatal diagnosis for disorders that are present at birth (congenital) or begin in childhood ("early-onset") in Chapter 26. However, some single-gene disorders, and many multifactorial genetic disorders, do not manifest themselves until adulthood. Affected individuals may have a normal and healthy childhood before any signs of the disease become apparent — which may not occur until they are in their 30s or later. For some of these disorders, it has become possible, using DNA testing, to identify persons who have inherited the gene for a single-gene late-onset disorder such as Huntington disease. It has also become

possible to identify, for a few disorders, persons who have inherited a gene that increases susceptibility to a late-onset multifactorial disorder. Both these uses of DNA testing have been called "predictive" testing, since the disease being tested for would not occur for many years, even decades. Testing for these, if carried out prenatally, could also identify fetuses carrying the relevant genes.

> Our concern is that if you institute screening without counselling and without the support necessary to launch screening, what you are going to end up with is a significant number of persons who are basically given information that only confuses them because you can't say for sure, yes they do have or don't have [the disorder] and at the same time you are not providing them with any kind of social support system to be able to deal with this kind of uncertainty.
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> *M. Buchwald, Canadian Cystic Fibrosis Foundation, Public Hearings Transcripts, Toronto, Ontario, November 19, 1990.*

The term "predictive" testing is therefore confusing, because it can be used to refer to two very different types of testing. First, prenatal diagnosis can test for the presence of a gene or genes that increase susceptibility to certain multifactorial disorders. Multifactorial disorders, such as many types of cancer, cardiovascular disease, and mental illness, result from a complex interaction of one or more genes and environmental factors. We know that these disorders have a partly genetic basis and that they tend to cluster in certain families. In some cases, scientists have discovered that the presence of a particular gene makes some individuals more susceptible to a disease than others in the general population. Having this "susceptibility gene" does not necessarily mean that the person will get the disease, because it also has an environmental component; some with the gene will not get the disease if they have a particularly healthy environment, diet, or way of life. Conversely, some people without the gene will get the disease if they are sufficiently exposed to the environmental factors that also play a role in causing the disease. We know, for example, that some women are at increased risk for breast cancer, given their family history, and it is becoming possible in some families to identify a gene that is responsible for this increased risk. But all women are at some risk for breast cancer, even if they do not have a susceptibility gene. Rather than use the term "predictive testing" for this type of testing, therefore, we use the term "susceptibility testing" to refer to the use of prenatal diagnosis to test for the presence of susceptibility genes in the fetus. No susceptibility testing is being done at present in Canada.

The second type of testing is for late-onset single-gene disorders. It is helpful to think of disorders with a genetic component as being on a continuum — at one end of the spectrum, having a particular gene makes a person somewhat more susceptible to an illness in some environmental circumstances; at the other end, having a particular gene makes it

impossible for the individual to live and function normally beyond the age of onset, regardless of the environment. Along this continuum, however, the disorders generally fall into one of two broad, albeit somewhat artificial, categories: multifactorial disorders, described above, and single-gene disorders. Prenatal testing can also be used to detect the presence of the gene for a late-onset single-gene disorder.

Late-Onset Single-Gene Disorders

Huntington disease: Progressive mental deterioration (dementia) and uncontrollable jerky movements appear on average in the late 30s. Personality changes often occur in the early stages of the disease (which can last for many years) and may have devastating effects on the family. Individuals eventually become bedridden and unable to feed themselves in the later stages; the disease is fatal and has no known cure.

Adult polycystic kidney disease: Adult polycystic kidney disease causes a progressive reduction in kidney function. The disease has several genetic types; it is not fully penetrant, so that not all those with the gene become ill, but 85 percent will show abnormalities on ultrasound by age 25. Treatment can slow progress of the disease.

Familial adenomatous polyposis: Many benign growths occur in the intestine, some of which lead to cancer. The disease is fatal if not treated by removal of the colon; the risk of one or more of the adenomas undergoing malignant degeneration is virtually 100 percent.

Myotonic dystrophy: Myotonic dystrophy is an untreatable disease that results in variable degrees of muscle wasting and cataracts. The disease is highly penetrant but varies in severity. The prevalence in the Saguenay region of Quebec is 1 in 475 — about 30 to 60 times higher than the prevalence in other regions of the world; prevalence is estimated at 1/25 000 for European populations.

Retinitis pigmentosa: Several types of retinitis pigmentosa lead to progressive loss of vision in later life. No treatment is available.

Familial hypercholesterolaemia: Familial hypercholesterolaemia leads to early coronary heart disease (with onset of symptoms in the 30s or 40s) and other degenerative vascular problems. Early diagnosis allows treatment that can modify progress of the disease.

Single-gene disorders may be recessively or dominantly inherited. In dominant inheritance, the child of an affected person has a 50:50 chance of inheriting the responsible dominant gene. For many dominant disorders, presence of the gene equates with presence of the disorder — all those with the gene who live long enough will become affected. (Huntington disease is one such disorder.) However, some particular dominant disorders are

not fully penetrant — that is, not everyone with the gene will manifest the disorder.

Unlike susceptibility genes, having a fully penetrant single-gene disorder is not a question of greater susceptibility or increased risk — presence of the gene equates with the eventual occurrence of the disease, even if no symptoms appear for many years. The relevant gene can be identified directly for some disorders; for others, closely linked genes or "markers" are still used instead, which makes prenatal diagnosis of the latter disorders less than 100 percent accurate. This situation will change in the coming decade, as it becomes possible to identify more and more disease genes directly using DNA technology. We therefore use the term "pre-symptomatic testing" to refer to the use of PND to test for the presence of genes for late-onset single-gene disorders (or their closely linked markers). PND of this type is currently being done for a few disorders in Canada, including Huntington disease.

Both susceptibility testing and pre-symptomatic testing raise important issues that do not arise with respect to PND for congenital disorders or early-onset disorders. We discuss these issues, as well as the current practice of pre-symptomatic testing and susceptibility testing, in the remainder of this chapter. It is important to bear in mind that we are concerned here with *prenatal* testing, which is done to help couples to decide how to manage a pregnancy. Children and adults can also be tested for susceptibility genes and late-onset single-gene disorders; in these cases, the objective of genetic testing is to provide information about the individual's own future health. This application of genetic diagnostic techniques is important, but it is outside our mandate. Throughout this chapter, therefore, the terms pre-symptomatic testing and susceptibility testing refer solely to testing done prenatally.

Prenatal Diagnosis for Late-Onset Single-Gene Disorders

Prenatal testing can be used to detect several dominantly inherited diseases of late onset (see box).[1] These disorders vary widely in their treatability and in their severity when not treated. As will be seen below, these differences in treatability and severity are reflected in people's decisions about whether to have pre-symptomatic testing and how they respond to the results.

Types of Tests

Most late-onset single-gene disorders are dominantly inherited — that is, if either the male or the female partner has the disorder, each child has a 50 percent chance of inheriting the gene from the affected parent. Until

recently, couples had no way to determine whether a fetus had inherited the gene. New developments in DNA technology, however, have made it possible to use prenatal testing to determine whether a gene has been passed on; fetal cells are extracted through chorionic villus sampling or amniocentesis, and the DNA is analyzed. At present, this testing takes one of two forms: the test may look directly at the gene, or it may look for linked DNA markers. The latter approach requires study of family members as well.

For some disorders, it is possible to identify the gene that causes the disease and so ascertain with 100 percent accuracy whether the fetus has the gene. This is now possible for myotonic dystrophy, some forms of retinitis pigmentosa, Becker muscular dystrophy, and the Li-Fraumeni syndrome of multiple cancers.

The situation is changing rapidly as more genes are identified, but, in the interim, it is not yet possible to identify the gene directly in many disorders. Instead, tests are used to look for the presence of linked markers — that is, genes that are closely linked to the defective gene. Particular genes located close together on the chromosome (such as a disease gene and a nearby marker gene) are usually transmitted together to the offspring. By studying very large families with a history of a particular disorder, researchers have discovered linked markers that are almost always found together with the disease gene in a particular family. A marker for Huntington disease was discovered in this way in 1983. This made it possible to identify which offspring of an affected individual had inherited the marker gene and therefore to predict that the defective gene was also inherited. The presence of the linked marker was a very reliable indication of the presence of the defective gene — the correlation was over 95 percent for the Huntington disease marker — but it was not definitive. This has changed recently; in future, a linked marker will no longer need to be used now that the Huntington disease gene itself has been identified.

Although most pre-symptomatic testing for late-onset single-gene disorders relies on linked markers, such technology is transitional. Once genes and their mutations have been identified, testing for linked markers will be phased out. In the future, it will be possible to test directly for all dominant disorders. Such ability to identify the genes causing single-gene disorders is increasing rapidly, in part as a result of the Human Genome Project.

PND for late-onset diseases that relies on linked markers can take two forms: exclusion testing and so-called definitive testing (though this is a rather misleading term, since it is not entirely accurate). We will briefly describe the situation for Huntington disease, as this is the disorder on which the most information is available and it serves to explain the current role of markers.

"Definitive Testing"

So-called definitive testing involves detailed family linkage studies to identify the form of marker that accompanies the disease gene within the family. If a closely linked marker is found, this can be used to reveal the health status of both the parent and the fetus. For example, definitive testing may reveal that a woman did not inherit the Huntington disease gene from her affected father, in which case there would be no need to test the fetus. If the woman did inherit the disease gene, then the fetus could also be tested. If the fetus has the same marker, its risk is very high (98 percent); if not, its risk is very low (2 percent). Because it does not identify the disease gene directly, however, definitive testing is not 100 percent accurate. This kind of testing is not a simple process — gathering the necessary information from the family and doing the DNA analysis may take from several months to more than a year. Moreover, definitive testing is not always possible, because of difficulties in acquiring or analyzing the DNA. Before the gene for Huntington disease was identified, definitive testing was an option for about 75 percent of eligible couples.

Exclusion Testing

Exclusion testing is used when a parent does not know whether he or she will get a late-onset disorder, and does not want to know, but wants to avoid the birth of a child who would develop the disease. Exclusion testing makes it possible to determine whether a fetus is at low risk of a late-onset disorder by comparing the fetal genotype with that of one of the grandparents on the affected side of the family. If testing shows the fetus inherited the marker that came from the unaffected grandparent on that side, the fetus will be at very low risk for the disease — because only one gene of the pair the fetus receives can come from that side of the family. It does not give information on the parent's status, since he or she will have two genes from that side of the family. Exclusion testing, by contrast with definitive testing, requires DNA only from the fetus, the couple, and one grandparent on the affected side of the family.

As we have noted, these approaches will likely be phased out in coming years, although exclusion testing may still have some advantages if a parent does not want information about his or her own status.

Current Practices in Canada

Pre-symptomatic testing for late-onset single-gene disorders, whether for adults or prenatally, is relatively new and is currently provided in Canada for just a few disorders (Huntington disease, myotonic dystrophy, adult polycystic kidney disease, and others). This type of DNA testing pre-symptomatically has been available since the mid-1980s in Canada, and information is limited about the nature and implications of the practice. Most of the information available concerns one disorder — Huntington

disease — which has been the subject of a continuing in-depth study known as the Canadian Collaborative Study of Predictive Testing for Huntington Disease.

The information emerging from the Canadian Collaborative Study is useful, since it illustrates issues common to all late-onset disorders. Prenatal pre-symptomatic testing for Huntington is currently provided at 14 of the 22 genetics centres in Canada; all 14 participate in the Canadian Collaborative Study. Since any one centre sees relatively few families with the disorder, the Canadian Collaborative Study was set up to collect data in a uniform way.

To help understand the practice of pre-symptomatic PND testing in Canada, and to evaluate the issues it raises, we commissioned two research studies in this area, both of which drew on information gathered through the Canadian Collaborative Study (see research volume, *Prenatal Diagnosis: New and Future Developments*). One study examined patterns of demand for pre-symptomatic or prenatal testing and the psychosocial aspects of prenatal testing. A questionnaire was used to obtain a sociodemographic profile of study participants and to ascertain their knowledge about and attitudes toward prenatal testing; it included questions, for example, about whether they chose to have prenatal testing and whether they knew the difference between exclusion testing and definitive testing. A psychosocial assessment of those who participated in prenatal testing was also done, and their reasons for decisions about pregnancy termination were explored.

Prenatal testing for Huntington disease has now been offered in Canada for about five years. This ongoing national program has provided the opportunity to study the knowledge and attitudes of people at risk who choose or decline prenatal testing. During this period, over 425 people have participated in predictive testing. Of the 38 who became pregnant and were eligible for prenatal testing, 14 (37%) have entered the prenatal testing program. Of the 14, only 7 actually took the prenatal test. The other 7 withdrew, primarily due to miscarriage or not wanting to consider termination of pregnancy as an option. Clearly, the demand for prenatal testing for this late-onset, autosomal dominant disorder is lower than the expected demand.

S. Adam and M. Hayden, "Prenatal Testing for Huntington Disease: Psychosocial Aspects," in Research Volumes of the Commission, 1993.

A second study discusses ethical aspects of predictive testing for Huntington disease, drawing on the experiences of the Canadian Collaborative Study as well as the relevant literature. Ethical issues covered include consent to predictive testing, the counselling process, and patient confidentiality; legal issues addressed include the concepts of wrongful birth and wrongful life, as well as physician liability.

The Canadian Collaborative Study has involved both adult and prenatal testing for markers linked to Huntington. In terms of prenatal testing, of the 47 couples enrolled in the study who became pregnant, 38 were eligible for prenatal testing. Of these 38 couples, 14 (37 percent) requested PND; 4 of these withdrew after pretest counselling, and for 3 others who withdrew termination of pregnancy was not an acceptable option. There were 7 remaining women (3 of whom had more than one pregnancy during the five-year study period) who underwent testing for a total of 11 pregnancies. From 11 prenatal tests, four pregnancies were designated low-risk; the remaining seven were found to be at high risk. Of the seven high-risk pregnancies, six were terminated.

The evidence suggests that prenatal testing for Huntington has been well received by the couples who have chosen it. Many parents at risk for developing Huntington want to avoid the birth of a child who will develop the disease. Shelin Adam explained to the Commission why a pregnant woman whose mother has Huntington disease sought PND:

> She knows what she has been through, living "at risk" for Huntington disease, and does not want to bring a child into this world that would have to go through that same sort of fear — every time she drops something, she thinks she has the start of the disease; every time she forgets something, she is worried. (*S. Adam, participant, Commission Colloquium on Prenatal Diagnosis, November 13, 1991.*)

For this woman, and for others in her situation, PND is seen as a valuable service, without which she would have given up the attempt to have children. But most eligible couples choose not to have prenatal testing. This is also true of prenatal testing for other late-onset disorders. In general, prenatal testing for late-onset single-gene disorders has a much lower utilization rate than testing for congenital anomalies or genetic diseases with their onset in childhood.

> [A] cause for some alarm is the strong belief displayed by so many respondents that a cure for [Huntington disease] is in the pipeline. All the talk about genetics research and the Human Genome Project may well have engendered unrealistic expectations about progress in this and other diseases ... Appeals for public support need to be leavened with the truth, which is that it always takes longer than we've planned.
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> *T. Powledge, reviewer, research volumes of the Commission, June 16, 1992.*

The utilization rate is also lower than was anticipated before the tests became available. Before testing was available for Huntington, studies surveying the attitudes of women with fetuses potentially at risk for Huntington indicated that between 32 and 65 percent would use prenatal testing. The actual utilization rate, at 18 percent, is

thus outside the lower end of the anticipated range. There are several reasons for the low utilization rate:

- According to the results of the Canadian Collaborative Study, the most important reason for not having PND testing for Huntington is the belief that a cure will be found by the time the child reaches the age of onset. There is no effective treatment or cure for this disease at present, nor is one expected in the near future, but people may reason that the same DNA technologies that have enabled testing for Huntington will, with luck and with sufficient resources, lead to treatments or a cure.
- The uncertainty of the test has led some couples to decline testing. Although this is now changing, the test for Huntington relied on linked markers and so did not provide the same level of certainty as DNA tests that identify a gene directly. The 2 to 3 percent level of uncertainty is much greater, for example, than is the case for PND for chromosome disorders.
- Since the test for Huntington is relatively new, many couples at risk already have a child or children who were not tested and whose status is unknown. Some couples in this situation decline testing because they do not want some of their children to know their risk status while others do not.
- Many couples consider that a child can have an enjoyable and productive life for decades before symptoms of the disease begin to be troublesome. The late Woody Guthrie is often cited as an example of someone with Huntington disease who was able to enjoy life and contribute to society for many years.

Experience with other late-onset disorders for which prenatal testing is possible has shown that the proportion of couples who request PND declines as the seriousness of the disorder decreases and its treatability increases. For example, adult polycystic kidney disease is a late-onset single-gene disorder that varies in severity and is partially treatable with dialysis and kidney transplantation. Although PND using linked markers has been available for this disorder since 1986, very few families have taken advantage of it. A study conducted in Manchester, England, between 1988 and 1991 found that only 1 couple out of 40 with high-risk pregnancies requested prenatal testing. Another study in Australia showed a similar experience, with only one request for prenatal testing out of 46 eligible families over a three-year period.

The use of prenatal testing is even lower for those late-onset disorders where early intervention and treatment are possible. Familial hypercholesterolaemia (high blood cholesterol) is an autosomal dominant disorder that results eventually in heart attacks and strokes. However, diet and drug therapy have proven effective in reducing cholesterol levels. Even though prenatal testing using DNA probes is possible in families known to

have the mutant gene, there have been virtually no requests for prenatal testing, presumably as a result of the success of treatment.

Issues in the Use of Prenatal Diagnosis for Late-Onset Single-Gene Disorders

The use of PND for late-onset disorders raises many of the same issues as the use of PND for congenital and early-onset disorders, discussed in the previous chapter. However, it also raises some important new issues, including the potential vulnerability of the child, the need for special counselling, and the disclosure of genetic information to family members. We examine these in turn.

Vulnerability of Children

The available evidence suggests that most of the small proportion of women who do seek PND for late-onset disorders choose to terminate the pregnancy if the disorder is detected. If they choose not to have an abortion, however, the resulting child who knows of his or her status may be placed in a very vulnerable position, for several reasons.

First, it is likely to be difficult to keep knowledge of the child's status a secret from other family members or from the child. Parents and other relatives who know that a child has the gene may perceive and treat him or her differently from siblings known to be at low risk. Needless to say, even if differential treatment is not conscious or deliberate, the effects on the child and his or her siblings could be very harmful.

There are also concerns for the child who knows he or she is at high risk. Since a very young child would not have the capacity to understand the information, it is only when the child is somewhat older that the implications of his or her status would start to become clear. This means that the child would have to deal with the information at a difficult time in the life cycle, when identity and self-image are being formed. The knowledge of being at very high risk could result in significant diminishing of self-esteem and self-worth for a developing child and many problems in adjustment, including anger at and resentment of parents and unaffected siblings.

It is not known how children and adolescents who have the knowledge that they are likely to develop a late-onset disease would deal with decisions about schooling, relationships, and marriage, but it is likely to place a severe burden on them. The potential for long periods of completely normal life could be destroyed by the knowledge that they will almost certainly begin to experience symptoms sooner or later, without them having chosen to have this knowledge.

A danger also exists that the genetic information revealed during PND testing could be disclosed by the family (deliberately or accidentally) to third parties, potentially leading to discrimination or stigmatization affecting the

child's schooling or subsequent employment. When PND is used to detect congenital anomalies or early-onset disorders, the condition being tested for is clearly evident early in life; "normal" life for the child is life with the disorder. With late-onset disorders, however, the children have many years of life unaffected by the disorder, yet could still be deprived of a "normal" life if others learn that they will develop the disorder later on.

Hence, there are significant differences in the potential harms to children from prenatal testing for late-onset disorders and the potential harms to children from PND for congenital or early-onset disorders. Moreover, at present there is no way to use knowledge of the child's condition to improve the child's health. No treatment has been discovered or developed that might prevent or delay the onset of Huntington disease. Thus, their situation is unlike that for some congenital disorders, where knowledge that the disorder is present in the fetus can help in the medical care of the fetus and child and in preparing parents to care for the child, and where the disorder is evident early in any case.

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The adverse effects of the knowledge for the resulting child may be great if the parents decide not to terminate after diagnosis of a late-onset disorder, and the benefits to the child are fewer than for diagnosis of a congenital disorder. For these reasons, many of those involved with Huntington disease (parents, relatives, and groups representing them, as well as testing practitioners) believe that prenatal testing should be refused in cases where parents are unwilling to consider terminating the pregnancy. This is the position of Canadian genetics centres participating in the Canadian Collaborative Study, as well as the position of the International Huntington Association and the World Federation of Neurology.

Commissioners agree that the decision about whether to offer testing where the parents are unwilling to consider termination is not easy. Given the potential harms of PND to the resulting child, we believe that testing for late-onset disorders is one instance where an exception can and should be made to the general prohibition on directive counselling. If termination is not a choice that the couple would be willing to make, counsellors should ensure that the potential harms to the child of knowing the PND test results are clearly outlined to parents. The facts usually act as a strong deterrent to having testing, and, when parents are unwilling to consider termination, counsellors should discourage testing and explain why they are doing so.

We do not believe, however, that parents should be asked for a commitment to terminate an affected pregnancy as a precondition for

having the test. We believe the test should be available, after appropriate counselling, to all eligible couples who request it even if they say in advance that they will not terminate an affected pregnancy. Requiring a commitment to terminate is inappropriate for several reasons:

1. Most parents can be relied on to make sensible judgements in light of their own circumstances. In fact, the available evidence shows that after appropriate counselling, most couples who reject the option of abortion decide not to have pre-symptomatic PND testing. Commissioners believe that, after appropriate counselling, few if any who could not contemplate termination would be likely to want prenatal testing.
2. It is often difficult for people to know what they will do in a given situation as long as it remains hypothetical. As we noted with respect to PND for congenital anomalies, many women said that the PND decision-making process became "real" to them only when the test revealed a disorder. It is possible that some women and couples faced with an actual finding that the fetus is affected would opt for termination, even if they previously thought they would not do so.
3. There is no way to enforce a commitment to terminate a pregnancy. If a woman says that she plans to terminate an affected pregnancy, perhaps to gain access to the test, then decides to continue the pregnancy, she cannot be compelled to terminate. Moreover, it would be unacceptable to try to create a legal mechanism that could compel her to undergo an abortion.
4. Finally, the number of couples who might decide to have the testing even if they would not abort is extremely small. The evidence from the Canadian Collaborative Study suggests that this would occur in Canada, at most, only a few times a year. It is therefore important to keep this issue in perspective.

For these reasons, we believe that it is inappropriate to deny couples access to PND testing for late-onset disorders on the basis of their unwillingness to consider abortion. Principles such as individual autonomy and respect for people's ability to make decisions in line with their own circumstances and values preclude this.

It is desirable to protect children identified as being at high risk, who, as we have seen, are in a very vulnerable position. Hence, it is acceptable and appropriate for genetics counsellors to emphasize to the couple the potential harms to the resulting child of using PND in this context, and to discourage the use of PND by couples who are unwilling to consider termination.

We also believe, however, that it is desirable to protect children identified as being at high risk, who, as we have seen, are in a very vulnerable position. Hence, it is acceptable and appropriate for genetics

counsellors to emphasize to the couple the potential harms to the resulting child of using PND in this context, and to discourage the use of PND by couples who are unwilling to consider termination.

Our position represents a departure from the usual practice in genetics counselling, which attempts to be non-directive. However, the clear potential for harm during a child's growing years and early adulthood makes it necessary to consider the interests of this vulnerable group. The same considerations do not apply in the case of PND for congenital and early-onset disorders. Hence, counselling practices need to be modified to reflect the distinctive needs of both parents and children when PND for late-onset disorders is at issue. The Commission recommends that

256. Provision of prenatal diagnosis for pre-symptomatic testing for late-onset single-gene disorders be restricted to genetics centres licensed by the National Reproductive Technologies Commission.

and that

257. Pre- and post-test counselling for such disorders be rigorous and extensive in nature, with particular attention paid to the potential implications for any child born at high risk of developing a late-onset single-gene disorder, and that provision of such counselling be a condition of licence for all genetics centres providing such testing.

Counselling and Support

Individuals who seek PND for late-onset disorders are generally well informed about the disorder in question. They have often lived with people who have the disorder and may be involved in caring for an affected parent. They still need intensive counselling and long-term support, however, often exceeding that normally provided in prenatal genetics counselling. For one thing, studies have shown that many individuals have difficulty understanding the technical aspects of the testing, particularly in the case of exclusion testing using linked markers. With respect to PND testing for Huntington disease, for example, Commission research showed that 89 percent of those surveyed for the study had difficulty fully understanding the technology because the current process of marker analysis was so complex (see research volume, *Prenatal Diagnosis: New and Future Developments*).

Given the complexity of both the testing and the counselling process, it is advisable that the DNA testing of parents and grandparents that is required as a basis for prenatal testing be carried out before the woman becomes pregnant. This provides sufficient time for the couple to assimilate information about prenatal testing. At present, many women who enter a prenatal testing program are already pregnant, which places them and the counsellors under severe time constraints. It is important, therefore, to educate the at-risk population about the desirability of carrying out DNA testing before pregnancy occurs.

Moreover, it is important to remember that couples undergoing definitive testing may be discovering their own health status, as well as that of the fetus. This can be a source of enormous stress. Discovering that one is almost certainly going to develop a serious and debilitating genetic disease is extremely difficult for any individual. Counselling is essential for individuals working through this situation.

> The counselling alternative ... clarifies coexisting fundamental values, permitting a resolution that arises out of the experience of the participants in the dialogue rather than being imposed by referral to a third party.
>
> Heavy emphasis in counselling on what might be called value clarification may provide a model for the resolution of related issues in testing for other late-onset disorders. The need for in-depth counselling was also described with respect to fully informed choice.
>
> *M. Cooke, "Ethical Issues of Prenatal Diagnosis for Predictive Testing for Genetic Disorders of Late Onset," in Research Volumes of the Commission, 1993.*

In short, the significance of counselling in relation to PND for late-onset single-gene disorders cannot be overstated. This is recognized in the Canadian Collaborative Study, which offers parents a minimum of three counselling sessions before they get the test results. However, the Canadian Collaborative Study is being offered as part of a funded research program, and it is not clear whether similar funds for intensive counselling will be available when these tests are provided as part of provincial health insurance plans. We believe it is essential that adequate resources continue to be available to support families at risk in the future. The Commission recommends that

258. Provincial/territorial ministries of health make available adequate resources for counselling in relation to prenatal testing for late-onset disorders.

Confidentiality and Access to DNA Test Results

Using PND testing for late-onset disorders raises many of the same concerns about confidentiality as PND for congenital disorders, but, in particular, there is concern about the potential for discrimination if this information is disclosed to third parties, including insurers, employers, and government agencies.

We refer to what we said in the previous chapter — namely, that the duty of confidentiality entails the obligation to protect information about an individual who has undergone genetic assessment and to ensure it is not released to others without the individual's explicit permission. Genetic information has the same legal protections as all other medical information; whatever the limits or exceptions to the duty of confidentiality are in civil or common law, they do not include a right to disclose information to insurers or employers without the patient's consent.

Some confidentiality issues, however, are unique to PND testing for late-onset disorders. As we have seen, most pre-symptomatic PND testing has so far used linked markers. This requires analysis of DNA from several relatives, including at least one with the disorder. The fact that PND for late-onset single-gene disorders often requires the involvement of other family members raises two kinds of issues: securing the consent of other members of the family to such testing; and regulating access to the results of such testing by other family members.

Consent to testing by other members of the family: Ethical difficulties may arise if a family member does not wish to be tested, but that particular individual's results are required to provide a diagnosis for a relative. Some ethicists believe that such individuals have a moral obligation to cooperate in a family linkage study — even at the risk of learning unwanted information — if their tissue sample is necessary to establish the pattern of inheritance that other family members need to know in order to establish their own risk and take steps that may be possible to safeguard their health or that of potential offspring.[2] All individuals have the right, however, to refuse treatment or investigation, even if some might wish that they would comply for the benefit of others.

Access to test results by other family members: Predictive testing takes place in a complex system of family inter-relationships, and the information revealed has a direct bearing on the health or reproductive risk of other family members. Ethical issues can therefore arise if the information generated through PND is withheld from other members of the family who might be affected. Do individuals have the moral right to withhold test results from family members?

Similar issues regarding the interaction of family members arise in the context of various chromosomal disorders. We believe that the only feasible approaches to these issues are tactful negotiation and common sense. The

available evidence shows that the majority of such situations can be resolved through counselling.

The ethic of care reminds us that the counselling alternative is clearly preferable to a judicial process for mediating rights claims.

The alternative is to place more emphasis on judicial mediation between conflicting claims. For example, some people have proposed imposing a *prima facie* legal obligation on family members to cooperate in linkage studies, or a *prima facie* legal obligation on patients to share PND test information with other family members who may be affected. These obligations would have to be balanced against competing rights to confidentiality and privacy; this balancing process would be mediated by courts or other judicial tribunals.

The ethic of care reminds us that the counselling alternative is clearly preferable to a judicial process for mediating rights claims. Whereas judicial mediation promotes an adversarial stance between conflicting rights-bearers, counselling clarifies co-existing fundamental values, permitting a resolution that arises out of the experience of the participants in the dialogue rather than being imposed by referral to a third party (see research volume, *New Reproductive Technologies: Ethical Aspects*).

Full protection of individual privacy and confidentiality is already the practice with respect to PND in general. We reaffirm the importance of these principles with respect to prenatal testing for late-onset disorders and believe that counsellors should continue to pursue, through mediation counselling, consent by other family members to testing and access to test results by other potentially affected family members.

Employment: The Commission heard concerns about the potential for discrimination if employers or insurers had access to genetic information about prospective employees or candidates for insurance. These concerns appear to be based in part on the perception that such information would be readily available to parties other than the patients and their health care providers. As we have noted, however, several protections exist for this information, including the requirement to maintain the confidentiality of medical information unless the patient gives explicit consent to its release.

In addition, the federal *Privacy Act* allows government departments or agencies to collect personal information about individuals only if it relates directly to an operating program or activity of the department or agency in question. Personal genetic information would be unlikely to satisfy this criterion, so federal departments and agencies would not be able to justify collecting it. Further, the Privacy Commissioner of Canada has interpreted the act to mean that legislation must specifically authorize the collection of personal genetic information. However, the Privacy Commissioner's interpretation is open to challenge in a court, and thus collection of information may be justified without specific statutory authority.

Sections 7 and 8 of the *Canadian Charter of Rights and Freedoms* have been interpreted as offering a limited right of privacy against intrusions by federal and provincial governments. These sections could be interpreted as preventing federal government bodies from invading individual privacy by collecting genetic information. The section 15 equality provision of the Charter would appear to reinforce this protection by prohibiting legislation or policies that have the effect of discriminating on the basis of genetic traits related to race, colour, ethnic origin, or mental or physical disability.

Federal and provincial human rights legislation prohibits discrimination in employment on the basis of disability except in cases where being free of a particular disability is a bona fide occupational requirement for the job being filled. Given that genetic testing for diseases of late onset provides no indication of an individual's *current* health or disability status, employers would not be justified in asking for such information as a basis for deciding on a person's ability to do a job. However, one gap in human rights legislation is that a genetic susceptibility to a late-onset disorder might not be perceived by the law as a disability, and so such people may not have protection.

In summary, there appears to be considerable protection against discrimination in employment on the basis of genetic information. We recognize, however, that if genetic testing of adults comes into wider use, these protections could be challenged or eroded. For example, employers might seek to expand the definition of bona fide occupational requirements by claiming that the presence or absence of a given genetic trait would indicate a person's unsuitability for a particular job and to justify testing on this basis. These issues are outside our mandate, which relates to new reproductive technologies. We believe, nevertheless, that society must be prepared to address such questions in the context of a public policy response to the general issue of new and evolving genetic capabilities.

Insurance: Although the issues surrounding genetic testing and insurance are somewhat different from those related to employment, we heard similar concerns about the potential for discriminatory use of genetic testing results. Some provincial human rights laws exempt insurers from provisions prohibiting discrimination on grounds of disability. Insurers can therefore question applicants for insurance about disabilities that may be genetic in origin, as this helps them to assess risk and set premiums in consequence. They can also differentiate among applicants or deny them insurance because of a disability; differentiation or exclusion must generally be based, however, on "reasonable and bona fide grounds."

The growing availability of genetic testing for a wider range of conditions could therefore add to existing barriers to disability, life, and other types of insurance. These issues have attracted considerable attention in the United States because of refusals to provide health insurance to individuals or even to entire families on the basis of genetic testing of one member. With Canada's system of universal health

insurance, no person would be denied basic health care, but genetic testing could result in a denial of disability insurance or other types of insurance.

In addition to the federal *Privacy Act*, human rights legislation, and the *Canadian Charter of Rights and Freedom*, other provisions found in data protection statutes, statutory torts legislation, the common law, and ethical and professional guidelines protect genetic information from being used to discriminate against a person or infringe on a person's right to privacy. For example, like the federal act, some provinces have privacy statutes that limit the collection, use, and disclosure of personal information. Furthermore, legislation exists that imposes obligations on physicians to maintain the confidentiality of health information in addition to their common law duty to do so.

However, there are gaps in these same laws and instruments, so that it is difficult to say for certain whether the law offers adequate protection of genetic information. For example, Quebec is the only province that has comprehensive data protection legislation that is currently being examined for possible extension to the private sector. Another gap in the protection offered by the law is where insurers are permitted to discriminate on the grounds of genetic disability. As well, because recent Supreme Court of Canada decisions affirm that the fetus under most applications of the law does not have legal rights, prenatal testing for susceptibilities or late-onset disorders may mean that, after the individual is born, he or she may be burdened with unwanted genetic information; if there are loopholes in the current protections with regard to access to test results or DNA samples, this information could be used as a basis for discrimination.

Thus, the precise level of protection offered by the law may not be apparent until cases pertaining to genetic privacy come before the courts. These general issues of protection of access to genetic information are outside our mandate, however, and should be addressed as part of a broader public policy response to the development of genetic science. We concur, however, with the perspective expressed by the Office of the Privacy Commissioner of Canada in a 1992 report, *Genetic Testing and Privacy*,[3] to the effect that insurers and other service providers should not be permitted to begin collecting information made newly available through genetic testing without a thorough review of the ethical and human rights implications of allowing this.

Prenatal Diagnosis for Susceptibility Genes

People with susceptibility genes are genetically predisposed toward multifactorial disorders, which differ from late-onset single-gene disorders in that they are caused by an interaction of genetic and environmental factors (such as diet and smoking). Although having a susceptibility gene increases the probability of getting the related disease, it does not

necessarily lead to the disease; the relevant environmental factors may be absent or inoperative, or other genes may act to protect the individual from the disease.

Multifactorial disorders include some of the most common diseases in our society today, such as many types of cancer, cardiovascular disease, and mental illness. It has been estimated that up to 60 percent of adults will eventually suffer from a multifactorial disorder.[4] It has now become possible to identify susceptibility genes for some of these disorders through DNA testing. Examples include colon cancer, insulin-dependent diabetes mellitus, heart disease, rheumatoid diseases, and chronic obstructive lung disease (see research volume, *Prenatal Diagnosis: New and Future Developments*).

The ability to identify susceptibility genes raises the question of whether it is appropriate to test for them, a question on which the Commission heard a range of views from Canadians. For example, as with pre-symptomatic testing for late-onset single-gene disorders, susceptibility testing for multifactorial disorders could take place either prenatally or during adolescence or adulthood. In the latter case, individuals would be tested in order to evaluate their risk for a late-onset multifactorial disorder and provided with information that could help them manage that risk. In the prenatal case, a pregnant woman could have her fetus tested to determine its risk status, presumably with the intention of aborting a fetus that had the gene, as no prenatal treatment or prevention strategies are available.

No such prenatal testing for susceptibility genes is being done in Canada at present, but there is a limited amount of adult testing of members of families with a history of a disorder. Considerable interest has been shown in exploring susceptibility testing, both within the health care system and by commercial interests (see Chapter 24). The main health-related justification for such testing is that it might enable individuals at higher risk for a particular multifactorial disorder to take preventive measures or receive treatment earlier in their lives. Since the disorders are caused by a combination of genetic and environmental factors, it is possible, in principle, to modify a person's micro-environment with the aim of avoiding exposure to the factors that trigger the disorder. For example, people with a genetic susceptibility to coronary heart disease could alter their diet to decrease their cholesterol intake, increase their activity level, and have their cholesterol level checked more frequently to

> Canada has a window of opportunity to anticipate and shape developments in the area of susceptibility testing in accordance with our collective values and priorities. Guidelines and safeguards must be established to ensure that if any such testing takes place, it will be in an ethical and beneficial manner, and that our response as a society is not driven solely by technological imperatives or commercial goals.

enable earlier diagnosis and treatment. It has even been suggested that population screening programs be established to test all adults for certain common susceptibility genes, although no such program exists in Canada. As we will see in the next section, the likely health benefits of susceptibility testing programs, in terms of better prevention or earlier treatment, are not clear.

As with the case for single-gene late-onset disorders, the other reasons for the interest in susceptibility testing are not related to health care. For example, insurance companies offering life or disability insurance have a strong interest in identifying individuals who are at higher risk of developing multifactorial disorders, so as to minimize the insurer's exposure to risk. Employers may also wish to know the genetic susceptibilities of potential employees: healthy employees are more productive and less costly to employ. There are no programs in Canada at present to screen applicants for genetic susceptibility to disease for employment or insurance purposes. However, this is not what prevents access to medical records and test results by insurers — it is the physician's legal duty of confidentiality that prevents access without the patient's explicit consent. This may need to be made more explicit with regard to insurers in particular.

