Commercial Interests and New Reproductive Technologies

The purpose of this chapter is to examine the role of commercial interests in providing and developing new reproductive technologies and to outline our general position in this regard; this position, amplified in preceding chapters, will be further discussed in detailed recommendations in subsequent chapters. Commissioners believe that the development and dissemination of reproductive technologies cannot be left to market forces and corporate goals; rather, the ethical principles we have described should guide any use. These guiding principles, together with the ethic of care, require that our recommendations ensure that any use of the technologies does not commodify human beings or commercialize reproduction.

The crucial principle to be taken into account with regard to the activities of commercial interests is protection of the vulnerable. Clearly, the interests of commercial firms and the interests of those to whom they sell are not identical (for example, one wants to increase price, one to decrease it), but in an open market it is assumed that buyers can protect their own interests. The situation is different when health care is involved — commercial firms can protect their own interests, but individuals cannot, and therefore they require protection through society's rules and regulations. Given that there are vulnerable interests to be protected, the question is not whether there should be regulation of commercial interests but rather what form it should take. Recognition of this need to protect interests that are not able to protect themselves in open market exchanges is at the heart of all professional and health care regulation — acknowledging that regulation is needed. But not only individuals have vulnerable interests that need protection from commercial interests; the wider Canadian community also embodies vulnerable interests in two ways:

- We all have an interest in the nature of the community in which we live — for example, that our society not be one in which people are treated as commodities. This is one reason why societies such as ours choose to regulate what is permitted and prohibited through laws such as those limiting the types of contracts people can enter into.
- The community is also vulnerable to spillover costs from nominally "private" transactions — if the wider community has to bear costs resulting from these transactions, the community also has an interest that it needs to protect.

Obviously, conflicts of interest are inherent in most commercial transactions, but conflicts arising in the medical context are different, in that the individuals' interests are vulnerable because they are at a disadvantage in terms of medical knowledge and its application. Regulation is therefore needed for commercial activities in the health care field. The existence of conflicts of interest is not the problem in itself; it is how such conflicts are resolved that may be a problem. Commercial organizations are designed, both in objectives and in their management, to promote a single interest (profit); they are not designed to balance conflicting interests. Patients do not have the means or knowledge to defend their vulnerable interests, and these interests will therefore be sacrificed when they conflict with profit — hence the need for regulatory protection and the role of government as the guardian of the vulnerable interests.

The existence of conflicts of interest is not the problem in itself; it is how such conflicts are resolved that may be a problem. Commercial organizations are designed, in both objectives and in their management, to promote a single interest (profit); they are not designed to balance conflicting interests. Patients do not have the means or knowledge to defend their vulnerable interests and these interests will therefore be sacrificed when they conflict with profit. Hence the need for regulatory protection and the role of government as the guardian of the vulnerable interests.

The idea of vulnerable interests that must be protected against commercial interests captures the concerns we heard from many Canadians with respect to the role of commercial interests in reproductive technologies. Many groups and individuals who appeared at the public hearings or made submissions to the Commission expressed concern that commercial motives may be driving the development and provision of reproductive technologies inappropriately. People were worried that the private sector's pursuit of profit may promote high-tech approaches to the treatment of infertility to the detriment of other alternatives and that industry funds research into drugs and treatments for infertility rather than its prevention. We also heard the concern that there are inadequate provisions for ethical review and monitoring in industry-based research

involving human subjects and that corporations may avoid Canadian research guidelines by conducting research and product testing in countries with less stringent regulations regarding safety and informed consent. Canadians also told us of their concerns about pricing and marketing practices for reproductive products and services — for example, that companies may be promoting ineffective or unsafe products and services. We also heard the view that the activities of private clinics impose costs on the public health care system, that physician ownership of clinics and laboratories represents a conflict of interest that may not be resolved to the benefit of the patient, and that the existence of private clinics unfairly restricts access to these services. Finally, Canadians told us they were concerned there was potential for commodifying human reproductive tissues and functions through the involvement of commercial interests and that inappropriate technology transfer — for example, from techniques developed by animal breeders — could also be an undesirable consequence of this involvement.

> It does appear that there exists some legislation governing the breeding of cattle. Are humans less important? As soon as some scientist or researcher finds a commercial application for some of what is happening today we will be away and running and, as stated before, it will then be too late to do anything about it.
>
> *Brief to the Commission from the Provincial Council of Women of British Columbia, July 1990.*

Canadians hold differing views about the appropriate role for commercial involvement in the development, marketing, and provision of products and services related to new reproductive technologies. However, many think that commercial interests have a useful though limited role and that relying solely on governments to fund the development of new reproductive technologies is unrealistic. Nevertheless, it is very clear that Canadians believe commercial activity should occur only in the context of a regulatory framework that ensures the profit motive is not the deciding factor behind the provision of reproductive technologies.

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Much of the public debate has centred on the role of the pharmaceutical industry in developing and marketing fertility drugs. However, the range of commercial companies potentially involved in new reproductive technologies extends far beyond the pharmaceutical industry. These companies fall into two broad categories — products and services.

The first consists of companies that manufacture new reproductive technology-related products, such as fertility drugs, medical devices used in assisted conception techniques, and gene probes used in prenatal diagnosis. The second category involves the commercial provision of services, such as medical laboratories, sperm banks, and private clinics offering *in vitro* fertilization or sex preselection.

> The public and private funding of IVF clinics leads to a conflict of interest for physicians involved and a two-tier system of health care with respect to this "treatment" for infertility ... Canadians do not have access to this technology on an equal basis and physicians whose research and training [have] been supported by public money can maximize their profits at private clinics.
>
> *Brief to the Commission from the Canadian Association for Women in Science, January 15, 1991.*

We have already stated (in Chapter 3) the Commission's position on the commercialization of reproduction. By commercialization we mean activities involving the exchange of money or goods and that are intended to generate a profit or benefit for those engaging in this exchange. Commissioners believe strongly that the ethic of care and the principle of protecting vulnerable interests mean that the development and dissemination of reproductive technologies cannot be left to market forces and corporate goals. We believe that the impact of market forces in the area of human reproduction could, if not properly regulated, undermine important social values and ethical principles and harm people by leading to inappropriate, unethical, or unsafe use of technology.

> It appears this new field has competing interests and availability is not ensured unless you are able to pay for it. IVF is being considered and utilized by many as a potential gold mine and not being seen as the complex mine field that it truly is. There are many hazards, known and unknown, associated with IVF and there is real danger in making these technologies a new commercial product. When used they must be used for the benefit of all infertile women and not for the benefit of doctors and commerce. Their accessibility should be ensured for all not just a few.
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> *Brief to the Commission from S. Andrews, private citizen, April 26, 1991.*

Within a framework of regulation, however, commercial companies can play a legitimate role in specific areas of research and development related to new reproductive technologies, as they can in other areas of medical care. Many women and couples who are infertile who might otherwise have been unable to have children have benefited from using fertility drugs. Diagnostic tools such as ultrasound and

specialized medical devices play an important and useful role in the diagnosis of congenital disorders and the treatment of infertility. Since companies that develop, produce, and market these products exist to make a profit, opposing all forms of commerce or commercialization would jeopardize Canadians' access to beneficial products and services. However, we believe that the provision of these products and activities in research and development in the area of human reproduction must occur under strictly regulated conditions.

> The impact of market forces in the area of human reproduction could, if not properly regulated, undermine important social values and ethical principles and harm people by leading to inappropriate, unethical, or unsafe use of technology.

Our specific proposals for how to limit and regulate commercial forces are discussed throughout Part Two of our report, as this issue arises in virtually every aspect of our mandate. We make recommendations regarding the appropriate role of commercial interests in the chapters on fertility drugs, assisted insemination, assisted conception, adoption, preconception arrangements, prenatal diagnosis, embryo research, and the use of fetal tissue. Indeed, the need to protect vulnerable interests by limiting or regulating commercial interests is part of the fabric of all the chapters and is woven into our deliberations and recommendations throughout the report.

The purpose of this chapter is to give the reader a general picture of the role of commercial interests in reproductive technologies in Canada today. We begin with a brief overview of the extent of commercial interests in the various areas of our mandate, then we go on to consider some of the general issues and concerns raised by the presence of commercial interests and present our stance on the appropriate role and regulation of these interests. We conclude the chapter with a brief discussion of the role of patenting in the field of new reproductive technologies.

The Extent of New Reproductive Technology-Related Commercial Interests in Canada

To assess the extent and nature of industry involvement in reproductive technologies, the Commission undertook a review of private sector activity in the field. We commissioned studies to evaluate the social and economic forces influencing the development of assisted reproductive techniques and to determine the extent of private sector involvement in the provision of fertility drugs, medical devices used for reproductive technologies, and commercial laboratory services. We also conducted surveys of pharmaceutical and biotechnology companies to determine the

extent of their involvement in the development of specific products used in reproductive technologies and commissioned research to examine the extent to which IVF clinics, sperm banks, and other services are privately run on a commercial basis. This section contains a brief outline of our findings regarding commercial involvement in products and services related to new reproductive technologies. (Detailed discussion is available in our research volume entitled *New Reproductive Technologies and the Science, Industry, Education, and Social Welfare Systems in Canada.*)

Commercial Involvement in New Reproductive Technology-Related Products

Commercial interests involved in the manufacture of new reproductive technology-related products can be divided into three groups — pharmaceutical companies, which manufacture fertility drugs; biotechnology firms, which produce genetic probes and test kits; and the medical devices industry.

Pharmaceutical Companies and Fertility Drugs

During our public hearings, many people suggested that the pharmaceutical industry has targeted fertility drugs as a major growth area and has engaged in extensive research and marketing in this area. Our evidence suggests that this is not the case. We found that the market for fertility drugs in Canada is small at present, accounting for about four-tenths of 1 percent of the total $4.2 billion pharmaceutical market in this country, or about $16 million annually.

Of the approximately 3 000 drugs listed in the 1991 *Compendium of Pharmaceuticals and Specialties*, approximately a dozen are used in the treatment of infertility. These fertility drugs are produced by just a few companies. A single company, Serono Canada Inc., currently accounts for approximately three-quarters of all fertility drug sales in Canada. Serono Canada Inc. is part of The Ares-Serono Group, based in Geneva, Switzerland, which is the major world producer of fertility drugs. Other companies that market fertility drugs in Canada are Merrill Dow, Ayerst, and Sandoz.

A survey of the members of the Pharmaceutical Manufacturers Association of Canada (conducted for the Commission in November 1991) showed that relatively few pharmaceutical companies are currently marketing drugs to treat infertility and that few have plans to move into this market. Information was also collected separately from Serono Canada Inc., which is not a member of the Pharmaceutical Manufacturers Association of Canada and so did not participate in the survey.

Most companies regard the infertility market as relatively unimportant because the potential users of fertility drugs (primarily women of childbearing age who are infertile) represent only a small fraction of the

total population. By contrast, the potential market for fertility control and post-menopausal products is much larger; products in these areas are therefore likely to generate a better return on investment. Also of interest is the fact that generic manufacturers have not moved into the infertility market, even though most fertility drugs are not patented; this is another reflection of the industry's perception that fertility drugs do not have significant volume and profit potential.

Because of the small market, even those companies that do produce fertility drugs often do not advertise or promote their fertility drugs in Canada, but instead put their promotional efforts behind products with greater profit potential. The major exception is The Ares-Serono Group, which specializes in fertility drugs and actively promotes its products in Canada and elsewhere.

Even if the market for fertility drugs is small in relative terms, and even if few firms are involved at present, Commissioners consider it important nevertheless to ensure that regulations are in place to protect vulnerable interests with regard to the activities of commercial companies. We have the opportunity to establish such protections in Canada now, and Commissioners believe Canada should seize this opportunity while it exists.

Biotechnology Companies

In Canada, the biotechnology "industry" consists of between 300 and 400 companies loosely identified as belonging in this category by their use of biological methods in research and manufacturing. These companies are found in many industrial sectors, from mining and aquaculture to waste management and health care. According to Industry and Science Canada, biotechnology is best seen as a technology used in many industries, not as an industry in itself.

Among the Canadian biotechnology firms active in the field of health care, some are the research arms of conventional pharmaceutical companies, demonstrating that the distinction between biotechnology firms and pharmaceutical companies is not a sharp one. Of the almost 300 Canadian companies and research institutes listed in the *Canadian Biotechnology Directory*, about 90 are listed as being active in the area of health care. Seven of these are involved in areas relevant to reproductive health, manufacturing and/or developing reproductive health care products such as diagnostic and therapeutic products for sexually transmitted diseases, pregnancy detection and assessment products, and hormone testing products (including fertility test kits).[1] One of these companies owns the rights to the gene probe technology used in paternity tests, and another is involved in trying to license the probe for the cystic fibrosis gene. In addition, certain biotechnology companies are developing and producing recombinant versions of existing fertility drugs (see Chapter 18).

A common impression that biotechnology companies are widely involved in new reproductive technology-related research may stem from

the fact that some of these companies, particularly in the United States, are involved in research related to genetic testing. Like many large pharmaceutical firms, some biotechnology companies on this continent are involved in research aimed at discovering the molecular genetic components of common multifactorial diseases such as auto-immune disorders, neurological disorders, blood diseases, and cancer. The driving force behind this research is the prospect of developing new and potentially profitable treatments (mainly drugs), based on a better understanding of the underlying disease processes.

It is important to distinguish the various categories of use of genetic testing, as the largest potential use is not related to reproduction per se. The first category is genetic testing in the population at large to identify individuals who have a single-gene disorder and who may benefit from treatment for that disease — for example, in Canada, newborn screening for phenylketonuria. Such disorders are uncommon, but there are more common diseases that are not single gene but do have a genetic component — multi-factorial disorders — the second category of genetic testing (see Chapter 27).

It is in this category (multi-factorial disorders) that some U.S. biotechnology companies see a potential for development, as it could involve a very large testing market. Given the private health insurance system in the United States, there is a large potential market in that country for techniques to identify risk status, especially if health insurance costs continue to be borne by employers. This is not the situation in Canada, where everyone is covered in the publicly supported system. A third category of genetic tests is those used to identify adults who do not and will not themselves have a genetic disease but who are carriers, meaning that they are at higher risk that their children will have a genetic disease. A fourth use of genetic testing is to identify the presence of a genetic disease in a zygote or fetus through preimplantation or prenatal diagnosis.

> First, we strongly believe that neither bodies, nor gametes, nor human embryos, nor any part of our reproductive potential, should be considered fungible or marketable commodities. Permitting the exploitation, conditioning and distribution of the seeds of life, human embryos and infants, in accordance with market forces, ignores the principles of human dignity and individuality.
>
> We demand that the principle of no charge for services that has always guided Canadian law and policy on blood and organ donations be upheld, and we recommend that marketing of gamete and embryo transfers be prohibited. [Translation]
>
> *G. Létourneau, Commission de réforme du droit du Canada, Public Hearings Transcripts, Montreal, Quebec, November 21, 1990.*

Biotechnology companies in other countries, particularly the United States, are involved in developing gene probes and tests. Their main motivation is to find large and profitable markets such as that provided by multifactorial disease. Gene testing could theoretically be used or applied in one of the four ways just described. However, the Canadian biotechnology industry is not involved in any significant way in such development or research, although one company, the Hospital for Sick Children Research and Development Limited Partnership, is involved in licensing the probe for the cystic fibrosis gene (which may have uses in the reproductive context for prenatal diagnosis). To date this has not proved profitable. If and when the hospital does start receiving royalties, it expects only modest returns.

There are many reasons for limited commercial involvement in developing genetic tests to apply to prenatal diagnosis (or other uses) in Canada. Ethical issues, for instance, are a major concern with respect to whether it is appropriate to engage in prenatal diagnosis for the most common (and therefore potentially most profitable) genetic conditions, such as susceptibility genes or late-onset genetic diseases, which may not manifest themselves until adulthood. Moreover, the demand for prenatal testing for treatable or adult-onset genetic diseases is less than some people originally expected, and the testing itself has proven to be more complicated than anticipated. Possibly the biggest obstacle to private sector involvement in Canada is the question of who will pay for costly testing and counselling in an era of health spending constraints. Provincial health insurance plans have not funded prenatal genetic testing except for conditions that cause serious congenital disabilities, and this makes it less likely that commercial activities in this area will be profitable. However, the possibility that inexpensive, over-the-counter test kits (even if they prove unreliable and open to misinterpretation) could be developed and marketed to large numbers of people may be motivating some U.S. companies to pursue research. What effect this might have, if such products are then marketed in Canada as well, is unknown.

In summary, it appears that very few Canadian biotechnology companies are engaged in research that is directly relevant to new reproductive technologies. In Canada, the vast majority of such research is being done in universities and funded by government granting agencies or private foundations. Nor are any biotechnology companies in Canada involved in gene therapy (see Chapter 29).

Any future application of such genetic tests to the area of reproduction should be monitored by the National Reproductive Technologies Commission, and governments should put measures in place to protect vulnerable interests.

Medical Devices Companies

Medical devices are health care products that are not drugs or medicines but are used for diagnostic or therapeutic purposes. According to the industry association, Medical Devices Canada (MEDEC), medical devices generally fall into one of several subgroups: diagnostics; medical imaging and therapy; medical/surgical supply; hospital equipment; implants; and assistive devices.

Some 600 companies sell medical devices in Canada; many are divisions of large multinationals or subsidiaries of major pharmaceutical firms. They supply the $2.5 billion market in Canada with products in 6 500 categories (see research volume, *New Reproductive Technologies and the Science, Industry, Education, and Social Welfare Systems in Canada*). Items range from bedpans to CAT scanners and medical information computer systems. Eighty percent of the medical devices sold in Canada are imported (mainly from the United States).

The medical devices that are most relevant to new reproductive technologies are diagnostics (used in laboratory testing to measure hormone levels); ultrasound equipment; and specialized equipment for use in IVF and other forms of assisted conception. According to industry experts, it is not possible from available data to assess how much of the medical devices industry is devoted specifically to new reproductive technologies, but it is considered very small indeed.

The diagnostics subsector of the industry manufactures test materials (often called "reagents") consumed in the process of laboratory testing, as well as sophisticated equipment and auto-analyzers used to process test samples. The total size of the "consumables" portion of the Canadian market is estimated at $350 million. Despite a major marketing thrust during the 1980s by some companies to promote fertility hormone test lines (seen then as a potential growth area), sales of reagents used in testing fertility hormones today account for only about 2 percent ($7 million) of the annual consumables market. For the diagnostics industry, fertility testing is seen as a very small specialized market, though for certain niche companies it may be an important one.

A second subsector of the medical devices market with relevance to new reproductive technologies is ultrasound. This form of imaging is now used widely in medicine generally. Ultrasound scanning in the field of women's reproductive health is most widely used in the assessment of pregnancy. Ultrasound technology is also used in investigation of infertility (to examine the uterus and fallopian tubes, for instance) and to monitor daily the development of eggs in the ovaries during IVF cycles.

In Canada, the ultrasound equipment market for all medical uses has recently been estimated at approximately $50 million annually — $32 million in hospital sales and the rest in sales to government laboratories, university research centres, and doctors' offices. Ultrasound is used widely

in many specialties of medicine and surgery for diagnosis, but no figures are available on what proportion of this use is relevant to reproductive problems.

A third relevant subsector involves specialized devices developed and manufactured specifically for use in IVF, assisted insemination, and related procedures. These items include aspiration needles used during egg retrieval, zygote transfer catheters (tubes), and various other catheters for use in assisted insemination or assisted conception. The total Canadian market for such items has been estimated at approximately $250 000 and is so small that it is not captured in industry data.

In summary, it appears that the market for new reproductive technology-related products in Canada is quite small and constitutes only a fraction of the total market for pharmaceutical, biotechnology, and medical devices companies. Of course, the fact that these markets are small does not mean that the profit motive is absent or that these companies manufacture new reproductive technology-related products out of compassion. On the contrary, like any other industry, the objective for these companies is to make a return on investment. Clearly, the profit motive must be the main driving force behind all research, development, and marketing decisions that companies make about their products — the underlying goal is to make money by making saleable products. This applies to the market for fertility drugs, which has been consistently profitable,[2] as well as to the market for genetic tests and medical devices.

Moreover, Canadian pharmaceutical, biotechnology, and medical devices manufacturers must be situated within the larger global economy. Most of these companies are subsidiaries of foreign-owned companies based in the United States or Europe. In the case of fertility drugs, the global market is estimated to be worth approximately half a billion dollars,[3] so the $16 million Canadian market represents 3.2 percent of the total world market. This means that product development and marketing decisions made in Canada are influenced or made by corporations with headquarters elsewhere. It also means that most research, development, and testing of new drugs or devices take place outside Canada, with only the marketing carried out here. Multinational companies conduct their research where the research facilities exist and where it is most profitable to do so; The Ares-Serono Group, for example, spends less than 1 percent of its research budget in Canada. As we discuss later in this chapter, this international dimension of the manufacture of new reproductive technology-related products raises important issues.

Commercial Involvement in New Reproductive Technology-Related Services

The second major category of commercial interests involves the provision of new reproductive technology-related services on a for-profit basis. This includes commercial laboratories, commercial sperm banks,

private (commercial) IVF and sex preselection clinics, and commercial preconception (surrogacy) agencies.

Commercial Medical Laboratory Testing

Medical laboratories provide a range of diagnostic testing services such as routine blood and urine tests, as well as more specialized tests. These laboratories may be associated with hospitals or public health departments, operating on a non-profit basis, or they may be commercial companies, operating for profit. Commercial laboratories conduct medical tests on the written request of a physician and are reimbursed by provincial health plans.

The overall market for commercial laboratory medical testing in Canada has been estimated at approximately $700 million annually. The bulk of commercial testing occurs in Ontario, and indeed some other provinces have no commercial laboratories. Our evidence suggests that commercial laboratories provide very few new reproductive technology-related services. In principle, commercial laboratories could provide two important new reproductive technology-related services: genetic testing and infertility testing. However, no commercial laboratories are used for genetic testing in Canada at this time; all molecular genetic testing is done by universities, teaching hospitals, or government-funded genetics centres. In the United States, by contrast, commercial genetic testing is a $150 million a year industry and growing.

There is some use of commercial laboratories for tests related to fertility assessment and assisted conception, but this constitutes a very small percentage of the overall commercial laboratory market in Canada. One estimate puts the figure for infertility testing in commercial laboratories at $7.5 million annually, or approximately 1 percent of the total. For Canada's largest commercial laboratory company (MDS Laboratories), fertility testing represents 1 to 2 percent of its revenues. The volume of fertility testing by commercial laboratories increased during the 1980s but has now levelled off. This may be partly because some physicians involved in private IVF clinics have set up their own laboratories as part of clinic services.

Commercial Clinics Providing Assisted Conception Services

Commercial laboratories have become a well-established part of the health care system in some provinces, and their services are covered by the provincial health plans. Most other commercial new reproductive technology-related services, however, operate on the margins of the health care system, billing patients directly for uninsured services on a for-profit basis. These include commercial IVF and sex preselection clinics and commercial sperm banks.

Commercial In Vitro Fertilization Clinics: The distinction between commercial and non-commercial clinics is not clear or easy to make in practice. Three categories of activity in health care that can be distinguished are for-profit (drug companies), not-for-profit (hospitals), and not-only-for-profit (physicians' own practices or clinics). However, this last category includes clinics where (1) the physician is on salary (from a hospital or university); (2) physician income comes only from reimbursements by the provincial medical insurance plan for services rendered; or (3) the patient pays a fee that not only covers costs but provides income for the physician.

For purposes of our analysis, the Commission defines a commercial clinic as any clinic that charges patients fees, unless these are charged simply to recover the clinic's costs of services and the physicians involved derive no additional income from these fees. A Commission survey showed that 4 of the 17 clinics providing IVF in Canada are commercial clinics according to this definition (see Chapter 20). The remaining IVF clinics operate on a non-profit basis, in affiliation with a university or teaching hospital. The four commercial clinics are the Toronto Fertility Sterility Institute; C.A.R.E. Centre (Mississauga, Ontario); IVF Canada (Scarborough, Ontario); and the Institut de Médecine de la Reproduction de Montréal (IMRM) Inc.

The first three are owned and operated by physicians. The fourth is funded in part by local business interests. These clinics charge a fee to their patients, as do most IVF clinics in Canada, since IVF is an insured service only in Ontario. However, at these four clinics, the patient's fee is designed not only to recover the costs of the procedure, but also to provide a profit to the clinic, so that a proportion provides income to the physician or provides a return on investment to the clinic's owners. These four clinics treated about one-quarter (640 of 2 494) of all IVF patients treated in Canada in 1991.

Commercial Sperm Banks: Our survey showed that there are some 15 sperm banks in Canada, of which 4 operate on a for-profit basis. The rest are affiliated with hospitals or teaching hospitals/universities. Donors are paid $75 per sample on average. This is usually described as compensation for the donor's time and inconvenience, not payment for the sperm itself. After processing, one donated sample is divided into "insemination units" — 8 to 10 is not an unusual number of units. These units are then sold to physicians involved in infertility treatment. One Toronto sperm bank charges doctors between $100 and $150 per insemination unit.[4] Thus, a $75 sample might yield $1 000 for the sperm bank.

The difference between the payment to the sperm donor and the price charged by the sperm bank for insemination units is not pure profit. Costs for testing the sperm, freezing and thawing, record keeping, and distribution must be taken into account. However, commercial sperm

banks do make a profit on the sale of sperm to doctors. Some doctors, in turn, may also mark up the price of the insemination unit charged to the patient, to help cover clinic overhead costs. The cost to the recipient varies greatly but averages $300 to $400 per cycle, which includes two or three inseminations.

There is little published information on sperm banking in this country, and the total value of the Canadian commercial trade in human sperm is not known. Some clinics in Canada use sperm from commercial banks in the United States. In the United States, assisted insemination is estimated to be a $164-million-a-year industry, according to a 1987 Office of Technology Assessment survey,[5] which included both sperm bank earnings and those of doctors providing AI. One U.S. commercial sperm bank, California Cryobank in Los Angeles, stores 100 000 frozen samples and ships 2 300 vials each month. In the United States, there is so little regulation of the industry that no one — not professional groups or governments at any level — knows how many commercial sperm banks exist. Approximately 45 sperm banks are members of the American Association of Tissue Banks, but only 12 are accredited by the association. This kind of activity in the United States shows what could happen in Canada without regulation.

Commercial Sex Preselection Clinics: In 1973, an American researcher, Ronald Ericsson, discovered a technique for separating sperm aimed at yielding samples that are richer in either Y-bearing sperm (which leads to boys) or X-bearing sperm (which leads to girls). He claims that women desiring a boy (or a girl) who are inseminated with sperm treated by his technique increase their chances of having a child of the desired sex to 69 percent for a girl, and 71 to 76 percent for a boy, although these claims have not been independently verified.

This sperm treatment technique has been patented and franchised to 57 clinics in the United States that specialize in this service, often called "sex preselection clinics." There is less interest in such clinics in Canada. However, one clinic using the technique opened in 1987, and a second one opened recently, both in Toronto. The procedure is not covered by the provincial medical insurance plans, and the charge is about $500 per insemination.

Other Commercial Services

In the United States, at least two other types of new reproductive technology-related commercial services exist. Fetal sexing clinics use ultrasound to provide prenatal diagnosis of the sex of the fetus for couples who might choose to abort a fetus of the undesired sex. In fact, an American physician has patented a technique for determining fetal sex at about 12 to 14 weeks' gestation and has opened several clinics offering this service — including one across the border from Vancouver, which he hopes

will attract Canadians. There are no fetal sexing clinics in Canada, and the physician in question does not have a licence to practise medicine in British Columbia.

Commercial surrogacy agencies arrange preconception agreements for couples who wish to hire a woman to conceive, bear, and then relinquish a child. An agency's fee for arranging such an agreement may run into the tens of thousands of dollars. There are no such agencies in Canada, and such activities would probably be deemed illegal under provincial adoption laws (see Chapter 23).

The Appropriate Role and Regulation of Commercial Interests

The preceding overview shows that new reproductive technology-related products constitute a small fraction of the pharmaceutical, biotechnology, and medical devices markets and are not seen as priority areas for research and development by most companies in these industries. Similarly, most new reproductive technology-related services are provided through the publicly supported health care system. In Canada, there are four commercial sperm banks, four commercial IVF clinics, two sex preselection clinics, and no commercial surrogacy agencies or fetal sexing clinics. Nevertheless, there is no guarantee that this situation will not change, and even limited commercial interests can have a significant impact on the way new reproductive technologies are developed and disseminated. Moreover, these interests could become much more prevalent, as they are in the United States — technological developments elsewhere could be imported into Canada, and new reproductive technology-related products and services could potentially provide a source of profit in this country. These areas are open to exploitation by business unless safeguards and regulations are put in place. As a society, we must think carefully about the appropriate role for commercial interests and about the best mechanisms for ensuring that they are kept within the desired boundaries and that regulations are in place to provide oversight and protect vulnerable interests. We have a window of opportunity to act, and we should not fail to use it.

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Commissioners see nine important aspects that must be addressed in assessing the role of commercial interests. We took these into account in considering the options for regulation and in formulating our recommendations throughout Part Two of our report. The nine aspects are as follows: research priorities; ethical review of research; conflicts of interest; testing of products and services; marketing; access; public subsidy of private clinics; commodification; and technology transfer. We outline these in the following pages, and our specific recommendations on these issues are discussed in subsequent chapters, in the context of the particular technologies or procedures to which they are relevant.

Research Priorities

When making research decisions, those with commercial interests invest in a line of research only if they think it will lead to some product or service that can be sold for a profit. For example, pharmaceutical companies fund research into infertility only if it is likely to lead to the development of a new patentable fertility drug or other potentially lucrative new reproductive technology-related product.

Many forms of research that would be beneficial to Canadians are not likely to lead to profitable products or services. For example, much research into the causes and prevention of infertility is unlikely to lead to the development of a saleable drug, device, or commercial service. Yet, as we have shown in our discussion of the ethic of care, preventing a disease, where possible, is generally preferable to treating it through drugs or surgery after it has already caused harm.

Thus, the kinds of research that are most valuable to commercial interests may not always be the kind that are most valuable to the Canadian public. If commercial interests were able to determine priorities for medical research in Canada, the resulting priorities could be distorted. The possibility of private capture of the public research process is something to which society should be alert and against which society should seek to guard itself. A consequence of the new federal patent legislation means that substantial funds have to be spent by pharmaceutical companies on research in Canada. If this money is channelled into the Medical Research Council and universities, especially in the context of static or declining public research resources, there is a danger the decision-making process regarding research priorities in those institutions will be skewed. The availability of money from pharmaceutical companies carries with it an in-built temptation to frame research questions in a way that might lead to potential applications that could be of benefit to that industry. It is incumbent upon universities and publicly funded research agencies to make this conflict overt; awareness of it should be incorporated into the thinking and approach of decision makers in these settings.

At the heart of this concern is how perceptions of the causes and treatment of disease could be distorted by research that is driven solely by commercial motives. The determinants of disease are in fact extremely complex, highly inter-related, and embedded in a social context, as we discussed in Chapter 4. To tease out only one strand of this web — the one that may be amenable to pharmaceutical treatment — contributes to a simplistic and inappropriate view of health and disease.

It is therefore important that acceptance of money with strings attached by universities and public funding agencies be viewed with great caution. In its discussions with the Commission, the Pharmaceutical Manufacturers Association of Canada argued that the current tax law requires that the money they give to agencies to support research must meet certain criteria of relevance to their commercial activities. This situation should be reviewed and the law amended if necessary so that money given to certain major public research funding agencies, without conditions, is still eligible for tax credits.

As well as the potential to influence research activities, the significant financial resources available in the pharmaceutical industry for research and development of new drugs, compared to the more limited public funds for basic research on human reproduction, may lead to an emphasis on treatment approaches and the relative neglect of research into preventive measures. The distinction between research into causes/prevention and that geared to developing new patentable drugs is not completely clear. Some pharmaceutical products, notably vaccines, are used specifically in prevention, while others are used to inhibit the progression of disease (for example, antibiotics), thereby preventing more serious health problems. For example, a vaccine against chlamydia (see Chapter 10) would be both profitable and of great benefit. Some drug research is focussed on gaining a better understanding of underlying disease processes, and this knowledge, while it may result in development of a new drug, also adds to the body of scientific knowledge that may lead eventually to prevention methods or ways to minimize the condition without drugs.

> The kinds of research that are most valuable to commercial interests may not always be the kind that are most valuable to the Canadian public. The possibility of private capture of the public research process is something to which society should be alert and against which society should seek to guard itself. It is incumbent upon universities and publicly funded research agencies to make this conflict overt; awareness of it should be incorporated into the thinking and approach of decision makers in these settings.

Currently, the private sector provides a relatively small proportion of funding for biomedical research carried out at universities and university-affiliated hospitals in Canada. In 1989-90, $577 million was spent on all

biomedical research conducted by Canadian faculties of medicine.[6] The private sector funded 8.3 percent (about $48 million), and just over 70 percent was funded by federal and provincial governments and not-for-profit foundations. (The private sector also conducts a certain amount of in-house research, estimated at $237 million for research in the medical and pharmaceutical fields in 1990.[7]) The federally funded Medical Research Council of Canada alone supports 30 percent of biomedical research carried out at universities in Canada. These public agencies help ensure that the health needs of Canadians, not commercial profit, remain the primary determinant of medical research priorities in universities in Canada.

The current economic situation has curtailed growth in government funding of research, and there is an increasing danger that commercial imperatives will have a greater influence on medical research in the future. This issue arises throughout our report, and we have made recommendations directed to ensuring that the public interest is respected in the determination of medical research priorities. We also discuss ways of improving the use of public research funds, to target areas of medical research that are neglected by commercial interests. We recommend in some cases that commercial interests be encouraged or required to contribute resources to public research funds.

We believe that commercial funding can play a legitimate role in medical research in Canada but that active steps are needed to ensure that this participation does not skew research priorities and activities in universities and publicly funded agencies. We discuss research funding and priorities and make recommendations regarding it throughout Part Two, in the context of infertility prevention, assisted conception, prenatal diagnosis, human zygote/embryo research, and research involving the use of fetal tissue.

We believe that commercial funding can play a legitimate role in medical research in Canada but that active steps are needed to ensure that this participation does not skew research priorities and activities in universities and publicly funded agencies.

Ethical Review of Research

Most medical research in Canada that involves human subjects is approved by a local research ethics board. Research ethics boards evaluate the scientific aspects of proposed research and consider ethical issues such as whether the procedure for gaining informed consent from research participants is appropriate. Research ethics board approval provides a valuable check to ensure that the interests of research subjects, and of the wider society, are respected in medical research.

Research ethics board approval is required for any publicly funded medical research involving human subjects. Universities and hospitals also require that research within their institutions have research ethics board approval. However, research ethics board review is not legally required, and some important forms of medical research may not be adequately reviewed. This is particularly true of commercially funded research that takes place outside hospitals or universities. For example, commercially funded research conducted by private physicians in their offices, or conducted in-house by commercial firms, may not be reviewed by a research ethics board.

We believe strongly that commercially funded research involving human subjects should receive the same ethical review as publicly funded research. Indeed, the presence of a profit motive means that commercially funded research is particularly in need of independent research ethics board approval. We have therefore made recommendations, throughout Part Two, to ensure that commercially funded medical research is also subject to research ethics board approval. This applies not only to research involving human subjects, but also to research involving human zygotes and the use of fetal tissue.

