Other Risk Factors and Infertility

We know that several other risk factors in addition to those already reviewed play a role in infertility, but the limited information available on these factors makes it difficult or impossible to assess how serious the risk is. As we have discussed, a lack of needed information characterizes the entire field of risk factors for infertility, but it is particularly evident for the factors examined in this section. In some cases, this is because their role in infertility has begun to be recognized only recently; in other cases, it is because we have evidence of their role in infertility and adverse reproductive outcomes when exposure is severe, but not in the milder exposures that more commonly occur.

Some of these risks are medical in origin, including diseases such as endometriosis and the unintended effects of medical intervention. Many of these risk factors, however, have to do with personal habits and choices: how the individual eats, exercises, controls fertility, uses substances such as alcohol or drugs, or deals with stress. Exactly what proportion of infertility these risk factors account for is not clear, but they are in the ambit of individuals to control. For instance, women who are trying to conceive or who are pregnant should aim to have moderate amounts of exercise, abstain from alcohol or drug use, and achieve or maintain a normal body weight. Preventing infertility by avoiding these risks is therefore both achievable and cost effective for the individual and for society.

Given the Commission's goal of consolidating the broadest possible understanding of all known risk factors for infertility, we surveyed the extensive literature on all these risk factors, selected the most scientifically rigorous studies, synthesized the findings to establish what is reliably known about these risk factors, and came to conclusions. This is the first time such a comprehensive review has been conducted. The review consisted of a thorough analysis of the extensive international literature

and a synthesis of the reliable information that could be obtained from well-designed studies. In all, Commission researchers reviewed more than 500 studies. The conclusions and findings from this review, presented here, in themselves represent a substantial contribution to this field. They also point to the clear need for further research, as these risk factors are relevant to the choices of many women and men who would like to have children. We begin with what is known about the relationship between eating disorders and infertility.

Eating Disorders, Weight, and Exercise

Researchers have identified very low and very high body weight and body fat as factors that may influence reproductive functioning. In particular, an inadequate ratio of body fat to body weight has been linked to infertility in women who exercise excessively, diet to achieve a below-average weight for their height, or have an eating disorder such as bulimia or anorexia nervosa. Excessive weight has also been associated with infertility in women. There has been very little research, however, on how these factors affect male fertility.

Researchers are not yet certain of how these risk factors affect female fertility, but it is suspected that they may disturb the functioning of the hypothalamus and the pituitary gland, which in turn may affect such body functions as hormone production. Even though it is not known exactly how it occurs, there is substantial evidence that infertility may be a consequence of abnormal eating behaviours, excessive exercise, and under- and overnutrition. These effects can be reversed, however, by achieving and maintaining healthy weight and exercise levels and through improved nutrition.

Undernutrition and Eating Disorders

In the Western world, although undernutrition is associated with poverty, drug use, and chronic alcoholism, a substantial amount is also related to self-imposed dietary restrictions, poor eating habits, and eating disorders. Undernutrition and eating disorders may affect women's fertility in terms of both their ability to conceive and their ability to have a healthy pregnancy and birth. Severe nutritional deprivation before and during pregnancy places the fetus at risk; growth retardation, low birth weight, and death or illness among newborns are more common in infants of poorly nourished mothers. As well, the risk of a particular type of congenital anomaly (neural tube defects) is greater in the children of malnourished women who have diets deficient in folic acid.

Eating disorders such as anorexia and bulimia may result in difficulty conceiving, or in pregnancy and birth complications. Anorexia is a

psychological disorder that involves extreme dieting to achieve weight reduction. Bulimia is a psychological disorder characterized by induced vomiting or other forms of "purging" such as excessive laxative use. One estimate is that 1 percent of young adult and adolescent women in the general population suffer from anorexia nervosa and that 1.7 percent suffer from bulimia.[1] The prevalence of eating disorders has been reported to be higher than this among infertile women: a Canadian study of 66 infertility patients showed that 7.6 percent had anorexia nervosa or bulimia nervosa, but further studies are needed to ascertain the frequency of eating disorders in women seeking treatment for infertility. The following discussion outlines some possible mechanisms for the association between infertility and eating disorders.

Women with anorexia nervosa often have primary or secondary amenorrhea (cessation of menstrual periods). Anorexic amenorrhea is not attributable solely to weight loss; rather, a combination of physical, psychological, and nutritional stress factors is involved. As well, it has been argued that the loss of body fat rather than body weight per se is a crucial factor. Women who suffer from bulimia have also been reported to experience menstrual disorders that could affect their ability to conceive. The combination of weight loss (although this is generally not as severe as that experienced by anorexic women), inadequate nutrition, chaotic eating behaviours, and psychological distress in bulimic women have been associated with reproductive problems (see research volume, *Understanding Infertility: Risk Factors Affecting Fertility*).

> A complex interplay of biopsychosocial factors appeared to influence the fertility of women who presented with eating disorders, who exercised, or who used dietary restriction as a method of weight control. Weight and percentage of body fat appeared to be critical factors that influenced reproductive functioning. A precise understanding of the physiological links was still unclear, though the majority of evidence suggested a disturbance in the hypothalamic-pituitary axis.
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> *S. Maddocks, "A Literature Review of the Physiological Manifestations Related to Infertility Linked to Weight, Eating Behaviours, and Exercise," in Research Volumes of the Commission, 1993.*

Both anorexia and bulimia have been associated with problems in fetal development and pregnancy outcome. Adverse effects such as low infant birth weight, complications of labour and delivery, and increases in perinatal mortality and morbidity have been reported. A recent Canadian study reported on 74 women who had been treated for anorexia nervosa or bulimia, 15 of whom later became pregnant. The researchers observed lower maternal weight gains and infants with lower birth weights for the seven women who were ill with anorexia nervosa or bulimia at the time of conception. The eight women in remission from the disease at the time of

conception were found to have healthier infants.[2] Few studies have been conducted on the effects of anorexia and bulimia on fertility; information from this small Canadian study should therefore be extended and the findings confirmed.

Although eating disorders are much less common in men, it is theoretically possible that undernutrition may affect their fertility. Although based on small numbers, two studies of 76 men with celiac disease and Crohn's disease (two diseases that affect the body's ability to absorb nutrients from food) found an association between nutritional deficiency and impaired semen quality and infertility.[3] However, the drugs used to treat the symptoms of Crohn's disease (such as sulphasalazine) may have contributed to the results, and further research is required.

Young people need to be aware that severe dietary restriction or eating disorders can affect their health, including their fertility ... Young women should be encouraged to identify and evaluate the images of women projected by the media and accepted by many in our society.

Serious eating disorders are tied closely to lack of self-esteem and negative self-image in women. Unfortunately, women get many messages that they are valued for their appearance and that perpetuate unrealistic expectations about women's body size and shape. A consequence of this focus on "ideal" body weight is that many young women feel that they could be more attractive or more popular if they could change their appearance to fit with what they perceive to be the ideal. This same preoccupation leads many young women to smoke as a means of "controlling" their weight. While severe forms of dieting are clearly linked to infertility, again we lack data on whether the dieting that many young women engage in has any impact on fertility.

Young people need to be aware that severe dietary restriction or eating disorders can affect their health, including their fertility. As is the case with sexuality education, this information is best presented in the context of developing individual self-confidence and self-esteem. Young women should be encouraged to identify and evaluate the images of women projected by the media and accepted by many in our society. The Commission recommends that

45. Health Canada initiate and promote consultation and information sharing with provincial/territorial ministries of health and education to ensure that goals and objectives for health education incorporate information about the effects of severe dietary restrictions and severe weight

control on health and fertility. This information should be conveyed in a context that encourages young people to question popular myths about female beauty and to develop a healthy sense of self-acceptance.

Most obese women are fertile, but obesity has also been reported to be associated with anovulation and menstrual cycle disturbances. There is some evidence that obesity is more common among infertile women. One study of 312 sterile women found that 8.7 percent were obese.[4] Negative effects on pregnancy development occur among obese women (mainly the risk of high blood pressure), and such women may also give birth to infants that are large for their gestational age, although this is generally considered a less serious problem than low birth weight.

Mild reproductive disturbances in obese men have also been reported by researchers; for example, testosterone levels have been reported to decline, which might affect sperm production or sperm function. More research is required on the relationship between male obesity and fertility.

We have already noted that a proportion of women undergoing infertility treatment have an eating disorder that could have affected their fertility. These women need to be informed of the importance of eating a healthy diet and achieving a normal weight to their wish to conceive and have a healthy pregnancy. Physicians and other health care workers should include weight and diet assessment as a part of the preliminary investigation preceding infertility treatment. The Commission recommends that

46. Physicians and health care workers ask women who are seeking infertility treatment about their eating habits to determine whether their diet and weight may be factors contributing to their infertility. Women who are severely underweight or overweight should be encouraged to restore their weight to a normal level for a reasonable time to see if they still do not become pregnant before embarking on any form of fertility treatment; counselling and support to help them accomplish this goal should be made available.

Excessive Exercise

There is no association between moderate exercise (for example, up to 60 minutes per day) and ovulatory dysfunction. However, excessive

exercise may cause delayed onset of menstrual periods, the absence of menstrual periods, and other problems that would make establishing a pregnancy difficult or impossible. Studies have consistently reported an association between infertility and vigorous extended daily exercise (for example, more than 60 minutes per day of running, aerobics, tennis, or downhill skiing). Infertility resulting from this level of exercise is reversible, however.

Researchers have not established an accurate estimate of the prevalence of exercise-induced infertility among women. Surveys show that the incidence of menstrual irregularities among competitive athletes ranges from 1 to 50 percent, compared to the estimated 2 to 5 percent in the general population. These widely varying results are attributable to differences in the way researchers define menstrual dysfunction and are influenced by whether the training intensity of the athletes is taken into consideration.

Some have hypothesized that certain risks to fetal development and pregnancy outcome may be associated with prolonged excessive exercise during pregnancy. These include hyperthermia leading to teratogenesis, miscarriage, premature rupture of membranes, placental abruption (premature separation of placenta), premature labour, and long-term low oxygen supply to the fetus (hypoxia).[5] Normal levels of activity during pregnancy do not carry these risks.

In summary, excessive strenuous exercise can have negative effects on fertility and pregnancy, but infertility associated with this factor is reversible. Pregnant women or women who are trying to conceive should be encouraged to undertake *moderate* exercise, as this is beneficial, but prolonged intensive daily exercise should be avoided. The Commission recommends that

47. (a) Physicians and other health care workers inform women of reproductive age of the possible effects of excessive exercise on their fertility; if they are trying to conceive or are pregnant, they should exercise in moderation.

(b) Physicians and health care workers routinely evaluate the exercise history of women seeking infertility treatment to determine whether excessive exercise (more than 60 minutes of vigorous activity per day) might be a contributing factor in their infertility. Women who are exercising to this extent, including high-performance

athletes, should be encouraged to reduce their level of activity to a moderate level to restore their fertility. This should be a first step before any form of fertility treatment is attempted.

Endometriosis

Endometriosis is a chronic condition in which endometrium (the tissue lining the uterus) is found in other parts of the body, including the fallopian tubes, the ovaries, the ligaments that suspend the uterus, the outside of the uterus itself, and, in severe cases, the intestines, bowel, and bladder. The endometrial tissue in these locations can bleed during menstruation, but the tissue and blood remain trapped in the body, and this may cause inflammation, the formation of cysts and scar tissue, and consequent medical problems. While many women with endometriosis have no symptoms, in others the symptoms include chronic pelvic pain, pain during sexual intercourse, and painful menstrual periods, bowel movements, and urination. Physicians classify endometriosis according to stages: Stage I (minimal disease), Stage II (mild disease), Stage III (moderate disease), and Stage IV (severe disease). The disease is generally thought to be progressive if left untreated, but whether in fact this is the case is not clear. Endometriosis has also been identified as a risk factor for infertility, but again the exact relationship is not clear. There is clear evidence that it can cause infertility when anatomical distortion or obstruction of the fallopian tubes occurs. Whether the presence of endometrial implants alone, without distortion or disruption of the fallopian tubes, can cause infertility is not known definitively, but it appears much less likely. Some women with mild endometriosis have difficulty conceiving, but others with mild or even moderate endometriosis do not experience any difficulty becoming pregnant.

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In the past endometriosis was considered a "career woman's disease" because it was diagnosed most often in childless women between the ages of 30 and 40. It is now known that this is false; endometriosis can affect any woman and is relatively common among adolescents. Estimating the prevalence of endometriosis among women of reproductive age is difficult because many experience symptoms long before they seek help

from a doctor, while others experience no symptoms at all. Despite these limitations, researchers estimate that 10 to 20 percent of all women of reproductive age have endometriosis.[6] It is therefore not surprising that endometriosis is often identified during preliminary infertility investigations: between 10 and 40 percent of infertile women are found to have endometriosis (see research volume, *Understanding Infertility: Risk Factors Affecting Fertility*); one study puts the incidence rate at 14 percent.[7] The answer to the key question of whether the condition is more common among infertile women than among fertile women has not been established, however. Women experiencing difficulty conceiving are usually investigated using procedures such as laparoscopy, so that if endometriosis is present it will be identified; it would not be justifiable to investigate healthy women in the same way, however, simply to establish whether they are more or less likely to have endometriosis.

Some clinicians consider endometriosis (even mild endometriosis, which causes no visible obstructions) that is found to co-exist with infertility to be its cause. The available evidence does not show a causal relationship, however, and a comprehensive investigation of potential factors in a large group of infertile women showed that endometriosis without adhesions did not alter the cumulative conception rate.[8] Nor does medical treatment of endometriosis enhance the chances of conception in infertile women. However, additional research is required to confirm this conclusion further.

> Medical investigators have developed a general understanding of basic cellular activities within peritoneal fluid during the menstrual cycle, and they have ascertained that both the peritoneal fluid environment and the reproductive cycles of infertile women with endometriosis are dysfunctional in comparison to those of healthy women. However, as yet, investigators offer only suggestions for the cause of the defects, and for the specific relationship or relationships between minimal or mild endometriosis and infertility, projecting that future research will confirm or modify their theories.
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> *A. Ponchuk, "The Physiological Links Between Endometriosis and Infertility: Review of the Medical Literature and Annotated Bibliography (1985-1990)," in Research Volumes of the Commission, 1993.*

In contrast to milder forms of the condition, it is quite clear that endometriosis that produces visible anatomic distortions and scarring to the reproductive organs and surrounding areas within the pelvic cavity does cause infertility. Bands of scar tissue can impair the function of the ovaries and fallopian tubes by binding them together. Scar tissue can also interfere with the release of eggs from the ovaries or the pick-up of the eggs by the finger-like fimbria at the end of the fallopian tubes. A further barrier to pregnancy is that severe endometriosis can make sexual intercourse very painful.