Given that commercial interests may wish to develop the concept of population testing for susceptibility genes, there are vulnerable interests to be protected, and governments should be considering what measures are needed to protect these interests. Canadians told the Commission that they are concerned about the use of DNA testing in harmful and discriminatory ways. Canada has a window of opportunity to anticipate and shape developments in the area of susceptibility testing in accordance with our collective values and priorities. Guidelines and safeguards must be established to ensure that if any such testing takes place, it will be in an ethical and beneficial manner, and that our response as a society is not driven solely by technological imperatives or commercial goals.

Before considering the possible uses of susceptibility testing, it is important to clarify what such tests would reveal. In the next section, we discuss what it means for an individual to have a susceptibility gene. We go on to consider the implications of susceptibility testing, both in the adult context and in the PND context.

What Does Susceptibility Testing Actually Tell Us?

Susceptibility testing is intended to provide individuals (or couples) with reliable information about the likelihood that they (or the fetus) will develop a multifactorial disorder later in life. The usefulness of this information is deficient in many important respects, however. First, many of the tests now available rely on linked markers, which means, as we saw earlier in this chapter, that the tests cannot establish definitively whether the relevant gene or genes are present. This will change as genes can be

identified directly, but secondly, and more important, even when a susceptibility gene can be identified reliably, this does not mean that the individual will become ill with the disorder in question. It is essential to remember that the disorder will not appear in all people with susceptibility genes, and that not all people with a disorder will have particular genes. Environmental factors are also involved in the onset of multifactorial diseases, and these cannot be measured by DNA testing.

Susceptibility testing by itself, therefore, provides only limited information. Although someone with the gene may have an increased likelihood of becoming ill, the data are not usually good enough to answer accurately questions about how many people who have the gene actually get the disorder — is it 0.5 percent, or 5 percent, or 50 percent? We also need to know how this risk compares to that of others in the general population who lack the genes — does having certain genes increase one's disease risk by 5 percent, by 100 percent, or by 1 500 percent?

Answering these questions would require correlational studies that compare the clinical and natural history of those with a particular genotype to those in the general population who do not have the genotype. However, simply looking retrospectively at a group of people identified as ill with the disease in question and comparing them to a group of well people for differences in the frequency of the gene raise the problem of biased ascertainment, because such an approach does not provide a random sample of people with the gene — the sample would include only those with the gene who became ill. Moreover, since the disorders in question are of late onset, the data needed to conduct such studies must be collected over the long term. The study group may need to be followed over several decades to obtain the necessary information on outcomes. This imposes a considerable burden on participants, who must be willing to make themselves available for the full duration of the study, and creates difficulties for funding, since research agencies are often unable or unwilling to commit funds to such long-term projects.

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We do not have good correlational data for the vast majority of susceptibility genes for multifactorial disorders. What we do know is that people with a particular multifactorial disorder often exhibit a particular genetic marker. But we also need to know how often these same genes are found in people who do not develop the disorder, or how much more likely people with the gene are to develop the disorder than people without the gene. In the absence of good information on the absolute risk for those

with the gene, as well as on the increased relative risk, susceptibility testing is likely to create unnecessary anxiety among those who have a susceptibility gene but whose risk is nonetheless quite low, and a false sense of security among those who lack a susceptibility gene but whose risk is nonetheless real.

For example, testing for the susceptibility gene for insulin-dependent diabetes mellitus (IDDM) would likely create unnecessary anxiety. There is no question that having the susceptibility gene for IDDM affects the likelihood of getting the disease — more than 95 percent of IDDM patients have the gene. However, although people with this gene are more likely to get IDDM than people without the gene, the vast majority of people who have the gene do not get IDDM. In fact, evidence suggests that only 1 person in every 150 who have the gene actually develops the disease. Most people with the susceptibility gene do not get the disorder because they are not exposed to the environmental factor or factors that trigger IDDM, or because they may have another gene that protects them. (The environmental factor involved is widely believed to be some sort of virus, although this has not been established definitively.) Telling people that they have the susceptibility gene for IDDM is therefore likely to cause unnecessary worry, even if they are also told that the likelihood of developing the disease is very low.

By contrast, testing for a recently identified susceptibility gene for breast cancer could create a false sense of security if the results are negative, as this genetic mutation accounts for only 9 percent of breast cancers.[5] As a result, being told that one lacks this particular susceptibility gene is likely to be misleading, unless it is also made clear that the vast majority of breast cancers are not associated with having this particular gene. In addition, there are probably other as yet unidentified susceptibility genes for breast cancer. People who lack the one identified gene may still be at significant risk for breast cancer, because they may have another gene or may be exposed to environmental factors that trigger the disease. In other words, the absence of the particular susceptibility gene being tested for does not mean that an individual lacks a genetic predisposition to the disorder. Furthermore, researchers are discovering that there are different genes that may indicate susceptibility to a particular disorder. Some individuals may have more than one of these, each of which changes the person's risk to a different extent. As a result, even the most sophisticated DNA susceptibility testing could miss a significant proportion of people with a genetic susceptibility. An understanding of these aspects of susceptibility testing is not easy to communicate, and they also mean that the benefits to be derived from this application of DNA testing are limited.

Finally, to complicate the picture still further, some people have what might be called "protective genes," which actually reduce their susceptibility to particular disorders. For example, protective genes have been identified for coronary artery disease and diabetes mellitus.

At its current state of development, therefore, susceptibility testing for multifactorial disorders on a population basis provides only very incomplete information on people's risks of developing them. It tells us only that some people have a greater risk (estimated with varying degrees of reliability) of developing a disease at some unpredictable point in the future.

The Implications of Adult Susceptibility Testing

In assessing the implications of allowing susceptibility testing, we need to consider the potential benefits, harms, and opportunity costs. We look first at adult susceptibility testing to establish a context for considering prenatal testing, the substance of our mandate in this area.

Potential Benefits

The major health-related benefit of adult susceptibility testing is that, in principle, it can allow individuals who know they are at higher risk of developing a particular multifactorial disease to avoid exposure to environmental factors that are known to trigger the symptoms of the disease and to seek earlier diagnosis and treatment. However, this presupposes that there is a proven treatment or prevention strategy for the disorder in question. People can derive some benefit from testing only if knowledge of their susceptibility allows them to avoid the disease. But, for most of these disorders, no effective intervention is available at present. For example, there is no known way to delay the onset of IDDM and hence no health benefit to individuals from knowing their genetic susceptibility.

The fact is that we know very little about the identity or interaction of the specific environmental factors that trigger multifactorial diseases. Moreover, some of the factors known to affect multifactorial disorders — such as the characteristics and quality of social relationships and human interaction — are very difficult to measure. Finally, it is likely that different environmental factors trigger different susceptibility genes for the same disorder. Hence, it is unlikely that a single prevention strategy would be effective in all cases of genetic susceptibility to a particular disorder.

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Even if a prevention strategy is identified, how likely is it that individuals at risk would change their behaviour and follow the recommended prevention strategy? Experience shows that rates of compliance with medical treatment regimes are often quite low, even when people are already acutely ill.[6] In the case of susceptibility genes, where an illness is not yet present to serve as a motivating factor, compliance rates

are likely to be lower still.[7] In the absence of specific strategies to provide continuing support and reinforcement, many people would find it difficult to follow a prevention regime for a disease that has yet to occur.

In summary, the ability of individuals and the health care system to react to and effectively use any information provided by susceptibility testing of the general population is likely to remain quite limited for a long time to come.

Potential Harms

Although the likely benefits of susceptibility testing for multifactorial disorders are quite minimal, the potential for harm is considerable. The use of susceptibility testing, like pre-symptomatic testing for single-gene disorders, creates a new category of people who are not ill but who know that they are susceptible to a specific illness. This could have a negative impact on people's self-image and sense of identity, as well as on their family and other relationships. Moreover, people could be stigmatized by disclosure of their risk status. The likelihood of stigmatization would probably decline with the development of tests for a greater number of these genes and with increasing awareness that almost all of us carry genes that make us susceptible to one multifactorial disorder or another. When testing first became available, however, those who carried the genes that could be tested for might well encounter stigma or bias in their personal, school, or work lives.

> A caring society is one that does not impose special burdens or inequitable requirements on any of its members simply because they happen to have a particular genetic make-up.

Moreover, information from susceptibility testing, if obtained by third parties such as employers or insurers, could be used to discriminate against the individual; we discussed this issue in the context of PND in general. It would be essential, therefore, to ensure that information from susceptibility testing, like all other medical records, was protected from any disclosure without the individual's consent.

> Would genetic screening be used in hiring and promotion? How will it affect access to health insurance, long term disability insurance and drug plans? To what extent will this technology impact negatively on the economic status of women? Will women's jobs become even more ghettoized than they have in the past?
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> *N. Riche, Canadian Labour Congress, Public Hearings Transcripts, Toronto, Ontario, October 31, 1990.*

There are concerns that employers or insurers could demand that applicants undergo

susceptibility testing as a precondition for gaining employment or buying life or disability insurance. The use of susceptibility testing in this context falls outside our mandate, but we are concerned about the potential for applying this technology for uses unrelated to health care. Unlike health care providers, employers or insurers would be under no obligation to respond to a diagnosis of genetic susceptibility with either therapeutic responses or preventive measures. The value of this information to employers and insurers would be based solely on financial considerations, not the interests of those being tested. For example, tests could identify actual or potential health care risks among employees or insurance applicants, thereby giving employers or insurers an opportunity to minimize their costs or liability. It would be neither the role nor the responsibility of employers or insurers to offer prevention, treatment, or even follow-up counselling for the individuals tested.

> We are concerned that women and men may be made more vulnerable economically because of the growth in diagnostic technologies ... The ability to screen for genetic disposition to conditions or illnesses will provide a tool that many employers, in their search for the perfect work force, are eager to use. Legislation has already been introduced in American jurisdictions permitting employers to demand and use the results of tests showing genetic disposition.
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> *C. Micklewright, British Columbia Federation of Labour, Public Hearings Transcripts, Vancouver, British Columbia, November 27, 1990.*

We are very concerned about any use of susceptibility testing to identify employees or insurance applicants as health care risks, particularly when the ability of individuals and the health care system to respond would be quite limited. In our view, a caring society is one that does not impose special burdens or inequitable requirements on any of its members simply because they happen to have a particular genetic make-up. Despite being beyond our mandate, then, the issue of susceptibility testing in the context of the workplace or insurance is one that does require investigation and, possibly, a public policy response to ensure that information acquired through such testing cannot be used in discriminatory ways. Commissioners thus conclude that there is a need to review the legal protections now in place with respect to insurance and employment practices to determine whether they are adequate in an era of DNA testing,

> There is a need to review the legal protections now in place with respect to insurance and employment practices to determine whether they are adequate in an era of DNA testing, and we urge that this be done while the current window of opportunity is still open.

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Opportunity Costs

The goal of avoiding the onset of multifactorial disorders is a worthy one. However, given the practical, ethical, and other difficulties of relying on susceptibility testing to realize this goal, we believe that alternative approaches would provide greater benefits and create fewer harms.

It is important to remember, for example, the potential effectiveness of environmental responses to multifactorial diseases. In the last several decades, mortality from cardiovascular disease has fallen by more than 40 percent, not as a result of identifying individuals who are at genetic risk but largely because of environmental change — such as changes in diet and smoking habits, increased physical activity, and changes in socioeconomic circumstances. Similarly, we know that improved prenatal care programs for pregnant women in disadvantaged circumstances will reduce the incidence of disease and disability throughout their children's lives.

Where environmental factors are associated with disease or ill health, then, it may be less effective to invest societal resources in discovering the individuals who are at genetic risk than to devote resources to changing the environment for everyone. In other words, the opportunity costs of emphasizing the genetic dimension of multifactorial conditions include the risk of diverting attention and research resources away from potentially more effective approaches, such as environmental change for communities or populations. Viewing diseases that have multiple causes as "genetic" tends to preclude remedies that attack the complex social determinants of health, which may well be equally or more important in causing the disease.

Genetic testing and disease prevention through improvements in the physical or social environment are not necessarily mutually exclusive undertakings. In fact, the purpose of identifying those with susceptibility genes is to permit environmental interventions that may allow them to avoid becoming ill. However, in assessing the costs of susceptibility testing, it is important to recognize just how expensive such testing would be if done appropriately and ethically. The cost would go far beyond the development and provision of the test, although this alone would be quite expensive. In addition, it would be necessary to establish and fund testing, counselling, and follow-up programs and to hire and train the personnel necessary to implement them. Susceptibility testing, if offered on a population screening basis, would identify many at-risk individuals, all of whom would require counselling. As we have seen, genetics counselling is personnel-intensive and time-consuming, because conveying risk information is complex and perceptions of risk differ widely. Unless appropriate counselling was provided, people could be lulled into a false sense of security or develop unnecessary anxiety about their risks, both of

which could jeopardize rather than promote their future health. Quality control mechanisms for the laboratories that do the testing would also be necessary to minimize the possibility of errors, as would safeguards to protect the confidentiality of information generated through testing.

Commissioners believe that the resources needed to develop such screening programs would be better spent on prevention programs that focus on improving the social and physical environment for whole communities or populations. For the foreseeable future, widespread susceptibility testing would not be an appropriate use of resources — it would provide minimal benefits at too high an opportunity cost and has the potential to cause serious harm.

The Commission does recognize the value of continuing studies, for example, to track certain multifactorial diseases in large families with a history of a particular disorder. But these studies must be viewed as research, not clinical services, with all those involved receiving the full protection accorded participants in biomedical research in Canada today. All such studies involving human subjects would have to be based at a university or hospital and would have to be approved by research ethics boards, which follow Medical Research Council of Canada guidelines for research involving human subjects.

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The time may come when population screening for particular susceptibility genes would be an appropriate use of resources. This is only a possibility at present, and many conditions would have to be met before such a program would be appropriate: the gene would have to be quite common in the population; reliable information would be needed about the actual risks posed by having the susceptibility gene; the disorder would have to be severe; an effective preventive strategy would have to be available; the gene would have to increase susceptibility by a significant amount; mechanisms for protecting the confidentiality of information and for assuring the quality and reliability of laboratory test results would have to be in place; and the appropriate forms of counselling and follow-up would have to be identified and funded.

These conditions for a successful population-wide screening program are not currently in place (see research volume, *Prenatal Diagnosis: New and Future Developments*), and establishing them would be possible only if susceptibility screening were first tried out in research pilot studies. The danger is, however, that screening would not be done as part of a unified,

well-planned public health program, based on the lessons of carefully monitored pilot studies, but would occur on an opportunistic and ad hoc basis. Consequently, Commissioners believe that safeguards should be in place to ensure that any transition from research to service be subjected to careful and rigorous review. In our view, programs for population screening of individuals for susceptibility to multifactorial diseases should not be funded or offered in the health care system. Studies aimed at tracking certain multifactorial diseases should be classified as research projects, not clinical diagnostic services, and all subjects involved in such studies should receive the full protection accorded participants in biomedical research.

The Implications of Prenatal Susceptibility Testing

We have outlined our concerns about adult susceptibility testing, which falls outside the Commission's mandate, in order to establish a context for the subject that is in fact within our mandate — susceptibility screening in the context of reproduction and reproductive technology. We believe that prenatal susceptibility testing is even less appropriate than adult testing, because the benefits are even fewer and the potential harms greater. Like prenatal testing for late-onset single-gene disorders, prenatal susceptibility testing puts children in a very vulnerable position if they are shown to be at higher risk. The potential harms to self-image and parent-child relations, which we discussed in the context of PND for single-gene disorders, apply equally to prenatal susceptibility testing, as does the potential for stigmatization and discrimination.

Although adults who agree voluntarily to undergo susceptibility testing may be willing and able to accept these potential dangers, it is not in the best interests of children to be subjected to them as a result of prenatal susceptibility testing. Moreover, there is little opportunity for parents to use information obtained prenatally about a child's genetic risk to help delay the onset of the disorder in question. As we have seen, few effective prevention strategies exist.

There has been no demand for the development and provision of prenatal susceptibility testing from couples with a family history of late-onset multifactorial

> The question has been raised whether society would approve of doing prenatal diagnosis to detect genes that have only an increased probability, not a certainty, of causing a serious disorder. Most geneticists would not approve, and existing guidelines suggest that it is not ethical. It might be concluded that prenatal testing for susceptibility genes is one possible use of prenatal diagnosis that has so many pitfalls and so few benefits that it should not be permitted.
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> *L. Prior, "Screening for Genetic Susceptibilities to Common Diseases," in Research Volumes of the Commission, 1993.*

disorders. This is in sharp contrast to calls for PND for early-onset genetic disorders and congenital anomalies but similar to the situation with respect to prenatal testing for late-onset single-gene disorders, where tests have been developed but rates of use have been much lower than originally anticipated. There has been no identified demand for susceptibility testing.

Couples using PND want information about the health status of the fetus that is useful and relevant to the health and functioning of their child. Susceptibility testing is simply unable to provide this sort of information; having a susceptibility gene does not necessarily mean developing the disorder, the incidence of the disorder is affected by complex but potentially controllable environmental factors, and the disorders concerned do not develop until adulthood. Moreover, since everyone carries an unknown number of susceptibility genes, there is no way to ensure that children are free of all genetic susceptibilities — in fact, it is very unlikely that any of us are.

Given these limitations and potential harms, it is not surprising that demand for prenatal susceptibility testing has been negligible. Spending resources on prenatal testing for susceptibility genes would not be an effective or responsible investment of scarce health care resources. The Commission therefore recommends that

259. Prenatal diagnosis *not* be offered for genes that increase susceptibility to disease, and that this restriction be a condition of licence to provide prenatal diagnosis services established by the National Reproductive Technologies Commission.

Conclusion

In our review of pre-symptomatic testing for late-onset disorders and testing for susceptibility genes, it is evident that many of the principles and recommendations developed in the context of PND for congenital anomalies and early-onset genetic diseases also apply to the provision of pre-symptomatic and susceptibility testing prenatally. We have not reiterated these here.

One distinctive issue arises when parents want prenatal testing for an adult-onset single-gene disorder but would continue the pregnancy regardless of what the test showed. As we have argued, the potential harm to the resulting child in this situation is such that testing should not be offered without full counselling emphasizing the lack of benefit to the child and the potential for serious harm.

To ensure that individuals and couples have the proper support to make the very difficult decisions regarding testing in the context of late-onset disorders, Commissioners believe that special efforts and resources must be provided to ensure that PND in this situation is accompanied by adequate and appropriate counselling. In the end, Commissioners find themselves returning to the basic logic underlying all PND — namely, that individual women and couples, when faced with difficult choices, are capable of making enlightened and appropriate decisions for themselves and their children when given proper and respectful support.

With regard to DNA testing for susceptibility to multifactorial disorders, despite its limitations, interest is substantial and will likely grow, particularly on the part of those with commercial interests. Many people look to the field of genetics to provide clear and understandable reasons for disease or ill health when in fact their determinants are very complex and include social, economic, and environmental factors. Susceptibility testing also has financial attractions for employers and insurers, and some biotechnology firms in the United States can see substantial profits in the future in the development and marketing of a range of test kits.

Given the commercial presence (both present and potential) in this area in other countries, and the vulnerable interests of individuals and society that therefore need protection, we believe that any pressure to introduce susceptibility testing in this country at this time should be resisted firmly and consistently. The premature application of susceptibility testing could be harmful to Canadians and would constitute a serious waste of resources. Given that we do not know how to use the limited information made available by such testing to improve prevention or treatment, susceptibility testing offers few benefits and creates many potential harms.

We have concluded, therefore, that susceptibility testing should not be provided prenatally (or on a population-screening basis) for the foreseeable future; although pre-symptomatic testing for single-gene late-onset diseases in families known to have the gene may be justified, testing for susceptibility genes on a population basis is not. Susceptibility testing should be provided to adults only in the context of research projects — such as family linkage studies or research pilot studies — with all the strictures and protections that entails.

Commissioners recognize that recommendations aimed at preventing or limiting the proliferation of susceptibility testing in the health care system are only part of the social response that is needed. Given that commercial interests may put resources behind developing and marketing DNA testing, there are vulnerable interests to be protected. Individuals do not have the expert knowledge to evaluate whether they need to be tested, and social harms may therefore result from widespread use of such testing. Governments should therefore ensure that these interests are protected. We do not find it likely that pressure for prenatal DNA testing for these categories of disorders will arise in the foreseeable future, and we have

made recommendations in several chapters to limit the use of DNA testing and technology in other categories (see Chapters 26, 28, and 29). However, pressure to apply these tests could also arise in other areas of society — in the workplace or in the insurance industry, for example — that are outside our mandate. The use of susceptibility testing in the health care system is just one of the many significant issues posed by the emerging role of genetics in our society. Clear leadership and forward-looking policy responses to these issues are required from governments to ensure that the power of genetic science and technology is used in an ethical and beneficial manner wherever they may be applied. The Commission recommends that

260. The Prenatal Diagnosis and Genetics Sub-Committee of the National Reproductive Technologies Commission monitor developments in DNA testing as they relate to reproductive technologies, with a view to recommending regulations or limits if needed.

Public information, consultation, and dialogue are the most effective bulwarks against misuse of these technologies in this rapidly changing field. The existence of a source for this information and a forum for consultation would help to ensure that the necessary dialogue takes place and that decision makers can develop policies that are both responsive to Canadians' social values and effective in achieving appropriate societal oversight and control of technology use.

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Sex Selection for Non-Medical Reasons

A child's sex is usually the result of chance — about half the time a girl is born and half the time it is a boy. However, some parents have tried to change these odds. Interest in trying to influence whether a boy or a girl is born is long-standing, and motivations for sex selection have varied over the centuries and from culture to culture. Numerous methods of sex selection have been proposed throughout history, including timing of intercourse, douching, and diet, as well as more exotic theories focussing on the phases of the moon, the direction of the wind, or even the direction of the bed.[1] Historically, interest has focussed on techniques to increase the likelihood of male offspring, since men have held a higher social, economic, and legal status in most societies.

These folk recipes have no proven effectiveness. In the past, most parents with a strong desire for a child of a particular sex would only be able to "keep on trying" until they had a child of the desired sex, sometimes having more children than they wanted in pursuit of their goal. However, recent technological developments have the potential to change the chances of having a child of one sex or the other. These new methods of sex selection are the focus of this chapter. Three distinct techniques are covered by the term "sex selection." These three methods are employed at different stages in the reproductive process, using different reproductive technologies.

First, *sperm treatment with assisted insemination* is used before conception and involves an attempt to influence which type of sperm cell fertilizes the egg. All eggs have an X chromosome, so if the egg is fertilized by a sperm that carries the Y chromosome it will lead to the birth of a boy (XY); if it is fertilized by a sperm that carries the X chromosome it will lead to a girl (XX). Semen is therefore treated in an effort to separate out the desired type of sperm, and assisted insemination using the treated semen is performed. Because the method is used before conception, it is

sometimes known as "preconception sex selection" or "sex preselection"; this terminology has been used loosely, however, and has therefore become unclear, so we refer to this technique as "sex-selective insemination."

The second method, *in vitro* fertilization and preimplantation diagnosis, involves *in vitro* fertilization followed by preimplantation diagnosis to determine the sex of the resulting zygote. Only zygotes of the desired sex are transferred to the woman's uterus. We refer to this method as *sex-selective zygote transfer.*

These first two methods seek to influence the sex of the fetus before pregnancy is established. The third method, *prenatal diagnosis to detect fetal sex and sex-selective abortion,* involves identification of the sex of the fetus during the pregnancy using prenatal diagnosis, with abortion of the fetus of the undesired sex. Identification of fetal sex is possible by chorionic villus sampling, ultrasound, or amniocentesis between approximately 10 and 16 weeks' gestation. Therefore, if the fetus is not of the desired sex, a second-trimester abortion could be performed. We refer to this as "sex-selective abortion." (Future developments involving the examination of fetal cells in the pregnant woman's blood may allow fetal sex to be determined earlier in the pregnancy.)

Because the three techniques use different technologies and are employed at different stages in the reproductive process, they raise different issues and must be examined separately. It is important to remember, however, that sex selection techniques can be used for medical reasons, in situations where male offspring are at high risk of severe genetic disorders resulting from genes on the X chromosome (for example, Duchenne muscular dystrophy). As discussed in Chapter 27, most Canadians consider use of sex selection techniques to prevent the birth of male offspring at high risk of a severe genetic disorder to be an appropriate use of prenatal diagnosis. As well, the Canadian College of Medical Geneticists has long approved prenatal diagnosis to determine fetal sex as an appropriate option to offer to women or couples at risk of having male offspring affected by an X-linked disorder.

The focus in this chapter is the use of sex selection techniques in cases where a couple wants to have a child of one sex or the other for non-medical reasons, not because an X-linked disease is likely. When we speak of sex selection in this chapter, therefore, it is in this non-therapeutic context. After a brief survey of the views of Canadians on this topic, we discuss each of the techniques in turn, including their ethical and social aspects and our analysis and recommendations.

The Views of Canadians

Commissioners were informed by the discussion of sex selection during our public hearings and in written submissions, as well as by the

views of Canadians across the country obtained through the Commission's survey research.

Public Hearings and Submissions

Most of the discussion in the public hearings concerned the use of prenatal diagnosis to determine the sex of the fetus and sex-selective abortion. This was an issue on which there is widespread agreement among Canadians. Almost all intervenors who commented on this form of sex selection were strongly opposed to it, except when it is used to avoid a serious sex-linked genetic disorder.

Representatives from a broad cross section of Canadian society — the medical sector, the community and social services sector, women's groups, religious groups, and concerned citizens — all voiced their opposition to sex-selective abortion because they believed it would have a discriminatory impact on women and/or because it involves abortion. A primary concern expressed by all these groups about sex-selective abortion is that the practice fosters, reinforces, and legitimizes discrimination on the basis of sex.

The Commission received testimony that the pressure to use sex-selective abortion to avoid female offspring is particularly strong for some women who are members of certain cultural or ethnic minorities. Representatives of these groups appearing before the Commission were especially concerned about the way clinics providing fetal sex identification target minority communities in their promotional activities. Particular concern was expressed about a clinic using ultrasound, established just across the U.S. border from Vancouver by a California physician. The physician is not licensed to practise in British Columbia, but witnesses told us that he has heavily promoted his service among Vancouver's large East Indian community. The response from the immigrant and visible minority community in Vancouver has been highly critical. At the Commission's public hearings in Vancouver, a representative of immigrant and visible minority women's groups denounced such clinics:

> Another cause for alarm is the misuse of pre-natal testing for the sex-selection of boys or girls. Given the preference in most cultures for male children, especially male first born children, boys will usually be selected over girls. This cross-culture preference for boys not only reflects the inequalities of the female role but further devalues the real lives of girls and women.
>
> *Brief to the Commission from Vancouver YWCA Board of Directors, December 1990.*

> We are opposed to having technologies directed against our communities that devalue women further and which are being legitimized in the name

> of culture and tradition. We are opposed to this racist stereotyping of the Indo-Canadian culture and here today represent that tradition of resistance which is firmly rooted in our culture and which has fought against the devaluation of women for centuries. *(S. Thobani, Immigrant and Visible Minority Women of British Columbia, Public Hearings Transcripts, Vancouver, British Columbia, November 26, 1990.)*

The Commission's survey of ethnocultural community organizations subsequently confirmed these concerns. The Commission surveyed 312 organizations that represent or serve ethnocultural communities to help identify their views on new reproductive technologies. Most of these organizations did not have an official position on the use of reproductive technologies. However, not a single respondent supported the use of PND for the purposes of sex-selective abortion. Moreover, an overwhelming majority of respondents would be concerned if their community were to be the target of those promoting sex selection technologies (see research volume, *Social Values and Attitudes Surrounding New Reproductive Technologies*).

> Pre-natal diagnosis should be done only for medical reasons, not for sex pre-selection ... some cultures prefer male children, and there might be cultural pressures to abort female fetuses.
>
> *Brief to the Commission from the North Shuswap Women's Institute, March 24, 1992.*

Many of the interventions the Commission heard assumed that the technique would be used, as it has been in some other countries, mainly to abort female fetuses. This led to concern that the widespread use of sex-selective abortion would lead to sex maldistribution, with a resulting preponderance of males in the population. Fears were expressed that sex maldistribution would have adverse effects on the most fundamental aspects of our society.

A related concern was that sex-selective abortion would be used to ensure that the first-born child was a boy, who would then receive the emotional and financial advantages that are widely believed to accrue to first-born children.

Although virtually all intervenors opposed sex-selective abortion for non-medical reasons, no single preferred method to control the practice emerged from our public consultation process. Some groups wanted a legal ban on sex-selective abortions, but most groups, while critical of sex-selective abortions, believed that prohibiting such abortions would require authoritarian measures and place grave restrictions on women's autonomy and reproductive freedom. They felt it would require intrusive and ultimately futile attempts to monitor the actions of pregnant women who were informed of the sex of their fetus and to determine whether sex preference was the sole reason behind a woman's request for an abortion.

Most groups therefore favoured other approaches — for example, trying to ensure that PND is not used to identify the sex of the fetus except in cases where there is a risk of a serious sex-linked disorder, or encouraging broader social change and education to promote the valuing of males and females equally.

> If sex selection is an option, boys will be chosen to be the first-born. What message does this give to daughters — second born, and second choice. Although experts have forecast profound social, psychological, and demographic consequences of sex selection, there is no unanimity on what exactly these consequences would be.
>
> *Brief to the Commission from L. Lavigne, St. Catharines, December 13, 1990.*

There was less discussion of the other two methods of sex selection — sperm treatment methods and sex-selective zygote transfer — perhaps because there is much less public awareness of them. Our survey of people's attitudes toward the sex of their children, discussed below, showed a relatively low level of awareness of sperm treatment methods — less than one in four Canadians surveyed — and certainly a much lower level of awareness than for other aspects of our mandate, such as preconception arrangements, IVF, or PND.

Parental Preferences Regarding the Sex of Children and the Use of Sex Selection

To obtain a detailed analysis of Canadians' attitudes and views, the Commission undertook the first national survey of preferences regarding the sex of children and attitudes toward sex selection. The survey involved a random selection of more than 500 Canadians who intend to have children. This research is described in our research volume entitled *Prenatal Diagnosis: New and Future Developments.*

The survey revealed that, contrary to what has been found in some other countries, a large majority of Canadians do not prefer children of one sex or the other. Many intervenors in our public hearings assumed that Canadians have a pro-male bias with regard to family composition; we found that this assumption appears to be unfounded with regard to the Canadian population as a whole.

When asked about their preferences with respect to future children, 71 percent of respondents wanted equal numbers of boys and girls, 14 percent wanted more daughters, and 15 percent wanted more sons. For respondents who did not yet have children, the numbers were even more striking — 82 percent wanted an equal number of boys and girls, 10 percent preferred more sons, and 8 percent preferred more daughters.

There has been much speculation about the preferences of prospective parents regarding the sex of their first-born child. Our survey showed that

for respondents who did not yet have children, the majority of respondents had no preference regarding the sex of their first child, while 26 percent preferred their first-born child to be a son and 21 percent preferred their first-born to be a daughter. Moreover, even those who did express a preference rated the importance of this preference as very low (1.8 on a scale of 1 to 5 for those who wanted a boy; 1.7 for those who wanted a girl).

> We feel that identifying sex for the purpose of embryo selection must be prohibited. At present, several studies have shown that embryos of the male sex would often be chosen, and the results are significant at the level of populations. When it is known, for example, that people the world over often prefer the first child to be a boy, we must see to what extent couples' and parents' social conditioning is now — must be controlled in this regard; there must be measures prohibiting embryo selection by sex. [Translation]
>
> *C. Coderre, Féderation des femmes du Québec, Public Hearings Transcripts, Montreal, Quebec, November 21, 1990.*

In other words, most prospective parents expressed a weak preference for an equal number of sons and daughters, and a few expressed a weak preference about the sex of their first-born child. However, these preferences were generally seen as unimportant, almost trivial. The survey showed that virtually all prospective parents want, and feel strongly about having, at least one child of each sex.

Previous international studies have consistently shown a significant difference between women and men in terms of their preferences regarding the sex of their children. According to most studies from other countries, fathers and mothers both express a pro-son bias, although the fathers' pro-son bias is usually much stronger. Our survey suggests that results of these studies cannot be generalized to Canada.

Most prospective parents expressed a weak preference for an equal number of sons and daughters, and a few expressed a weak preference about the sex of their first-born child. However, these preferences were generally seen as unimportant, almost trivial. The survey showed that virtually all prospective parents want, and feel strongly about having, at least one child of each sex.

The attitudes of women respondents in our survey were almost perfectly sex-neutral — the average woman respondent wanted an equal number of boys and girls and had no preference regarding the sex of the first child. Male respondents did indicate a small pro-son bias: the average male respondent placed more importance on having at least one son than on having at least one daughter and on having a boy as the first child. However, the survey showed that each of these biases is slight, and it is clear that for men, as for women,

biases in favour of either sex are trivial compared to the value of having at least one child of each sex.

Previous surveys of parental preferences have often assumed that people who express a preference regarding the number or order of sons and daughters would be likely to use sex selection techniques. We wanted to know whether this is the case. The likelihood of actually using sex selection techniques depends primarily on the importance people attach to their preference. As these preferences were often described as unimportant in our survey, it seems that few people would actually make use of sex selection techniques, particularly if they involve drawbacks such as moral conflicts, cost, intrusiveness, inconvenience, or delay.

This was borne out by the way respondents in our survey described their personal willingness to use sex selection techniques. None of the respondents would use sex-selective abortion if it was to be their first child. Fewer than 4 percent could imagine any circumstance in which they would use PND and abortion to avoid having a child of the undesired sex. Those few who would consider terminating the pregnancy would do so only if they already had one child or more of the same sex, and the fetus was also of that sex. Finally, this minority who would consider sex-selective abortion would do so only if the results of PND were available before the twelfth week of pregnancy (which is currently not the case). Thus, it is clear that very few Canadians would be prepared to contemplate a second-trimester abortion for sex-selective reasons.

> The solution to sex selection is not to restrict abortion, but to challenge the social and cultural conditions that create these pressures on women to make such a drastic "choice." We have to directly confront and challenge a social structure and culture from which such misogynist values spring.
>
> *Brief to the Commission from the Ontario Coalition for Abortion Clinics, May 1991.*

Canadians were more willing, however, to consider sperm treatment methods and sex-selective insemination. Approximately 21 percent of respondents could imagine some circumstance in which they might use such a technique. However, the survey data indicated that less than 2 percent would use sex-selective insemination for their first child. Somewhere between 6 and 9 percent of respondents said they would use sex-selective insemination either to have a girl after having one or more boys, or to have a boy after one or more girls. These situations — where sex-selective insemination is used with the goal of having at least one child of each sex — are the only circumstances in which a significant number of respondents said they would be willing to use sex-selective insemination.

The survey conducted for the Commission contradicts certain widely held beliefs about the preferences of Canadians with regard to the sex of

their children. Yet the results of other recent surveys of Canadians are consistent. For example, a public opinion survey of 2 722 people across Canada, conducted for the Commission by Decima Research between December 1991 and July 1992, also showed no bias in the preferences of Canadians regarding the sex of their children. Twenty-five percent agreed that it is very important to have at least one male child, while 24 percent agreed that it is very important to have at least one female child. The Decima survey also confirmed the overwhelming opposition in Canada to the use of sex-selective abortion. Only 2 percent of respondents approved of the termination of a pregnancy because the "sex of the fetus is not what the parents had hoped for," while 92 percent disapproved and 6 percent expressed no opinion.

The survey conducted for the Commission contradicts certain widely held beliefs about the preferences of Canadians with regard to the sex of their children. Yet the results of other recent surveys of Canadians are consistent.

It should be remembered, however, that answers to hypothetical questions on surveys may not be the same as actual behaviour. This is particularly the case if the technology were to be easily available and publicly countenanced.

Prenatal Diagnosis of Fetal Sex and Sex-Selective Abortion

The diagnostic techniques that constitute the core of PND — amniocentesis, chorionic villus sampling, and targeted ultrasound — are capable of providing a great deal of information about the fetus, including its sex. This has made it possible, in principle, for parents to discover the sex of the fetus and to terminate the pregnancy if they had hoped for a child of the other sex. In this section, we discuss the current regulations regarding the identification of fetal sex through PND and the issues it raises.

Current Situation

Intervenors at our public hearings expressed concern that prenatal testing to determine fetal sex for non-medical reasons is being done routinely at genetics centres. Our research shows that this is not the case. The joint guidelines of the Canadian College of Medical Geneticists and the Society of Obstetricians and Gynaecologists of Canada (CCMG/SOGC) state clearly that "Determination of fetal sex for nonmedical reasons, using either invasive or noninvasive means, is not considered to be appropriate."[2] The

data obtained from our survey of genetics centres across the country showed that these guidelines are being adhered to.

The reason for this is straightforward: a prospective parent's desire to know the sex of the fetus is not a medical reason for providing access to PND, since sex is not a disease. As discussed in Chapter 26, the rationale for the PND system in Canada is to help couples at higher risk of having a child with a serious genetic disease or congenital disorder; identifying fetal sex to satisfy parental preferences falls entirely outside this approach to PND.

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The Commission's research showed that women are sometimes referred to genetics centres by family physicians or obstetricians for prenatal testing to determine fetal sex for non-medical purposes. However, such referrals are rare and are strongly discouraged by the genetics centres. Women referred on this basis would typically be counselled by staff of the genetics centre but would not be offered PND testing. A survey conducted for the Commission found that genetics centres counselled 14 women in 1990 whose reason for requesting testing was sex selection — six in Quebec, five in British Columbia, and three in Ontario. In all but one case, which involved unusual circumstances, the centre refused to provide testing.