The presence of a profit motive means that commercially funded research is particularly in need of independent research ethics board approval.

As we noted earlier, much of the research conducted on new reproductive technology-related products takes place outside Canada. In some countries, research ethics boards do not exist, raising the possibility that companies may seek to avoid ethical guidelines in developed countries by testing drugs or devices in developing countries, where standards of safety and informed consent are not as rigorous.

It is generally accepted that abuses did occur in the past with drugs such as contraceptives, but the industry denies that they still occur. We were unable to find evidence or documentation regarding such practices. It would, of course, be unacceptable if the burden of experimentation were to fall on women in the developing world, while the benefits accrued to the relatively privileged citizens of Western nations. To help prevent such a situation, Canada has a moral responsibility to ensure that fertility drugs, and new reproductive technologies generally, are developed and used in a responsible way both in Canada and abroad. Our recommendations concerning Canada's international role in preventing the abuse of new reproductive technologies are presented later in this part of our report.

We believe strongly that commercially funded research involving human subjects should receive the same ethical review as publicly funded research.

Conflicts of Interest in Particular Situations

As explained at the beginning of this chapter, the existence of commercial interests in the provision of new reproductive technologies creates conflicts of interest; vulnerable interests need protection if appropriate resolution of those conflicts is to occur. If pharmaceutical companies become involved in the provision of services related to reproductive technologies, a conflict arises in which vulnerable interests may not be protected. A profit-seeking organization that establishes or purchases an infertility treatment clinic, for example, enabling it to set clinical policy, is not subject to professional controls and monitoring or guided by social and personal expectations (as physicians are expected to be) that it will seek patients' interests first. A similar conflict of interest could arise, with no means to protect vulnerable interests, if pharmaceutical companies set up or directly fund data bases or registries to keep track of the outcomes of fertility drugs used — hence the need for an intervening arm's-length mechanism through which to channel such funding.

Similarly, when commercial IVF clinics own laboratories that provide fertility testing, or when physicians who own laboratories can refer patients to those laboratories for tests, a conflict of interest arises in which protection, in the form of regulation of commercial activities, is needed to ensure the conflict is resolved appropriately.

Commissioners believe that allowing these conflicts of interest to persist without regulatory oversight is not to the benefit of Canadians. It is unrealistic to expect for-profit enterprises to regulate themselves in ways inimical to profits. We have therefore made recommendations regarding the ownership and management of clinics, data bases on treatment, and laboratories with this in mind.

Testing of Products and Services

The issue of product and service testing for safety and efficacy provides a cogent illustration of a conflict of interest in the development and use of medical technologies; the interests of commercial firms and of people seeking treatment do not coincide exactly.

For commercial firms, in the absence of legal requirements, the profit motive determines what products to research and how extensively to test for safety and efficacy. Although it is often in the interests of companies to conduct a certain amount of testing and follow-up apart from that legally required, companies cannot be expected voluntarily to do the research and long-term follow-up needed to ensure that new drugs, devices, or services are safe and effective when used by large numbers of people over a significant length of time. It is in the interests of patients, however, that such testing be stringent and ongoing.

Companies that market unsafe or ineffective products and services may find themselves subject to lawsuits, and sales may be hurt by a poor reputation, so they have a certain interest in product testing. By themselves, however, these motivations are not sufficient to protect the health of Canadians. The federal government must also require adequate testing and follow-up of new reproductive technology-related products and services to protect the interests of patients.

At present, regulations regarding the testing of medical products and services vary greatly. For example, pharmaceutical products, including fertility drugs, must be approved by the federal government before they go on the market. Pharmaceutical companies must provide evidence of a drug's safety and efficacy before this approval is granted (see Chapter 18). Long-term follow-up on the outcomes of drug use is seriously lacking, however. Nor are all medical devices and diagnostic tests closely regulated. The regulations require submission of test results and pre-marketing approval for only a small fraction of the medical devices and diagnostic tests on the market today. There is no requirement that new services, such as assisted conception techniques, be tested and approved before being provided by commercial clinics if they are provided by physicians.

We believe that appropriate testing and follow-up are essential for all new reproductive technology-related products and services, and we make recommendations throughout Part Two to ensure this. For example, we recommend ways of improving the drug approval process. We also propose a regulatory system for the provision of assisted conception and prenatal diagnosis services; the proposed National Reproductive Technologies Commission would be responsible for approving new procedures and services before they are introduced at licensed clinics. We also recommend a system of record keeping and data linkage, which would allow for improved long-term follow-up.

Marketing of Products and Services

Once a product has been developed or a commercial clinic established, companies use marketing strategies they have found effective to recoup their investment and maximize profits.

Questions have been raised about whether companies are providing the objective information that doctors and patients need as the basis for informed choice; questions have also been raised about the accuracy and comprehensiveness of information provided by pharmaceutical companies to doctors and pharmacists. Similarly, concerns have been expressed that commercial IVF and sex preselection clinics do not provide prospective patients with sufficient objective information and non-directive counselling to ensure that they can exercise informed consent.

Complete, accurate, and objective information is a precondition of informed choice, and doctors and patients must have access to such information. We make recommendations to this effect, including the

standardization of written information materials and consent forms, the monitoring of promotional literature, the need for non-directive counselling, and the provision of independent information by the National Reproductive Technologies Commission and the federal government.

Equal Access

Patients must pay for services provided at commercial clinics; those who are unable to afford the fee will not have access to the service. This creates a two-tier system, in which access to services depends on ability to pay.

The Commission strongly opposes the development of a two-tier health care system. We believe that medical services that are safe, effective, and ethically appropriate should, wherever possible, be included in provincial health plans. Some of the services currently provided are not safe or ethically appropriate, and these should not be provided at all. Others are unproven and should not be provided as treatment unless and until their safety and efficacy have been demonstrated. But we believe, based on our review of the evidence and our ethical assessment, that some reproductive technologies should be included in the publicly funded health care system. Commissioners saw the evidence that having children is an important part of people's lives. The ability to have children is not a luxury or a frill, so that effective assisted conception services for people who are infertile are as or more important than many other services already provided in the health care system. We therefore conclude that if effective and safe procedures exist and can be provided at a reasonable cost, they should be provided through the health care system. In addition, equal access to legitimate medical services is a basic principle of Canada's health care system, and we have structured our recommendations regarding the funding of services and the licensing of clinics with this in mind.

The Commission strongly opposes the development of a two-tier health care system. We believe that medical services that are safe, effective, and ethically appropriate should, wherever possible, be included in provincial health plans. Some of the services currently provided are not safe or ethically appropriate, and these should not be provided at all. Others are unproven and should not be provided as treatment unless and until their safety and efficacy have been demonstrated.

Public Subsidy of Private Clinics

Commercial clinics are seen by some as operating parallel to and complementing the publicly supported health care system. In this view, whereas the publicly supported health care system provides medically

necessary services to all on the basis of medical need, commercial clinics provide what are considered optional services to those who are willing to pay. Commercial clinics are perceived as not affecting the public health care system, but simply providing additional services that the public system is unwilling to provide.

Commissioners are strongly opposed to such a view. There are compelling reasons for approved procedures to be carried out only in licensed, publicly supported clinics; principal among them is the strong evidence that commercial clinics impose many hidden costs on the public health care system. For example, although *in vitro* fertilization and embryo transfer are not an insured health service in most provinces, the cost of laboratory tests associated with the procedure is borne by the health care system. Similarly, the public health care system must cover the costs associated with the multiple births that often result from the use of fertility drugs administered at private IVF clinics. Moreover, public resources would be needed to monitor these clinics and ensure their compliance with standards of safety and informed consent, and public resources are used to train their medical and nursing personnel.

> The predominant force driving the pharmaceutical industry is identical to the driving force behind any other business or commercial venture — the need to make a profit on investment ... That raises the question of whether some NRTs should be provided through the private market. There are private chains of clinics in the United States, and the public/private balance could be shifted in this area. If it were to be, then we have to contemplate not only a private, profit-driven pharmaceutical industry, but a private profit-driven industry which is actually using the products of the pharmaceutical industry.
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> Under those circumstances, it seems to me that the problems of surveillance and of appropriate utilization become even more acute. At present we are dealing with physicians whose professional motivations are to try to serve patients best, and whose limitations are simply the time and effort and the information that they have available to them. Physicians, to some extent, have interests that are at variance with those of the drug companies.
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> *R.G. Evans, reviewer, research volumes of the Commission, September 28, 1992.*

There are very strong reasons to resist private medical services or direct commercial offer of genetic testing or reproductive technology to the public. These services need to be developed within a social framework, and quality control and monitoring of service delivery are essential to protect those using the services. For example, counselling is expensive because it takes professional time, and this is likely to be minimized in private commercial services doing genetic

testing. Governments have a responsibility to ensure that ad hoc private provision of these kinds of services does not occur.

Given that public funds are currently subsidizing the profit-making activities of commercial clinics providing uninsured services in many ways, we believe that this is an inappropriate use of public resources, which should be used only to provide medical services that are found effective, safe, and ethically acceptable for all Canadians. Our recommendations throughout the report reflect this conviction.

Commodification

The profit motive, taken to its extreme, would lead to a global market in reproductive materials and services. It would be possible to make a profit from the buying and selling of eggs, sperm, zygotes, embryos, and fetuses, as well as from preconception arrangements involving the hiring of "surrogate mothers." Indeed, commercial interests in other countries have already explored some of these possibilities.

As we have discussed, we believe that certain aspects of the human experience must never be commercialized. Among the activities that we see as ethically unacceptable on the basis of the principle of non-commercialization are the buying and selling of gametes, zygotes, embryos, or fetuses, and the use of financial incentives in preconception or adoption arrangements. To allow commercial exchanges of this type would undermine respect for human life and dignity and lead to the commodification of women and children. We recommend stringent prohibitions on these forms of commercialization throughout Part Two, in the context of assisted insemination, assisted conception, prenatal diagnosis, and research involving human zygotes/embryos and fetal tissue.

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Technology Transfer from Animals to Humans

Many of the new reproductive technologies used in assisted conception — such as *in vitro* fertilization, assisted insemination, and embryo freezing — are also used in animal breeding. Indeed, many of these techniques were developed initially to improve the commercial value of livestock (just

as some techniques developed originally for use in human beings have been transferred to animals). For example, the genetic alteration of animal embryos is used to create new breeds of animals with commercially valuable properties.

Transfer of technology from agribusiness to human medicine is worrisome to many people who think that the transfer of technology will carry with it a transfer of values. The goals of new reproductive technology use in animals are quite different, however, from the goals of new reproductive technology use in people. New reproductive technologies are used in animals to increase the number and commercial value of the offspring, not to treat infertility. If a given technology is adapted for use in human beings, however, the concern is that it may be used for purposes similar to those motivating its use in animals, leading to the commodification of women and children.

> Technical aspects of reproductive manipulation may be similar for humans and domestic animals, but the objectives are quite different. With humans the purpose of reproduction manipulation is to benefit the individual, whereas artificial insemination (AI) and embryo transfer (ET) in domestic animals are done to improve production, which benefits farmers and, ultimately, consumers.
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> *K. Betteridge and D. Rieger, "Embryo Transfer and Related Technologies in Domestic Animals: Their History, Current Status, and Future Direction, with Special Reference to Implications for Human Medicine," in Research Volumes of the Commission, 1993.*

We do not believe that technologies developed originally for commercial animal breeding purposes will be used in similar way with human beings. The values of Canadians (including both potential patients and physicians) are such that use in this way is highly unlikely. To guard against the possibility that technologies developed in animals could be transferred for inappropriate uses for human beings, and to protect the vulnerable interests involved, we make recommendations in several chapters to prohibit various uses that we consider unethical and therefore unacceptable. In addition, many of our recommendations regarding the licensing of facilities that provide new reproductive technology-related services will ensure that they are used only for non-commercial therapeutic purposes within the health care system. Finally, we have recommended the establishment of boundaries by criminalizing some uses of technology in human beings. (We discuss the transfer of technology issue in more depth in Chapter 25.)

In summary, commercial interests raise significant issues and concerns. There is an inherent difference of interests in any commercial transaction between seller and buyer. In the area of new reproductive technologies (as in all areas of medical care), there are vulnerable interests to be protected — interests of both individuals and the wider community.

If it remains unregulated, commercial activity in new reproductive technologies has the potential to undermine basic ethical principles and social values. In particular, active federal regulation is required to ensure that unethical uses of technology are prohibited; that Canadians' health priorities are respected; that commercial research is subject to ethical review; that the safety and efficacy of commercial products and services are properly tested; that accurate information is available to patients and physicians regarding these products and services; that conflicts of interest are managed with protection of vulnerable interests; that equitable access to services is protected; that public resources do not subsidize private profit; and that commodification is prevented.

With these boundaries and guidelines in place to protect vulnerable interests, however, we believe that commercial interests can play a legitimate role in developing and providing products and services that might not otherwise be available and that can be of benefit to many Canadians.

Patenting

Our mandate directed us to examine the role of patenting in relation to new reproductive technologies. A patent gives the inventor of a new product or process the right to prevent others from copying, using, or selling the invention for a specified number of years (typically 17 to 20 years) unless the inventor licenses someone else to make use of the product or process. In Canada, patenting is governed by the federal *Patent Act*.

One function of patent law is to encourage commercial investment in the development of useful innovations. Since we have argued that commercial interests can play a valuable (if circumscribed) role in developing new reproductive technology-related products and services, it might seem appropriate to provide a (limited) form of patent protection for some kinds of developments.

As we pursued this question, however, we discovered that very little is known about the implications of patent protection in this area. Indeed, there is some uncertainty about the extent to which the existing patent law already applies. There is no current catalogue of materials, instruments, or processes related to new reproductive technologies that have already been patented, for example, largely because not all inventions that could be used for new reproductive technologies are described in such specific terms in patent documents — to do so would potentially limit the application of the invention, which inventors understandably may not want to do.

The basic principles of patent law, formalized more than 200 years ago, were not designed to deal with some of the issues raised by modern technology, and the law is therefore in a state of flux. The very idea of patenting has become unclear, as various "hybrid" forms of intellectual

property rights have evolved to meet the issues raised by new technology. For example, in Canada, a distinct patent regime has evolved for plant breeders, and pharmaceutical manufacturers also face different requirements that place greater constraints on how patent holders can use their discoveries and place more emphasis on the larger interests of society. For example, the prices of patented drugs must be reviewed by the Patented Medicine Prices Review Board to protect the public interest.

Insofar as patenting is appropriate for new reproductive technology-related discoveries, it should perhaps take the form of a "hybrid" regime. However, we believe that this entire topic needs further study. It would not be helpful for this Commission to say that patent protection should or should not be extended to new reproductive technology-related discoveries. Given the diversity of new reproductive technology-related discoveries (from medical devices such as aspiration needles to genetically altered cell lines) and the shifting nature of patent law, such a statement would inevitably be simplistic and misleading. It is more helpful, we believe, to discuss the basic issues that need to be considered when assessing patenting policy in this area and to outline the principles that should guide such a policy and the boundaries within which it should operate.

To begin with, we believe that two clear boundaries must be set on patenting — patenting should not extend to medical treatments or to human eggs, sperm, zygotes, embryos, or fetuses.

Medical Treatments

A significant part of the first boundary is already in place. Innovative medical treatments performed on the human body are not subject to patent protection in Canada. There are several public policy reasons for this, including the need for unimpeded access to medical treatments, the need for impartial evaluation of their success, and the avoidance of conflict of interest for physicians. So an innovative treatment for infertility performed on the body would not be patentable, just as a new technique for treating cancer could not be patented.

However, innovative diagnostic tests and medical devices used in medical treatments can be patented in Canada. It is not entirely clear why medical tests and devices are patentable, while medical treatments are not. This distinction seems to have worked in the past in other areas of health care, but it would be necessary to ensure that the patenting of new reproductive technology-related gene probes and medical devices did not preclude adequate testing of their safety and efficacy and did not create conflicts of interest for new reproductive technology service providers or impede access to treatment.

Zygotes, Embryos, and Fetuses

Commissioners believe strongly that human zygotes, embryos, and fetuses are inappropriate subject matter for intellectual property protection. (Zygotes, embryos, and fetuses would not normally be classified as "innovations," but if they have been the subject of genetic alteration or other research, some may attempt to classify them in this way.) Inherent in the moral point of view and respect for human life is abhorrence of any recognition of property interests of one human being in another; as entities that may have the potential for human life, zygotes, embryos, and fetuses should not be patentable.

Intellectual property rights have not been recognized historically in relation to human fetuses and embryos. Although the *Patent Act* does not expressly forbid the patenting of higher life forms, to date none has been patented in Canada, nor have the courts addressed the issue of whether higher life forms are patentable. In the only case to date in this area, the 1989 *Pioneer Hi-Bred Limited* case, a patent was refused for a new type of soybean plant, but the case did not answer the question of whether a higher life form is patentable, because it was decided on other grounds.

However, the Patent Office does allow the patenting of innovative "microbial life forms." In addition to lower organisms, such as altered viruses, yeasts, and algae, the term "microbial life forms" also refers to cell lines derived from higher organisms, including human beings. Generally speaking, then, human cell lines are patentable if they meet the standards laid out in the *Patent Act*. Patentable inventions must be a novel creation or innovation, not just the discovery of a pre-existing naturally occurring phenomenon, they must be reproducible, and they must have some useful function. However, if researchers find a way to make human cells reproduce indefinitely (a process called immortalizing the cell line) and find a use for them, these cell lines can be patented, even though they already "exist" in nature, if they meet the act's criteria. Similarly, the processes associated with handling, preserving, altering, and using these cell lines can also be patented.

Human cell lines are derived from various tissues of the body, including fetal and embryonic tissue. Although embryos and fetuses cannot be patented, processes, techniques, and cell lines, not only using adult human tissue, but also using tissue from embryos and fetuses, may be entitled to such protection if they meet the act's criteria. For example, pancreatic cell lines used to make insulin are patented, as is the process for making insulin, and human cells that were used to make artificial skin have also been patented. Developing and perfecting such techniques and keeping such cell lines could require a sizable financial investment, beyond what public agencies may be willing or able to provide. Pharmaceutical or biotechnology firms might provide the investment if they have a reasonable expectation of profit, which in turn may depend on the type and extent of patent protection.

Thus, it is possible that the current patent protection for human cell lines will have beneficial consequences for Canadians; at the same time, however, concerns have been raised about the patenting of human cell lines. Some people view this as the first step toward commodifying human life. Will patenting of cell lines derived from human tissue encourage forms of research that may be unethical or socially undesirable? For example, cell lines derived from human tissue could be useful not only in improving transplantation therapy but also in developing cosmetic products. How can limits be set to encourage research into appropriate but not inappropriate uses?

These are some of the issues that need to be addressed by any proposal regarding new patent protection or alterations to existing patent protection in this area. It may be possible to shape a patent regime that promotes desirable research while avoiding these problems of commodification and unethical research. Although clearly zygotes, embryos, fetuses, eggs, and sperm should not be patentable, the problems of commodification and unethical research have more to do with the larger regulatory system within which the patent regime operates than with patenting per se.

We have recommended stringent legislation against the buying and selling of gametes, zygotes, embryos, and fetal tissue. This legislative prohibition would set the boundaries within which any patenting of microbial life forms would operate. Provided such a prohibition is in place, patent protection for cell lines may not, by itself, lead to the commodification of human life. However, if a law prohibiting the sale of gametes, zygotes, embryos, and fetal tissue were not in place, withdrawing patent protection from cell lines would not by itself eliminate the problem of commodifying human life. Patents are not the only reason why people might buy and sell gametes or fetal tissue.

We have also recommended establishment of a licensing system to regulate the use of zygotes and fetal tissue in research, including a requirement for research ethics board approval of all such research (see Chapters 22 and 31). If such a licensing scheme is put in place, patent protection for cell lines will not promote or allow the use of fetal tissue in cosmetics, or other socially undesirable research. Again, if this regulatory regime is not established, then withdrawing patent protection would not solve the problem, since patents are not the only reason why people might engage in unethical research.

In other words, although patenting human cell lines raises certain concerns, we need to distinguish those problems that are intrinsic to patenting from those that result from the lack of adequate safeguards elsewhere in the regulatory system. Moreover, it is important to remember that traditional intellectual property regimes are no longer clear-cut legal categories. Many different kinds of intellectual property regimes are possible, and governments can create "hybrid" regimes. Moreover, governments can require additional approvals that modify the rights of the

patent holder in order to protect the public interest. For example, the government could establish a rigorous approval process for certain new reproductive technology-related products, just as pharmaceutical companies must receive federal approval before marketing their patented drugs.

Clearly, this topic deserves further study. The possible forms of regimes are too many, and the existing literature too sparse, for us to generate a specific proposal for how patent legislation should be drafted. Instead, we have outlined the principles that we believe should inform public policy in this area. We believe it is important to encourage research that can potentially benefit human health, and that patenting can play a role in encouraging private investment in such research. However, any patent policy must operate within clear boundaries that preclude the patenting of medical treatments, and of human zygotes, embryos, fetuses, eggs, and sperm. Moreover, patenting in the fields of medical care, health, and reproductive technologies must be situated within a larger regulatory system that deals with issues of commodification, access to treatment, conflicts of interest, quality control, the ethical review of research, and other related matters.

We believe that the best body to engage in this further study of patenting is the National Reproductive Technologies Commission, given the access it will have to information regarding the development and provision of new reproductive technology-related products and services and its representative nature. We therefore recommend that

206. The National Reproductive Technologies Commission, in collaboration with Industry and Science Canada (Canadian Intellectual Property Office), undertake further study of the issue of intellectual property protection in the area of new reproductive technologies with a view to making recommendations to the federal government for any necessary amendments to the *Patent Act*.

Conclusion

In this chapter we have provided an overview of the extent of commercial interests in the development and marketing of new reproductive technologies in Canada. We have also discussed our view about the appropriate role of these interests and the need to provide limits and regulation so as to protect vulnerable individual and societal interests.

We found that new reproductive technologies are not a large part of the pharmaceutical, biotechnological, medical devices, or commercial medical services sectors in Canada; nonetheless, the experience in the United States shows that commercial interests may drive the development and provision of new reproductive technology-related services and technologies if they remain unregulated and may lead to the development and provision of unsafe, inappropriate, or unethical services. It is essential, therefore, that the federal government, as the guardian of the public interest, strictly regulate the research, testing, and marketing activities of commercial interests. Vulnerable interests must be protected, including those of patients, research subjects, and the broader community. We believe that the federal government has full constitutional authority to exercise this role, both under its power to regulate trade and commerce and intellectual property, and under the peace, order, and good government clause. The role of government is to protect the public interest; the current window of opportunity will not remain open indefinitely, and we believe it is therefore incumbent upon the federal government to act while it is still possible to do so in this rapidly evolving field. The implementation of our strong recommendation for a National Reproductive Technologies Commission would be the major instrument in ensuring this needed regulation.

It is essential, therefore, that the federal government, as the guardian of the public interest, strictly regulate the research, testing, and marketing activities of commercial interests ... The current window of opportunity will not remain open indefinitely, and we believe it is therefore incumbent upon the federal government to act while it is still possible to do so in this rapidly evolving field.

Our specific recommendations on how best to limit or regulate commercial interests so that vulnerable interests are protected (to be carried out by policies of the NRTC sub-committees) are discussed in chapters dealing with specific technologies, procedures, and services. These recommendations include prohibiting the inappropriate commercialization of technologies and services; strengthening the procedures governing the testing of new products and services and their approval for use; monitoring the promotional and marketing activities of commercial interests; ensuring ethical review of industry-funded research; and licensing service provision to ensure quality control and provision of objective information to prospective patients. Adoption of these recommendations would ensure that the commercial impetus is contained and regulated so that the vulnerable interests of individuals and society are protected.

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Prenatal Diagnosis and Genetic Technologies: Introduction and Social Context

For many Canadians, genetic research and the application of genetic technology embody a basic human conflict — the drive to expand the boundaries of knowledge and apply it for the benefit of humankind, contrasted with the equally real feeling that some mysteries of life should not be tampered with. This perceived conflict is often heightened by the fact that the field is evolving rapidly, often without the social debate necessary to develop a public understanding and response to its implications, and without reliable information available for the public upon which to base such a debate.

Although many areas of study relate to genetics, the Commission's mandate was to examine in particular those aspects of genetic knowledge and technology that apply to human reproduction. Myriad other endeavours are related to genetics — the mapping of human genes currently taking place as part of the international Human Genome Project (see box), for example, or the genetic manipulation of livestock and plants. These issues were outside the Commission's mandate and indeed constitute a vast field of study on their own. Although the Commission's work was necessarily limited to genetics as it relates to new reproductive technologies, it was clear during our work that many of the broader issues involving genetics are troubling for Canadians and should continue to be addressed by other bodies as they evolve.

The Commission identified four applications of genetic knowledge and practice that relate to reproduction. Although each uses genetic knowledge and technology to identify genetic make-up before birth, the application of technology is very different in each case, as are the issues raised by its use.

The first application — prenatal diagnosis for genetic diseases and anomalies — employs techniques such as amniocentesis for identification of fetal anomalies. It has become a well-known part of pregnancy care for

women who are at higher risk. Canada's approach to introducing and regulating some PND techniques such as amniocentesis has served as a model internationally. Canadians see PND for those at risk of having an affected fetus as a valuable health care service, yet there were aspects of PND delivery that warranted the Commission's attention. The challenge facing Commissioners was to determine whether PND is offered in the best interests of women and society, to assess the effect of PND use on societal attitudes toward disability and people with disabilities, and to recommend how best to manage the system, ensuring that Canada is prepared to deal with emerging issues and developments in this field.

The Human Genome Project

The Human Genome Project is an international effort, spearheaded and coordinated by the United States, to determine the structure and location of the estimated 100 000 human genes. First conceived in 1986, the project involves research teams around the world working to sequence the DNA, which is contained within human cells. It is hoped that the information gained will lead to the eventual cure of many genetic diseases. To date, about 5 percent of the genes have been identified and mapped, and researchers expect to complete the project by the year 2005. Countries involved include Japan, France, Britain, Germany, Denmark, and Italy, and Canada joined the project in 1992. The Commission did not examine the Human Genome Project per se, as our mandate asked us to examine genetic research and technology as they relate to human reproduction, and reproductive technology in particular.

A second use of PND technology is prenatal testing for late-onset disorders (diseases or conditions that can be identified before birth but do not manifest themselves until adulthood) and susceptibility genes (genes shown to increase an individual's susceptibility to certain conditions that may or may not develop later in life, such as cancers or heart disease). This technology is not in general use at present, and the Commission therefore had the opportunity to research and deliberate on its implications before development goes further. We found, for example, that this technology raises issues with respect to informed consent and confidentiality, as well as concerns about appropriate counselling for those contemplating or receiving testing, and whether it is an appropriate use of medical resources.

Ethical and social issues are also raised by a third use of PND technology — sex selection for non-medical reasons. Genetic technology can reliably identify the sex of a fetus prenatally; this capacity can be used to identify fetuses at risk of genetic diseases linked to one sex or the other. The Commission had to evaluate whether using genetic technology to identify fetal sex is appropriate or acceptable when the presence or absence of genetic diseases is not at issue.

The fourth area of interest to the Commission, gene therapy, is the newest and most complex. This use of technology not only identifies genetic diseases and anomalies, but seeks to cure these conditions by introducing normal genes either pre- or post-natally. Although gene therapy is an emerging technology and has not been attempted in human beings in Canada, it is an expanding field. It is one that raises concerns for many Canadians if the technology were to be used to change the genetic make-up of human beings for reasons other than severe disease. The Commission had a rare opportunity to examine and evaluate a technology, and to analyze its social, ethical, and generational implications, before it becomes a reality in this country. There is an opportunity to recommend policy to set parameters around further development in light of these implications.

The Commission examined these four areas of application of genetic knowledge using the same approach as we did with the other reproductive technologies. Current practices, as well as potential implications for society and for future generations of Canadians, were investigated through wide-ranging research projects in fields such as ethics, sociology, law, and other disciplines, as well as through field studies at clinics across the country. Our findings are detailed in our research volumes entitled *Prenatal Diagnosis: Background and Impact on Individuals*; *Current Practice of Prenatal Diagnosis in Canada*; and *Prenatal Diagnosis: New and Future Developments*. We reached our conclusions and recommendations in light of our ethical principles and also using the approach of evidence-based medicine, which we discussed in Part One of this report. The wide ethical and social implications of technology use were evaluated with the help of commissioned studies, data gathering, and analyses.

> As the public becomes more and more involved in the debate over new reproductive technologies, PND in particular, professionals are being called upon to explain their role in modern medicine and to justify the development of controversial technologies. Increasingly, scientists and health care professionals have to pay close attention not only to professional interests but also to their societal responsibilities. These challenges help to promulgate informed and expert information and opinion on complex and challenging issues.
>
> *I. MacKay and F.C. Fraser, "The History and Evolution of Prenatal Diagnosis," in Research Volumes of the Commission, 1993.*

The Commission investigation revealed interesting and, in some cases, worrisome data. We found, for instance, that researchers and practitioners in these fields overall have not managed to convey adequate information to the public about what genetic services in Canada do. There was little public awareness and much misunderstanding of the technologies. We

found that the counselling and information needs of some women undergoing PND were not met. Variation in beliefs and attitudes toward the prenatal diagnostic procedures by physicians referring patients for genetic testing in particular alerted us to troubling implications for patient care and access.

The gaps in public information are not solely the responsibility of researchers and practitioners. Despite the complexity of the issues surrounding these technologies, sensational and oversimplified articles continue to appear in the science, business, and popular press. Although most of these technologies have very limited application and in fact affect only a small proportion of the population, there is a perception that genetic testing has become a large industry, with widespread use of the technologies. Misinformation has contributed to the formation of public knowledge and attitudes in this area.

Another theme that emerged from our investigation of PND and applied genetics was the importance of assessing technology before it is introduced into wide practice. For instance, Canada has been a leader in the field of clinical testing of invasive prenatal diagnosis technologies used at specialized genetics centres, such as amniocentesis and chorionic villus sampling; but non-invasive screening technologies in use in the wider medical community, such as prenatal ultrasound scanning, have not followed the same careful path of technology assessment. Ultrasound use has proliferated to a point where today at least 80 percent of pregnant women in Canada are screened, at enormous cost to the health care system, while there is still debate about whether this procedure is of benefit. These and many other issues are examined in the next four chapters.

From a public policy perspective, addressing the issues raised by PND and genetic technologies involves questions of how to ensure effective and ethical management of the introduction and use of the technologies; it is important to put in place mechanisms to ensure the provision of accountable, effective, and safe health care for women and their children.

The Commission's investigation confirmed the view that these powerful technologies have the potential for rapid development. As existing technology is improved and new technologies are introduced, decisions in this area will become more complex and difficult. The Commission concludes that coordinated national and provincial efforts are called for, to reflect a societal commitment to monitor developments and to set in place systems to ensure adherence to standards of research and practice. The following chapters show how this conclusion flows from the evidence before the Commission.

Our conclusion reflects Commissioners' commitment to an ethic of care, to weighing of individual and collective interests, and to protection of vulnerable interests. The implications of applications of genetic knowledge and technologies vary according to the use proposed and the interests involved; the policy responses must take this into account. The goal of our

recommendations is to achieve an integrated system of services and standards and to provide a policy framework that allows for responsiveness as technology evolves, but within a framework that always takes social and ethical aspects into account.

Research and practices in genetic reproductive technologies occur within the framework of the health care system, but the issues they raise have implications for society as a whole. The remainder of this introductory chapter examines the values and attitudes of Canadians with respect to this field and the common themes raised by Canadians about the use of the technologies.

The Views of Canadians

The use of genetic knowledge and technology as relevant to human reproduction was an area of concern for participants in public hearings, private sessions, roundtables, panel discussions, and written submissions. Many individuals and groups presented their views. The Commission heard many concerns about specific technologies — addressed in each of the following chapters — but we also heard opinions about genetics in general. The Commission's national surveys revealed aspects of the overall social context in which PND and genetic technologies are developed and used; some of these concerns were discussed in a general sense in Part One. Some of the issues seemed to produce general agreement among Canadians. There was significant support evident for the use of PND to detect genetic disease, for example, with 84 percent of Canadians overall in favour of its use. An even stronger consensus emerged on the issue of sex selection — 92 percent of Canadians are strongly opposed to the abortion of a fetus when the sex was not the one the parents hoped for.

The public dialogue on the applications of genetics to human reproduction led Commissioners to appreciate the range of views apparent among Canadians — an appreciation that informed our investigations. Some groups representing those carrying or affected by a genetic disorder, for example, argued for the need for genetic research with the goal of effective treatment or cure; others expressed concern about the implications of such research and advocated a moratorium. Several themes in the area of genetics and new reproductive technologies emerged and seemed to define many Canadians' views about new reproductive technologies in general.

"The Future Is Here"

Growing public awareness of and concern about the power of genetics were evident in public consultations with the Commission. Many Canadians expressed fears about what the rapidly increasing capacity to

detect genetic make-up would mean for their work opportunities, how they live, and, particularly, the health care they receive and their options with respect to reproduction. Others called for a social policy debate on the emerging role of genetics in Canadian society.

For some, discoveries in the world of genetics are moving at a rate that is simply too fast for society to comprehend, let alone manage. In our national survey, for instance, 35 percent of respondents agreed with the statement that medical science is moving too fast for society to keep up. Many feel that the future is upon us without the chance of proper evaluation and assessment by members of society other than scientists and doctors.

> In the meanwhile it appears that every week new so-called advances are being made in the fields of human reproductive technologies and recombinant DNA research ... We have reached a stage in a technological development where the unthinkable is already being done and the ability to impose total genetic control seems just beyond our reach.
>
> *F. Bazos, private citizen, Public Hearings Transcripts, Toronto, Ontario, November 20, 1990.*

Some felt that genetic technology was market-driven — that commercial interests, not the interests of society, have determined the nature and direction of developments. Some advocated a moratorium in the research, to give governments and the public time to assess the social, ethical, and legal implications before science moves further, but there was little testimony on how this could be implemented in practice.

Some responded on a personal level, showing concern about whether women are being pressured or compelled to use genetic diagnostic technology simply because it exists, not because they wish to do so. Concerns were raised that the proliferation of such technologies compels women to feel that using the technology is "the responsible thing to do," despite the fact that some intervenors felt not enough societal debate had taken place on the usefulness or impact of the technologies.

> The potential for the dehumanization and depersonalization of humankind is very real and very frightening. Scientists who practise genetic manipulation, a term considered by many to be offensive, are in fact tampering with nature.
>
> *C. Johnson, Federated Women's Institutes of Canada, Public Hearings Transcripts, Winnipeg, Manitoba, October 23, 1990.*

The Commission examined current practices, existing guidelines, and research in these fields in Canada. We developed recommendations that, if implemented, will protect the vulnerable interests of individuals and of

society and promote greater public information and accountability. Our recommendations will also allow a well-informed public debate about the implications of the use of genetic technology. Our commitment to evidence-based medicine and our guiding principles, including the appropriate use of health care resources, helped us map out a strong framework within which ethical and accountable research and development in these areas can occur. The details of our recommendations with respect to particular technologies, and how their implementation would ensure ethical and responsible development in this area, are explained in the chapters that follow.