There is no "cure" for endometriosis; physicians can only reduce the symptoms of the disease, by surgically removing endometrial tissue that has implanted outside the uterus, or by using drug therapy. Drugs commonly prescribed for endometriosis suppress ovulation, preventing the monthly build-up and shedding of endometrial tissue, and are effective in reducing pain. Drug treatment is thought to help cause the implants to shrink and disappear, but there is no evidence that this is effective in treating infertility.

Researchers have considered how endometriosis might affect reproduction. Both the peritoneal fluid environment and the reproductive cycles of infertile women with endometriosis have been shown to vary from what is considered normal. Researchers have reported abnormalities in some of the phases in the menstrual cycle in women with endometriosis; this in turn may affect their fertility. As well, variations in the volume and content of peritoneal fluid in the cavity surrounding the internal organs have been observed that might help explain the occurrence of endometriosis and a relationship between endometriosis and infertility. A link between the altered peritoneal environment of women with endometriosis and the survival and motility of sperm within their bodies has also been suggested. This alteration might cause problems with sperm-egg interaction, embryo implantation, or early embryonic development, or it may cause spontaneous abortion.

So many mechanisms have been proposed to explain the occurrence of minimal or mild endometriosis that this, in itself, is evidence that we do not yet understand what leads to this condition. It is clear that further research is needed in such areas as the possible contribution of abnormalities in peritoneal fluid in the development of endometriosis. It may also be that multiple co-existing factors are responsible for both endometriosis and infertility. It is evident that we know little in a definitive way about this condition and that it needs to be studied further.

Since the causes of endometriosis are not well understood, it is impossible to know how to prevent women from developing endometriosis and thus reduce the prevalence of infertility resulting from severe forms of this disease. However, educational efforts could help to inform women of the possible impact of endometriosis on their fertility and encourage them to consider this in making their childbearing plans. For example, one 1990 survey found that only about half the 618 Canadian women interviewed

Since the causes of endometriosis are not well understood, it is impossible to know how to prevent women from developing endometriosis and thus reduce the prevalence of infertility resulting from severe forms of this disease. However, educational efforts could help to inform women of the possible impact of endometriosis on their fertility and encourage them to consider this in making their childbearing plans.

knew about endometriosis. Another quarter of the women recognized the term, but knew little or nothing about the condition.[9] Such a finding suggests a need for efforts to inform women of the symptoms of endometriosis, and the need to provide information about the possible impact on their fertility to those with the condition. The Commission recommends that

48. Health professionals such as physicians, gynaecologists, and nurses ensure that women who have endometriosis know about the possible implications of the condition for their fertility so that they can take this information into account when making their childbearing plans.

Substance Use and Abuse

Alcohol

Many studies have confirmed the existence of an association between chronic alcohol abuse and negative effects on male reproductive function, such as impotence, testicular atrophy (shrinking of the testes), sperm abnormalities, and reduced sperm production. Chronic alcohol use by men has also been associated with a reduction in testosterone levels, even after only a few months of daily alcohol consumption. Exactly what level of alcohol consumption produces these problems is not known, however. It is therefore clear that people who abuse alcohol are more likely to experience reproductive problems. Whether the amounts of alcohol that Canadians commonly consume have an effect on their reproductive health is not known.

The situation is similar with regard to women — chronic alcoholism has been associated with menstrual irregularities — but researchers have not found any statistically significant associations between low or moderate levels of alcohol intake and a woman's ability to conceive.

However, the risks associated with heavy alcohol consumption (defined as more than six drinks, glasses of wine, or bottles of beer per day)[10] during pregnancy are well documented; they include spontaneous abortion and fetal anomalies. The evidence is also clear that heavy drinking has a high risk of causing alcohol-related birth anomalies, ranging from full fetal alcohol syndrome (growth retardation, central nervous system dysfunction, characteristic facial anomalies, and often congenital heart disease) to one or more of such problems. Fetal alcohol syndrome is reported to be the third most common known cause of congenital anomalies and mental

retardation in newborns.[11] It is also the most preventable cause of these conditions. At any given level of alcohol intake during pregnancy, far more children will have alcohol-related birth anomalies than will have full fetal alcohol syndrome. As a result, many more children in the population will have intellectual deficits and minor physical problems than will have the full syndrome. The proportion of children affected decreases with reduced levels of alcohol intake, so that at less than two drinks per day the risk of these problems is minimal. At the same time, results of animal studies suggest that even a single episode of heavy drinking at a critical time in pregnancy may cause fetal damage.

Alcohol Consumption in Canada

The prevalence of alcohol consumption has declined slightly over the last 10 years in Canada. This has occurred largely among the younger and older segments of the population: between 1985 and 1989 the proportion of young people between the ages of 15 and 19 who were current drinkers dropped from 81 percent to 74 percent. Regardless of age, a higher percentage of men than women consume alcohol; men also consume alcohol more frequently and in greater quantities.

On average, Canadians consume 3.7 drinks per week. The Addiction Research Foundation estimates that approximately 477 000 Canadian adults (3 percent of the adult population) are alcoholics; 70 percent of these are men.

Efforts to prevent alcohol abuse, and thus to reduce the impact of alcohol as a risk factor for infertility and adverse birth effects such as fetal alcohol syndrome, must begin with young people. The earlier people start drinking regularly, the more likely they are to develop alcohol problems. *Opportunities for Health: A Report on Youth*, from the Chief Medical Officer of Health, published by the Ontario Ministry of Health, suggests that although the number of young people who drink has declined over the past few years, binge and problem drinking have increased.

To reduce alcohol consumption among young people, a comprehensive strategy is required that involves programs to influence both the environment and the individual. The social conditions and personal circumstances that lead individuals to abuse alcohol need to be recognized and addressed. Easy access to alcohol and the glamorization of drinking through advertising and the media promote consumption. Preventive efforts designed to influence the environment can include, for example, limiting access to alcohol by strictly enforcing drinking age regulations. School policies and programs can also help shape young people's attitudes toward alcohol consumption; providing leisure and recreation activities as an alternative to adolescent drinking and teaching young people in health education programs how and why to avoid alcohol use are necessary

components of a strategy to prevent alcohol abuse. The Commission recommends that

> **49. Health Canada, in cooperation with provincial/territorial ministries of health and education, review and evaluate existing programs to reduce alcohol consumption among young people and, where necessary, develop new or improved initiatives to accomplish this objective.**

Educational efforts are also necessary to inform women of the adverse effects of alcohol consumption during pregnancy. Women who are hoping to conceive or for whom pregnancy is a possibility should be aware that much of fetal development occurs before they are even aware or certain they are pregnant. Strongly worded labels on alcoholic beverages, advising pregnant women of the risks of consuming alcohol during pregnancy, may reduce the likelihood that those who wish to conceive or who are pregnant will drink alcoholic beverages. A 1987 report by the U.S. Department of Health and Human Services concluded that health warning labels can have an impact on consumers if the labels are designed effectively. In the United States, manufacturers of alcoholic beverages are now required by law to include warnings about the risks of alcohol consumption to pregnant women and fetuses.

In Canada, no such law exists, although a pilot project is under way to evaluate whether labelling influences drinking behaviours. Alcohol consumption represents more than a risk to fertility; the dangers associated with drinking and driving are also cause for concern, and chronic alcohol consumption is associated with a host of other adverse health risks. It would therefore make sense to have warnings regarding all these risks on alcohol labels, similar to the approach that has been taken with health warnings on cigarette packages. Warnings about the effects of alcohol on fertility should not be directed solely to women — men too have fertility risks from chronic alcohol consumption, and both sexes are at risk from the range of other adverse health effects. If the results of the pilot project show they have an effect, the Commission recommends that

> **50. Health Canada make it mandatory for manufacturers to include on all containers of alcoholic beverages health warnings about the risks of alcohol consumption, including risks to the fetus.**

and that

51. Physicians and health care workers provide information about the reproductive health effects of alcohol consumption to women who plan to become pregnant and to couples trying to conceive.

Couples who are experiencing infertility need to be made aware that although moderate consumption of alcohol by either partner has not been shown to affect fertility, chronic consumption of alcohol has been linked to fertility problems in men. Men are less likely to consult a physician when a couple wants to become pregnant, and providing information to their partners about the effects of alcohol use on male fertility may be a way of helping this information get to them.

Because of the association between heavy alcohol consumption and harm to the fetus, as well as the fact that a safe level of alcohol consumption for pregnant women has not been established, it is common sense for women who are trying to conceive to avoid consuming alcohol. Unless there is no possibility they will become pregnant, women of childbearing age should avoid heavy alcohol consumption or binge drinking, not only for their own health but because of the possible risks to the fetus in an unplanned or undetected pregnancy. The Commission recommends that

52. Physicians and health care workers provide information to couples seeking infertility treatment on the effects of alcohol consumption on fertility and on pregnancy outcomes and make sure couples trying to conceive understand the importance of minimizing alcohol use.

and that

53. Physicians and health care workers routinely evaluate the drinking history of both partners in couples who are infertile. If a problem is identified, counselling and support should be offered to change alcohol consumption before they undergo infertility treatment.

Illicit Drugs

Some drugs used illicitly may inhibit the activity of the central nervous system (anaesthetics, analgesics, sedatives, and tranquilizers). Others stimulate the activity of the central nervous system (anti-depressants, stimulants, and hallucinogens). Drugs in both categories have the potential to affect reproductive function by influencing various body processes and nervous system functioning associated with the production of sex hormones by the pituitary. Changes in hormone production could in turn affect ovulation or sperm production. Psychoactive drugs might also influence reproductive function by affecting the autonomic nervous system, which controls erection and ejaculation in men and sexual arousal in women.

Illicit Drug Use in Canada

Cannabis (marijuana/hashish) is the most commonly used illicit drug in Canada. In 1989, approximately 6.5 percent of Canadian adults had used it in the past year, and approximately one in five of these used it at least once a week. More than twice as many men as women were users, with the highest rate of use in the 20 to 34 year age group.

In 1989, approximately 1.4 percent of Canadian adults had used cocaine or crack at least once in the past year. The highest rate of use was among adults 25 to 34 years of age: approximately 4.9 percent of men and 1.8 percent of women in this age group had used cocaine in the past year.

Use of LSD, speed, and heroin in the year preceding the survey was reported by 0.4 percent of Canadian adults.

Source: Canada. Health Promotion Directorate. Health and Welfare Canada. *National Alcohol and Other Drugs Survey: Highlights Report.* Ottawa: Minister of Supply and Services Canada, 1990.

One problem with assessing the effects of illicit use of such drugs is that regular users often engage in other unhealthy practices, making it difficult to separate the effects of drug use from these other factors. It is estimated, for example, that 67 percent of women who are addicted to heroin support their habit by prostitution, which puts them at higher risk of contracting sexually transmitted diseases. As a result, there is a high incidence of pelvic inflammatory disease, and consequently tubal infertility, among heroin users. Malnutrition and the concurrent use of other drugs are also confounding factors. Despite these research complexities, there is strong evidence to suggest that certain illicit drugs have an adverse effect on the fertility of men and women.

Cocaine

Cocaine use in men has been associated with problems with sperm motility, density, and morphology. One group of researchers found that cocaine consumption over a period of two years was strongly associated with low sperm concentration (compared to men who had never taken cocaine). Cocaine use over a five-year period was associated with low sperm counts, low sperm motility, and a greater incidence of abnormally shaped sperm. These researchers also found that the frequency of cocaine use was less strongly related to infertility than was the duration of use or how recently it had been used. They concluded that, given the number of men who use cocaine (particularly men between the ages of 20 and 35), it could play a significant role in infertility. Other researchers have found that cocaine directly affects the first stages of sperm production and can cause constriction of the blood vessels, which in turn may have harmful effects on testicular function.

Cocaine use during pregnancy is potentially harmful to both the woman and the fetus. Some studies suggest that the risks are severe, including maternal heart attack and higher rates of spontaneous abortion and fetal death, as well as congenital anomalies, growth retardation, and stillbirth. Cocaine has a well-documented constrictive effect on blood vessels. An increased frequency of neurological problems and brain damage in fetuses (resulting from the death of areas of brain tissue when their blood supply is cut off) has been reported by several groups of researchers. However, the many reports on adverse effects must be interpreted with some caution, as it is difficult to isolate the effects of cocaine use itself from the impact of poor diet, poor social circumstances, and other problems that are common among chronic cocaine users. Evidence of an increased likelihood of placental abruption due to cocaine use is fairly clear, however.

Heroin

In men, frequent use of heroin has been reported to reduce sex drive and affect sexual performance. The effect of heroin consumption on male sex hormone levels is not clear, as both increases and decreases have been reported. In women, heroin abuse has been associated with menstrual irregularities, including lack of ovulation. (Morphine use has also been found to have similar consequences.)

Marijuana

Some researchers have reported an association between marijuana use and declining levels of the hormones that control ovulation. It is not possible to say definitively whether marijuana or one of its components causes infertility, but some researchers believe that it may delay conception. Overall, however, relatively little is known about the effects of

marijuana use on human reproduction.

It is not clear how heroin, morphine, and marijuana affect pregnancy outcome. All three drugs pass easily through the placenta, and heroin use during pregnancy has been associated with negative effects such as withdrawal symptoms, which have been observed in 40 to 80 percent of infants born to heroin-addicted women.[12] The symptoms can last as long as three weeks after birth.

Low birth weight in infants born to women who used heroin during pregnancy has also been reported. It is difficult in most cases, however, to dissociate the effects of heroin use from other factors contributing to the poor health of the pregnant woman. Finally, no consistent associations have been drawn between heroin use during pregnancy and the risk of congenital anomalies in infants.

In view of the risks to general health associated with the use of illicit drugs, it is obviously common sense for all individuals to avoid their use. Women and men also need to be aware of the potential effects of illicit drugs on their reproductive health. The evidence suggests that we should be particularly concerned about use of these drugs by young people, especially those between the ages of 20 and 34. These individuals may experience a reduced ability to conceive; they may also have an increased risk of problems in pregnancy or birth complications if they have a pregnancy while using drugs.