Our survey also showed that some centres receive inquiries from women by telephone regarding sex-selective abortion. These callers were rarely seen for counselling, although some centres would, if asked, provide the telephone numbers of U.S. programs that provide prenatal testing to determine fetal sex.

In short, there are few explicit referrals or requests for prenatal testing to determine fetal sex for non-medical reasons in Canada. Some women may indeed prefer to have a girl or a boy, quite apart from any socially generated pressure. In such situations, however, the social harm of providing testing is felt to outweigh the woman's or couple's preference, and the centres consider it reasonable to limit the woman's autonomy; these requests are therefore refused under CCMG/SOGC guidelines.

However, if women do have a valid medical indication for testing (for example, on the basis of their age or family history) and undergo the procedure, they will often be informed about the sex of the fetus at the same time as they are told about the presence or absence of a disorder or anomaly. The sex of the fetus is currently included in the laboratory report of test results sent to the genetics counsellor caring for the woman. This information is included even if it is not relevant to the genetic disorder being tested for, and generally it is made available to patients who request

it. Some genetics counsellors in Canada reveal fetal sex routinely, while others reveal it only if the woman or couple ask specifically for that information.

The fact that fetal sex is often disclosed to patients who have been tested for a valid medical indication creates the possibility that someone who wanted to have a child of one sex could gain access to PND for this purpose, provided they met the medical indications. Testing might be warranted for medical reasons, yet the real reason for seeking testing might be to discover the sex of the fetus; for example, a 36-year-old woman who is eligible for PND because of her age might actually want testing to discover the sex of the fetus, not because of the risk of a chromosomal disorder.

> Genetic manipulation opens the door to control over embryo selection and quality. Here again, the long-term effect can be disastrous and this manipulation can have an effect on the genetic heritage. If many parents chose to have boys, for example, the result could be real demographic unbalance. [Translation]
>
> *Brief to the Commission from le Comité "Vieillir au féminin," de l'Université du troisième âge de l'Université de Moncton, January 18, 1991.*

Genetics centres are conscious of this potential for misuse of testing and do exercise control over the availability of testing, but there is no way to prevent such misuse entirely. Requests for PND that are intended to determine the sex of the fetus rather than disorders are difficult to identify; geneticists told the Commission that these probably occur in a few cases, but there is no evidence that the phenomenon is widespread. Indeed, as we discussed earlier, our public opinion surveys showed that the number of Canadians who would consider a second-trimester abortion for sex-selective reasons is very small indeed.

Despite the existence of professional guidelines discouraging prenatal testing to determine fetal sex for non-medical reasons, some practitioners in the PND community are ambivalent about the practice.[3] To determine how Canadian geneticists view this practice, the Commission conducted its own survey of the attitudes of 200 genetics counsellors in Canada. Half of this group were asked whether they approved of PND to determine sex for non-medical reasons. Only 2 percent of respondents personally approved of PND to determine fetal sex for non-medical reasons. However, a significant minority would attempt to accommodate a request for such testing, despite personal disapproval. The survey showed that 20 percent of the geneticists surveyed would recommend that their centre provide PND to determine fetal sex (if it were allowed) if a couple requested it, and 41 percent would be willing to give the couple the name of another centre that would do the test (see research volume, *Current Practice of Prenatal Diagnosis in Canada*).

Willingness to provide PND to determine fetal sex (if it were allowed) increased when the details of a hypothetical case were provided. The other half of the group of genetics counsellors was asked how they would respond to a request for PND to determine the sex of the fetus from a pregnant woman from a culture where the preference for sons is strong. In the hypothetical situation described, the woman already has three daughters, and her husband has told her he will send her back to their country of origin without her children if she has another daughter.

Under such circumstances, 14 percent of Canadian geneticists said they personally approved of providing the test; 26 percent would recommend that their centre provide the test; and 55 percent would refer the woman to another centre if their own centre would not provide it. On the other hand, many geneticists recognize that threats of divorce or abortion should not always be taken at face value. One recent study found that most geneticists view such threats as a bluff to gain access to prenatal testing for sex selection reasons.[4]

These findings are consistent with other information about the attitudes of Canadian medical geneticists. A minority would provide prenatal diagnosis to determine the sex of the fetus, particularly in difficult circumstances. For example, a 1985 survey showed that 30 percent of doctoral-level geneticists in Canada would perform PND for a couple with four daughters who wanted a son and who would abort a female fetus, and a further 17 percent would offer referral in this situation to another centre that offered the test.

The Commission's surveys showed that only 4 percent would consider sex-selective abortion under any circumstances, and then only if the abortion could be performed in the first trimester. Since information about the sex of the fetus is not currently available before 10 to 12 weeks' gestation, there is every reason to believe that the number of sex-selective abortions in Canada is very low indeed.

Despite the existence of clear professional guidelines, the evidence suggests that a determined couple can gain access to the PND system to acquire information about the sex of the fetus, and that some referring physicians and geneticists would be willing to help such a couple, or at least would not obstruct them.

There is no reason to think, however, that this is a frequent occurrence in Canada. On the contrary, the Commission's surveys showed that only 4 percent would consider sex-selective abortion under any circumstances, and then only if the abortion could be performed in the first trimester. Since information about the sex of the fetus is not currently available before 10 to 12 weeks' gestation, there is every reason to believe that the number of sex-selective abortions in Canada is very low indeed.

Future developments in PND, however, may make information about the sex of the fetus more easily available. Ultrasound is already a widely

used diagnostic technique, and future technical improvements may increase its capacity to reveal the sex of the fetus earlier in pregnancy. Similarly, research into the testing of fetal cells in the pregnant woman's blood may one day yield a reliable and non-invasive way of revealing fetal sex early in pregnancy. The relative simplicity of blood tests, coupled with the possibility of a first-trimester abortion, might reduce the existing barriers to sex-selective abortions. Moreover, taking blood or providing ultrasound — unlike chorionic villus sampling and amniocentesis — can in principle be performed more widely in the medical community rather than solely at specialized genetics centres. The existing CCMG/SOGC guidelines relate to activities at genetics centres and would therefore be inadequate to prevent misuse of these techniques. This suggests that guidelines covering these more broadly based activities would be needed if we determine that PND for sex selection should continue not to be available.

Issues and Recommendations

The Commission's public hearings and survey research revealed an overwhelming consensus against the use of PND and sex-selective abortion. More than 90 percent of those surveyed found it unacceptable to abort a fetus because the parents wanted a child of the opposite sex. Commissioners share this view for several reasons. First, sex-selective abortion offends the principle of respect for human life and dignity because it entails the deliberate termination of a pregnancy, for reasons related only to the sex of the fetus, at a stage when it is likely that the pregnancy would have resulted in a live birth. Our perceptions of the value of human life cannot help but be altered when a potential life at this stage of development is ended intentionally for no reason other than the sex of the fetus. Whether the procedure is used to select male or female fetuses — and even if it were used in a gender-neutral way — the devaluation of and disrespect for human life and dignity inherent in the practice make it morally unacceptable and ethically unjustifiable.

Our perceptions of the value of human life cannot help but be altered when a potential life at this stage of development is ended intentionally for no reason other than the sex of the fetus. Whether the procedure is used to select male or female fetuses — and even if it were used in a gender-neutral way — the devaluation of and disrespect for human life and dignity inherent in the practice make it morally unacceptable and ethically unjustifiable.

In addition, the use of PND to determine fetal sex contradicts the very purpose and role of these procedures within the health care system — namely, to determine whether serious genetic diseases or congenital anomalies are present. Sex is not a disease, so the sex of the fetus is not

medically relevant except in cases where a disease or anomaly is sex-linked. Acceptance of PND to determine fetal sex for non-medical reasons is contrary to the underpinnings of the PND system in Canada — the diagnosis and prevention of serious and untreatable genetic disease. Some are concerned that allowing sex-selective abortion could lead to easier acceptance of selective abortion on other grounds, such as height or skin colour, if this ever became feasible.

We believe it is important that the PND system be used only for the detection of serious genetic and congenital anomalies. We discussed why PND should not be used to test for trivial disorders in Chapter 26 — such use reflects inappropriate views of diversity, of the respect owed to human life, and of parenthood, and it violates the principle of appropriate use of resources, since it fulfils no medical need. Those arguments apply here with equal force.

Moreover, using PND in support of sex-selective abortion for non-medical reasons could violate principles of sexual equality. Indeed, some commentators have argued that sex-selective abortion for non-medical reasons could amount to wrongful discrimination under human rights law and the *Canadian Charter of Rights and Freedoms* if the practice is used in a way that reflects and perpetuates the subordinate status of women as a group in Canadian society. As the Canadian Research Institute for the Advancement of Women argued in their submission to the Commission,

> The philosophy behind sex selection is questionable in itself: what is more sexist than choosing a child purely on the basis of its sex? By increasing our emphasis on the importance of sexual difference, we can only create more rigid gender roles for men and women. *(Brief to the Commission from the Canadian Research Institute for the Advancement of Women, September 20, 1990.)*

We are aware that the preference for sons is strong among some Canadians, and that members of some ethnocultural groups in Canada value sons more highly. Indeed, those who make a business of providing diagnosis of fetal sex often justify their actions in terms of "respecting cultural minorities." It is important, however, to look more carefully at the nature and source of these cultural differences.

The preference for sons is strong in some countries, and PND and sex-selective abortion are used in those countries to abort female offspring. In India, for example, most PND procedures are performed for sex selection rather than the detection of genetic or congenital disorders (see research volume, *Prenatal Diagnosis: New and Future Developments*).

Some immigrants from these and other societies with a strong cultural tradition of preferring sons may carry these cultural values to Canada. However, as the Immigrant and Visible Minority Women of British Columbia emphasized during the Commission's public hearings, culture is neither monolithic nor static. On the contrary, traditional practices are often questioned and revised by the members of the culture, and culture

generally is in a constant state of evolution. Many people in these countries have not discriminated against females in these ways and are in fact working actively to counter such tendencies.

The preference for sons is strong in some countries, and PND and sex-selective abortion are used in those countries to abort female offspring. In India, for example, most PND procedures are performed for sex selection rather than the detection of genetic or congenital disorders.

Moreover, many of the social and economic reasons underlying a cultural preference for sons in other countries do not apply in Canada. The economic and social reasons for preferring sons include, for example, the fact that a son is responsible for caring for parents in their old age; that a daughter seldom has the earning power to support aging parents; and that daughters represent a considerable economic burden in come countries because of the practice of paying dowries. However, selective abortion to avoid female offspring cannot be justified by such factors in Canada; rather, in this country it would be a matter of satisfying a parent's preference for sons — a preference that would perpetuate the devaluation of women.

We are aware that the preference for sons is nonetheless strong in some sectors of society. As a result, some women may still face considerable pressure to have sons. It has been argued by some that providing PND to determine fetal sex would help these women cope with family pressure to have sons.

To allow couples to identify and abort female fetuses because of a cultural preference for sons would devalue all women and jeopardize the achievement of sexual equality in this country.

As we have seen, a significant number of geneticists in Canada said that they believe it appropriate to provide PND in the case of a woman whose husband is threatening to break up the family if she does not produce a son. It is understandable that genetics counsellors would feel sympathy for patients in such difficult circumstances. As well as our concern for the individual woman trying to satisfy family or cultural demands, we must also take into account, however, justice for all women. The provision of PND to determine fetal sex might ease the plight of one woman temporarily. However, to allow couples to identify and abort female fetuses because of a cultural preference for sons would devalue all women and jeopardize the achievement of sexual equality in this country.

Providing PND to determine fetal sex in this situation does not solve the problem that put the woman, and other women in her community, in this difficult position in the first place. On the contrary, it perpetuates and reinforces the problem — it ultimately harms the status of women in her

community and, indeed, in Canada as a whole. Moreover, she herself will continue to be regarded and valued for her ability to produce sons.

It is therefore shortsighted to accommodate a woman's request for PND and sex-selective abortion of female fetuses in order to alleviate family pressures on her. If the reason for the preference for a son is the existence of sexist pressures within the community, then fulfilling such a request will provide little long-term benefit for the woman. Indeed, reinforcing these pressures will only harm the woman later on, as well as her sisters, daughters, and granddaughters. As one analyst has commented,

> Arguments that sex selection will lead to a better quality of life for families, children, or women are comprehensible only in the context of a sexist society that gives preferential treatment to one sex, usually the male. *(D. Wertz, "Prenatal Diagnosis and Society," in Research Volumes of the Commission, 1993.)*

It is important, therefore, to ensure that the ideal of respecting cultural differences is not used to rationalize coercion against vulnerable members of the group or the oppression or subordination of women generally. Respect for cultural differences is a valuable, indeed defining, characteristic of Canada. However, respect for cultural diversity must be situated within the context of Canada's fundamental principles, including its constitutional and international commitments to the protection and promotion of human rights. These principles include respect for sexual equality and the protection of the vulnerable.

This view is supported by the Canadian Medical Association in its discussion of sex selection:

> Nor is the Association persuaded that the mere fact that a particular outlook is culturally entrenched establishes the ethical acceptability of that outlook. The disenfranchisement of women in some cultures is a case in point ... Another way of putting that is to say that Canada insists on maintaining the pre-eminence of certain fundamental principles as a condition of membership within Canadian society itself.[5]

The Commission therefore rejects the use of PND with sex-selective abortion as inconsistent with our guiding principles — respect for human life and dignity, sexual equality, protection of the vulnerable, and the balancing of individual and collective interests. Finally, sex selection for non-medical purposes is also a misuse of collective resources. To allow allocation of scarce health care resources to provide PND with sex-selective abortion would clearly be unethical. This applies even where those services would be purchased in a private market because, as explained elsewhere in this report, such services virtually always entail significant costs to the public purse as well.

For all these reasons, Commissioners reject the use of PND with sex-selective abortion. It violates the Commission's ethical guidelines and distorts the underlying premises of the PND system. Commissioners are strongly of the view that PND to determine sex and sex-selective abortion

have no role in the health care system.

> The Commission rejects the use of PND with sex-selective abortion as inconsistent with our guiding principles — respect for human life and dignity, sexual equality, protection of the vulnerable, and the balancing of individual and collective interests. Finally, sex selection for non-medical purposes is also a misuse of collective resources.

We believe that the existing CCMG/SOGC guideline, which states that fetal sex determination for non-medical reasons is an inappropriate practice, is an important starting point for the regulation of this form of sex selection. Because of this guideline, patients requesting PND to determine fetal sex for non-medical reasons have usually been denied access to the services of genetics centres in Canada. To ensure that the guideline continues to be followed by all genetics centres providing PND, adherence to this guideline should be made a condition of receiving a licence to provide PND services. The Commission therefore

261. Affirms the existing Canadian College of Medical Geneticists/Society of Obstetricians and Gynaecologists of Canada guideline that prenatal diagnosis to determine fetal sex for non-medical reasons not be offered. Adherence to this guideline should be a precondition of securing and maintaining a licence to provide prenatal diagnosis services from the National Reproductive Technologies Commission.

As noted earlier in this chapter, the CCMG/SOGC guidelines may be inadequate to cover future developments in PND, such as ultrasound to identify fetal sex or testing of fetal cells in pregnant women's blood. It is possible for these newer, non-invasive tests to be provided outside licensed genetics centres and hence outside the reach of the CCMG/SOGC and the National Reproductive Technologies Commission. Indeed, private clinics specializing in the use of ultrasound to determine fetal sex already exist in the United States. The possibility exists that private "fetal sexing" clinics could be established in Canada in the future, using ultrasound, blood tests, or other technologies.

We resolutely oppose the establishment of private clinics or physicians' practices providing detection of fetal sex for a fee. To prevent this, we recommend that any clinic or practice providing PND to determine fetal sex be defined as providing a "genetic service" and hence be required to obtain a licence from the National Reproductive Technologies Commission. This will prevent clinics or practitioners from using these newer techniques to determine fetal sex for non-medical reasons, since a condition of licensing

will be adherence to the CCMG/SOGC guideline. The Commission recommends that

> **262. The requirement that all clinics and physicians providing prenatal diagnosis be licensed by the National Reproductive Technologies Commission extend to any clinic or physician providing services aimed at identifying fetal sex (including the use of ultrasound or blood tests on pregnant women). The Commission recommends further that adherence to guidelines prohibiting the use of prenatal diagnosis to determine fetal sex for non-medical reasons be a condition of such licence.**

Disclosure of Fetal Sex After Testing for a Genetic Disease

A more complicated issue concerns the disclosure of fetal sex to patients who have a valid medical reason for undergoing PND. For example, every pregnant woman over 35 years of age has a legitimate entitlement to prenatal testing and could use this entitlement to obtain information about the sex of the fetus. Knowledge about fetal sex may have some influence on abortion decisions among women having PND because of their age, especially if the pregnancy was not intended (see research volume, *Prenatal Diagnosis: New and Future Developments*). There may be cases, for example, where a genetic anomaly not linked to fetal sex is discovered, but information about the sex of the fetus might "tip the balance" in making a decision about termination.

In many cases, the woman prefers not to know the sex of the fetus. However, in cases where the patient does want to know, many geneticists feel ambivalent about whether to provide this information. On one hand, many counsellors believe that knowledge of fetal sex can add to the pleasure parents derive from a pregnancy, helping to personalize the fetus, and thereby strengthening bonding. Also, many geneticists believe, as a general principle, that doctors should disclose all information in the patients' records that the patient requests to know. Anything other than full disclosure is viewed as paternalistic and possibly a violation of the patient's legal right to know information in his or her medical records. On the other hand, many geneticists do not feel comfortable disclosing the sex of the fetus except in cases of a sex-linked disease, because this information is not relevant to the health of the fetus.

It is not clear whether a legal duty to disclose fetal sex exists in either the United States or Canada, as the courts have not yet tackled this question directly. In the United States, some practitioners of PND refuse

to provide information about the sex of otherwise healthy fetuses until the legal ambiguity of this issue is clarified; other practitioners provide full disclosure, to avoid potential legal problems.

In Canada, current practice is to disclose the sex of the fetus if asked. However, it is not clear whether any legal requirement to comply with such a request exists. Generally speaking, patients have a right to the information in their medical records but not to the documents themselves. In the province of Quebec, for example, an individual has a statutory right of access to personal medical information. In other provinces, some of which do not have statutes dealing specifically with access to medical information, the same general principle applies: the individual has a right of access, upon request, to the medical information in his or her medical records.

We strongly support the general principle of full disclosure of medical information in support of informed choice, which is an integral part of the shift away from a paternalistic model of the physician/patient relationship to a partnership model. We do not wish to weaken that principle. The issue, however, is not simply whether patients have a right to the information in their medical records; it is also important to discourage misuse of non-medical information that is revealed by genetic testing.

However, the exact scope of this legal principle is unclear — including its application to the disclosure of non-medical information regarding the sex of the fetus — as there have been relatively few court cases to date. In one province, Manitoba, the PND centre had a policy in the late 1970s of not revealing the sex of the fetus until the twentieth week of gestation. In the early 1980s, in view of increasing human rights activity and legislation, the hospital's legal advisers suggested that this practice should be changed, and that patients probably had a legal right to this information. The current policy in Manitoba, as elsewhere, is to give information on the sex of the fetus if requested. In all centres there must be valid medical indications for having the test in the first place.

We strongly support the general principle of full disclosure of medical information in support of informed choice, which is an integral part of the shift away from a paternalistic model of the physician/patient relationship to a partnership model. We do not wish to weaken that principle. The issue, however, is not simply whether patients have a right to the information in their medical records; it is also important to discourage misuse of non-medical information that is revealed by genetic testing.

We believe, as a general principle, that prenatal testing should not be seen by either physicians or patients as a mechanism simply for identifying the sex of the fetus. If the reason for prenatal testing is to detect disease, then it is the presence or absence of disease that is relevant. Information on the sex of the fetus is not medically relevant — it does not tell the

physician or the patient about the health of the fetus (except in cases of X-linked diseases or diseases that affect one sex more severely than the other). Because this information is not medically relevant, and because it can be misused for sex-selective purposes, we considered the possibility that it should be withheld from the patient. This could be done in various ways.

One possibility would be to amend the legislation governing access to medical records and to create an exception in the case of information regarding the sex of the fetus. We believe that this would create a dangerous precedent, and that even a well-crafted exception could be misused. Since our studies have shown that very few Canadian women would consider undergoing sex-selective abortion, the risks of limiting the right of patients to their records seem greater than the risk that the information will be misused.

Another possibility would be to allow access to information about the sex of the fetus, but to make that information more difficult to get. For example, the laboratories that perform prenatal testing could be instructed not to include information about the sex of the fetus in the report they forward to the genetics counsellor or referring physician (except where medically relevant). The laboratory would identify and record the sex of the fetus — this is part of the standard testing procedure and is inherent in the notation system used to record chromosomal findings; it is also used as a quality control measure (the sex identified by testing can be compared with the sex of the child born). However, the laboratory would not forward that information to the genetics centre. The counsellor or physician would then be able to inform the patient whether a genetic disease was present or absent, but would not be able to inform her of the sex of the fetus. If the patient was determined to find out the sex of the fetus, she could contact the laboratory directly, which would disclose the information to her. To do this would require a certain amount of effort and inconvenience on the woman's part — it would make access to information about fetal sex more difficult, but not impossible.

There is some merit in this idea. It would reinforce the idea that the purpose of PND is to detect disease, not to satisfy parental preferences about the sex of their children. And since the capacity of genetic testing to uncover information about the fetus will likely expand in the future, it would be important to establish the principle that the only legitimate purpose of genetic testing is to diagnose health-related information. Since this would constitute a change of practice, it would be important to tell patients that prenatal test information would not include the sex of the fetus, unless it is medically relevant. Patients would then be tested knowing that fetal sex would not be disclosed. If patients were genuinely

It would be important to establish the principle that the only legitimate purpose of genetic testing is to diagnose health-related information.

concerned about detecting fetal disorders, rather than sex selection, this change in policy would not affect their wish to undergo PND for valid medical reasons.

Although we considered this proposal seriously, we concluded that it was not practical. Laboratories would receive calls from women who were simply curious about the sex of the fetus but who would have no intention of using that information prenatally, as well as from women who were determined to know the sex of the fetus and who might be inclined to have a sex-selective abortion. This would shift responsibility from physicians to the laboratories and increase their costs without preventing some potential misuse of this information; laboratories are not set up to deal with these sorts of requests — they rarely deal directly with the public and do not have the personnel and financial resources to verify and respond to such requests.

There is no simple and foolproof way of guaranteeing that couples do not misuse information regarding the sex of the fetus. However, given the evidence that very few Canadians are prepared to contemplate sex-selective abortion, particularly in the second or third trimester, we believe that the danger of misuse is quite low. We are willing to put our trust in the humanity and good judgement of Canadian women and couples.

Yet we cannot ignore the possibility that inappropriate pressures may be applied to women within some segments of Canadian society. Nor can we ignore the possibility that future developments in PND testing — which may be capable of providing information about fetal sex earlier in pregnancy — could lead more Canadians to consider sex-selective abortion.

Clearly, this is an issue that deserves further study and continuing monitoring. We believe that the Prenatal Diagnosis and Genetics Sub-Committee of the National Reproductive Technologies Commission should actively monitor the situation in Canada for evidence that information regarding the sex of the fetus is being misused. If such evidence is found, the National Commission should consider whether a legal mechanism should be put in place to limit the patients' right to access to information in their medical records. The Commission recommends that

263. The guidelines established by the National Reproductive Technologies Commission for licensed prenatal diagnosis clinics indicate that information on the sex of the fetus be given to the woman or referring practitioner only upon direct request. Patients should be informed prior to testing that the usual practice is to reveal this information only if it is medically relevant to the health of the fetus.

Regulating the disclosure of fetal sex during routine ultrasound to monitor pregnancy is even more difficult. Particularly when ultrasound is used later in pregnancy, the practitioner (or even the patient) may become aware of the sex of the fetus as the image appears on the ultrasound screen. Because the practitioner/patient interaction is not mediated by laboratory testing, the possibility of disclosure of fetal sex is greater.

Although it may rarely be impossible to avoid the inadvertent disclosure of fetal sex during routine ultrasound examinations, we think it is important to ensure that appropriate guidelines and standards of practice exist for physicians providing prenatal ultrasound — whether it is an obstetrician, a radiologist, or a general practitioner — stating that the sex of the fetus should not be evaluated intentionally or disclosed intentionally to the patient before the third trimester. The current standards of the Canadian Association of Radiologists pertaining to ultrasonography practice do not address the issues of fetal sex determination or disclosure of fetal sex.

The adoption of guidelines would prevent practitioners from intentionally offering fetal sex detection and acquiring patients on this basis. Equally important, such guidelines would also support practitioners who do not wish to disclose fetal sex to patients earlier in pregnancy, but who find it difficult to turn down patients' direct requests.

Adoption of such guidelines would prevent practitioners from intentionally offering fetal sex detection and acquiring patients on this basis. Equally important, such guidelines would also support practitioners who do not wish to disclose fetal sex to patients earlier in pregnancy, but who find it difficult to turn down patients' direct requests. Patients know that practitioners using ultrasound often can tell the sex of the fetus and may ask for this information out of curiosity. It is sometimes difficult for practitioners not to comply with such requests, particularly in close physician/patient relationships, unless they have recourse to an explicit professional guideline or standard that fetal sex is not to be examined for and disclosed.

It is highly unlikely that a woman would request or obtain a sex-selective abortion during the third trimester, however, so there is little reason not to disclose fetal sex if ultrasound at this stage of pregnancy incidentally reveals this information. We do not believe that the use of ultrasound at any stage simply to detect sex is justified; nevertheless, because knowledge of the sex of the fetus is of interest to families and can help promote bonding between the woman and fetus, we believe disclosing the sex of the fetus, if it is observed incidentally during the third trimester

and requested by the woman, should be allowed. The Commission recommends that

264. The Society of Obstetricians and Gynaecologists of Canada, the Canadian Association of Radiologists, and the College of Family Physicians of Canada review practice guidelines to ensure that practitioners using prenatal ultrasound do not perform ultrasound for sex identification (except where medically indicated) and do not deliberately examine for or volunteer information on fetal sex, except for medical reasons, and upon request, prior to the third trimester.

Sex-Selective Zygote Transfer

The second currently known method of sex selection is sex-selective zygote transfer. This is an invasive, expensive, and technologically complicated procedure involving both *in vitro* fertilization and preimplantation diagnosis.

The woman's eggs are retrieved through laparoscopy, the eggs are fertilized *in vitro* with her partner's (or a donor's) sperm, and the sex of the resulting zygotes is determined through preimplantation diagnosis, which can detect whether the zygote has an XX or an XY chromosome complement. Only zygotes of the desired sex are then transferred to the woman's uterus. Although this technique is different in important respects from the use of PND and sex-selective abortion, Commissioners believe that it, too, is unethical and medically inappropriate, for many of the same reasons.

First, sex-selective zygote transfer is not an appropriate use of resources. It uses a sophisticated, expensive, stressful, and inefficient diagnostic procedure for what is clearly a non-therapeutic objective. It is difficult to imagine many couples wishing to follow this route simply to have a child of the preferred sex. Both the IVF procedure and the preimplantation diagnosis test are expensive, adding up to thousands of dollars per cycle. Similarly, using preimplantation diagnosis to detect the sex of the zygote for non-medical reasons distorts the role of preimplantation diagnosis, which is to identify the presence of severe genetic diseases at a very early stage in the development of the zygote.

Sex-selective preimplantation diagnosis also carries risks for the woman involved, from the use of ovulation induction drugs to the egg

retrieval procedure. Subjecting women to medical procedures involving risk is unethical except where there is a clear therapeutic purpose — that is, to treat disease and promote health. In actual practice, preimplantation diagnosis is likely to be pursued very rarely, because of its intrusive nature and expense.

Use of preimplantation diagnosis to identify zygotes of a particular sex also conflicts with the principle of respect for human life and dignity. As we discuss in Chapter 22, zygotes do not have the same moral status as embryos or fetuses; they do not have a fixed and individuated identity or a central nervous system, and the probability that they will result in a liveborn individual is low — perhaps one in five in those situations where both partners are likely to be fertile. Nonetheless, zygotes are not just human tissue; the potential they embody means that refusing to transfer a zygote solely on the basis of its sex is inconsistent with the respect owed to it.

In the view of Commissioners, these objections are such that any use of preimplantation diagnosis for purposes of non-medical sex selection is not justified and should be prohibited. Since preimplantation diagnosis requires the use of IVF technology, it is currently carried out in IVF clinics. We have concluded that all proposals to use preimplantation diagnosis on zygotes should be approved by the Assisted Conception Sub-Committee of the National Reproductive Technologies Commission. We further recommend that the guidelines covering IVF clinics prohibit the use of preimplantation diagnosis to determine fetal sex for non-medical reasons. Even though it is very unlikely practitioners or couples would be willing to pursue preimplantation diagnosis for this purpose, it is important we reassure Canadians that it is not occurring, by making adherence to these guidelines a condition of licensing by the National Reproductive Technologies Commission. The Commission recommends that

Any use of preimplantation diagnosis for purposes of non-medical sex selection is not justified and should be prohibited.

265. The National Reproductive Technologies Commission guidelines for licensed *in vitro* fertilization clinics prohibit the use of preimplantation diagnosis to determine fetal sex for non-medical reasons. Adherence to these guidelines should be a condition of licensing by the National Reproductive Technologies Commission.

Sex-Selective Insemination

Current Practices

The various methods of trying to influence the sex of a child before conception can be grouped into two categories. First, there are "natural" methods, such as timing of intercourse, altered coital position, alteration of vaginal acidity, and dietary changes to alter the content of cervical secretions. The reliability of these methods is unknown. Some research has tested whether particular timing of intercourse relative to the time of ovulation has an effect on the sex of resulting offspring, but recent studies have generally not confirmed this.[6]

Our focus in this section is on the other group of methods, which involve laboratory treatment of sperm. Several sperm separation methods have been designed in the last 20 years to separate the two kinds of sperm — those carrying the Y chromosome (leading to male offspring) and those carrying the X (leading to female offspring). Taking advantage of presumed differences in density and motility, sperm separation attempts have been performed by electrophoretic, flow fractionation, and cell-sorting techniques. Immunological techniques have also been used in an effort to separate the two kinds of sperm.

It is difficult to assess the effectiveness of these techniques. The results of studies have been inconclusive, and the studies have been criticized for poor follow-up and lack of control groups.[7] However, many reviews of the evidence have come to the same general conclusion: while theoretically possible and clinically feasible, none of these sperm separation techniques has proved very reliable. Some have proved just effective enough to encourage continued research and development and the establishment of commercial clinics offering sex-selective insemination.

The best-known and most widely used technique was developed by an American researcher, Ronald Ericsson, in 1973. It is based on evidence that Y-bearing sperm swim faster than X-bearing sperm. The technique involves washing the sperm and layering it on increasingly thick albumin protein, through which some sperm swim faster. This technique has been used to retrieve sperm samples rich in Y-bearing sperm for assisted insemination. Ericsson claims a 72 percent success rate in producing male children (rather than the usual 52 percent), but this claim has not been verified independently.[8]

Producing X-bearing sperm is more difficult. The slower sperm left over from Ericsson's albumin test cannot be used, because the sample will include a high percentage of abnormal Y-bearing sperm as well as healthy X-bearing sperm. The most promising technique for producing samples rich in X-bearing sperm is a filtration technique developed originally to prepare semen samples with better sperm motility. Researchers discovered incidentally that the method also enriches the proportion of X-bearing

sperm by up to 22 percent. Because isolating X-bearing sperm is more difficult, and because there is some evidence that the use of fertility drugs to induce ovulation may increase the chances of having a girl, drugs such as clomiphene are often used in conjunction with this filtration technique. This also results in an increased frequency (8.5 percent) of twins. Various other combinations of sperm-sorting techniques and ovulation induction drugs have been used in the hope of increasing the likelihood of conceiving a girl. Ericsson claims a 69 percent success rate for couples seeking a girl, although independent confirmation is not available.

The effectiveness of this or any similar sperm separation technique is an open question, as they have not been confirmed independently. What objective data are available suggest that the child is of the desired sex well under 80 percent of the time for both boys and girls, compared to the usual chance of about 50 percent.[9] In the absence of better data, these forms of sex-selective insemination must therefore be seen as experimental, not proven techniques. The procedure is intrusive and may need to be repeated, as any given insemination with treated sperm has a less than 10 percent chance of resulting in a liveborn child. Despite these limitations, it is likely that some sperm separation method will eventually be able to influence the likelihood of having a boy or girl fairly reliably.

The procedure is intrusive and may need to be repeated, as any given insemination with treated sperm has a less than 10 percent chance of resulting in a liveborn child.

Whatever the current effectiveness of sperm separation techniques, entrepreneurs have judged that there is a market for sex-selective insemination. Private clinics have been opened in the United States, the United Kingdom, Canada, and elsewhere to provide this service for a fee. Private clinics are particularly active in the United States, where the Ericsson technique has been franchised to over 50 clinics through a business firm. In the United Kingdom, the establishment of private clinics offering sex-selective insemination has led to the Human Fertility and Embryology Authority's consultation initiative on sex selection. Here in Canada, one sex-selective insemination clinic using the Ericsson technique has been in existence in Toronto since 1987, and a second one recently opened in Toronto. The procedure is not covered by provincial medical insurance plans, and the charge is about $500 per insemination.

Issues and Recommendations

Trying to influence the sex of offspring before conception raises different issues from either sex-selective abortion or sex-selective zygote transfer. For example, sorting sperm does not raise the same issues of respect for human life as aborting a fetus or discarding zygotes because of

their sex. However, the practice does raise important questions regarding both the potential for discriminatory use that would offend sexual equality principles and the appropriate use of resources.

Sexual Equality

For reasons discussed earlier, Commissioners find it unacceptable for sex-selective insemination to be used in a way that undermines or jeopardizes equality — that is, to select first-born sons, to select families with more sons than daughters, or to perpetuate the cultural devaluation of women. There is strong evidence, however, that sex-selective insemination would not likely be used in this way in Canada. The marked preference for boys that may have characterized public opinion in Canada in the past has clearly eroded. Although some parents have a weak preference regarding the sex of their first-born child, fewer than 2 percent of Canadians say they would actually consider using sex-selective insemination to try to satisfy that preference. Instead, the use of sex-selective insemination in this country is more likely to be directed to enabling couples to have at least one child of each sex in their family. As we saw earlier in this chapter, this is very important to most Canadians — indeed, it is the only desire regarding the sex of children that Canadians feel strongly about and are willing to take steps to fulfil. This is still only a minority, however — 8 percent of couples with two sons would consider sex-selective insemination to have a girl, rather than continuing to have children in the hope that one would be a girl. A similar number of couples with two daughters would consider using sex-selective insemination to have a son.

Our survey of parental preferences therefore suggests that sex-selective insemination, if used, would be used in a gender-neutral way by most people in this country. This is consistent with the experience of Ericsson's clinics in the United States. According to Ericsson, a survey of 7 000 couples at his clinics revealed that less than 1 percent wanted to use the service for their first-born. Instead, couples used it for their last child, to have a child of the sex they did not already have. In fact, Ericsson says that 51 percent of requests at his clinics are for girls.[10] But the technique for conceiving females involves taking fertility drugs and is therefore more complicated and expensive; more services are in fact provided to try to produce boys.

The use of sex-selective insemination in this country is more likely to be directed to enabling couples to have at least one child of each sex in their family. As we saw earlier in this chapter, this is very important to most Canadians — indeed, it is the only desire regarding the sex of children that Canadians feel strongly about and are willing to take steps to fulfil.

A 1989 study by Nan Chico, a professor of sociology in California, found that couples who contacted Ericsson's clinics for more information about sex-selective insemination already had an average of two children of the same sex and were seeking "mixed families." Her study of 2 505 letters to Ericsson's clinics found that those desiring a first-born male accounted for 1.4 percent of the total, and that there was nearly a 50:50 balance in requests for boys and girls.[11]

There are important differences between the male and female experience, and the desire to have the distinctive relationships that come from having sons and from having daughters is not, in and of itself, evidence of sexism.

We believe that the use of sex-selective insemination by couples to have a child of the sex they do not already have is not necessarily sex-discriminatory. As the CFAS/SOCG note, this reason for seeking sex-selective insemination "implies that parents are expressing less of a gender preference *per se* and more of a desire to enhance family development with the sort of unique relationship that only a brother/sister or mother-daughter/father-son interaction can afford."[12] Boys and girls are different, and the widespread desire to have at least one child of each sex reflects the fact that parents find joy and delight in these differences. The desire to have a son after two daughters, or a daughter after two sons, is a natural one that reflects a desire to enjoy children of both sexes, not a bias in favour of one sex or a devaluation of the other.

Of course, it is possible that some couples could be motivated by sexist stereotypes, such as the wish to pass on a family business to a son rather than a daughter. We recognize that such stereotypes exist in society. But the existence of sexism in our society is not grounds to conclude that this technology would necessarily be used for sexist reasons. There are important differences between the male and female experience, and the desire to have the distinctive relationships that come from having sons and from having daughters is not, in and of itself, evidence of sexism.

Another aspect to be taken into account is whether sex-selective insemination would significantly affect the overall sex ratio in society at large. If many couples used sex-selective insemination to select boys, while few couples used it to select girls, the resulting inequality in the sex ratio in the general population could have serious social repercussions. Our research suggests, however, that there is little danger of this occurring, for several reasons.