Hope for Treatment and Cure

Along with concerns about the need for social control over the development and use of genetic technology, Commissioners heard from Canadians who were personally affected by genetic disease. Many told their stories to the Commission and emphasized that PND had offered them a chance to have a healthy child, while genetic research offered the hope of treatment or cure.

> Gene therapy must be encouraged to help people with diseases have hope for a treatment in their lifetime. In the next decade the window on our genetic blueprint is going to open wider and wider and it is important that we develop the kinds of programs that make this knowledge useful and applicable, so people like myself won't just get the news that they are likely to die of a disease or their children will likely have a disease but will have some options: options for treatments, options for predictive testing and options for family planning.
>
> *T. Jung, private citizen, Public Hearings Transcripts, Vancouver, British Columbia, November 27, 1990.*

We heard throughout our consultations that it may not be the technologies themselves but rather how technologies are applied that causes concerns for Canadians. In the case of gene therapy, for example, the Commission heard that research into the identification and treatment of specific genetic diseases and anomalies is acceptable and in fact should be encouraged; but the application of the same kind of technology to identify and alter non-medical characteristics would be unacceptable even if it became possible. We heard from people opposed to the use of PND for various reasons, but we also heard from couples who had had a child die of a severe genetic disease and who felt that PND had given them their only chance of having a healthy child; without it, they would have felt unable to have children.

The Potential for Discrimination

People with Disabilities

Some Canadians fear that the application of genetic knowledge to identify fetuses with anomalies could lead to social discrimination against specific groups of people or segments of society. Those representing people with disabilities were concerned that the use of PND might devalue these groups in Canadian society or perpetuate discriminatory attitudes. We also attempted to find out how different sectors of society see these issues — for instance, ethnocultural or Aboriginal communities. We learned, for example, that the issues may have particular significance to some people in Aboriginal communities, where some feel that people with disabilities are thought to have a special relationship with the Creator.

> Just as society is beginning to open the door to people with disabilities, who have been shut out for so long, NRTs are creating new ways of devaluing the disabled by attempting the creation of the perfect child.
>
> *J. Rebick, National Action Committee on the Status of Women, Public Hearings Transcripts, Toronto, Ontario, October 29, 1990.*

We heard two overall concerns about the use of genetic technologies from people with disabilities. They saw the use of PND to identify fetuses with genetic diseases and anomalies as being aimed largely at eliminating such conditions, and they were concerned it would lead to social devaluation of people with disabilities. They felt that the uncritical existence and acceptance of these technologies reflect and reinforce discriminatory attitudes toward people with disabilities. The second concern was that public resources used in the research, development, and delivery of PND and genetic technologies would detract from the already limited resources available for programs and supports for people with disabilities and their families.

> With the tremendous advances being made in recombinant DNA technology, the capability exists to detect a greater number of disease-related genes, often in presymptomatic individuals. Who should have access to this information? What right has the patient to confidentiality? How might this affect the relationship between industry, employer, and potential employee?
>
> *J. Jung, Regional Medical Genetics Centre, Fetal Development Clinic, and Reproductive Endocrinology Committee of the University of Western Ontario, Public Hearings Transcripts, London, Ontario, November 2, 1990.*

Women

Groups representing women told the Commission that prenatal diagnosis used to detect the sex of the fetus could be used in discriminatory ways. Many women told the Commission that any acceptance of non-medical sex selection would devalue women in society.

Many intervenors were also concerned about the impact of the technologies on the pregnant women who use them. Women's groups asked whether all women have equal access to the technologies, whether they are subject to pressure or coercion to use the technologies or to abort a pregnancy if a genetic disease or anomaly is found, and whether patients receive appropriate counselling and support to help them make personally appropriate choices about testing, treatment, and care.

We heard clearly that Canadians do not condone the use of reproductive technologies in discriminatory ways. We investigated the potential effects of the use of genetic knowledge applied to prenatal diagnosis in such ways at great length. The Commission's recommendations reflect our ethic of care, and we strongly reject the non-medical use of PND or genetic technologies, or their use in discriminatory ways that devalue being female.

Individuals Identified as Being at Genetic Risk

The Commission also heard concerns that genetic screening technologies could be used in the population at large, and that individuals identified as being at risk of genetic disease or susceptibility could be discriminated against. The use of genetic identification outside the context of reproduction is outside our mandate — this is one of the broader issues raised by genetic knowledge alluded to at the beginning of this chapter. However, the concern raises issues that are relevant to our mandate with regard to the confidentiality of information gained through prenatal testing. We make recommendations with regard to protection of information gained from prenatal genetic testing so that it is not misused, and so that individuals with particular genotypes are not discriminated against in employment or insurance coverage.

Concerns About Future Developments and Technology Transfer from Animals

During the Commission's public hearings, some intervenors raised concerns about the similarities between technologies used in domestic animal breeding and those used to assist conception in human beings. Among the concerns raised were that women and reproduction could be exploited and commodified if techniques perfected in the agriculture industry were transferred to the human situation without regard to social and ethical values.

As we discussed in Chapter 24, the transfer of technology between animals and human beings is common in medicine and in fact is generally considered desirable. Indeed, the Medical Research Council's research guidelines require that the safety and efficacy of techniques to be used in people be researched first using animals, if possible. Animal models are also used widely where possible in research intended to benefit human beings. This approach is also part of the international standards set under the Helsinki Declaration. Research involving laboratory animals has permitted the evaluation of new surgical techniques, immunization, new drugs, transplantation, and other strategies. Such research is a widely accepted part of medicine, if carried out in an ethical and regulated way with protections for the animals involved.

> I personally feel that the manipulation or engineering of the human genome is an unacceptable form of public health management.
>
> *D. Tkachuk, private citizen, Public Hearings Transcripts, Vancouver, British Columbia, November 26, 1990.*

The concern about technology transfer with respect to the manipulation of zygotes is not that they were tested originally on animals, but rather that they were developed to increase the profitability of livestock breeding and that, if they were applied in a similar way in human beings, it would be detrimental to the best interests of women and of society. Commercial interests and the interests of women and society are not identical. Some intervenors feared that technology transfer from commercial livestock breeding to human medicine could bring with it commercial values and goals. This is an important issue, and one that should be examined to see whether measures are needed to limit or regulate any such transfer. In the view of Commissioners, transfer of technologies from use in animals to use in human beings is detrimental only if inappropriate technologies, or inappropriate uses of a technology, are transferred. It is important that the goals are not transferred along with transfer of knowledge and technology. Research with animals, where possible, is an ethical prerequisite to research with humans. Applying knowledge about reproductive technologies gained through research involving animals is desirable, then,

> Canadians are deeply concerned about what technological development has done to nature. I don't think we can assume that they are or should be less concerned about what technology can do to themselves, to human nature.
>
> *C. Cassidy, Citizens for Public Justice, Public Hearings Transcripts, Toronto, Ontario, October 29, 1990.*

provided such applications occur in an ethically acceptable way and in a way that results in benefits for women and society.

Animal Research and Assisted Human Conception

Successful zygote transfer occurred up to 44 years earlier in domestic animal species than in human beings (sheep, 1934; pig and cow, 1951; horse, 1974). However, the source of zygotes was either surgery or uterine flushing, not *in vitro* fertilization of eggs. IVF was not used on domestic animals because animal zygotes would not develop *in vitro* past the two- to eight-cell stage, and zygotes at that early stage of development failed to implant in the uterus. Since animal zygotes had to be at a more developed (morula or blastocyst) stage before they implanted, animal breeders relied on uterine flushing or surgery, not IVF, as their source of zygotes.

When scientists started researching IVF techniques in human beings in the 1960s, therefore, they were not applying a technology that was already in use in animal breeding. On the contrary, research on human IVF led to the first birth of a child conceived *in vitro* in 1978, whereas subsequent work in cattle resulted in the birth of the first IVF cow in 1982. So the use of IVF in human medical research predated its use in animal breeding.

The use of endoscopy and ultrasonography during IVF procedures in human beings has stimulated their analogous use in animals, and the recent discovery that growth hormones used in conjunction with ovarian stimulation in human beings enhances the maturation of eggs for retrieval has led to the use of similar procedures in pigs, sheep, and cattle.

Conversely, knowledge gained from efforts to enhance livestock production has greatly improved techniques to alleviate infertility in human beings. Many aspects of human IVF procedures regarding the handling of zygotes were derived from studies on animals. For example, the first successes with frozen human zygotes were owed entirely to processes developed in animals.

The recent discovery that adding somatic cells to the *in vitro* culture medium may improve the maturation of human zygotes was also based on research related to livestock breeding. The development of techniques to support the maturation of animal zygotes to the morula or blastocyst stage has been the focus of a great deal of research because, as noted earlier, animal zygotes can be transferred successfully only at those later stages. The "co-culturing" technique using somatic cells has proved the most successful of these techniques and is now being applied to human zygotes; if successful, IVF practitioners may decide in future to transfer human zygotes at the blastocyst stage (four to seven days) instead of at the two- to eight-cell stage (two to three days). This would enable better identification of developmentally compromised zygotes; if only healthy zygotes were transferred, a better chance of live birth is thought to be likely.

The Commission investigated the history of assisted reproduction in livestock and its relationship to human assisted reproduction. The research clearly confirmed the interdependence between technologies developed for use in livestock and those used in human beings; a glance at the dates of milestones in assisted reproduction shows that the migration of knowledge and procedures has been two-way (see box). This two-way process of technology transfer is likely to continue. Some of the areas for potential transfer of technology developed in work on animal breeding to the human situation include the following:

- the evaluation of zygote viability before transfer, based on metabolic activity;
- the improvement of techniques of freezing and thawing, particularly of eggs; and
- genetic diagnosis by molecular techniques.

As we have made clear, however, only some technologies and only some uses of these technologies are acceptable for technology transfer. Any use of technology in humans should be in the service of ethically appropriate goals. With this in mind, in the remainder of this introduction to prenatal diagnosis we briefly review some specialized and experimental techniques of zygote manipulation in animals and their possible future relevance to human IVF research.

Micromanipulation of Zygotes and Embryos

Micromanipulation is a rapidly advancing technique whereby early animal zygotes or gametes can be altered structurally and functionally using minute, specialized instruments while looking through a microscope.

Broadly speaking, zygotes can be divided or combined at various developmental stages up to and including the blastocyst stage. The simplest application is "embryo splitting" to produce limited numbers of genetically identical animals. This has been used commercially to a limited extent for several years. Most recently, this technique has been extended to produce zygotes and calves from separated cells (blastomeres) from 4- to 16-cell cattle zygotes. This has been referred to, inaccurately, as "cloning" (see below).

Parts of different zygotes of the same or even different animal species can also be combined. This procedure is potentially significant in the preservation of endangered species because it may allow the embryos thus created to be gestated in the uterus of another closely related species. The cells of the "combined" zygote that invade the uterine wall come from the host species, while the inner cell mass giving rise to the embryo comes from the related endangered species.

In October 1993, researchers from the United States reported the first successful splitting of human zygotes into component cells, permitting a

zygote with the same genetic information to develop from each one of the cells. It has been said that this technique may be of use in future to assist infertile couples by making more zygotes available.

However, this technique of zygote splitting and manipulation has no foreseeable ethically acceptable application to the human situation, and points to the need in Canada for a system of appropriate limits, accountability, and regulation with regard to new reproductive technologies. Its use in human zygotes offends respect for human life and dignity and provides no benefit that cannot be achieved in other, ethically acceptable ways. For example, if the goal were to enable a couple to have two children using IVF techniques, zygotes not needed for a first attempt could be frozen for later use, or a second egg retrieval procedure could be done.

Cloning (Nuclear Substitution)

Forty years ago, researchers discovered that tadpoles could develop from embryos produced by substituting the nucleus from a frog embryo cell for that of an egg that had had its nucleus removed. Since then, embryos have been produced by similar techniques in other species — amphibians, fish, mice, rabbits, sheep, pigs, and cattle.

The nucleus of a cell is taken from a zygote and placed in the cytoplasm of an egg. The resultant embryo is thus composed of the nuclear genetic material of the embryonic animal and the cytoplasmic structures and contents of the egg. The significance of the procedure in some species (it does not work in mice, for example) is that each of the cells from a particular zygote can be used to produce another zygote when put into an egg. This process may produce several embryos with exactly the same nuclear genotype as the one original zygote. Moreover, after each resulting zygote has gone through several cell divisions, the process could be repeated. In animals, breeding is directed, so that valuable zygotes can be identified. In theory, there may be no limit to the number of copies of a commercially valuable zygote that might be produced in this way. An important difference in humans is that the qualities of the zygote that could give rise to these multiple "copies" cannot be known in advance.

This technique is in commercial use, and patent rights are currently under legal dispute. Recent reports from these operations have shown increased spontaneous abortion rates, excessive birth weights, congenital anomalies, and perinatal death in calves arising from "cloned" zygotes. These problems will have to be rectified before this technique could become commercially useful. Even if it were possible in human beings, this technique would have no foreseeable ethical application.

Sex-Selective Zygote Transfer

An ability to select the sex of offspring would be of substantial benefit to livestock producers in a variety of situations. For example, commercial

dairy farming requires a continual supply of heifers, but bull calves are of less commercial value. In contrast, in beef operations, bull calves are considered more desirable because of their higher rates of weight gain, though heifer calves may be required for some types of specialized beef production. For a variety of reasons, animal researchers are seeking to develop non-invasive methods of sexing at the zygote stage. For example, it may be possible to distinguish between male and female zygotes *in vitro* on the basis of quantitative differences in metabolic activity. Such a discovery, if transferable to human beings, might have advantages over the biopsy method currently used to test for sex-linked genetic disorders. Any such transfer of knowledge should be evaluated in light of the values it supports or promotes. Our recommendations on this subject are set out in Chapter 28, where we recommend that sex selection for non-medical reasons be prohibited.

Genetic Alteration of Zygotes

Genetic alteration of animal zygotes is of interest in two ways at present: the production of livestock with higher rates of growth and the possibility of transferring genes into animals so they produce novel proteins, particularly pharmaceutical compounds of significance to human medicine. Particular human genes could be transferred to cattle, for example, in order to produce pharmaceutically important proteins in milk, which could then be concentrated and purified to provide a supply of these compounds for treatment of diseases. In the popular press, this has become known as "genepharming."

In 1982, researchers found that injecting the rat growth hormone gene into one-cell mouse zygotes sometimes produced mice that had greater-than-normal growth after birth. This report was of immense significance to all areas of the life sciences; to animal scientists it was of interest because increased growth rates may be a highly desirable trait for purposes of livestock production. Major efforts were therefore directed to achieving a similar result in domestic animals. These studies led to the successful transfer, incorporation, and expression of human and bovine growth hormone genes in pigs and sheep. These "transgenic" animals transmit these traits to their offspring, so that potentially valuable strains of animals showing increased growth and reduced fat, both desirable features, can be produced.

Although many therapeutically important proteins such as human insulin and growth hormone can be produced by animals developed from zygotes that have had a foreign gene inserted, there are limitations. Gene transfer must take place at the zygote stage and has a high failure rate; in addition, breeding of the resulting animals must be highly controlled, and host animals may not be able to produce many of the desired complex proteins because they lack the appropriate metabolic pathways and mechanisms. Gene transfer into zygotes has also led to various health

problems in animals in these strains, from lethargy and infertility to diabetes. It is speculated that the cause of these problems may be inappropriate promoters used in conjunction with the genes that were transferred, which may have caused excess amounts of other gene product to be produced; research is currently under way to find more appropriate promoters.

The use of gene transfer to produce animals with new characteristics is still under investigation, but it potentially has major implications for food production and human medicine. For example, production of dairy cattle that produce lactose-free milk could provide a new source of this important food for people who are lactose-intolerant. The transfer of genes associated with resistance to specific disease could significantly reduce both production losses and the need for antibiotics in animal production. The transfer of genes coding for human cell-surface proteins could even, theoretically, provide donor organs (kidneys, livers) of animal origin that would escape rejection by the human host's immune system.

Although these uses of technology are outside our mandate, many ethical and other questions are raised by such uses of animals.

There is no foreseeable application of gene transfers of the types just described in human zygotes. As we discuss in Chapter 29, even if a zygote could be diagnosed, for example, as lacking the normal gene for growth hormone, it could simply not be transferred to the uterus; one of the couple's other zygotes would be transferred instead.

Ectogenesis

Ectogenesis refers to the idea of supporting the development of a zygote into an embryo and fetus outside a uterus until it is "born" or able to exist independently. Biologists develop techniques for culturing animal embryos in order to observe and learn about the intricate process of development. But no embryologist has succeeded in culturing animal embryos continuously through the whole period of gestation. In the first 10 or 11 days of development in the mouse or rat (which are similar in some respects to the first six to seven weeks of human development), it is possible to maintain a zygote in culture and watch it develop for several days. By doing this for overlapping three-day periods, it is possible to cover the whole period — but not with the same zygote. No one has succeeded in culturing an early animal embryo through the period of

> The idea that human zygotes could develop and grow into infants in an artificial womb is seen as quite inappropriate by most Canadians. Such research, if pursued, would dehumanize motherhood; some have even envisaged it as opening the way to "baby farms" and femicide. Commissioners regard such research as ethically reprehensible, and we have recommended that it be prohibited.

implantation to or beyond the period when the placenta normally becomes its major life support (10 or 11 days after fertilization in the case of the mouse). In a larger zygote with a longer gestation period, such as that of human beings, the problem would be still more intractable.

This technology has no foreseeable ethical application to human beings in any case. The idea that human zygotes could develop and grow into infants in an artificial womb is seen as quite inappropriate by most Canadians. Such research, if pursued, would dehumanize motherhood; some have even envisaged it as opening the way to "baby farms" and femicide. Commissioners regard such research as ethically reprehensible, and we have recommended that it be prohibited.

The concerns raised by Canadians about the use of PND and genetic technologies formed an important part of the backdrop for the Commission's inquiry. These concerns show the importance of examining and evaluating each technology and its current and potential uses to determine whether and under what circumstances society should accept its use, and what conditions society should put in place to govern uses found to be ethically acceptable and socially desirable. In the remaining chapters in this section we present the results of our investigation of the four applications of genetic technology in reproduction — prenatal diagnosis for genetic disease and congenital anomalies; prenatal diagnosis for late-onset disorders and susceptibility genes; sex selection for non-medical reasons; and genetic alteration, including gene therapy. We outline the issues involved in each and conclude with the Commission's recommendations for action.

General Sources

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Prenatal Diagnosis for Congenital Anomalies and Genetic Disease

Prenatal diagnosis is increasingly familiar to Canadians. Various diagnostic tests, including amniocentesis, chorionic villus sampling, ultrasound scanning, and others, have become part of the experience of pregnancy for many women. PND has provided hope and assurance to many individual women and couples at risk of having children affected by genetic disease or congenital anomalies.

On the other hand, the use of these powerful technologies raises issues, dilemmas, and challenges that are complex and difficult. From a public policy perspective, addressing these issues involves questions of how to ensure clear and enlightened management of the introduction and use of technologies found to be ethically acceptable, and how to ensure the provision of effective and safe services based on these technologies for people across this country. In all these areas, there are vulnerable interests to be protected, and all the technologies are developing rapidly. This makes it important to put in place structures and processes to set boundaries for technology use and to ensure that any use of technologies within those boundaries occurs in safe and beneficial ways.

Before turning to current practice and to the views of Canadians on prenatal diagnosis, it is essential to know something of the nature and incidence of the congenital anomalies and genetic diseases that these techniques are designed to detect. Basic information on the disorders is therefore provided in Appendix 1, while the chances of these occurring and the tests used to detect them are described below.

The Risk of Congenital Anomalies and Genetic Disease

The risk that a child could be born with a congenital anomaly or genetic disease is inherent in the human condition. This risk is unavoidable, and every couple must face it. Some couples, however, are at much greater risk than others; if they are aware of the risk, this can be a source of considerable anxiety to prospective parents, who naturally want their children to be healthy. Prenatal diagnosis is intended to help individuals and couples at increased risk to manage a pregnancy in light of knowledge about the fetus.

Congenital disorder: a disorder that is present at birth.

Genetic disorder: a disorder that is inherited from one or both parents.

Multifactorial disorder: a disorder that is attributable to a complex interaction of genetic and environmental factors.

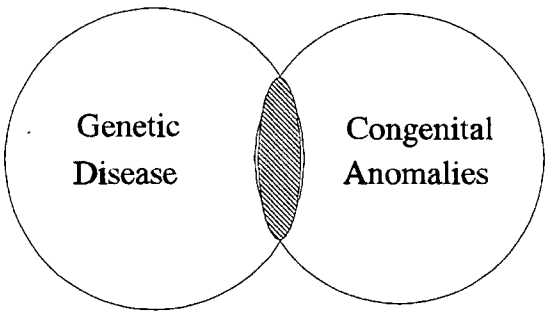
Teratogenic disorder: a disorder that arises as a result of the embryo or fetus being exposed to harmful agents or substances *in utero*.

The various disorders that fall into the category of congenital anomalies or genetic disease differ in two important respects. First, they differ in their cause. Some disorders have a wholly genetic basis — that is, the disorder results from an anomaly in the genetic material inherited from the parents, either at the chromosomal level or in the sequence of DNA within the genes that compose the chromosome. Other disorders are clearly the result of environmental factors that interfere with the normal development of the fetus, such as the pregnant woman's exposure to radiation or to a viral illness. Many disorders are attributable to a complex interaction of genetic and environmental factors. These are called "multifactorial diseases." Finally, many disorders are of unknown or unidentified cause.

Second, these disorders differ in their time of onset. If a disorder resulting from a genetic anomaly is present at birth, it is considered a "congenital" genetic disease; if it develops during adulthood, it is called "late-onset." For some genetic diseases, the genetic anomaly, though present at birth, may not interfere with the person's development or functioning until months after birth (Tay-Sachs disease) or even until adulthood (Huntington disease).

In short, and as shown in Figure 26.1, not all genetic diseases are congenital (since the disorder may develop only in childhood or adulthood), and not all congenital anomalies are genetic in origin (since they may result from exposure to toxic agents *in utero*); indeed, most studies conclude that the largest category of congenital anomalies is of unknown cause (Table 26.1).

Figure 26.1 Relationship Between Congenital Anomalies and Genetic Disease



The risk of having a child affected by either a congenital anomaly or a genetic disease is not insignificant. Recent studies have concluded that somewhere between 3 and 8 percent of infants are born with either a serious congenital anomaly or a genetic disease that will cause medical problems before adulthood (Tables 26.2 and 26.3). It is difficult to give more precise statistics on the incidence of these disorders for a variety of reasons: researchers use different methods of identifying the disorders, some more intensive than others, and the definition of a "serious" congenital anomaly may differ somewhat from study to study. The figures given in Tables 26.1, 26.2, and 26.3 reflect the particular methodology used; other reputable studies arrive at slightly different numbers. Nevertheless, these figures give a general indication of the incidence of different kinds of disorders.

We explain the different kinds of disorders, explore who is at greatest risk of having a fetus affected by a disorder, and discuss how PND can help people at increased risk to make reproductive decisions in Appendix 1 to this chapter. As explained there, all women and couples face some risk of having children with a congenital anomaly or genetic disease. No one is exempt. As we have noted, the estimated incidence of these disorders in the general population varies from study to study, but data on newborns show that people in the general population (that is, those not known to be at higher risk because of a factor such as family history) face about a 4 percent chance of having a child with a genetic disease or congenital anomaly. This approximate risk does not vary much between cultures or over time where comparable data are available, suggesting that these background risks are inherent in the human condition.

Nevertheless, some women and couples have different kinds and levels of risk for a congenital anomaly or genetic disease in addition to the general background level of risk. For example, some are at higher risk of having a child with particular sorts of disorders — women over the age of 35, known

carriers of a genetic disorder, those with a family history of multifactorial disorders, people who have been exposed to a known teratogen, and so on. This is where the use of prenatal diagnosis may be valuable.

Table 26.1. The Causes of Congenital Anomalies

Cause	% of infants with congenital anomaly
Chromosomal	10.1
Single-gene	17.6
Multifactorial	23.0
Unknown	43.2
Teratogens	3.2
Uterine factors	2.5
Twinning	0.4

Source: Nelson, K., and L.B. Holmes. "Malformations Due to Presumed Spontaneous Mutations in Newborn Infants." *New England Journal of Medicine* 320 (1)(January 5, 1989): 19-23.

Table 26.2. The Incidence of Genetic Diseases (Onset by Age 25)

Category	% of total births
Single-gene	0.36
Autosomal dominant	0.14
Autosomal recessive	0.17
X-linked recessive	0.05
Chromosomal	0.18*
Multifactorial	4.64
Genetic unknown	0.12
Total	5.32

* Under-ascertainment likely for this category due to methodology.

Source: Baird, P.A., et al. "Genetic Disorders in Children and Young Adults: A Population Study." *American Journal of Human Genetics* 42 (1988): 677-93.

Table 26.3: The Incidence of Congenital Anomalies

Category	% of total births
Anomalies with a known genetic component	2.66
Anomalies with no known genetic component	2.62
Total	5.28

Source: Baird, P.A., et al. "Genetic Disorders in Children and Young Adults: A Population Study." *American Journal of Human Genetics* 42 (1988): 677-93.

The Role of Prenatal Diagnosis

Before the introduction into the clinical setting of amniocentesis in the 1970s and CVS and obstetrical ultrasound in the 1980s, there was no way to diagnose accurately whether a fetus had a congenital anomaly or genetic disorder. Since then, however, there has been a tremendous increase in the capacity of medical technology to determine through PND testing whether fetuses in higher-risk pregnancies are in fact affected. It is also increasingly possible, through carrier screening and screening of pregnant women, to identify adults in the population who are at increased risk of having an affected fetus. These techniques give couples information on which to base reproductive decisions.

Diagnostic Testing

Some techniques, known as "diagnostic" tests, are intended to determine whether the fetus has a congenital anomaly or genetic disease. These techniques include amniocentesis, CVS, and specialized or "targeted" ultrasound. The first two techniques involve taking fluid or tissue samples containing fetal cells in order to carry out chromosome, biochemical, or DNA analysis. Targeted ultrasound is an imaging technique that involves intensive, prolonged visualization of the fetus using sound waves to look for anatomical or structural anomalies. (It is important to distinguish this targeted ultrasound from routine ultrasound, discussed below.)

Because amniocentesis and CVS are invasive and expensive and carry risks for both the fetus and the pregnant woman, they are offered only to women who have higher-risk pregnancies. The same is true for targeted ultrasound, which requires highly specialized equipment and personnel. In Canada, these tests are provided only to women who have been referred to a specialized centre, usually by their family doctor or obstetrician, because of a specific factor that puts them at higher risk.

Common Diagnostic Tests

Amniocentesis: Amniocentesis is the most common invasive prenatal diagnostic procedure in Canada. It is normally carried out between 15 and 17 weeks of pregnancy. Fluid is removed from the uterus using a needle inserted through the abdominal and uterine walls under ultrasound guidance. The fluid taken out contains fetal cells that are grown in culture and examined in different ways, depending on whether the couple is at higher risk for chromosomal disorders, genetic metabolic disorder, or a neural tube defect. Results usually take two to four weeks.

Chorionic villus sampling (CVS): The chorionic villi are fronds that extend from the fetal membranes into the uterine wall as the placenta forms. A sample of these fronds can be taken by suction through a tube inserted into the uterus through the vagina or through the abdominal wall. CVS can be done several weeks earlier in pregnancy than amniocentesis, and the tissue can be cultured or examined directly without culture, which means test results are available more quickly. However, CVS is more difficult to interpret than amniocentesis and cannot diagnose some disorders — for example, neural tube defects.

Ultrasound: Ultrasound examination involves the transmission of high-frequency sound waves through tissue and the display on a screen of the echoes produced by these waves. In the context of PND, it can be used as both a *screening* test and, when used in a more focussed way for a lengthier examination, a *diagnostic* test. Most pregnant women in Canada now have ultrasound *screening*, usually at about the eighteenth week of pregnancy, to estimate gestational age, to see whether there is more than one fetus, and to look for placental abnormalities and conditions that may require medical attention. This is variously described as "Level I" ultrasound or "routine" ultrasound. In the process, ultrasound screening may produce images that raise the suspicion of a congenital anomaly. If so, the woman is normally referred for further testing to provide a definitive diagnosis, sometimes by a more intensive *diagnostic* ultrasound examination (also known as Level II and III ultrasound or "targeted" ultrasound). Since Level I ultrasound is simply a screening test, it is not a reliable way to diagnose fetal anomalies. Level II and III ultrasound involves a detailed examination of the fetus, section by section, lasting up to an hour, and can accurately diagnose many congenital anomalies. Ultrasound is also used in PND as an adjunct to amniocentesis and CVS, to help guide the needle or tube.

This, in turn, has led to increased efforts to improve identification of higher-risk pregnancies. In the past, high-risk pregnancies were identified almost entirely on the basis of either family history or the pregnant woman's age. However, several "screening" techniques have recently been developed to help identify more accurately those in the general population who are at higher risk. These include carrier screening tests and prenatal screening tests.

Carrier Screening

Carrier screening involves testing men and women in population groups known to be more likely to carry particular genetic disorders to identify which individuals carry the gene. For example, carrier screening is available to identify the carriers of Tay-Sachs disease among Ashkenazi Jews. If both members of a couple are identified as carriers of this disease, they are at higher risk of having an affected fetus, and so they would be offered PND in any pregnancies they were to have subsequently.

Prenatal Screening

Unlike carrier screening, which aims to test prospective parents before conception, prenatal screening tests are designed to be offered to all pregnant women. Their aim is to identify particular women likely to be carrying an affected fetus so that they can be offered more definitive prenatal tests. The techniques include routine ultrasound and the testing of a pregnant woman's blood for levels of fetal proteins (see box). An abnormal result in one of these tests suggests that the fetus has an increased likelihood of having a congenital anomaly; in these cases, the woman would be offered a diagnostic test to confirm or dispel that suspicion. (In the case of routine ultrasound screening, the scan may sometimes incidentally identify a major structural anomaly, such as anencephaly.)

In most cases, the result of prenatal diagnostic testing is reassuring. According to a Commission survey of genetics centres in Canada, approximately 5 percent of the diagnostic tests carried out show that the fetus has a serious congenital anomaly or genetic disease; in cases where a serious congenital anomaly or genetic disease is found, about 80 percent of women and couples choose to terminate the pregnancy.

Prenatal diagnosis cannot and does not identify all disorders or eliminate all reproductive risks. PND is most useful for identifying chromosomal disorders, and, theoretically, all chromosomal disorders could be detected by examination of the chromosomes of the fetus. Although PND can be used currently to detect only several hundred of the several thousand known single-gene disorders, recent scientific and technological developments in genetics make it likely that the ability to test prenatally for single-gene disorders will increase rapidly in coming years.

These chromosomal and single-gene disorders account for a relatively small percentage of congenital anomalies. They are far less common than multifactorial disorders and disorders of unknown cause — and most disorders in these categories cannot be detected at present and will not be detectable in the foreseeable future. For example, many disorders of function (such as blindness, deafness, and muscle paralysis) are not detectable by either analysis of fetal cells or targeted ultrasound

examination. The most common type of multifactorial disorder that can be detected is neural tube defects, such as spina bifida and anencephaly.

Screening Tests

These are tests designed to be offered, where available, to all pregnant women, not just those at higher risk. If an abnormal result is revealed in one of these screening tests, the woman is at higher risk of having an affected fetus and so would be offered a diagnostic test to provide a definitive diagnosis of the condition of the fetus.

Blood tests: Several tests can be done on a pregnant woman's blood to provide information about the likely condition of the fetus. These include maternal serum alpha-fetoprotein (MSAFP) testing, triple testing, and, perhaps in future, the testing of fetal cells from the pregnant woman's blood.

Maternal serum alpha-fetoprotein: This test relies on the detection of alpha-fetoprotein (AFP) in maternal blood. AFP is produced by the fetus; a higher than normal level of AFP in the pregnant woman's blood suggests the possibility of an abnormal fetal opening, such as a neural tube defect (anencephaly, spina bifida), allowing the concentration of this protein to become higher in the amniotic fluid and the pregnant woman's bloodstream. Concentrations of AFP rise in some other fetal conditions as well. Thus, a pregnant woman's blood can be screened to detect an increased likelihood of anomalies in the fetus.

Triple testing: As the name suggests, this test relies on a combination of three different indicators in the pregnant woman's blood sample, including AFP. A high risk of a chromosomal disorder is indicated by variations in the extent to which AFP, human chorionic gonadotropin hormones, and estriol hormone are present. For example, triple testing can be used to detect an increased risk of Down syndrome.

Ultrasound scanning: Ultrasound scanning can be used as a diagnostic test or as a screening test. (See "Ultrasound" in previous box.)

Carrier screening: Whereas other screening tests involve testing pregnant women after conception has occurred, carrier screening involves testing both men and women *before* conception to determine who is a carrier of a particular genetic disease. Carrier screening programs try to identify carriers within a particular ethnic group that is at risk for a specific single-gene disorder. For example, Mediterranean populations are screened to identify carriers of thalassaemia. Identified carriers would be offered diagnostic tests on all subsequent pregnancies, as the fetus would be at risk of inheriting the genetic disorder.

Diagnostic testing is offered only to those who are at identified higher risk. Here again, we know more about who is at higher risk from chromosomal disorders and single-gene diseases, since these have relatively clear and predictable patterns of incidence. Even for recessive disorders, however, the risk is usually identified because the couple has a child who

is affected — thus showing that they have a one in four risk in any future pregnancy. Little is known about who is at higher risk of multifactorial disorders and disorders of unknown cause.

The higher the identified risk and the easier it is to detect a disorder, the more likely it is that a woman will be referred to a genetics centre for diagnostic testing. For example, although chromosomal disorders associated with pregnancies later in a woman's childbearing years account for approximately 10 percent of congenital anomalies in liveborn individuals, 78 percent of women tested at genetics centres in Canada are referred because of their age. Conversely, although multifactorial disorders and disorders of unknown cause account for more than 66 percent of congenital anomalies, fewer than 10 percent of women are referred in order to be tested for such disorders.

In short, testing for chromosomal disorders accounts for the largest proportion of PND, because there is a test to detect these disorders and because it is possible to identify people at higher risk for them. Multifactorial disorders, though much more common than chromosomal disorders, are less commonly tested for, because it is more difficult to know who is at higher risk, and for most there is no way to detect such disorders in the fetus. We have no reason to think that this will change markedly in the foreseeable future.

The usual background risk of a congenital anomaly or genetic disorder being present at birth (which is about 4 percent for any couple in the general population) is always present for high-risk couples, as well as for those not offered diagnostic testing. By having diagnostic testing, a couple is simply identifying whether the condition for which they are at higher risk — over and above the background risk — has occurred. Essentially, these couples are trying to establish for themselves the same level of risk that is part of every pregnancy. A normal test result puts high-risk couples back into the same risk group as everyone else. If a disorder is found, the couples can make decisions about treatment (if available), care, or termination.

Using PND cannot be expected to eliminate or greatly reduce disabling conditions in the population at large. Most of these result from prematurity, viral or bacterial diseases, accidents or violence, and aging.