> Most of the studies surveyed ... indicate that licit and illicit drugs can affect the physiological parameters linked to male and female fertility to varying degrees. However, none of them clearly demonstrates that any one of these drugs causes infertility. Consequently, considerable care should be taken in interpreting research into the effects of these drugs on fertility.
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> At the same time, it is impossible to overemphasize the need for experimental methods that lend themselves to multifactorial analysis. Human beings do not live in antiseptic laboratories. Attempts must therefore be made to assess the impact of multiple variables that cannot be submitted to very strict experimental control. Furthermore, the majority of people dependent on licit and illicit drugs do not limit their consumption to only one of those drugs. For example, smokers are more likely to consume alcohol than non-smokers ... Multiple drug use may have harmful effects that a simplistic statistical analysis cannot reveal.
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> *H. Boyer, "Effects of Licit and Illicit Drugs, Alcohol, Caffeine, and Nicotine on Infertility," in Research Volumes of the Commission, 1993.*

Health education in schools can help to reduce illicit drug use among young people by imparting information about the risks and by teaching skills to help them resist social pressures to use drugs. Public education programs can also help to convey messages about the risks of using drugs, and both federal and provincial/territorial governments have been involved

in this area. Specific efforts targeted at high-risk groups such as drug users, prostitutes, and youth who have dropped out of school are also required, as these individuals are less likely to be reached through such traditional channels as school programs. Heavy consumers of drugs within these groups must be reached with messages that encourage them to seek help, and counselling and treatment services must be made available to them. In particular, special programs are required to help young women who become pregnant while abusing drugs to stop using them.

In view of the number of known or suspected risks to reproductive health and fertility associated with the use of illicit drugs, people who are trying to conceive should avoid their use. Physicians should routinely ask couples seeking infertility treatment about their drug history, to ensure that use of drugs is not a factor contributing to their infertility. The Commission recommends that

54. Health Canada and provincial/territorial ministries of health coordinate their efforts to develop school-based and public education programs for young people concerning drug use.

55. Federal, provincial, and territorial governments ensure that funding for school health and public education programs related to drugs also include funding for the evaluation of program effectiveness.

56. Health Canada and provincial/territorial ministries of health develop specific programs targeted at high-risk individuals such as drug users, prostitutes, and street youth regarding drug use and, in particular, ensure that counselling and treatment programs be made available to help women who become pregnant while abusing drugs to stop using them.

57. Physicians routinely take a drug history from couples seeking infertility treatment to ensure that illicit drug use is not a possible contributing factor to their infertility.

Caffeine

Caffeine, widely consumed in coffee, tea, and soft drinks, enters the bloodstream very easily and is distributed throughout various body tissues. Its presence can be detected in the brain, testicles, secretions of the uterus, early embryonic cells, fetal tissue, amniotic fluid, and breast milk. Very few specific studies have been conducted on the effects of caffeine consumption on male and female fertility. Some studies have indicated a delay in conception as a result of caffeine consumption by women, but the methodology of these studies has been strongly criticized.[13]

Many studies have looked at the risk of congenital anomalies or spontaneous abortion as a result of caffeine intake (moderate drinking of coffee, tea, or colas) during pregnancy. The data on which to base judgements about moderate caffeine intake are fairly sound; in general, they show that the risks are minimal. Although some studies have shown a higher incidence of spontaneous abortion, premature labour, fetuses that were small for their gestational age, and congenital anomalies in these studies, it is difficult to isolate the effects of caffeine from other factors such as cigarette smoking. In summary, most well-designed studies have shown no link between caffeine and fetal anomalies. Data on which to base judgements about higher levels of caffeine intake are not available.

Although no clear link has been established between caffeine consumption and reduced fertility or pregnancy complications, it would nevertheless seem prudent for women who want to become pregnant to consume caffeine in moderation, particularly because research shows that caffeine does pass through the placenta to the fetus. The existence of a few studies suggesting an association between caffeine consumption and a delay in conception, notwithstanding their methodological shortcomings, suggests that women should err on the side of caution.

Less is known about the effect of caffeine consumption on male fertility. A few studies have associated caffeine consumption with potentially beneficial effects on male fertility, including increased sperm density and motility. Further research is required to determine whether there is an association between caffeine consumption and increased (or decreased) male fertility.

Stress and Psychological Factors

There is a very large literature on the effect of stress and psychological factors on infertility; it is a field in which there are many hypotheses but relatively few studies with data meeting a good standard of evidence. It is a difficult and complex area to study and in which to show cause and effect. Several psychological factors are suspected as potential risks to fertility. Some researchers believe that psychological problems associated

with psychosexual maladjustment, stress, lack of self-esteem, anxiety, mood disorders, depression, and psychosocial distress can have adverse effects on fertility in both men and women. The extensive literature devoted to these questions is often speculative, anecdotal, and contradictory. Psychological stress can result in decreases in testosterone levels and sperm counts in men and amenorrhea in women. Whether such stress-induced changes in hormone levels or reproductive functioning account for infertility is unknown. Definitive associations or cause-effect relationships between stress or other psychological factors and infertility have yet to be well documented in either men or women. A major difficulty in designing studies is how to measure stress and other psychological problems, as they are common in both fertile and infertile people.

Recently, researchers have begun to hypothesize about how stress might affect sperm production and ovulation. Stress stimulates several hormonal responses that help the body adapt to real or perceived threats by affecting the cardiovascular, energy-producing, and immune systems. Proper reproductive function depends heavily on the healthy functioning of these three major body systems, but it remains unclear how the body's reaction to stress might specifically affect or compromise reproductive ability.

There is a very large literature on the effect of stress and psychological factors on infertility; it is a field in which there are many hypotheses but relatively few studies with data meeting a good standard of evidence. It is a difficult and complex area to study and in which to show cause and effect.

Stress may also play a role in infertility by interfering with sexual desire or performance. Problems cited in this area include impotence, retarded ejaculation, ejaculation prior to intromission, infrequent intercourse, and vaginismus. However, no firm conclusions about the impact of stress on sexual desire or performance in men or women can be drawn on the basis of existing research in this area.

Psychosocial distress has been reported to be more common in couples who are infertile than in other couples. Researchers recently reviewed 30 existing studies to determine whether (1) stress causes infertility; (2) the experience of infertility (and/or associated treatment) brings about a certain level of stress; or (3) the two are interdependent, each having a causal effect on the other.[14] They found some evidence for all three hypotheses, particularly for the latter two. They concluded that in a small but consistent percentage of patients who are infertile, stress is likely to precede infertility and could play an important causal role in infertility among members of this group.

Recent studies have examined whether being treated for infertility places additional stress on couples who are infertile and sometimes exacerbates an infertility problem. A decrease in semen quality has been

reported in men whose female partners were undergoing *in vitro* fertilization.[15] A recent study of women undergoing infertility treatment, conducted at Concordia University in Montreal, found that, contrary to popular belief, it is not the treatment itself that creates the most stress for women, but rather finding out that the treatment has been unsuccessful. The authors suggest that women who are infertile need to be informed about and helped to cope with treatment failure — they need to develop strategies to help them deal with the stress occasioned by this.[16]

Medical Intervention and Infertility

Infertility can be an intended or unintended consequence of medical intervention or treatment. The infertility may be desired — for example, as a result of contraceptive use or after a tubal ligation or vasectomy. In some cases, medical intervention may be necessary and the resulting infertility anticipated — for example, after a hysterectomy. Much less frequently infertility may be an unintended side effect of a diagnostic or treatment procedure. In this section we discuss infertility associated with each of these categories.

Method of Contraception

Although the use of contraception indicates a desire to control fertility, certain methods of birth control carry a risk of unintended infertility or delay in the return to fertility when the method is discontinued. Other methods of contraception do not present such risks, but nor do they protect fertility. Methods that provide no protection against the transmission of STDs and thus no protection against this cause of infertility include the rhythm method, natural family planning, periodic abstinence, coitus interruptus/withdrawal, IUDs, oral contraceptives, post-coital contraceptives, hormonal implants, and injectable progesterone. Contraceptive methods that provide protection against STDs include condoms and, to a lesser extent, diaphragms, cer-

> Professionals and the public should be educated that the concomitant use of two contraceptive systems (dual protection) is necessary for both pregnancy control and the prevention of infection-based infertility. There is a need for public and professional education regarding the expert use of contraceptives with a view to protecting against unwanted pregnancy and an equal concern for future reproductive health.
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> *N. Barwin and W. Fisher, "Contraception: An Evaluation of Its Role in Relation to Infertility — Can It Protect?" in Research Volumes of the Commission, 1993.*

vical caps, and spermicides. These categories are particularly important for individuals who are likely to have more than one sexual partner, or whose partner has had other sexual partners.

Commission research, reported in Chapter 9, shows that, excluding those who are surgically sterilized, about 4 out of 10 Canadian women between the ages of 18 and 49, who are married or cohabiting with a male partner, use some form of contraception. The 1984 Canadian Fertility Survey shows that if those who are surgically sterilized are included, 7 out of 10 Canadians between the ages of 18 and 49 are using contraception.

Sterilization

Voluntary sterilization is the most widely used form of contraception in Canada. As shown in Table 14.1, in 1984 approximately 35 percent of those women 18 to 49 years of age who used some form of birth control had undergone a tubal ligation; and 12.7 percent of the women surveyed indicated that their male partner had undergone a vasectomy. (Tubal ligation involves surgery to block or sever the fallopian tubes so that the egg and sperm cannot meet. Male sterilization by vasectomy involves cutting and sealing the vas deferens, the tube that carries sperm from the testes.)

As shown in Table 14.2, in 1991-92, 22.9 percent of cohabiting women aged 18 to 44 years had a tubal ligation, and 18 percent of their male partners had a vasectomy. Overall, in 41 percent of couples, one or both members were sterilized. Not surprisingly, the proportion who have had surgical sterilization rises with age, and in 61 percent of couples in the 40 to 44 age group one or both members were sterilized. Data gathered by the Commission in 1991-92 suggest that the difference in the proportion of women who have undergone a tubal ligation and the proportion of men who have undergone a vasectomy is narrowing.

Voluntary sterilization is most likely to be chosen by men and women who are over the age of 35 and have had all the children they want. Uncertainty remains, however, about the percentage of those who have been surgically sterilized who come to regret this decision and seek to regain their fertility. One study of couples in Quebec found that about 15 percent of all sterilized couples felt "some regret" about their choice, and 10 percent would have tried to have another child were it not for the sterilization. A Scandinavian researcher who conducted a literature review estimated that between 1.3 and 12.7 percent of women who had undergone sterilization regretted their decision to some extent.[17] Research shows that women who regret having had a tubal ligation and who seek reversal are more likely to have been sterilized at an early age and to have had complex marital histories.[18]

Regret about sterilization may occur when a partnership has ended, for example by divorce or death, and the man or woman would like to have children with a new partner. Some couples may regret their earlier decision

Table 14.1. Percent Distribution of Women 18 to 49 Years of Age Using Contraceptives, by Method of Contraception and Age Group, Canada, 1984

Age group	Number of respondents	Percentage using contraception	Percent distribution of women using contraception, by method						
			Total	Female sterilization	Male sterilization	Pill	IUD	Condom	Other*
18-24 years	1 323	56.9	100.0	2.1	1.6	76.6	6.5	8.1	5.0
25-29 years	986	67.7	100.0	16.5	7.9	39.2	11.7	14.5	10.2
30-34 years	925	74.8	100.0	35.7	16.8	17.3	13.4	10.0	6.8
35-39 years	846	78.5	100.0	54.1	17.8	6.5	8.6	7.4	5.7
40-44 years	644	76.2	100.0	61.3	21.6	2.9	3.9	4.7	5.7
45-49 years	591	63.6	100.0	67.6	15.4	0.3	1.6	8.8	6.4
Total (18-49 years)	**5 315**	**68.4**	**100.0**	**35.3**	**12.7**	**28.0**	**8.3**	**9.1**	**6.6**

* Including diaphragm, spermicides, rhythm, withdrawal, and others.

Source: Balakrishnan, T.R., K. Krotki, and E. Lapierre-Adamcyk. "Contraceptive Use in Canada, 1984." *Family Planning Perspectives* 17 (5)(September-October 1985), Table 3.

Table 14.2: Percentage of Cohabiting Couples Who Were Contraceptively Sterilized (Either Tubal Ligation or Vasectomy) in 1991-92

	Tubal ligation and vasectomy combined			
Age group	**Number**	**Sterilized (%)**	**Tubal ligation (%)**	**Vasectomy (%)**
18-24 years	119	—	—	—
25-29 years	291	15.8	7.6	8.2
30-34 years	429	40.0	21.0	19.1
35-39 years	387	58.7	31.0	27.6
40-44 years	272	60.9	40.1	20.9
Total (18-44 years)	**1 501**	**40.8**	**22.9**	**18.0**

Note: Percentages may not sum to overall rates due to rounding.

Source: Commission analysis of data from Dulberg, C.S., and T. Stephens. "The Prevalence of Infertility in Canada, 1991-1992: Analysis of Three National Surveys," in Research Volumes of the Royal Commission on New Reproductive Technologies, 1993.

to be sterilized when one partner or both decide they would like to have additional children. Couples in this situation can attempt to have the sterilization surgically reversed — although the surgery can be complicated and success is not guaranteed in reversing tubal ligation or vasectomy. An alternative to reversal for a vasectomy is for the woman to attempt to conceive using donor sperm, although in this case the man will not have a child who is genetically related to him. In the case of tubal ligation, a woman can attempt *in vitro* fertilization, which bypasses the fallopian tubes.

Health Canada data on the number of individuals who undergo a rejoining of the vas deferens or fallopian tubes provide an upper estimate of the number of sterilization reversals being performed in Canada, although some of this surgery is done for reasons other than the desire to regain fertility after sterilization. For example, tubal surgery may be done for tubal blockage as a result of sexually transmitted diseases. In 1980-81, 1 711 procedures on the fallopian tubes or vas deferens were performed; in 1989-90, 4 433 were performed.[19] Estimated success rate for reversal of tubal ligation is 60 percent, and for vasectomy 39 to 78 percent.

Based on a survey of fertility clinics conducted for the Commission, it was estimated that between 5 and 15 percent of patients requesting *in vitro* fertilization had had tubal ligation. A similar percentage of people seeking assisted insemination were reported to have requested that procedure because of a vasectomy. In total for 1991, therefore, an estimated 10 percent (630 of 6 300) of couples having one of these treatments (3 400 assisted insemination, 2 900 *in vitro* fertilization; see research volume, *Treatment of Infertility: Current Practices and Psychosocial Implications*) would have previously had surgical sterilization. Given that there are approximately 1.5 million Canadian couples, in which the female partner is between the ages of 18 and 44, who have been surgically sterilized, this figure represents an extremely small proportion of all sterilized couples. It does, however, represent a significant minority of couples seeking infertility treatments in a given year. Moreover, more women are being sterilized at a younger age, and this may affect the number of couples seeking reversal of sterilization (see research volume, *The Prevalence of Infertility in Canada*).