First, our surveys showed no significant pro-son (or pro-daughter) bias in the population; therefore, sex-selective insemination is likely to leave the sex ratio unchanged. Second, even if there were a pro-son or pro-daughter bias in parental preferences, this is unlikely to have a significant impact on the sex ratio, because relatively few couples would actually act on their preference. As we have shown, preferences about the sex of children tend

generally to be weak. Few couples attach enough importance to it to undergo substantial inconvenience, expense, or risk to try to increase the chance of having a child of the desired sex. Undergoing sex-selective insemination is intrusive, unproven, expensive, and tedious. A sperm sample must be delivered to the clinic, the woman must time her visit to the clinic to coincide with ovulation, and the couple must abstain from intercourse during this time. The process usually has to be repeated several times, since establishing a pregnancy usually takes several cycles.

> The kinds of sex selection methods that significant numbers of people would be willing to use are ineffective at present, while those that are effective are unacceptable to all but a handful of people. There is no reason to believe this will change in the foreseeable future.
>
> *M. Thomas, "Preference for the Sex of One's Children and the Prospective Use of Sex Selection," in Research Volumes of the Commission, 1993.*

It is not surprising, therefore, that sex-selective insemination is not very popular even in countries where it is widely available. One other possibility should be considered, however. As discussed in our research volume entitled *Prenatal Diagnosis: New and Future Developments*, if the sperm separation method for selecting one sex were much more reliable and easier to use than that for the other sex, then an imbalance in the sex ratio could occur because that method would be used more. The possibility that differences in the techniques for selecting boys and girls could alter the sex ratio should not be ignored. On the other hand, given that only a relatively small number of people appear to be willing to use sex-selective insemination, the potential for a sudden change in the ratio is very small.

We believe, therefore, that certain uses of sex-selective insemination are not inherently inconsistent with the principle of sexual equality and may be gender-neutral in their motivations and implications. Nonetheless, other aspects must also be taken into account in coming to our recommendations. First, there are segments within the Canadian population where males are valued more highly, putting pressure on women to undergo such techniques for discriminatory, sexist reasons. This would have to be protected against if sex-selective insemination were allowed. We would also need to ensure that it was not used in a gender-biased way in terms of the order and number of sons (or daughters) in each family.

Some have proposed that these problems could be overcome by establishing a system to limit access to couples who already had at least two children of one sex and none of the other and who wanted to use sex-selective insemination to have a child of the other sex. This would ensure that sex-selective insemination could not be used to have a first-born son,

or to have more sons than daughters, but only to have at least one child of each sex.

We gave this proposal very serious consideration. However, we rejected it for several reasons. Although Commissioners recognize and sympathize with the strong desire of many couples to have at least one child of each sex, we do not believe that society should lend any substance to the notion that families in which all the children are of the same sex are less than ideal. Society should not promote the view that a family of all girls — or all boys — fails to meet some arbitrary standard of what constitutes the ideal family. The availability of even tightly controlled sex selection would signal approval of it, which may in turn promote change in the current attitudes of Canadians that the sex of a child is of little importance. Moreover, using sex-selective insemination could have a detrimental effect not only on a child of the opposite sex born despite the procedure, but on earlier children. If a couple with two daughters used sex-selective insemination to have a boy, the girls could well interpret this as reflecting on their adequacy in their parents' eyes, as could a girl born after a procedure that did not "work."

Certain uses of sex-selective insemination are not inherently inconsistent with the principle of sexual equality and may be gender-neutral in their motivations and implications. Nonetheless, other aspects must also be taken into account in coming to our recommendations ... We do not believe that society should lend any substance to the notion that families in which all the children are of the same sex are less than ideal ... Moreover, using sex-selective insemination could have a detrimental effect not only on a child of the opposite sex born despite the procedure, but on earlier children.

Appropriate Use of Resources

In addition to all the caveats just enumerated, the principle of appropriate use of resources must be considered.

Sex-selective insemination is not a medically necessary service. It is not intended to treat or avoid disease or to promote human health. In addition, having a child of a particular sex is not so important in people's lives as to justify the use of public resources to achieve it. Helping couples who are infertile or helping couples at high risk of passing on a genetic disorder to have a healthy child are legitimate aims on which to spend public resources, whereas satisfying parental wishes to have children of each sex is not.

It might seem that allowing private clinics to offer sex-selective insemination for a fee would not constitute an inappropriate use of public resources, since it would then be consumers, not the provincial insurance plan, who would pay for the service. However, as we saw in Chapter 20, the activities of private clinics often impose costs on the public health care

system. In the case of private IVF clinics, these costs are substantial. In the case of sex-selective insemination, they would be less significant. Nevertheless, these clinics could generate such costs; for example, the initial medical examination of clients and laboratory testing of the male partner's sperm (before sperm-sorting techniques are used) could be charged to the public health insurance plan. Similarly, in the case of techniques aimed at conceiving a girl, the use of fertility-enhancing drugs could be charged to provincial drug plans or to private supplementary health insurance (although most provinces do not cover drugs such as clomiphene for any purpose).

More important in this case, however, is that ensuring that sex-selective insemination was being provided in private clinics in a safe and ethical way would require a strict system of licensing and monitoring. This alone would present significant costs to the public purse, and Commissioners would be strongly opposed to the use of scarce public resources for this purpose. Although a scheme might be devised to recoup some of these costs through licensing fees, given the potential harms we identified earlier, we believe that there is no legitimate reason to allow these services to be provided at all.

Similarly, unproven sex-selective insemination techniques should not be defined as "medical research." To define these techniques as medical research implies that they should be funded out of medical research budgets and that, if their efficacy becomes proven, these techniques should be considered for funding as medical services within the public health care system. The Commission believes, however, that it would be a serious distortion of the health care system, and an inappropriate use of public funds, to view sex-selective insemination as a medical service.

In summary, we believe that sex-selective insemination for non-medical reasons should not be allowed, for the following reasons:

- It would constitute an inappropriate use of public resources to provide this service. Even if it is provided in private clinics for a fee, the only way to ensure it is not used in a sexist way (for example, as a result of pressure on women to use it to have male children) would entail significant public resources (for example, monitoring, data collection, and analysis), which would constitute an inappropriate use of resources.
- Although people who choose to use the technique might well do so in ways that are not inherently sexist (for example, to have a child of each sex), its availability would nonetheless reinforce the message that the composition of a family, in terms of the sex of the children, is important.
- Even if use of the technique were restricted to situations where the couple was trying to have a girl after two boys (or vice versa), the existing children could feel that their own sex is not valued as much as the other, as could a child born after a procedure that did not "work."

- The technique is unproven, and, although it could be verified and improved by additional research, to spend research dollars to prove that it works would be inappropriate given other priorities for medical research.

Private clinics offering sex-selective insemination currently fall outside systems of accountability such as ethical review boards and professional organizations. In Chapter 19 we recommended that any clinic or physician offering assisted insemination with sperm treated with the aim of separating X- and Y-bearing sperm be required to obtain a licence from the National Reproductive Technologies Commission; we also outlined the conditions of licence for offering assisted conception services. The Commission recommends further that

266. As a condition of licence for offering assisted conception services, sperm treated with the aim of separating X- and Y-bearing sperm be provided only for individuals who have a clear medical indication (for example, X-linked disease). In such cases, there should be
(a) disclosure of objective information to patients about the lack of reliability of any technique used; and
(b) record keeping and annual reporting to the National Reproductive Technologies Commission with respect to the sex of the children resulting from insemination following such sperm treatment.

Conclusion

We have looked at three techniques that could be used to influence or select the sex of children: prenatal diagnosis with sex-selective abortion; preimplantation diagnosis with sex-selective zygote transfer; and sperm treatment with sex-selective insemination. Each of the three techniques raises different ethical and social issues. At the same time, all three techniques raise concerns related to fundamental values and the kind of society Canadians want to live in. For example, groups representing women from minority communities were concerned about the use of reproductive technologies, particularly sex selection, to exploit stereotypical attitudes associated with race or culture. Commissioners took these concerns very seriously in coming to our recommendations. We support

the efforts of these groups to resist pressures for sex selection within their communities and to promote wider adoption of fundamental values such as sexual equality. In so doing, we recognize the importance of protecting these values in the larger Canadian community as well by ensuring that they are not undermined or compromised by our recommendations.

More specifically, Commissioners view the practice of PND and sex-selective abortion for non-medical reasons as contrary to the Commission's guiding principles and incompatible with generally held Canadian values. This practice violates the principles of respect for human life and dignity, sexual equality, protection of the vulnerable, and the appropriate use of resources. Moreover, it has the potential to distort the role of PND within the health care system, which is to identify serious disorders in the fetus or zygote and to avoid the birth of a child with a serious genetic disease or congenital anomaly.

Existing CCMG guidelines disapprove of the use of PND to determine fetal sex for non-medical reasons, and to date these guidelines have generally worked to ensure that PND is not misused for this purpose. However, further action is required to remove any ambiguity about the legitimacy of this practice and to ensure that safeguards are in place to deal with future developments in PND technology.

The challenge has been to translate the broad public consensus against sex-selective abortion for non-medical reasons into measures that will not create other, more difficult problems. Any attempt to limit abortion for sex-selective reasons would prove impossible to enforce and would risk eroding other aspects of women's reproductive autonomy. Instead, Commissioners decided upon a two-part approach: first, NRTC-licensed PND centres should be prohibited from providing PND to determine fetal sex for non-medical reasons; second, when prenatal testing is done for a medical reason, information on the sex of the fetus should be given to the patient only on direct request or if it is medically relevant. Commissioners believe that this approach will prevent PND from being misused for sex-selective purposes, without infringing on women's privacy and reproductive autonomy or violating the principle that patients should have access to their medical records.

Where prenatal testing is done outside genetics centres, through ultrasound or blood tests administered by obstetricians, radiologists, or general or other practitioners, the same general conditions and standards of practice should apply. We have recommended that professional guidelines be reviewed and amended if necessary to ensure that practitioners do not provide prenatal detection of sex for non-medical reasons and do not deliberately examine for or volunteer information on fetal sex before the last trimester of pregnancy except for medical reasons.

We believe that an approach based on licensing centres is also appropriate to prevent misuse of the second technique — preimplantation diagnosis and sex-selective zygote transfer — as preimplantation diagnosis for non-medical reasons will not be allowed.

With respect to the third technique — sperm treatment and sex-selective insemination — evidence suggests that the great majority of Canadians do not have a gender bias with respect to the sex of their children and that they would consider using sex-selective insemination only with the aim of having at least one child of each sex. We are sensitive to and empathize with the desire to have at least one child of each sex and to establish the unique family relationships that come from having both sons and daughters. We believe that sex-selective insemination, if used in support of these goals, is not in itself unethical, although it is not a medical service. It may be consistent with sexual equality, if used in a gender-neutral way.

We have shown clearly, however, that additional factors must be taken into consideration in deciding whether sex-selective insemination should be permitted. These include questions such as whether permitting this practice would reinforce the view that the sex of a child is important; whether it would make existing children feel that their own sex is lacking in some way; and whether it would involve the appropriate use of resources. In addition, because the technique is unproven, it would be unethical to offer the procedure in the absence of research aimed at determining its effectiveness and safety; however, such research is not of sufficient value to justify devoting scarce research dollars to it.

These considerations led us to conclude that sex-selective insemination services should not be available in Canada, and our recommendations reflect this view. We recommend that sex-selective insemination services be provided only where there is a medical indication, and only in licensed settings with corresponding requirements for informed consent, data collection, and reporting.

Finally, Commissioners conclude that all three techniques raise important issues that must be addressed at the international as well as the domestic level. The opening of fetal sexing clinics just across the border in the United States, aimed in part at attracting Canadian clients, shows that these issues cannot be addressed solely in a domestic context. As we have discussed at several places in our report, we believe that the National Reproductive Technologies Commission should promote and participate in efforts to develop international guidelines on new reproductive technology-related issues of international importance. These should include guidelines relevant to sex selection for non-medical purposes.

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Gene Therapy and Genetic Alteration

Twenty years ago, geneticists invented procedures for isolating single, identifiable genes and for "splicing" those genes into a foreign chromosome in such a way that the inserted gene would become functional and would duplicate in the process of cell division. This ability has given rise to various applications in agriculture and pharmaceuticals and is the basis for much of the biotechnology industry. It is also an ability that is evolving rapidly, giving rise to concerns about the development of technology outstripping society's capacity to make reasoned decisions about its acceptability and use. We heard these concerns and many other related to genetic alteration in our public consultations.

As we saw in the previous three chapters, developments in DNA technology have also enabled the identification of some of the specific genes responsible for particular genetic diseases. The potential of "gene splicing" to treat genetic disease in human beings was immediately evident. Generally speaking, there are few effective cures for genetic diseases, whether they are of early onset or late onset; this is why most couples decide to terminate a pregnancy when PND reveals that the fetus is affected by a severe genetic disorder. However, these recent scientific discoveries mean that it may become possible to treat some severe genetic disorders by altering the gene in question. This field of research is known as human gene therapy.

The Commission's mandate did not ask us to examine and make recommendations on all uses of genetic knowledge; it asked us to examine genetic manipulation and therapeutic interventions to correct genetic anomalies in the context of human reproduction and to make recommendations in the public interest with respect to them. Our concern in this chapter, as with the technologies examined in the previous chapters, is on the use of gene therapy and alteration in the reproductive context. Thus, our examination does not focus on therapy or alteration used after

birth, but many of the issues are similar. To conduct our review of these issues, we listened to Canadians, commissioned research and analysis, and considered the issues through the prism of our guiding principles and our evidence-based approach to technology assessment. Given that the field is developing so rapidly, with the exact direction of those developments still uncertain, this area will need continued public discussion to guide appropriate policy development.

Human gene therapy involves the insertion of genetic material into a human being with the intention of correcting a particular genetic defect. Specifically, a genetic defect resulting from an alteration in the DNA of a particular gene is corrected by inserting a normal DNA sequence for that gene into the individual's cells. One approach to inserting this genetic material is to remove cells containing the genetic defect from the individual, alter them in culture by adding the normal gene, then return the altered cells to the body. Another approach is to use altered viruses to deliver the gene — for example, into the respiratory tract if that is where the defect is expressed (as in the case of cystic fibrosis).

Gene therapy may be the only hope for some severely affected individuals who would otherwise die or be very severely disabled by a genetic disease. In addition, the knowledge that some severe genetic conditions may be amenable to gene therapy may broaden the options open to couples at risk of passing on a genetic disease. For disorders that are not treatable by any other means except gene therapy, the availability of this treatment could encourage some people who might otherwise terminate a pregnancy to continue it to term.

This is a new and rapidly developing field, but it has taken two decades of laboratory and animal studies to test the safety and feasibility of this approach and to develop the appropriate techniques for human application. The first approved clinical trials involving human gene therapy began in September 1990,[1] in the United States, and research has moved rapidly since then. A recent survey listed 15 research protocols involving 59 patients at nine different institutions in the United States, France, Italy, and China.[2] Gene therapy is, however, still very much an experimental technique.

At present, no gene therapy research involving human subjects is being done in Canada. However, several research centres in Canada are doing laboratory or animal work related to gene therapy. For example, groups at the Royal Victoria Hospital in Montreal, Mount Sinai Hospital Research Institute and the Hospital for Sick Children Research Institute in Toronto, and the Terry Fox Laboratory in Vancouver are investigating the use of retroviruses to transfer genes into blood-producing cells. Physical methods of DNA transfer into cells are being researched, and the use of electroporation is being examined at the Toronto General Hospital.

The development of gene therapy has created both hopes and fears. As one researcher commented in a study (see research volume, *Prenatal Diagnosis: New and Future Developments*) prepared for the Commission,

> The prospect of using directed genetic alteration to treat serious inherited disorders ... raises the hopes of patients and their families, but also the fears of those who perceive it as tampering with the secrets of life, or at least creating unknown hazards. (*L. Prior, "Somatic and Germ Line Gene Therapy: Current Status and Prospects," in Research Volumes of the Commission, 1993.*)

As we will see, there are reasons for these divergent responses, since gene therapy does indeed contain both significant potential benefits and unknown risks.

In evaluating these benefits and risks, it is important to keep in mind that the term "gene therapy" has been used to cover a wide range of procedures that are used for different purposes and in different contexts. The term gene "therapy" is misleading; as we will see, in some cases it is more accurate to call it gene "alteration," because no treatment of an individual with a disorder is involved. There are two major categories of genetic alteration: the first, somatic cell gene therapy, involves the introduction of the corrective DNA into the somatic cells (the non-reproductive body cells) of an affected individual. Since the altered genetic material is not inserted into the reproductive (germ) cells, the alteration is not passed on to subsequent generations. The second category involves the introduction of the corrective DNA into the germ cells, with the result that the genetic change can be passed on to subsequent generations.

There are two possible purposes for genetic alteration. The genetic alteration may be intended to treat disease, or it may be intended to enhance particular desired qualities, such as height or intelligence. Only the former is appropriately called gene therapy, since the term "therapy" implies the treatment of disease. Although enhancement is often discussed under the term "gene therapy," this is inappropriate, as its aims are entirely different. To emphasize this important distinction, we refer to it as "non-therapeutic genetic alteration" or "genetic enhancement" and treat it separately in this chapter.

Genetic alteration can be performed during adulthood, childhood, or prenatally on zygotes and fetuses. Although all of the current gene therapy research involving human beings is done on children or adults, if post-natal gene therapy proves effective, prenatal treatment may be considered. For example, a fetus diagnosed as having a severe single-gene disorder could potentially be treated through somatic cell gene therapy *in utero*. Similarly, if it becomes feasible to identify zygotes with genetic disorders through preimplantation diagnosis, the suggestion may arise that they be treated through genetic alteration *in vitro*. If this were done early in development, it is probable that the cells giving rise to the testes or ovaries (the "gonads")

in the resulting fetus would also be altered. This is not "germ-line therapy" per se but zygote therapy that may also alter the germ line as a side effect.

The Views of Canadians

Some indication of public views and attitudes can be gained from the input the Commission received at hearings and in submissions, although much of that input was on use of genetic knowledge in general. Recent surveys in the United States also provide some relevant information.

Public Hearings and Submissions

The topic of gene therapy received less attention in our hearings and submissions than some other aspects of our mandate. However, what was said was thoughtful, and a wide range of positions on the medical and ethical acceptability of gene therapy was expressed. For example, we heard from many people whose lives have been touched by severe genetic disorders; for them, somatic cell gene therapy is seen as a valid response to severe genetic diseases that cannot be treated effectively at present.

Although there was general support for the provision of somatic cell gene therapy for disease, there was more scepticism about the concept of altering a zygote's DNA at a time when the gonads would also be affected. These reservations reflect concerns about the unknown consequences of changing the DNA of cells when these changes may be passed on

> As a member of a family affected by a genetic disease and as a representative of other families affected by genetic diseases, I would like to emphasize that we are greatly affected by the policies or guidelines established in this area of reproductive technology. Many of our families are benefiting from the existing technology in the area of prenatal diagnosis ... Ultimately, our families look forward with profound interest to the day in the future when advances in this area and the area of gene therapy remove the death sentence now imposed on children afflicted with Tay-Sachs and the allied diseases ... it is important to note that the ideal solution in the eyes of a parent such as myself who was told that their baby was dying would be for the medical technology to be there to save my baby's life ... Should research into the areas of gene therapy be stopped or slowed down? No. This is not gene therapy to raise a child's IQ or change a child's looks. In my eyes, as in the eyes of the parents in our group, we ... just wanted our children to live.
>
> *H. Reiter, National Tay-Sachs and Allied Diseases Association of Ontario, Public Hearings Transcripts, Toronto, Ontario, October 31, 1990.*

to the next generation, the risks of permanent alterations in the human gene pool, the ethical implications of research involving human zygotes, and the potential for discriminatory use of technology.

Among those who discussed the topic, there was unanimous opposition to the concept of enhancement genetics intended to "improve" normal levels of human intelligence, strength, beauty, or other personal characteristics. This is seen as highly discriminatory in intent and totally antithetical to the values of Canadian society.

> We must refrain from trying to design or redesign human beings or perfect them according to our own notions ... The technologies we are discussing may have a place in alleviating suffering and combatting disease but should never be used as a means of seeking to reinvent human beings.
>
> *P. Marshall, The Evangelical Fellowship of Canada, Public Hearings Transcripts, Toronto, Ontario, November 20, 1990.*

There was also strong agreement that all forms of gene therapy should be regulated on a national basis and that there should be national regulations prohibiting non-therapeutic gene alteration or genetic enhancement.

These views are in line with the emerging international consensus on the acceptability of gene therapy. An international survey of 20 policy statements issued between 1980 and 1990 by legislative bodies, government agencies, professional organizations, and religious bodies concluded that

> Without exception, all 20 of these policy statements accept the moral legitimacy of somatic cell gene therapy for the cure of disease. Evaluations of germ-line genetic intervention for the cure or prevention of disease are mixed, with a majority of the policy statements opposing such intervention. None of the 20 statements supports the enhancement of human capabilities by genetic means.[3]

It is important to note, however, that some Canadians appearing before the Commission expressed opposition to all forms of gene therapy and recommended an outright moratorium on any such techniques. This opposition was based in part on broader reservations about the safety and wisdom of genetic manipulation technologies.

Surveys of Opinion

Most information on public attitudes toward gene therapy comes from the United States, where several public opinion surveys have been conducted. Since the mid-1980s, public reaction in the United States to gene therapy has been characterized consistently by high levels of approval for the use of gene therapy, but low levels of actual knowledge and information about the procedure.

For example, a survey of attitudes toward gene therapy conducted in April 1992 found that Americans were "at once deeply enthusiastic about the new science of gene therapy, in which patients receive healthy copies of genes they lack, but admittedly ignorant of any details about who might benefit or how. For example, 89% said they approved of using the novel approach to thwart genetic disorders, yet 60% confessed that they [had] heard almost nothing about the technique."[4] The same survey also revealed that a sizable minority approved of the use of genetic alteration for non-therapeutic enhancement as well as for treating disease. For example, 42 percent said that they approved of genetic alteration to improve the intelligence of children.

Such a high level of approval for gene therapy arises in part, no doubt, from the nature of media coverage of the topic. As we will see, there are serious technical and ethical limitations to the use of genetic alteration. These difficulties tend to be downplayed by the media, which have focussed instead on the glamour of high-tech medicine and the possibility of "miracle medicine" breakthroughs. This is perhaps inevitable, given the space and time limitations imposed by media coverage formats, as well as the complexity of the technology and the issues surrounding it. In an understandable desire to establish for media audiences the link between the discovery and the ultimate application or treatment, the intervening development processes and difficulties are usually minimized; the length and uncertainty of the stage between initial discovery and clinically useful application are often compressed or ignored. In addition, the range of potential applications of gene therapy is treated as large and ever-increasing — gene therapy is presented as revolutionizing wide areas of medical practice in the near future. Such an approach to covering these subjects also contributes to an oversimplified body-as-machine, doctor-as-mechanic view of disease, in which the genetic causes of disease are emphasized at the expense of the complex web of causation involving social and cultural factors, as well as physiological and immunological factors.

> We recommend that techniques involving the reshaping of human genes in any way be limited to the very narrow sphere of prevention and cure of specifically identifiable genetic diseases associated with human suffering and misery, and not extended in any way to positive eugenic programs of species improvement.
>
> *Brief to the Commission from the Mennonite Central Committee Canada, December 18, 1990.*

It is essential to develop a more informed and balanced public debate about the merits and limits of gene therapy. We look first at the most developed form of gene therapy — somatic cell gene therapy. We then consider the more speculative (and troubling) forms — gene therapy of a zygote that may alter the germ line, or genetic alteration of the germ line in

adults with the goal of prevention, and non-therapeutic genetic alteration. Our major focus, however, is on the possible uses of gene therapy in the reproductive context.

Somatic Cell Gene Therapy

Somatic cell gene therapy is the form of gene therapy on which research is most advanced and is an active area of biomedical research. It is still highly experimental, however, and its ultimate usefulness in the treatment of genetic disease is unknown. We examine the range of conditions potentially amenable to this form of therapy, then consider the issues it raises.

Potential Uses of Somatic Cell Gene Therapy

Genetic disorders differ very widely in the extent to which they could be corrected by existing or foreseeable gene therapy procedures. For example, chromosomal disorders (such as Down syndrome) are not amenable to gene therapy. These disorders involve the absence or duplication of fragments of chromosomes or entire chromosomes; as a result, the chromosomes have many extra or missing genes. Because no techniques are available to insert or remove sufficient DNA to correct such large defects, gene therapy does not apply to chromosomal disorders.

Similarly, most multifactorial disorders — which are the most common category of genetic diseases and include, for example, much cardiovascular disease — are beyond the reach of somatic cell gene therapy at its current level of development.

> Genetic therapy on embryos, fetuses and adults with serious genetic defects (such as cystic fibrosis or Tay-Sachs Disease) would be of great good to humanity and particularly to women in our capacity as primary caregivers on a global level. The darker side of genetic engineering is its potential to damage the human gene pool and to link with eugenic ideology and practice on a more powerful scale than has been possible previously ... If the human gene pool is understood as the collective property of humanity, then control of interventions in it and the judgement of risk and benefit are a public matter and need the participation of people who are not medical doctors, research scientists, lawyers, or statisticians. In addition to the need for representation by medical interests on the national ethics board, the [Canadian Advisory Council on the Status of Women] strongly recommends the inclusion of women's and labour group representatives, community health activists, and other lay people.
>
> *Brief to the Commission from the Canadian Advisory Council on the Status of Women, March 1991.*

Multifactorial disorders are determined by a combination of genetic predisposition and interaction with the environment. As we saw in the previous chapter, the genetic components are not understood sufficiently to warrant serious contemplation of genetic intervention.

Gene therapy is therefore relevant primarily to single-gene disorders. However, even within the category of single-gene disorders, there are wide differences in the potential usefulness of gene therapy. Recessive disorders (for example, Tay-Sachs disease) are much more amenable to gene therapy than dominant disorders. Recessive disorders can, in principle, be corrected simply by inserting a normal gene somewhere in the chromosomes of an affected cell (this is called "gene insertion"), without replacing or repairing the defective gene. Dominant gene disorders, on the other hand, are manifested even though the person has only a single copy of the defective gene. This is because defective dominant genes often alter the proteins that are the body's building blocks, which results in structurally abnormal tissues, so that normal function is not possible. Adding a normal gene in this case is not enough, because the aberrant gene product interferes with the ability of the normal gene product to form normal tissue. This means such disorders usually can be corrected only by repairing the defect in that dominant gene itself or by replacing it with a normal gene. (This is called "gene replacement.") This may involve replacement of the entire gene or of the aberrant nucleotides within the gene. For simplicity, we will speak of replacing genes, although in some cases only a part of the gene is replaced.

This is an important difference because, at present, only gene insertion is feasible in human beings. It is possible to insert a normal copy of the gene that is defective, which will then supplement the defective gene, but it is not yet possible to correct the mutation itself. To replace or repair the defective gene itself would require the ability to "target" the inserted genetic material with precision, so that it could be inserted in place of the original defective material. Such targeting is not currently possible, and, although research is proceeding, there is no guarantee that the required precision will be achieved in the near future.

As a result, only recessive single-gene disorders are amenable to gene therapy at present. As explained in Chapter 26, recessive disorders are manifested only if a person inherits a "double dose" of the defective gene. A person who has one copy of the defective gene will be healthy (although he or she will be a carrier of the genetic disease), because the normal gene can "cover" for the defective gene, producing enough of the protein for normal functioning. Inserting one copy of the normal gene into someone with a double dose of the defective gene may, therefore, be enough to restore health, even without trying to alter the defective genes. Some examples are severe combined immunodeficiency syndrome resulting from adenosine deaminase deficiency; deficiencies in liver enzymes; and some recessive central nervous system disorders like Tay-Sachs disease. The first approved clinical trial of gene therapy, begun in September 1990 at the

National Institutes of Health in the United States, involved such a recessive single-gene disease. The gene for the enzyme adenosine deaminase was inserted into children with severe combined immunodeficiency. This trial is continuing, and the inserted genes appear to be succeeding in increasing the children's immune response.[5] However, even if the trials for some recessive disorders prove successful, it is doubtful that somatic cell gene therapy will prove effective even for all recessive single-gene diseases, as many technical problems remain to be solved. The three most pressing of these technical problems are insertion methods, accessibility of the tissue, and regulation of the gene product.

> Genetic manipulation should be limited at present to corrective measures ... to work aimed at the eradication of abnormalities significantly impairing the capacity for or the quality of life. We would see this type of corrective genetics limited to somatic-line therapy, which would have an impact only on individuals affected by the disease. On the other hand the use of germ-line therapy which would produce a permanent alteration in the gene human pool should be implemented only after a full discussion and general agreement within our society.
>
> *M. Buchwald, Canadian Cystic Fibrosis Foundation, Public Hearings Transcripts, Toronto, Ontario, November 19, 1990.*

Methods of Insertion

Inserting genetic material into a human cell in such a way that it becomes integrated into the genome and becomes functional requires the precise identification and manipulation of submicroscopic amounts of genetic material. Current methods have not proved entirely satisfactory, with the result that the challenges associated with delivering healthy DNA sequences to the appropriate somatic cells remain formidable. The absence of appropriate methods of inserting genetic material constitutes a major impediment to the use of somatic cell gene therapy for some recessive diseases for the foreseeable future.

Accessibility

Another limitation to gene therapy is that the target organ for the genetic material must be accessible. This is not so much of a problem when the genetic disease manifests itself in changes in a protein or enzyme that circulates throughout the body — these diseases can be addressed by inserting the gene into any appropriate accessible tissue, as this will change the circulation level of that substance. But for other genetic diseases that affect particular tissue types, the usefulness of gene therapy will depend on the accessibility of the tissue. Gene therapy may be possible

if the clinical consequences of a disorder arise from changes occurring in a single accessible tissue, such as bone marrow or liver. However, several gene disorders affect relatively inaccessible tissues such as brain tissue (for example, Tay-Sachs disease), and these are not currently amenable to gene therapy.

Regulation of Gene Product

It is not enough for the genetic material to be inserted. The product of the inserted gene must also be regulated properly — that is, the gene must produce its particular protein at the proper time and in the proper amount. Too much of a protein may be as harmful as too little. Therefore, genes that require very precise regulation of expression are poor candidates for gene therapy because the current understanding of gene regulation is insufficient to ensure such precise control.

In summary, the present technology largely limits the use of gene therapy to single-gene recessive disorders where there is an accessible tissue and little regulation of the gene product is required. This means that gene therapy is relevant at present to only a small fraction of the total number of recessive disorders, which in turn is a fraction of the total number of single-gene disorders, which in turn is a small fraction of the total number of disorders in which genes are important. Although somatic cell gene therapy research is moving quickly, there is still a long way to go with respect to its feasibility. Even if some of these technical difficulties are solved, as some undoubtedly will be, there is no reason to think that gene therapy will ever become a miracle cure for genetic disease in general.

The Commission's particular interest is in the prenatal use of somatic cell gene therapy on fetuses *in utero*. Many of the limitations just mentioned apply with particular force to the prenatal use of gene therapy; for example, accessibility is an even more serious obstacle when dealing with a fetus *in utero*.

There are also additional risks in applying somatic cell gene therapy prenatally. If done at a very early stage of development — for example, when the zygote is accessible *in vitro* after preimplantation diagnosis — there is the risk that the insertion of somatic cells may result in de facto germ-line gene therapy; that is, that the entire range of cells in the zygote, germ-line as well as somatic, will be affected. Thus, any gene therapy done before the body organs begin to develop could result in germ-line gene alteration. Rather than alter the zygote at this early stage, it seems more appropriate not to transfer those zygotes diagnosed as affected by the disorder in question.

The other stage when the developing fetus could be treated is after PND by CVS or amniocentesis (that is, after at least 10 weeks' gestation). At that stage of development it would be possible to "see" and reach the tissues of the fetus using ultrasound guidance. Such procedures would pose risks for the pregnant woman, both from the invasive nature of the

procedure and from unintended consequences of inserting new genetic information into the fetus. Given these risks, many couples would probably opt to terminate the pregnancy if the fetus was found to be affected with a serious disorder.

Given the greater obstacles and risks of prenatal treatment, as well as the current state of knowledge about the results of post-natal treatment, little research is being conducted into fetal applications at present, even in animal models. Somatic cell gene therapy on the fetus *in utero* would be the only way to treat some genetic diseases, however. Some disorders could be treated only if they were corrected during fetal development, before they have caused irreversible damage. This is true of Lesch-Nyhan syndrome and some other severe central nervous system disorders. (Many in-born errors of metabolism can be dealt with after birth, since the mother's metabolic system usually keeps the circulating level of the substances normal in the fetus, but single-gene conditions that result in congenital anomalies must be dealt with earlier.) In addition, some tissues may be more amenable to effective gene insertion during the rapid growth that takes place during fetal development than they are after birth. Hence, fetal gene therapy, while currently speculative, may come to play a valid, if very limited, role in the treatment of genetic disease.

Issues Raised by the Use of Somatic Cell Gene Therapy

There seems to be no reason to object in principle to somatic cell gene therapy, which can be seen as a natural extension of commonly used medical procedures. For example, people with diabetes who are unable to produce normal amounts of insulin are given this missing gene product by daily injection. If the insulin-producing gene could be inserted into someone with diabetes, the effect would be the same as the daily injection, except that gene therapy would provide lifetime relief. The same permanent result would occur if the diabetic received a tissue or organ transplant, which would also provide cells containing the normal gene. By itself, then, the idea of somatic cell gene alteration does not seem to raise any new moral problems. Although somatic cell gene therapy is not inherently objectionable, its actual application does raise several important issues, including risks, informed consent, confidentiality, and appropriate use of resources.

Risks

The methods used to insert genetic material may expose the patient to infectious viruses and increase the risk of cancer. At the current state of the technology, it is not possible to control how or where the inserted DNA integrates into the host cell. Thus, there is a risk that the random integration of inserted genes could result in the activation or deactivation of genes that influence susceptibility to cancer or promote the body's ability

to suppress the development of tumours. This could increase the possibility that the person would subsequently develop cancer, although the probability is quite small. A risk of cancer resulting from treatment is not unique to gene insertion — it also occurs in other life-saving treatments, such as anti-rejection medications used in kidney transplant patients.

Another risk is that if genetic material integrates successfully but the treatment is insufficient, the procedure may simply prolong a severe disorder, without actually curing the disease or even alleviating the suffering.

Given these risks at this time, the use of somatic cell gene therapy is appropriate only for diseases that lead to severe debilitation or death and that cannot be treated successfully by any other means.

In the case of fetal applications of gene therapy, as well as unintended consequences of the insertion of new genetic information into the fetus, there are additional risks to the pregnant woman, resulting from the intrusiveness of the procedure. If post-natal gene therapy proves safe and effective in the future, however, the use of gene therapy *in utero* could be considered for fetal conditions that cause irreversible damage before birth.

Informed Consent

As with all medical research, an individual's involvement in gene therapy should be informed and voluntary. The person should be fully informed about the nature and risks of treatment and should make the decision about whether to participate completely free of any pressure. Sufficient information must therefore be provided about the proposed treatment and the patient's role in it, in a form that can be understood, to enable the patient to decide whether to participate. The patient should also know that it will remain unknown for many years whether adverse long-term effects occur. The level of disclosure should be proportionate to the likelihood and scale of possible harm, but even the remote possibility of adverse consequences should be disclosed.

Several problems arise with respect to informed consent for gene therapy. First, gene therapy is irreversible (just as most surgery is), so the right to revoke one's consent is less meaningful than for continuing medical treatment. It is particularly important, therefore, to ensure that the highest standards of informed consent are met.

Second, in reproductive contexts, both the fetus that receives the DNA alteration and the pregnant woman are being treated. The woman's decision about whether to consent to treatment must therefore be based not only on information about potential risks and benefits to the fetus but also on potential harms to herself. In-depth counselling should be provided to ensure full review of the state of knowledge concerning the risks of changing the DNA in the fetus — what the known risks are as well as what

is unknown — the relative risks and benefits of alternative treatments, and the reversibility of any side effects.

Confidentiality

As with PND and genetic testing, information obtained during somatic cell gene therapy research trials could be prejudicial to individuals being treated or to their families. Any information obtained must therefore be reported in a manner that conceals the identity of individuals being treated. No one outside the research team should be permitted to handle data that could reveal patient identity. Identifying information should be disclosed only with the individual's express authorization. There may be problems in maintaining anonymity, since there is widespread interest in gene therapy among the public, as well as in scientific, government, and other communities. The potential for wide publicity may make it difficult to assure people's privacy, since there could be many ways for the media to identify who is being treated. Acknowledgement of the risk of media exposure should be part of the process of informed consent.

Appropriate Use of Resources

Somatic cell gene therapy is expensive. If the procedure proves effective, costs will likely decline as techniques are refined and treatment becomes more widely available. It will always be a relatively expensive procedure, however, since considerable expertise and expensive laboratory support are required. But there are also substantial costs associated with treating children born with a genetic disease, who often require procedures that are as expensive or invasive. For example, children with immunodeficiency may have several bone marrow transplants, which are likely to be more expensive than gene therapy if the latter becomes part of clinical practice. Commissioners therefore believe that it is appropriate to provide public funding for research into somatic cell gene therapy for serious disorders for which there are no alternative treatments.

Of course, researchers should not neglect the development of other possible treatments for the genetic diseases in question. For example, some success has been achieved in treating adenosine deaminase deficiency through the drug PEG-ADA. Clearly, the appropriateness of funding further research into gene therapy for this disorder or other disorders will depend on the success of drug treatment.