Prenatal diagnosis does not provide all the answers about the health of the fetus, but there is a strong desire for the answers it can provide on the part of women and couples who are at higher risk. Using PND cannot be expected to eliminate or greatly reduce disabling conditions in the population at large. Most of these result from prematurity, viral or bacterial diseases, accidents or violence, and aging. Thus, there will always be a risk of having a child with a congenital anomaly or genetic disease. Human development is too complex to allow easy or simplistic answers, and the application of PND cannot be expected to provide them. Thus, much of

what will be stated in the rest of this chapter turns on the recognition that risk entails probabilities, not certainties, and that managing reproductive risks and making decisions with respect to PND will never be easy or straightforward, no matter how powerful the technology.

Issues Raised by Prenatal Diagnosis

As noted in Part One of this report, few previous inquiries into new reproductive technologies, either in Canada or internationally, have included PND in their research or recommendations. However, we believe that the impact of PND technology on reproductive health care, and on society generally, is as great as that of any other reproductive technology. PND raises many of the issues discussed in Part One with respect to new reproductive technologies as a whole. It involves many of our most basic beliefs and values as individuals and as a society; challenges our capacity as a society to manage rapidly changing technology and scientific knowledge with wisdom and humanity; and constitutes a key component of Canada's health care system.

> Many people now fear that the development of new reproductive technologies will exert great pressure on couples, and particularly on women, to use one technology or another. And prenatal diagnosis is often cited as an example in this regard. Our methods of assessing technology, or our methods of technological assessment, must therefore be reviewed from new perspectives if we are to protect the freedom of communities effectively. [Translation]
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> *H. Doucet, Faculté de Théologie, Université Saint-Paul, Public Hearings Transcripts, Ottawa, Ontario, September 18, 1990.*

With the increasing power of PND technologies come dilemmas and implications for individuals and society alike. Decisions that are intensely personal and painful (for example, a decision about whether to abort a fetus found to be severely affected) have important implications for society. These must be addressed if PND is to be used in a way that is both beneficial for individuals and socially responsible.

In the small proportion of cases where a serious disorder is identified, the majority of couples decide to abort. This raises important questions about the impact of PND on society's view of abortion and whether, as some people fear, it will lessen society's respect for human life. There is also the concern that the use of PND to identify and terminate affected pregnancies will lead to or reinforce prejudice or discrimination against people with disabilities and to intolerance of diversity and "imperfections" in society. Moreover, the extent to which women's decisions regarding PND and

abortion are subject to social pressure or legal coercion will affect the status of women in society and the equality of the sexes. These and other issues are discussed later in this chapter.

The rapid development of prenatal diagnostic technologies also raises the issue of technology proliferation. We found evidence that some screening technologies are being widely disseminated before they have been adequately assessed and without adequate support in place, such as the availability of genetics counselling and follow-up diagnostic facilities for those with abnormal test results. These issues provide specific examples of the need to provide only evidence-based health care throughout the system — care that has been assessed for benefits and risks. We return to this question later in the chapter as well.

> The social status and realities of those with congenital disabilities, and societal attitudes toward them, warrant serious consideration in the face of advancing PND technologies. There is a need for public discussion about the selection aspect in particular, with a focus on society's fear of disability and the reasons why some disabilities are viewed as socially tolerable, while others are not. As well, society's past and current treatment of those with disabilities, the fears that persist around disability and persons with disabilities, and the question of public policies regarding social and economic support for those with special needs, including women in the caregiving role, deserve closer study. This broader view will allow medicine and society to more adequately address the choices generated by PND.
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> *J. Milner, "A Review of Views Critical of Prenatal Diagnosis and Its Impact on Attitudes Toward Persons with Disabilities," in Research Volumes of the Commission, 1993.*

The introduction and use of prenatal diagnostic technologies cannot be allowed to be a function of either technological imperative or policy drift. A conscious and coordinated approach is needed to ensure that PND is provided in an ethical, safe, and beneficial manner in Canada, now and in the future.

Our Approach to the Study of Prenatal Diagnosis

Consistent with our recognition of the many issues raised by PND, we commissioned qualitative examinations by prominent ethicists, geneticists, and other scholars (see research volumes, *Prenatal Diagnosis: Background and Impact on Individuals*; *Current Practice of Prenatal Diagnosis in Canada*; and *Prenatal Diagnosis: New and Future Developments*). At the same time, in our public consultations, private sessions, and consultations with interested organizations and expert bodies, we were anxious to learn about

issues and concerns surrounding PND and its use. In addition, we commissioned studies on a range of PND topics: the history and evolution of PND; risk assessment of PND techniques; and the social context of PND, including attitudes toward persons with disabilities and ethical issues such as informed consent and choice.

Also commissioned was a series of field studies examining the actual delivery of PND in Canada today, both in genetics centres and in the referral system. Examples include a survey of genetics centres; a survey of referring physicians and their behaviour and attitudes toward PND; trends in the use of prenatal ultrasound; Manitoba's experience with its maternal serum alpha-fetoprotein screening program; and a demographic and geographic analysis of the users of PND services. We also examined women's experience of technology use during pregnancy; women's attitudes, perceptions, and experiences regarding PND; and the reactions of women to prenatal diagnosis of a genetic disorder leading to pregnancy termination.

Given the scope and complexity of PND, the Commission's objective was not limited to fashioning specific responses to specific problems. Instead, much of our approach to PND was predicated on the importance of providing a long-term perspective and situating PND within the larger context of health care in Canada.

Given rapid evolution of the technologies, we focussed on developing recommendations regarding a regulatory structure that would enable policy makers to deal not only with current techniques but also with future developments. Our approach has been to see beyond the origins and dissemination of specific diagnostic technologies and to consider how to create a more inclusive and systematic approach to the assessment, limitation, or introduction and use of prenatal diagnostic technologies in general.

Current Practice of Prenatal Diagnosis in Canada

This section outlines the current practice of PND in Canada. This includes at least four elements: the 22 genetics centres that provide the major diagnostic PND tests; the 10 000 or more general practitioners (GPs) and obstetricians who provide primary care of pregnant women, who may refer patients to genetics centres, and who play an increasing role in providing screening tests; the women and couples involved; and the programs and funding that support these services.

Genetics Centres

At the core of the PND services system in Canada are 22 genetics centres, which provide the three major categories of diagnostic PND tests

— amniocentesis, CVS, and targeted ultrasound. All three require highly specialized equipment and personnel to carry out the tests and interpret the results; hence, they are provided only to women at identified higher risk. To receive one of these tests, a pregnant woman must be referred to one of the specialized centres, usually by her family practitioner or obstetrician.

All the genetics centres are situated in urban areas — 16 are in university medical centres or tertiary care hospitals associated with university medical centres, and 6 are in large community hospitals. Prince Edward Island, New Brunswick, Labrador, the Northwest Territories, and the Yukon do not have a genetics centre. Women from these areas must be referred to the nearest centre, which may involve travelling considerable distances.

There are also 35 formal outreach sites associated with the genetics centres. The most extensive network is in Alberta, which has 18 outreach sites, compared to 8 in Ontario, 4 in the Maritimes, 3 in Newfoundland, and 6 in British Columbia. The services provided at these outreach sites vary. In some provinces, public health nurses at the outreach site provide routine referrals to the genetics centre for pregnant women who might not otherwise see a referring physician in time; in other provinces, amniocenteses are available at the outreach site, and the samples are shipped to the centre for analysis.

The laboratories associated with genetics centres analyze MSAFP samples taken at the centre, as well as MSAFP samples collected by other practitioners in the community. In 1990, 37 163 women were screened for MSAFP through laboratories associated with genetics centres, which often also provide the infrastructure for carrier screening programs.

We commissioned a survey of genetics centres to determine how many women are being referred and for which conditions; how many tests are being performed and what their results are; and, more generally, how the centres are operated. The detailed results are provided in the Commission's research studies, in the volume entitled *Current Practice of Prenatal Diagnosis in Canada*. We provide a brief summary here.

Referrals

In 1990, more than 22 000 women were referred for prenatal diagnostic services at genetics centres in Canada because of an identified higher risk of having a fetus with a congenital anomaly or genetic disease. The most common reason for referral was because the woman was over the age of 35 (known as "advanced maternal age"), which increases the risk of chromosomal disorder. Advanced maternal age accounted for about 78 percent of referrals (Table 26.4). The remaining 22 percent were referrals for a variety of reasons, including having had a previous child with a chromosomal abnormality (2.4 percent), a family history of chromosomal abnormality (2.3 percent), an abnormal MSAFP result (3.6 percent),

abnormal ultrasound (3.1 percent), family history of single-gene disorder (1.6 percent), possible teratogen exposure (1.4 percent), and anxiety on the part of the pregnant woman about the health of the fetus (1.3 percent).

Table 26.4. Reasons for Referral to Genetics Centres for Prenatal Diagnosis

Risk of chromosomal disorder	83.0%
Advanced maternal age	77.7
Previous chromosomal	2.4
Previous family chromosomal	2.3
Parental chromosomal	0.5
Chromosome marker abnormality	0.1
Risk of single-gene disorder	1.6
Risk of structural anomaly	10.6
Abnormal MSAFP*	3.6
Abnormal ultrasound*	3.1
Previous family neural tube defects	2.5
Teratogen	1.4
Pregnant woman's anxiety	1.3
Other	3.5

* May also indicate increased risk of chromosomal disorder.

Source: Hamerton, J.L., J.A. Evans, and L. Stranc. "Prenatal Diagnosis in Canada — 1990: A Review of Genetics Centres." In Research Volumes of the Royal Commission on New Reproductive Technologies, 1993.

Counselling

Women who are referred to a genetics centre receive counselling before being tested, in order to clarify the nature of their risk and to ensure that their choice to undergo testing is an informed one. The type of counselling and level of intensity depend on the reason for referral. Where the risks are well known and information is relatively straightforward to convey, as in the case of advanced maternal age, counselling is done by genetics associates at some centres (often nurses with special training in genetics), by family physicians, by obstetricians, or through group counselling. The average duration of a counselling session for patients referred to genetics centres for advanced maternal age was one hour, and partners were encouraged to attend.

Counselling for referrals because of family history are more complex, often requiring complicated statistical analysis and clinical interpretation.

This is done by medical geneticists. Such sessions are considerably longer and may involve repeat visits.

Tests Performed

After the counselling, some women decide not to proceed with the testing, particularly if they were referred for an invasive test, such as amniocentesis or CVS, which carries a small risk (less than 1 percent) of miscarriage. Almost 10 percent of patients referred for amniocentesis or CVS in 1990 declined the procedure. Some of these women (137) were offered targeted ultrasound, although ultrasound cannot pick up many of the chromosomal disorders for which the women would have been referred for invasive testing originally. Some women did not have a test for other reasons — for example, fetal death was discovered at the time testing was to have been done, or the woman miscarried before testing.

However, the majority of women referred to genetics centres did have a test (19 795 out of 22 222, or 89 percent). Of these, most had amniocentesis (15 454), while a much smaller number had either CVS (2 097) or targeted ultrasound (2 244) (Table 26.5). The latter number does not include all targeted ultrasounds conducted, because women are often referred to practitioners specializing in this procedure instead of to a genetics centre for this test.

Table 26.5: Amniocentesis, CVS, and Targeted Ultrasound Performed at Genetics Centres in Canada (1990)

Type of test	Number of women tested	% of women referred
Amniocentesis	15 454	69.5
Chorionic villus sampling	2 097	9.4
Targeted ultrasound	2 244	10.1
Total	19 795	89.0*

* Approximately 10 percent of referred women did not have a test, either because they decided not to undergo the test after counselling or for other reasons (for example, miscarriage before the test).

Source: Hamerton, J.L., J.A. Evans, and L. Stranc. "Prenatal Diagnosis in Canada — 1990: A Review of Genetics Centres." In Research Volumes of the Royal Commission on New Reproductive Technologies, 1993.

Of the 19 795 women who were tested in 1990, 95 percent received reassuring test results. However, a fetal disorder was detected for the remaining 5 percent of women tested — about 990 cases. Of these, 792 women (80 percent) decided to terminate the pregnancy. The decision to

terminate is affected by many factors, including the severity of the disorder, its treatability (although in most cases the disorder detected is not treatable), the stage of pregnancy, and the circumstances and values of the individuals making the decision. The 792 constituted just over 3 percent of all women referred to genetics centres in 1990. To put this in perspective, about 6 percent of the 393 000 women who gave birth in Canada in 1990 were referred for prenatal testing; of the more than 92 600 therapeutic abortions performed annually in Canada, about 0.86 percent are done after PND.

Variations in Access

There were some marked regional variations in patient referrals. The rates varied from 7.0 percent of all pregnant women in Ontario to 1.5 percent in Newfoundland — a more than fourfold variation — as shown in Table 26.6.

Table 26.6. Referral Rates by Province (1990)

Province/region	% of pregnant women referred
Newfoundland	1.5
Maritimes	2.7
Quebec	5.9
Ontario	7.0
Manitoba	5.8
Saskatchewan	1.8
Alberta	4.1
British Columbia	6.1

Source: Hamerton, J.L., J.A. Evans, and L. Stranc. "Prenatal Diagnosis in Canada — 1990: A Review of Genetics Centres." In Research Volumes of the Royal Commission on New Reproductive Technologies, 1993.

There is a similar pattern for one specific category of referral — advanced maternal age. Although 52 percent of pregnant women aged 35 or over were referred across Canada, the number varied widely between provinces. The highest rate was in Quebec (64.5 percent); British Columbia, Manitoba, and Ontario were in the middle (between 49 and 57 percent); and in the other provinces the rates were much lower (30 percent in Alberta and the Maritimes, 23 percent in Saskatchewan, and 15 percent in Newfoundland) (Table 26.7).

In other words, there is more than a fourfold difference in referral rates between different parts of the country. Some of these differences may be the result of differences in women's choices; however, as discussed later in this chapter, data from our research and surveys of Canadians across the country suggest that regional differences in individual values or preferences are unlikely to explain this fourfold difference in referral rates. Values and preferences are very similar across the country, whereas physicians' attitudes were found to vary markedly between provinces. There may also be practical considerations, however, such as the distance that may have to be travelled to have a test, that play a role in whether a physician deems it worthwhile for a woman to have a test. It may also be that women who are referred may balance the decision to have a test with the amount of inconvenience the trip would cause and their financial circumstances.

Regional differences in individual values or preferences are unlikely to explain this fourfold difference in referral rates.

Table 26.7. Referral Rates for Advanced Maternal Age by Province (1990)

Province/region	% of eligible women referred
Quebec	64.5
Ontario	56.7
British Columbia	54.6
Manitoba	49.3
Maritimes	30.7
Alberta	30.1
Saskatchewan	23.1
Newfoundland	15.0

Source: Hamerton, J.L., J.A. Evans, and L. Stranc. "Prenatal Diagnosis in Canada — 1990: A Review of Genetics Centres." In Research Volumes of the Royal Commission on New Reproductive Technologies, 1993.

It would seem, however, that at least part of the explanation lies in the referring practices of physicians. Family and general practitioners and obstetricians in some provinces are much more likely to offer referrals for certain indications than are their colleagues in other provinces.

There were also some variations in referral rates on the basis of place of residence, income, and education. A study done for the Commission showed that people in rural or northern communities were less likely to be referred to a genetics centre, as were people of lower income or education.

Unlike the practice of many infertility clinics (discussed in Chapter 20), there is no evidence that genetics centres deny access to any woman on the basis of factors such as income, education, or marital status. Those who are referred are accepted if they meet the genetic risk criteria (for example, they are 35 years of age or over). Variations in access arise, therefore, at the point of referral, because of the way physicians offer or withhold referrals, the way women accept or decline referrals, or how difficult it is to get to a centre.

> Fewer than expected family/general practitioners are referring women for prenatal diagnostic services, a problem that is magnified in rural and northern areas because they are usually the only physicians practising. The obverse of this is that the vast majority of obstetricians/gynaecologists (who make most of the referrals) are concentrated in the largest urban centres in every province. The implication is that women living in rural or northern communities who want prenatal diagnostic services may have to travel to an urban location just to get a referral. They will have to travel to yet another urban location for the prenatal diagnostic service itself.
>
> *P. MacLeod et al., "A Demographic and Geographic Analysis of the Users of Prenatal Diagnostic Services in Canada," in Research Volumes of the Commission, 1993.*

Guidelines and Accreditation

The Canadian College of Medical Geneticists (CCMG) established a system of guidelines and accreditation for the provision of PND services more than a decade ago, and the first genetics centres received accreditation in 1981. Centres satisfying the accreditation requirements are accredited for five years.

The criteria and written standards established by the CCMG cover such things as the availability of non-directive counselling, the adequacy of laboratory support, record-keeping practices, qualifications of the staff, and so on. Centres lose accreditation in a particular subspecialty if they do not have a CCMG-qualified staff person in that specialty. When the accreditation committee believes that problems it has identified can be rectified within a specific period, it may award provisional accreditation pending correction.

Accreditation is voluntary, however. Of the 22 centres, only 10 — all of them university-based — were accredited by the CCMG for the delivery of services in 1990. (The unaccredited university centres are at Memorial University, Dalhousie University, Laval University, the University of

Montreal, and the University of Saskatchewan.) None of the general hospital centres is accredited, and none has applied for accreditation. Although lack of accreditation does not necessarily indicate a lower standard of service, it does make it impossible to evaluate, compare, and monitor the quality of prenatal diagnostic services across Canada, as this would depend upon the cooperation of all the centres.

Practitioners Involved

Although the size and composition of the 22 genetics centres vary, almost every centre has the following mix of professionals and related medical personnel: MD geneticists, PhD geneticists, MSc genetics associates, registered nurses, laboratory technicians, and ultrasound technicians (Table 26.8). Professional guidelines and qualifying exams exist for most of these personnel. The Royal College of Physicians and Surgeons of Canada developed a certification program in 1989, with CCMG input, for physicians who specialize in medical genetics; training requirements for PhD geneticists providing genetics services are set by the CCMG.

Table 26.8: Practitioners Involved in PND at Genetics Centres

Type of practitioner	Number
MD geneticists	60
PhD geneticists	41
Genetics associates	57
Total*	158

* Does not include radiologists or obstetricians who specialize in targeted diagnostic ultrasound for fetal anomalies, who often belong to radiology units that are separate from, but associated with, the genetics centres. It also does not include some community obstetricians who are associated with the genetics centres, and who may provide some routine counselling and testing.

Source: Hamerton, J.L., J.A. Evans, and L. Stranc. "Prenatal Diagnosis in Canada — 1990: A Review of Genetics Centres." In Research Volumes of the Royal Commission on New Reproductive Technologies, 1993.

The category of "genetics associate," which is relatively new, evolved as the demand for PND and genetics counselling grew faster than the supply of trained MD and PhD counsellors. Genetics associates have either a background in counselling, such as social work or psychology, and learn genetics on the job, or training in nursing, genetics, or other paramedical skills and learn the practical side of counselling on the job (Table 26.9).

As the number of genetics associates has grown, the need for formalization of their training and functions has been recognized. In response, a master's-level training program has been established at McGill University, and a second is being developed at the University of British Columbia. The Canadian Association of Genetic Counsellors has been incorporated and is currently developing guidelines for training and procedures for accreditation.

Table 26.9. Type of Training of Genetics Associates

Type of training	Number
Formal genetics counselling training	14
Master's degree in genetics	4
Bachelor's or Master's degree in nursing	16
Diploma in nursing	16
Other	7
Total	57

Source: Hamerton, J.L., J.A. Evans, and L. Stranc. "Prenatal Diagnosis in Canada — 1990: A Review of Genetics Centres." In Research Volumes of the Royal Commission on New Reproductive Technologies, 1993.

Referring Practitioners

In addition to the 200 or so medical professionals at genetics centres, there is a much larger network of practitioners involved in PND in Canada — namely, the 10 500 specialists and family and general practitioners who see pregnant women, and who may refer them to genetics centres for diagnostic testing. These practitioners constitute what might be termed the referral system that refers higher-risk patients to the genetics centres (Table 26.10).

As well as making referrals, an increasing number of practitioners also provide PND screening tests. For example, many now perform routine ultrasound in their offices, refer for routine ultrasound to a local facility, or take MSAFP samples.

Whether and how these practitioners offer referrals, give advice, or provide screening tests have a powerful effect on the evolution and provision of PND services in Canada. To understand how this larger referral system works, we commissioned two surveys. The first was a major nation-wide survey (which included obstetricians and family and general practitioners who had performed five deliveries or more in the year preceding the survey, radiologists doing obstetrical ultrasound, and

paediatricians) that analyzed responses from 3 072 medical professionals involved in PND outside the genetics centres. The second survey analyzed information from 642 practitioners involved in Manitoba's MSAFP program (see research volume, *Current Practice of Prenatal Diagnosis in Canada*).

Table 26.10: Number of PND Practitioners Outside Genetics Centres* (1990)

Type of practitioner	Number in Canada
Obstetricians	1 528
GPs/family practitioners practising obstetrics	8 021
Radiologists doing prenatal ultrasound	991
Total	10 540

* Involved in PND through referring patients to genetics centres; doing preliminary counselling; providing routine ultrasound; taking MSAFP samples.

Source: Renaud, M., et al. "Canadian Physicians and Prenatal Diagnosis: Prudence and Ambivalence." In Research Volumes of the Royal Commission on New Reproductive Technologies, 1993.

Referrals: According to the first survey, almost all referrals to genetics centres were made by either obstetricians (56 percent) or general/family practitioners (40 percent) (Table 26.11). The role of general practitioners and obstetricians in referrals was found to vary according to local health care practices. For example, a GP may refer to an obstetrician who then refers to a genetics centre, or the GP may refer directly to the centre.

Significant provincial and regional variations in referral practices were found. Although obstetricians accounted for 56 percent of all referrals nation-wide, the figures ranged from over 80 percent in some centres (North York, Ottawa, and Saskatoon) to less than 25 percent in Vancouver. Similarly, while GPs accounted for 40 percent of referrals across Canada, the figures ranged from 72 percent in Calgary to 22 percent in St. John's.

Also, as noted earlier, there were very marked variations by province in the overall proportion of pregnant women referred by both obstetricians and GPs. These variations may reflect in part the fact that the relevant professional associations for GPs and obstetricians (the national and provincial medical associations and colleges of physicians and surgeons) have not adopted and promulgated policies about when doctors should offer referrals. The CCMG and the Society of Obstetricians and Gynaecologists of Canada (SOGC) have voluntary guidelines, but there is evidence that some referring physicians are basing their referral decisions on their own values, rather than medical need. For example, our nation-wide survey of

referring physicians showed that 15 percent of respondents opposed abortion after PND, no matter how serious the condition or anomaly. At the other extreme, 16 percent responded that it is socially irresponsible for women at higher risk not to have PND and to give birth to an affected child. In addition, it was found that 40 percent of referring physicians believe that it is physicians, not women or couples, who should decide which fetal anomalies justify abortion; 51 percent said it would be inappropriate to offer amniocentesis to a woman who refuses to consider abortion if an anomaly is diagnosed.

Table 26.11. Source of Referrals to Genetics Centres (1990)

Type of practitioner	% of referrals
General or family practitioners	40
Obstetricians	56
Other*	4

* Includes referral by other physicians; referral through MSAFP program; self-referral; referral by public health nurses or fetal assessment units; referral through outreach programs.

Source: Hamerton, J.L., J.A. Evans, and L. Stranc. "Prenatal Diagnosis in Canada — 1990: A Review of Genetics Centres." In Research Volumes of the Royal Commission on New Reproductive Technologies, 1993.

These results show that a disturbing proportion of referring physicians do not accept the principle that patients should make their own informed choice about whether to have PND and whether to have an abortion after diagnosis of a fetal disorder. Moreover, when we examined regional variations in physicians' responses, we found that they closely matched the regional variations in referral rates. For example, respondents from Quebec were least likely to oppose the termination of pregnancy after a fetal disorder is detected by PND, while those from Saskatchewan expressed the highest level of opposition to aborting affected fetuses. The fact that pregnant women in Quebec are three times more likely to be referred to a genetics centre than women in Saskatchewan suggests strongly that many referring practitioners in Saskatchewan are basing their referral decisions more on their personal values than on medical indications. Our national survey did not show

The CCMG and the Society of Obstetricians and Gynaecologists of Canada have voluntary guidelines, but there is evidence that some referring physicians are basing their referral decisions on their own values, rather than medical need.

regional variations in Canadians' attitudes toward PND sufficient to explain the difference in referral rates.

The nation-wide survey concluded that the more serious doctors consider anomalies to be, and the more they accept the option of abortion, the more likely they are to extend access to prenatal diagnostic procedures by providing referrals (and vice versa). This is of great concern to Commissioners, because respect for the pregnant woman's autonomy requires that it be her values and priorities, not the doctor's, that determine her decision to accept or decline PND testing.

When we examined regional variations in physicians' responses, we found that they closely matched the regional variations in referral rates ... Our national survey did not show regional variations in Canadians' attitudes toward PND sufficient to explain the difference in referral rates ... Respect for the pregnant woman's autonomy requires that it be her values and priorities, not the doctor's, that determine her decision to accept or decline PND testing.

Referral rates are also affected by physicians' knowledge of these tests. For example, many of the physicians in the Manitoba study did not have accurate knowledge about the cut-off age for referrals, which may be leading to under-referrals to genetics centres.

Screening Tests: As well as providing referrals to genetics centres, an increasing number of practitioners in Canada also provide PND screening tests. Many now take blood samples for MSAFP screening, perform routine ultrasound in their offices, and/or refer for routine ultrasound to a local facility.

Here too, however, we found wide variations in the way services are provided. For example, the kind of information and counselling physicians provide before taking MSAFP samples varied greatly. In the Manitoba program (Manitoba is the only province with a MSAFP provincial program, although Ontario recently introduced provincial MSAFP screening as part of its triple-testing program), written information regarding the test was provided to physicians for distribution to patients. However, of the respondents to the Manitoba survey, only 30 percent provided this information to the woman before taking a MSAFP sample, 54 percent provided only oral information, and 6.6 percent provided no information at all. (About 10 percent did not respond to the question.)

There were also wide variations in the proportion of women to whom MSAFP screening was offered. In the Manitoba survey of practitioners, 3.5 percent did not respond to the question, 6.2 percent of GPs and obstetricians did not offer the test to any pregnant women, 11.1 percent offered it to pregnant women for specific reasons, such as positive family history, while the remaining 79.2 percent offered or provided it to all pregnant women. Among the 79.2 percent of practitioners who screened

all pregnant women, there were wide variations in how the woman's consent was secured: 37.7 percent of doctors provided the test only if the woman gave her specific consent; at least 22 percent did the test without securing the patient's consent; and 19.4 percent provided the test unless the woman specifically declined — that is, the doctor did not seek specific consent, but if the woman asked what the test was for and then did not want it, she did not have the test.

Substantial regional variations were found in the way the other major screening test — routine ultrasound — is provided. For example, 89 percent of Quebec respondents in the national survey thought it appropriate to use ultrasound to screen for fetal anomalies, compared to 60 percent elsewhere in Canada. Further, while 40 percent of physicians in Manitoba and Alberta did not think it essential to order an ultrasound scan during pregnancy, only 4 percent of physicians in Quebec shared this opinion. (In part this reflects the policy of the Quebec health ministry, which has stated that ultrasound should be the PND screening test of choice in Quebec.)

Substantial regional variations were found in the way the other major screening test — routine ultrasound — is provided.

Moreover, there is evidence that some physicians are overstating the capacity of routine ultrasound to detect fetal anomalies and to reassure patients that the fetus is healthy. Routine ultrasound (unlike the "targeted" ultrasound done at specialized centres) is not intended to screen for fetal anomalies, and it is not capable of identifying many structural anomalies, including some major ones. It may incidentally pick up some anomalies, but its efficacy as a screening tool in this regard is questionable (see discussion later in this chapter).

As with variations in referral practices, variations in the way prenatal screening tests are provided reflect the absence of established standards for the practices of GPs and obstetricians in this area, as well as the lack of monitoring of these practices. Although the CCMG has guidelines (also adopted by the SOGC) on when to refer patients to genetics centres, these are voluntary and often not adhered to. Standards regarding information provision, consent procedures, and counselling for MSAFP testing are needed, as are standards for routine ultrasound and referrals for both MSAFP testing and ultrasound. There are, moreover, no qualifying exams for GPs or obstetricians who wish to provide these PND services.

It is in this large network of referring physicians, rather than in the genetics centres, that much of the variation in PND referral and testing practices occurs ... These variations raise serious doubts about whether women in Canada can expect to receive uniform, high-quality PND services, regardless of where they live and who their doctor is.

It is in this large network of referring physicians, rather than in the genetics centres, that much of the variation in PND referral and testing practices occurs. The data show that the level of knowledge and patterns of practice differ a great deal among physicians in the referral system. These variations raise serious doubts about whether women in Canada can expect to receive uniform, high-quality PND services, regardless of where they live and who their doctor is. In short, how a population is served depends not just on the presence of a genetics centre, but also on having knowledgeable practitioners providing primary care to pregnant women. The same is true, of course, of screening and referral in other areas of medicine.

Patients' Perspective

Three surveys of women's perceptions, attitudes, and experiences of PND were carried out for the Commission in which women were encouraged to discuss their feelings at length and in depth. The studies provide helpful insights into women's experiences and feelings as they undergo PND and face the decisions it entails. The three studies were quite different in design, samples, and methodology. In one study, 70 women referred for PND because of their age were interviewed before they received genetics counselling; they and an additional 52 women were also surveyed by questionnaire after counselling (total of 122, with a response rate of 91 percent).

Another study focussed on a selected group of 37 women (selected because they were not likely to be heard by the Commission in any other way) who had had a variety of experiences with PND, ranging from MSAFP screening to PND and abortion of an affected fetus. Based at a community health centre, the project recruited 5 teenagers, 10 immigrant and refugee women, 6 women with disabilities or deafness, 4 Aboriginal women, 3 parents of children with disabilities, and 9 single parents. Each woman had a semi-structured interview with the investigator, lasting from 1.5 to 4.5 hours; the women's recorded stories were analyzed to identify issues and common themes.

In the third study, two groups of women who had terminated a pregnancy after PND were interviewed at length by a psychologist at intervals ranging from six months to several years later. In one group were 76 women who had known they were at increased risk for a disorder (mostly because of their age) and who had received thorough genetics counselling before amniocentesis. The second group comprised 124 women who were not known to be at higher risk but who had had an unanticipated fetal disorder, detected by routine ultrasound, that was then confirmed by diagnostic testing. The two groups therefore differed in their preparedness for the test result and in the time available for decision making.

Several common themes, as described below, emerged from these three studies (see research volume, *Prenatal Diagnosis: Background and Impact on Individuals*).

Overall Approval

Overall, the majority of women had generally favourable views of PND testing, because the tests provided reassurance, identified problems, and helped them to manage their risk. Even women who had had stressful experiences because of false-positive MSAFP results said they would have the test with their next pregnancy. The women also felt ambivalence, however, describing the testing process as a benefit that has emotional costs attached. The women had to process complex technical information about risks, explore their attitudes toward disability and abortion, balance the desire to know as much as possible with acceptance of the pregnancy, and experience the discomforts of testing and the anxiety of waiting for results, while at the same time trying to enjoy the pregnancy.

Women had worries about the testing procedures, particularly the risk of miscarriage. Although the statistical risk is less than 1 percent, some women said they would feel guilty if they lost a healthy child as a result of having the test; indeed, as we have seen, some women decline amniocentesis for this reason. Anxiety while waiting for results and the length of the waiting period were also mentioned as sources of stress.

Referral and Counselling

Several other specific concerns were raised about the referral and counselling process. Some mentioned the incompleteness of the information provided by referring physicians about why they were being referred to a genetics centre, the nature of the tests, and other aspects of the process.

The women also thought counselling should go beyond the medical facts to include more discussion of their feelings about PND, disability, and abortion. Comments were made about the impersonal or detached attitudes of some practitioners, compared to the more open, supportive approach of other practitioners, and the need for "high-quality" interaction between practitioners and patients.

In one way or another, some women in each of the three studies perceived subtle pressures to have the recommended diagnostic test. In many instances, this was mainly because of the limited time available in which to schedule counselling sessions and tests. In other cases, however, particularly for some of the younger, less educated women, there was a sense of being swept along by an imposing process. There were no suggestions that overt coercion had occurred, although several referring physicians were reported to have asked why anyone would want the test if they would not abort an affected fetus. However, only one woman reported

that her physician actively encouraged abortion if the fetus was found to be affected.

Deciding to Terminate a Pregnancy

For many women, a real appreciation of the seriousness of the PND process came only when the test result was abnormal, triggering a set of choices that required rapid decisions. No matter how supportive and non-directive the counselling, the task of sorting out what was right in light of their own values and priorities, evaluating risks and percentages, and weighing of options proved difficult and stressful for all the women interviewed, but more so for some than for others.

Women in the first two patient perspective studies expressed a range of views about having a child with a disability. Some were confident they could handle having such a child. Others said they would abort a fetus in the case of a very severe disability, but not for Down syndrome or spina bifida. Still others felt that to bring a child with Down syndrome into the world was not fair to the child.

In the third study, the great majority of women felt in retrospect that their decision to abort had been the correct choice for them. This decision is not easy with a wanted pregnancy, and a few of the women had had serious emotional or psychological problems, including guilt (10 percent). Four years later, some women reported that they still felt guilty. It was not possible, however, to design the study to show whether the frequency of psychological or emotional problems among the women in the study was higher or lower than in the general population or among women who decided to continue the pregnancy and have a child with a disability.

Even though most women felt they had made the decision that was correct for them, the experience of termination was difficult, particularly for those who had a fetal disorder detected unexpectedly during ultrasound late in the pregnancy: the women talked about the uneasiness of the ultrasound staff, the feeling of being a "number" as more scans were conducted, the shocking news, the urgency of making a decision, and the lack of personal support during the termination, as well as the lack of information about its aftermath and the sense of not being treated as parents who have just lost a much-desired child. We make recommendations later in this chapter with regard to support for those in this situation.

The Growth of Prenatal Diagnosis Services in Canada

Genetics centres are provincially funded, based on negotiation between the centres and provincial ministries of health, with some provinces having genetics advisory committees advising the minister of health regarding policy and funding in this area. Currently, there is a great deal of variation

across the country in the methods of funding. Some provinces use global budgets, others use line-item budgets; some provinces pay personnel at the centres through salaries, others pay on a fee-for-service basis; some provinces separate PND from other genetics services, while others combine all genetics services into one budget category.

Such a funding situation makes it difficult to determine the precise amount spent on PND in Canada, or to compare the expenditures in different provinces. It is clear that expenditures are considerable, however, and increasing. All but one of the genetics centres reported a significant overall increase in the demand for PND services between 1985 and 1990 and predicted that such demands will rise further over the next five years.

The largest increase has been in referrals of pregnant women later in their reproductive years, for increased risk of chromosomal disorders. More women and more referring physicians are becoming aware of the guideline recommending that referral be offered to pregnant women who are 35 years of age or older, and this is leading to higher rates of referral. There are also more women in this age group because of the baby boom population.

In addition, as a result of scientific developments, more people are likely to be referred for DNA diagnosis of single-gene disorders in future. Demand is also likely to increase if screening tests continue to be developed or preventive strategies become available.