Surgical sterilization must be viewed as permanent; it is essential that the decision and all its implications be considered carefully to minimize the likelihood that it will be performed on people whose desire to have children is likely to resurface or where change in life circumstances is likely to lead to regret about sterilization. The Commission recommends that

58. Physicians counsel couples considering surgical sterilization to ensure that they view the decision as permanent and to inform them what the likelihood of pregnancy is after reversal of tubal ligation or vasectomy.

Oral Contraceptives

As shown in Table 14.1, oral contraceptives (the pill) are the next most common form of contraception after surgical sterilization. Twenty-eight percent of Canadian women between the ages of 18 and 49 use the pill, the majority of them under the age of 34. In Chapter 10, we emphasized that women who use the pill for pregnancy prevention need to be aware that it provides no protection against sexually transmitted diseases. Women who are not in long-term monogamous relationships should therefore be encouraged, particularly by physicians prescribing oral contraceptives, to ensure that their partners use condoms for protection against STDs. Some data show that use of the pill may reduce the likelihood that an infection will move into the upper genital tract and may thereby lessen the risk of STD-induced pelvic inflammatory disease; it is not known how or why this is the case. However, use of the pill has also been reported to increase the risk of cervical infection caused by chlamydia; it is therefore important for physicians to recognize that oral contraceptives on their own are not appropriate for women who are not in long-term monogamous relationships. The Commission recommends that

> **59. Physicians and health care workers counsel young women and men who are not in long-term monogamous relationships about the need for dual forms of protection against pregnancy and sexually transmitted diseases. In particular, oral contraceptives should be used in conjunction with a barrier form of contraception to protect against not only pregnancy but also sexually transmitted diseases.**

As discussed in Chapter 10, there is also a need for school and community sex education programs to convey to young women (and men) that oral contraceptives, while offering an effective means to avoid pregnancy, do not protect them against sexually transmitted diseases. Pharmaceutical companies can also promote awareness of this important message by including package inserts in oral contraceptives to communicate the importance of using condoms for protection against sexually transmitted diseases by individuals who may be at risk.

Some women who stop using oral contraceptives may experience a delay before they become fertile again. One study of 5 580 fertile women who had stopped using contraception to conceive found that the proportion of previous pill users who conceived in the first month was 30 percent less than users of other contraceptive methods, but this difference disappeared by the third month.[20] A similar study confirmed that conception delays were temporary among oral contraceptive users, but found the delay to be

longer. While most of the difference disappeared by 24 months, very small differences were detectable up to three years later.

Women who are using oral contraceptives and plan to become pregnant in the future should be informed of the possibility of a delay before they are fertile again, so they can take this into account in their childbearing plans.

Intrauterine Devices

The IUD, which prevents pregnancy by stopping a fertilized egg from implanting in the wall of the uterus, is used by 8.3 percent of women who use some form of contraception. Women aged 25 to 34 are the group most likely to use an IUD. In the late 1970s and early '80s case control studies showed an association between the use of IUDs and several health risks, including pelvic inflammatory disease, ectopic pregnancy, and spontaneous abortion. Following this information, as well as the controversy surrounding the Dalkon Shield® and its removal from the North American market, there was a dramatic decline in the use of IUDs. The Dalkon Shield® is associated with a higher risk of pelvic inflammatory disease, and data on women who used it had been included in these earlier studies.

A recent international study by the World Health Organization used the largest data base of any IUD study, including 22 908 IUD insertions and more than 50 000 woman-years of follow-up, to evaluate the possible relationship between pelvic inflammatory disease and IUD use.[21] The study found a higher risk of PID during the first 20 days after IUD insertion. After that time, there was little difference between the incidences of PID among IUD users and other contraceptive users; the risk was low and constant during follow-up. The short-term risk of PID during the first days after insertion is likely related to the insertion procedure rather than the IUD itself. If bacteria are present in the woman's vagina at the time of insertion, or if they are introduced during the procedure, there is an increased risk of infection. This means IUDs should not be replaced routinely, but should be left in place for their maximum lifespan if the woman wishes to continue use.

Other studies have shown that in women who have had only one sexual partner, there is no increased risk of tubal infertility (which may result from PID) associated with IUD use.[22] However, the risk of pelvic inflammatory disease is greater in IUD users who were more likely to have been exposed to sexually transmitted diseases than among IUD users who were at low risk of exposure. This is to be expected, because the IUD does not provide protection against sexually transmitted diseases. Women who have had multiple partners, or whose partner has had multiple partners, are at greater risk of contracting a STD and subsequent pelvic inflammatory disease. This points to the need for physicians to ensure that a woman does not have a sexually transmitted disease, and is not at risk of exposure to STDs, before inserting an IUD. Women should be advised

to seek prompt medical attention if they experience symptoms of an infection after IUD insertion. They should also be warned that an IUD does not provide protection against sexually transmitted diseases. It also suggests the need for a trial to evaluate whether antibiotic use prior to an IUD insertion reduces the risk of subsequent infection.

The estimated incidence of ectopic pregnancy among IUD users is approximately 102 per 1 000 woman-years (a unit used to measure use — for example, 500 women using an IUD for two years would account for 1 000 woman-years of IUD use).[23] This is 2.5 times less than the chances of ectopic pregnancy in women who are sexually active and who use no contraception, but 200 times greater than the chances of ectopic pregnancy in women who use oral contraceptives (because they are very unlikely to become pregnant at all) and 10 times greater than for women whose partners use condoms. It would appear that the IUD does not cause ectopic pregnancies, but, unlike the oral forms of contraception, which prevent fertilization and thus also ectopic pregnancy, IUD use does not prevent ectopic pregnancy in predisposed women. Women who have a history of pelvic inflammatory disease (which increases their risk of ectopic pregnancy) or a previous ectopic pregnancy should therefore choose other forms of contraception.

In rare cases, women conceive despite using an IUD. The pregnancy rate is estimated to be 20 in 1 000 woman-years.[24] In these situations, there is an increased risk of pregnancy complications such as premature delivery if the device cannot be removed, which sometimes occurs because the thread attached to the IUD has retracted into the uterus. If the device is removed early in pregnancy, however, the risk of pregnancy complications is very low.

Research shows that the majority of women who stop using the IUD return to fertility in 12 months or less. One study found that 89 percent of women under the age of 30, and 78 percent of women 30 years of age and over, became pregnant within 12 months of having an IUD removed.[25]

Condoms

Condoms are the method selected by 9.1 percent of women using contraception (see Table 14.1). Condom use lessens the risk of transmission of STDs and subsequent infertility. In Chapter 10, we described the clear and urgent need for prevention programs to encourage condom use by sexually active young people. However, the values and mores that contribute to the inequality of women also make it difficult for some women to persuade their partners to use or to insist they use a condom. This points to the need for contraception methods to be developed that are much more directly under the control of women (as may become the case with vaginal condoms) as well as for education of both men and women to change attitudes toward condom use.

Other Forms of Contraception

Other forms of contraception (rhythm methods, natural family planning, periodic abstinence, coitus interruptus/withdrawal, spermicides, diaphragms, cervical caps, post-coital contraceptives, hormonal implants, and injectable progesterone) are used by 6.6 percent of women using contraception in Canada (see Table 14.1). Spermicides, diaphragms, and cervical caps provide some protection against STDs and subsequent infertility, but the rest do not. Injectables and implants have also been linked with delays in the return of fertility after their use is discontinued (see research volume, *Understanding Infertility: Risk Factors Affecting Fertility*): these types of contraceptives either are not available, however, or are used rarely in Canada. This is also the case for post-coital contraceptives (the morning-after pill).

Based on our review of what is known about the various methods of contraception, the Commission recommends that

60. Physicians inform women about the protection against sexually transmitted diseases provided by various forms of contraception and whether their use may be associated with a delayed return to fertility after contraceptive use is discontinued. Women who have had more than one sexual partner (or whose partner has had other partners) should be counselled to use protection against both pregnancy and STDs. Oral contraceptives should not be prescribed for those individuals without counselling about the need to protect against STDs as well as pregnancy.

Surgical Procedures in Women

Some surgical procedures for women may make it difficult or impossible for them to conceive. Hysterectomy always leads to infertility, as it involves removal of the uterus and usually the fallopian tubes and may also include removal of the ovaries. Certain other surgical procedures are associated with a low risk of complications that may lead to infertility.

Cervical surgery can affect fertility, as it may lead to incompetent cervix, a condition that results in the inability to carry a pregnancy to term. Cervical traumas associated with surgeries, such as conization of the cervix, dilation and curettage, and induced abortion, or with childbirth (either in natural delivery or with instrument use) are reported to be responsible for 30 to 50 percent of cases of incompetent cervix. However,

in most cases women who are infertile because of an incompetent cervix can be treated successfully with a procedure that involves circling the cervix with a suture. This improves the fetal survival rate in women with the condition from between 20 and 50 percent to between 70 and 90 percent (see research volume, *Understanding Infertility: Risk Factors Affecting Fertility*).

Many studies have been undertaken to determine whether induced abortions affect subsequent fertility and pregnancy outcomes since they are a frequently performed surgical procedure; in 1990, more than 92 600 abortions were performed in Canada, with the highest rates among women between the ages of 18 and 24.[26] The risk of infertility associated with induced abortion is complex to assess because factors such as the abortion technique used, the conditions under which the abortion is performed, whether the abortion is a first or subsequent abortion, and the age and other characteristics of the woman involved may influence the outcome, as well as the surgery itself. Despite these complexities, the most recent and rigorous studies do not demonstrate an increased risk of infertility or complications in a subsequent pregnancy after induced abortion. Statistics Canada data show that the rate of complications following abortion is low, at 1.1 percent in 1991. This is consistent with existing research studies, which show that between 1 and 2 percent of women have a significant post-abortion complication.

Complications that could lead to infertility include pelvic inflammatory disease, endometrial lesions, or haemorrhaging leading to the need for a hysterectomy. However, secondary hysterectomies (removal of the uterus) as a complication following an abortion are very rare: in Canada, the rate is less than one in 10 000 procedures. Estimates of the incidence of pelvic inflammatory disease following an induced abortion range from 0.1 percent to 5.0 percent, depending on the study.[27] The risk of developing pelvic inflammatory disease following an abortion is strongly influenced by whether the woman had a history of sexually transmitted diseases and PID and whether she was infected at the time of the abortion. We believe that research should be conducted to determine the benefit of screening women in high-risk groups who wish to undergo an induced abortion to ensure they do not have a sexually transmitted disease before the procedure is performed. The preventive use of antibiotics for such women should also be assessed and the results taken into account when the *Canadian Guidelines for the Prevention, Diagnosis, Management and Treatment of Sexually Transmitted Diseases in Neonates, Children, Adolescents and Adults* are updated.

Research has also examined whether there is an increased risk of ectopic pregnancy, spontaneous abortion, or premature delivery associated with subsequent pregnancies among women who have undergone an induced abortion. The risk of ectopic pregnancy following an abortion, if it exists, is too low to be detected in large-scale studies. Studies concerning the possible association between abortion and future spontaneous abortion

or premature delivery suggest that the risk is minimal. Whether repeated abortions over time are a risk factor for infertility is not yet known — some studies have reported an association, while others have found no association.

Caesarian sections do not appear to be a risk factor for infertility, although there is a slightly higher risk of spontaneous abortion in subsequent pregnancies than following a vaginal delivery.

Surgical Procedures in Men

Some forms of surgery on the male genital organs and accessory organs may have a subsequent effect on fertility. For example, urological procedures involving resection of the bladder neck or the prostate have been reported to lead to infertility through retrograde ejaculation. Following removal of the prostate glands to treat cancer, impotence has been reported in 60 to 90 percent of cases. The great majority of these procedures are performed at an age when it is likely that no further children are desired, so their impact is of importance not for fertility but for sexual functioning.

Testicular cancer may occur in younger men and has been reported to cause lowered fertility. Surgical removal of both testes, which might have to be done to remove a cancerous growth, will obviously result in infertility. Ways to modify treatment procedures to prevent subsequent infertility are being explored, and sperm samples can be frozen and stored before surgery if the man wants to retain the capacity to father a child later.

Radiation Therapy

The levels of radiation exposure that have a documentable effect on fertility are usually approached only when radiation is used in the treatment of cancer. The average man or woman will not be exposed to levels of radiation that could impair their fertility. Women and men who are to undergo radiation therapy should of course be informed of the possible effects on their fertility, and men who foresee wanting to have children should be made aware of the option to freeze their sperm in the event that they become infertile following a surgical procedure or radiation treatment; it is not possible to freeze eggs at present, but a couple could consider the possibility of freezing zygotes.

Diagnostic Testing Procedures for Infertility

Like other invasive medical procedures, testing procedures used to diagnose infertility in women and men have risks, including a slight risk that the procedure itself will lead to complications that may affect fertility.

Laparoscopy is the most commonly performed diagnostic procedure to assess fertility in women. It involves the introduction of an instrument

through the abdominal wall, or into a hollow organ, to visualize the tissues. It is used to observe the ovaries, fallopian tubes, and external walls of the uterus, and it is also used in egg retrieval for *in vitro* fertilization. In rare cases, the instrument used to elevate and manipulate the uterus during the procedure may perforate the uterus, resulting in internal bleeding. The risk of this occurring has not been documented for laparoscopies used in infertility diagnosis, but a 3 percent chance of this occurring has been reported during sterilization procedures via laparoscopy.[28] This is not usually a serious complication, and we found no data concerning the impact of it on fertility.

Hysteroscopy involves the insertion of a small scope through the cervix to visualize the interior of the uterus, to identify the existence of tumours, adhesions, and/or congenital anomalies. The test has a small risk of exacerbating an undiagnosed pelvic infection. Physicians should therefore ensure that women undergoing this procedure have been screened to eliminate the risk of a pelvic infection.

Hysterosalpingography is a test to determine whether a woman's fallopian tubes are structurally intact and her uterus is shaped normally. It involves the injection of a radiopaque dye directly into the uterine cavity. Normally the dye fills the uterine cavity and then flows through the fallopian tubes into the peritoneal cavity. If the dye does not pass through the tubes, then a blockage may be identified, either through X-ray or by observation during a laparoscopy. The incidence of infection following a hysterosalpingography has been reported to be between 0.3 and 3.1 percent in various studies. Our review did not reveal any studies of the impact of this test on fertility.