Regulating Somatic Cell Gene Therapy

Commissioners believe that the therapeutic intent of somatic cell gene therapy is broadly consistent with the ethic of care. However, further research or future clinical application in this area must be managed in a socially responsible way. At present, any proposal for somatic cell gene therapy research in Canada would be carried out within the context of the

Medical Research Council of Canada's *Guidelines for Research on Somatic Cell Gene Therapy in Humans*.[6] The MRC applies these guidelines to all researchers who receive MRC funding for medical research involving somatic cell gene therapy. These guidelines are also applied by a wide range of hospitals, funding bodies, and universities in Canada. For the foreseeable future, then, any gene therapy project in Canada would originate from an institution that is covered by MRC guidelines.

These guidelines cover many of the issues we have identified as important for the ethical application of gene therapy, including informed consent, confidentiality, and limiting gene therapy to serious diseases for which no alternative treatments are available. Commissioners believe that the MRC's guidelines on somatic cell gene therapy research provide a solid foundation for the management of this research in Canada. However, they need to be implemented fully and supplemented in several ways, as discussed later in this chapter.

One key feature of the MRC's guidelines involves the recommendation that these guidelines be applied in a two-tiered fashion, first at the local level by research ethics boards of hospitals and universities and then, in the case of a positive review by the local research ethics board, in a second review by a national committee. A similar two-step process has been established in the United States for federally funded gene therapy research, with review both at the local institutional level and by the Recombinant DNA Advisory Committee of the National Institutes of Health.

However, the national review committee proposed by the MRC has yet to become a functioning reality. There has not been a pressing need for this committee to date, because research in Canada has not yet involved human subjects. However, this will soon change. Commissioners believe that the national review committee proposed by the MRC should be established immediately, to provide assistance to local research ethics boards and to ensure consistent national treatment of gene therapy research activities.

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Somatic cell gene therapy has the capacity to generate scientifically difficult and ethically demanding questions that might place an unfair burden on the resources of local research ethics boards and that would benefit from the broader perspective and additional analytic resources implicit in a national review function. Also, a national review committee would maintain consistency of treatment of these potentially highly controversial research projects across Canada. It is unreasonable to expect the system of locally controlled, volunteer-based research ethics boards alone to provide an adequate framework for protecting either research

subjects or the national interest in monitoring the evolution and application of gene therapy.

We also believe that the MRC guidelines need to be supplemented in two important ways. First, public reporting should be an essential element of any national review function, given the growing public interest in therapeutic advances and strong public concerns about potential abuses of this technology. A high level of public availability of information must be associated with the process of approving and funding research involving human beings. Commissioners believe it will be important for the MRC's proposed national review committee to report publicly on somatic cell gene therapy research in Canada on a regular basis — both the failures and successes — perhaps in the MRC president's annual report.

Second, with regard to matters within its mandate, Commissioners believe that special safeguards are required for fetal applications of somatic cell gene therapy. Any research projects involving fetal applications of somatic cell gene therapy should be undertaken only with the greatest of care, given the vulnerability of the recipient, the technical difficulty of the procedure, and the need to respect the autonomy of the pregnant woman.

Proposals for fetal gene therapy research must be assessed carefully to ensure that they do not promote development of an adversarial relationship between a woman and her fetus, and that they constitute an appropriate use of resources.

Commissioners view the potential development of fetal gene therapy with considerable misgivings. To the extent that these developments encourage increased interest in and capacity to support the health of the fetus, they are useful. To the extent that the possibility of performing somatic cell gene therapy condones coercion or undermines the autonomy of women, however, some very real concerns must be addressed. Proposals for fetal gene therapy research must therefore be assessed carefully to ensure that they do not promote development of an adversarial relationship between a woman and her fetus, and that they constitute an appropriate use of resources.

To ensure this careful assessment, Commissioners believe that gene therapy research and/or subsequent clinical treatment involving fetuses should be approved by the Prenatal Diagnosis and Genetics Sub-Committee of the National Reproductive Technologies Commission, as well as by the MRC's proposed national review committee on gene therapy. While the MRC review process is invaluable, medical and scientific perspectives predominate, both at the local research ethics board level and nationally. Moreover, the few representatives of the general public are often drawn from a narrow range of professional groups, with little reflection of women's groups, the community health sector, or other relevant interests.

The National Commission, by contrast, would embody a wider range of perspectives and would be more publicly accountable than the MRC's national review committee. Hence, the MRC national review committee and the National Commission Prenatal Diagnosis and Genetics Sub-Committee would provide complementary forms of assessment, based on their different expertise and perspectives. The MRC national committee would apply expertise primarily to the scientific merits of research proposals, while the National Commission Sub-Committee would focus primarily on social and ethical issues.

Moreover, approval by the Prenatal Diagnosis and Genetics Sub-Committee of the National Commission would help integrate fetal gene therapy with the larger PND system in Canada. If and when fetal applications of somatic cell gene therapy prove clinically feasible, it will be important to ensure that there is close cooperation between the prenatal diagnosis system, which may reveal to at-risk couples that their fetus is affected by a genetic disease, and the practice of gene therapy, which would be available as an option for treating that disease. The Commission therefore recommends that

267. Any proposal for somatic cell gene therapy research involving human fetuses as subjects be reviewed and approved by the Prenatal Diagnosis and Genetics Sub-Committee of the National Reproductive Technologies Commission, following review and approval by the Medical Research Council national review committee for gene therapy.

and that

268. The National Reproductive Technologies Commission develop guidelines concerning the appropriate indications for fetal applications of somatic cell gene therapy as the field evolves, with a view to increasing the National Reproductive Technologies Commission's regulatory involvement if the need arises.

Germ-Line Genetic Alteration

Potential Uses of Germ-Line Genetic Alteration

The term "germ-line gene therapy," although widely used, is in fact misleading. "Therapy" implies treatment of an individual (a person or a

developing fetus) for a disease that has been identified. Genetic alteration aimed specifically at the gonads to alter the gametes is therefore not therapy — there are no existing affected individuals. It is quite incorrect, therefore, to refer to genetic alteration done in adults with the aim of altering the germ cells as "therapy" — it is a "preventive" strategy. For purposes of analysis, it is important not to describe this, misleadingly, as "therapy," as there is much less willingness to undertake risk (both individually and societally) in order to prevent disease than to do so for therapeutic purposes.

It is possible, however, to consider genetic therapy involving the zygote or the fetus — that is, genetic alteration aimed at curing disease in that zygote or fetus. If done very early in development during the zygote stage, this could affect the germ line. There are two windows of opportunity during which the developing entity is theoretically accessible for genetic therapy before birth. The first is after IVF and preimplantation diagnosis have shown that the zygote is affected. If gene insertion were done at this stage, before the process of cell differentiation and the development of body organs (organogenesis), then the genetic change would be present in most or all cells — and could thus affect the germ line of the resulting fetus as well. Some have argued that this not only would treat that particular zygote but might prevent the transmission of the gene to future generations. However, rather than taking the risk of altering genes that will be passed on to the next generation, there is the less risky option of simply not transferring affected zygotes.

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The next window of opportunity (before birth) is much later, after organogenesis; treatment of an affected fetus at that time would be unlikely to affect its germ line. A major reason for interest in gene therapy before birth is that it might be able to treat certain genetic diseases that are not amenable to therapy after birth — for example, diseases that cause irreparable harm early in fetal development or that affect multiple body systems.

Germ-line genetic alteration has also been discussed (under the misnomer "germ-line therapy") in terms of relevance to adults who either have, or are carriers of, a genetic disorder. But if an adult manifests a genetic disease, then altering his or her germ cells would not treat that disease, which would continue to affect the body cells; it would mean simply that the disease gene would not be passed on to offspring. It is incorrect to call this therapy — the aim is preventive, not therapeutic. The difficulties associated with altering the gametes or gonads of adults are enormous, to the point where few proponents of germ-line alteration consider this a viable option. Germ-line genetic alteration is much more

complicated than somatic cell gene therapy. Whereas somatic cell gene therapy uses gene insertion, germ-line therapy would require gene replacement (which is not feasible in human beings at present) of all the germ cells affected. If a normal gene were simply inserted, without removing the defective gene, then the genetic disease could still be passed on to future generations.

Research with animals has demonstrated that intergenerational transmission of genetic information inserted into zygotes (so the gonads contain the altered gene) is possible. However, the failure rate of insertion and transmission to offspring is high. Moreover, animal germ-line alteration is done for different purposes than human germ-line alteration would be. Germ-line genetic alteration in animal zygotes is not done to treat disease, but to create "transgenic" breeding lines of animals, either to establish an animal model of a human disease that will be inherited, enabling the production of animals that can be used in research, or to produce animals that make commercially valuable proteins. Neither of these purposes applies to human beings. At present, therefore, genetic alteration in human beings that affects the germ line is a wholly untested procedure. Moreover, as discussed in the next section, genetic alteration intended to affect the germ line is both unnecessary and unwise.

Genetic alteration intended to affect the germ line is both unnecessary and unwise.

Issues in the Use of Germ-Line Genetic Alteration

Many of the issues raised by somatic cell gene therapy would also apply to germ-line genetic alteration — for example, requirements for informed consent and confidentiality. However, in addition, several unique and very troubling aspects of germ-line genetic alteration distinguish it from somatic cell gene therapy.

First, the risks associated with germ-line alteration are much greater than those surrounding somatic cell gene therapy. As we have seen, it is not possible to target an inserted gene precisely to a specific chromosomal site, raising the possibility that an inserted gene could interfere with other vital gene functions or even activate genes related to cancer development. The consequences of random insertion, while serious, are less severe in the case of somatic cell gene therapy, since a "mistake" would affect only a single target cell or tissue. In genetic alteration of the zygote, however, this "mistake" would be incorporated into most or all its cells.

Moreover, there is no reason to risk these consequences, for there is an easier and less risky alternative to treatment of the zygote. Treating a zygote at a stage when the germ line would be affected first requires determining which zygotes have a genetic disorder, which means that preimplantation diagnosis would have to be performed. It would therefore

be possible not to transfer the zygotes found to be affected and to transfer only those found to be unaffected. Couples who are at risk of passing on a genetic disorder have a very good chance that at least one of their zygotes will not have the defective gene, although the exact odds depend on the kind of genetic disorder. (Recall that preimplantation diagnosis would be done on more than one zygote at a time, since multiple eggs would normally be retrieved for fertilization and preimplantation diagnosis during *in vitro* fertilization procedures.)

For example, if four eggs have been retrieved and fertilized *in vitro*, and if both parents are carriers of a recessive gene, then the odds are that three of the four zygotes tested by preimplantation diagnosis will turn out to be healthy and unaffected by the genetic disease. On average, one of the four zygotes will be diagnosed as having the genetic disease, but it does not have to be transferred to the woman's uterus; three healthy zygotes can be transferred, without any need for gene therapy. There is therefore no justification for performing gene therapy on affected zygotes when healthy zygotes can be obtained for transfer.

Similarly, if one parent has a dominant disorder, the odds are that two of four zygotes tested through preimplantation diagnosis will turn out to be healthy and so can be transferred without gene therapy. Even in the very rare instance that both parents have a dominant disorder, there is still a 25 percent chance of producing a healthy zygote.

Finally, if the genetic disease is X-linked, half the zygotes with a male chromosomal complement will be affected. Preimplantation diagnosis can be used to identify the female zygotes and the unaffected male zygotes, which will be healthy and can be transferred.

In all these cases, then, preimplantation diagnosis can be used to identify healthy zygotes for transfer. Hence, it is difficult to envision the real-world situations in which genetic alteration involving a zygote at an early enough stage of development to affect the germ line would be an appropriate response. Few couples are likely to prefer transfer of an altered zygote to not transferring those affected.

It is difficult to envision the real-world situations in which genetic alteration involving a zygote at an early enough stage of development to affect the germ line would be an appropriate response.

The only situation in which preimplantation diagnosis could not be used to identify normal zygotes is if both members of the couple are affected by a recessive disorder (and are not just carriers of it). In this case, it is virtually certain that all their zygotes will be affected by the disease. This would be extremely rare, however, as the average incidence of a recessive disorder is 1 in 20 000. The random likelihood that two affected individuals would mate is therefore exceedingly small. Moreover, even if they do, if both are healthy and functional enough to achieve pregnancy, the condition affecting them cannot be among the most devastating of the

genetic diseases. Indeed, such diseases are likely to be relatively mild (for example, deafness) and certainly not devastating enough to warrant attempting manipulation of the DNA of a zygote. Further, couples in this situation could also consider using donor gametes.

The same logic applies to the possibility, mentioned earlier, that germ-line genetic alteration could be applied to the gametes of an adult who is a carrier of a genetic disease. It is not currently feasible to perform genetic alteration of sperm or eggs. But, even if it were to become possible, in order to alter the carrier sperm the sperm carrying the disease would have to be distinguished from those that do not, or else *all* the sperm would have to be altered.

A misguided argument has been made that gene therapy on zygotes that also affects the germ line is desirable, even if other options are available to avoid or treat affected offspring, because it has the advantage of serving a preventive function, by reducing the transmission of genetic disease to future generations. Fetuses that have been treated by somatic cell gene therapy, or zygotes from high-risk couples that have been tested by preimplantation diagnosis and found normal, do not have a genetic disease, but some are still carriers of the disease and so risk passing it on to future generations. DNA alteration of such zygotes would eliminate the risk. (The same preventive argument is made for research into germ-line genetic alteration on adult gametes or gonads.)

For example, it has been argued that "society should pursue the development of strategies for preventing or correcting, at the germ-line level, genetic features that will lead to, or enhance, pathological conditions" as a way of ensuring that present and future couples can "exercise their rights to reproductive health."[7]

The idea of eliminating the risk of transmitting genetic disease may sound attractive, but it is in fact based on a misunderstanding of human genetics. All of us are carriers of various recessive genetic disorders — that is, we all carry genetic mutations that, if found in a double dose, could be deleterious, even fatal. To set as our aim the elimination of all risk of passing on genetic disease would involve genetic alteration of the gametes or gonads of all adults.

For example, if a recessive disorder occurs in 1 in 10 000 live births, which is relatively frequent for a recessive disorder, then approximately 1 individual in 50 is a carrier for that disorder, although that individual will be quite normal and healthy. To prevent this 1 in 10 000 chance of a recessive disorder, one would have to alter the DNA of 1 individual in 50 — and this would have to be done for all the hundreds of recessive single-gene disorders that exist.

The fact is that all human beings carry a few genes that would be deleterious if passed on to offspring in a double dose. The risk of passing on genetic disease is inherent in the human condition; it makes no sense to try to alter this in this way. Not only is the goal of a genetically "perfect"

human being impossible to achieve, but human beings in all their diversity have value in themselves.

Moreover, even if it were feasible, it is not necessarily desirable from an evolutionary perspective. The fact that we all possess a certain amount of genetic mutation is what provides the reservoir for the species to adapt to changing environmental circumstances. The risks of genetic alteration of the germ line therefore do not affect just the individual involved. The human genome has evolved over millions of years, in complex and subtle homeostasis with the environment. For example, we know that having carriers of certain genetic disorders is beneficial to a population. The best-known example is the gene for sickle-cell anaemia, which provides greater resistance to malaria. Many other examples are suspected as well. We simply do not know enough to contemplate intentionally changing the human genome in the way required for a germ-line prevention program to have any appreciable effect.

The behaviour of humanity has always had consequences for the composition of the gene pool.

It is important, however, not to exaggerate the possible impact of germ-line genetic alteration on the DNA of the species as a whole. Many medical treatments affect the likelihood that particular genotypes will be passed on — it can be argued that the gene pool of the next generation is altered by any medical treatment or social support that allows people with a disease with a genetic component, who would formerly have died at an early age, to survive and reproduce. We do not withhold treatment of individuals for that reason. The behaviour of humanity has always had consequences for the composition of the gene pool. For example, technological innovation and cultural change affect the human gene pool. As one observer put it,

> ... it seems to me that the possibilities for what can be accomplished directly through genetic engineering are being exaggerated. After all, the human gene pool is enormous; there are over three billion human beings, and a large percentage of them at any given time are fertile. To effect a really significant change in a gene pool of that size through genetic engineering would call for delicate microsurgery on a lot of people. If we wanted to introduce far-reaching and practically irreversible changes into the shape of human life, we could do so far more effectively in the old-fashioned ways, by technological innovation and cultural change.[8]

It is nonetheless important to note that germ-line genetic alteration would be unique in that it involves intentional interference in human evolution. This imposes a greater responsibility to consider the impact of decisions regarding it on our species and on the interests of future generations.

Commissioners are of the opinion that the question of the impact of technology on future generations is one that touches on gene therapy, susceptibility testing, and other new reproductive technologies, and thus should be treated in a disciplined manner over the long term by setting up a framework to clarify what is prohibited, how activities will be regulated, and how decisions will be made.

> It is nonetheless important to note that germ-line genetic alteration would be unique in that it involves intentional interference in human evolution. This imposes a greater responsibility to consider the impact of decisions regarding it on our species and on the interests of future generations.

Regulating Germ-Line Genetic Alteration

It is clear that germ-line genetic alteration is inconsistent with the Commission's guiding principles. There are many risks and potential harms, without any clear benefit to any individual. It is not an appropriate use of resources, and it jeopardizes, rather than protects, those who are vulnerable. Since any foreseeable germ-line genetic alteration would involve embryo research, it would be covered by the legislative and licensing mechanisms we propose in Chapter 22. However, we believe it is important to emphasize the unacceptability of germ-line genetic alteration by including it in the licensing conditions for infertility clinics, which in practice would be the source of human zygotes (or eggs) in Canada. The Commission therefore recommends that

269. No research involving alteration of the DNA of human zygotes be permitted or funded in Canada. This prohibition would be monitored and enforced by the Embryo Research Sub-Committee of the National Reproductive Technologies Commission.

and that

270. The Prenatal Diagnosis and Genetics Sub-Committee of the National Reproductive Technologies Commission have as part of its guidelines for centres licensed to provide PND and genetics services that no genetic alteration of a human zygote be permitted.

Non-Therapeutic Genetic Alteration

Genetic enhancement involves the attempt to enhance or improve an already healthy genetic structure by inserting a gene for "improvement." This non-therapeutic use of genetic technology might take the form of altering either somatic cells or germ cells.

Like gene therapy, the scope of genetic enhancement feasibility is quite narrow. Genetic alteration to improve complex human traits, such as beauty, intelligence, vigour, and longevity, is far beyond our technical capabilities and will be so for the foreseeable future. These complex traits are multifactorial in nature; that is, they are a function of complex interactions between genetic and environmental factors. As a result, enhancement of any particular gene is not likely to have the desired effect.

Genetic enhancement may be possible in principle for some simpler physical characteristics, such as height. However, the risks involved are totally disproportionate to any benefits that might be gained. These risks include not only all the risks discussed earlier with respect to somatic or germ-line gene alteration (such as inducing cancer), but others that are unique to genetic enhancement. As one scholar has commented,

> Any alteration or addition [to the normal genome] is likely to have deleterious, not beneficial results. Any gene acts on the background of many other genes that also have evolved over millennia.[9]

For example, although attempts to increase the size of mice by inserting growth hormone genes have succeeded in increasing their size, they have also led to a variety of deformities and functional disturbances.

Moreover, the motivation for non-therapeutic gene alteration requires close examination. Proponents argue that genetic enhancement is really no different from cosmetic surgery, and that the desire to improve oneself is natural and commendable. However, comparing enhancement genetics to cosmetic surgery or to other ways of helping individuals "make the best of themselves" is misleading and neglects the potential harms. We see three major types of risk in connection with genetic enhancement:[10]

- *Social risks*: A caring society values people for themselves and for their uniqueness. Our ethical principles tell us that all individuals should be valued equally. Genetic enhancement raises the prospect of a society where some people would be accepted only if they were "improved" — they would not be acceptable as themselves. This is a form of commodifying individuals — people are treated as things that can be changed according to someone else's notions of human perfection. This shows a lack of respect for human life and dignity and intolerance for human diversity, which is likely to lead to discrimination against and devaluing of certain categories of people. Any use of genetic enhancement raises troubling and potentially

discriminatory judgements about what sorts of enhancement would be allowed and who would have access to them. In the case of gene therapy, the issue of who should receive the alteration is clear — those with a severe disease should be eligible for medical treatment. But in the case of genetic enhancement, the selection process, by definition, cannot be based on medical need. It must therefore be based on other, as yet unspecified, criteria. Would it be a lottery or, more likely, those most able to pay?

As there is no therapeutic objective, the goal of such alteration would be to pursue non-medical objectives, which might be economic, social, cultural, ethnic, or other. What are these objectives, and whose objectives are they? There is also the danger that people might be pressured to undergo such a procedure and be subject to discrimination if they refused. Finally, use of technology in this way might promote a social program of eugenics or indeed change our concept of what it is to be a human being.

- *Medical risks*: Many of the risks of cosmetic surgery are documented, but we do not know the risks of inserting genetic material, such as the risk of disrupting a tumour suppressor or activating a cancer-related gene.
- *Opportunity costs*: The non-therapeutic use of genetic alteration technology would draw away needed resources and skilled personnel from real medical problems. To allow DNA alteration in healthy individuals when there are so many other pressing calls on social attention and resources would be irresponsible and unethical.

The desire to improve the longevity, talents, and vigour of ourselves and our children is not inherently objectionable. However, this can best be achieved by improving the social and environmental factors that shape our daily lives — such as improved education or a healthier environment — rather than through the risky and potentially discriminatory use of genetic enhancement by those with the money or power to gain access to the technology.

In short, Commissioners find any non-therapeutic use of gene alteration unacceptable both in principle and in practice. It is not clear who would benefit or at what cost; there is the great risk of discriminatory use; and it is unacceptable to impose serious risks on healthy individuals for unclear benefit.

Our recommendations earlier in this chapter on somatic cell gene therapy have already made clear that research on genetic alteration in human beings is appropriate only for the treatment of serious diseases when no alternative treatment exists. Any non-therapeutic use of genetic alteration technology is also inconsistent with the existing MRC guidelines, which we have endorsed and supplemented with our recommendations.

It is extremely doubtful that any use of this technology for individual enhancement would ever be proposed by a genetics centre; but, if this ever did occur, the National Reproductive Technologies Commission would be able to turn down any such proposal.

It is important to remain vigilant about the possible misuse of technology that can change DNA, and it is important for the general public to become more aware of the issues it raises. Although these areas are outside our mandate, and the uses of genetic technology in general (for example, to "improve" individuals) are outside the span of new reproductive technologies and the National Reproductive Technologies Commission, we believe that a mechanism for keeping a watching brief on this area is desirable. Hence, we conclude that the National Council on Bioethics in Human Research (NCBHR) should consider this to be an area that warrants continued attention. The Commission recommends that

271. No research involving the alteration of DNA for enhancement purposes be permitted or funded in Canada. Proposals for any such project should be refused by the Medical Research Council national review committee on gene therapy.

and that

272. The National Council on Bioethics in Human Research address the question of non-therapeutic genetic alteration and monitor developments in this field.

Conclusion

The widespread and intense interest in all aspects of DNA technology that can alter genetic make-up includes both ardent hopes for the development of cures for severe, often fatal, genetic diseases and equally intense concerns about the potential abuses of science's increasing capacity for genetic manipulation. Our recommendations take into account the potential uses of these technologies in the context of human reproduction. Other applications of DNA technology are outside our mandate; we believe, however, that their implications for society warrant continued vigilance and public dialogue on whether and under what circumstances such applications might be permitted. This is why we have recommended that

existing bodies charged with various review responsibilities maintain a watching brief and promote the necessary dialogue through publications, discussion papers, and other public education tools. In addition, Commissioners believe that the current stage of development of DNA technology in Canada provides a unique window of opportunity for enlightened policy responses that, if adopted now, will help set the future course of how our new capacity to alter genetic make-up is used in this country.

With respect to both germ-line genetic alteration and enhancement genetics, Commissioners are of the opinion that the risks associated with any such research on human zygotes or human subjects are completely out of proportion to any potential benefits, and that publicly funded research of this type should not be conducted in Canada.

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Somatic cell gene therapy in general is outside our mandate. Nevertheless, to ensure appropriate limits on those aspects of somatic cell gene therapy that are within our mandate (that is, its use in the reproductive context), and to ensure that such uses, if permitted, can be appropriately regulated, we believe that a broader approach is necessary. Only if a mechanism is in place to review all proposals for somatic cell gene therapy can we ensure that the oversight we recommend for prenatal or reproductive uses occurs. This would mean that the following division of responsibilities should be in place with respect to somatic cell gene therapy:

- The Medical Research Council would continue to regulate human gene therapy research in general and immediately establish its recommended national review committee to review all proposals for somatic cell gene therapy research involving human subjects.
- Any proposal for the application of somatic cell gene therapy to fetuses would also be subject to approval by the Prenatal Diagnosis and Genetics Sub-Committee of the National Reproductive Technologies Commission.
- As part of its regulation of research involving human zygotes, the National Reproductive Technologies Commission would prohibit any genetic alteration of human zygotes, as such alteration may affect the germ line.
- The National Council on Bioethics in Human Research would address the question of the use of DNA technology that alters genetic make-up (for example, non-therapeutic uses or "preventive" uses) with respect

to the ethical and social implications, including consideration of the interests of future generations.

We believe that this division of responsibilities will serve Canadians well, now and in the future, with regard to DNA technology that alters genetic make-up, both by overseeing present-day research and by stimulating an informed and reasoned public debate about any future uses of DNA alteration technology in health care, or indeed any other use that is proposed.

General Sources

Prior, L. "Somatic and Germ Line Gene Therapy: Current Status and Prospects." In Research Volumes of the Royal Commission on New Reproductive Technologies, 1993.

Specific References

1. The first administration of genetically altered material into human beings occurred in 1980. However, this experiment was premature and not an approved clinical trial. It was quickly stopped, and the researcher was censured. A voluntary moratorium was in effect regarding human gene therapy between 1980 and 1990, although laboratory and animal research continued.

2. Adapted from "Human Gene Transfer/Therapy Patient Registry — Summary." *Human Gene Therapy* 3 (6)(December 1992), p. 729.

3. Walters, L. "Human Gene Therapy: Ethics and Public Policy." *Human Gene Therapy* 2 (2)(Summer 1991), p. 117.

4. Angier, N. "Many Americans Say Genetic Information Is Public Property." *New York Times*, September 29, 1992.

5. Blaese, R.M. "Development of Gene Therapy for Immunodeficiency: Adenosine Deaminase Deficiency." *Pediatric Research* 33 (Suppl.)(1)(1993): 49-55.

6. Medical Research Council of Canada. *Guidelines for Research on Somatic Cell Gene Therapy in Humans.* Ottawa: Minister of Supply and Services Canada, 1990.

7. Zimmerman, B.K. "Human Germ-Line Therapy: The Case for Its Development and Use." *Journal of Medicine and Philosophy* 16 (1991), p. 593.

8. Porter, J. "What Is Morally Distinctive About Genetic Engineering." *Human Gene Therapy* 1 (4)(Winter 1990), p. 423.

9. Prior, L. "Somatic and Germ Line Gene Therapy: Current Status and Prospects." In Research Volumes of the Royal Commission on New Reproductive Technologies, 1993.

10. For an exploration of these issues, see Anderson, W.F. "The First Signs of Danger." *Human Gene Therapy* 3 (4)(1992): 359-60.

Judicial Intervention in Pregnancy and Birth

The use of legislation and court decisions to control a pregnant woman's behaviour in situations where a fetus is thought to be at risk* — that is, judicial intervention in pregnancy and birth — provides an example of how technological developments can raise new ethical issues for society. The increasing incidence of judicial intervention has occurred in part because recent technological and medical developments have contributed to the ability to visualize, and hence to conceptualize, the fetus as an entity separate from the pregnant woman.

Technology, by enabling us to "see" the fetus, in particular through clearer and more detailed ultrasound images, provides a graphic depiction of the fetus that was previously not possible. Other medical technologies have reinforced this impression among medical practitioners and in society generally: prenatal diagnosis contributes to the perception of the fetus as a separate being with a specific medical condition that can be detected before birth; the ability to sustain newborns of lower and lower birth weight outside the womb changes perceptions of a fetus at the same stage of development *in utero*; and the emerging capacity to perform fetal surgery for certain conditions reinforces the view of the fetus as a separate patient. This new way of conceptualizing the fetus is even apparent in popular media images and illustrations portraying the fetus as an isolated entity suspended in an unidentifiable medium — seldom acknowledging the presence of the pregnant woman's body, without which the fetus cannot exist.

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* Legislation and policies that apply specifically to pregnant women and women of childbearing age in the workplace (for example, exclusionary or protectionist laws and policies concerned with exposure to harmful substances in the workplace), while relevant to our mandate, are covered in Chapter 13, "Exposure to Harmful Agents in the Workplace and the Environment and Infertility."

The tendency to see the fetus as a separate entity is evident in a good deal of legislative and judicial activity in jurisdictions across North America. Although this is more evident in the United States, the tendency exists in Canada as well. The province of New Brunswick has extended its child protection law to include the fetus in its definition of "child," and in 1989 the Law Reform Commission of Canada proposed a new category of "crimes against the fetus." In one reported Canadian case, a woman was required to undergo a Caesarian section considered necessary for the health of the fetus, and in another a woman who was 8-1/2 months pregnant was ordered to remain in a hospital ward until she had given birth. A woman's consumption of alcohol during pregnancy was also characterized by a court as physical abuse — in other words, existing child welfare legislation was construed to apply to the fetus. (See box for developments in the United States.)

Judicial Intervention in Pregnancy and Birth: Recent Developments in the United States

One major area of legislative activity in the United States involves the extension or creation of criminal offences to deal with the infliction of harm on a fetus. General homicide provisions have been extended to include the unlawful killing of a viable fetus, and a new offence of "feticide" has been created in several states. As well, offences relating to fetal abuse or neglect have been developed, including the offence of failure to provide the necessities of life, such as food and medical care, to a child conceived but not yet born. As an indication of the degree to which the criminal law is being employed in this context, the American Civil Liberties Association reported that in the first six months of 1990, South Carolina prosecuted 18 women for criminal neglect arising out of drug use during pregnancy.

Another use of the criminal law involves the sentencing of pregnant women who are charged with offences to "protective" incarceration in the belief that prison would provide a safer environment for their fetuses. Women who have been convicted of child abuse or related offences have also been ordered to use contraceptives or offered sterilization as a condition of probation.

In addition to the use of the criminal law, judicial intervention in the United States has taken the form of forced blood transfusions over the religious objections of a pregnant woman in the interests of the fetus, and court-ordered Caesarian sections. Advance directives declining medical treatment in case of supervening incompetence ("living wills") have been deemed to be of no force and effect during pregnancy. As well, courts have suggested that a child could sue the mother for damages arising as a result of the mother's actions during pregnancy.

Changing ideas about the fetus, fostered by technological development, have the potential for both positive and negative consequences. On the positive side, for example, society has become increasingly aware of the effects on the health of the fetus of nutrition and tobacco and alcohol use

during pregnancy. Information gained through prenatal diagnosis can allow fetuses with certain anomalies to be treated at birth, and, in much rarer cases, treatment prenatally can lead to the birth of a healthier child.

At the same time, society must be aware of the ethical and legal difficulties inherent in regarding the fetus as a patient who is separate from the pregnant woman. Considering the interests of the fetus in isolation from those of the woman has the potential to establish adversary relationships that, at their extreme, can lead to efforts to force the pregnant woman to act in the interests of this "separate patient." This may mean that a woman's right not to be subject to unwanted interference with her physical integrity is taken away from her, with serious implications not just for that woman, but for all women who become pregnant.

Judicial intervention tends to occur when the ethic of care has broken down — situations that the Commission seeks to prevent. What should society do to protect the fetus? Should it empower the courts to over-ride a pregnant woman's refusal of health care? Should it enact legislation of some kind? Or are other measures more appropriate? In the next few pages we consider the issues raised by judicial intervention in pregnancy and birth. We outline the views of Canadians and discuss the issues from both a legal and an ethical perspective, with a view to reaching conclusions and recommendations that reinforce or re-establish the ethic of care in such cases.

Judicial Intervention Defined

Our mandate directed us to examine "judicial interventions during gestation and birth." This examination involved considering how legislation and court decisions are or may be used to control a pregnant woman's behaviour. Such judicial intervention usually occurs when a woman is believed to be endangering the fetus she is carrying by refusing medical treatment believed necessary for fetal health, by abusing drugs or alcohol, or by engaging in behaviour such as prostitution. The matter is typically brought before the courts by a children's aid society, a health care facility, or, in some cases, a physician.

Judicial interventions during gestation and birth can take several forms. Canadian courts, for example, have ordered pregnant women to refrain from specified behaviours and to undergo certain medical procedures considered necessary for the health of the fetus. (See box for how Canadian law has been used as the basis for judicial intervention.) U.S. courts have issued similar directives, ordering women to engage or not to engage in certain behaviours during pregnancy, to undergo Caesarian section and other medical treatment, and to be incarcerated until they had given birth.

Judicial Intervention in Canada

Several legal avenues have been used to justify judicial intervention in pregnancy and birth, but most cases have involved child welfare law. These cases are considered by many legal scholars to be exceptional, and the use of the law for this purpose has been heavily criticized. If such uses continue to be repeated in future, they will no doubt give rise to court challenges under the *Canadian Charter of Rights and Freedoms*.

In *Re Children's Aid Society for the District of Kenora and J.L.*, the Ontario Provincial Court ordered Crown wardship of a child born suffering from fetal alcohol syndrome. The Court held that the child was "in need of protection," within the meaning of the provincial child welfare act, both *prior to* and after its birth, on the grounds that the mother's excessive consumption of alcohol during pregnancy constituted physical abuse of the child and that her refusal to seek treatment during pregnancy endangered the child's health. Although the apprehension occurred after birth, this case is significant in its characterization of prenatal abuse and in its finding that existing child welfare legislation could be construed to apply to a fetus.

Another case had a different outcome. In *Re A. (in utero)*, which involved an application for Crown wardship of a fetus, an interim order was sought subjecting the fetus to the supervision of the Children's Aid Society. The terms of the order would have required the mother to submit to prenatal medical supervision or, in the event of her refusal, to be detained in hospital until the birth of the child and undergo all medical procedures deemed necessary for the well-being of the fetus. The court noted that the Society had legitimate concerns for the welfare of the fetus, but it refused the application on the basis that Ontario's child welfare legislation does not accord a fetus the right to protection. The court also held that its *parens patriae* jurisdiction did not authorize judicial intervention on behalf of the fetus, stating:

> ... here the child is actually inside of the mother. It is, therefore, impossible in this case to take steps to protect the child without ultimately forcing the mother, under restraint if necessary, to undergo medical treatment and other processes, against her will. I believe that the *parens patriae* jurisdiction is just not broad enough to envisage the forcible confinement of a parent as a necessary incident of its exercise. Even if it were, however, the court should be very wary about using its powers in such instances, as its routine exercise could possibly lead to some abuse of pregnant mothers.

The criminal law has also been used as a basis for judicial intervention.

(*continued in next box*)

Judicial Intervention in Canada *(continued)*
Canadian Cases

Criminal Law
The criminal law was used to intervene in pregnancy in *R. v. McKenzie*, a case where a pregnant woman was convicted of communicating for the purpose of prostitution and failing to appear in court. The judge stated "... the only way to protect this child is to have this child born in custody ..." Accordingly, he sentenced the woman to 60 days in jail and ordered that she remain in a hospital ward until the child was born.

Constitutional Issues
Constitutional arguments have been raised in only one reported Canadian case of judicial intervention. *Joe v. Director of Family and Children's Services* involved an appeal of an order made under the Yukon *Children's Act*. The act provides that where a fetus is subject to a serious risk of fetal alcohol syndrome or other injury as a result of a pregnant woman's use of addictive or intoxicating substances, a judge can order the woman to participate in supervision or counselling. The court concluded that the section interfered with the pregnant woman's right to liberty under section 7 of the Charter and that the term "fetal alcohol syndrome" was so vague as to result in a lack of substantive fairness. Because Ms. Joe had complied with the order by the time of the appeal, however, this issue was moot.

Few cases have reached the courts in Canada, because the women most likely to encounter this situation are often in no position to resist and therefore they comply with the wishes of a physician or child welfare authority. An examination of the cases that have been reported shows that the women most likely to be subjected to judicial intervention are disproportionately poor, Aboriginal, or members of a racial or ethnic minority — all factors that influence their capacity to resist intervention. Whether overt discrimination is at work or whether the life circumstances of these women are such that their behaviour during pregnancy is more likely to come under scrutiny is difficult to disentangle.

Judicial intervention is an issue for all women in Canada, however, regardless of socioeconomic status, because its implications go beyond the consequences for an individual woman; it is an issue for women more generally if becoming pregnant means that they waive the constitutional protections afforded other citizens.

The Views of Canadians

An understanding of these issues was evident in the testimony Commissioners heard. It was clear, for example, that Canadians are aware

of the difficult situations that give rise to attempts at judicial intervention and would like to find a way of responding to these situations that is respectful of women's autonomy and constitutional rights while also providing the means to demonstrate concern for at-risk fetuses. Thus, we heard from Canadians both a concern that women not be coerced or their rights infringed and a concern for society's responsibilities in relation to the well-being of the fetus. The Commission also heard thoughtful recommendations about what society's response should be in these situations.