Dealing with increased demand will in turn require an increase in the resources available to genetics centres for laboratory and counselling services. In our survey, when asked to predict their staffing needs in five years, genetics centres projected a need for approximately 40 additional full-time MDs, 40 genetics associates, 20 outreach personnel, and smaller numbers of PhD geneticists and nurses.

These numbers are, of course, speculative and could change dramatically with changes in PND technology or with provincial funding decisions regarding development of screening tests. If current projections are accurate, however, there will be a shortage of trained genetics associates in the near future, since the training programs at McGill University and the University of British Columbia are not yet graduating large numbers.

The Views of Canadians

PND involves very personal and often difficult decisions by individuals and couples, but it also has implications for society more generally. This was brought home to Commissioners by the breadth, diversity, and intensity of views brought forward during our consultative and research activities. To come to a better understanding of public perceptions of PND, we collected information in two ways. First, we listened to Canadians (including users and providers of PND services, groups representing people

who have some of the conditions detected through PND, persons with disabilities and groups representing them, and others concerned about the social and ethical implications of these technologies) through our public hearings, panel discussions, private sessions, and submissions. Second, to understand how Canadians in general view PND, we commissioned survey research on the values and attitudes of Canadians with respect to these activities.

Public Hearings and Submissions

Canadians have a wide spectrum of views on PND, and many of the oral and written presentations received by the Commission were insightful, thought provoking, and moving. The Commission is grateful for the time and effort put in by individuals and groups that made presentations to us.

> Testing benefits a pregnant woman by providing her with information about the status of her fetus and thus the option to terminate her pregnancy by early abortion or to carry the fetus to term while making necessary preparations for the accommodation of her child's needs. For those few disorders whose manifestations can be prevented, delayed, or ameliorated by interventions *in utero*, or by early delivery by Caesarian section or just by Caesarian section, testing provides an opportunity to reduce the magnitude of disability ... A universal prenatal screening program [without] adequate social supports for disabled individuals threatens to promote the public perception that women are expected to bring only perfect babies into the world. Such a perception hides the fact that it is society's responsibility to assist disabled children and their families throughout life. A program with a coercive and anti-disability bias would limit reproductive choice and must therefore be avoided.
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> *K. Sandercock, Vancouver Women's Reproductive Technologies Coalition, Public Hearings Transcripts, London, Ontario, November 1, 1990.*

Social and Ethical Dimensions

Interventions concerning the social and ethical dimensions of PND produced considerable debate during the Commission's hearings, reflecting the complexity of the questions involved and the difficult nature of the issues to be resolved. These issues included the potential impact of PND on attitudes toward abortion, the "medicalization" of pregnancy, societal attitudes toward people with disabilities, and the potential for discrimination against people who carry the gene for certain diseases.

Abortion: Women in Canada have the option of terminating a pregnancy if a fetal anomaly is detected through PND. Members of some religious and anti-abortion groups oppose this practice. They believe that to allow the abortion of fetuses with disorders reflects and perpetuates a lack of respect

for human life. Representatives of these groups who conveyed their views to the Commission stated that using PND to identify fetuses affected with a congenital anomaly or genetic disease is appropriate only if it enables treatment of the disease *in utero* through fetal therapy, or if it enables parents and physicians to prepare for the birth and treatment of an affected child. They acknowledged that PND may be used in many cases by couples who would otherwise have terminated a pregnancy if testing were not available to provide evidence that the fetus was healthy.

> The message that it is not only permissible but preferable to abort any foetus that may be born with a disability resounds loud and clear from the advice given and the approach adopted by many within the medical community. Canadians who have a disability find this message repugnant and totally unacceptable. The implications for them in their day to day lives is to live in an environment of hostile and denigrating attitudes. The primary purpose of prenatal testing is to try to diagnosis disabling conditions in advance. The recommended "solution" to that diagnosis is abortion.
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> *Brief to the Commission from the Canadian Association for Community Living, April 30, 1991.*

Many other groups and individuals felt strongly that if a fetus is affected by an anomaly or disorder, the choice of a course of action must be left entirely to the pregnant woman or couple. Other witnesses expressed concern that the availability of PND creates subtle pressures for abortion. We heard allegations that women or couples unwilling to consider abortion in the event that a fetus was affected were not offered PND services, despite the fact that PND in this instance might either reduce anxiety by showing that the fetus was unaffected or give them time to prepare for the birth of a child with a disability.

If such pressure occurs, it has obvious implications for individual autonomy in matters of reproductive health and well-being; it was therefore one of the aspects of PND on which we sought accurate data. Our research shows that any pressure for women to commit themselves to aborting an affected fetus comes from referring physicians, not from the genetics centres.

Medicalization of Pregnancy: The Commission received several representations concerning the effects of PND in medicalizing pregnancy; some argued that medicalization gives medical professionals and society at large increased power to control women's reproductive functions and choices. For example, some witnesses were concerned that the universal availability of PND would mean that it would become compulsory eventually, with possible repercussions — such as loss of hospital or medical insurance benefits — for those who declined to have testing. (See Part One, Chapter 2, for a more detailed discussion of the concept of medicalization and its relevance to new reproductive technologies.)

Attitudes Toward Disability: Several intervenors spoke eloquently about the need for society to examine what the use of PND says about our attitudes toward disability and members of society who have disabilities.

Others questioned whether the allocation of resources to PND diverts attention from the non-genetic causes of disability, including accidents, socio-economic status, and inadequate prenatal care.

We were told that societal supports are generally inadequate for women or couples who have a child with a disability and that, in these circumstances, intervenors questioned whether aborting the fetus or carrying it to term was a real choice.

Potential for Discrimination: Finally, intervenors expressed concern that people who carry the genes for certain diseases, particularly those that begin to affect an individual only later in life, could be subject to discrimination — in employment, in access to health or life insurance, or in other ways — if the information revealed by PND was not protected. This issue will presumably grow in importance as knowledge about the genetic component of health expands — for example, with respect to late-onset diseases such as Huntington disease and Alzheimer disease, as well as with respect to individual susceptibility to conditions such as heart disease, cancer, and a range of other conditions. This topic is discussed in Chapter 27.

> There are many circumstances where knowledge of the fetus's condition can have a significant and beneficial impact on the overall obstetric management.
>
> For example, if a woman is known to be carrying a fetus with a non-lethal structural abnormality such as an intestinal obstruction in an otherwise normal fetus, then arrangements can be made in advance to optimize the fetus's outcome by arranging for her to deliver in a tertiary level centre with immediate access to neonatology and paediatric surgery. The couple will also have time to emotionally and psychologically prepare for the delivery and the fact the child will be immediately transferred to an intensive care setting or undergo surgery.
>
> *J. Johnson, Genetics Committee, Society of Obstetricians and Gynaecologists of Canada, Public Hearings Transcripts, Toronto, Ontario, November 19, 1990.*

> Advocacy of termination solely on the basis of race would be met with loud, impassioned cries of protest, but termination on the basis of gender is dreamed of by some, and abortion on the basis of a fetal abnormality is considered the best thing to do. Best for whom? Those of us who are disabled question the criteria.
>
> *M. Gibson, Spina Bifida and Hydrocephalus Association of Ontario, Public Hearings Transcripts, Toronto, Ontario, November 20, 1990.*

The concern was also raised that employers or insurance companies might demand *post*-natal genetic testing as a precondition of being offered employment or insurance. The issues surrounding genetic screening in the workplace are important, but they lie outside our mandate, which is limited to prenatal genetic diagnosis as one of the new reproductive technologies. In countries where private insurance covers health care, PND does indeed become a key issue for insurance regulation. In Canada, however, where basic health care is guaranteed, this is less of a concern.

How Prenatal Diagnosis Is Delivered

Some of what we heard focussed on concerns about inequality of access to PND on the basis of socioeconomic status, education, or place of residence. Witnesses argued that the use of PND seems to rise with the level of income, education, and employment; that having a higher level of education seemed to make it more likely that a woman or couple either would be aware of PND or would be able to secure a referral if they wished to have testing.

> We do not want to ignore or abolish medical technology — we want to use it. We want to ensure that women are given the information they need to enable them to make a choice around using it, and the necessary support for decisions which they need to make based on the use of that technology. We need to establish a true partnership between women and the practitioners who serve them.
>
> *Brief to the Commission from the Toronto Women's Health Network, November 30, 1990.*

Concerns were also expressed about the nature of counselling. Some witnesses thought that the counselling provided as part of PND services might fail to give prospective parents a full appreciation of their range of options, including the possibility of raising a child with a disability and an indication of the supports available, from an unbiased perspective free of stereotyping or prejudgement.

We also heard calls for research into two principal areas concerning: (1) the long-term effects of the use of some of these technologies on women and children, and (2) efforts to improve the accuracy of diagnoses. The issues raised by Canadians are discussed at more length below.

Commission Surveys of Canadians

Two large surveys of Canadians carried out across the country for the Commission documented a high level of awareness of and support for PND. Responses to these surveys showed high levels of awareness of the existence of some prenatal diagnostic techniques, such as amniocentesis and ultrasound, but fewer respondents were aware of the full range of

techniques available to assess the health of the fetus or of the nature and purpose of specific techniques. Levels of awareness are higher among women than among men, and among respondents with higher levels of formal education.

- The vast majority of those surveyed would be prepared either to use PND themselves (79 percent) or to allow others that option (81 percent). About 18 percent were opposed to either personal use or wider availability of PND services.
- A marked majority of those surveyed also support the availability of the option to terminate a pregnancy after PND, with only 16 percent opposed in all circumstances. The level of support depends on the severity of the disorder. For example, 73 percent of people surveyed strongly supported the availability of abortion if a disorder that is fatal early in life is diagnosed in the fetus, while approximately 60 percent supported the availability of abortion for disorders that make it almost certain that independent living will not be possible.

Sixteen percent of referring physicians believe that intentionally giving birth to a child with a genetic defect at the time when both PND and abortion are available is socially irresponsible. The existence of this view, even if only among a minority, supports the need to establish safeguards to protect the principles of autonomy and informed consent to PND.

Aspects of the Use of Prenatal Diagnosis in Canada

In thinking about the issues and in integrating a wide range of individual perspectives and experiences, professional orientations, and expert advice into a coherent set of policy recommendations that address them, we applied our guiding principles. The context of the ethic of care and the intent to prevent or avoid harm wherever possible directed our reasoning. The ethic of care seeks to empower *all* concerned, rather than some at the expense of others. Hence, we considered both what harms could be done to individuals and society by the use of PND, whether these can be prevented by safeguards and, if so, whether these are in place; and what harms could be done to individuals and society by *not* providing PND.

It is important to remember that harm can arise either way: that is, either by withholding or by providing PND. Withholding PND for severe disorders could cause harm to individuals and couples at higher risk of having an affected fetus. On the other hand, the technologies involved are too

> We found that Canadians recognize the seriousness of the issues to be weighed in reaching these decisions and are willing to give others the opportunity to deal with the choices in the way they see fit.

complex and powerful to be provided without a context of adequate guidelines and safeguards to protect vulnerable interests (of individuals and of society). We therefore had three goals in mind: to safeguard against the inappropriate, unethical, or discriminatory use of PND; to remove obstacles to appropriate access; and to deal with deficiencies in the PND system that result in the (direct or indirect) withholding of appropriate services.

Our guiding principles require that both individuals and society be considered in reaching our recommendations. Individual women and couples who have PND testing are constantly searching for the choices that are "right" for them. Many of these choices will also be acceptable to society as a whole; choices can vary greatly between families without in any way transgressing the bounds of societal acceptability. We found that Canadians recognize the seriousness of the issues to be weighed in reaching these decisions and are willing to give others the opportunity to deal with the choices in the way they see fit.

The Commission's objective is not to render definitive or immutable answers but rather to recommend how the serious issues raised by PND can continue to be addressed in the years to come, guided by our ethical principles. We focus on four broad sets of issues in the remainder of this section:

- the counselling and decision-making aspects of the PND process;
- the moral and legal issues of confidentiality and liability;
- the relationship between disabilities and choices about whether to terminate a pregnancy; and
- access to prenatal diagnostic services.

Counselling, Information, and Support

Throughout this report we have been guided in part by the principle of autonomy and its corollary, informed choice. As discussed in Chapter 3, this ideal requires that individual women and couples have adequate information, support for decision making (for example, through counselling), and an adequate range of options from which to choose.

The Medical Genetics Counselling Process

Within the genetics centres, genetics counselling is provided at various levels of complexity, ranging from referrals for maternal age, where little work is needed to identify the risks and options involved, to referrals for a family history, which may require highly complex statistical analysis and clinical interpretation. Counselling is a very demanding process that often taxes the skills and professionalism of the counsellor and challenges and engages the individual woman's or couple's deeply held values. (See box, which outlines the goals of medical genetics counselling.)

The Medical Genetics Counselling Session

The aims of the counsellor are to

- provide estimates, in understandable form, of the probability of having an affected child, and of the risks and benefits of contemplated procedures;
- provide information about the nature, burden, and possible variability of the disorder and about what treatments and supports are currently possible for a child born with a particular disorder;
- try to allay anxiety based on misperceptions and help the woman or couple to deal with that which is well founded;
- try to appreciate the couple's perception of risk and burden and where they fit on the spectrum of views regarding abortion, the disabled, quality of life, and attitudes toward life (for example, are they optimistic, realistic, fatalistic?). Every family is different, and, recognizing this, counsellors must try not to project their personal views into the situation;
- try to help the couple, without being directive, to reach a decision best suited to their own situation, by pointing out pros and cons and acting as a sounding board and resource person. The counsellor wants to empathize with the couple or individual, yet must remain objective to be effective. It is a tenet of genetics counsellors not to be directive, fully recognizing that this is not easy.

Quality of Information

The provision of accurate information in an understandable format is a fundamental component of the broader counselling process. The Commission collected brochures and other informational materials provided to patients by Canadian genetics centres; many of the materials were found to be complex, technical, and difficult to read.

Thirty items of patient education material from 14 centres were analyzed for reading level, writing style, and visual appeal. Twenty of the 30 items tested required a reading level above Grade 12; 18 items were rated as having a "poor" writing style; and 16 had "poor" visual appeal. In terms of an overall rating, 26 items were rated either "poor" (16) or "fair" (10), while only 4 were rated "good" (2) or "excellent" (2). Written materials were not always available in the language of the people served, particularly in centres that served large immigrant populations.

Many of the individual items, however, had positive features that, taken together, could provide the basis for improving patient education

materials provided by genetics centres. The Commission therefore recommends that

> **207. The Canadian College of Medical Geneticists coordinate a collaborative effort by genetics centres, with the input of concerned women's groups and organizations representing people with disabilities, to develop more appropriate educational materials on prenatal diagnosis.**

The Commission also recommends to provincial/territorial health ministries that

> **208. These materials be made available to women and the general public through physicians' offices, public health units, local hospitals with obstetrical units, community centres providing prenatal classes, and other appropriate means.**

and that

> **209. Centres with large immigrant populations ensure that written materials and, in particular, consent forms are available in the relevant languages, and that provincial/territorial health ministries ensure that funds are available for this purpose.**

Complexity and Time Constraints

Women and couples often find genetics counselling sessions helpful, and perhaps even comforting, but satisfaction is not universal. Several of the reasons for dissatisfaction are implicit in the nature of this counselling. The facts themselves may be unpalatable or threatening. People may have great difficulty accepting that they carry a gene for a deleterious condition or that their next child is at risk for a serious disorder.

In addition, counselling done before pregnancy or before testing can only provide probabilities — expressed, for example, as a 1 in 4 chance or a 1 in 100 chance that the next child will have the condition. But probabilities, no matter how precise, are unsatisfying. People being counselled would like to have simple yes or no answers, yet ambiguity is often unavoidable in genetics counselling situations.

In addition, even though a fetus is known to be affected, it is not possible to predict the severity for some disorders except in terms of range. This is because some particular disorders show a great range in severity.

For example, the gene for neurofibromatosis may be detected, but this does not predict how seriously the eventual child will be affected by the disorder, whose effects range from only minor skin changes in some to devastating disability and early death in others.

Moreover, many people being counselled have no first-hand knowledge of the disorder that has been diagnosed. For example, many people will never have encountered a child with cystic fibrosis, even though it is the most common single-gene disorder in Canada. This means that some prospective parents are almost entirely dependent on their counsellors for information about disabilities and may have difficulty imagining the various possibilities and options.

> Firstly, concerning the way I see the multidisciplinary team: I see it among practitioners, physicians, or nurses, in the context of the hospital itself, when the woman is contacted and told, for example, that she is carrying a fetus with an abnormality.
>
> Before a decision is made about abortion, would it not be appropriate, in fact, to introduce a multidisciplinary team that discusses the prognosis of the child the woman is carrying? Of course, trisomy is a serious problem, a very severe abnormality, but it is well known that there is difficulty detecting the degree of severity — who knows? [Translation]
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> *Y. Grenier, private citizen, Public Hearings Transcripts, Montreal, Quebec, November 21, 1990.*

Because of the time constraints imposed by the PND context, women and couples may feel there is insufficient time to reach a thoughtful decision. The time frame for decision making may be particularly tight when the woman or couple wishes to consider termination if the fetus is affected; the later in pregnancy an abortion is done, the more risk and trauma it involves for the woman. Although results are usually available earlier, in some cases they may not be received until the pregnancy has reached the twenty-first or twenty-second week of gestation (for example, cases where a test must be redone, which happens in 1.1 percent of amniocenteses). Even without re-testing, amniocentesis results may not be available until after the sixteenth week of gestation.

Counsellors at genetics centres are required by the CCMG guidelines to be non-directive. Non-directiveness is not always welcomed by those receiving counselling. Some women and couples find the information complex and overwhelming and ask the counsellor what he or she would do in their place. Some are frustrated when the counsellor insists that it is their decision.

Even with optimal counselling, it can be expected that some women and couples will feel frustrated and angry at the circumstances in which they find themselves.

In view of this, we believe that the counsellor should provide written summaries of genetics counselling sessions not only to the referring

physician but also to the women and couples counselled (which we found was done by some centres). Reports of counselling carried out before testing could be of benefit to women and couples in deciding about PND; similarly, reports of post-test counselling could benefit women and couples with an affected fetus who are considering their options. Even though in some cases there may not be time for them to be useful in that pregnancy, the family then has it on hand for future reference and decision making about reproduction.

We are concerned that the resources devoted to counselling may not be keeping pace with increasing demand for counselling services ... The need for more and different kinds of counselling resources will likely expand with growing diversity in Canadian society.

We are concerned that the resources devoted to counselling may not be keeping pace with increasing demand for counselling services. As medical knowledge and PND technology develop further, more information will be available about the fetus at earlier stages of gestation, and the need for counselling will tend to increase as a result. The need for more and different kinds of counselling resources will also likely expand with growing diversity in Canadian society. Counselling must be adapted continuously to meet the needs of users and be sensitive to language, social, and cultural factors in addition to the other requirements already identified.

If these concerns are to be addressed, provincial/territorial health ministries will have to increase their funding for counselling. Genetics centres are often funded through global budgets, which include salaries for personnel. At present, resource allocation for PND counselling often fails to recognize its personnel-intensive nature and the time involved in providing genetics services. If testing is to be offered, health ministries must provide appropriate levels of support, and genetics centres should also use these resources as effectively as possible. For example, genetics counsellors, not physician geneticists, would be able to offer counselling when the reason for referral is that the woman is 35 years of age or older. The Commission recommends that

210. Provincial/territorial health ministries develop a formula for funding genetics centres based on caseload to ensure that adequate resources for counselling are available. For a given number of women and couples referred annually for counselling (and this is to be an agreed-upon mix of straightforward and complex cases), the ministry of health should provide funding for a

given ratio of physician, genetics associate, and support personnel. Such a formula would allow more comparable care to be delivered across the country.

Supportive Counselling

We have particular concerns about the adequacy of supportive counselling to deal with the emotional and psychological needs of patients. We found that most genetics centres offer high-quality informational counselling before testing, to review testing results, and to re-evaluate recurrence risks. However, just as in any medical care, the genetics counsellor may not be sufficiently expert in the recognition or management of the complex psychological and emotional problems that may arise, particularly when a fetus is found to be affected.

When a severe disorder is diagnosed, the woman or couple involved faces very difficult decisions and may require additional supportive counselling. If a decision to terminate the pregnancy is made, follow-up counselling may be offered; several genetics centres offer social work, pastoral care, or psychological support services in such cases. Genetics associates often have significant involvement in follow-up and emotional support for the women or couples involved. However, genetics centres may lack adequate psychological, psychiatric, or social work resources to help provide care in complex situations.

> The mourning reaction (to abortion) should be anticipated and respected. A psychiatric consultation in the pre-termination period should be followed by a contact with the couple sometime later at home. Patients suggested that this contact be initiated by the medical team because people often do not feel comfortable contacting the psychiatric team themselves. Involvement with a parents' group or association could prevent the feeling of isolation expressed by many couples. Family members and friends often do not understand the sorrow as well as people who have had a similar experience.
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> *L. Dallaire and G. Lortie, "Parental Reaction and Adaptability to the Prenatal Diagnosis of Genetic Disease Leading to Pregnancy Termination," in Research Volumes of the Commission, 1993.*

It is important to remember that women and couples undergoing a termination following PND may need support, just as parents whose child has died do. Hence, counselling support should be offered throughout the process. We found that there is a lack of personal support during the termination procedure and its aftermath. We believe that special attention

should be given to the counselling needs of women and couples in cases involving termination following the discovery of a serious fetal disorder.

In addition, access or referral to self-help groups or associations of people who have had a child with the same disorder may help reduce the feeling of isolation and provide support and helpful advice. The Commission recommends

> **211. To the Canadian College of Medical Geneticists, the Society of Obstetricians and Gynaecologists of Canada, the Canadian Association of Genetic Counsellors, and all practitioners involved in prenatal diagnosis that steps be taken to ensure that the woman having termination because of a serious fetal disorder and her family receive support from medical and paramedical staff, just as those who lose a child after birth do, from obstetrical and ward personnel before, during, and after termination, as well as from genetics centre personnel.**

The Commission also recommends that

> **212. All centres providing prenatal testing have, within their centre or by referral, facilities to provide women with counselling, including grief counselling, appropriate to their situation. This should be a condition of licence.**

The Commission recommends further that

> **213. To help reduce the feelings of isolation expressed by many women and couples, referral to self-help groups or associations be offered (where they exist) to people who have experienced a termination because of a fetal disorder.**

Consent, Choice, and Individual Autonomy

Genetics counselling is part of a decision-making process that results, ideally, in a free and informed choice by women considering whether to undergo PND. How do women and couples make decisions once they have received all the information, counselling, and support that is available?

Our evidence shows that there is a distinction between problem solving (the search for the one correct technical answer, a process heavily dependent on the practitioner's expertise) and decision making (the balancing of probabilities and personal priorities, risks, and desires — a process that centres around the patient's wishes) (see research volume, *Treatment of Infertility: Current Practices and Psychosocial Implications*). In the context of PND, informed consent and choice must be understood as matters of decision making, not problem solving. There is no single "right" answer for all women and couples, only answers that are right for the individual woman or couple, based on personal circumstances and values.

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What is right for the woman or couple is often not immediately clear, either to the counsellor or to the people receiving counselling, whose perception of risk and burden may vary widely. The specific family situation may be crucial, and the woman or couple may have more day-to-day experience of a condition than the counsellor. For example, a couple may already have a child with cystic fibrosis or spina bifida. Some may equate aborting a fetus who has the same disorder with disloyalty and rejection of their loved child; others may reject the idea of bringing another such child into the world. A woman who has worked with children with Down syndrome may be much more anxious about her pregnancy than one who has not. A person with polycystic kidney disease that was entirely asymptomatic and discovered only on routine examination at the age of 30 may be much more willing to take the 50 percent chance of passing the gene on to a child than someone whose disease is more severe and who has already had a kidney transplant. Regardless of the decision of the woman or couple,

> The ultimate consequence of the genetic-risk standard and its associated discourse is a denial of abnormality, a fear of difference, and a reinforcement of couples' and women's narcissism, that is, the perception of the other as an extension of oneself, and even the projection of oneself, leading, ultimately, to an unwillingness to accept otherness. This, then, in short, defines how technology and science make the other into a tool and, as a corollary, how they make abnormality or handicap even more devastating. [Translation]
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> *Brief to the Commission from M. De Koninck, Chaire D'Étude sur la Condition des Femmes, and M.-H. Parizeau, Professeure, Faculté de Philosophie, Université Laval, February 1991.*

counsellors should be expected to respect that decision and to provide support and help.

Issues of liability also arise with respect to gaining informed consent when performing PND procedures. As discussed in Part One (Chapter 4), physicians have a legal obligation to secure the informed consent of patients to all procedures, which requires disclosing the benefits and risks involved. The current legal status of informed consent rests on the principle that if the physician fails to inform a patient of what is termed a "material" risk or a "special risk with serious consequences" associated with the proposed treatment, the failure can give rise to a lawsuit for negligence. Hence, providers of PND must inform patients of all material risks associated with PND procedures (that is, risks that could affect whether the patient would agree to the procedure). Similarly, if a referring physician neglects to inform women 35 years of age or older about PND testing, and if an affected child is born, there could be a claim of negligence.

In the context of decision making, the principle of autonomy directs attention to questions of consent, options, and the social context for choice. Are women in fact free to choose whether they will have PND? If the fetus is affected, are they free to choose whether to have an abortion or whether to continue the pregnancy? Are there undue pressures from doctors, spouses, friends, relations, or other sources that influence their decisions? In assessing these questions, the Commission found that it is important to distinguish the genetics centres from the referral system.

Consent to Testing

Option to Refuse Prenatal Tests: Commission research found that women at the genetics centres recognize that they have the choice of accepting or declining testing. Indeed, approximately 10 percent of patients referred for amniocentesis or CVS do decline the procedure. This varied from about 20 percent in Ontario centres outside Toronto to 3.7 percent in Halifax. Newfoundland (17.3 percent) also had a relatively high percentage who declined; rates for Saskatchewan (7.7 percent), Manitoba (6.1 percent), Alberta (4.6 percent), and Quebec (4.4 percent) were lower.

These figures must be interpreted with caution, as record-keeping differences between centres may have influenced their accuracy. However, there is some indication that in areas where referral to a more distant centre is necessary, the women who are referred have usually decided in advance to have testing. The higher refusal rates in Ontario may indicate that when women do not have to travel as far for counselling and testing, they may be more likely to go to the centre for counselling and put off the decision about whether to accept the test until after the counselling (see research volume, *Current Practice of Prenatal Diagnosis in Canada*).

The fact that about 10 percent of women decline testing suggests that women do see refusal as an option. It is also important to remember that most women who object on principle to PND would not go to a genetics

centre in the first place. Hence, we believe that informed consent to PND testing is being given at genetics centres.

This cannot be taken for granted, however; vigilance must be maintained to ensure that informed consent remains a reality. Overall, referring physicians are opposed to the coercive use of PND. In fact, mandatory testing would be resisted by genetics centres and the CCMG and would be unacceptable to the vast majority of people in any society that values individual autonomy. Indeed, it would probably be struck down as inconsistent with the *Canadian Charter of Rights and Freedoms*.

During our public hearings we heard it said that some women choosing PND have been told that they must commit themselves to an abortion if a disorder is found. Our data from across the country showed that this is not the case at genetics centres, and the CCMG guidelines (to which genetics centres must adhere in order to get CCMG accreditation) state clearly that such a commitment is not required. It is possible, however, that women are being told this by physicians who refer them to genetics centres.

Commitment to Terminate: During our public hearings we heard it said that some women choosing PND have been told that they must commit themselves to an abortion if a disorder is found. Our data from across the country showed that this is not the case at genetics centres, and the CCMG guidelines (to which genetics centres must adhere in order to get CCMG accreditation) state clearly that such a commitment is not required. It is possible, however, that women are being told this by physicians who refer them to genetics centres.

The policy of the centres, laid out by the CCMG, is that the woman or couple should have the right to make a decision when faced with the actual, rather than a hypothetical, situation, because people often respond differently in the two situations. Furthermore, even if a couple does not wish to consider terminating the pregnancy after a disorder is found, the information provided by PND may still help them prepare for the birth of an affected child and appropriate medical care for the fetus before birth and at delivery.

Our data did show, however, that at one centre with insufficient resources to do all the prenatal tests requested, women who would not consider abortion under any circumstances were advised against (though not refused) PND. This was to allow testing of more women who were leaving that decision until after the test.

We cannot take the principle of informed consent for granted. Evidence from our survey of referring physicians showed that approximately half supported the idea of requiring a commitment to abortion before providing PND. Moreover, 12 genetics centres have not applied for accreditation from the CCMG, so it is difficult to monitor their

compliance with the CCMG guidelines. The Commission therefore recommends that

> **214. All genetics centres providing prenatal diagnosis services formally adopt an explicit policy (consistent with current Canadian College of Medical Geneticists guidelines) that agreement to terminate a pregnancy is not a precondition or requirement for undergoing prenatal testing. The Commission recommends further that adoption of such a policy be a condition of licence established by the National Reproductive Technologies Commission for centres providing prenatal diagnosis and genetics services.**

The Social Context for Choice

Most people in Canada think that the choice of whether to have PND when at risk for a serious disorder, and whether to have an abortion if a disorder is diagnosed, should be left to each woman or couple in accordance with their own values and circumstances (see research volume, *Social Values and Attitudes Surrounding New Reproductive Technologies*).

Various social pressures influence this choice. If a woman decides to terminate the pregnancy, some may view her decision as unethical. On the other hand, a woman who decides to continue a pregnancy and have an affected child may face disapproval from some members of the community who will view the decision as irresponsible. Another aspect she must consider is that the resources available for parents who choose to raise children with disabilities are limited, and that children with disabilities may be subject to prejudice and discrimination. For some individual women, economic and social realities make the possible alternative — raising a child with a disability — so formidable that it does not appear to be a genuine choice for them.

People receiving counselling should be fully informed, therefore, not only about the risks and the disorders involved, and about what the disorder means in terms of day-to-day functioning for the affected individual and lifelong consequences for themselves, but also about the social pressures they

Most people in Canada think that the choice of whether to have PND when at risk for a serious disorder, and whether to have an abortion if a disorder is diagnosed, should be left to each woman or couple in accordance with their own values and circumstances.

may experience, so that they have an opportunity to consider how such pressures might affect them (see research volume, *New Reproductive Technologies: Ethical Aspects*). These social pressures are important. We believe that women's capacity to make informed choices about PND would be improved if economic and social supports for families affected by disabilities were increased.

It is also important to realize that social pressures are not the only, or even the primary, factor in many decisions. For many families, lack of support or services is not the primary reason they do not wish to have an affected child. Although there is no question that increased support is necessary in the interests of social justice, this would not provide an acceptable alternative to PND and abortion of affected fetuses for many women and couples. To say that it would neglects the devastating impact of some mental and neurological disabilities, which require lifelong care, often overwhelm the parents' lives, and inflict suffering on the affected individual and, as a result, on family members and others who witness that suffering. In addition, parents — especially the woman, who often bears the primary responsibility for care — are left with few choices about pursuing other goals.

It is also important to realize that social pressures are not the only, or even the primary, factor in many decisions. For many families, lack of support or services is not the primary reason they do not wish to have an affected child.

Counselling and Informed Choice in the Referral Network

As noted earlier in this chapter, there are serious problems regarding counselling and informed consent within the referral network for PND. For example, given the demonstrated inadequacies with informed consent to MSAFP screening in Manitoba that our data show, we believe that women who consent to MSAFP screening should be required to sign a consent form that contains relevant information about the test.

Similar problems regarding informed consent arose in the context of referrals for women who were 35 years of age or over. In the Commission study of 70 such women referred to a genetics centre for PND, many were told that referral was "automatic" at their age (see research volume, *Prenatal Diagnosis: Background and Impact on Individuals*). Other Commission research found that some women do not realize that they can decline referral (see research volume, *New Reproductive Technologies: Ethical Aspects*).

Practising physicians, particularly obstetricians, tend to be much more directive than geneticists according to the evidence provided by our surveys.

Insofar as general practitioners and obstetricians do provide information, there are concerns about the directiveness of counselling. The Commission's survey of referring physicians found that 50 percent agreed with the statement that parents should have absolute right to freedom of choice regarding abortion, yet 40 percent thought that physicians, not parents, should decide which fetal anomalies justify abortion (see research volume, *Current Practice of Prenatal Diagnosis in Canada*).

> It is urgent that we look critically at these technologies and consider the serious problems they create for women. We note, firstly, the intensive use of their bodies: the heavy reliance on treatments, the overmedication, the complexity of treatments, and the fact that they are increasingly numerous. Ultrasound is an example. Initially, this treatment was limited to women at risk; then, most women had one ultrasound during their pregnancy; later, they had three or four. And one of my colleagues was telling me this morning that, in some centres, women routinely had to have an ultrasound at every visit. So it has become routine in hospitals; it has become ordinary. [Translation]
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> *A. Robinson, Groupe de recherche multidisciplinaire féministe, Public Hearings Transcripts, Quebec City, Quebec, September 26, 1990.*

Other findings were also relevant: for example, 16 percent of all physicians responding, and 27 percent of Quebec physicians, believed that it is a socially irresponsible act to have a child with a genetic disorder when PND is available. Similar proportions felt it would be justified to have laws to limit the transmission of genes causing severe disorders. Thus, practising physicians, particularly obstetricians, tend to be much more directive than geneticists according to the evidence provided by our surveys.

The finding that many practising physicians (who determine whether and how referral for PND is offered) have attitudes that are less respectful of patient autonomy is an indication of the need for greater physician education and awareness in this regard. This has implications for medical school curricula, residency training, specialty examination content, and continuing medical education. The values and opinions of physicians must not be imposed on patients. The Commission recommends that

215. For women who consent to MSAFP screening, signed consent forms be required prior to taking blood for the test and that information about the test be contained on the consent form.

216. The Society of Obstetricians and Gynaecologists of Canada and the College of Family Practitioners of Canada encourage their members to pursue continuing medical education to increase their knowledge and understanding of the capabilities and limitations of prenatal diagnosis, the proper provision of accurate information, and the process of informed consent and choice.

and that

217. Specifically, increased efforts should be made in the continuing medical education of referring physicians to emphasize the right of individual women and couples to reproductive autonomy, to decide for themselves whether to have prenatal testing, and, if a serious disorder is detected, to decide whether to terminate or continue the pregnancy. These decisions must be based on the principle of informed choice, that is, with full knowledge of all the available options, benefits, and risks, and full and informed consent to undergo a prenatal diagnosis procedure.

Confidentiality

Disclosure of Genetic Information to Family Members

PND sometimes unexpectedly reveals sensitive information that, if disclosed, could benefit some individuals but harm others. This may give rise to serious ethical problems. For example, the test might reveal that the pregnant woman's partner is not the biological father of the fetus she is carrying. In this situation, our data show that a woman's partner would not usually be told; rather, the woman would be told he is not the father and the decision about what to do left up to her. If DNA testing becomes used more often, such situations will

Doctors are under a legal duty to maintain the confidentiality of medical records. This legal duty is recognized in common law and civil law, as well as in various statutes and professional guidelines, and may even be protected by section 7 of the *Canadian Charter of Rights and Freedoms*.

arise more often. Ideally, the pregnant woman should be informed in private, before she consents to testing, that the test may reveal paternity or, sometimes, that the partner is not the biological father of the child.