Endometrial biopsy is used to determine whether certain hormone levels, and the body's response to them, are normal. It involves the removal of a small sample of the endometrium for analysis. We found no data on the risk of infection or infertility following this test. If the woman is pregnant at the time of testing, there is a risk of removal of a conceptus during biopsy (0.6 to 6.3 percent).[29]

Vasography is a test used to detect the location of blockages or leaks in the duct leading from the testicles to the prostate (the vas deferens). Radiopaque dye is injected into the vas deferens to trace the path of the semen. One study found that 3 percent of 509 azoospermic men experienced obstruction of the vas deferens *after* undergoing a vasography.[30] Reducing the risk of complications is possible by performing a vasography on one vas deferens initially, instead of both. Only if an obstruction is found will a vasography be required for the other vas deferens as well, because one open vas deferens is sufficient to allow sperm to be transported out of the body during ejaculation.

Testicular biopsy is recommended only when a man has an extremely low sperm count that cannot be explained. It involves making a very small incision in the scrotum to remove a small quantity of testicular tissue for examination under the microscope. Some studies have reported that

testicular biopsies may lead to a temporary decrease in sperm production. Infection has been reported in only a few cases as a result of this procedure, and infertility as a result of undergoing a testicular biopsy is likely to be very rare.

Prescription Drugs

The use of certain prescription drugs is associated with fertility problems as a side effect. Infertility caused by chemotherapy treatment for cancer is common in both men and women, but it is not considered to be a permanent effect of this treatment. As well, pregnancy loss and some teratogenic effects in the fetus have been reported from chemotherapy treatment for cancer during pregnancy (the effects varying with the dose and length of the treatment period).

Use of barbiturates has been associated with menstrual abnormalities in women and with hormonal changes in both men and women, although neither of these conditions necessarily implies fertility problems. Barbiturates have also been reported to pass quite easily through the placenta to the fetus.

It is suspected that anti-depressants may have side effects on erection and ejaculation ability in men and menstruation in women. As well, neuroleptic drugs may cause a decline in the volume of sperm produced. To date, however, no studies have directly examined the reproductive effects of these two types of drugs. Very few epidemiological data are available on the effects of these drugs when taken during pregnancy, but the risk of teratogenic effects as a result of *in utero* exposure is thought to be very small.

Studies have documented that drugs to control high blood pressure have the side effect of loss of sexual desire in some patients, difficulty in achieving or maintaining erection, and difficulty in achieving orgasm. These drugs have also been associated with menstrual disorders. Researchers note that it is difficult to determine with certainty whether these effects are a direct result of drug use, or whether they are related to the condition for which the drugs are taken. Some anti-hypertensive drugs have been associated with a substantial risk of oligohydramnios (too little fluid around the developing fetus) and fetal distress or death when taken in the latter part of pregnancy. But no studies of congenital anomalies in infants born to women who have been treated for hypertension have been reported.

Certain drugs used to treat gastrointestinal illnesses have been associated with sexual dysfunction and limited sperm production. However, gastrointestinal illnesses themselves can affect the reproductive system by altering concentrations of certain hormones. Our review did not identify any good data on the effects of these drugs on fetal development.

It is clearly important that physicians inform their patients about the risks associated with any drug they prescribe, including its possible effects

on their fertility. These risks must be weighed against the potential benefits of taking the drugs and the need to treat the illness. There are, however, obstacles to informing about the risks — good data may simply not be available, or such data as do exist may not have been widely disseminated in an arm's-length and objective way. Currently, many doctors receive much of their information on drugs from pharmaceutical companies or from the *Compendium of Pharmaceuticals and Specialties*. No body or mechanism exists at present to assemble good data regarding drugs and to make this information accessible to physicians (see Chapter 18).

General Sources

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Preventing Infertility

As we have seen, our knowledge about the contribution of various risk factors to the overall prevalence of infertility is incomplete. Nevertheless, what remains compellingly clear is the urgent need for national leadership and cooperation among the key partners — the federal government, the provinces and territories, health professionals, educators, volunteer groups, and others — so that as many people as possible can be spared the pain of wanting but not being able to have a child.

We have made specific recommendations to reduce the prevalence of infertility by preventing exposure to risk factors in the sections dealing with each of those factors. In some areas, such as sexually transmitted diseases and smoking, the risk is sufficiently clear and the route to prevention sufficiently known that it is possible to make fairly detailed recommendations; in other areas, such as environmental and workplace hazards, the need for more information limits the ability to develop effective prevention measures, but we have outlined some steps that can be taken. What is clearly evident, however, is that we lack any comprehensive or coordinated approach to promoting the reproductive health of Canadians generally or preventing infertility in particular. What is also evident from the Commission's work in this field is that prevention is a feasible and desirable approach. We have the ability to design programs to address specific known risk factors, and methods of evaluating those programs for effectiveness are being developed.

Prevention of infertility is a subject that naturally prompts questions about prevention in general and infertility prevention in particular. Does prevention work, and can it be effective enough to make a discernible impact on the prevalence of infertility and the demand for infertility treatment? How do we know when an infertility prevention program is effective or successful? What types of prevention approaches work for what

kinds of risk factors? Posing questions of this type is consistent with the Commission's evidence-based approach to new reproductive technologies.

The Commission has concluded that there are indeed risk factors for infertility, such as sexually transmitted diseases and smoking, that can be addressed through prevention programs; that some risk factors, especially environmental and workplace exposures, can be identified, studied, and contained with appropriate countermeasures; that other risk factors, including those related to weight, eating disorders, and exercise, may be amenable to counselling and related responses; and that the potential effects of the less reversible risk factors, such as endometriosis and biological aging, can be addressed through timely and accurate information about their implications for individual decisions about childbearing.

As many Canadians recognized in their testimony before the Commission, the current emphasis on treating infertility after it has occurred must be rebalanced to include more attention and resources to preventing infertility in the first place. Although this perspective is tempered with the recognition that some infertility will not be amenable to prevention — even if we had unlimited resources to devote to this effort — there remains a strong sense among Canadians that many women and men who seek infertility treatment would not have needed such services if timely and appropriate prevention programs had been in place.

> There is a need to increase public awareness of the risk factors that lead to infertility. Nurses are in a key position to disseminate information about the causes of infertility through educational programs aimed at reaching those involved in at-risk activities ... The need for health promotion and disease prevention strategies related to the infertility is extremely important for adolescents.
>
> *Brief to the Commission from the Association of Registered Nurses of Newfoundland, April 28, 1992.*

In this chapter, therefore, we set out our strategy for a national action plan to reduce the prevalence of infertility and, in general, to improve the reproductive health of Canadians. We developed this plan in keeping with our commitment to our guiding principles and an evidence-based approach to health care provision. We believe that one entity must be given formal responsibility for developing policy and identifying broad strategies. We therefore propose the establishment of a permanent sub-committee of the National Reproductive Technologies Commission, the Infertility Prevention Sub-Committee, and our recommendations to this effect are presented at the end of this chapter.

In calling for a greater emphasis on infertility prevention, the Commission is among the many and growing voices advocating a new approach to health, some of which are detailed later in this section. While medical care can be vital in restoring health when specific problems occur,

there is increasing recognition that acute care is actually quite limited in its ability to influence overall health. We discuss this shift in emphasis from acute care to prevention in this section. This shift implies that adequate resources should be devoted to prevention. To date, however, that has not been the case; this has presented further obstacles to an effective and comprehensive approach.

Commissioners believe that the best strategy for preventing infertility in men and women involves a coordinated and integrated approach within a larger context; to be successful, a national prevention effort must place prevention in the larger context of social and health policy in Canada. For instance, as we note in the chapter on aging and infertility, workplace policies and the availability of accessible and affordable child care could have a significant impact on the decision to delay childbearing. Similarly, broadening definitions of occupational health and safety to include reproductive health could result in the more timely identification of hazards to reproductive health and the development of measures to reduce exposure to them. Prevention thus requires a multifaceted approach, with coordinated action on many fronts simultaneously and the involvement of a diverse range of partners in these efforts. This will help to overcome some of the barriers we described — the lack of definitive knowledge of the links between various risks and infertility, the inter-relationships among the various risk factors, and the complexity of the contexts and systems within which risk factors arise and prevention responses must take place.

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The most important priorities for a national reproductive health strategy that emerged from our review of the evidence on risk factors for infertility are as follows:

- reducing the incidence of sexually transmitted diseases, particularly among young women;
- reducing smoking among women and men and preventing smoking among young people; and
- increasing public awareness of the effect of delaying childbearing on fertility.

Also important are the expansion of scientific and medical knowledge about workplace and environmental risks to infertility, and encouraging women and couples who want to have a child not to drink alcohol, use drugs, or

exercise excessively and to maintain sound eating habits and a healthy body weight.

The Commission has identified several key areas for action in reproductive health, where priorities need to be identified and strategic plans for action established, including the following:

- Research into risk factors for infertility, so that we have the information needed to guide prevention policy — evaluation of prevention programs is an essential part of this research effort, as is stable and continuing funding of research, program development, and evaluation.
- Education of the public and practitioners to promote awareness and understanding of risk factors and how to protect reproductive health. Public education programs should be non-judgemental, reflect the pluralistic nature of Canadian society, and address the complex issues surrounding sexuality in our society. They should also be evaluated periodically to determine whether they are having the desired effect.
- Working with provincial/territorial education ministries and school boards to incorporate information on fertility protection into school-based health promotion programs. In addition, special programs will be needed to reach young people at high risk who are not in school.
- Developing and providing relevant and clear information to assist women, men, and couples in making decisions related to their reproductive health, to prevent specific problems, and to seek appropriate assistance when necessary. This information must be culturally relevant to different target groups, including adolescents, Aboriginal people, and those who speak neither English nor French.
- Persuading all levels of government to fund and support reproductive health promotion and infertility prevention programs and their evaluation.
- Identifying and encouraging needed legislative change, such as changes in occupational health and safety and environmental legislation, to make it more effective in protecting reproductive health.
- Facilitating the involvement of key partners, such as the education, legal, and social service sectors, in prevention and promotion efforts. Pharmaceutical companies have a role to play with respect to including information inserts regarding condom use in packages of contraceptive hormones.
- Identifying and promoting professional and support services such as counselling and outreach that are not in place but are needed to make prevention possible. This should be within the context of larger prevention and health promotion efforts, building, for instance, on campaigns to reduce smoking so that they include risks to fertility, or on existing contraceptive counselling so that it includes STD

prevention and targets specific populations, particularly adolescent women.

- Encouraging relevant changes in the training of health care providers in reproductive health promotion and infertility prevention at both the undergraduate and postgraduate levels. Curricula should address the factors that affect fertility, as well as the general reproductive health and well-being of both women and men. Continuing medical education in these areas is vital not only for physicians, but for all health care providers, whether they are working in the institutional or community health sector or in private practice.

We believe the National Reproductive Technologies Commission has a key role to play in these efforts, and we discuss the various initiatives we propose at the end of this chapter.

The Role of Prevention

There appears to be strong support in many parts of the country for initiatives that redirect resources toward disease prevention and health promotion. The federal government has been involved in formulating new conceptual frameworks for health and health care services. As early as 1974, the Department of National Health and Welfare in its document *A New Perspective on the Health of Canadians: A Working Document* took a strong position showing that factors other than health care services — such as human biology, environment, lifestyle, and health care organization — are key determinants of health. In 1986, the Department of National Health and Welfare issued a paper entitled *Achieving Health for All: A Framework for Health Promotion*, which set out three major strategies for promoting health: fostering public participation, strengthening community health services, and coordinating healthy public policy. In the same year, an international conference on health promotion sponsored by the World Health Organization, the Department of National Health and Welfare, and the Canadian Public Health Association produced the *Ottawa Charter for*

> We have been disturbed by the media coverage of these hearings pitting women who are cautious about new reproductive technologies against women who feel they may benefit from them. We believe an approach including public education, research, and funding that emphasizes prevention benefits all women.
>
> *R. Kilpatrick, Association of Ontario Midwives, Public Hearings Transcripts, Toronto, Ontario, November 20, 1990.*

Health Promotion, setting out a blueprint to help the international community develop strategies for promoting health.

The federal government has not been alone in trying to encourage a shift of effort and resources toward prevention and health promotion. Over the past few years, many provincial governments have appointed commissions and task forces. A common theme in their recommendations has been the need for initiatives that shift resources from curative treatments toward prevention.

> What reason is there for resorting on a wide scale to the use of technologies which counter infertility without first carrying out some in depth research into the causes and treatment of infertility? No serious, ongoing effort has been made to inform teenagers about sexually transmitted diseases which are one of the leading causes of sterility and involuntary infertility. While education and training may not be sensational or newsworthy approaches, from a social standpoint, they are extremely effective. Once more, prevention is being overshadowed by the rush to find a cure. [Translation]
>
> *Brief to the Commission from Confédération des organismes familiaux du Québec, February 2, 1991.*

In 1983, the Quebec government commissioned a provincial study on health promotion (*Objective: A Health Concept in Quebec: A Report of the Task Force on Health Promotion*). The task force set out 10 measurable health objectives and what was needed to achieve these objectives. Following this review, a 1986-87 commission of inquiry (Commission d'enquête sur les services de santé et les services sociaux — commonly known as the Rochon Commission) assessed the operation and financing of the health and social service systems in the province. Among its 27 recommendations for improving these systems was a proposal to reorganize infertility health services along a continuum — starting with health promotion, followed by treatment of infertility and, finally, recourse to reproductive technologies. In response to these and other reports of the task forces that it had struck throughout the 1980s, the Quebec Ministry of Health and Social Services released a document in April 1989 entitled *Improving Health and Well-Being in Quebec: Orientations*. The ministry proposed four major strategies for future action — one

> We also urge the Commission to recognize that the real problem is not how to "cure infertility" but rather how to lay the framework for a series of strategies that will prevent infertility and enhance the reproductive wellbeing of all Canadian women.
>
> *S. Ballangall, YWCA of Canada, Public Hearings Transcripts, Toronto, Ontario, November 20, 1990.*

of which was the prevention of health problems and the promotion of health and well-being.

Ontario has also been active: the Ontario Premier's Council on Health Strategy was established in 1987 in response to the recommendations of three major provincial inquiries into health and health care. The Council's mandate was to provide leadership and guidance in achieving health for all citizens of Ontario. It developed guiding principles that included greater emphasis on promoting and maintaining health and access to a balanced system of treatment. Based on these principles, the Council outlined a vision of health that took account of the importance of economic and social determinants of health, as well as the importance of equitable access to affordable and appropriate health care.