The Canadian Bar Association, for example, stated that "The fetus should be protected by the provision of medical, social, and educational services to pregnant women and to women at risk generally in society." In a similar vein, the British Columbia Association of Social Workers wrote,

> Any state efforts to protect the fetus must recognize that the well-being of the fetus is best protected by ensuring pregnant women have adequate socio-economic resources. This means social programs and social policies should attend to the well-being of women before, during and after pregnancy. The conditions of pregnant women's lives cannot be ignored in the context of society's compelling interest in fetal well-being. *(Brief to the Commission from the British Columbia Association of Social Workers, February 1991.)*

The Manitoba Association for Childbirth and Family Education summed up the concerns of many witnesses:

> [We] would certainly agree that women who are willingly pregnant have a moral obligation to safeguard their unborn babies to the best of their ability. However, we feel that judicial intervention in pregnancy and childbirth is a very poor way to achieve this ... [P]unishing a woman for abusing drugs, failing to get medical attention or otherwise endangering her fetus places all the responsibility for the well-being of the unborn on the shoulders of the mother without offering any concrete support to her. A punitive approach doesn't address the poverty or social problems which may have created the abusive situation [in the first place]. *(A. Basham, Manitoba Association for Childbirth and Family Education Inc., Public Hearings Transcripts, Winnipeg, Manitoba, October 23, 1990.)*

Legal Issues*

Much of the recent debate about judicial intervention has centred on the legal status and rights of the individuals involved and the status of the fetus. Two points are particularly relevant. First, under Canadian law, a fetus does not have independent legal or constitutional rights; whether we look at Anglo-Canadian common law or Quebec civil law, a human being

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* See Annex for dissenting opinion.

does not acquire legal rights until he or she is born alive. It follows that a third party cannot volunteer to defend the "rights" of a being that has no legal existence.

Second, women have constitutionally protected rights to equality, liberty, and security of the person, as well as the right to refuse medical treatment. These constitutional rights of women, which are set out in the *Canadian Charter of Rights and Freedoms* and interpreted through court decisions, are fundamental to human dignity and autonomy, for they are basic concepts in human rights. Like other women and men, pregnant women therefore have a constitutional right to refuse unwanted medical treatment or control that threatens their bodily integrity or interferes with their ability to make independent decisions about their medical care.

It follows that compelling a pregnant woman to conform to certain standards of behaviour, or requiring her to undergo surgery or other invasive procedures, would constitute an unacceptable violation of her individual rights and her equality rights. It would also have adverse effects on the rights of women generally in Canadian society by imposing on pregnant women a standard of behaviour not required of any other member of society. As the Supreme Court of Canada has confirmed, discrimination on the basis of pregnancy constitutes sex discrimination.

Permitting judicial intervention therefore has serious implications for the autonomy of individual women and for the status of women collectively in our society. All individuals have the right to make personal decisions, to control their bodily integrity, and to refuse unwanted medical treatment. These are not mere legal technicalities; they represent some of the most deeply held values in society and form the basis for fundamental and constitutional human rights.

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A person can be found mentally incompetent to make these decisions under provincial mental health laws only in a very narrow range of circumstances; drug and alcohol addiction (whether during pregnancy or not) would rarely, if ever, qualify as such a circumstance. The use of mental health legislation to commit or treat a pregnant woman against her will, even where the language of the statute appears to be applicable, would clearly offend Charter principles.

Moreover, the legal consequence of being found mentally incompetent is simply the appointment of a legal guardian to make decisions on one's behalf. That guardian must, in all cases, make those decisions in the best interests of the incompetent person in question, and not in the perceived best interests of some third party, such as the state or the fetus.

As numerous intervenors pointed out in their testimony before the Commission, women do not give up their right to control their own bodies

or to determine the course of their medical treatment just because they are pregnant. A woman has the right to make her own choices, whether they are good or bad, because it is the woman whose body and health are affected, the woman who must live with her decision, and the woman who must bear the consequences of that decision for the rest of her life. In this respect, pregnant women are no different from any other responsible individual; to treat pregnant women differently from other women and men, or to impose a different standard of behaviour on them, is neither morally nor legally defensible.

Canadian Case Law: The Status of the Fetus

In its 1989 decision in *Tremblay v. Daigle*, the Supreme Court of Canada held that the fetus is not a legal person under Quebec civil law, the Anglo-Canadian common law, or the Quebec *Charter of Human Rights and Freedoms*. The Court also rejected the argument that the potential father had the right to veto the pregnant woman's decision with respect to the fetus, or that a parent or third party could volunteer to defend the rights of the fetus, which has no legal existence.

In considering the general issue of fetal rights, the Court stated that "A foetus would appear to be a paradigmatic example of a being whose alleged rights would be inseparable from the rights of others, and in particular, from the rights of the woman carrying the foetus." In its subsequent decision in *R. v. Sullivan and Lemay*, the Court also held that the fetus is not a person for purposes of the *Criminal Code*.

In its decision in *Borowski v. Attorney General of Canada*, the Saskatchewan Court of Appeal held that the fetus is not protected under section 7 of the Charter and so does not enjoy a constitutional right to "life, liberty and security of the person." The U.S. Supreme Court came to a similar decision under the U.S. *Bill of Rights*. Legal recognition of the fetus has also been rejected in Britain and Australia and under the *European Convention*.

The Ethical View

The Commission's position on judicial intervention in pregnancy and birth, while consistent with the legal and constitutional considerations just described, relies primarily on our ethical stance and guiding principles, which we have applied throughout our report and in our recommendations. Although many legal and constitutional arguments can be made, our conclusions with respect to judicial intervention

Although many legal and constitutional arguments can be made, our conclusions with respect to judicial intervention rest largely on our ethical reasoning.

rest largely on our ethical reasoning. In our view, it is ethically (as well as legally) wrong to suggest that pregnant women's rights to make decisions about their medical care and treatment should be changed or lessened because they are pregnant.

Canadian Case Law: The Rights of Pregnant Women

In its 1988 decision in *R. v. Morgentaler*, the Supreme Court of Canada ruled that, by interfering with their bodily integrity and subjecting them to serious psychological stress, the abortion provisions of the *Criminal Code* (section 251) violated women's rights to liberty and security of the person. The Court found that the abortion provisions impaired women's rights under the *Canadian Charter of Rights and Freedoms* (section 7) and could not be seen as "reasonable limits" that are "demonstrably justified in a free and democratic society" (section 1).

In her decision, Justice Wilson characterized section 251 as a violation of pregnant women's constitutional rights on the basis that "In essence, what [the section] does is assert the woman's capacity to reproduce is not to be subject to her own control. It is to be subject to the control of the state. She may not choose whether to exercise her existing capacity or not to exercise it. This is not, in my view, just a matter of interfering with her liberty in the sense ... of her right to personal autonomy in decision making, it is a direct interference with her physical 'person' as well. She is truly being treated as a means — a means to an end which she does not desire but over which she has no control."

In its 1989 decision in *Brooks v. Canada Safeway Ltd.*, the Supreme Court also ruled that discrimination based on pregnancy constitutes sex discrimination, which is prohibited under federal and provincial human rights law and under the Charter. In his judgement, Chief Justice Dickson asserted that "it is difficult to conceive that distinctions or discriminations based upon pregnancy could ever be regarded as other than discrimination based upon sex."

Consistent with the ethic of care — which is concerned with preventing conflicts instead of trying to resolve them after they arise — we begin by asking questions about how to ensure the best possible prenatal health and the maximum degree of well-being for both the pregnant woman and the fetus. Regardless of whether a fetus is a "person" with "rights," it is clear that the interests of the fetus are worthy of protection: what transpires before birth — the behaviour of the woman during pregnancy, the provision of medical treatment to her and to the fetus — can seriously affect the health and well-being of the child that is eventually born. Society therefore has an interest in promoting the prenatal health and well-being of the fetus and of the woman carrying it.

From the woman's perspective, however, considering the interests of her fetus separately from her own has the potential to create adversary situations with negative consequences for her autonomy and bodily integrity, for her relationship with her partner, and for her relationship with

her physician. Judicial intervention is bound to precipitate crisis and conflict, instead of preventing them through support and care. It also ignores the basic components of women's fundamental human rights — the right to bodily integrity, and the right to equality, privacy, and dignity. Importantly, as we will see, such measures are also unlikely to be effective and may not in fact protect the fetus.

If we impose a legal obligation upon a woman to care for her fetus — even if it were possible to legislate a caring and nurturing relationship — the potential for curtailing women's choices and behaviour becomes staggering. The kinds of substances and activities that could pose a danger to the fetus are many, varied, and increasing: cigarettes, alcohol, drugs (both legal and illegal), environmental pollutants, strenuous exercise, saunas, and inadequate nutrition. As scientific knowledge develops, the list is becoming longer. Many women's management of pregnancy could be subject to challenge and scrutiny, and pregnancy could become the source of potential liability suits against women who failed to comply with certain standards of behaviour. In some cases, fearing a less-than-perfect outcome, a pregnant woman might feel compelled to seek abortion instead of care.

> [There are] questions about the relationship of the pregnant woman to the fetus. That relationship should, surely, be regarded as being different, both legally and morally, from the relationship of the health care facility, of reproductive researchers, and of corporations, to the fetus. When the fetus is within the woman's body, the maternal/fetal relationship may arguably be regarded as a unity, and the competent woman's informed decisions about the fetus and her pregnancy should prevail ... the goal should be to protect and enhance the health of both the fetus and the pregnant woman without infringing upon the woman's reproductive autonomy. Ensuring that a child does not suffer from events that occurred while it was a fetus need not require treating the fetus as a patient, or according the fetus a status independent of the pregnant woman.
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> *C. Overall, reviewer, research volumes of the Commission, August 19, 1992.*

Moreover, the threat of judicial intervention could have significant negative effects on fetal and maternal health. If women knew that they could be confined against their will, forced to submit to medical treatment, or charged with criminal offences, they might well avoid seeking medical care. Unfortunately, those who might avoid seeking care would likely be those who need it most — for example, women who are dependent on drugs or alcohol. As a result, health problems would escape detection and treatment — precisely the opposite effect sought by those who would use judicial means to intervene.

Physicians and Judicial Intervention

Several professional associations have prepared reports concerning a physician's responsibility to a pregnant woman and her fetus. The Royal College of Physicians and Surgeons of Canada has suggested that where the physician's view of what is in the best interests of the fetus conflicts with the view of the pregnant woman, the role of the physician is to provide counselling and persuasion, but not coercion.

The American College of Obstetricians and Gynecologists has also taken the position that it is important for the physician to avoid a coercive role, noting that coercion violates the principle of informed consent and threatens the doctor/patient relationship. The College concludes that resort to the courts is counterproductive and almost never warranted. The American Medical Association has reached similar conclusions and has also suggested that criminal sanctions or civil liability for behaviour by a pregnant woman that could be harmful to the fetus are inappropriate.

The resort to judicial intervention also has serious implications for the relationship between a pregnant woman and her physician. If the physician is perceived to be potentially coercive instead of a caregiver, the woman might begin to withhold information or stop seeking prenatal care, with detrimental consequences for her health and that of the fetus. These dangers are recognized by many professional associations of physicians. Moreover, experience with judicial intervention has shown the uncertainties inherent in diagnosis and treatment; in several cases of judicial intervention, the medical treatment deemed essential by the courts later turned out not to have been necessary. For example, a woman who went into hiding in defiance of a court order to undergo a Caesarian section later gave birth vaginally to a healthy child. Thus, medical and judicial judgements — even those made with the best of intentions — can be mistaken. In addition, the very limited time frame within which most such decisions must be made and acted upon makes the process of judicial intervention unlikely to lead to fully considered, principled, or constitutional conclusions.

Finally, judicial intervention both emerges from and reinforces a social perception of the role of women in reproduction that instrumentalizes them and devalues their humanity and individuality. At the core of the impulse toward judicial intervention in pregnancy and birth is the view that pregnant women are the means to an end — the birth of healthy children. To the extent that judicial intervention reinforces the notion that a pregnant woman's role is only to carry and deliver a healthy child, it denies her existence as an autonomous individual with legal and constitutional rights and is dangerous to the rights and autonomy of all women.

In summary, judicial intervention offers no satisfactory answer to ensuring the well-being of the fetus: it precipitates crisis and conflict, it

ignores women's fundamental constitutional and human rights, it contributes to an instrumentalized view of their role in reproduction — with adverse consequences for women individually and as a group — and, most important, it is not effective in achieving its goal of protecting fetal well-being.

Judicial intervention offers no satisfactory answer to ensuring the well-being of the fetus: it precipitates crisis and conflict, it ignores women's fundamental constitutional and human rights, it contributes to an instrumentalized view of their role in reproduction — with adverse consequences for women individually and as a group — and, most important, it is not effective in achieving its goal of protecting fetal well-being.

Society cannot care for a fetus, in the absence of the pregnant woman's cooperation, without taking control of the woman herself. The physical relationship between the fetus and the pregnant woman and the dependency of the fetus on the pregnant

North American Case Law: Right to Refuse Medical Treatment

The right of individuals to have control over their own bodies is a longstanding principle of Canadian law. An important aspect of this principle is the right to refuse unwanted medical treatment. This right is set out clearly under the Quebec *Civil Code*, as discussed in the 1992 Nancy B. case, which held that a patient has the right to refuse respiratory support. This principle is also protected under Anglo-Canadian common law, as discussed in the 1990 *Malette v. Shulman* case.

In the 1991 case of *Fleming v. Reid*, involving involuntary psychiatric patients, the Ontario Court of Appeal held that the right to be free from non-consensual invasions of one's bodily integrity and to make decisions with respect to one's medical treatment are also protected under section 7 of the Charter.

In its 1990 decision in *In re A.C.*, the District of Columbia Court of Appeals discussed the specific situation of pregnant women in the following terms: "[I]t would be an extraordinary case indeed in which a court might ever be justified in overriding the patient's wishes and authorizing a major surgical procedure such as a caesarean section ... Indeed, some may doubt that there could ever be a situation extraordinary or compelling enough to justify a massive intrusion into a person's body, such as a caesarean section, against that person's will."

Any limits imposed on the rights of pregnant women to refuse unwanted medical treatment would amount to a violation not only of their right to security of the person under section 7 of the Charter, but also, in accordance with the Supreme Court of Canada decision in *Brooks v. Canada Safeway Ltd.*, of their right to sex equality under section 15.

woman for sustenance make this impossible. By forcing medical intervention, society would be requiring pregnant women to do something that is asked of no other individual: to undergo medical treatment for the benefit of another. Even a living child has no right to force a parent to undergo medical procedures for the child's benefit, however morally compelling the case might be. This infringement of bodily autonomy and physical integrity is not justified on any grounds.

This imperative will not change even as research pushes the boundaries of what can be done to treat a fetus *in utero*. For example, if and when surgery on a fetus moves beyond the research stage for a range of conditions, there may be increasing pressure on pregnant women to consent to such procedures. Whether these techniques remain experimental or move into the realm of accepted practice, they must be offered only in the context of the ethical and legal considerations set out in this chapter — that is, in the context of the pregnant woman's autonomy and with her informed consent, based on full knowledge of the nature and risks of the proposed treatment.

An Approach Based on Support and Care

If we reject judicial intervention in pregnancy and birth on moral, practical, and legal grounds, we must return to the question of how to ensure the health and well-being of the fetus and the pregnant woman. How should society respond to a situation where a woman is not caring for her fetus or engaging in behaviour that may harm it? In the Commission's view, the answer lies in examining the reasons for that behaviour and seeking solutions that address them.

Some of the situations that give rise to attempts at judicial intervention are among the most difficult and tragic imaginable. The potential for harm is evident; the dangers to a fetus of alcohol abuse, drug addiction, or sexually transmitted diseases are real and potentially devastating. These situations are all the more distressing because the caring and nurturing assumed to be inherent in the relationship between woman and fetus appear to be absent.

Although many cases involving refusal to follow medical advice or to accept surgical or other medical treatment have involved drug or alcohol abuse, a woman's reasons for choosing a particular course of action may include her socioeconomic circumstances, her educational level, her religious convictions, her cultural beliefs, her fears, or other deeply held values or personal beliefs. Of relevance in this regard is the fact that most of the women who have been subject to judicial intervention to date have been Aboriginal women and women of colour.

Whatever the circumstances, judicial intervention does not provide a solution, because it does nothing to address the circumstances that bring

about attempts to intervene or to create the social conditions and support that help to ensure a successful pregnancy and healthy outcome for both the woman and the child.

Whatever the circumstances, judicial intervention does not provide a solution, because it does nothing to address the circumstances that bring about attempts to intervene or to create the social conditions and support that help to ensure a successful pregnancy and healthy outcome for both the woman and the child.

In reaching this conclusion, Commissioners are acutely aware of the tragic nature of some of the situations that give rise to efforts to intervene in a pregnancy. As members of the helping professions, physicians and child welfare workers face situations that call on their basic human instinct to help where possible — an impulse that is rightly very difficult to resist because it is so fundamental to who they are and the job they do. The decision to respect a woman's autonomy and physical integrity and not to intervene must surely be one of the most difficult decisions any human being would ever be called upon to make. That is why the Commissioners' decision in this matter was reached through long and careful deliberation and consideration of the issues from all sides. We made this decision not because harm to a fetus is acceptable or even tolerable, but because the dangers posed by judicial intervention far outweigh any benefits that a given individual intervention might yield.

A societal interest in pregnancy and birth — to maximize the chances for the birth of a healthy child — is a goal Commissioners strongly endorse; it is an important and worthy goal. But our examination of the legal, ethical, and social implications of judicial intervention leads to the inescapable conclusion that judicial intervention is neither an acceptable nor an effective method of achieving that goal.

In line with the ethic of care, we believe that the best approach is to seek ways to ensure that the needs of both the woman and the fetus are met — in other words, to prevent a situation developing in which child welfare, medical, or other authorities might consider judicial intervention appropriate or necessary. The ethic of care offers a means of avoiding the conflicts inherent in judicial intervention by promoting two fundamental values: respect for the rights and autonomy of the pregnant woman and concern for the health and well-being of the fetus. The best way to accomplish this is not by compelling pregnant women to behave in certain ways, but by providing a supportive and caring environment in which they can make informed decisions and choose from among realistic options before and during pregnancy.

The situations that lead to judicial intervention are inherently distressing because of the commitment we, as a society and as individuals, have to respect human life and dignity — the life and dignity of the pregnant woman, expressed through her autonomy, and that of the fetus, as a potential person. Judicial intervention sacrifices the human dignity

and rights of one for the potential well-being of the other. Taking the alternative route of care and assistance means that the human life and dignity of both woman and fetus are respected — and it may even accomplish what legislation or court decisions cannot: establish a caring and nurturing relationship.

Taking the alternative route of care and assistance means that the human life and dignity of both woman and fetus are respected — and it may even accomplish what legislation or court decisions cannot: establish a caring and nurturing relationship.

Clearly, the vast majority of women will act in a way they believe to be in the best interests of their fetus. The best way to promote prenatal health is therefore to provide the information and support necessary to enable pregnant women to make healthy choices for the well-being of themselves and their fetuses and informing them — in non-coercive, non-judgemental ways — about the implications of their decisions. This includes providing safe and accessible contraception and abortion services; offering accessible and culturally appropriate prenatal care and social services to pregnant women; counselling pregnant women about healthy lifestyles and ensuring they have the means to make these choices, including financial assistance where necessary; and providing information, outreach, and supports in the forms pregnant women need to make informed choices and realistic decisions about care and treatment, particularly for addictions.

The Canadian Bar Association pointed out, in its brief to the Commission, that recourse to judicial intervention should be seen as a failure — a failure to provide policies and programs that sustain a woman's right to manage her pregnancy and to support her decisions with appropriate services and resources in the community. By itself, prohibiting judicial intervention does not fulfil our responsibility as a society to promote the health and well-being of pregnant women. Meeting this responsibility also requires appropriate programs, services, and outreach designed specifically to support pregnant women who are in the difficult circumstances we have outlined. This is not the case at present. In fact, overall, the behaviour that attracts judicial intervention may be less threatening to fetal and neonatal health than the well-documented effects of poverty on a much larger number of pregnancies.

As we discuss in Chapter 14, a variety of appropriately designed supportive programs for pregnant women can at the same time help to ensure the well-being of the fetus. In particular, with respect to pregnant women who endanger the health of their fetuses by using alcohol or drugs, the Board of Trustees of the American Medical Association has recommended that "[p]regnant substance abusers should be provided with rehabilitative treatment appropriate to their specific physiological and psychological needs." Similar conclusions have been reached by this Commission and by others studying the problem of drug use during pregnancy. What is required is ready access to facilities and services that

provide outreach, counselling, and treatment designed specifically for pregnant women that are appropriate to their needs.

Conclusion and Recommendations

In summary, trying to use the law and the courts to protect fetal health can only be counterproductive. Such laws may, on the surface, have appeal, because we all support the goal of the well-being of the fetus, and enacting them may appear to be a logical extension of society's interest in the health of the fetus. But there is nothing in our experience to demonstrate that such laws work in practice. Indeed, there is strong evidence to the contrary, particularly because the instruments available to the courts — forcing action under penalty of fines or incarceration — are brutally blunt and patently unsuited to the goal of promoting anyone's health or well-being. Clearly, if protecting the fetus is the goal, other methods are needed.

A societal interest in pregnancy and birth — to maximize the chances for the birth of a healthy child — is a goal Commissioners strongly endorse; it is an important and worthy goal. But our examination of the legal, ethical, and social implications of judicial intervention leads to the inescapable conclusion that judicial intervention is neither an acceptable nor an effective method of achieving that goal. Because the woman's consent and cooperation are needed to ensure a positive outcome for the fetus, it follows that the most effective way of caring for the fetus is through appropriate support and caring for the pregnant woman. The Commission therefore recommends that

273. Judicial intervention in pregnancy and birth not be permissible. Specifically, the Commission recommends that

- **(a) medical treatment never be imposed upon a pregnant woman against her wishes;**
- **(b) the criminal law, or any other law, never be used to confine or imprison a pregnant woman in the interests of her fetus;**
- **(c) the conduct of a pregnant woman in relation to her fetus not be criminalized;**
- **(d) child welfare or other legislation never be used to control a woman's behaviour during pregnancy or birth; and**
- **(e) civil liability never be imposed upon a woman for harm done to her fetus during pregnancy.**

274. Unwanted medical treatment and other interferences, or threatened interferences, with the physical autonomy of pregnant women be recognized explicitly under the *Criminal Code* as criminal assault.

and that

275. All provinces/territories ensure that they have in place

(a) information and education programs directed to pregnant women so that they do not inadvertently put a fetus at risk;

(b) outreach and culturally appropriate support services for pregnant women and young women in potentially vulnerable groups; and

(c) counselling, rehabilitation, outreach, and support services designed specifically to meet the needs of pregnant women with drug/alcohol addictions.

In conclusion, it is the Commission's view that almost all pregnant women will take steps to maximize their chances of a healthy birth if they have ready access to the information, prenatal care, social services, and income support necessary to do so. In the Commission's view, extending care to the fetus by giving the pregnant woman the support she needs provides the best hope for enhancing the health and well-being of both the fetus and the woman carrying it.

General Sources

Rodgers, S. "Juridical Interference with Gestation and Birth." In Research Volumes of the Royal Commission on New Reproductive Technologies, 1993.

Uses of Fetal Tissue

The most widely known use of fetal tissue, largely as a result of extensive media coverage, is in trials of transplantation treatment that may some day prolong and enhance the lives of thousands of Canadians. Therapeutic use of fetal tissue could result in considerable alleviation of human suffering. The treatment now under research may improve the daily lives of people with such diseases as Parkinson, Alzheimer, and diabetes and many other problems; it may one day enable these patients to move their bodies freely, to remember, or to discontinue insulin injections as the transplanted fetal tissue supplies what is needed. Using fetal tissue transplants to correct these diseases is possible in theory, but whether fetal tissue transplantation research will realize these expectations is simply not known. This means that all the usual ethical concerns about research involving human beings must be applied, and the potential for benefit must therefore be weighed against the fact that the treatment may prove not to work.

It is also essential to recognize that this field of research raises serious social and ethical issues to be considered and addressed. The only reliable source of fetal tissue for transplantation is elective abortions. To some, this makes fetal tissue transplantation inherently wrong; others are concerned about the dangers of commodifying fetal tissue or creating pressure on women to have abortions in order to donate fetal tissue. The possible risks of coercion, commercialization, and promotion of abortion must be evaluated and taken into consideration in deciding whether the use of fetal tissue should be allowed and, if so, under what circumstances.

Transplantation is only one of many medical and scientific uses of fetal tissue, and, although this research has received the most publicity, it represents only a small fraction of the use of fetal tissue at present. Fetal tissue from both spontaneous and elective abortions is studied to learn about normal and abnormal fetal development, as well as the genetic or

environmental causes of congenital diseases, and it is used in the diagnosis of viral diseases and the development of vaccines, in the testing of new pharmaceutical products, and in the education and training of medical and health professionals. Indeed, the use of fetal tissue in medicine goes back at least to the 1920s, and fetal tissue procurement organizations in the United States and Britain have been distributing fetal tissue to researchers for 30 years.

The other uses of fetal tissue raise many of the same ethical issues as fetal tissue transplantation, so that transplantation should be situated in the broader context of fetal tissue use. Although fetal tissue transplantation was mentioned specifically in the Commission's mandate, we looked for information pertaining to all existing and potential uses of fetal tissue. Whether or not fetal tissue transplantation proves successful, society must address the question of the ethical uses of fetal tissue.

In approaching the task of deciding whether to endorse, condemn, or limit the use of fetal tissue in research, the Commission considered many aspects and questions. If the Commission were to endorse some uses of human fetal tissue, should a woman's informed consent be required before tissue from an aborted fetus could be used for research? Or by terminating her pregnancy, would she also have relinquished whatever interests she might have had in the tissue? If her consent were required, what should the timing of it be — could the choice to abort be kept separate from the decision to donate tissue from the fetus? How could society ensure that a woman's consent to either abortion or use of tissue was not coerced? Should specification of the recipient for the tissue be prohibited, to remove any possibility that a woman might conceive with the idea of using the tissue for a specific recipient?

In approaching the task of deciding whether to endorse, condemn, or limit the use of fetal tissue in research, the Commission considered many aspects and questions.

The Commission also needed to consider the potential for financial exploitation or coercion. If research shows that fetal tissue transplants treat disease effectively, what safeguards would need to be in place to ensure that women would not be under pressure to donate fetal tissue? Also to be considered is that increasing demand for fetal tissue could prompt Canadians to look abroad for supplies in jurisdictions where international guidelines on obtaining human tissue are ignored.

These are just a few of the concerns raised by the use of fetal tissue. If fetal tissue transplantation research proves to be successful and matures into more widely used practice, it will be even more important that a clear framework for only ethical use be in place. The Commission's research and Canadians' input to us have shown the importance of establishing a legislative and regulatory framework for this activity. Moreover, this

framework must be national in scope because the interests to be safeguarded transcend provincial boundaries.

In this chapter we document what we learned from Canadians across the country and from our research into the current and future uses of fetal tissue, both in Canada and abroad. We then review some of the laws, regulatory mechanisms, and government policies that have restricted or shaped research and treatment in this field, in Canada and in other jurisdictions. In light of this background, we go on to outline the ethical, legal, and social implications of fetal tissue use. Our recommendations for policy development in this area conclude the chapter.

The Views of Canadians

Commission Surveys

Early in our mandate, the Commission conducted two surveys on the views of Canadians on new reproductive technologies. The results of the first, a qualitative study involving personal interviews and group discussions held in 1990, helped us to understand how much Canadians knew about fetal tissue use and the issues it raises. The second, a telephone survey of approximately 1 500 Canadian adults, gave us some additional insight into Canadians' views and opinions on the subject (see research volume, *Social Values and Attitudes Surrounding New Reproductive Technologies*). Then, between December 1991 and July 1992, we undertook a values survey; questionnaire responses from 7 664 Canadians randomly chosen from across the country were analyzed. In all, more than 9 000 Canadians were asked for their opinions on this topic.

Results from these surveys suggest that fetal tissue transplantation is less familiar to Canadians than other medical procedures in our mandate, such as *in vitro* fertilization and prenatal diagnosis. In the 1990 telephone survey, fewer than half of those interviewed (42 percent) were aware of research using fetal tissue to treat disease. In the 1992 values survey, 62 percent said they were aware of the use of fetal tissue in medical research, although only 18 percent said they were well informed about it.

Although the overall level of awareness of fetal tissue transplantation research was not high, many survey respondents viewed it as a positive development that could be of benefit to society because it might result in treatments or cures for debilitating diseases. In the 1990 telephone survey, for example, 84 percent of respondents stated that the use of fetal tissue to treat fatal diseases should be allowed, while only 12 percent opposed it. Respondents who endorsed fetal tissue transplantation often likened it to organ donation. When asked whether they personally would want to undergo treatment using fetal tissue if they were suffering from a serious disease, 72 percent said that they would.

There was also widespread support (77 percent) for the use of fetal tissue in medical research, while 16 percent opposed it. In both the 1990 and 1992 surveys, the level of support for the use of fetal tissue in treatment or research was slightly higher among men than among women (a margin of four to nine percentage points) and among individuals with higher levels of education.

As shown in Table 31.1, there was widespread agreement (77 percent) that fetal tissue should not be used for non-medical, commercial purposes. Respondents feared that permitting this use of fetal tissue would promote the commercialization of human reproduction. During the personal interviews, the need for regulation and control emerged as a key concern; participants predicted that any prospect of financial gain could increase the demand for fetal tissue and prompt the creation of financial inducements for women to initiate and terminate pregnancies. Participants also objected if the proposed use was purely cosmetic, which they considered trivial by comparison with curing neurological disease and advancing scientific knowledge.

Table 31.1. Permissibility of Using Fetal Tissue

Use	Allow	Do not allow
To treat disease	84%	12%
Medical research	77%	16%
Commercial purposes	18%	77%

Source: Angus Reid Group Inc. "Reproductive Technologies — Qualitative Research: Summary of Observations." In Research Volumes of the Royal Commission on New Reproductive Technologies, 1993.

Submissions to the Commission

The Commission also heard a wide range of views from experts and interested parties, laypersons, and interest groups at public hearings and through written submissions and telephone calls. Some anti-abortion, family, and religious groups argued that fetal tissue should not be used in research or therapy because this may promote abortion. Some stated that the use of fetal tissue from miscarriages and ectopic pregnancies was ethically acceptable, but that the use of tissue from elective abortions was not. Some felt, for example, that women might be more likely to abort a pregnancy if they believed they were thereby contributing to medical

research. Concerns were also raised that the demand for human fetal tissue would create social pressures encouraging women to abort pregnancies about which they were ambivalent. Some people also believed that if fetal tissue research expands, doctors might encourage women to abort in order to secure an adequate supply of fetal tissue. Others thought that the care of women having an abortion could be compromised because of researchers' desire to obtain tissue at a specific stage of fetal development. Some speculated that commercialization of fetal tissue would occur and would encourage women to initiate and terminate pregnancies in response to financial incentives.

Others were concerned that women might initiate a pregnancy in order to recover fetal tissues for a particular recipient, such as an aging parent with Parkinson disease or a child in need of organ or tissue transplantation. At least one case has been reported in the medical literature (in Hungary) where a pregnancy appears to have been terminated expressly to provide fetal tissue for transplantation.

> No woman, professional/lay person, or medical personnel [should] receive any inducement or reward, monetary or otherwise, for making fetal tissue available or to terminate a pregnancy.
>
> *Brief to the Commission from the Canadian Baptist Federation, October 29, 1990.*

Some objections to the use of fetal tissue for transplantation hinged on the misperception that the tissue used is taken from fetuses that are still alive. This misperception may result from the fact that after a fetus (or an adult human being) dies, the various tissues of the body die at different times — some cells and tissue remain alive (or "viable") for several hours. Fetal cells taken after fetal death may be viable for some time and, if placed in an appropriate culture medium *in vitro* or if cryo-preserved, may remain viable for months or years. Some fetal tissue research requires that the tissue be viable in this sense, just as research with tissues taken from an adult may require it. It is important that this use of viable or living fetal tissue not be confused, however, with the use of a viable or living fetus.

> We urge the Canadian government to: outlaw buying and selling of human fetal tissue; nationalize such tissue; [and] appoint a Government Board to oversee the acquiring, distribution, use, and disposal of such tissue. Membership should be appointed from the medical, scientific, religious communities, and half should be female. The Blood Bank is a good model to follow in running this organization.
>
> *Brief to the Commission from the Halifax Monthly Meeting [Quakers], December 20, 1990.*

Commissioners heard a full range of views on these issues. From representatives of Alliance for Life in Montreal, we heard:

> Scientific research should not be conducted on embryos or on fetal tissue resulting from induced abortion, nor should such tissue be utilized for transplantation into other people suffering from disease. Such uses would legitimize abortion [and] have the potential of encouraging acceptance of it, and of increasing the type and numbers of abortions, as well as the gestational age at which [abortion] is performed. In all cases of induced abortion it is impossible to get proper informed consent. *(A. Kiss, Alliance pour la vie, Public Hearings Transcripts, Montreal, Quebec, November 21, 1990.)*

We also heard from representatives of the Canadian Abortion Rights Action League in Halifax, who said:

> It is argued that women will be forced to become pregnant and to abort. We point out that there is no evidence to support this theory. Women in society in general need to be vigilant against coercion of any kind for any reason. It is argued that commercialization of fetal tissue will proliferate. Again, this is an example of scare-mongering. Canada has no tradition of commercializing donated blood or body parts ... It is said that women will be asked to delay abortions to maximize chances of success for recipients. However, where research is underway, there is a clear policy to separate the abortion procedure from fetal tissue transplant therapy.
>
> Finally, opponents argue that fetal [tissue] transplantation shows disrespect for life and a disrespect for fetuses. This argument can only be made by people who wish to grant legal status to the fetus. In fact, such an argument grants a greater status to fetus[es] than to people, inasmuch as research on human cadavers is an established part of medical education and practice and does not imply a disrespect for human life nor for human beings. *(K. Holmwood, Canadian Abortion Rights Action League, Public Hearings Transcripts, Halifax, Nova Scotia, October 18, 1990.)*

These two views summarize a great deal of the input Commissioners heard on this issue. What we found most interesting about the written and oral submissions was that, apart from the obvious difference of opinion about the status of the fetus, the values expressed by participants had much in common. No one favoured the commercialization of fetal tissue. All opposed the exploitation of vulnerable women, the deliberate undertaking of a pregnancy to produce fetal tissue for a particular use, and the use of abortion methods that were not in the best interests of the pregnant woman.

Thus, despite the range of views, there was also a significant degree of congruence on some aspects of these issues. Indeed, it seems that many of the concerns and disagreements among Canadians about fetal tissue use stem from a shortage of information about this research, about the feasible

sources of fetal tissue and its alternatives, and about the mechanisms for regulating research. To help address this lack of information, we commissioned a series of studies examining research involving the use of fetal tissue, its future directions, its current conduct in Canada and abroad, the source of fetal tissue, and current regulations in Canada and abroad. (For a brief review of policies in other countries, see Appendix 1.) We focussed particularly on research into whether fetal tissue can be used to alleviate disease, since this is the aspect that generates most public concern. Our findings are discussed in the next few sections.

> Apart from the obvious difference of opinion about the status of the fetus, the values expressed by participants had much in common ... Thus, despite the range of views, there was also a significant degree of congruence on some aspects of these issues.

Uses of Fetal Tissue

Fetal tissue has a wide variety of uses, including experimental transplantation treatment, basic medical research, the development and testing of pharmaceutical products, pathology testing, viral diagnostics, and medical education.

The best-known use of fetal tissue involves research into the development of experimental treatments, such as fetal tissue transplantation for Parkinson disease. However, fetal tissue is also used in basic research to increase knowledge about human functioning and disease processes. This may involve, for example, the study of the form and structure of organs or cells using dead tissue. Other basic research involves *in vitro* culture of living tissue or cells to study the biochemical and physiological processes of fetal development and the genetic or environmental bases of various diseases. Disciplines involved in this research include anatomy, pathology, genetics, cytogenetics, endocrinology, biochemistry, and molecular biology.

Fetal tissue can also be transplanted into animals to create animal models of various human diseases. For example, fetal blood-generating cells (haematopoietic stem cells) have been transplanted into a strain of mice that are unable to reject the cells because the mice have an inherited immune deficiency. The cells give rise to human blood cells in the mice, offering an animal model in which disorders of the human blood system (including leukemia and AIDS) can be studied.

Fetal tissue has also been used for many decades in the development and production of pharmaceutical products, such as vaccines against polio, measles, rubella, and other diseases. The 1954 Nobel prize for medicine was awarded for work on the polio vaccine using fetal kidney cell cultures.

It has been reported that fetal cells in culture are also used to screen new pharmaceutical products for toxicity or to identify carcinogens or agents causing congenital anomalies. For example, the U.S. National Institutes of Health funded research examining fetal tissue to determine the carcinogenicity of tobacco smoke from active and passive smoking.

Fetal tissue is also used in the diagnosis of human viral diseases, including hepatitis, influenza, and HIV. Cultures prepared from fetal tissues allow a more accurate and rapid diagnosis of certain viruses than any other method, and some viruses can be isolated only in spongioblasts derived from fetal brain tissue.

However, the most frequent category of fetal tissue use is for pathological examination or testing. Fetal tissue from spontaneous abortions is subject to a routine pathology examination in hospitals. Abnormalities may be identified, helping to diagnose the cause of the pregnancy loss. This is part of normal patient care and helps physicians care for and advise women on future pregnancies. Fetuses from therapeutic abortions are also examined by hospital pathology services. Hospitals in Canada have a general policy of examining all tissue removed surgically, as part of quality assurance, and indeed this is required under provincial/territorial legislation. In the case of therapeutic abortions, the pathology examination is used to verify the pregnancy, to ensure that fetal tissue has been evacuated during the abortion, and to check for any abnormalities in the fetal tissue.

The most frequent category of fetal tissue use is for pathological examination or testing ... Hospitals in Canada have a general policy of examining all tissue removed surgically, as part of quality assurance, and indeed this is required under provincial/territorial legislation.