Dilemmas could also arise if testing revealed a chromosomal translocation carried by one of the partners, which would show that his or her near relatives were also at risk of having affected children. A lack of disclosure in this situation could harm the relatives, as they might wish to avoid having children affected by the disorder.

Generally speaking, doctors are under a legal duty to maintain the confidentiality of medical records. This legal duty is recognized in common law and civil law, as well as in various statutes and professional guidelines, and may even be protected by section 7 of the *Canadian Charter of Rights and Freedoms*.

However, there are three recognized exceptions to the duty of confidentiality: where there is consent by the patient, authorization of a court, or the risk of harm to third parties. For example, there are requirements to protect public health by reporting certain infectious diseases or an intentional threat to a third party. If a genetics counsellor wants to contact relatives at risk of having an affected child, it is not a question of public health or of avoiding intentional harm to another; rather, it is a question of providing third parties who are relatives with additional significant information they might not otherwise have.

A U.S. President's Commission (for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research) report in 1983 recommended that, in cases where there is a high probability of serious harm to an identifiable individual, a breach of confidence could be considered ethically acceptable if there were first a serious attempt to persuade the primary patient to allow the information to be divulged to identifiable relatives, if failure to inform could cause serious harm, and if the information released was limited to necessary genetic information. No court to date has rendered a judgement about such disclosures in the specific context of human genetics, so it is not known whether these guidelines would serve as a defence in the event of a suit by the person whose confidential records were disclosed without their consent or whether the failure to disclose would be considered negligent. Opinion varies among geneticists about how to deal with such problems,[1] but in general, as we have noted elsewhere (see Chapter 27), they believe that disclosure can usually be achieved by discussion, education, and tactful negotiation.

One other situation where full disclosure may raise ethical questions involves test results that are ambiguous; either the significance of test results is not clear (for example, mosaicism or an unusual chromosome that might, or might not, be a normal variant), or test results are conflicting. Even though disclosing such results could create so much anxiety that the woman might be better off not knowing, in our society full disclosure is now the norm. We consider failure to disclose paternalistic,

as the assumption that a woman would not be able to deal with the information is disrespectful of her autonomy.

Protection of Privacy and Confidentiality

As noted earlier, concerns have been raised that information gained through PND may be wanted by insurance companies and employers.[2] Release of such information by the physician without the patient's consent would be a clear violation of the legal duty of confidentiality. Whatever the exceptions to confidentiality in civil or common law, they would not include a right to disclose information about the fetus to insurers or employers without the patient's consent.

PND records are protected by the same rights to privacy as other medical records. Indeed, the duty of confidentiality is particularly important here, given the private nature of the decision to have PND and the fact that information about the fetus and eventual child is involved, making consent to disclosure by the individual in question impossible. The records must therefore be protected from unauthorized access by third parties; we provide for this in our recommendations.

In the next chapter we briefly review the protections that now exist with regard to misuse of information about an individual's genetic make-up, but most of the concerns about the use of genetic information by employers or insurers relate to testing of individuals *post*-natally. This is an important issue but one that is outside the mandate of the Commission.

Liability

Physicians have a responsibility to inform pregnant women about their options with respect to managing the pregnancy. Offering at-risk women and couples the option of PND is considered a standard of care by the SOGC, the CCMG, and the American College of Obstetricians and Gynecologists. This has important implications for physicians. If a physician fails to inform an at-risk couple of the availability of PND and the woman subsequently delivers a child affected by a serious disorder that would have been detected by PND, that physician could be liable for damages in a civil suit for failure to inform them. In the United States, for example, physicians have been sued for failure to offer prenatal testing based on risks such as the woman's age, ethnicity, the

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previous birth of an affected child, or exposure to teratogens such as rubella.

Whether the behaviour of a medical professional constitutes a fault, which can lead to a charge of negligence, or merely an error, which does not, will depend on how the act or omission measures up to the standards of the profession. According to the standards of medical geneticists, a genetics counsellor has a duty to explain the magnitude of a risk and the burden of the disorder, in a way that the woman or couple can understand, and to attempt to ensure that those being counselled do in fact understand the information provided (whether the person being counselled does comprehend is of course impossible to guarantee). If counsellors fail to inform patients adequately regarding the option of PND — or fail to provide preconception counselling if that is indicated — they can be sued for damages or injury. The purpose of such court actions is to get compensation — that is, to restore the patient, as far as possible, to the position they would have been in had the practitioner not acted negligently.

In the context of PND, the claim of negligence arises where there is misinformation or failure to supply information to a woman or couple who subsequently have an affected child that they would otherwise not have conceived or would have aborted. The claim for damages may be made by the parents or made on behalf of the child. As we will see, the courts have responded very differently to these two types of claims.

Wrongful Birth

Claims of damages by the parents have been referred to as involving "wrongful birth." The initial defence against such a claim was that the health care worker did not cause the damage; it was caused by a gene or, in some cases, a teratogen. However, negligence in establishing or imparting risk information has come to be seen by the courts as depriving women or couples of their right to prevent the conception or birth of a child with a disability, and failure to provide information has come to be seen as a direct cause of the injury.

There have been no reported cases in Canada of a wrongful birth claim arising from PND malpractice. Two Quebec cases arising from malpractice in sterilization are relevant to this issue, however. In *Cataford v. Moreau* (1978), a tubal ligation was done negligently, and a healthy eleventh child was born to the woman who had sought sterilization through tubal ligation. The parents were awarded medical and hospital expenses. However, the award with respect to the cost of rearing the child was modest, not only because of existing state support by way of family allowance but also because the court considered the birth of a child a benefit, if not a blessing.

In *Engstrom v. Courteau* (1986), a man with hereditary cataracts had a vasectomy after his first child was born with the disorder. No post-operative sperm count was done, and his second wife subsequently became

pregnant and gave birth to another child with the disorder. The Quebec Superior Court allowed a claim for wrongful birth.

In the few PND-related wrongful birth suits in the United States, awards have generally been intended to cover the cost of raising an affected child over and above what would have been the cost of raising a child without the disorder. In other words, having a child per se is not considered a damage, even though the parents might not have had a child had they known the risk. The period of compensation may also extend beyond the age of majority, since parents have a moral and, in some jurisdictions, a legal obligation to support a dependent child beyond the age of majority. In some cases, awards were also made for the mental suffering of the parents.

Wrongful Life

Cases in which the child is the plaintiff in a suit brought by its parents on its behalf have been termed "wrongful life" claims. In general, the courts in both Canada and the United States have resisted making awards for wrongful life. For example, in the two Quebec cases mentioned above, the Quebec Superior Court rejected wrongful life claims on the grounds that there is no legal right not to be born; thus, having been born cannot be claimed as damage by a child. Among the reasons given for not allowing wrongful life claims are the following:

- Whereas parents have a right to control their reproduction, a child has no independent right not to be born. To accept such a right would imply that the physician was under a legal obligation to terminate the fetus's life (regardless of the parent's wishes).
- To accept the child's claim that it would be better off not to have been born is contrary to public policy, since it would devalue the life of an existing child and would thus be a violation of the sanctity of human life.
- Had the negligent action not taken place (that is, had the parents been warned), the child would not exist in order to sue. Since the aim of compensation is to restore the plaintiff (as far as possible) to the position they would have been in had the negligent action not occurred, "compensating" the child would seem to require returning it to a state of non-existence.

To summarize these two topics, wrongful birth suits brought by parents for reproductive risk malpractice are now widely accepted in U.S. jurisdictions. It is likely that such a suit would be allowed in Canada where avoidance of the risk could have been achieved by not conceiving the child or by aborting the fetus after PND. It is likely, however, that a wrongful life suit would be rejected in Canada.

As we also discuss in Chapter 30, "Judicial Intervention," the Commission is of the view that it would be wrong to permit wrongful life suits to be brought against women who bear a child affected by a disorder. We believe also that such suits would not be successful in Canadian courts. The Commission does not believe, therefore, that new legislation is needed to change the way Canadian courts are handling such cases.

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Disabilities

If a severe disorder is identified prenatally, many women and couples decide to terminate the pregnancy. As we have seen, this has given rise to concerns that the current practice of PND is antithetical to the interests of people with disabilities and contributes to their marginalization in society. Some critics have also argued that PND is being used as a means of reducing the incidence of disabilities so as to reduce the "burden" on society of providing supports for people with disabilities. These concerns must be taken seriously and evaluated honestly. Among the questions on which Commissioners needed information were the following:

- What is the actual impact of PND on the frequency of disabling disorders in Canadian society? Is PND being done in order to reduce the incidence of such disorders in the population?
- How do individual women and couples, practitioners, and society deal with the question of the severity of a disability as it relates to PND?
- How do social attitudes and the availability of supportive programs for people with disabilities and parents of children with disabilities affect the decisions made by women and couples about PND and about terminating a pregnancy?

The Impact of Prenatal Diagnosis on Frequency of Disorders

There are two reasons why PND cannot eliminate or substantially reduce the overall incidence of genetic disorders and disabling conditions in the population.

First, the majority of congenital anomalies and genetic disorders cannot be detected by PND, nor is it possible to identify the majority of people at higher risk for these disorders and offer them diagnostic testing. Even for disorders for which population screening is offered in some parts of the country (for example, MSAFP testing for neural tube defects; carrier

screening for thalassaemia), and even though the frequency of these particular disorders is reduced, these conditions account for only a very small proportion of all disorders. Furthermore, although the frequency of individuals with these disorders is reduced in the population, the frequency of the underlying genes is not altered.

Second, most disabilities are not genetic or congenital in origin. Most disabilities result from other factors, such as accidents, low birth weight, prematurity, viral or bacterial diseases, birth traumas, acts of violence, and aging. This means that using PND to test for genetic disorders may influence the frequency of particular categories of disorders, but it cannot be expected to and will never substantially decrease the overall incidence of disability in the population, because categories of disability affected by congenital anomalies account for such a small proportion of all disabilities.

PND is not designed to have a substantial impact on the incidence of disabilities in the population. Rather, it is designed to give those at higher risk of having an affected fetus options in dealing with their particular risk and to give them the same chance as other Canadians of having a healthy family.

The Effects and Severity of Disabilities

Prenatal diagnosis should be provided only to identify serious disorders. Some people are concerned that society's perception of what constitutes a serious disorder will change and that PND will, over time, lead to greater intolerance of even minor anomalies. It is important, therefore, to say something about what constitutes a "serious" disorder. A disorder can be serious because of the suffering it causes for the child and/or because of its emotional, physical, and financial effects on the parents and family. These are related but vary from one disorder to another.

Tay-Sachs disease, for example, is a particularly severe disorder in terms of the suffering it causes for the child; affected children have short and painful lives. Down syndrome can be burdensome for parents; though such children often lead long and happy lives, they may require constant care. If congenital heart disease is also present, Down syndrome can cause severe suffering for the child, but even in cases where the child's symptoms are not so serious, the child may be incapable of functioning independently.

Perceptions of the severity and impact of a disorder are, to some extent, subjective — they depend on the experiences and circumstances of the people involved. For example, a couple who has been trying for some years to have a child may view a given disorder or disability differently from a couple who did not plan the pregnancy and who already has several children. Genetics centres accept that since it is the parents who would have to care for an affected child, they are the only ones in a position to evaluate these factors.

Some disorders cause neither significant suffering to the child nor hardship for the parents — for example, webbed toes or extra digits.

Children with these minor anomalies do not suffer any ill health from them, and caring for them does not create any unusual hardship for the parents. Allowing PND and termination for such disorders would be unethical for several reasons. First, it reflects inappropriate views of disability, of the respect owed to human life, and of the nature and value of children and the parent-child relationship. It also violates the principle of appropriate use of resources, since it fulfils no real medical need.

It is important, therefore, that PND be used only to detect serious disorders. PND may incidentally reveal the existence of trivial disorders, but this is not the purpose of such procedures. It is not possible, however, to establish a definitive list of serious disorders. The severity and impact of a disorder can change over time, with changes in society and in the treatability of disorders. Moreover, we do not believe it is necessary to establish such a list; the literature and our own field survey show that couples usually do not seek PND for trivial reasons and that the likelihood of termination is related to the severity of the disorder identified. (The related question of PND to determine the sex of the fetus for non-medical reasons is discussed in Chapter 28.)

The literature and our own field survey show that couples usually do not seek PND for trivial reasons and that the likelihood of termination is related to the severity of the disorder identified.

We heard from many genetics centres that they are having difficulty getting adequate funding from provincial governments to provide testing for serious disorders; requests for funds to provide a new PND test are often turned down or are accepted only after long and difficult negotiations. Examples of tests that are not funded in some provinces include metabolite measurements or enzyme assays for patients with certain inborn errors of metabolism and DNA mutation analysis for families at risk of Tay-Sachs disease. In at least one province, funding has to be negotiated case by case for testing of fetal chromosomes after routine ultrasound has picked up a physical anomaly, even though chromosomal testing in these circumstances is recommended by nationally recognized guidelines. Some geneticists try to provide these tests anyway, seeking reimbursement from the provincial ministry after the fact, or paying for them out of research budgets. However, this can create uncertainty, delays, backlogs, and anxiety for both practitioners and couples at risk. Given these circumstances, provincial health ministries seem unlikely to provide funds for testing intended to detect trivial disorders.

We see no evidence that Canadian women are seeking PND for trivial disorders, that genetics centres are offering PND for trivial disorders, or that provincial/territorial governments are funding PND for trivial disorders. This is an important issue, however, and one about which a tolerant and inclusive society cannot afford to be complacent. We believe, therefore, that this area of medical activity should be monitored and

reported on, and that there should be more opportunities for public input on decisions about which PND tests should be provided. Greater public awareness is the best bulwark against the inappropriate use of PND for trivial disorders. Our recommendations later in this chapter are intended to establish such a system of public monitoring and debate.

> We see no evidence that Canadian women are seeking PND for trivial disorders, that genetics centres are offering PND for trivial disorders, or that provincial/territorial governments are funding PND for trivial disorders.

Public Policy and Social Attitudes Toward Disabilities

Support Programs for People with Disabilities: A frequent concern expressed at our hearings by people with disabilities was that providing resources for PND may divert money from programs providing support to people with disabilities and parents caring for children with disabilities.

We firmly endorse the importance of adequate social support for parents bringing up a child with a disability, both as a matter of justice for people with disabilities and as a matter of informed choice for the parents. Adequate support is essential if the decision to continue a pregnancy and have a child with a disability is to be a viable and socially accepted option. Moreover, recent medical advances in the treatment of children with disabilities have increased the need for social support. The deinstitutionalization of people with disabilities and the fact that people with disabilities are living longer often mean that parents (usually the mother) must care for a child well into old age. The economic and social costs of this can be substantial.

> We firmly endorse the importance of adequate social support for parents bringing up a child with a disability, both as a matter of justice for people with disabilities and as a matter of informed choice for the parents. Adequate support is essential if the decision to continue a pregnancy and have a child with a disability is to be a viable and socially accepted option.

We do not believe, however, that there is a trade-off between providing PND and providing support for people with disabilities. On the contrary, we believe that the two can go hand in hand.

For one thing, as noted previously, the incidence of disability in the population will be little affected by the provision of PND. Most childhood disability originates from other factors, and, as society ages, the overall proportion of people with disabilities is increasing. Statistics Canada figures for 1991 indicate that almost 16 percent of all Canadians reported some kind of disability, up from 13 percent in 1986.

It does not seem likely, therefore, that funding for PND will affect the funds available for social support for people with disabilities. Indeed, attitudes toward people with disabilities are changing as society becomes more informed about their needs and more aware of how constitutional and human rights protections must be reflected in public institutions and policies. The growing public profile of this issue is being reflected in increased attention to the needs of people with disabilities by all levels of government. Thus, concerns expressed about PND need to be placed in context of positive changes in Canadian policies and institutions with respect to disability and the participation of people with disabilities in all aspects of society.

The question of how best for society to provide support for people with disabilities is beyond our mandate. But we affirm our support for social policy and public education initiatives intended to provide adequate support for people with disabilities and to promote their equal treatment, acceptance, and participation in Canadian society.

Attitudes Toward People with Disabilities: Historically, Canadians with disabilities have faced significant prejudice and hostility, and society is still capable of such attitudes. Indeed, the Commission heard from some groups representing people with disabilities that as much suffering is caused by attitudes toward disability as results from the disability itself. Prejudice or hostility toward people with disabilities is unacceptable; the question is whether the existence and continuing development of PND technology promote such attitudes.

> We do not believe that there need be any conflict between the interests and needs of couples at risk and those of people with disabilities. To suggest that Canadians choose one or the other is an example of the adversarial stance that an ethic of care seeks to avoid, when in fact the aim should be to provide good care for all.

Some critics say that using PND to identify and abort affected fetuses is discrimination on the basis of disability, which in effect is prejudice against disabled persons in society. We do not accept this view. We believe it is possible to uncouple the issue of the availability of PND from issues surrounding society's attitudes toward and treatment of people with disabilities.

As explained earlier in this chapter, all couples face the possibility of having a child with a disorder or disability, even if the risk is low for most. If such a child is born, most parents feel emotionally committed to him or her. Almost all families love their children and do their best to respond to the challenges of child-rearing. But the commitment to value and nurture an existing child with a disability is not the same as the commitment to nurture a fetus where an anomaly has been detected. Lack of commitment to continue a pregnancy does not mean that commitment to an existing child or person is diminished.

Some people referred for PND are already caring for an affected child. These couples usually care deeply about their child, and many have struggled to improve social support and acceptance for people with disabilities. However, they may feel unable to cope with raising another affected child and so seek PND for future pregnancies. It is clear that these families are able to uncouple the issue of PND and possible termination of a pregnancy from their attitudes toward their existing child and toward people with disabilities in general. Many couples at risk wish to avoid having another child with severe disabilities. To assume that this desire represents hostility or prejudice toward existing children or adults with disabilities is, we believe, an oversimplification, both morally and psychologically.

Another concern we heard is that prospective parents may be given biased information about various disorders during PND counselling. Some representatives of people with disabilities worried that doctors are providing parents with stereotyped and inaccurate information about living with disability. They claim that some doctors, particularly in the referring network, are telling parents that a child with cystic fibrosis or Down syndrome leads a painful or worthless existence. Many parents feel it would be selfish to abort an affected fetus solely on grounds of hardship to themselves; as a result, they believe, there may be a tendency to exaggerate the extent to which a disorder or disability causes suffering to the child.

> To argue that the status of people with disabilities would be improved if PND were less available is misleading.

Giving parents biased information would violate the principle of autonomy. It is therefore essential that information be as objective and accurate as possible. We have already recommended that the CCMG coordinate a collaborative effort by genetics centres to develop improved educational materials on PND and the disorders it can detect, and that groups representing people with disabilities be included in that effort. The Commission recommends further that

218. As part of its collaborative effort to develop appropriate counselling materials on prenatal diagnosis, the Canadian College of Medical Geneticists conduct a rigorous review of counselling protocols and information materials to ensure that disabilities and living with a disability are represented fairly and accurately. People representing those with disabilities, people at risk, and women should be included in this process.

We must not let the availability of prenatal testing create the illusion that disabilities are avoidable — most are not. Disabilities will always be

with us, whether PND is used or not. Society must offer support to people with disabilities. But to argue that the status of people with disabilities would be improved if PND were less available is misleading. Given that most disabilities are not congenital and cannot be diagnosed prenatally, it seems likely that society's approach to people with disabilities will not stand or fall on the availability of prenatal diagnosis services or the way they are provided. In fact, evidence suggests that in countries where PND is practised, there is greater rather than less interest in the welfare of people with disabilities as a result of increased medical and social awareness of their needs and rights.[3]

We do not believe that there need be any conflict between the interests and needs of couples at risk and those of people with disabilities. To suggest that Canadians choose one or the other is an example of the adversarial stance that an ethic of care seeks to avoid, when in fact the aim should be to provide good care for all.

Termination of Pregnancy

In the great majority of cases where a serious fetal disorder is diagnosed prenatally, no treatment of the fetus is available. The choice is usually between terminating the pregnancy or preparing for the birth of a child with a disorder or disability. As we have seen, most women in these circumstances decide to terminate the pregnancy.

This has raised the concern that the availability of PND might encourage the indiscriminate use of abortion. To assess this concern, we examined the likelihood of termination after PND, the way higher-risk families approach reproductive decisions in the absence of PND, and the views of Canadians about the termination of pregnancy in the context of PND.

Likelihood of Terminations

When a serious fetal disorder is detected by PND, approximately 80 percent of women decide to terminate the pregnancy. About 20 percent of women decide to carry on with the pregnancy, which suggests that the decision to terminate a pregnancy after a disorder is diagnosed is not taken lightly. Indeed, the decision to terminate is complicated, involving many factors. In particular, the severity of the disorder has a profound effect on the likelihood of a decision to terminate. As Table 26.12 indicates, the proportion of women in Canada who elected to terminate a pregnancy after a fetal disorder was detected varied greatly with the nature of the disorder.

The disorders in the last two groups listed have less serious or less predictable effects than disorders in the other two categories. In the case of Turner syndrome, the most frequent problems are short stature and infertility, but cardiovascular and other physical anomalies are also common.

Table 26.12 Pregnancy Termination After Diagnosis of Fetal Disorder

Type of disorder	% of women who terminated pregnancy
Trisomies 13, 18, and 21 (Down syndrome)	83
Neural tube defects	76
Turner syndrome	70
XXY, XYY, XXX syndromes, balanced translocations, mosaics	30

Source: Adapted from Hamerton, J.L., J.A. Evans, and L. Stranc. "Prenatal Diagnosis in Canada — 1990: A Review of Genetics Centres." In Research Volumes of the Royal Commission on New Reproductive Technologies, 1993.

Generally speaking, children with XXY, XYY, and XXX syndromes can be somewhat less intelligent than they otherwise would be and have certain learning and behavioural problems, but many such children exhibit only mild signs. The fact that fewer women choose to terminate a pregnancy when one of these disorders is detected shows that women and couples consider carefully the severity and burden of the disorder before making a decision to continue or terminate a pregnancy.

In short, PND is not inexorably linked to abortion when disorders are discovered. Information gained through PND may be used by one couple in a decision to terminate, while another couple may use the same information to prepare for the birth of a child with a disorder. It is evident that the decisions of women and couples are nuanced and situation-specific.

Coping with Higher Genetic Risk in the Absence of Prenatal Diagnosis

When discussing the relationship between PND and abortion, most people focus on the difficult decision women and couples face when a fetal disorder has been diagnosed. But this is just half the story; couples at higher risk also face a difficult decision when PND is not available. The desire to have children is deeply rooted, and most Canadians want to have children. Where PND is not available, a couple's knowledge that they are at higher risk for congenital or genetic disorders poses a serious threat to this goal.

Couples who want families are willing to take the usual risks that accompany reproduction. Studies have shown that when a couple does not

realize that a congenital disorder is genetic in origin, they tend to have the same number of children as others in their community; as a result, they may have several affected children. When they know that the disorder has a genetic basis, unless PND with the option of termination is available, couples give up their plans to have children (or more children) rather than risk having an affected child. This is often deeply distressing to the couple, particularly if it is their first and only child who is affected.

When they know that the disorder has a genetic basis, unless PND with the option of termination is available, couples give up their plans to have children (or more children) rather than risk having an affected child. This is often deeply distressing to the couple, particularly if it is their first and only child who is affected.

When PND is made available to those who want it, higher-risk couples who had stopped having children often have repeated pregnancies at short intervals in order to have healthy children and a family of the desired size. Their family size increases to become similar to that of couples who are not at genetic risk.[4] For example, before PND was available for thalassaemia, couples with one affected child who knew about the one in four recurrence risk tried not to conceive. They avoided having further affected children but were unable to reach their goal of having a healthy family. In other words, PND allows high-risk couples to manage their risk and have the same chance as others to have healthy children.

Public Attitudes

Canadians' attitudes toward abortion are complex. Most support a woman's right to choose, but individual opinions vary widely about the personal circumstances in which abortion is appropriate. Most Canadians recognize that the diagnosis of a severe congenital anomaly in a wanted pregnancy is tragic and that it is with great regret that a woman or couple in these circumstances chooses to terminate the pregnancy.

Most Canadians do not feel they can tell others what they should do in these circumstances. A substantial majority (about three-quarters) say that if the fetus has a severe anomaly, the parents should have the option to terminate the pregnancy. Canadians recognize that termination in this situation is not a benefit but rather the opposite; nevertheless, they believe the option should be available.

Public support for having this option available to couples at risk is therefore a case of public respect for the extremely difficult situation of these couples — a situation in which all the options are difficult and none of the choices is easy. Commissioners believe that couples in this situation merit society's understanding and support, and we affirm our support for the availability of PND services to identify severe disorders and for the

freedom of women and couples to choose among the options based on the information PND provides.

Access

Representations to the Commission on behalf of women's groups, people with disabilities, women of colour and members of visible minorities, professional associations, and others were eloquent about the need for women in Canada to have equal access to safe, high-quality PND services. As we have seen, however, there are substantial and worrisome variations in PND availability and use across the country. In this section, we examine some sources of variation in PND use: distance from a genetics centre; variations in referral patterns; and socioeconomic status.

Distance from a Centre

Utilization rates generally decline with distance from a genetics centre. In most provinces, genetics centres are located in one or two of the largest cities. Given the infrastructure and the skilled and experienced personnel needed, this makes sense from the perspective of functional requirements and appropriate use of resources. Like other medical technologies that depend on expensive infrastructure and skilled personnel, genetics centres should serve a catchment area of appropriate population size.

The further a woman lives from a centre, however, the less likely she is to use these services. The geographical distribution of referring obstetricians and gynaecologists also has an effect. As we have seen, they are more likely to make referrals than general practitioners, and, since they are concentrated in urban centres, a woman living in an urban centre is more likely to be referred. Women living in rural or northern communities who want prenatal diagnostic services may have to travel to an urban location to get a referral, then travel to yet another location for the actual PND service. This is a difficult, expensive, and time-consuming process. Women in remote communities may not in fact see a referring physician in time to get a referral for prenatal testing. Other women may be offered a referral but be unable to afford the time or money required to travel to the centre.

The problem is exacerbated in provinces with no genetics centre (Prince Edward Island, New Brunswick, the Northwest Territories, and the Yukon). Women from Prince Edward Island and New Brunswick are referred to Halifax for testing; women from the Northwest Territories are usually referred to Edmonton or Winnipeg, depending on which is closer (although some amniocenteses are performed in Yellowknife and the fluids sent to Edmonton for analysis); and women from the Yukon are tested in Vancouver.

Table 26.13. Geographical Distribution of Genetics Centres in Canada

Province	Population	Number of centres	Population/ centre
Nfld.	572 600 (2.2%)	1 (4.5%)	572 600
P.E.I.	130 500 (0.5%)	0 (—)	—
N.S.	890 200 (3.4%)	1 (4.5%)	890 200
N.B.	722 900 (2.7%)	0 (—)	—
Que.	6 749 400 (25.5%)	3 (13.7%)	2 249 800
Ont.	9 698 500 (36.6%)	10 (45.5%)	969 850
Man.	1 088 000 (4.1%)	1 (4.5%)	1 088 000
Sask.	1 000 400 (3.8%)	2 (9.1%)	500 200
Alta.	2 459 200 (9.3%)	2 (9.1%)	1 229 600
B.C.	3 120 600 (11.8%)	2 (9.1%)	1 560 300
Yukon/N.W.T.	79 800 (0.3%)	0 (—)	—
Canada	26 512 100 (100%)	22 (100%)	1 205 100

Source: Adapted from Sova, G. *1991 Corpus Almanac and Canadian Sourcebook*, 26th ed. Don Mills: Southam Business Information and Communications Group, 1990; and Hamerton, J.L., J.A. Evans, and L. Stranc. "Prenatal Diagnosis in Canada — 1990: A Review of Genetics Centres." In Research Volumes of the Royal Commission on New Reproductive Technologies, 1993.

Needless to say, having to travel out of province is difficult for many women. Some people have called for the establishment of more genetics centres to reduce these geographic inequalities. The existing distribution of centres generally makes sense, however, in terms of the size of the population each serves. As Table 26.13 shows, the average genetics centre in Canada serves a population of 1.2 million people, or roughly 4.5 percent of the total Canadian population. In this context, it would not be sensible or efficient to establish a genetics centre, for example, to serve the 79 800 people in the Yukon and Northwest Territories or the 130 500 people in Prince Edward Island.

Indeed, if we look at the distribution of genetics centres by region, rather than province, each region of the country appears to have its fair share of centres. For example, Atlantic Canada has 2 of the 22 centres across Canada (9.1 percent), to serve 2.3 million people (8.7 percent of the Canadian population); the Prairies have 5 of the 22 centres (22.7 percent), to serve 4.5 million people (17.2 percent of the population).

The solution to the problem of distance to genetics centres is not necessarily to build more centres. Rather, it is to improve the extent to which centres can reach out to remote areas — for example, through satellite clinics — and to improve the ability of women in remote communities to gain access to health care professionals who can provide referrals and to afford travel costs. Although we recognize the constraints facing provincial/territorial ministries of health, we believe that the importance of these choices — which may have lifelong consequences for the families involved — is such that access to services should remain a high priority in resource allocation decisions. The Commission therefore recommends that

219. All pregnant women in Canada should have reasonable access to prenatal testing. Where this is difficult (as in rural and northern areas), genetics centres should establish outreach programs so that at least pretest counselling services can be available to all women closer to home. Funds for this purpose should be provided by provincial/territorial ministries of health. Further, provincial/territorial ministries of health should provide subsidies for those who want testing but are unable to afford the cost of travel from remote areas to a genetics centre.

220. In areas where obstetricians or family physicians are not available to provide referrals, there should be a designated individual in the public health system, such as a public health nurse, who is knowledgeable about prenatal diagnosis, so that women contemplating testing can obtain information close to home and, if they wish, be referred to the appropriate centre.

and that

> **221. Interprovincial barriers to access to prenatal diagnosis services should be removed to allow women to receive prenatal testing at the most appropriate centre dealing with their particular risk. Samples should be taken locally and shipped for analysis to the appropriate centre, even if it is in another province. Funding in these cases should be provided by the ministry of health of the woman's province or territory of residence to the local centre to cover costs of taking a history and sample and shipping it to the centre doing the analysis, as well as for the analysis.**

Reasonable access also requires that women have the option of terminating or not terminating the pregnancy after PND, and that when termination is the choice, the procedure be accessible and covered in each province/territory as an insured health service.

Variations in Referral Patterns

As we have seen, there are wide variations in referral rates; for maternal age, for example, the rate ranges from 64.5 percent of eligible women in Quebec to 15 percent in Newfoundland — a more than fourfold difference. Similar variations exist for overall referral rates.

Commission surveys of people across Canada show that regional variations in attitudes toward PND cannot account for this fourfold difference in use. On the contrary, regional variations in people's willingness to use PND themselves were quite small (Table 26.14). Nor were there any regional variations in people's awareness of PND or their willingness to allow its availability for others.

As discussed earlier in this chapter, the more significant reason for these variations is that physicians in some parts of the country are less likely to offer referrals, whether because of lack of knowledge of the tests or their personal views about the appropriateness of using PND for certain disorders. The Commission's study uncovered extremely wide attitude disparities among physicians in different provinces. Disparities occurred in terms of when to use various tests, how grave certain conditions are considered to be, how directive physicians should be, and how readily they accept selective abortion. As a result, the study showed, the experiences of women who want prenatal testing depend on where they live; there seem to be provincial "cultures" that influence medical attitudes — and no doubt behaviours — and therefore the experience of pregnant women.

Table 26.14. Willingness of Canadians to Use Prenatal Diagnosis

Q: If you or your partner were expecting a child, would you use prenatal diagnosis of the fetus?

	Canada %	Maritimes %	Quebec %	Ontario %	Prairies %	B.C. %
Yes	69	70	75	65	67	66
Depends	7	7	5	7	8	10
Don't know	2	1	2	3	3	1
No	22	22	18	25	22	23

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

The wide divergence in attitudes among referring physicians is troubling in a country with a public health care system that has access as one of its basic principles. The Commission recommends that

222. Provincial colleges of physicians and surgeons and medical associations emphasize to their members that failure to discuss with patients the option of referral for a medically indicated prenatal diagnostic service is unethical and constitutes unacceptable medical practice. Information in this regard should be incorporated into medical school curricula and intern and residency training and examinations.

Socioeconomic Factors

People of lower socioeconomic status are not referred for and do not use genetics services as often as higher-income women and women with higher levels of education, who are over-represented among those referred to genetics centres. Centres provide services to all women referred who have an indication of higher risk, so the reasons for this must lie in the referral process. We have outlined some factors that may underlie it — for example, the attitudes of referring physicians, the cost of travel, or the

values of the individual women and couples. But it may also result from lack of awareness about what tests are available or difficulty understanding the issues raised throughout the PND process. As we have recommended, brochures and counselling should be understandable to people with varying levels of education and language skills, and these materials should be widely distributed to the public.

Overall, we found significant problems of access to PND services in Canada. Many women with legitimate medical indications for PND counselling and testing are not offered or do not have equal access to prenatal diagnostic services. The solution is not to establish new genetics centres; rather, we need new ways of encouraging practitioners outside the genetics centres to work more effectively with the centres, to offer referrals to all women who have appropriate indications, and to ensure that women who want to make use of the services have access to them.

Many women with legitimate medical indications for PND counselling and testing are not offered or do not have equal access to prenatal diagnostic services.

The Commission's Stance*

In this chapter, we have discussed several important and legitimate concerns about the use of PND and its implications for society. Having reviewed these concerns, the Commission concludes that, if provided in the proper way (with appropriate, unbiased counselling, leading to informed consent), using PND is both beneficial to individual women and couples at risk and consistent with social values regarding equality for persons with disabilities and respect for life.

It is important that, as these technologies develop in Canada, we have a structure and process to decide whether we want to apply new technologies and, if we wish to apply them, to ensure that this occurs in a regulated and accountable way.

But this is not to say that PND should be allowed to develop according to a technological imperative or without boundaries. There are vulnerable interests of individuals and of society to be protected. The PND system requires monitoring and public input to ensure that PND is used in an ethical, safe, and beneficial manner. This is a rapidly changing area of technology, and it is important that, as these technologies develop in

* See Annex for dissenting opinion.

Canada, we have a structure and process to decide whether we want to apply new technologies and, if we wish to apply them, to ensure that this occurs in a regulated and accountable way. This needs to take into account the two quite distinct parts of the system — the genetics centres and the larger medical community. Our recommendations on how to ensure this are spelled out in the next two sections.

Using Prenatal Diagnosis Technologies Appropriately

The Role of Technology Assessment

The last two decades have seen rapid development and dissemination of PND technologies. Amniocentesis, CVS, and diagnostic ultrasound are all established components of the PND system in Canada; prenatal ultrasound is offered routinely in many provinces; MSAFP is emerging as a significant screening test; and new technologies now in development include using fetal cells in pregnant women's blood for PND, preimplantation diagnosis, and others.