> In terms of public policy priorities, we recommend that research funding be redirected to the following areas:
>
> Firstly, to research into the causes of infertility linked to the environment, to sexually transmitted diseases, and to the use of certain methods of contraception.
>
> Secondly, to research into the long-term effects of all reproductive technologies, including so-called "routine" prenatal exams and hormonal drugs.
>
> Thirdly, to research into no-risk contraceptive methods. [Translation]
>
> *M. Bégin, Canadian Research Institute for the Advancement of Women, Public Hearings Transcripts, Ottawa, Ontario, September 20, 1990.*

Increased emphasis on prevention and health promotion was also one of the key directions for change identified by the Premier's Commission on Future Health Care for Albertans in 1989. The Premier's Commission recommended that, by April 1995, a minimum of at least an additional 1 percent of the total Alberta health budget be allocated to health promotion and illness prevention programs.[1]

In 1989, the Nova Scotia Royal Commission on Health Care identified several principles to guide change in the provincial health care system, including the need to attain a better balance between the curative and preventive components of health care. Health promotion and disease prevention accounted for 2 percent of the budget of the Nova Scotia Department of Health in 1990-91. In response to that commission's recommendations, the department plans to increase its spending on community health to 4 percent of total departmental spending. These funds will be channelled to the development, implementation, and evaluation of comprehensive health promotion and disease prevention programs.

The 1990 Saskatchewan Commission on Directions in Health Care also called for greater emphasis on health promotion. It recommended that the mandate of traditional public health programs be expanded to place

more emphasis on health promotion and maintenance of good health through programs of disease prevention, public education, personal and group counselling, and monitoring of environmental and community factors that affect the health of individuals.[2]

Similarly, the 1991 report of the British Columbia Royal Commission on Health Care and Costs noted that almost all health care funds are devoted to treatment; less than 1.5 percent of funds are spent on trying to prevent illness or injury. This report, too, makes a strong and clear call for a shift in priorities: "More money should be spent on the prevention of illness or injury and on protecting health. The least amount of money possible should be spent on providing the necessary high quality curative services."[3]

> For the sake of the public's health, your Commission should formulate social policies aimed at modifying lifestyles or behaviours that cause infertility, much in the same way as there are social policies aimed at eliminating certain lifestyles or behaviours associated with the use of toxic substances (alcohol, tobacco, drugs). There is no logic in increasing the number of infertility treatment clinics without addressing the lifestyles that cause infertility. Similarly, it would make no sense to increase the number of lung cancer treatment centres without also stepping up our efforts to eliminate smoking. [Translation]
>
> *L. Simard, Action Famille, Public Hearings Transcripts, Montreal, Quebec, November 22, 1990.*

In short, prevention is an idea whose time has come. The approach we are advocating, based on our guiding principles, the ethic of care, and evidence-based medicine, is part of a broader trend evident not only in the reports of provincial royal commissions and inquiries and documents issued by provincial/territorial and federal health departments, but also in the work of community health organizations, health policy advocates, and consumers across the country. It is clear, then, that prevention is going to assume a more prominent role in the future of public policy, resource allocation, and individual decision making in this country.

Obstacles to Shifting Resources to Prevention Programs

Despite clear recognition by governments of the need for greater emphasis on prevention, substantial change in provincial budget allocations has not occurred. The greatest proportion of health dollars continues to be spent on acute care. At present and for the foreseeable future, new dollars are not likely to be made available to be allocated to prevention and health promotion. This means that shifts *within* existing provincial budgets will be necessary to make a new emphasis on prevention and health promotion anything more than words. Deciding where these shifts should occur is very difficult, however, because the evidence on

which to make such decisions is incomplete — few data have been collected, for example, on what medical treatments work, which are ineffective (or even harmful), and what approaches to prevention are successful. Such decisions are also very difficult politically, given the strong public perception that more medical care means better health. Canadians need to understand that not all medical care is of equal value, and that it may often be wiser to allocate funding to effective prevention than to ineffective treatment.

Establishing the relative frequency and severity of various risk factors for infertility in the Canadian population is an important initial step in any priority-setting exercise aimed at deciding what resources are needed to tackle the prevention of infertility. Since resources are inevitably limited, such a study could help to direct the most effective resource allocation. Without a systematic effort to establish the relative importance of various identified causes of infertility, there is a risk that important preventable causes of infertility will not receive the attention they deserve. This could lead to resources being focussed on treatment of problems deemed treatable. In turn, this tends to displace attention from the relative costs of this approach versus a prevention-oriented approach, or from attempts to introduce prevention where it could be potentially beneficial.

P. Millson and K. Maznyk, "Pilot Study on Determining the Relative Importance of Risk Factors for Infertility in Canada," in Research Volumes of the Commission, 1993.

Resistance to reallocating funds to prevention also stems from the fact that it is much easier to advocate the allocation of resources to meet the needs of identifiable individuals than to devote them to serving unidentified individuals. Preventive programs also help individuals, but it is difficult to identify who they are, whereas medical programs relate to particular individuals in a direct, immediate, and documentable way. It is easier to justify public expenditures when moving media stories and articulate advocates of identifiable individuals are involved. People sympathize with someone anxiously awaiting medical treatment they perceive to be needed, even if it has not been proven to be of benefit. It is less easy to generate public sympathy for the unidentifiable people helped by promotion and prevention programs, even if the suffering avoided is equally real and even, in collective terms, greater. It is difficult to stop providing expensive treatments that deal with identifiable individuals, even if the treatment is of questionable value to many of those who receive it.

Reallocating funds from medical treatments to prevention does not require, however, that effective programs be closed down. There is room within many therapeutic programs to save money by allocating resources appropriately within them — through early discharge programs, for example, or establishing criteria for receiving a given treatment based on evidence of what works for what indications. Rigorous application of these

and other approaches would make it largely unnecessary to withdraw funding from efficacious treatment programs in order to generate funds for prevention.

In categories of cases where no proof of effectiveness exists, or where treatments have been demonstrated ineffective, we believe funding should be withdrawn and reallocated to effective prevention programs. We recognize, however, that many groups (health care workers, physicians, hospital employees, pharmacists, and others employed in the health care industry) have a strong interest in maintaining or increasing funding for treatment; these groups, together with the public, can exert significant pressure against resource reallocation, giving politicians little room to manoeuvre when they try to shift resources to fund prevention programs.

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Another impediment to resource reallocation is that prevention programs seem to have required a greater burden of proof before being funded than medical treatments. Even though many medical and drug treatments have not been proven effective through appropriate testing and evaluation, they are widely used and funded by provincial health care systems. Yet funding requests for prevention programs are often turned down because their impact has not been established with certainty. Even where prevention programs have been shown to be effective, funds may not be provided to maintain or extend a program.

> Prevention programs are hard to evaluate. Not all infertility is preventable, and it would be difficult to count the number of cases of infertility averted. However, common sense dictates that prevention programs are the most obvious and the least expensive step in reducing infertility, and that these programs must be available to all potential parents.
>
> *M. McGovern, Women's Issues Group, Canadian Federation of University Women, North York, Public Hearings Transcripts, Toronto, Ontario, October 31, 1990.*

A further difficulty inherent in using assessments of prevention programs is that it is not always possible to generalize from the results of one effective program. For example, sexuality education and support services designed to alter the sexual attitudes or behaviours of high school students cannot be applied to youth who have dropped out of school, even if they have been demonstrated effective in a high school setting.

Prevention programs must be designed with the identified needs, knowledge base, and motivations of specific target groups in mind.

One reason cited for the shortage of data evaluating the results of prevention programs is the difficulty of measuring these results. For example, many prevention programs are intended to elicit behaviour changes in individuals, and both the change and whether the change produced the intended results are difficult phenomena to measure. Similarly, people are exposed to many factors, including peer pressure, media images, and the home environment, that make it difficult to assess whether it was the prevention program itself or other factors that actually influenced behaviour. However, many preventive programs are just as easy to measure as many treatment programs. Many medical treatments (for example, coronary bypass surgery in patients over 65 years of age) are equally problematic to assess because other factors (such as social support, socioeconomic status, diet, exercise, tobacco use) influence the health of patients who have undergone the procedure. However, even in a short time, it is possible to measure reduced incidence of disease (for example, sexually transmitted diseases, reduction in incidence of low birth weight) in a population that has received a prevention program, so that prevention programs are not necessarily more difficult to evaluate than medical treatments.

In the view of the Commissioners, it is generally inappropriate to subject preventive efforts to more stringent effectiveness criteria than medical treatments before funding them. The effectiveness of the great majority of treatments — like the effectiveness of most prevention programs — remains unproven. Society's approach to resource allocation for medical treatments and prevention programs should be the same — both need to be evaluated rigorously before they are disseminated widely and then regularly after that to determine their continuing effectiveness. Funding for prevention programs should include funding designated for measuring outcomes. This is analogous to the evidence-based approach we recommend for treatment programs.

Society's approach to resource allocation for medical treatments and prevention programs should be the same — both need to be evaluated rigorously before they are disseminated widely and then regularly after that to determine their continuing effectiveness. Funding for prevention programs should include funding designated for measuring outcomes. This is analogous to the evidence-based approach we recommend for treatment programs.

We recognize that this is not a simple task. Prevention is a complex undertaking in its own right, and one that cannot be taken for granted in terms of the need for information to support program evaluation and provide guidance of resource allocation and policy decisions.

Moreover, we also recognize that the standards of evidence for treatment and prevention may vary, even though an evidence-based approach should apply to both. There is an additional onus, for example, on those responsible for disease prevention and health promotion programs aimed at those who consider themselves healthy to ensure that they do no harm. This is not always the case with treatment; for instance, even in the absence of definitive evidence, a risk of causing harm by trying an untested procedure may on occasion be justified to help someone with a very serious illness if there is no alternative treatment available. Such a risk would not be justifiable in the context of prevention, which might require a higher standard of evidence of the effectiveness of a new program before its use could be justified if the potential for harm is great.

Building on Success

Despite the difficulties associated with evaluating prevention programs, there is enough evidence to show that some programs are effective in preventing exposure to some of the risk factors for infertility. For example, a comprehensive approach to reducing smoking among Canadians, including legislation, public education, school programs, and high taxation, has significantly reduced the prevalence of this risk factor.[4] Building on this successful approach to include a specific infertility prevention component could add significantly to these successes.

Similarly, AIDS education that combines information and skills building and motivates individuals to use these skills has been shown to reduce high-risk behaviour significantly. Such an approach has also proven successful in reducing pregnancies among adolescents and college students.[5] As discussed in this Part, an approach that combines these three elements could also reduce rates of sexually transmitted diseases among young people by "piggybacking" infertility prevention onto existing efforts.

It is clear, then, that the real issue in prevention is not feasibility but political will. Given that prevention programs can be evaluated, there is nothing in principle preventing governments from making informed decisions about prevention program development and resource allocation in general and infertility prevention and reproductive health promotion in particular. This Commission has concluded that preventing infertility and promoting reproductive health have at least as much to contribute in terms of rationalizing the use of scarce resources as treating fertility problems after they have occurred. Other inquiries have reached similar conclusions;

This Commission has concluded that preventing infertility and promoting reproductive health have at least as much to contribute in terms of rationalizing the use of scarce resources as treating fertility problems after they have occurred.

what is missing is the will to make policy in light of this information. In our view, the onus is no longer on advocates of prevention to make their case but rather on policy makers to show why they have not acted to make prevention a more important part of government priorities and agendas for action.

Cost Effectiveness

Some advocates of prevention cite cost effectiveness (saving money) as the reason why resources should be shifted from medical treatments to prevention, assuming that prevention will cost less than treatment. There are two problems with this argument. For prevention programs to be more "cost effective," they must yield more health benefits than use of the same funds in treatment. In other words, the cost of the prevention program must be less than the cost of providing medical treatment to people affected by the health problem in question — prevention must result in better health status for a larger number of people. Some prevention programs, such as fluoridation of drinking water and childhood immunizations, clearly meet these standards and save substantial health care dollars. However, many other prevention programs are less cost effective than acute care would be, because they are aimed at preventing diseases that affect only a relatively small proportion of the population. Programs that aim to reduce individual exposure to risk factors associated with infertility may well be cost effective in the long term when compared to medical treatments for infertility, as many of these have substantial direct and indirect costs associated with them, but the data that would make it possible to determine this do not exist.

> When so many determinants of reproductive health are outside the medical care system, viewing change in that system alone as the way to produce reproductive health is using the wrong tool to do the job.

This brings us to the second problem with the cost-effectiveness argument and to the discussion that began this section. Evaluating programs solely on the basis of cost effectiveness ignores the ethical basis for preventing the harms associated with injury, disability, and disease. There are compelling reasons for a compassionate society to protect the fertility of individuals that go well beyond economic arguments. Infertility treatments are invasive and not always successful; like any medical treatment they entail risks, and there are also emotional and financial costs associated with them. The most humane approach is to help people protect their fertility, rather than providing treatment to help them conceive after they have already become infertile — to avoid harm rather than try to ameliorate its effects after the fact.

The cost-effectiveness argument paints too limited a picture, because it tends to frame the issues in terms of resource reallocation within the

health care system. It is important to be clear that prevention is not simply — or even mainly — the concern of the health care system. In fact, effective prevention will be possible only if there is change outside the medical system — in the educational, legal, and social sectors as well. Prevention is a shared responsibility of a broad range of sectors in society and has important implications for individual Canadians as well. When so many determinants of reproductive health are outside the medical care system, viewing change in that system alone as the way to produce reproductive health is using the wrong tool to do the job. What is needed is a coordinated and multifaceted response — no individual sector has all the tools or resources to do what is needed. The Commission is therefore urging strong national leadership to begin the job of mounting a concerted effort to encourage all relevant sectors to work together to prevent infertility and promote the reproductive health of Canadians.

We recognize that provincial budgets are under tremendous pressure and that policy makers are hard pressed to find funds to maintain existing services. In this environment, reallocating resources to prevention will be difficult. Moving toward an evidence-based approach to medicine, however, with new funding provided only for treatments that have been demonstrated to be beneficial for specific medical conditions, together with evaluation of unproven treatments now in use, would permit reallocation for prevention. Prevention programs that are funded in this way should also be evaluated to determine their effectiveness. In other words, the same approach that we are advocating for assessing and funding medical treatments should also be used with prevention initiatives.

It is critical that we use our common resources effectively to achieve optimal health for all Canadians. If policy makers continue to pay only lip service to this concept, prevention will not be given the necessary emphasis, and we will continue to see an increasing proportion of our tax dollars being consumed by medical care; eventually, the health care system will collapse under the strain. This does not have to be the result if we make the decision now to move in a new direction.

Moving toward an evidence based approach to medicine, however, with new funding provided only for treatments that have been demonstrated to be beneficial for specific medical conditions, together with evaluation of unproven treatments now in use, would permit reallocation for prevention.