Finally, fetal tissue and fetal specimens are used in the education and training of medical, nursing, and other health sciences students so they can learn about normal human development and the disease processes that may affect it.

Some commentators include all these uses of fetal tissue under the general heading of "research." Indeed, circumstances do exist in which each of these uses of fetal tissue could be part of an experiment or research project. However, it is important to realize that most of these uses of fetal tissue have been routine for many years, an everyday part of clinical practice, pharmaceutical methods, or medical education. Although some uses of fetal tissue involve research and experimentation, to describe all uses of fetal tissue as "research" ignores the extent to which certain uses of fetal tissue are well established in the health care system. Taken together, these diverse uses of fetal tissue have provided invaluable new knowledge about human health, have prevented much human suffering (for example, from polio), and have led to greater understanding of disease processes.

Potential Usefulness of Fetal Tissue for Transplantation

The particular use of fetal tissue that has received the most public attention is transplantation. In the past two decades, human organ transplantation and tissue replacement using organs and tissues (from adults and children) have found a valuable role in medical care. Transplant recipients' survival rates have increased significantly. Better procedures and new anti-rejection drugs have revolutionized the therapeutic potential of transplanting human organs and tissues. As a result, procedures once considered experimental, such as corneal and kidney transplants, have become recognized and valuable medical procedures.

Fetal tissue has certain unique biological properties that make it particularly valuable for transplantation. Because of these advantages over adult tissue as a transplant material, there appears to be a strong possibility that some forms of fetal tissue transplantation could become recognized medical practice in the next few years. The advantages of fetal tissue as a transplant material include

- its capacity for growth and differentiation;
- its ability to survive culture and manipulation *in vitro*;
- its different immunological properties; and
- its potential to restore function in a transplant recipient.

Growth and Differentiation

In general, fetal tissue cells, both human and animal, exhibit a remarkable capacity for change and differentiation; they are also more able to migrate and form new intercellular connections and to extend new fibres both in transplant recipients (*in vivo*) and in the laboratory (*in vitro*), making them particularly useful for transplantation.

Differentiation refers to the process whereby cells become more and more specialized — in both form and function — to do a particular job in the body. The capacity for differentiation is greatest at early stages of fetal development and diminishes as the fetus develops; the capacity is largely lost in many tissues by the end of fetal development. Once this has happened, each cell has assumed its lifelong assignment — for example, to be a skin cell — and there is very little possibility of its changing function — to become, for example, a bone cell (redifferentiation).

Culture *In Vitro*

Fetal cells are more resistant to damage, both during *in vitro* manipulations and after transplantation. One reason is that they are able to survive at lower oxygen levels than adult tissue cells. Another is that

immature fetal cells are less strongly attached to one another than adult tissue cells are, making fetal cells less likely to rupture while they are being separated and prepared for transplantation.

Cells in early fetal tissues may continue to divide in the laboratory, while the cells from many adult tissues, such as brain and heart cells, do not. Fetal cells also divide more rapidly and more often than those adult cells, such as liver cells, that will multiply under appropriate laboratory conditions. Selection of specific cell types *in vitro* may be aided by this robustness.

The capacity of fetal cells to divide and grow *in vitro* has led to research interest in the development and maintenance of cultured fetal cell lines. If these cell lines could be frozen and thawed successfully, they could provide a secure source of material for both research and therapy, reducing the need for continuing access to new sources of fetal tissue.

Immunogenicity

The most important obstacle to successful transplantation is the rejection of transplant material by the recipient. The host immune system recognizes the transplanted material as genetically distinct from itself — as it does with infectious bacteria or viruses — and initiates a destructive immune response.

In recent years, transplant results have been improved dramatically by the use of more advanced methods of matching potential donor tissue with that of the recipient, and by the use of drugs, such as cyclosporin, that suppress the body's immune response. Immunosuppression is not always successful, however, and tissue and organ rejection remains a major problem. Serious side effects from immunosuppressive drugs are frequent, and patients are more susceptible to infections that can result in death. Moreover, the drugs often must be taken for a lifetime.

The proteins on cell surfaces (antigens) that provoke an immune response begin to appear only as development proceeds in various tissues, so that fetal tissues may provoke less immune response. In addition, fetal tissues do not contain cells that elicit graft-versus-host disease (where the cells in the graft harm the host), which makes them more desirable for transplantation.

Restoration of Function in Transplant Recipients

Extensive animal studies have looked at the growth and functional capacity of transplanted animal fetal cells of various types. It has been found that these fetal cells may produce high levels of certain substances in their host — including factors that induce blood vessel formation and neuron survival — that can enhance their growth as grafts and that may also facilitate regeneration by surrounding tissues in the recipient.

Animal studies indicate that there is demonstrable and clinically significant growth and functional recovery by transplanted fetal cells in animal models for Parkinson disease and Type I (juvenile or insulin-dependent) diabetes. Such studies provide the rationale for clinical trials using fetal tissue transplantation in human patients when conventional treatments fail.

Given all these characteristics of fetal tissue, it is not surprising that researchers in the area of transplantation have looked to fetal rather than adult tissue as a source of transplantation material. Indeed, the use of human fetal tissue for transplantation is not new. The first attempts at transplanting fetal pancreas tissue to treat diabetes occurred in the 1920s. However, recent scientific developments mean the number of potential disorders that may be treatable through fetal tissue transplantation has increased. Studies in the Commission's research volumes outline the disorders being explored for possible treatment in this way. Most research to treat the diseases is at an early stage and is often theoretical or involves animal experiments, but fetal tissue has been used in human subjects in Parkinson disease, Alzheimer disease, and diabetes mellitus, among others. However, the only research in Canada using fetal tissue transplantation in human subjects at present is one trial for Parkinson disease, at the Victoria General Hospital in Halifax (see Appendix 2).

Future Directions in Fetal Tissue Research and Treatment

It is difficult to predict what the future of this research will be, but hopes are that fetal tissue transplantation will be useful in treating a range of disorders. For example, fetal neural tissue transplants may be used in the near future to treat Alzheimer disease. It has also been speculated that patients with other neurological disorders may benefit in the more distant future. Similarly, fetal liver tissue transplants may be used in the future to treat diseases currently treated through the use of bone marrow transplants; many blood disorders are theoretically future candidates for this approach. It has been speculated that eventually fetal liver tissue might be able to be used to restore function that has been depleted by anti-cancer therapy, thereby allowing use of higher doses of anti-cancer medication or irradiation. (For further information on future directions for fetal tissue transplantation, see research volumes.)

Fetal tissue may also be used more in future to create models of human disease in animals, so they can be studied more easily, and to produce antibodies for therapeutic purposes. It is important to remember, however, that many of these future uses of fetal tissue are quite speculative, and some are many years away from being investigated.

Information on Uses of Fetal Tissue in Canada

Although the future uses of fetal tissue remain speculative, Commissioners wanted to know how fetal tissue is being used in Canada today. We discovered, however, that relatively few data were accessible regarding the use of fetal tissue in this country; in part, this is because of the large number of sites at which medical research takes place and because of the range of funding sources for medical research, including both governmental and non-governmental sources. As a result, data on research projects and uses of fetal tissue in research are not centralized in one location.

Non-governmental sources have supported various forms of fetal tissue research in Canadian laboratories, including fetal tissue transplantation research. For example, The Parkinson Foundation of Canada helps fund the clinical trial of fetal tissue transplants for Parkinson disease in Halifax.

The leading federal agency supporting research in the health sciences, including fetal tissue research, is the Medical Research Council of Canada, which provides about 30 percent of the funds for medical research in Canada. Our consultations with Canadian scientists suggested that the MRC has provided funds totalling several million dollars over the last three decades for research using fetal tissue. This research has investigated a wide range of subjects, including the regulation and effects of fetal hormone secretion, the normal and pathologic development of fetal organs, the chromosomal make-up of cells from normal and abnormal fetuses, and aspects of fetal tissue metabolism, including generation or elimination of toxic or therapeutic compounds. The research has been directed to understanding fetal health and disease, as well as health and disease in pregnant women; in fact, Canadian research has made significant contributions to knowledge that has provided the foundation for advances in reducing illness and death in newborns.

The Minister of the Department of National Health and Welfare stated in the House of Commons in July 1988 that federal funds would not be used for research involving the use of fetal tissue transplantation in human beings.[1] Since then, the MRC has received no requests for funding for such research.

The U.S. government banned federal funding of transplantation of tissue from elective abortions in 1988; the ban was rescinded by President Clinton in January 1993. The Canadian decision regarding federal funding of fetal tissue transplantation research will not likely be revisited until the Commission has reported.

In summary, it was not possible to obtain complete data on the use of fetal tissue in research in Canada. This is not the case in Britain, where a centralized fetal tissue bank collects and distributes fetal tissue to

researchers and publishes annual reports listing the research projects that receive fetal tissue from the bank.

It is clear, nevertheless, that many research groups in Canada have used human fetal tissue for their investigations during the last three decades and that many studies are currently in progress. As far as we can determine, these research projects have been carried out at universities, hospitals, or other non-profit institutions, using tissue collected from local hospitals. In recent years, they have been conducted with institutional research ethics board approval, in accordance with the 1987 MRC *Guidelines on Research Involving Human Subjects*, which have been adopted by all schools of health sciences in Canada and their affiliated teaching hospitals and research institutes.

However, these research projects are just one aspect of the handling and use of fetal tissue in Canada. As we noted earlier, fetal tissue is used in many other ways, such as pathology testing and medical education, and we felt it was important to get Canadian data on the entire spectrum of fetal tissue use. We wanted to know how much fetal tissue is collected and who has access to it, for what purposes, and according to what guidelines. To get a sense of this larger picture, we surveyed every health care facility from which fetal tissue could be obtained. This was one component of a larger study intended to identify how all reproductive tissues obtained in these facilities are used or handled. (The results of this survey as they pertain to the handling of gametes and zygotes/embryos were discussed in Chapter 22.)

Health Care Facilities, Abortion Clinics, and Medical Laboratories in Canada

As detailed in our research volume entitled *Background and Current Practice of Fetal Tissue and Embryo Research in Canada*, a survey of Canadian health care facilities offering obstetrical or gynaecological services was conducted for the Commission between November 1991 and February 1992. Among the 642 facilities on which the survey results are based, 80 reported that they did not handle abortuses or fetal tissue. Of those that did, most reported that they disposed of fetal tissue after it had undergone routine pathology testing. However, 83 facilities said they provided tissues to other institutions, laboratories, or individual researchers, while 5 facilities said they retained these tissues, at least in part, for in-house research.

The research team conducting the survey thought some of the respondents might not have been aware of how their facility handled reproductive tissues, or of the purpose for which tissues were distributed to outside agencies. To get a clearer picture of the overall use of fetal tissue, the Commission undertook a follow-up survey in May and June 1992 of the 60 medical laboratories identified in the previous survey as recipients of reproductive tissue, including fetal tissue. Of the 48 medical

laboratories that responded, 31 reported handling abortuses/fetal tissues in particular. Of these, all used fetal tissue for pathology analysis. This is clearly the most common use of fetal tissue in Canada. After examination or testing, nine laboratories disposed of the fetal tissue in-house, while others sent tissue to medical waste firms for disposal. Only one laboratory reported using fetal tissue in research.

To complete the picture, the Commission surveyed 23 medical waste firms identified as receiving reproductive tissues. None of these firms reported any use of fetal tissue other than disposal.

These surveys revealed a pattern of fetal tissue use in Canada; the most common, and indeed routine, use of fetal tissue is the examining of tissue from spontaneous and therapeutic abortions in the pathology laboratory, followed by disposal of the tissue through incineration. The pathology testing is done in hospitals and in laboratories; the disposal may be done by hospitals, laboratories, or medical waste firms.

In the relatively few facilities (either hospitals or laboratories) that do conduct research using fetal tissue, a considerable range of projects is being carried out: one example is a study to develop simple, long-term methods of assessing the health of the fetus during pregnancy; another is the clinical trial of fetal tissue transplantation treatment for Parkinson disease being conducted in Halifax. This latter project will play a significant role in establishing international standards for assessing the usefulness of fetal tissue transplantation treatment for this disorder (see Appendix 2).

Our survey indicated that scientists obtain fetal tissue for research either directly from hospitals and abortion clinics or from other investigators who themselves obtain the tissue from a hospital or clinic. No payments are involved, except for the service of transporting the tissue.

Although the survey was comprehensive in its coverage, its results may be incomplete and inaccurate in various ways. One of the more interesting results was that many hospital administrators were not aware of how reproductive tissues were handled and disposed of in their facility. The respondent filling out the questionnaire in each facility may not have been aware of some studies in the facility using fetal tissue samples from abortuses, and there may be no one within the facility who formally collects such data. Another finding was that one-third of the hospitals or clinics handling fetal tissue and disposing of fetal tissue reported having written protocols; two-thirds did not.

Moreover, there may have been differences in the way respondents interpreted the term "fetal tissue research." For example, someone who examines the chromosomes of cells from spontaneous abortions as part of a larger project on chromosomal genetic disorders might think of themselves as engaged in "cytogenetics research," not "fetal tissue research." No standardized terminology is used to discuss and categorize the different uses of fetal tissue.

We believe it is important for Canadians to have accurate and reliable information about the use of fetal tissue in Canada, and that proper record keeping and reporting mechanisms must therefore be in place. Our recommendations at the end of this chapter address this issue.

Pharmaceutical Manufacturers and Biotechnology Companies in Canada

Cell lines in culture, derived from human fetal tissue, have been used for several decades by pharmaceutical and biotechnology companies in the development of vaccines such as the human polio vaccine. Fetal cell lines have also been used to develop various pharmaceutical products and diagnostic tests. We felt it was important, therefore, to determine whether private sector companies in Canada were using fetal tissue.

The Commission surveyed all 67 member companies of the Pharmaceutical Manufacturers Association of Canada in 1992 to assess their use of human fetal tissues in research and development. Of the 55 pharmaceutical companies that responded, none reported any use of fetal tissue, although some believed that the industry may in future invest in research using fetal tissue related to the treatment of Parkinson disease.

The same questionnaire was sent to 26 biotechnology companies that were identified as potential users of human reproductive tissues. Of the 20 biotechnology companies that responded, only 1 reported research related to fetal tissue. It uses human cell lines originally developed from fetal lung fibroblast in the late 1950s and 1960s.

It would appear that there is little use of fetal tissue by the private sector in Canada, although no information is available on the differences between the companies that responded and those that did not. When asked to explain why there was not more interest in fetal tissue, respondents cited concerns about the expense involved and the potentially controversial nature of such research. It is important to note, however, that this survey dealt with the use of fetal tissue in Canada. There is some evidence, discussed below, that fetal tissue is used by pharmaceutical and biotechnology firms in other countries, including firms whose Canadian subsidiaries responded to the Commission's survey.

The Use of Placental Tissue

As part of our survey, we also examined the handling and use of placentas. The research use of placental matter does not raise the same ethical concerns as research involving zygotes, embryos, and fetal tissue. Indeed, placental matter is usually seen as a waste product and is treated in the same way as other waste products of medical procedures.

However, the handling of placental matter has come to public attention as a result of recent newspaper reports that placentas are being sold by Canadian hospitals and exported to France, and that no consent is

obtained for this. Our investigation showed that more than 100 hospitals in Canada sell placentas, for about 35¢ each, to one medical waste firm (Bocknek Ltd.), which then forwards them to the Institut Mérieux in Lyon, France. The Institut Mérieux uses placentas to produce various pharmaceutical products, such as human albumin, polyvalent immune globulins for intramuscular use, and histamine-protective immune globulin, all used in the care of patients. The Institut Mérieux processes between 3 000 and 4 000 tons of placentas each year, collected from 8 000 hospitals worldwide; between 1 and 2 percent of this material comes from Canada. This is the only case we discovered of human reproductive tissue of any kind being exported from Canada.

> Those tissues going to medical waste firms were simply being disposed of, with the one exception of placentas ... The placentas sold by health care facilities are forwarded by the medical waste firm receiving them to the Institut Mérieux in France for production of pharmaceutical products such as vaccines, gamma globulin, and other therapeutic agents.
>
> Provincial human tissue gift acts in Canada forbid the selling of human tissues for medical or therapeutic research. It is evident that placentas are not viewed by these hospitals as coming within the acts but are seen as a waste by-product of childbirth and are classified as "discarded human body material" that would otherwise have to be incinerated.
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> *SPR Associates Inc., "Report on a Follow-Up Survey of Use and Handling of Human Reproductive Tissues (Survey of Medical Laboratories and Medical Waste Disposal Firms)," in Research Volumes of the Commission, 1993.*

Some people have expressed concern that the placentas exported to France are used in the production of cosmetics. Indeed, some of the surveyed hospitals that sold the placentas listed cosmetics among the end uses of the material. So far as we can determine, however, placental material exported from Canada to the Institut Mérieux is used only to produce pharmaceutical products. In the past, a subsidiary of the Institut Mérieux did make cosmetics from human placental tissue using placentas collected in France. When contacted, however, the Institut Mérieux was most emphatic that this is no longer done.

This is not the only use of placental matter; our survey revealed that eight health care facilities retained placental tissue, and nine medical laboratories reported they used placentas for research purposes. Our survey identified more research projects in Canada using placentas than projects using zygotes, embryos, or fetal tissue. Placentas are of great scientific interest because they are the point of connection between the fetal blood vessels and those of the pregnant woman.

We have serious reservations about the current practice of selling placentas to the Institut Mérieux without the woman's consent. We do not

object to the selling of placental material per se. It would cost money to dispose of placental material through incineration, like other medical waste products, a cost that would have to be borne by the public health care system. If these costs can be saved, and if the waste tissue is used to produce pharmaceutical products that are of benefit, this is appropriate. However, we believe that women should be informed that placentas are used in this way and should be given the option of having their placental material disposed of through incineration, if they object. Some women may have religious or other objections to the possible use of their placentas in creating pharmaceutical products, and these should be respected. The Commission recommends that

276. Hospitals obtain consent from women, by means of written consent forms, regarding the disposal of placentas.

Uses of Fetal Tissue in Other Countries

There are few firm data regarding the use of fetal tissue in other countries. Few countries have centralized registries or have conducted national surveys. Arrangements to obtain fetal tissue for study are usually negotiated on an individual basis between researchers and hospitals or clinics in most countries.

An exception is Britain, which since 1957 has had a centralized fetal tissue bank in London, run by the United Kingdom Medical Research Council. Between 1981 and 1986, 124 researchers received fetal tissue from the bank, which distributes between 4 000 and 5 000 tissue samples each year, derived from some 800 fetal specimens. Of these projects, most involved virology (27 percent), molecular biology and genetics (23 percent), immunology (17 percent), tissue culture (15 percent), descriptive embryology (7 percent), haematology (3 percent), and bacteriology (2 percent). Little research is being done into transplantation — the bank has not supplied any fetal tissue for research into transplantation since 1983. Fetal tissue is obtained from local obstetricians, who receive no payment for the tissue. The woman's permission is required before fetal tissue is sent to the bank. The tissue is then distributed to researchers at no cost, except transportation charges. A requirement is that the research for which the tissue is sought has obtained the approval of a local institutional ethics committee.

Similar details regarding fetal tissue use are not available for other countries. However, some information can be gleaned from funding

agencies, agencies that obtain fetal tissue for distribution, and published studies.

In the United States, the National Institutes of Health is the major source of federal funds for medical research. It provided more than $11 million in funding in 1987 for 116 projects involving fetal tissue. These projects used fetal tissue for a variety of purposes: to study the genetic basis of certain diseases (for example, retinoblastoma); the carcinogenicity of tobacco smoke; the process of lung maturation; the transmission of AIDS; and the development of cell cultures used to study disease resistance. As noted earlier, in 1988 the U.S. government imposed a ban, since rescinded, on federal funding of transplantation research using fetal tissue from elective abortions.

A substantial amount of private sector research that involves fetal tissue is also being conducted by U.S. biotechnology and pharmaceutical companies. However, no reliable information exists on the number of companies using fetal tissue or the nature of their research. Examples of private sector research include the development of cell lines for toxicity testing, particularly for medical products that may be used by pregnant women, the development of vaccines, and the development of techniques for transplantation therapy.

Very little is known about how U.S. companies acquire fetal tissue. In some cases, tissues are acquired from specialized procurement agencies. For example, the International Institute for the Advancement of Medicine, a non-profit tissue procurement agency that is the largest U.S. distributor of fetal tissue for research, has supplied fetal tissue to 86 institutions, 19 of which were for-profit corporations. However, private companies in the United States may also receive tissue through informal arrangements with abortion clinics. A 1988 survey by the National Abortion Federation, with responses from more than half its 300 U.S. clinic members, revealed that 11 clinics provided fetal tissue for research programs, which in two cases were carried out by commercial laboratories.

The Council of Europe recently released a report on the use of reproductive tissue, including fetal tissue, in Europe. According to the report, research using fetal tissue is going on in the areas of pathology/testing, viral identification and vaccine development, anatomy/embryology, molecular genetics, the development of animal models of human disease, and transplantation. The Council of Europe report also notes a "persistent rumour" that human fetal tissue is used by European cosmetics firms, but states that this rumour is "without foundation." Animal fetal tissue is used by some French cosmetics firms, and human placental material has been used by cosmetics firms in the past; there appears to be no evidence, however, that human fetal material has been used or is being used by cosmetics firms.[2]

There have been other rumours regarding the commercial use of fetal tissue. In a book on global traffic in commodities, for example, James Ridgeway stated that human fetal tissue has been shipped from South

Korea to Fort Detrick, Maryland, for use by the U.S. Army in investigations of haemorrhagic fever, and that "100 000 fetuses a year end up in research laboratories" around the world. This has been cited as evidence of "a rapidly growing market for human fetuses." However, the Commission was unable to establish the basis for this claim, which remains unsubstantiated.[3]

The solution is to ensure that any fetal tissue used in research is obtained in a controlled, accountable, and ethical way.

Nevertheless, we take very seriously the possibility that fetal tissue could become commercialized and the object of international trade. We believe that the solution is not to ban the use of fetal tissue — since this would deprive society of valuable medical research and treatment, and could also drive the activity underground. The solution is to ensure that any fetal tissue used in research is obtained in a controlled, accountable, and ethical way. This is one of the goals of our recommendations later in this chapter.

Obtaining Fetal Tissue

To be suitable for most research uses, including uses in transplantation research, fetal tissue must have viable cells, be free of significant genetic anomalies, and be uncontaminated by infectious agents — bacterial, viral, or fungal. Some research projects can be carried out with tissue that does not meet these requirements, but others, particularly transplantation research, cannot be. These criteria must therefore be considered when evaluating the potential sources of fetal tissue.

Current Sources of Tissue

Some research questions can be answered using fetal tissue from spontaneous abortions — in fact, research on such tissue has provided insights into the causes and consequences of disease processes that affect the fetus. We know, for example, that approximately half of early spontaneously aborted fetuses have chromosomal abnormalities; this knowledge was gained by studying the chromosomes in their cells. Scientists have also learned about the development of fetal anomalies from the study of tissues from spontaneous abortions.

Other research questions cannot be answered by studying fetal tissue from this source. For example, fetal material from spontaneous abortions cannot be used for transplantation research. Difficulties in obtaining this material include the unpredictable timing of the event, and tissue death and degeneration. In addition, the tissue from spontaneous abortions is

often infected. This, coupled with the high incidence of chromosomal abnormalities, renders tissue from spontaneously aborted fetuses largely unsuitable for many research projects, including transplantation. For these reasons, fetal tissue from spontaneous abortion is rarely used for clinical research applications.

For reasons associated with tissue viability, condition, and availability, elective first-trimester abortion provides more suitable fetal tissue for some kinds of research, particularly research involving transplantation to treat disease.

Fetal material from spontaneous abortions cannot be used for transplantation research. Difficulties in obtaining this material include the unpredictable timing of the event, and tissue death and degeneration. In addition, the tissue from spontaneous abortions is often infected.

More than 90 000 abortions are performed annually in Canada (92 665 in 1990).[4] About 90 percent of these take place within the first trimester. The overwhelming majority of these procedures are performed between the fifth and twelfth weeks of gestation, usually by vacuum aspiration. Fetal tissue from these procedures, although fragmented, is generally usable and can be collected without contamination. Tissues at these stages of development are useful for many types of research and optimal for some. Fetal tissue used in the transplantation research project being carried out in Halifax is from fetuses aborted in the first trimester.

Altering the method of abortion may allow collection of tissue better suited for use in transplantation research. For example, researchers in Sweden have used other techniques, such as forceps or a manual syringe under ultrasound guidance, to obtain less fragmented fetal tissue. Similarly, a modified vacuum aspiration technique has been used in the United States. These are experimental techniques, and their safety for the woman undergoing the abortion has not been established. We make recommendations with regard to this later in this chapter.

Some areas of fetal tissue transplantation research (for example, fetal pancreatic tissue transplants) must use tissues from second-trimester abortions. The most common method of abortion at this stage is the dilation and evacuation technique. This procedure is considered to be the safest for the pregnant woman, and tissue obtained from this procedure is generally usable.

Termination of pregnancy later than the second trimester is unusual and is almost always done only when a severe abnormality has been discovered in the fetus at this stage of pregnancy. It can be performed by replacing the amniotic fluid with a concentrated saline solution or by stimulating uterine contractions with drugs (for example, prostaglandins). Tissue from fetuses at this stage of development is less usable for most research purposes, as it is more differentiated and mature, and because there is often a genetic anomaly. Moreover, these methods of abortion

rarely yield viable fetal cells — almost never in the case of saline injection and only rarely in the case of prostaglandin induction.

Alternative Sources of Fetal Tissue for Transplantation and Other Research

Many of the ethical and legal issues raised by using tissue derived from therapeutic abortions could be avoided if it were possible to use alternative material. Several possibilities are therefore under investigation — some more promising than others. However, their practical clinical use is likely many years away.

Ectopic Pregnancy

In an ectopic pregnancy the embryo implants in a woman's fallopian tube instead of in her uterus. The condition is life-threatening to the woman unless the fetus aborts spontaneously or is removed surgically. Between 40 and 64 percent of ectopic pregnancies abort spontaneously in the first trimester. This material is rarely recognizable or viable in culture and therefore is generally not usable for fetal tissue transplantation or other research.

Ectopic pregnancies that do not abort spontaneously require surgical removal of the fetus to save the woman's life. The surgically removed fetal tissue is usually normal and thus more useful than the fetal tissue from spontaneously aborted ectopic pregnancies. However, the low incidence and unpredictable occurrence of ectopic pregnancies restrict the availability and usefulness of this source of tissue. Moreover, because surgical removal of the fetus often damages the woman's fallopian tube, the recent trend has been to abort ectopic pregnancies non-surgically through the use of a local injection of methotrexate in an effort to preserve the fallopian tube. This procedure renders the fetal tissue unsuitable for research and transplantation.

Human Fetal Cell Lines

Continuously propagated cultures (cell lines derived from fetal tissue) have obvious advantages as a potential source of fetal tissue for transplantation. Theoretically, cells from a few fetuses might be made to proliferate *in vitro* to provide a virtually limitless supply of transplantable tissue. There are several serious difficulties with this scenario, however. Fetal tissue cell lines currently in existence continue to grow and divide only because they have been specially treated to behave this way. As a consequence, the cells are also likely to keep dividing after transplantation, possibly resulting in tumours. Because of the length of time they are kept in culture, fetal tissue cell lines may also develop abnormal antigens that make them identifiable as foreign by the recipient and which are likely to lead to their rejection.

In the future, it may be possible to avoid rejection, as well as the potential spread of cancerous cells, by implanting fetal cell lines that are "encapsulated." Other approaches to the propagation of non-cancerous lines of human endocrine, neurological, or stem cells by various means, including treatment with growth factors, are under development. It is unlikely, however, that fetal tissue cell lines will be able to replace fetal tissue in the near future in transplantation research. Even if cell lines can be used to replace fetal tissue for transplantation in the future, cell lines will not be able to replace fetal tissue for all other research purposes — for example, cultured cells would not be useful for basic research into fetal development.

Umbilical Cord Blood

Umbilical cord blood obtained from normal placentas at birth is a readily available potential source of blood stem cells. These could, in theory, replace the transplantation of fetal liver cells in the treatment of certain blood disorders. Indeed, at least two children with a rare inherited blood disease have been treated by transplantation of cord blood from compatible newborn siblings. However, umbilical cord blood is useful only for compatible recipients, because the cells in it are more immunologically mature than fetal tissue cells and they may recognize the host body as "foreign," going on to mount a catastrophic graft-versus-host reaction.

Non-Human Fetal Tissue

Non-human fetal tissue has also been considered for transplantation into human beings. However, species differences greatly limit the usefulness of this approach. All cells express species-specific antigens that can be recognized as foreign by the recipient, so survival of grafts across species requires that they be protected from rejection. Grafts from other species have been considered for clinical application, but the potential toxic effects of prolonged use of the immunosuppressive drugs now available have discouraged pursuit of this approach.

Microencapsulation

Microencapsulation of animal tissues, allowing useful products to leak out of the capsule while preventing antibodies from getting in, is one approach being worked on. It may prove useful eventually in treating endocrine or metabolic disorders through implantation. Where direct contact between graft and host cells is needed for neurological

Despite active research into alternative materials for transplantation, it seems that, for the present, fetal tissue from elective abortion provides the only reliable source of tissue for transplantation research.

or other applications, it may be less useful, although researchers at Brown University in the United States, working with a commercial company, are awaiting government approval to begin clinical trials for patients with Parkinson disease on a newly patented capsule containing dopamine-producing rat tumour cells.[5] Several other laboratories are pursuing this line of work, and several U.S. companies have recently been formed to use similar approaches.

Despite active research into alternative materials for transplantation, it seems that, for the present, fetal tissue from elective abortion provides the only reliable source of tissue for transplantation research. Alternative therapies that do not involve transplantation may also be developed — for example, the development of new drugs to treat Parkinson disease or to improve disease prevention.

Potential Availability of Fetal Tissue

Given that elective abortion currently provides the only reliable source of fetal tissue for transplantation research, it is relevant to know how the present availability of fetal tissue from this source is related to the potential demand for it, should transplantation treatment prove effective.

Fetal tissue is currently collected for research and therapeutic use from about 1 percent of induced abortions performed in Canadian hospitals. Present research thus uses only a small fraction of the available fetal tissue. U.S. studies have found more than 90 percent of women undergoing abortion would consent to the use of tissue for research or transplantation, and some Canadian observers believe the same would hold in Canada. It is probable that fetal tissue could therefore be collected from most of the abortions performed annually in Canada.

We can compare this potential availability of tissue with the estimated annual incidence of the diseases most likely to be treatable by human fetal tissue transplantation in the near future. Approximately 8 000 new cases of Parkinson disease and 4 000 cases of insulin-dependent diabetes mellitus are diagnosed in Canada each year. However, since other methods of treatment work for all but the most serious cases, less than 10 percent of such patients would be possible candidates for fetal tissue transplants in the near future. The annual number of new cases of leukemia and congenital immunodeficiency disorders is approximately 4 000, and about 100 cases of Huntington disease occur each year, but the availability of other methods of treatment means the use of fetal tissue would be indicated only in some of these cases. The figures therefore suggest that the tissue available from therapeutic abortions would be more than sufficient to accommodate the need for tissue for therapeutic uses in the foreseeable future.

It is impossible to make accurate longer-range predictions. On one hand, some speculative future applications of fetal tissue transplantation could involve many more patients. On the other hand, the development of

preventive measures, alternative treatments, or alternative sources of transplantable tissue could eliminate much of the potential future demand for fetal tissue. Another factor in any longer-term prediction is change in the incidence or methods of abortion. For example, if the use of RU-486 became widespread, the supply of fetal tissue usable for research or treatment would diminish. These factors render attempts at longer-range prediction largely futile.

Regulations Relevant to Fetal Tissue Use in Canada

On the basis of the evidence we have reviewed, we judge that there is a real possibility that research involving the use of fetal tissue could result in considerable alleviation of human suffering. It is also evident to us that, at present, elective abortion provides the only practical source of fetal tissue for such treatment. Even if transplantation proves largely unsuccessful, a wide range of other research, diagnostic, and educational uses of fetal tissue can and already do provide important health benefits to society.

We are very conscious of the need to address the many ethical and social questions raised by fetal tissue use and to safeguard against the possible risks of coercion, commercialization, and the promotion of abortion. We need to determine whether it is possible, through legislation or other regulatory mechanisms, to eliminate these risks while allowing society to realize the benefits. In approaching this question, we looked first at the current system of laws and professional guidelines that relate to fetal tissue use in Canada.

> Strict guidelines [should] be formulated under the Health Act specifying under what conditions fetal tissue can be obtained for research; and that the effectiveness of fetal tissue transplants [should] be monitored by a national committee on bioethics. Monitoring and guidelines should: (a) prevent abuse of the technology, such as ensuring that no fetus is aborted solely to provide transplant tissue; [and] (b) ensure that the abortion method used is one that is best suited to the welfare of the woman involved, rather than for the optimal preservation of the fetal tissue for transplant.
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> *Brief to the Commission from the Provincial Council of Women of British Columbia, July 24, 1990.*

At present, the principal laws governing the research use of human tissue are the provincial tissue transfer laws. These are based largely on the 1971 *Uniform Tissue Gift Act*, developed by the Conference of Commissioners on Uniformity of Legislation in Canada (the Uniform Law Conference of Canada). The act requires obtaining the consent of living persons for the transplantation of their tissue into another person.

It is not clear whether many of the provincial human tissue gift acts (HTGAs) include fetal material in the definition of "tissue." Two clearly do not. The acts of Manitoba and Prince Edward Island specifically exclude fetuses from the definition of tissue. On the other hand, the wording of the Quebec *Civil Code* may be broad enough to regulate transplantation of fetal tissue. If fetal material is covered under the *Civil Code* and other provincial acts, their provisions will require asking the woman from whom a fetus is removed for her consent to the use of the tissue. If that consent is not given, the tissue cannot be used for transplantation.

Even if fetal tissue is not interpreted as "tissue" under various HTGAs in the common law provinces, it may well be considered "body parts." HTGAs generally prohibit the sale of body parts as well as tissue. This is consistent with laws prohibiting the sale of human organs in the United States and most of Western Europe. The acts provide procedures that can be used to secure the donor's consent for the use of body parts after the donor's death for use in therapy, research, or education. The acts also appear to leave it open to use procedures other than those set out in the acts to obtain body parts for use in transplantation.

If a court or legislature ultimately decides that the transplantation of fetal material is not regulated by HTGAs, the common law or civil law will apply. Historically, there was a common law presumption that when a patient entered a hospital, he or she implicitly abandoned to science any tissue or body parts removed during surgery. This abandoned material might then be used for research or education. That presumption of abandonment might be rebutted if the patient expressed a specific interest in retaining the body part.

However, recent developments in the United States suggest that this presumption may be changing. In *Moore v. Regents of the University of California*,[6] physicians used a patient's spleen, which had been surgically removed for health reasons, to develop a highly profitable cell line. They did not inform the patient that they were intending to use the spleen for this purpose. The Supreme Court of California concluded that a physician must disclose personal interests unrelated to the patient's health in order to satisfy the physician's fiduciary duty and to obtain the patient's informed consent to the medical procedure. In *Moore*, Mr. Justice Panelli concluded as follows:

> Even if the splenectomy had a therapeutic purpose, it does not follow that [the physician] had no duty to disclose his additional research and economic interests ... [T]he existence of a motivation for a medical procedure unrelated to the patient's health is a potential conflict of interest and a fact material to the patient's decision.[7]

The findings in this case are not, of course, binding on Canadian courts, and the facts can be distinguished from the situation of using fetal tissue for transplantation, education, or non-commercial research. Still, the reasoning in this case suggests that the legal thinking in this area may

be evolving. In addition, the requirement of full and informed consent in the medical treatment context (as well as for research or other uses) is consistent with constitutional law principles relating to human dignity and autonomy. It can therefore reasonably be assumed that consent should be sought for use of tissue or body parts, including fetal tissue, taken from patients if the intended use is not routine pathological examination but research, creation of cell lines, banking, treatment (including transplantation), or education.

However, the form and timing of this consent have not been legally defined, and the practice of hospitals in terms of seeking such consent varies. The most common practice in Canada is to ask patients who enter hospital to sign an admission form containing a general waiver regarding the use of tissue removed during surgery. The wording of this waiver varies. For example, it may ask the patient to give the hospital authorization to "dispose" of tissues and body parts. Some hospitals treat the patient's consent to dispose of tissue as implicitly including authorization to use the tissue in research or education. In other cases, the hospital admission form may simply include a more explicit reference to the possibility that surgically removed tissue may be used for research purposes. Most hospitals in Canada operate on the assumption that the general waiver signed by patients when they are admitted to hospital is sufficient for legal purposes. Only the revised Quebec *Civil Code* (in force January 1, 1994) specifically provides that consent must be obtained for any research on human cells, tissues, and substances.

Some hospitals seek consent to the use of tissue removed during a particular operation, rather than (or in addition to) a general waiver regarding the use of any and all tissue that may be removed during the course of the patient's stay in hospital. This operation-specific consent may take two forms. Hospitals may include a clause regarding the use of removed tissue in the consent form for the particular operation. This is common in the United States, where standard consent forms for elective abortions contain a clause asking for consent to the use of fetal tissue for research or education. One standard formulation of this clause is as follows: "I further understand that in accordance with applicable law, any tissue removed may be examined and retained for medical or educational purposes and may be disposed of in accordance with the custom practised."

More rarely, patients may be asked to sign a separate consent form regarding the use of removed tissue, in addition to the consent form for the surgery itself. This makes it clear that consent to the procedure does not require consent to the particular use of the tissue.