As with any rapidly developing technology, our concern as a society must be that we are leading rather than being led by the existence of the technology. This requires the disciplined application of technology assessment. We need to have a clear understanding of how specific PND technologies work and how they are assessed as part of the process of ensuring appropriate use of these tests by practitioners. Resources for the provision of health care are not unlimited, and any new technology should be assessed for evidence that it is beneficial in terms of outcomes.

In addition, technology assessment provides information that is important in ensuring realistic public and patient expectations about what these technologies can and cannot do, what answers they can and cannot provide. Thus, technology assessment has a valuable role in curbing society's tendency to look to "miracle medicine" as a cure-all. Unrealistic expectations can lead to undue pressure (often patient-generated) to provide unproven technologies.

As with any rapidly developing technology, our concern as a society must be that we are leading rather than being led by the existence of the technology.

Throughout this report we have emphasized the basic principle of evidence-based medicine — namely, that widespread use of medical treatments, procedures, or technologies should occur only after rigorous evaluation in clinical research trials. In this section, we examine how the technologies already in place (amniocentesis, CVS, ultrasound, and MSAFP) were assessed, as a way of identifying the lessons of this experience and developing recommendations about how this should be done in the future.

We begin with the major diagnostic tests (amniocentesis, CVS, targeted ultrasound), which are provided by the genetics centres in Canada; then we look at the major screening tests (routine ultrasound, MSAFP), which are being provided more widely; finally, we conclude with newer technologies (DNA analysis of fetal cells in a pregnant woman's blood, preimplantation diagnosis, and magnetic resonance imaging), which are at an earlier stage of development.

Diagnostic PND

Amniocentesis: Amniocentesis is currently provided in the second trimester of pregnancy, when the fetus is at 15 to 17 weeks' gestation. This is the most thoroughly studied and evaluated PND procedure. It is the most commonly used invasive PND procedure in the second trimester, with hundreds of thousands of amniocenteses having been done worldwide over the last 20 years, and it has been shown to be safe and effective. Success rates of up to 99.5 percent in obtaining a cytogenetic diagnosis have been reported in a study involving more than 7 000 cases.[5]

Life-threatening risks to the pregnant woman are almost non-existent; complications include leakage of amniotic fluid, transient vaginal spotting, and uterine contractions. Fetal injuries are rare. Fetal loss as a result of the procedure is in the order of 1 in 250. The risk of miscarriage for amniocentesis, as for other invasive prenatal tests, should be seen in light of the fact that approximately 8 percent of recognized pregnancies end in spontaneous abortion, and that the older a woman is, the more likely this is to occur, even if no testing is done.

In Canada, amniocentesis was assessed for effectiveness before being introduced widely as a service. Indeed, evaluation and standards-setting work with respect to amniocentesis, funded by the Medical Research Council of Canada and carried out by the CCMG and the genetics centres, helped set international standards in this area. The Commission found that the use of amniocentesis occurs in the context of written protocols detailing the appropriate indications for its use.

Chorionic Villus Sampling: Like amniocentesis, CVS was assessed for effectiveness before being used widely in Canada, and it is used in the context of written protocols detailing the appropriate indications for use.

The major drawback of amniocentesis is that it is performed relatively late in pregnancy. This led to research into CVS, a first-trimester procedure that allows for earlier diagnosis and decisions about the pregnancy. CVS is also more useful in detecting certain kinds of disorders, such as single-gene disorders. However, it is more difficult to interpret than amniocentesis and has slightly higher risks associated with it. For example, the need for retest with CVS is 7.5 percent, compared to 1.1 percent for amniocentesis.

Complications for the pregnant woman may include bleeding, cramping, and infection. Fetal loss rates as a result of CVS are slightly higher than those associated with amniocentesis. As yet, no study has examined whether there are any long-term effects of CVS, but some studies have been done on infants and children, and these have been generally reassuring. Recently, some concern has been raised about a possible relationship between CVS and limb damage when the test is performed very early in the pregnancy (before 10 weeks), but the available data are inconclusive, and more study is required to assess this possibility fully. Full information about this possible risk should be disclosed before consent to testing is obtained, and centres should ensure that this information is taken into account in decisions about the timing of CVS testing. The Commission recommends that

223. In view of recent reports of a possible relationship between early CVS and congenital limb deformities, data on all types of limb deformities in CVS-exposed infants be collected and analyzed to make more definitive outcome data available, and that the current state of knowledge on this risk be disclosed to all women contemplating the test.

Early Amniocentesis: Research is being done to determine whether early amniocentesis (performed before 15 weeks' gestation) could provide the benefits of CVS (early detection) without its drawbacks (more difficult to interpret and higher risks). Recent studies suggest that early amniocentesis is associated with higher rates of fetal loss and amniotic fluid leakage than second-trimester amniocentesis,[6] but the differences in risks are not statistically significant; the risks are lower than those associated with CVS.

Although the safety of early amniocentesis has yet to be established definitively in clinical trials, some researchers believe that if its safety can be shown, early amniocentesis may eliminate the need for CVS.[7] Further evaluation, by means of a large multicentre randomized control trial, is needed to compare first-trimester amniocentesis and CVS as a basis for resource allocation decisions (see research volume, *Prenatal Diagnosis: Background and Impact on Individuals*) and before any introduction into routine practice in this country. For now, Canadian guidelines indicate that amniocentesis should be performed for routine indications between 15 and 17 weeks' gestation. Facilitation of such a multicentre trial should be considered a priority by the National Reproductive Technologies Commission as well as by agencies such as the MRC.

Targeted Ultrasound: Targeted ultrasound to detect fetal anomalies is provided by highly trained personnel using specialized equipment, usually in a facility associated with a genetics centre; the procedure can take up to an hour or more. (Routine ultrasound, discussed below, is often provided by obstetricians in their own offices and takes only a few minutes.)

The evidence shows that targeted ultrasound is quite effective as a diagnostic procedure, that is, to identify whether a suspected structural anomaly or malformation is present in the fetus. For example, a recent British study suggested that over 90 percent of major structural anomalies that are lethal or severely disabling can be detected through targeted ultrasound in referred high-risk pregnancies.[8]

The available evidence has shown no specific risks or biological consequences of targeted ultrasound.[9] The question of whether there are as yet undetected long-term effects has been raised, and it would be answerable by using data on exposed individuals, then using record linkage approaches to evaluate longer-term outcomes.

Targeted ultrasound carried out in referral centres, often associated with genetics centres, is used in accordance with written protocols developed by the SOGC, spelling out the appropriate indications for its use.

In summary, the Commission concludes that the major prenatal diagnostic tests provided at specialized genetics centres in Canada have been properly assessed for safety and efficacy and are now being provided for appropriate indications in the context of written protocols.

Screening Tests

The history of the assessment and use of PND screening tests (routine ultrasound and MSAFP) has been very different from that of the major diagnostic tests. Indeed, the Commission has serious reservations about the way screening tests have been assessed and provided. The number of physicians and personnel involved is much larger than for specialized tests done at genetics centres, making it more difficult to apply quality control or assessment.

The Commission has serious reservations about the way screening tests have been assessed and provided.

Routine Ultrasound: Obstetrical ultrasound is now offered as a routine part of prenatal care — at least 80 percent of all pregnant women have this procedure in much of the Western world. It is offered to determine the gestational age of the fetus, to identify multiple pregnancies, and to look for placental abnormalities. As well, an increasing number of physicians use ultrasound to identify women who are at higher risk of having a fetus with a congenital disorder. However, the effectiveness of routine ultrasound to identify such fetuses is not at all clear. It varies greatly with the timing of

the routine examination and the expertise of the ultrasonographer, with between a third and three-quarters of major malformations being detected.[10] Many structural anomalies cannot be detected by routine ultrasound. Research conducted for the Commission suggests that, in some cases, routine ultrasound is being used inappropriately to reassure women that they are not carrying a fetus with Down syndrome. The value of routine ultrasound for this purpose is uncertain, and women might be given a false sense of security by apparently normal findings.

Even if routine ultrasound is not useful as a PND screening test, it might be appropriate for other reasons. However, the effectiveness of routine ultrasound for these other purposes is also unclear. Although there is no question that routine ultrasound can help to date pregnancies and detect multiple pregnancies, we do not know how much of a difference this actually makes in terms of birth outcomes.[11]

> Obstetrical ultrasound scanning has grown exponentially since its introduction and, as various authors have noted, the procedure spread before it was even evaluated ... Enthusiasm preceded any evidence of its effectiveness or safety. Although it is now a key component of prenatal care, there do not appear to be any explicit empirical standards that would warrant its routine use. Opinions differ on the number of ultrasound scans that should ideally be performed during pregnancy, and indeed on whether there is any valid clinical reason for doing them at all. Consensus conferences, it should be noted, have produced a variety of opinions. In France ... the consensus reached was two ultrasound scans per pregnancy. The U.S. National Institutes of Health, on the other hand, indicated in 1984 that there is no evidence justifying a firm and final opinion on this point.
>
> *M. Renaud et al., "Canadian Physicians and Prenatal Diagnosis: Prudence and Ambivalence," in Research Volumes of the Commission, 1993.*

Despite the lack of evidence regarding effectiveness, there has been a massive increase in the number and cost of ultrasounds performed in Canada during the last 10 years (Table 26.15). The bulk of this increase (75 percent) is attributable to an increase in the per capita use of routine ultrasound, rather than an increase in the number of pregnancies (12 percent). It is essential to determine whether routine ultrasound is in fact effective in managing pregnancies more safely and effectively, because this has important implications for resource allocation and for medical practice.

If routine ultrasound does not help manage pregnancies more safely and effectively, the current number of tests is clearly too high. If routine ultrasound does achieve this purpose, however, the distribution of tests is seriously skewed (even if the overall number of tests is about right), because between 15 percent and 20 percent of women never receive screening.

Regional variations in the use of routine ultrasound account in part for this skewed distribution. According to the Commission's survey of referring physicians, 40 percent of physicians in Manitoba and Alberta do not consider it essential to order an ultrasound scan during pregnancy; in Quebec, only 4 percent of physicians share this opinion. In fact, Quebec physicians generally order two ultrasound scans per pregnancy, and it is only in Quebec that the great majority of physicians (89 percent, compared to 60 percent elsewhere in Canada) find it acceptable to use ultrasound to screen for anomalies. These variations in physician attitudes are reflected in provincial utilization rates — the percentage of all pregnant women having an ultrasound exam ranges from 97 percent in Quebec to 62 percent in Manitoba. These regional variations stem in part from the lack of formal guidelines regarding when it is appropriate for general practitioners and obstetricians to provide or to refer for routine ultrasound.

Table 26.15. Number of Obstetrical Ultrasound Procedures*

Year	Number of procedures	Costs ($)
1982-83	358 722	21 174 894
1984-85	490 783	31 871 971
1986-87	636 515	43 748 019
1988-89	813 347	66 618 851
1990-91	998 492	74 649 481

* Number of ultrasound procedures associated with obstetrics and gynaecology and paid for under the provincial medical care insurance plans for Quebec, Ontario, Manitoba, Saskatchewan, Alberta, and British Columbia. Figures for the Atlantic provinces are not included, as ultrasound there is paid for under provincial hospital insurance plans, not medical insurance plans.

Source: Adapted from Health and Welfare Canada data, 1991.

Perhaps because of its non-invasive nature, the wide dissemination and use of routine ultrasound followed a very different pattern from introduction of the major diagnostic tests discussed previously. Unlike amniocentesis and CVS, the dissemination of routine ultrasound came well before any technology assessment of it and was not accompanied by formal guidelines regarding the appropriate indications for its use. Only in Manitoba do physicians providing ultrasounds have to be licensed and have a minimum of six months' training before they can meet the criteria for licensing.

It is essential to control this rapid proliferation of routine ultrasound and to determine whether the substantial funds now being devoted to it are justified. Two responses are called for. First, there is a need for further well-designed, sufficiently large studies to evaluate the clinical effects of routine prenatal ultrasound. This would be a major undertaking, since a trial powerful enough to detect clinically significant effects of routine prenatal ultrasound on perinatal morbidity and mortality might require a sample size of over 12 000. We believe, nevertheless, that a major multicentre randomized control trial would help to determine the effectiveness and value of routine ultrasound as a procedure to help manage normal pregnancies. We therefore conclude that the National Research Technologies Commission should consider the pros and cons of underwriting some of the cost of such a trial. We would point out, however, that large amounts of money are already being spent to provide these services. If provincial/territorial ministries of health were to collaborate in developing the trial, and if they were to agree to structure their funding for routine ultrasound in such a way as to ensure that all service provision became part of the trial — for example, funding could be contingent upon appropriate data collection — the trial could be conducted for only the additional cost of data collection and analysis, instead of as an add-on to current service provision. Similarly, collaborative efforts at the international level could ensure that sufficient data on which to base judgements about effectiveness were collected quickly and at only a small additional cost relative to the current cost of providing services.

> The dissemination of routine ultrasound came well before any technology assessment of it and was not accompanied by formal guidelines regarding the appropriate indications for its use.

A second important aspect is that a program framework must be developed that will serve to contain both utilization rates and total costs for routine ultrasound. A Commission study of ultrasound use rates in British Columbia and in Ontario during the last 10 years showed clearly that the British Columbia approach, in which ultrasound can be provided only by licensed (hospital) facilities and is paid for out of hospital budgets, is far more effective in containing use and costs than is the Ontario system, which does not restrict practice location. This means that Ontario physicians with ultrasound equipment in their offices can bill for prenatal ultrasounds that they decide are needed and that they conduct in their own offices.

In the nine years preceeding 1991, expenditures for prenatal ultrasound increased twofold in British Columbia but fourfold in Ontario. While the number of hospital-based ultrasounds increased by only 16 percent in Ontario between 1983-84 and 1989-90, the number of non-hospital ultrasounds increased by about 300 percent. Thus, provincial health policy has implications for both the use and the costs of routine

ultrasound. We believe that the British Columbia approach not only controls costs but makes possible quality control and the establishment of standards of training for personnel. It also eliminates the potential for self-referrals, which have been shown in many studies of medical practice to lead to unnecessary use. The Commission recommends that

224. Provincial/territorial ministries of health review the program framework within which routine ultrasound scanning during pregnancy is offered. The Commission concludes that requiring facilities that offer ultrasound to be licensed would promote women's best interests and best medical practice.

and that

225. Provincial/territorial ministries of health eliminate potential conflicts of interest by ensuring that those ordering routine obstetrical ultrasounds do not usually provide them.

Also, as discussed in greater depth in Chapter 28, ultrasound should not be used to identify the sex of the fetus, except for medically indicated reasons, before the third trimester. Commission research shows that it is highly unlikely that anyone would resort to abortion of a fetus of unwanted sex at this stage in pregnancy. The Commission recommends that

226. 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 the purpose of sex identification (except where medically indicated), and that they do not offer information on fetal sex except for medical reasons and upon request before the third trimester of pregnancy.

MSAFP Screening: Alpha-fetoprotein is produced by the fetus; a higher than normal level of AFP in a pregnant woman's blood may indicate the presence of an abnormal fetal opening, such as a neural tube defect. This has led to the development of programs to measure the concentration of AFP in pregnant women's blood. It is a safe, relatively inexpensive, and

easily performed method of screening pregnancies and identifying those at higher risk for neural tube defects.

The interpretation of test values is complex — results must be adjusted for the woman's age, weight, and race and the gestational age of the fetus, as well as for risks based on family history and population frequency; each laboratory conducting these tests must therefore establish normative values based on extensive testing experience. The results of MSAFP screening tests are expressed as probabilities. Since the test cannot determine with certainty whether the fetus is unaffected or affected, women with test results outside the normal range are offered further testing (targeted ultrasound or amniocentesis) to make a definitive diagnosis. The American Society of Human Genetics has developed guidelines for population-based MSAFP screening, which have been affirmed by the CCMG.

MSAFP screening is not a conclusive test. Several factors other than fetal anomaly may cause increased concentrations of AFP. Moreover, not every neural tube defect results in abnormally elevated MSAFP. The level of MSAFP may be above average but still within the "normal" range. In fact, deciding on the upper limit of "normal" MSAFP levels is very difficult. If the limit is set high, then some neural tube defects will be missed, with false-negative test results; if the limit is set low, resulting in false-positive test results, unnecessary amniocenteses will be performed. The cut-off values, therefore, are a matter of judgement in trying to achieve an optimal ratio.

In terms of safety, there have been no reports of complications arising from taking blood samples for purposes of MSAFP screening in the Manitoba program, although the further testing by amniocentesis entails the usual risks of that procedure. In Canada, MSAFP screening is offered as a province-wide program only in Manitoba (although the province of Ontario implemented a program, which includes MSAFP screening, offered to all pregnant women). The Manitoba program has proven effective in detecting neural tube defects — there has been a 50 percent decline in the incidence of liveborn infants with neural tube defects since the program was introduced in 1985. In 1989, about 60 percent of pregnant women in Manitoba were screened.[12] The results are comparable to those of similar programs in other countries.

There are some serious problems with counselling and informed consent in Manitoba's MSAFP program, discussed earlier in this chapter. In terms of sample analysis and follow-up, however, we believe that MSAFP screening is working effectively and being used appropriately in Manitoba's program. Written information is available for patients and physicians, the program has experienced laboratory personnel, and clear written guidelines are in place regarding how abnormal results should be followed up and by whom.

The same cannot be said with respect to the growing use of MSAFP screening in other provinces, which is marked by an absence of defined program guidelines and inconsistency in the availability of follow-up

counselling. In Canada in 1989, 50 180 women were screened in eight provinces; somewhat fewer than 10 000 of these tests were done in Manitoba. Of the 37 825 MSAFP tests done in Ontario, 10 000 were done through private laboratories. British Columbia also had substantial numbers tested, but British Columbia does not have an established provincial program, and Ontario established its program only recently.

This proliferation of MSAFP testing outside established programs is worrisome. Our research suggests that the indications for which MSAFP testing is offered vary dramatically across the country. In some locations, MSAFP is being offered routinely by physicians; in other locations, it may be offered routinely or only to those at higher risk, depending on the physician.

The nature and quality of follow-up counselling also vary. In locations where a genetics centre analyzes the MSAFP samples, the centre also does follow-up counselling. But in other cases, particularly where private laboratories analyze the samples, counselling is left to the general practitioner or obstetrician, who may not have the knowledge or experience to provide appropriate counselling. As with routine ultrasound, these variations reflect the lack of clear guidelines and standards for providing MSAFP screening and counselling.

The Commission believes that MSAFP should be used only as a routinely offered screening test where there is a program, funded by government, that includes well-designed information for women, education of physicians about the program, and the necessary facilities and resources to ensure accurate interpretation and follow-up, including counselling, when the results are abnormal.

Given the problems associated with the proliferation of MSAFP, the Commission believes that MSAFP should be used only as a routinely offered screening test where there is a program, funded by government, that includes well-designed information for women, education of physicians about the program, and the necessary facilities and resources to ensure accurate interpretation and follow-up, including counselling, when the results are abnormal. Furthermore, given recent information emerging about the potential benefits of increased levels of folic acid in the diet of pregnant women in reducing the risk of neural tube defects, decisions about whether and how to extend MSAFP testing more widely should take into account how new knowledge about the effectiveness of this or other preventive strategies will influence the demand or need for MSAFP testing.

The decision about whether to offer MSAFP on a population basis is complex. We are not in a position to recommend what provinces should be doing in this regard, particularly as the technology is changing rapidly. This is one of the questions on which the Prenatal Diagnosis and Genetics Sub-Committee of the National Reproductive Technologies Commission may want to conduct assessments and make recommendations. We do believe, however, that if MSAFP is to be offered routinely, it must be in the context

of a properly designed program within the public health care system. The Commission recommends that

227. MSAFP screening be offered on a population basis only within the confines of a program that adheres to the guidelines established by the American Society of Human Genetics and affirmed by the Canadian College of Medical Geneticists; that such programs be offered on the basis of informed choice and have the necessary laboratory, counselling, and prenatal diagnosis resources in place; and that such programs be affiliated with a licensed genetics centre.

228. Where the resources to develop such programs and the associated counselling are not available, the test be offered by licensed genetics centres only to patients at high risk.

and that

229. Provincial/territorial ministries of health not reimburse physicians or laboratories for MSAFP screening conducted outside such programs.

Triple Testing: MSAFP was designed to look for abnormally elevated MSAFP levels. Recently, however, it has been shown that decreased levels of MSAFP are an indication of increased risk for fetal chromosomal abnormalities. The test is less accurate when used to detect Down syndrome than when used to detect neural tube defects, but accuracy rates have been improved by also measuring other biochemical markers that tend to be altered in the presence of some chromosomal disorders. These additional markers are the hormones human chorionic gonadotropin and unconjugated estriol; when the three tests are conducted together, the procedure is referred to as "triple testing." In addition to these hormonal markers, other biochemical markers may improve the efficiency of serum screening for certain obstetrical and genetic risks such as certain fetal anomalies and intrauterine growth retardation.[13]

It has been suggested that triple testing results could replace the use of advanced maternal age as the main indication for amniocentesis to detect chromosomal disorders, and that this would cost less, detect more disorders, yet require fewer amniocenteses.

While there are many potential benefits to triple testing and other tests being developed, it is vital that any maternal blood screening be offered on a population basis only within the context of a well-developed program with sufficient resources to permit the support and counselling that are essential accompaniments to informed choice. Good planning, personnel and resource identification, funding allocation, and testing through pilot programs are necessary prerequisites. In the absence of these factors — planning, resources in place for support, and counselling — population screening through testing could prove to be more harmful than beneficial.

Triple testing is one of several newer tests being developed; we discuss how such future technologies should be assessed and turn to our recommendations in the next section.

Assessing New Prenatal Diagnosis Technologies

Several prenatal diagnostic procedures either are under development or are already developed but so far in limited use (see box). We can assume that the pace of technology development is not going to lessen, because the desire for information about the fetus in higher-risk pregnancies, together with continuing scientific discovery, is likely to produce a steady stream of innovations. It is essential, therefore, to put in place the right kind of technology assessment model. In thinking about what this model should look like, we can draw certain lessons from the way PND technologies have been introduced and assessed in Canada previously.

As we have seen, the record of technology assessment in Canada is mixed. With regard to PND, we found that although the picture at the periphery has been quite different, among the genetics centres providing the major diagnostic tests there has been a high level of cooperation and discipline in the introduction of new technologies and a clear commitment that new technologies should not be made available except in the context of clinical trials until their safety and accuracy have been assessed. The assessment, introduction, and use of both amniocentesis and CVS have constituted good examples of technology assessment that give operational meaning to the broader concept of evidence-based medicine.

Canada has been a leader in the field of clinical testing of prenatal diagnostic techniques before their introduction to clinical practice:

- The first Canadian guidelines for the delivery of prenatal diagnostic services were published in 1974, as a joint effort of the Genetics Society of Canada (antedating the CCMG), the Canadian Paediatric Society, and the SOGC. This was the first attempt in the world to establish national guidelines for service delivery in this area. These guidelines were updated in 1983, 1991, and again in 1993.
- A collaborative multicentre trial of amniocentesis in 1976, supported by the MRC, demonstrated the safety and effectiveness of this

technique and helped establish international standards for amniocentesis.

- Canada recently completed the first randomized clinical trial comparing CVS with second-trimester amniocentesis. This was made possible by a voluntary agreement among all Canadian genetics centres that CVS would be available only within the context of the trial.
- A proposal for a clinical trial comparing early amniocentesis with second-trimester amniocentesis has been developed with the cooperation of centres across the country, and funding for a trial is being sought before the procedure is offered as service.

Much of the credit for these achievements rests with the CCMG. As soon as amniocentesis was first provided in Canada in the early 1970s, it was evident that guidelines, quality control, procedures for accreditation of practitioners, and accredited training programs were needed. The formation of the CCMG in 1975 was intended to ensure that such services are delivered in a safe, effective, and non-directive manner.

The track record in Canada for assessing new prenatal diagnostic technologies at the centres has thus been very good. On the other hand, if we look at how PND testing provided in the larger medical community (such as routine ultrasound and MSAFP) has been introduced and assessed, a very different picture emerges. Routine ultrasound, for example, has simply proliferated, rather than being assessed and then introduced, showing that we cannot take for granted the disciplined introduction of technologies in the PND system. The same is true of MSAFP screening, which is being used in very different ways in different provinces. Only Manitoba has evaluated population screening before making it more widely available, although Ontario has recently embarked on a provincial program.

Why have these screening tests been allowed to proliferate without proper assessment? One reason is that, because these tests are non-invasive, they are relatively easy to administer — no special expertise is required to draw a blood sample or even to perform routine ultrasound, and the procedures pose few immediate risks to the pregnant woman or the fetus. As a result, many thousands of physicians in Canada could, if they so desired, provide these tests. By contrast, fewer than 100 medical professionals work at the 22 genetics centres. Needless to say, it is much more difficult to control the introduction and dissemination of new techniques under the former conditions.

The rapid and widespread adoption of routine prenatal ultrasound suggests that the lessons learned and models developed by centres in the past with respect to invasive tests have not been applied effectively to less invasive tests. This is very worrisome, as the extent of invasiveness and

New PND Technologies

***Preimplantation diagnosis*:** Preimplantation diagnosis is an experimental form of prenatal diagnosis involving *in vitro* fertilization (see Chapter 20). Eggs are obtained from the woman, fertilized *in vitro*, and allowed to proceed through several cell divisions, after which one or more cells are removed for examination. If the chromosomal and/or genetic disorder in question is not discovered, the embryos can be placed in the uterus. This avoids the need to decide whether to terminate a pregnancy should PND reveal a genetic disease, since the diagnosis is made *before* the pregnancy is established. However, even if preimplantation diagnosis proves feasible, most couples at higher risk will likely continue to prefer prenatal diagnosis techniques such as amniocentesis, which are less invasive and more reliable. The survival rate for embryos implanted after testing by preimplantation diagnosis is around 20 percent, whereas it is over 99 percent for amniocentesis. Data on the safety and efficacy of preimplantation diagnosis are scant and continue to be collected. The available data indicate that preimplantation diagnosis is a difficult, invasive, expensive, and inefficient technique with very limited indications.

***Prenatal diagnosis from fetal cells in maternal blood*:** Small numbers of fetal cells can be found in the blood of pregnant women. Because new techniques for amplifying DNA have opened up the possibility of making a diagnosis of genetic disease from very few cells, researchers are studying using these fetal cells for PND. Whereas other PND tests on maternal blood samples rely on biochemical markers, this tests the fetal cells themselves and thus the fetal chromosomes and genes. If successful, PND from fetal cells in maternal blood could provide a non-invasive, relatively safe, and economical method of detecting chromosomal and single-gene abnormalities at an early stage of pregnancy. This approach is still experimental, and its accuracy and effectiveness are not yet known. Clinical trials are under way in the United States and France, but PND by fetal cell analysis is not considered reliable enough for diagnostic testing at this time.

***Magnetic resonance imaging* (MRI):** MRI is a way of viewing the body and its component parts. It is similar to ultrasound scanning in that it is non-invasive and capable of providing good tissue detail in normal and abnormal pregnancies. It is considered to have the potential to complement ultrasound scanning, in that an ambiguous finding could be clarified. However, MRI is very expensive and not widely available. At present, MRI technology still does not permit real-time imaging, and the equipment is not as portable as ultrasound equipment. Thus far, studies on the safety of MRI do not report any measurable adverse effects at levels used for diagnostic purposes. However, the potential biological effects on the fetus have not yet been examined sufficiently to justify recommendations about its use as a service.

***Embryoscopy*:** Embryoscopy uses an endoscope to view the embryo. It is a very new technique still under development. Few data are available on risks associated with embryoscopy, but it appears that the risks are greater than those of amniocentesis and other prenatal diagnosis procedures, particularly loss of the pregnancy resulting from infection, bleeding, or spontaneous abortion. There is also a significant risk of preterm labour and delivery. Any use of embryoscopy constitutes research.

immediate risk should not be the primary factors determining whether technology assessment occurs before a technology comes into wide use. The use of non-beneficial technologies subjects people to unnecessary procedures and furthers inappropriate medicalization. Moreover, there are substantial opportunity costs involved in providing useless or non-beneficial technologies, which contravenes the principle of appropriate use of resources. For all these reasons, the use of non-beneficial technologies is unethical. This means that all tests, whatever their invasiveness or risks, should be examined against the same stringent, results-based criteria.

Moreover, the fact that a test is non-invasive or easy to administer says nothing about the often extensive laboratory and analytic resources required to provide meaningful results or adequate counselling about the results. A non-invasive test may be easy to administer, but the knowledge required to give appropriate counselling on abnormal results is not likely to be linked to the ability to administer the test. For example, if the analysis of fetal cells in pregnant women's blood proves feasible, this could mean that blood samples are taken widely before the resources and facilities for interpretation and follow-up are in place.

> The track record in Canada for assessing new prenatal diagnostic technologies at the centres has thus been very good. On the other hand, if we look at how PND testing provided in the larger medical community (such as routine ultrasound and MSAFP) has been introduced and assessed, a very different picture emerges.

What is required, therefore, is a conscious adoption of an evidence-based approach for all current and future PND technologies. The new PND technologies being developed vary in risk and invasiveness. It is likely that some of the more invasive, risky, and expensive tests (such as preimplantation diagnosis) will receive the same thorough assessment as amniocentesis and CVS before being introduced. In this regard, when evaluating proposals regarding the use of preimplantation diagnosis, the Assisted Conception Sub-Committee of the National Research Technologies Commission may wish to consult with the Prenatal Diagnosis and Genetics Sub-Committee, since it may have additional insights, based on its experience in the area of genetic testing. Most of the new PND technologies are being assessed according to what is sometimes called the "scientific consensus" model, that is, informal exchange of information, small pilot projects, and articles published in learned journals. This may lead to clinical research trials to establish whether a procedure is safe and effective, but often it is used widely before that assessment.

The scientific consensus model has served Canada well, at least for the assessment of diagnostic PND techniques. However, it would be desirable to develop a more formal process of technology assessment, to ensure that all new prenatal tests are assessed thoroughly. Such a process is needed

particularly for those procedures offered in the wider medical community. A more formal process could also help to ensure that funding is available to conduct the large trials that are needed to produce the information on which evidence-based medicine can be practised. For example, a large multicentre trial of routine ultrasound would cost several million dollars; given that up to $100 million is spent annually in Canada on these tests, however, it is important to determine whether they should continue to be offered.

> It would be desirable to develop a more formal process of technology assessment, to ensure that all new prenatal tests are assessed thoroughly.

It is important to recognize that clinical trials that seek to estimate small risks require such very large numbers of participants that the technologies being evaluated could almost be considered to be in general use. The significant differences are that (1) the collaborating centres agree to use the same protocols in the same way and to record their data in the same way; (2) if the trial is randomized the participating women must agree to randomization (randomization for purposes of a trial is ethical when a procedure is not known to be of benefit, because people with indications receive the procedure without participating in the trial); and (3) funding for testing comes out of research budgets.

To date, the MRC has funded the clinical trials that have been done in this area. However, the MRC does not have enough money to fund expensive new trials at this time, so the burden of funding trials will increasingly fall on provincial/territorial ministries of health. That is quite appropriate, since it is provincial/territorial ministries that are responsible for funding and managing the health care system, and technology assessment is part of that responsibility. However, not all provinces/territories are able to fund their own clinical trials, and this would lead to unnecessary duplication in any case. Hence, a formal process is needed to set priorities and coordinate the funding of clinical trials in this area.

There has also been a lack of involvement of ministries of health and community representatives in policy decisions about technology use. Again, a more formal process could respond to this concern. We believe that PND technology assessment requires the input of many groups, and that the appropriate forum for this process is the National Commission that we recommend be established. The Commission recommends that

230. The National Reproductive Technologies Commission establish and chair a Prenatal Diagnosis and Genetics Sub-Committee, with membership from relevant professional bodies, provincial/territorial health ministries, Health Canada, and groups and individuals

representing the interests of patients, people with disabilities, and other key segments of the community,

(a) to develop standards and guidelines for prenatal diagnosis technology assessment based on the principle that any new technology used at centres providing prenatal diagnosis and genetics services must be thoroughly assessed before its introduction and dissemination as a service;

(b) to develop, fund (or coordinate funding from the provinces/territories), and implement a process for the regular and continuing identification and assessment of new prenatal diagnostic tests and procedures, for the purpose of determining the feasibility of use in service conditions; this should include trials of new prenatal diagnosis techniques provided not at centres but in the wider medical community;

(c) to monitor and advise on all relevant issues relating to the prospective or retrospective assessment of prenatal diagnosis technologies and their introduction and dissemination; and

(d) to ensure that all participating patients have full information on risks before they consent to take part in a clinical trial of a technology.

The assessment process we have just outlined will complement rather than compete with the technology assessment and resource allocation decision-making processes of provincial/territorial ministries of health. It is virtually impossible to prevent the proliferation of a technology once provinces/territories have agreed to fund or approve its acquisition and use (for example, by including it as an insurable service under provincial/territorial health insurance plans). Perhaps the single most important factor in preventing the inappropriate proliferation of PND technologies or procedures is the funding decisions of provincial/territorial ministries of health.

In the past, provincial/territorial ministries of health have often funded techniques before they were properly assessed, relying on the various professional colleges and medical associations to set guidelines and on the cooperation and self-discipline of individual practitioners to refrain from using them in unproven ways.

The experience with amniocentesis and CVS shows that such an approach is possible. But it is one thing to rely on the voluntary cooperation of 22 genetics centres and quite another to ensure the cooperation of more than 10 000 family/general practitioners and obstetricians. The proliferation of routine prenatal ultrasound shows that reliance on individual physicians to establish limits is inappropriate — it is not their role — and doing so may lead to rapidly increasing costs.

The decision not to fund technologies until they are properly assessed is especially important when a new technology or procedure has the capacity to be disseminated widely and used by a wide range of practitioners (for example, MSAFP screening and others that will come). Ministries of health should therefore demand and fund more rigorous technology assessment before agreeing to fund a service. This has been recognized in recent health care reforms in virtually all provinces/territories. Provincial/territorial health ministries and Health Canada have the capacity, even in times of financial restraint, to help stimulate and fund clinical trials of new technologies, and it is desirable that they do so.

Ministries of health should therefore demand and fund more rigorous technology assessment before agreeing to fund a service.

The existence of a Prenatal Diagnosis and Genetics Sub-Committee within the National Reproductive Technologies Commission would be of great benefit to provinces as they grapple more actively with issues of technology assessment in this field. First, it would fund the most urgent clinical trials, thereby supplementing provincial/territorial technology assessment processes. The PND and Genetics Sub-Committee could also work with the Conference of the Deputy Ministers of Health to identify clinical trials (and pilot studies of programs) that should be organized cooperatively and funded jointly by provinces/territories. This would reduce unnecessary duplication of trials, since the results from one province or territory are likely to be more widely applicable. For treatments that are relatively unusual, this would allow provinces/territories to work together to obtain a sufficiently large sample size for a trial to give conclusive results. For other treatments, collaboration among the provinces/territories would allow a sufficiently large sample to be assembled much more quickly than could be done by a single province or territory acting alone.

In general, the standards- and guideline-setting and data collection functions of the Prenatal Diagnosis and Genetics Sub-Committee (discussed in more detail below) would provide essential information on which provincial/territorial health ministries could base resource allocation and other decisions. The Sub-Committee would provide information about what facilities and practitioners are doing and about the quality and results of these activities, as a basis for planning and resource allocation. This

information would enable the development of appropriate standards of care and better information upon which to base decisions about new facilities and new technology acquisitions.