It is clear that most prevention efforts, however, will have to take place outside the health care system if they are to be effective. The education, social services, and legal systems are essential partners in effective prevention strategies and programs. Tackling the issue of infertility at its source means adopting a comprehensive, coordinated strategy for protecting the reproductive health of Canadians; reallocation of some

resources within the health care system is not enough and should be only part of Canada's response.

A Comprehensive Response

In earlier chapters of this Part, we recommended programs, guidelines, and legislation that could help to reduce the exposure of individuals to the various factors that pose a risk to fertility. They ranged from improving sex education programs in schools to evaluating substances in the workplace and the environment for their reproductive health effects. In this final section, we review the role we propose for the Infertility Prevention Sub-Committee of the National Reproductive Technologies Commission in leading, supporting, and supplementing existing efforts by governments, health professionals, educators, volunteer groups, and others to reduce the prevalence of infertility in Canada and to improve the overall reproductive health of Canadians.

We have noted that there is no infertility prevention policy or strategy in Canada at present that is national in scope. Existing programs address aspects of reproductive health in a fragmented way, with little coordination between federal and provincial/territorial governments, health organizations, health care professionals, and those involved in public education. This is in contrast to what has been achieved, for example, in the field of reducing tobacco consumption, where a national committee, with representatives from federal and provincial/territorial governments and non-governmental health organizations, has successfully developed a national strategy involving a full range of actions by many sectors and groups to reduce tobacco use in Canada.

Infertility in particular, and sexual and reproductive health in general, clearly merit a similar comprehensive and coordinated response, because they are issues that affect all Canadians. It is essential that efforts to prevent known reproductive health hazards, such as sexually transmitted diseases, be integrated and coordinated to maximize their efficiency. At the same time, it is necessary to intensify and coordinate public and private research efforts directed at improving the existing pool of knowledge about the incidence, impact, and prevalence of reproductive health risks, whether caused by environmental, workplace, medical, or other factors. It is important that programs directed to infertility prevention and reproductive health be evaluated for effectiveness. Finally, it is imperative to raise public awareness about reproductive health hazards and to increase public accountability in decision making related to the development and

implementation of programs and initiatives aimed at infertility prevention. The Commission therefore recommends

61. The establishment of a permanent sub-committee of the National Reproductive Technologies Commission, with primary responsibility in the field of infertility prevention and reproductive health promotion.

The Infertility Prevention Sub-Committee would play an important role in all the areas just enumerated. As we explained in Chapter 5, the Infertility Prevention Sub-Committee would be one of six permanent sub-committees of the National Commission, along with those dealing with assisted insemination services, assisted conception services, prenatal diagnosis, embryo research, and the provision of fetal tissue for research and other designated purposes. Like National Commission members themselves, we recommend that at least half the Infertility Prevention Sub-Committee members be women, and that all members be chosen with a view to ensuring that they have a background and demonstrated experience in dealing with a multidisciplinary approach to issues, as well as an ability to work together to find solutions and recommend policies to address the complex challenges of infertility prevention and reproductive health promotion in a way that meets the concerns of Canadian society as a whole.

The Infertility Prevention Sub-Committee would have several functions. In addition to the priorities identified at the beginning of this section, the Sub-Committee could decide to establish ad hoc working groups to deal with one of more of these functions, if appropriate:

- Promoting and supporting consultation and cooperation among federal and provincial/territorial departments of health, labour, and the environment, among agencies such as the Canadian Centre for Occupational Health and Safety and the Canadian Centre on Substance Abuse, provincial workers' compensation boards, and other governmental bodies with responsibilities related to the field of reproductive health.
- Consulting with the provinces/territories, directly or through the Conference of Deputy Ministers of Health, on matters related to infertility prevention and reproductive health.
- Advising the federal and provincial/territorial governments on legislative and regulatory issues related to infertility prevention and reproductive health promotion, including in the areas of environmental protection and occupational health and safety.

- Consulting with health care professionals, community and public health personnel, educators, family planning organizations, and others involved in public education efforts in the field of reproductive health.
- Initiating, evaluating, disseminating, and contributing to the exchange of existing and new data and research on suspected reproductive risks, their incidence, and their reproductive effects.
- Assessing available information on existing and new infertility prevention and reproductive health promotion programs and initiatives and advising on how these can be designed and delivered more effectively.
- Working with other National Commission Sub-Committees on issues related to infertility prevention and reproductive health promotion, including training, ethical, legal, and related matters.
- Encouraging the federal government and federal research funding organizations to place greater priority on the funding of infertility-related research, including research related to program evaluation, in the public, quasi-public, and private sectors.
- Encouraging the federal and provincial/territorial governments to enhance support for infertility prevention initiatives and activities by health, labour, community, and other organizations with an interest and expertise in the field of reproductive health promotion.
- Promoting, on behalf of the federal government, international cooperation in research, information gathering, and public health initiatives related to infertility prevention. (See, for example, our recommendations in Chapter 13 with respect to a cooperative international effort to assess existing data on workplace and environmental exposures that may pose risks to reproductive health.)
- Promoting public awareness and discussion about the causes, incidence, and preventability of infertility in Canada, in part through the National Commission's annual report.

As suggested earlier, heightening public awareness about reproductive health hazards and increasing accountability in decisions about infertility prevention priorities and strategies are integral aspects of the mandate we propose for the Infertility Prevention Sub-Committee. Public awareness about reproductive health hazards will be increased as a result of the Infertility Prevention Sub-Committee's activities in promoting and disseminating further research into the causes and preventability of infertility in Canada. In addition to the National Commission's annual report, we anticipate that the Sub-Committee will make use of a variety of public consultation mechanisms to inform Canadians of new research findings in this area and to promote informed debate on their regulatory and policy implications.

Public debate and accountability will also be promoted by the composition of the Infertility Prevention Sub-Committee, which should include a balance of National Commission and outside membership, designed to ensure multidisciplinary perspectives and broad representation of the various interests involved. In particular, we recommend that this Sub-Committee include membership with a particular interest and expertise in the area of reproductive health and infertility prevention, including, for example, members from federal and provincial/territorial governments, health care professionals, community and public health personnel, educators, non-governmental health organizations, and other community organizations such as women's groups and family planning groups.

We are confident that with such a range of input, the Infertility Prevention Sub-Committee will be in a better position to identify and monitor research priorities, to evaluate existing initiatives, and to plan and coordinate future programs in a way that responds to widespread public demands for greater emphasis on infertility prevention and reproductive health promotion in any public policy response to the challenges posed by new reproductive technologies.

Conclusion

It should be clear from the discussion in this chapter that preventing infertility and promoting reproductive health are extremely complex. The old adage about medicine being as much an art as a science applies with equal force to prevention in general and infertility prevention in particular. A great deal obviously remains to be learned about all aspects of prevention as a dimension of health care, social policy, and other public policy fields. This assessment should not, however, be interpreted as meaning that prevention is not a viable response to infertility. Instead, the Commission's research has shown that there is both an opportunity for creativity in program design and a concomitant need for the disciplined and evidence-based development of initiatives that are effective in preventing infertility and promoting reproductive health.

Our research has shown further that the cost to individual Canadians and to society of failing to pursue these issues through further research and program development, together with the cost of failing to act on what we know already, will be great. There is a growing body of research and practical knowledge about what works and what does not work with respect to prevention as a policy response to public health issues. There is every reason to believe that this momentum will increase, leading to the development of more targeted, more sophisticated, and ultimately more effective efforts to prevent infertility.

There is a growing body of research and practical knowledge about what works and what does not work with respect to prevention as a policy response to public health issues.

Finally, our review of this field has shown that preventing infertility and promoting reproductive health are, for the most part, not the preserve or the responsibility of the health care system. Indeed, when the social determinants of behaviour that puts fertility at risk are considered, and when workplace and environmental risk factors are taken into account, it becomes clear that the health care system is not the main custodian of prevention efforts. Thus, whatever the outcome of the current debate about the appropriate proportion of health care resources that should be devoted to prevention and acute care, it must always be remembered that this debate also needs to be initiated and action taken in other sectors as well, including those dealing with schools, the workplace, and the community. This is why the approach we recommend is premised on coordination and collaboration among all key partners with the tools and resources to make the reproductive health of Canadians and the prevention of infertility a priority, with the Infertility Prevention Sub-Committee to provide focus and impetus for these efforts.

The Commission's research shows that infertility affects at least a quarter of a million Canadian couples at any given time. Unfortunately, our current knowledge does not allow us to make accurate predictions of the proportion of infertility that could be prevented. We believe, nevertheless, that a substantial proportion of infertility could be prevented if the range of measures we suggest were implemented to prevent individual exposure to the factors that pose a risk to fertility; there would be additional, more general benefits to the health of Canadians from these measures as well. We have outlined in this chapter the most urgent priorities for action and how we think they should be addressed.

Clearly, however, even if we had unlimited financial resources to devote to these efforts, and even with the most effective prevention programs in place, many people will still find themselves unable to have the children they want. In the next few chapters, therefore, we examine practices and procedures that can assist infertile couples to conceive and have healthy children.

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Adoption

During our public hearings and other consultations, adoption was the most frequently mentioned non-technological alternative for couples who are not able to have a child together. Couples in this situation may contemplate adoption as a solution, as an alternative to infertility treatment, or as an option if treatment proves unsuccessful. For example, in a study done for the Commission, 30 percent of IVF patients surveyed had applied for adoption by the time their treatment was under way or completed.

The attitudes expressed by intervenors reflect Canadians' views generally: fully 90 percent of people responding to a national survey conducted for the Commission considered adoption an acceptable option for couples who cannot conceive a child together. Indeed, more than half the respondents in another national survey said they would adopt a child if they were in this situation. Fewer respondents indicated they would choose other options, such as assisted insemination and *in vitro* fertilization, or choose to live without children.

However, the Commission's review of the adoption situation in Canada revealed that, in practice, adoption is not an easy alternative for most couples and is even less likely to provide a means for single people or people in non-traditional relationships to form a family. Although hard data are difficult to come by — in part because adoption systems and record-keeping methods vary between provinces and even within provinces — it is clear that trends over the past two decades are making domestic adoption a less accessible option and a more complex and difficult choice than ever before. Far more people are applying to adopt than there

> Far more people are applying to adopt than there are infants available for adoption in Canada.

are infants available for adoption in Canada. These findings place options such as donor insemination and *in vitro* fertilization in another light as we consider how societal resources should be apportioned to help people have children.

> Our daughter ... is the joy of our lives. Adopting her was no less of a miracle than our subsequent GIFT children. And this cannot be emphasized enough ... It is not really talked about as a therapy or anything, but adoption is one complete answer for infertility. It is a wonderful answer, with no physical risks, other than the birth mother's pre-existing pregnancy.
>
> [We] are greatly distressed that adoption is as difficult as it is today, because it is very difficult.
>
> *In Camera Sessions, Personal Experiences, Toronto, Ontario, May 1, 1991.*

Analogous to what we heard about many of the technological options, people who conveyed their experiences to the Commission talked about their frustration with the long and complex adoption process. As explained later in this chapter, this results in part from the disparity in number of available infants and numbers wishing to adopt in Canada. Indeed, Commissioners were struck by the similarities between the experiences of couples awaiting adoption and those undergoing infertility treatment. Both processes involve intense emotions and considerable stress, which are heightened, couples reported, by the uncertainty of the outcome and the feeling that they have no control over the process or its result. Many who embark on infertility treatment will not have a child, just as many who apply for adoption will not be successful. For older couples in particular, these strains are intensified by the sense that they are racing against time, with the chances of a successful outcome declining as they approach the age of 40.

When Commissioners reviewed the current state of adoption in Canada, some of the reasons for these frustrations became clear. Just under 1 700 infants were placed for adoption in Canada in 1991, the latest year for which figures are available. Indeed, research conducted for the Commission shows that for every infant placed for adoption by public adoption agencies across Canada, eight applicants are waiting to adopt. Given this, the availability of IVF and AI as options take on added importance. We estimate that between 2 000 and 4 000 children were born as a result of assisted insemination, *in vitro* fertilization, and related reproductive technologies in 1991. Thus, while the number of Canadian infants available for adoption has been declining, the number of

Indeed, research conducted for the Commission shows that for every infant placed for adoption by public adoption agencies across Canada, eight applicants are waiting to adopt.

infants born in Canada through assisted conception has been rising and now exceeds the number of infants adopted in Canada.

Although adoption was not mentioned in the Commission's mandate, Commissioners considered it important to review the current situation, given the assumption apparent in testimony before the Commission that adoption is a viable non-technological alternative for infertile couples. We therefore discuss current trends in adoption and the implications for people who are involuntarily childless in this chapter.

Methods of Adoption in Canada

Public adoption: facilitated by a public child welfare agency or provincial ministry facility; no fees

Private adoption: facilitated by non-government agency or private practitioner; prospective parents pay a fee for the service; services may be provided on a for-profit or non-profit basis

International adoption: coordinated by a public child welfare agency, a private practitioner, or, in some instances, the adopters themselves

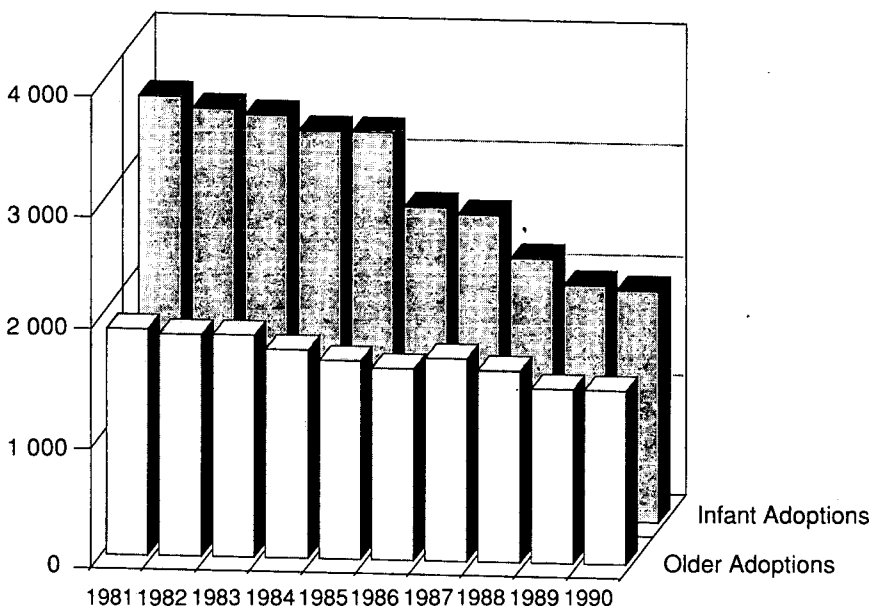
Trends in Adoption in Canada

Records on adoptions from 1981 to 1990* were examined in research conducted for the Commission. As shown in Figure 16.1, the data revealed several important trends, reflecting dramatic changes in adoption over the past 10 years. The number of infants available for adoption in Canada has declined by more than half in the past decade, despite overall growth in the population. In 1981, 3 521 infants were placed

The number of infants available for adoption in Canada has declined by more than half in the past decade, despite overall growth in the population.