In short, considerable uncertainty surrounds the legal status of fetal tissue and the state of the law regarding the need for consent to the use of removed fetal tissue for transplantation, research, or education. There is also some lack of uniformity across Canada in provisions governing commerce in human tissue and body parts, which likely includes fetal material.

Considerable uncertainty surrounds the legal status of fetal tissue and the state of the law regarding the need for consent to the use of removed fetal tissue for transplantation, research, or education. There is also some lack of uniformity across Canada in provisions governing commerce in human tissue and body parts, which likely includes fetal material.

Some groups suggested to the Commission that fetuses are not legally parts of the pregnant woman's body, but rather persons in their own right. In this view, any legal obligation that may exist to obtain informed consent would require the fetus itself to consent to the use of its tissue (through some proxy). As we have discussed in Chapter 30, although the Supreme Court of Canada has not yet ruled on the status of the fetus under the *Canadian Charter of Rights and Freedoms*, it has decided that a fetus is not a person under Quebec civil law, the Quebec Charter, common law, or under the Canadian *Criminal Code*. It is therefore very unlikely that the Court would find that a fetus has independent rights under the Canadian Charter. This means that no consent or other legal obligations would be owed to the fetus. The consent that would be required, if any, is therefore that of the woman.

In addition to these possible legal requirements, the Medical Research Council's *Guidelines on Research Involving Human Subjects* govern fetal tissue acquisitions. Compliance with these guidelines, adopted in 1987, is necessary where the research in question is funded by the MRC, but the guidelines have also been adopted widely by research institutions, universities, hospitals, and other granting agencies in Canada. The guidelines state that the woman's permission to use "separated tissue and placental material" in research should be sought "wherever possible." In research designed to use fetal tissue from therapeutic abortions, the guidelines also state that the research protocol must not influence the choice of procedure used for the abortion.

> The use of tissues or cells obtained from elective abortions [should be acceptable] in research designed to improve understanding of health and disease, or to provide means of treating intractable disease, [provided that]: research requirements must exert no influence on any aspect of the abortion, including the decision to abort, the timing and the procedures used; consent of the mother to use the tissues or cells must be obtained; [and] the research protocol must be approved by a Research Ethics Board as outlined in the [MRC] Guidelines [on Research Involving Human Subjects].
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> *Brief to the Commission from the Medical Research Council of Canada, April 1991.*

However, like the common law, the MRC's requirement of "consent" is unclear. The MRC guidelines do not provide much guidance regarding the

extent, form, or timing of this informed consent. For example, what kind of information should be given to the pregnant woman, and when should her consent to tissue donation be sought? Is it enough to include a general waiver within a hospital admission form or a clause within the consent form for the abortion procedure?

We believe that the pregnant woman's consent to the use of fetal tissue should be separate from the consent to hospital admission or to the abortion procedure. A clause in the abortion consent form may be overlooked by patients who are focussing on the risks and benefits of a surgical procedure. Unless there is a separate form, the woman may not realize that her consent to the abortion does not require her to consent to the use of the tissue. Moreover, this clause does not provide enough information to allow the woman's informed consent to use of the tissue. For example, it does not provide information regarding protection of her anonymity or the possible need for serological testing of her if the tissue is to be used specifically for transplantation.

Hence, we believe that a separate consent form should be required for uses of fetal tissue other than for the routine examination of the tissue that is a part of the medical care of the patient. All other uses of fetal tissue — including education and research — should require the separate consent of the woman undergoing the abortion. We discuss the requirements of informed consent further below.

We believe that the pregnant woman's consent to the use of fetal tissue should be separate from the consent to hospital admission or to the abortion procedure.

Canadian legislation and guidelines also have other gaps. For example, there is no guidance regarding who should be allowed to obtain and distribute fetal tissue or who should have access to it. There should also be guidelines outlining whether the timing or method of abortion can be modified, as well as guidelines with respect to the timing of request for permission to use fetal tissue in research. Such guidelines are common in other countries and are needed in Canada (see Appendix 1, The Regulation of Fetal Tissue Use in Other Countries).

Issues and Recommendations

We have grouped our recommendations into five areas of concern: the ethical uses of fetal tissue; obtaining tissue and informed consent; the commercialization of fetal tissue; the funding of research using fetal tissue; and accountability.

The Ethical Uses of Fetal Tissue

Commissioners heard arguments that the use of fetal tissue in research (whatever the source) violates the principle of respect for human life, since it treats fetuses as a means. In the Commissioners' judgement, this is not the case. Research and other use of tissue and organs from children and adults who have died are allowed. Most Canadians accept that organ transplantation and research on human cadaver tissues for valid scientific purposes are consistent with respect for human life; by analogy, we conclude that research on human fetal tissue is acceptable under controlled conditions. Indeed, attending to the ethic of care would suggest this research not only should be permissible but should be pursued, if it appears to hold the best likelihood of leading to effective treatment. However, this should be done only in circumstances that ensure tissue is obtained with safeguards against coercion, commercialization, and unethical use in place and is used for purposes that respect human life and dignity. In light of these considerations, the Commission recommends that

> The range of current and future applications of human fetal cadaver gives evidence of the importance of these applications for the advancement of knowledge and the improvement of medical therapy. However, increasing use of this tissue will also have ethical, legal, and social implications.
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> *A. Fine, "Human Fetal Tissue Research: Origins, State of the Art, Future Applications, and Implications," in Research Volumes of the Commission, 1993.*

277. The provision of human fetal tissue for use in research, or for any purpose not related to the medical care of the woman herself, be subject to compulsory licensing by the National Reproductive Technologies Commission.

In the next few pages we outline some of the aspects of regulating fetal tissue provision that we believe should be part of the conditions under which facilities obtain and hold a licence to provide fetal tissue.

Respect for human life clearly imposes certain limitations on research using fetal tissue. It is important to ensure, for example, that fetal death has been determined before tissue is taken. Concerns have been raised that fetuses might be kept alive artificially to improve the chances of securing more viable tissue. We found no evidence of this. When the standard vacuum aspiration technique is used to terminate a pregnancy in the first trimester, this would not be a concern, as only fragmented tissues, not intact fetuses, are recovered. If other abortion methods (such as saline

or prostaglandin inductions or low vacuum procedures) are used, however, it is possible that an intact fetus would be recovered; to guard against the possibility of abuses in such cases, the determination of fetal death should be made by someone other than the researcher who is to use the tissue. The Commission recommends that

278. When abortion methods other than standard vacuum aspiration in the first trimester are used,
(a) research use of fetal tissue be permitted only after fetal death has been established; and
(b) fetal death be established by a physician not associated with subsequent use of the tissue.

We found that there are no Canadian guidelines establishing appropriate criteria for fetal death. Because the fetus is at a much earlier developmental stage, the criteria for death focussing on brain function that have been developed for newborns are not necessarily applicable. Since it would be unethical to use tissue from a living fetus, appropriate definitions of fetal death are required and must be developed with input from those with relevant expertise. The Commission recommends that

279. Determination of fetal death be based on national standards of fetal death, and that these be developed by Health Canada in conjunction with the provinces/territories, relevant professionals, and ethicists.

Respect for human life precludes the use of fetal tissue for any purpose other than scientifically valid research intended to improve understanding of human functioning and disease, or to provide improved means of diagnosing and treating disease. Accordingly, the Commission recommends that

280. Fetal tissue use in research be permitted only if the research is directed to understanding human functioning or disease, or to diagnose or treat disease.

Obtaining Tissue and Informed Consent

There is no empirical evidence to support the claim that permitting research using fetal tissue encourages abortion. For example, we found no

reports of changes in the incidence of abortion in locations where well-publicized clinical trials of fetal tissue transplantation are under way. Nevertheless, this possibility should be guarded against by establishing a structure that creates a clear separation between the clinical care of the pregnant woman and her decision-making processes, and the researchers using fetal tissue. This separation is important in guarding against the possibility that researchers who want to obtain fetal tissue could influence a woman's decision to have an abortion. This safeguard will ensure that abortion is not encouraged by caregivers and will take into account respect for human life. Such a separation is also required by respect for the woman's autonomy, since it will ensure that women will not be subject to pressure or coercion to terminate a pregnancy, to modify the abortion method used, or to consent to the use of fetal tissue in research. The precise mechanisms for separating the decision to terminate a pregnancy from consideration of any subsequent tissue use are discussed below.

Separating Consent to Abortion from Consent to Tissue Use

Any request or discussion of use of fetal tissue for research should be deferred until after the woman gives informed consent to an abortion. This would apply to all settings where the option of abortion is discussed, including family practices, genetics clinics, family planning clinics, abortion clinics, and specialists' services. Only after a woman has chosen to abort a pregnancy, and has consented in writing to the procedure, should she be informed about the possible uses of fetal tissue. Women should not be pressured in any way to give consent, which is why it is important that the issue of fetal tissue use not be raised at all until after her decision is made. It should also be made clear that her decision regarding consent to the use of fetal tissue will not in any way affect the quality of her clinical care. Each decision — to have an abortion, and to consent to tissue use — should be made independently of the other.

The method for seeking consent to fetal tissue use should be in keeping with the principles of full disclosure and autonomy. The woman should also be informed of the provisions to protect the anonymity of donors. If the tissue is to be used for research involving transplantation into a human patient, she should be informed of the need for serological testing, including HIV testing. (Such testing is not necessary for research not involving transplantation.)

It is possible that a potential commercial application may emerge after some time; for example, a cell line derived from fetal tissue may on further study turn out to have unanticipated or commercially useful purposes. The woman should be informed of this possibility, and her consent should include the understanding that she will not receive any benefit from such use.

We believe that consent procedures of this type will help to guard against the possibility that researchers who want to obtain fetal tissue

could influence a woman's decision to have an abortion. The Commission recommends that

281. (a) Any use of fetal tissue (other than routine examination or tests as part of medical care) requires the informed consent, in writing, of the woman undergoing therapeutic abortion.

(b) This consent must be obtained separately from, and subsequent to, her decision to terminate the pregnancy.

(c) Consent to fetal tissue use must be sought in a manner that makes it clear that the woman's decision with respect to the use of fetal tissue will not affect the quality of her medical care.

(d) Consent to the use of fetal tissue in research and education should be obtained. When the tissue is to be used for research involving transplantation into a human patient, specific authorization for this use should also be obtained; in this case, the woman should be informed and consent to serological testing, including HIV testing.

(e) The woman should be informed that, if a project has commercial potential, no commercial or other financial benefit will accrue to her.

We believe that these recommendations will ensure the necessary separation of the decision to terminate a pregnancy from consideration of whether and how the tissue will be used. It will help ensure that the possible donation of fetal tissue does not affect the woman's decision to terminate the pregnancy or the medical care provided by her physician. To protect this separation even further, we believe several other steps are also required relating to protection of the woman's privacy, the method of abortion, the designation of tissue recipients, and co-authorship credit.

Anonymity

Privacy must be respected in any research project. Once the tissue has been collected, any information that would allow either the woman or her partner to be identified should be removed. Non-identifying information about either partner could accompany the tissue, but only if needed and only if specified in advance in the research protocol.

For example, a researcher involved in transplantation research may need to know certain facts about the woman and her pregnancy (for example, her age, medical history, HIV status, the stage of pregnancy, the sex of the fetus). The researcher would list such parameters in the research protocol, and this information would then be included with the tissue. However, information about the personal identity of the woman would never accompany the tissue. The Commission recommends that

282. No personally identifying information regarding the woman accompany fetal tissue.

Method of Abortion

A decision to permit use of fetal tissue in research should not alter a woman's health care in any way; in particular, it should not influence the choice of abortion method. As noted earlier, prolonging a pregnancy or altering the abortion method can increase the likelihood that resulting fetal tissue will be more suitable for transplantation purposes. However, the method of abortion should be chosen on the basis of what is best for the woman and never on the basis of the suitability of fetal tissue for transplantation research. Any method used must have been demonstrated not to increase the risk for the woman in any way and must not involve prolonging the pregnancy.

At present, Canada has no uniform guidelines or legislation concerning the permissibility of modifying abortion procedures expressly to facilitate recovery of fetal tissue. We are of the view that this situation is undesirable. The Commission recommends that

283. The abortion method and timing be chosen solely to protect the health and interests of the woman involved.

Prohibiting Designation of the Recipient of Fetal Tissue

Given the current availability of fetal tissue from therapeutic abortions and the relatively limited use of it, it does not seem likely that in the foreseeable future there will be heightened pressure from researchers or potential transplant recipients for women to donate fetal tissue for research. However, in specific cases where compatible tissue would be of possible benefit in transplantation, there might be pressure to consent to a donation, particularly from near relatives.

At present, Canada has no law that would prevent such "directed" donations, and the issue of directed donation is not mentioned in the MRC guidelines. This means it would be possible for a woman to consent to donate fetal tissue on condition that it be used to treat someone she designates.

Permitting fetal tissue to be used to treat a designated person creates the possibility that a woman might initiate a pregnancy deliberately to produce fetal tissue for transplantation to a loved one, or that she might be persuaded to terminate a wanted pregnancy in order to benefit someone important to her. This is using a fetus as a means to an end and would contradict the principle of respect for human life. It would devalue human reproduction and, consequently, human life. Indeed, we found that most Canadians are deeply uncomfortable with and reject the idea of a woman becoming pregnant for these reasons.

> While women undoubtedly are entitled to access to abortion, there may be some ethically justified limitations on their freedom to determine the use of embryonic and fetal tissue. Analogously, blood donors are not free to specify to what use their blood is put. And no one has the freedom to compel clinics to make use of their excised organs.
>
> *C. Overall, reviewer, research volumes of the Commission, May 29, 1992.*

We conclude that regulations should prohibit health professionals or facilities from any role in facilitating the use of fetal tissue in a designated or intrafamilial recipient; this would ensure that pregnancies were not undertaken with the intention of providing fetal tissue for a designated recipient. Women undergoing abortion should not know the identity of recipients of fetal tissue participating in research trials or therapy, nor should recipients know the source of the tissue. The Commission recommends that

284. Designation of recipients of fetal tissue by women undergoing abortion be prohibited.

In Britain, a centralized fetal tissue bank (analogous to a blood bank) has been established to receive fetal tissue and distribute it to approved research projects. This tissue bank serves as an intermediary, guaranteeing that there is no contact between the woman and the recipient of fetal tissue. Because of the limited extent of fetal tissue use in transplantation at this time, we do not believe it is necessary to recommend a centralized structure of this type. However, this issue should be re-evaluated by the National Reproductive Technologies Commission if fetal tissue transplantation use proves effective and expands in the future.

Benefits from Providing Fetal Tissue

Finally, to protect the separation of clinical and research responsibilities, we believe that the supplier of fetal tissue should not derive benefit from doing so. A supplier should not receive funding from research grants involving the use of fetal tissue or derive any other indirect financial benefit as a result of tissue provision. This prohibition should not prevent cost recovery for providing processing, transportation, or services such as microbiological testing of the tissue. In addition, a supplier of fetal tissue should not be given co-authorship credit for this role in any publications that emerge as a result of the research use of fetal tissue if this is the only contribution to the research. According to a survey, 30 percent of doctors in Canada accepted the idea of co-authorship credit for the supplier of fetal tissue.[8] Nevertheless, Commissioners believe that this creates a conflict of interest, and it means that the obtaining of consent to abortion may be subtly influenced. The Commission recommends that

285. Physicians supplying fetal tissue do not receive co-authorship credit for this role in publications resulting from the research use of that fetal tissue, or any direct or indirect financial benefit.

Commercialization and Patenting

The non-commercialization of reproduction is one of our guiding principles. Apart from its threat to human dignity, the commercialization of fetal tissue could open the door to exploitation of poor women, especially in developing countries, who might be persuaded to begin and end pregnancies for money. It is therefore important to develop measures to limit the possibility of trade in fetal tissue.

In 1989, the World Health Assembly, concerned about commercial trafficking in human organs, adopted a resolution to prevent the purchase and sale of human organs. It called on member states to introduce, as part of their organ transplantation policies, a set of guiding principles,[9] including the following:

- Giving or receiving payment (including any other compensation or reward) for organs should be prohibited.
- Advertising the need for or availability of organs, with a view to offering or seeking payment, should be prohibited.
- Physicians and other health professionals should be prohibited from engaging in organ transplantation procedures if they have reason to believe that the organs concerned have been the subject of commercial transactions.

- Organs should be made available to patients on the basis of medical need, not on the basis of financial or other considerations.

We believe that these principles should also apply to fetal tissue. As we have noted, laws prohibiting the sale of human organs are now in place in Canada, the United States, and most of Western Europe. However, not all of those laws in Canada include fetal tissue explicitly or implicitly. This is why the Commission recommended that the commercial exchange of fetuses and fetal tissue be prohibited under threat of criminal sanction (see Chapter 5). The Commission recommends further that

286. Provincial human tissue gift acts be amended specifically to prohibit the sale of fetal tissues and any payment to the woman from whom the tissue is obtained.

A further step is needed to ensure that any Canadian use of fetal tissue obtained in countries without laws or guidelines dealing with tissue and organ donation does not encourage unethical or harmful practices in those countries. Given the dearth of relevant legislation in much of the world, we believe that importation of fetal tissue by Canadian research facilities, including biotechnology and pharmaceutical companies, should be regulated.

Although it is our conclusion that the sale of fetal tissue should be prohibited, medical facilities that recover fetal tissues, preserve, differentiate, and diagnose them; prepare them for transportation; and transport them should be able to recover the costs of such services, as is the case with organ transplants. These service charges (as distinct from commodity sales) are permissible under the World Health Assembly's ethical guidelines and should continue to be allowed. (Since these expenses are not incurred by the woman giving permission to the use of fetal tissue, no financial payment should ever be made to her.)

No profit should be made on these services, however; they should be provided only on a cost-recovery basis. One U.S. company that provides fetal pancreatic islet cells free of charge for use in diabetes clinical trials is planning to market these cells in the next few years. Proposed service charges for the acquisition, preparation, storage, and transportation of these cells would make the company a profitable business. The company estimates that there is a potential $8 billion market worldwide for the treatment of diabetes.[10] We believe that so-called "service charges" should not provide a source of profit for private industry dealing with fetal tissue, since this would amount to the commodification of fetal tissue. Service charges in this country should be set at appropriate levels, that is, simply to recover costs. The Commission recommends that

287. The prohibition of the commercial exchange of fetuses and fetal tissue extend to tissue imported from other countries, so that no fetuses or fetal tissues are used in Canada for which women have received payment, or where a profit has been made by an intermediary.

and that

288. The costs of handling fetal tissue be recoverable only on a not-for-profit basis.

Resolving the issue of commercialization of fetal tissue still leaves the more complicated question of the appropriateness of patenting products or processes developed through research on fetal tissue. For example, researchers may discover a new way to culture fetal neural cells, discover and maintain a particular cell line that produces a therapeutically useful product, or discover a way to treat cultured cells that increases their production of neurotransmitters. Transplanted neural tissue that has been cultured in this way might be particularly useful in treating disease; alternatively, the substances produced by the altered cells might be of use in treatment. Developing and perfecting such techniques might require significant financial investment, however, and governments may be unable or unwilling to develop and support this research. Pharmaceutical, biotechnological, or other companies might invest in the development of potentially beneficial products or processes, but only if there is a reasonable expectation of profit. The possibility of profit may depend on the existence of intellectual property protection, such as patent or copyright.

We discussed the issues raised by patenting such innovations in Chapter 24. To recapitulate, Commissioners believe strongly that fetuses should never be an appropriate subject for patents. However, if they are intended to benefit human health, and if the safeguards we have recommended for obtaining and using fetal tissue are in place, innovative products and processes using fetal tissue as a source may warrant some limited form of patent protection. However, this is an area we have identified as requiring further study before policies are made, bearing in mind the principles we outline in that chapter.

Commissioners believe strongly that fetuses should never be an appropriate subject for patents. However, if they are intended to benefit human health, and if the safeguards we have recommended for obtaining and using fetal tissue are in place, innovative products and processes using fetal tissue as a source may warrant some limited form of patent protection.

Funding of Fetal Tissue Research

A variety of public and private agencies provide funds for research projects involving fetal tissue use. The largest source of public funds for this research is the Medical Research Council. However, as noted earlier, the MRC decided not to fund a particular type of fetal tissue research — transplantation research using tissue from elective abortions — after the Minister of the Department of National Health and Welfare objected to such funding in 1988.

We believe that there is clear justification for public funding of many forms of research using fetal tissue, including both basic research and research into transplantation. Basic research involving fetal tissue has had a proven record for many decades and has played an important role in the development of vaccines and antibodies, in the diagnosis of viruses, and, in general, in understanding many facets of human health and disease.

Whether fetal tissue transplantation research will result in the development of beneficial and efficacious treatments is not known; however, we believe that funding of this research is justified. The potential benefits are substantial, particularly in terms of reducing the human suffering caused by disease. The ethic of care means we must avoid or prevent this suffering if possible. Obviously, many of the most important benefits cannot be measured in economic terms, but if we consider the impact on medical care, productivity, and other factors, their impact could be enormous.

In supporting research that may lead to effective treatment of disease in the future, it is important not to neglect the immediate needs of those currently affected by these diseases — both must be taken into account in resource allocation decisions. Nor should promising research into alternative treatments or prevention strategies for these diseases be neglected. Fetal tissue transplantation is unlikely ever to replace the need for more conventional approaches and treatments.

The recent situation in the United States suggests what can happen when public funding for fetal tissue transplantation research is withdrawn. Rather than adopting legislation to control fetal tissue transplantation research, the U.S. federal government withdrew funding in 1988, as a result of pressure from the anti-abortion lobby, thereby creating a legislative and regulatory vacuum. Despite the unanimous recommendation of a government-appointed advisory committee that the funding prohibition be lifted, the Bush administration subsequently extended the ban until 1992. (As previously noted, the ban was lifted by the Clinton administration.)

This funding prohibition had several unintended effects. Rather than being halted entirely, some fetal tissue transplantation research continued with private funding, which meant that it escaped the review and accountability mechanisms that accompany public funding. The United

States also lost some highly qualified researchers to other countries, including Canada.

The U.S. experience shows the pitfalls of trying to ban public research funding or allowing research to go on in a regulatory vacuum. We believe that MRC's ban has discouraged other agencies from funding such work in Canada (as did the ban in the United States). We believe that federal funding of fetal tissue transplantation research would support potentially life-saving research, while also providing, through accountability for the use of public funds, a mechanism to monitor and regulate the ethical use of fetal tissue. The Commission recommends that

289. Research projects using fetal tissue (including those related to transplantation in human beings) be eligible for public funding by the Medical Research Council of Canada and other agencies, provided they meet applicable ethical and scientific research standards and tissue is obtained in accordance with the recommendations of the Royal Commission on New Reproductive Technologies.

Accountability

In the absence of national or provincial laws or guidelines governing the use of fetal tissue, research proposals are reviewed by hospital, clinic, or university research ethics boards. These differ in composition, expertise, and approach and operate without the benefit of a common set of detailed guidelines. Moreover, private sector research involving fetal tissue is not necessarily subject to research ethics board review and approval. To date in Canada, there has been no way of approving or accrediting individual physicians or clinics as sources of fetal tissue or to ensure that appropriate records on the collection and distribution of fetal tissue are kept.

The experience of such agencies as the National Disease Research Interchange in the United States and the Medical Research Council Tissue Bank in Great Britain suggests that there are advantages to a government-supported central organization for monitoring fetal tissue use. The ethical, safety, and record-keeping standards of these organizations are clearly superior to the unregulated and undocumented individual arrangements through which Canadian researchers currently obtain such tissue. A key advantage of centralized oversight is that it can also bring the private sector under legislative and regulatory control; another is that information can be made available for the public on the use of fetal tissue.

Licensing will ensure that use of fetal tissue for research or education taking place in both the public and private sectors uses only tissue that

has been obtained in compliance with the ethical guidelines we have recommended with respect to informed consent, the determination of fetal death, the separation of clinical and research responsibilities, and the absence of designated donation, among other matters. As a condition of licence, fetal tissue would be provided only to researchers/users who have obtained research ethics board approval for the use. Since some research ethics boards may not have broad representation, and to help ensure consistency of approach, clear guidelines set by the National Reproductive Technologies Commission should be used by these boards in their decisions on any research project proposing to use fetal tissue. Taken together, these measures will ensure that the use of fetal tissue is for legitimate purposes, related to education or improving human health, and is obtained in an ethical way. It will also enable information to be collected that allows the public to know about the use of fetal tissue in Canada, thus enhancing accountability.

As a condition of licence, fetal tissue would be provided only to researchers/users who have obtained research ethics board approval for the use ... Clear guidelines set by the National Reproductive Technologies Commission should be used by these boards.

The specific details of the licensing scheme we recommend are set out below.

Licensing Requirements for the Provision of Human Fetal Tissue to Users

The Commission recommends that

290. Compulsory licensing be required for the provision of human fetal tissue by any physician, centre, clinic, or other individual or facility providing human fetal tissue for research (including transplantation research) or for any purpose other than medical care of the woman, routine pathology testing, or disposal.

291. Providing fetal tissue without a licence issued by the National Reproductive Technologies Commission, or without complying with the National Reproductive Technologies

Commission's licensing requirements, as outlined below, constitutes an offence subject to prosecution.

and that

292. The National Reproductive Technologies Commission establish a permanent Fetal Tissue Sub-Committee to monitor the supply and use of fetal tissue, to develop standards and guidelines to be adopted as conditions of licence, and to oversee the implementation of the licensing program.

The Commission recommends that

293. In particular, the following requirements be adopted as conditions of licence:

(a) Unless obtained using first-trimester standard vacuum aspiration, only fetal tissue from fetuses that have been pronounced dead by a physician not associated with the subsequent use of the tissue can be provided for use in research.

(b) The full and informed consent of the woman, sought independently of and subsequent to the decision to abort, and including specific consent for use of fetal tissue in research involving transplantation, must be obtained in relation to any fetal tissue provided for use.

(c) Donation of fetal tissue to designated recipients should not be permitted.

(d) The exchange of fetal tissue should not occur on a for-profit basis; payment should be limited to the reasonable costs of handling, transporting, or testing of such tissue.

(e) The use of fetal tissue in research (or any other use) should be permitted only if the research is directed to understanding biological mechanisms with potential medical relevance or treating disease.

(f) Fetal tissue should be provided only for projects that meet ethical research guidelines developed by the Fetal Tissue Sub-Committee of the National Commission and that have received prior institutional research ethics board approval, including scientific and ethical review. Written documentation of such approval must be obtained before any fetal tissue is provided for use and must be held on file by the provider for five years.

(g) Licensed individuals or facilities providing human fetal tissue for use would be required to comply with record-keeping, data collection, and data reporting requirements established by the National Reproductive Technologies Commission.

(h) Licence holders would be required to report annually to the National Reproductive Technologies Commission in accordance with requirements established by the National Commission with respect to the form and content of information, including information on the number and type of projects for which fetal tissue has been supplied.

The Role of the Fetal Tissue Sub-Committee

We referred to some of the functions of the Fetal Tissue Sub-Committee in the licensing conditions set out above. However, in light of the key role the Sub-Committee will play in ensuring the ethical and accountable use of fetal tissue in Canada, it is also important to note the Sub-Committee's other functions here.

The Fetal Tissue Sub-Committee would be established and chaired by the National Reproductive Technologies Commission. It would be one of six permanent sub-committees, along with those dealing with infertility prevention; assisted conception services; assisted insemination services; prenatal diagnosis; and embryo research. Like National Commission members themselves, we recommend that at least half the members of the Fetal Tissue Sub-Committee be women, and that all members be chosen with a view to ensuring that they have a background and demonstrated

experience in dealing with a multidisciplinary approach to issues, as well as an ability to work together to find solutions and recommend policies to address the issues raised by the use of fetal tissue in research in a way that meets the concerns of Canadian society as a whole.

As well as setting and revising the licensing requirements for the provision of human fetal tissue to users, the Fetal Tissue Sub-Committee would

- develop ethical research guidelines to be applied by institutional or local research ethics boards in reviewing and approving projects involving the use of fetal tissue and ensuring that such guidelines are applied in an appropriate fashion;
- compile, analyze, and report to the public (through the National Commission's annual report) information documenting the use of fetal tissue in Canada and documenting that local research ethics boards are applying the National Commission's guidelines in an appropriate fashion; and
- monitor developments in the area of research using fetal tissue with a view to keeping the public informed, promoting public dialogue, and anticipating or proposing the need for further regulatory involvement in this field.

Conclusion

Transplantation is only one subcategory of fetal tissue use in research; only a very small proportion of fetal tissue currently used in research is used for transplantation research. Many important and far-reaching health benefits have been gained, however, from other studies and research using fetal tissue.

At present, virtually all use of fetal tissue in transplantation constitutes research. Indeed, fetal tissue transplantation is considered the treatment of choice in only one instance — to treat DiGeorge syndrome, a rare inherited immunodeficiency disease for which fetal thymus tissue transplantation is the recommended treatment.

Fetal tissue transplantation may be found to be of little or no therapeutic value — in which case there is not likely to be any increase in the demand for fetal tissue for this purpose. On the other hand, if these techniques are found to be of benefit in treating disease, significant increases in the demand for fetal tissue could result. If treatment based on cell lines was found to be as effective as the direct use of fetal tissue, this, too, would alter the situation. We cannot predict what will happen in the future as research evolves. What we must do instead is to ensure that, whatever the outcome of research, we have already set in place limits and boundaries to prevent misuse and coercion and, within those limits, have

put in place a regulatory system and licensing to ensure only beneficial and ethical uses of fetal tissue.

The progress in adult organ transplantation over the last two decades, as well as early results in fetal tissue transplantation, suggest that there is a reasonable possibility that some forms of transplantation will move from research to clinical practice in the next few years. The possibility of benefit to people suffering from disease means we have an ethical obligation to pursue it — if it can be done without harm to others. The regulatory system we have outlined offers a means of ensuring this and is a response to issues of national importance.

The use of fetal tissues or cells is acceptable in research designed to improve understanding of human functioning and to explore means of treating human disease. We judge it important, however, that any use of human fetal tissue be in the context of the boundaries, regulatory system, and guidelines we have outlined.

In summary, the Commission concludes that the use of fetal tissues or cells is acceptable in research designed to improve understanding of human functioning and to explore means of treating human disease. We judge it important, however, that any use of human fetal tissue be in the context of the boundaries, regulatory system, and guidelines we have outlined. If fetal tissue transplantation is found in future to be more effective than other therapies for the treatment of a disease, its use should be permitted — provided the tissue is collected, distributed, and used in the ethical manner we have outlined. We would also encourage research, however, into alternatives to treatments using fetal tissues.

Appendix 1: The Regulation of Fetal Tissue Use in Other Countries

For background information on the use of fetal tissue, we examined the regulation of this research in other jurisdictions, including Australia, Germany, Holland, France, the United States, Sweden, and the United Kingdom, as well as the Council of Europe.

In Australia, it is legal to use fetal tissues from therapeutic abortions in research involving transplantation with the consent of the woman and, where practical, her partner. Research protocols must be approved by a properly constituted ethics committee, and the abortion procedure must be totally separated from the research. The woman's specific consent is required if tissues or cells are to be propagated in culture or transplanted into a human recipient. The decision about whether to approach a pregnant woman about the possible use of fetal tissue for such research

lies with the woman's clinician, not with the researcher. The information sought through the proposed research must not be available through research using non-human fetal tissue, nor should any element of commerce be involved in the transfer of fetal tissue.

In Germany, the law permits research use of tissues obtained with consent, but the 1987 Clinical Code relating to the use of embryos and fetal tissue was reformed to criminalize the taking of these materials without consent.

In Holland, there are clear rules on the use of fetal tissue for research. When an abortion clinic is asked for tissue, it must ensure that the research project is scientifically valid, that it has been approved by an ethics committee, and that the clinic and the research institute have a written agreement. The woman's consent is always obtained. It is understood that any tissue retrieved will be destroyed, unless consent to any other use is obtained. The clinic may not receive any financial or other inducement to provide fetal tissue. There can be no direct link between the doctor performing the abortion and the prospective researcher, and the researcher may not influence the method of abortion. No tissue may be released for research or other uses related to cosmetics.

In France, the National Ethics Consultative Committee for Life and the Health Sciences issued an opinion in 1984 stating that the use of fetal tissue for transplantation should be limited to exceptional cases where the disease being treated is rare, there are no equally effective alternative treatments, and the intended beneficiary would receive a manifest advantage (such as survival). Only tissues from fetuses of less than 20 weeks' gestational age should be used, and only after death has been confirmed. Maintaining the fetus artificially in order to remove viable tissue is not permitted. The decision to donate tissue should not influence the timing or method of abortion. The woman and her partner have a right to veto the use of fetal tissue if the abortion is for medical reasons. However, in cases of abortions without medical indication, the woman's consent to use of the tissue for transplantation is not required because this might be seen as legitimating the abortion. No commercial or industrial use of fetal tissue is allowed, and public authorities restrict research involving fetal tissue to institutions that can demonstrate they have the necessary competence and facilities.

In 1986, the Parliamentary Assembly of the Council of Europe adopted Recommendation 1046 regarding the research use of human embryos and fetal tissue. It is essentially identical to the French guidelines, except that it requires the consent of the woman and her partner even in cases of elective abortion.[11]

In the United States, fetal tissue use is regulated primarily at the state level. Between 1969 and 1973, all 50 states enacted legislation based on the *Uniform Anatomical Gift Act*, which allows the donation of fetal tissue or organs provided that there is documented consent from either the woman or her partner and the other partner is not known to object. It also

allows the donor to designate the recipient of the tissue, which could be a patient, researcher, or institution, although this provision is widely criticized. The *Uniform Anatomical Gift Act* prohibits the physician who certifies death from participating in the removal or transplantation of tissue. Several states have passed laws that place additional restrictions on fetal tissue research. For example, nine states prohibit the use of fetal tissue obtained from therapeutic abortions in research.[12]

The Swedish Society of Medicine issued provisional guidelines approving the use of fetal tissue for transplantation research in 1985 (and reaffirmed them in 1990). These guidelines state that tissue can be taken only from dead fetuses; that the woman must have given her informed consent after a "reasonable period of counselling" (to allow for consultation of close relatives); that the decision to donate tissue should not in any way affect the method or timing of the abortion; that there should be no communication between the woman and the recipient; that only isolated cells of nerve tissue may be used for transplantation; and that approval for every project involving fetal tissue transplantation should be given by a regional research ethics committee.[13]

The British Medical Association produced interim guidelines in 1988. They are similar to the Swedish guidelines, but also state that there should be no financial reward for donating fetal tissue and that the generation of a pregnancy solely to produce fetal tissue for donation is unethical.[14] In 1989, a government committee recommended that a government organization be responsible for procuring and distributing fetal tissue, to ensure that there is a complete separation between the researchers who receive the tissue and the physicians who manage the pregnancy and abortion.[15]

By comparison with practices elsewhere in the world, then, there is relatively little regulation of the use of fetal tissue in Canada. Canada has no legislation or professional guidelines dealing with such issues as the separation of research and clinical care, modifications to abortion procedures, artificial maintenance of fetal life, the designation of tissue recipients, or the appropriate aims of fetal tissue research. The Commission believes, however, that the use of fetal tissue in transplantation research, and fetal tissue research more generally, is appropriate only if governed by clear principles and safeguards with respect to these and other issues.

Appendix 2: The First Canadian Research Using Fetal Tissue Transplantation in Human Beings

In June 1991, the Commission met with researchers and administrators at Dalhousie University and Victoria General Hospital where the first Canadian clinical trial of fetal tissue transplantation was begun. This trial

is the only clinical fetal tissue transplantation research in Canada and concerns the treatment of Parkinson disease. One of the objectives of the meeting was to learn what process the hospital followed before approving the trial. Among those present were the Dean of the university's medical school, the President of the hospital, and the Chair of the ad hoc committee established by the hospital's Board of Commissioners to examine the information and recommend a decision-making process.

The two-year approval process involved several stages of review. Although the medical faculty's research committee had endorsed the scientific validity of the proposed research, the hospital's own research review committee chose to send the proposal to independent experts around the country for external scientific review. The Research Review Committee at the Victoria General Hospital unanimously endorsed the scientific validity of the study. Next, the committee sent the proposal to three independent reviewers at Canadian bioethics centres.

The result of both the scientific and ethical reviews was a recommendation by the research review committee to the hospital administration that the proposal be considered acceptable on both scientific and ethical grounds. It then fell to the hospital's lay Board of Commissioners to make the ultimate decision to approve or not to approve the proposal. The board struck a three-member ad hoc committee, whose task was to examine in detail the background information forwarded by the research review committee and to recommend to the full Board how the decision would be made.

For four months the committee studied various aspects of the proposal and sought additional information about the costs and funding of the proposed research. We heard from the chairperson that the most difficult aspect of the committee's decision dealt with the relationship between the transplantation process and the source of the fetal tissue. Meanwhile, the proposal was being considered by yet another internal organization, the hospital's Ethics Consultation Service. Comprising nurses, social workers, psychologists, a lawyer, and a minister, the service considered the pros and cons of the proposed research from the perspective of the patient with Parkinson disease, the woman undergoing the abortion, and the fetus.

From the moment the proposal became public and throughout the years of decision making, the hospital and the university were besieged with telephone calls and letters from people opposed to fetal tissue from therapeutic abortions being used in the research. Demonstrations outside the entrance of the hospital were commonplace; some individuals contacted the hospital to say they would withhold financial pledges to the hospital if the research project went ahead.

In 1990, following the longest and most detailed assessment of any research proposal in its 131-year history, the hospital approved the trial. The Board of Commissioners expects a status report in 1994. In the meantime, it follows the project's progress informally.

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