Without the country-wide data collection and assessment made possible by the existence of a Prenatal Diagnosis and Genetics Sub-Committee, some provinces/territories would be in a poor position to evaluate new PND technologies. Most provinces have only one or, at most, two genetics centres; without the context of comparative data from the entire country, it is difficult to assess quality and results at any individual genetics centre.

Most provinces have only one or, at most, two genetics centres; without the context of comparative data from the entire country, it is difficult to assess quality and results at any individual genetics centre.

The data collection function and recommendations of the Sub-Committee would therefore provide important benefits to provincial/territorial ministries of health in managing an increasingly complex health care system. If a province or territory chose to make decisions about resource allocation that departed somewhat from the approach elsewhere, the health ministry would at least be in a position to know the baseline of services and standards from which it is departing and why it is doing so.

In short, the technology assessment process we propose, coordinated by the Prenatal Diagnosis and Genetics Sub-Committee, and the existing provincial/territorial technology assessment process are mutually reinforcing. The technology assessment promoted and monitored by the Sub-Committee would be for naught if provinces/territories agreed to fund technologies that have not been assessed properly; conversely, the provinces/territories would be unable to make informed resource allocation decisions without the data collection made possible by the Sub-Committee.

To promote this cooperation, a formal consultation process should be established between the Prenatal Diagnosis and Genetics Sub-Committee and the provincial/territorial ministries of health, through the Conference of Deputy Ministers of Health, and any existing provincial advisory committees or equivalent mechanisms. The Commission recommends that

231. Issues of technology assessment and use be the topic of at least annual consultations between the National Reproductive Technologies Commission's Prenatal Diagnosis and Genetics Sub-Committee and the Conference of Deputy Ministers of Health and other representatives of provincial/territorial ministries of health.

An Accountable, Well-Managed System: The Genetics Centres

Canadian society is at a crossroads in terms of the management of techniques and resources applicable to PND. If common policies and clinical standards were adopted, then the various elements of PND we have examined could be made to function better to serve Canadians equitably and ethically across the country.

If this is not done, an increasingly inequitable patchwork of PND services will develop out of a series of piecemeal decisions — some taken by health care ministries under pressure from various interested groups; others taken by practitioners working in the absence of clear policy guidelines; some taken by professional organizations; and others taken by trial and error or by default. Not only would this situation be regrettable, allowing it to occur would be unethical, as it would create greater potential for harm to individuals and reduce the likelihood that safe, proven care is provided equitably and that resources are used responsibly. Given the social implications of misuse of these techniques and procedures and the vulnerable interests to be protected, there are cogent reasons for a coordinated response across the country.

We therefore present a blueprint for the further evolution of PND practices in Canada with the goal of achieving a more integrated system of services and standards across the country within boundaries established to ensure that only ethically and socially acceptable use occurs. As discussed throughout this chapter, there are two very different components to the provision of PND services in Canada: the genetics centres and the referring physicians. We begin with the reforms required in the genetics centres and the referral network before describing in more detail the role of the Prenatal Diagnosis and Genetics Sub-Committee of the National Commission.

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Our research shows that the genetics centres have, generally speaking, provided PND services safely and ethically. In large part, this has been a result of the efforts of the CCMG and the effectiveness of its guidelines regarding the accreditation of genetics centres, record keeping, the provision of non-directive counselling, the appropriate indications for testing, and training and accrediting service providers.

Participation in the CCMG accreditation process is voluntary; at present, 12 of the 22 centres providing PND have not applied for or received accreditation. The lack of accreditation does not necessarily mean lower standards, but only if all centres participate can we track what is happening in PND practices across the country and ensure that standards and quality control are maintained.

For example, CCMG guidelines state that, in the absence of any other indication, a pregnant woman's anxiety is not reason enough for PND testing; nevertheless, we found that some PND tests are being performed for this reason, including invasive tests that carry risks to the fetus and the pregnant woman. It is important to be able to identify such practices and take appropriate measures to prevent them. Similarly, although we found no evidence to support the charge that genetics centres are requiring a commitment to terminate a pregnancy as a precondition for access to testing, it is essential that decisions or policies involving such fundamental values not be left to the discretion of individual physicians.

In addition, Commission research uncovered variability in the quality and quantity of record keeping by genetics centres. For example, three centres reported that they did not routinely collect follow-up information on pregnancy outcomes after testing, and one other followed up only high-risk cases. If the continued development of prenatal services is to be monitored properly, data collection by the centres must be standardized.

In summary, the existing accreditation system, based on voluntary compliance, is inadequate in several ways. Since it is voluntary, we have no way of knowing whether appropriate guidelines are being followed consistently at all 22 genetics centres, as there is no way to require unaccredited centres to comply with the guidelines. There is no way to assess the training and expertise of counselling at all centres. We have no means of tracking the evolution of PND practice and ensuring that standards and quality control are maintained. The comprehensive data gathering necessary to support continuing technology assessment is not taking place. To remedy these flaws, we conclude that there should be mandatory licensing of genetics centres. However, before licensing, we recommend that the 12 genetics centres that are not accredited apply to the CCMG for review and prior accreditation so that the elements just enumerated can be assessed by that body, which has the experience and expertise to assess many aspects of service provision as well as the credentials of centre personnel. In addition, however, the Commission recommends that

232. All genetics centres or other facilities providing prenatal diagnosis for genetic disorders and congenital anomalies be subject to compulsory licensing by the National Reproductive Technologies Commission.

As a condition of licence, genetics centres would have to comply with appropriate guidelines, to be established by the Prenatal Diagnosis and Genetics Sub-Committee of the NRTC. These would include such aspects as the qualifications of practitioners employed at the centre, record keeping, counselling, informed consent, and a code of practice. Breaching these conditions would be grounds for loss of licence.

The licensing process we propose carries forward the existing accreditation process developed and put in place over a decade ago by the CCMG. Indeed, we believe that it would be appropriate for the NRTC to build on the existing CCMG procedures and requirements in establishing its conditions of licence. CCMG members have the knowledge and have demonstrated the operational experience required for this task and should be heavily involved, but the NRTC, through its licensing process, should assume the ultimate approval authority.

It is essential that the current voluntary accreditation process be formalized in law under the aegis of the Prenatal Diagnosis and Genetics Sub-Committee. One reason is to ensure that accreditation is mandatory rather than voluntary and thus allow effective quality control and evaluation of outcomes. But bringing the accreditation process under the umbrella of the National Commission would also serve two other important goals: it would ensure that information on PND practices in Canada is available to the public; and it would provide a mechanism for public input into the formulation and revision of the guidelines governing those practices. To date, there has been little public input into the formulation of guidelines for the provision of prenatal diagnosis and little public information available about the practices of genetics centres in Canada. We believe that the public should have the opportunity to participate in the process of formulating guidelines and the opportunity to know whether guidelines are being complied with.

Bringing the accreditation process under the umbrella of the National Commission would also serve two other important goals: it would ensure that information on PND practices in Canada is available to the public; and it would provide a mechanism for public input into the formulation and revision of the guidelines governing those practices.

Licensing Requirements for Prenatal Diagnosis Services

The Commission recommends that

233. The compulsory licensing requirements for prenatal diagnosis services apply to any

physician, centre, or other individual or facility providing prenatal diagnosis services for which the Prenatal Diagnosis and Genetics Sub-Committee of the National Reproductive Technologies Commission deems a licence necessary. In particular, we recommend that licence applicants be required to obtain prior accreditation by the Canadian College of Medical Geneticists. At this time, we recommend that the compulsory licensing requirement apply to the following prenatal diagnosis services:

(a) amniocentesis
(b) chorionic villus sampling (CVS)
(c) any other prenatal testing of pregnant women aimed at obtaining information on the health status of the fetus with regard to congenital anomalies and genetic disease, other than provincial/territorial MSAFP screening programs or other provincial/territorial programs involving testing of pregnant women's blood and provincially/territorially licensed diagnostic ultrasound programs.

The Commission recommends that

234. Providing such prenatal diagnosis services without a licence issued by the National Reproductive Technologies Commission, or without complying with the National Commission's licensing requirements, constitutes an offence subject to prosecution.

and that

235. The Prenatal Diagnosis and Genetics Sub-Committee of the National Reproductive Technologies Commission develop, with input from relevant bodies, standards and guidelines to be adopted as conditions of licence.

The Distinction Between Recognized and Experimental Prenatal Diagnosis Procedures

In addition, the Commission recommends that the following requirements be adopted as conditions of licence:

236. Only procedures of proven safety and effectiveness for diagnosing the genetic disorder or congenital anomaly in question should be offered as routine testing. Procedures whose safety or effectiveness has not yet been clearly established should be offered only in the context of clinical trials.

237. Guidelines for determining which prenatal diagnosis procedures are of sufficiently proven safety and effectiveness to be offered as services, and which procedures remain experimental in nature, requiring further research, should be established by the Prenatal Diagnosis and Genetics Sub-Committee of the National Reproductive Technologies Commission.

238. In particular, the following should be considered experimental in nature, until their safety and effectiveness are more fully established:

- **(a) chorionic villus sampling performed before 10 weeks' gestation;**
- **(b) early amniocentesis;**
- **(c) preimplantation diagnosis;**
- **(d) PND from fetal cells in the blood of pregnant women; and**
- **(e) embryoscopy.**

239. Prenatal diagnosis procedures that remain experimental in nature should be offered only in the context of research — most often as multicentre randomized clinical trials. Guidelines for carrying out such trials at licensed centres, including specific patient consent, record keeping, and other requirements and safeguards, should be established by the Prenatal Diagnosis and Genetics Sub-Committee of the National Reproductive Technologies Commission.

240. The Prenatal Diagnosis and Genetics Sub-Committee of the National Reproductive Technologies Commission should coordinate the data collection, monitoring, and research evaluation necessary to assign a given procedure to either the experimental category or the category of recognized treatment or diagnostic procedure.

Impermissible Procedures

The Commission recommends that

241. The Prenatal Diagnosis and Genetics Sub-Committee of the National Reproductive Technologies Commission have as part of its guidelines for licensing of genetics centres that no genetic alteration of a human zygote/embryo be permitted.

242. We affirm 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, and adherence to this guideline should be a condition of licence.

Patient Information, Consent, and Counselling

The Commission recommends that

243. Prenatal diagnosis services should be provided in a manner that protects the patient's privacy and safeguards patient records from unauthorized access by third parties. Standard procedures and safeguards for ensuring the privacy and confidentiality of patient and medical records should be developed by the National Reproductive Technologies Commission.

244. Standard information materials and consent forms should be developed by the Prenatal Diagnosis and Genetics Sub-Committee of the National Reproductive Technologies Commission and should be distributed to all patients contemplating the use of prenatal diagnosis services.

245. Information materials should be in accessible language and format.

246. Consent forms should fully identify the specific procedures being consented to. Patients should be given ample time to discuss and fully

comprehend consent forms, and consent forms should be signed by the patient before any procedure is initiated.

247. The decision about whether to terminate a pregnancy should remain entirely with the woman; prior willingness or unwillingness to terminate a pregnancy should never operate as a precondition for prenatal diagnosis.

248. Genetics counselling should be an integral part of prenatal diagnosis services and should be provided by counsellors with appropriate training and expertise. For this reason, among others, we recommend that prior accreditation of a facility by the Canadian College of Medical Geneticists, which is equipped to assess this, be required.

249. Materials for patients about counselling and procedures should be developed by the Prenatal Diagnosis and Genetics Sub-Committee of the National Reproductive Technologies Commission. These should be designed to ensure that patients are fully informed of the probability, nature, burden, and possible variability of the disorder for which diagnosis or treatment is being provided, and that they are helped to reach a decision that best meets their particular situation and needs.

250. Counselling prior to and following termination of pregnancy, including grief counselling, should also be available, either on site or by referral.

Reporting, Licence Renewal, and Revocation of Licences

In addition to the specific conditions of licence outlined above, the Commission recommends that

251. Prenatal diagnosis services follow record-keeping, data collection, and data-reporting requirements established by the Prenatal Diagnosis and Genetics Sub-Committee of the National Reproductive Technologies Commission.

252. Licensed prenatal diagnosis services report to the National Reproductive Technologies Commission on their activities, in a standard form, annually or in the event of any change substantially affecting the conditions of licence.

253. Prenatal diagnosis services be required to apply to the National Commission for licence renewal every five years.

and that

254. Licences to provide prenatal diagnosis services be revocable by the National Reproductive Technologies Commission at any time for breach of conditions of licence.

These measures would ensure that services provided at the core of the PND system are consistent across the country and are monitored to ensure that they are provided in a safe and ethical manner.

The services and facilities that constitute the core of the PND system may change over time. With the increasing availability of non-invasive PND techniques, the need may arise for the licensing of facilities other than genetics centres. For example, private laboratories in Ontario with no affiliation to a genetics centre are offering MSAFP screening. We have recommended that at this time MSAFP be provided on a population screening basis only in the context of provincial programs administered in collaboration with genetics centres, which can provide the necessary counselling. We do not think any private laboratories should be providing population screening tests without this, as such laboratories do not have

the counselling personnel and expertise necessary to follow up on test results.

In the future, it may become appropriate or necessary for some prenatal genetic testing to be provided by facilities unaffiliated with genetics centres. If this occurs, it is important that these facilities have the expertise and resources to provide the follow-up counselling and diagnosis required when results fall outside the normal range. Hence, the Prenatal Diagnosis and Genetics Sub-Committee should monitor the role of private laboratories and require licensing where necessary. One potential example is testing of fetal cells in maternal blood samples for genetic disease if this becomes feasible. Such testing should be available only through a licensed centre.

An Accountable, Well-Managed System: The Referral Network

Our research has documented several difficulties with the provision of prenatal diagnosis services in the larger network of physicians who see pregnant women, provide certain PND screening tests, and offer referrals to the genetics centres. These include:

- wide variations in physicians' knowledge about the availability of and appropriate indications for PND;
- failure by some physicians to offer referrals to all women who are eligible for testing;
- wide variations in the services offered to women in different provinces;
- variations in informed consent procedures for MSAFP screening and inadequate follow-up counselling;
- inappropriate use of routine ultrasound to reassure women about the absence of chromosomal disorders; and
- directive counselling and inappropriate attitudes on the part of some physicians with respect to women's reproductive autonomy and their right to choose or not to choose abortion following PND.

In short, there is a clear need for standards for clinical practice for practitioners in service settings other than genetics centres. At present, there is no mechanism to give patients some reasonable assurance of consistent standards of practice. This is a very difficult area to regulate, however, given the thousands of general/family practitioners and obstetricians who see pregnant women. Indeed, any physician can see a pregnant woman and refer her to a genetics centre; for example, an ophthalmologist could examine a pregnant woman's eyes, diagnose an X-linked disorder causing blindness, and refer her to a genetics centre.

It would not be realistic, therefore, to require that all service settings or medical professionals involved in providing PND-related services (other than those already enumerated) apply for special accreditation or licence. However, we support the provincial/territorial licensing of facilities providing routine prenatal ultrasound. In addition, to ensure some standardization in the practices of referring physicians, better forms of self-regulation are required. The relevant medical associations (such as the provincial medical associations and colleges, the Society of Obstetricians and Gynaecologists of Canada, and the College of Family Physicians of Canada) should develop and disseminate explicit written guidelines for their members with respect to the appropriate provision of PND-related services. There is also a need to ensure better knowledge of PND through physician education and training and to encourage more consistent standards of practice with respect to the use of tests and referrals. We have already made several recommendations regarding specific aspects of these issues earlier in this chapter. In addition, the Commission recommends that

255. 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 the purpose of 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.

The Role of the Prenatal Diagnosis and Genetics Sub-Committee

We have already referred to the role of the Prenatal Diagnosis and Genetics Sub-Committee of the National Reproductive Technologies Commission in our earlier discussion of technology assessment and in our licensing recommendations for PND services. However, it is worth drawing these points together, because of the significant role the Sub-Committee will have in preserving the integrity of the PND system in Canada.

The 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; embryo research; and the provision of fetal tissue for research and other designated

uses. Like National Commission members themselves, we recommend that at least half the members of the Prenatal Diagnosis and Genetics 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 monitor developments in this field and propose policies in a way that reflects the interests and concerns of Canadian society as a whole.

The Prenatal Diagnosis and Genetics Sub-Committee would have several functions. It could decide to establish ad hoc working groups to deal with one or more of these functions, if appropriate:

- Setting and revising, from time to time, the licensing requirements for genetics centres (including guidelines for distinguishing between recognized and experimental procedures; guidelines for carrying out clinical trials; record-keeping requirements; and other requirements outlined in our recommendations), to be applied through the National Reproductive Technologies Commission hearing process. Professional associations, patient and other interested groups, and the general public would have input into this process. As noted above, CCMG review and accreditation would also be a specific condition of licence.
- Developing standard information materials, counselling materials, and patient consent forms to be used in the provision of PND services.
- Monitoring the assessment and introduction of new PND technologies; deciding which clinical trials of PND are most urgent; and funding or coordinating provincial/territorial funding for them. Annual consultations with the Conference of Deputy Ministers of Health would be an important part of this function.
- Gathering relevant country-wide data and information about facilities, technologies, and practices, which can be used as a basis for the Sub-Committee's guideline- and standard-setting activities, as well as by the provinces/territories in their own planning and resource allocation decisions. Publication of data on the provision and outcomes of prenatal diagnosis in Canada in the National Commission's annual report would facilitate understanding of the activities of each genetics centre within the national context and act as a uniform information base on which federal and provincial/territorial health ministries and relevant public authorities can base legislative, programmatic, or regulatory initiatives relating to the provision of prenatal diagnostic services in Canada.
- Discussing and setting policy on new issues and dilemmas as they arise, including identifying related training and education issues to bring to the attention of those responsible, monitoring the practices of private laboratories and other non-licensed PND providers, and ensuring appropriate levels of regulation on an ongoing basis.

- Working with other sub-committees of the National Commission on issues that relate to the mandate of more than one sub-committee, such as
  (a) embryo research;
  (b) preimplantation diagnosis; and
  (c) gene therapy.
- Disseminating information and promoting public awareness and debate regarding the provision of PND services in Canada, in part through the publication of the NRTC's annual report, as well as through periodic initiatives such as the preparation and/or publication of studies or position papers on emerging issues in the field of PND — for example, related to the development of new diagnostic tests or procedures. In addition, the Sub-Committee could sponsor public consultation initiatives, such as consensus conferences and wide circulation of position papers, to ensure the development of broadly based social consensus on potentially controversial issues surrounding the provision of prenatal diagnostic services and to discourage the use of prenatal diagnostic tests or procedures in ways that would undermine the confidence of the Canadian public in the prenatal diagnosis process.

The last function, disseminating accurate information on which to base a more informed public debate, is a particularly important part of the mandate we propose for the National Commission with respect to PND. We have emphasized the importance of public input in the formulation of licensing requirements governing the provision of PND services in Canada and public information about whether these are being adhered to. The measures we propose will ensure that the activities of the PND system are reported to the public in a timely and accessible way, so as to enable public discussion on policy making in this field. As we have suggested, the publication of the National Commission's annual report is an appropriate mechanism for this public reporting.

Accountability would also be promoted by the composition of the Prenatal Diagnosis and Genetics Sub-Committee, which should include a balance of NRTC and outside membership, ensuring broad representation of the various interests involved. This is why we have recommended that the Prenatal Diagnosis and Genetics Sub-Committee have a multi-disciplinary make-up, including membership from relevant professional bodies, federal and provincial/territorial health ministries, and individuals representing the concerns of patients, women, people with disabilities, and other key segments of the community. Where appropriate, the Sub-Committee should also consult directly with the public on issues under consideration — for example, by circulating draft policies or position papers for comment (see Chapter 5).

Finally, public education is needed to ensure more complete and accurate public understanding of PND in Canada. As we have seen, the issues involved are complex, and there are many misconceptions about the nature and implications of PND and genetics testing.

Disseminating accurate information on which to base a more informed public debate is a particularly important part of the mandate we propose for the National Commission with respect to PND ... Public education is needed to ensure more complete and accurate public understanding of PND in Canada. As we have seen, the issues involved are complex, and there are many misconceptions about the nature and implications of PND and genetics testing.

In our view, these goals of public accountability and public education can be achieved only by including PND under the umbrella of the NRTC. Although other bodies, such as professional associations or genetics centres, often seek to involve the public in some aspects of their decision-making processes, only the NRTC can ensure a comprehensive system of public accountability and public education regarding PND.

Indeed, the NRTC is needed to play a more general coordinating role, bringing all interested parties and perspectives to the same table. PND is a widespread and growing field of medical activity, one that impinges on the lives of many Canadians and has many social and ethical implications. It is vital to ensure that all those involved in the system — pregnant women and their partners, medical geneticists, community health care providers, physicians, provincial/territorial and federal health care funding agencies, and the general public — have the information they need for informed decisions and the opportunity to influence decisions that will affect them. The coordinating role of the Prenatal Diagnosis and Genetics Sub-Committee will help ensure that PND programs continue to develop appropriately and in the context of the values of Canadians. This is particularly important as well with regard to practice in the wider medical community. We have seen marked variation in practices with regard to consent and other aspects in the referral network, showing the importance of establishing and ensuring adherence to standards and guidelines. The Prenatal Diagnosis and Genetics Sub-Committee could assist the relevant professional bodies in bringing this about — for example, by providing appropriate information.

Conclusion

If we are to ensure that PND services are provided in a way that is both beneficial to individuals and couples and consistent with social values,

certain changes are required. The reforms we have proposed would promote the autonomy of patients and the appropriate use of resources, while also protecting vulnerable interests of individuals and society and ensuring only ethical uses. In general, and in line with our ethic of care, one goal of our recommendations is to foster a spirit of cooperation among all participants.

In the system we envisage, some regional differences in the use of services would remain — reflecting levels of demand and budgetary resources — but we should see far less variation in referrals to genetics centres. Although there will still be differences between practitioners on various aspects of PND, there would be far less variation in adherence to clinical, counselling, and other standards of practice. There will be mechanisms for public input and public accountability with regard to the evolution of the system. Finally, there will be far fewer opportunities to introduce new diagnostic tests without appropriate assessment and monitoring, as well as far more in the way of disciplined across-Canada assessment and use of new technologies. These reforms will ensure that at-risk women and couples have equal access to a wide range of proven beneficial services.

We believe that Canada has a unique capacity to put in place a structure for the provision of PND services that will serve Canadians now and adapt to the coming changes in technology and demand.

Is this vision feasible? We believe that Canada has a unique capacity to put in place a structure for the provision of PND services that will serve Canadians now and adapt to the coming changes in technology and demand. The necessary factors are in place: we have a strong history of voluntary cooperation by the genetics centres and the CCMG in the disciplined introduction of new PND technologies; there is good will among referring practitioners who have the interests of their patients at heart; we have a single-payer system of health care, which allows for control over the proliferation of new technologies; and we have strong incentives for cooperation on the part of provincial/territorial ministries of health, which are very cognizant of the need to manage the health care system more efficiently and of the need for better data on which to base planning and resource allocation decisions.

The reforms we propose offer the potential to manage more efficiently within existing resources and even to save resources. Although additional resources will be required to establish this structure and work through the first round of facility accreditation and quality assurance activities, there will be significant savings over time. This is because new technologies that do not work or do not provide benefit will not become part of the system. Thus, there are not only ethical but financial reasons for supporting the approach we propose. Canada has a unique opportunity to make this area of clinical practice a vibrant example of evidence-based medicine. PND in

the framework we envisage would exemplify how the health care system should strive to work to the benefit of those who use and provide its services.

The track record of the medical genetics community has been impressive in terms of determining the efficacy and safety of the various prenatal diagnostic techniques *before* they are introduced widely. For example, the randomized across-Canada collaborative clinical trials of amniocentesis and chorionic villus sampling are models that other areas of medicine could do well to follow. Seldom have health care providers done as well in collaborating and limiting new technology until it is assessed — that is, in providing evidence-based services. Yet the public and various interest groups are relatively unaware of this.

At our public hearings and in submissions to the Commission, we noted a high level of suspicion and mistrust of services provided by the genetics community from some members of the public. We heard perceptions that prenatal diagnosis is being used as a "search and destroy" mission to "weed out defective fetuses"; we heard that prenatal diagnosis counselling is biased and predicated on the assumption that it is better to abort a fetus found to have an anomaly than to consider raising a child with a disability; we heard statements that some of the newer developments in this area are being used for eugenic purposes and that women were coerced into terminating pregnancies. These themes were raised by vocal and well-organized groups representing women, people with disabilities, and the pro-life movement, as well as some concerned individuals.

At our public hearings and in submissions to the Commission, we noted a high level of suspicion and mistrust of services provided by the genetics community from some members of the public.

It has become evident that the genetics community needs to find better ways of communicating about how it carries out its work and needs to listen closely to what women are saying about their treatment experience. Not enough attention has been given to how patients view the experience or how the public perceives genetics services. There is a great deal of misinformation and a need for accurate, unbiased, and accessible information about genetics and about what

It has become evident that the genetics community needs to find better ways of communicating about how it carries out its work ... There is a great deal of misinformation and a need for accurate, unbiased, and accessible information about genetics and about what services are actually provided, and in what ways, across the country ... The system we propose should make knowledge about activities in genetic medicine more open and accessible to the general public.

services are actually provided, and in what ways, across the country. The referral network of the physicians in particular needs to realize more clearly the need for providing full information and for respecting the autonomy and decision making of women.

The system we propose should make knowledge about activities in genetic medicine more open and accessible to the general public. Lack of knowledge leads to concerns about what "might be going on." Clear, open information is a much better basis for decisions about use of genetic knowledge, use in which the values of Canadians have an influence.

Appendix 1: Causes and Risks of Congenital Anomalies and Genetic Disease

This appendix lists the major causes of congenital diseases and early-onset genetic disorders and discusses who is at most risk of having children affected by these disorders. It shows that while some people are at much higher risk of having affected children, all of us are at risk, and it is often difficult to identify who is at higher risk.

Unknown Causes

The largest category of disorders comprises congenital anomalies whose origin or cause is unknown. Estimates reached by various studies of the proportion of anomalies that fall into this category range from 43 to 70 percent of cases. The exact percentage found in any one study depends to some extent on the expertise of physicians and on the diagnostic investigations done, but even in the most rigorous studies (such as Nelson and Holmes[14]) more than 4 congenital anomalies in 10 were of unknown origin.

Chromosomal Disorders

These diseases are caused by extra or missing chromosomes or parts of chromosomes. For example, people with Down syndrome (trisomy 21) have three copies of chromosome 21 instead of the usual two. Down syndrome is characterized by developmental retardation and various physical anomalies; other, more severe chromosomal disorders result in profound retardation and early death. These and other significant chromosomal abnormalities can arise during formation of the gametes (eggs and sperm) during fertilization, or during cell division in early embryonic development.

Every couple is at some risk of having a fetus with a chromosomal abnormality, but some couples are at higher risk than others. In particular, the risk increases in pregnancies later in a woman's childbearing years. The incidence of chromosomal abnormalities in the general population, based on studies of the chromosomes of consecutive newborns, is about 1 in 200 liveborn individuals (0.5 percent). However, the likelihood of a woman having a child with a chromosomal anomaly rises steeply from about age 35. For example, the risk of having a liveborn infant with an abnormal number of chromosomes is about 1 in 380 births when the woman is age 30, 1 in 180 at age 35, 1 in 60 at age 40, and 1 in 20 at age 45.[15] In some rare cases, chromosomal anomalies are inherited, so family history may also identify some women at higher risk. Still, the majority of infants with chromosomal anomalies are born following low-risk pregnancies, simply because most pregnancies are in women under the age of 35.

Single-Gene Disorders

Genes are responsible for producing the proteins that make human development and functioning possible. Changes in the sequence of chemical bases in a gene can mean that the particular protein is not made or does not function properly. If this is one of the proteins or enzymes essential to early development, the embryo or fetus will die *in utero*, be spontaneously aborted, or be delivered as an infant with severe anomalies. Indeed, the incidence of genetic anomalies is one of the reasons for the high rate of spontaneous abortion (see Chapter 7).

If the essential gene becomes important only in early childhood, an apparently normal infant will stop developing, become very ill, and die. For example, Tay-Sachs disease is a single-gene disorder in which the signs appear during the first year of life. The disease causes nervous system degeneration with blindness, severe mental retardation, seizures, and paralysis. Death usually occurs by five years of age.

Finally, an abnormal gene might cause a disorder only in later life. Huntington disease, for example, causes a progressive deterioration of the brain, typically starting in adulthood or middle age and leading to death, usually within 10 to 20 years.

Each single-gene disorder is relatively rare, with most recessive single-gene disorders having a birth incidence of 1 in 15 000 to 1 in 100 000. Even the most common such disorder in Western countries, cystic fibrosis, occurs in only 1 birth in 2 500. However, since there are approximately 4 000 known single-gene disorders, the combined likelihood of having one disorder or another is much higher. It is estimated that 1 in 277 liveborn individuals will have a single-gene disease that is evident before age 25.

Who is at risk of having a fetus with a single-gene disorder? In some cases, the gene responsible is a spontaneous dominant mutation, not found in either parent. There is no way to pinpoint who is at risk of having a

fetus with a genetic disease caused in this way. In the majority of cases, however, the gene is inherited from one parent or both. The parents may not themselves exhibit any signs of a disorder, since (in cases of recessive diseases in both parents and X-linked diseases in the woman) the abnormal gene may be "covered" by a healthy gene. Although the parents are healthy, they are "carriers" of the abnormal gene and may pass it on to their children.

The Transmission of Single-Gene Disorders

Single-gene disorders are transmitted in one of three ways:

Recessive disorders: For recessive disease to occur, both genes in the pair — one received from the mother and one from the father— must be abnormal, since one normal copy of a gene is able to provide enough protein or enzyme to cover for its malfunctioning partner. If the parents each have only one abnormal member in the pair, they themselves are unaffected. Indeed, all of us probably carry at least one such gene that would be harmful in "double dose." However, when both parents carry the same defective gene, on average one-quarter of their offspring will have both genes faulty and thus be affected. Examples of recessive disorders are phenylketonuria (which results in retardation and seizures but can be treated by diet) and adenosine deaminase deficiency (which results in severe immune deficiency and early death). Another more widely known recessively inherited disease in Caucasian populations is cystic fibrosis, which leads to severe chronic respiratory and digestive problems and a reduced life expectancy.

Dominant disorders: In dominantly inherited disorders, only one member of the gene pair needs to be abnormal to cause the disease; the normal member of the pair is unable to cover for its malfunctioning partner. If the affected person reproduces, the abnormal gene will be passed on average to half their children, who will also be affected. Huntington disease is an example of a dominantly inherited single-gene defect.

X-linked disorders: In X-linked recessive disorders, the problem gene is located on the X chromosome. Since females have two Xs, if one is normal, that female will be healthy. Since males have only one X, if a male has the X-linked disease gene, he will be affected — there is no partner gene to "cover" it. In families where the mother has a gene for an X-linked recessive disorder, therefore, on average half the daughters will be healthy unaffected carriers of the gene, but half the sons will have the disease. An example of an X-linked, single-gene disorder is haemophilia. This bleeding disorder can now be partially controlled with injections of blood clotting factors.

Some people know that they are carriers of such genes, because of a family history of a particular single-gene disorder or, most often, because a previous child was born with that disorder. Others may know that they are at increased risk of being a carrier because of their ethnic descent. For example, Mediterranean populations are more likely to carry thalassaemia;

Ashkenazi Jews are at increased risk for carrying Tay-Sachs disease; black populations are more likely to carry sickle-cell disease; and Mennonite populations in Canada are at increased risk of carrying cystic fibrosis.

In the great majority of cases, however, people do not know that they are carriers of a single-gene disease. In fact, it is believed that everyone carries one or more abnormal recessive genes. If the disorder is recessive, the gene may be passed on for generations without producing a child with an observable disorder. Hence, even for those couples who have no reason to suspect that they are carriers of any particular genetic disorder, there is a small (though unknown) chance that both parents will carry the same genetic anomaly, and hence that the fetus may have a single-gene disorder.

The risk that an abnormal gene in the parent will result in a disorder in the child depends on whether the disorder is transmitted in a dominant, a recessive, or an X-linked way. If dominant, the risk that a child will be affected is one in two, even if only one parent has the gene; if X-linked, there is a one in two chance that male offspring will be affected; if recessive, and if both parents carry the gene, there is a one in four chance that the child will be affected.

Multifactorial Disorders

Multifactorial disorders result from complex interactions between environmental factors (which may include the chemical, social, and emotional environment) and the genes of an individual. Most of them are relatively mild and do not have an onset until adult life. Many adult-onset disorders fall into this multifactorial category; examples include some forms of diabetes, hypertension, heart disease, ulcers, thyrotoxicosis, and certain cancers. These disorders constitute by far the most frequent category. It is likely that most familial chronic diseases of adult onset fall into this group. However, some multifactorial disorders are congenital and can be quite severe — for example, neural tube defects (spina bifida and anencephaly).

Who is at risk for having a fetus with a multifactorial disorder? Because these disorders are partly the result of genes, they tend to run in families, so family history will identify some of those at greatest risk. A couple that has had a child with a multifactorial anomaly is identified as being at significant risk of recurrence. Evidence also suggests that some ethnic groups may be at higher risk of particular disorders — for example, Sikhs have higher rates of neural tube defects than the general population. However, a couple may be at risk of having an affected fetus even in the absence of a family history of the disease or anomaly; for example, one of the most frequent multifactorial disorders, neural tube defects, occurs in the general population in Canada at a rate of at least 1 in 820 births.

Teratogens

Another category of congenital anomalies arises as a result of the embryo or fetus being exposed to harmful agents or substances ("teratogens") *in utero*: for example, infections of the pregnant woman, such as rubella, toxoplasmosis, herpes, syphilis, and cytomegalovirus disease; diseases in the pregnant woman that affect the hormonal or metabolic milieu of the developing fetus, such as diabetes, phenylketonuria, and endocrine tumours; and other exposures, such as alcohol, inadequate nutrition, drugs, irradiation, chemical substances, and increased body temperature. Evidence from animal research shows that genes may influence the susceptibility of the embryo or fetus to such agents, but this is difficult to demonstrate in human beings. Some examples of congenital anomalies and the agents associated with their genesis include those cases of cleft lip and spina bifida resulting from the pregnant woman's use of anti-convulsants; caudal dysplasia resulting from the woman's diabetes; and fetal alcohol syndrome resulting from excessive alcohol consumption by the pregnant woman.

There is a popular misconception that exposure to drugs or to chemicals in the environment is responsible for a large proportion of congenital anomalies. This belief results perhaps in part from the explosion of litigation, particularly in the United States, involving children with congenital anomalies. However, the evidence is that drugs and chemicals account for a very small percentage of anomalies.[16] Nevertheless, some exposures are an unavoidable risk in all pregnancies; for example, every woman is vulnerable to infection during pregnancy.

Uterine Factors

Some uterine factors can cause malformations in the fetus before birth — for example, an abnormality in the shape or size of the uterus may mean the fetus does not have enough space to develop normally.

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