* Statistics were gathered from the provinces, and a national survey of approximately 350 adoption service providers was conducted (202 public service agencies, 130 private practitioners, and 16 private adoption agencies). The data come with some caveats. For example, it is rare to find complete and comparable adoption records in provincial ministries over a substantial period of time. Nor has there been a sustained effort to collect specific categories of adoption information across the country, making it difficult to combine or compare information from various provinces. The fact that the Commission had to rely on estimates in some cases underscores the need for data collection in support of public policy in this area.

Figure 16.1. Domestic Adoptions: Number of Children and Number of Infants Adopted in Canada, 1981-1990



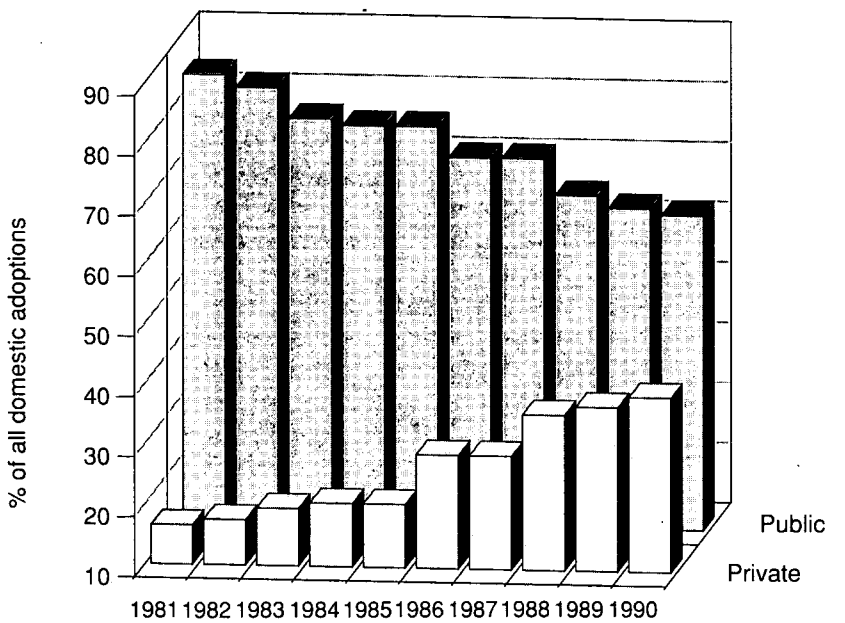
Source: Daly, K.J., and M.P. Sobol. "Adoption as an Alternative for Infertile Couples: Prospects and Trends." In Research Volumes of the Royal Commission on New Reproductive Technologies, 1993.

for adoption, compared to 1 698 in 1990. Given that Canada's population increased by 9.3 percent over the same period, the decline appears even more dramatic.

This trend is attributable largely to two factors: the general availability of contraception, which has reduced the overall number of pregnancies that might result in a child becoming available for adoption, and the fact that many more young women are choosing to keep their children in circumstances where, in the past, they might have chosen to place them for

The assumption that the availability of abortion has reduced the number of infants available for adoption appears to be unfounded.

Figure 16.2. Public and Private Domestic Adoptions as a Percentage of All Domestic Adoptions



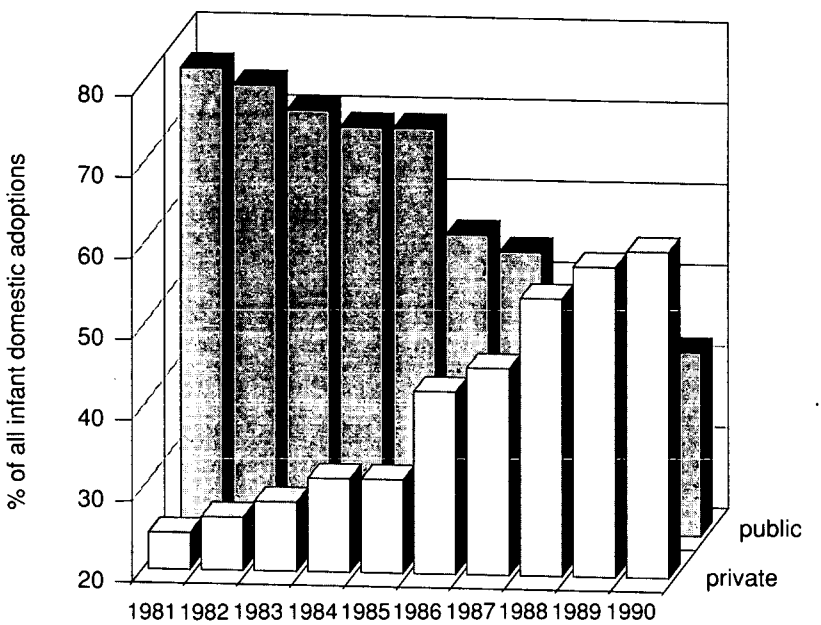
Source: Daly, K.J., and M.P. Sobol. "Adoption as an Alternative for Infertile Couples: Prospects and Trends." In Research Volumes of the Royal Commission on New Reproductive Technologies, 1993.

adoption. Of all births to unmarried mothers, data for 1959 suggest that 64 percent ended in adoption, whereas recent data available for unmarried women under 25 years of age suggest less than 4 percent gave them up for adoption. The assumption that the availability of abortion has reduced the number of infants available for adoption appears to be unfounded. Among women under the age of 25, who make up the vast majority of those who place infants for adoption, the number of abortions declined steadily over the past decade, yet the number of infants available for adoption also declined.

Adoptions can be facilitated by public or private agencies (see earlier box). Within the shrinking number of domestic adoptions, the proportions

of private and public adoptions are also shifting significantly, as shown in Figure 16.2. The number of children placed through public agencies has declined significantly in the past decade, as has the rate of such adoptions as a proportion of total domestic adoptions. The number of private adoptions, by contrast, held steady over the decade. However, private adoptions as a percentage of all domestic adoptions rose dramatically. Figure 16.2 shows this clearly, but the trend is even more marked if adoptions of infants under the age of one in particular are considered (see Figure 16.3).

Figure 16.3. Public and Private Infant Adoptions as a Percentage of All Infant Domestic Adoptions



Source: Daly, K.J., and M.P. Sobol. "Adoption as an Alternative for Infertile Couples: Prospects and Trends." In Research Volumes of the Royal Commission on New Reproductive Technologies, 1993.

Figure 16.3 also illustrates the current reality of adoption in Canada: infants are available for adoption primarily through private rather than

public adoption agencies. In 1990, for example, the number of applicants for public adoption exceeded the number of infants actually placed for adoption by a factor of almost eight to one. Overall, the ratio of applicants to children of all ages placed for adoption is about three to one.

Infants are available for adoption primarily through private rather than public adoption agencies ... Overall, the ratio of applicants to children of all ages placed for adoption is about three to one.

As a result of these trends, the number of people who want to adopt far exceeds the number of children available for adoption in Canada. This is no doubt one reason for the rising number of international adoptions, along with the desire of couples to avoid the long wait for domestic adoption of an infant. International adoptions are now thought to outnumber domestic adoptions (public and private combined); best estimates (extrapolated from the figures for Quebec, which is the only province that keeps complete records) are that for every two domestic adoptions of infants, three international infant adoptions take place.

Canada's Adoption System

Those who want to adopt a child in Canada can choose one of three methods: public, private, or international adoption. All provinces and territories except Quebec and Newfoundland permit both public and private adoption. Quebec prohibited private adoptions in 1980; since then, all adoptions, including international adoptions, have been coordinated through a public system. Since 1972, all adoptions in Newfoundland have been coordinated through a public system as well. No independent agencies or practitioners provide adoption services for a fee; only government social workers are permitted to act as service providers. Ontario requires all private practitioners to be licensed. In Alberta, agencies operate on a non-profit basis and a licence is required only if the agency is charging a fee to adoptive parents. No other province or territory requires private agencies or practitioners to be licensed, and none places an upper limit on the fees private agencies can charge.

> We desperately need more educated professionals in the issues of adoption to help us and our children cope with all the feelings in, around and about adoption. Perhaps, in time, there will be a Parent's Aid Society that works together with Children's Aid Societies to help the whole family.
>
> *Brief to the Commission from the Adoptive Parents Association of Halton, November 8, 1991.*

Public Adoption

Public adoptions are financially the most accessible type of adoption, as no fee is involved. Applicants must pass a screening process, however, and waiting lists for public adoption are long — six years on average to adopt a healthy infant, compared to three years for privately arranged adoptions where no fee is involved and just under two years through private agencies or practitioners that charge a fee. In fact, some 16 percent of the public agencies contacted for the National Adoption Study have closed their waiting lists — they are not accepting any new applications from people wishing to adopt.

In testimony and submissions to the Commission, many people described the various public adoption systems as difficult and frustrating, citing long waiting lists, the small number of children available for adoption, and application and screening procedures that prospective parents see as complex and intrusive, contributing to their feeling of powerlessness and lack of control over the adoption process.

On the other hand, public systems offer several advantages, primarily in the services offered to birth and adoptive parents. Thirty-two percent of public adoption agencies, for instance, offer support groups for new adoptive parents, compared to 21 percent in the private sector. Two-thirds (66 percent) of public providers offer short-term support to the birth parents, compared to 47 percent of private providers. The availability of this structured support, including professional staff, can be important for both the biological and the adoptive parents.

A benefit of public adoption for the children is the large pool of adoptive families from among whom agency personnel can select prospective parents. Other features of public adoption include more complete records of children's medical and social history (and storage of these records for an indefinite period); alternative resources in the event of a disruption in the adoption; more equitable access, regardless of socioeconomic status; and continuing availability of counselling services for all parties involved. This helps to ensure, through the structure and operation of the adoption process, that the best interests of the child are promoted.

Private Adoption

Private adoption is an appealing alternative for those who can afford it. Prospective parents face shorter waiting lists and a greater chance of adopting an infant, and they have more control over how the adoption is handled. These factors are reflected in the rise of private adoptions as a proportion of all domestic adoptions during the 1980s. The number of private adoptions remained relatively steady over this period, but they rose from 17.4 percent of domestic adoptions in 1981 to 39 percent by 1990, while the number of public adoptions declined.

Prospective parents using a private agency can expect to pay fees of up to $6 000, with the average being about $3 600. For adoptions facilitated by a private practitioner (a lawyer or social worker), the average fee is about $3 100 according to data provided to the Commission, although some practitioners involved in private arrangements charge no fee. The higher fees usually mean that the adoptive parents have agreed to pay for additional services, such as pre- and post-adoption counselling for the birth parents, other expenses of the birth mother, and home study updates.

One of the perceived advantages of private adoption is that it offers both the birth mother and the adoptive parents more opportunities to control the adoption process and have more personal influence in decisions about it. Research conducted for the Commission shows, for example, that private adoptions are more likely than public adoptions to be "open" — with birth and adoptive parents knowing about and even meeting each other. Some have argued that it is in the best interests of the child to know about his or her birth parents and for adoption arrangements to be open. The research showed that twice as many private practitioners as public service providers (41 percent compared to 20 percent) have facilitated a fully open adoption, where birth parents and adoptive parents meet before the placement and exchange identifying information. Similarly, 62 percent of private practitioners have facilitated an adoption where the birth and adoptive parents exchanged information anonymously through the practitioner; 55 percent of the public agencies surveyed had done this.

> We came through the [private] adoption route ...
>
> IVF was a piece of cake compared to everything else.
>
> We were treated by the Children's Aid workers and case workers and social workers as less than human, and it cost us a fair amount of money in trying the adoption route ...
>
> And we came up with nothing.
>
> *In Camera Sessions, Personal Experiences, Ottawa, Ontario, May 14, 1991.*

At the same time, private adoption raises questions about whether and how the best interests of children are being served. Private adoption is available only to those who can afford the fees, giving rise to apprehension about commercialization of this activity. Nor is private adoption closely regulated in 10 of the 12 provinces and territories that permit it. This raises concerns about standards in adoption services — for example, the training and qualifications of personnel involved in placing children for adoption, follow-up and support services for adoptive families, and the content, completeness, and availability of adoption records. It could also be argued, however, that if a private system encourages openness in adoptions, adopted children could benefit.

International Adoption

International adoption has become the most common method of infant adoption for Canadians, reflecting the small number of infants available for adoption within the country. Canadians made an estimated 2 448 international adoptions in 1991.

One adoptive parent who testified before the Commission placed the cost of adopting a child from outside Canada at between $12 000 and $15 000. In addition to the financial cost, international adoptions may pose challenges to the adoptive family. For example, as in some domestic adoptions, poor pre- and post-natal conditions may result in future physical or mental disabilities in the child, while missing or incomplete medical records may compound the difficulties associated with caring for and raising the child.

International adoptions also raise complex issues for families — such as the challenge of raising a child of a different racial or ethnic background — and for Canadian society, including such issues as how to ensure that international adoptions conform to Canadian standards with respect to ethics, law, and the protection of the child's best interests. Among the ethical issues involved are the possible pressures on parents in difficult financial or social circumstances to allow their children to be adopted by families in wealthier countries and the potential for international adoptions to encourage the view that children can be "bought" or "sold."

Custom Adoption

The Commission also learned during its public hearings that adoption in Aboriginal communities can take place without the formal involvement of public agencies or officials. People in these communities follow their traditional rules or customs in a practice known as custom adoption. Whether permitted by provincial or territorial law or practised without this authority, custom adoption is among the means for Aboriginal people to ensure that their children remain in Aboriginal communities and in contact with their family and cultural origins.

As the Commission was told in Whitehorse and Yellowknife, custom adoptions involve a fertile couple or woman "giving" a child to a childless cou-

> Some women who are indeed infertile ... in talking with their own family members and elders [have been told] ... children are a gift and if you haven't received that gift, then maybe your love should be shared in some other way with the extended family. And that's why it's ... so much more common for them to take in the child of a sister or a cousin because there isn't quite the same pressure, I feel, on them having their own natural child ... access to custom adoption is probably a little more free than down south.
>
> *L. Hudson, Tawow Society, Fort Smith, Public Hearings Transcripts, Yellowknife, Northwest Territories, September 12, 1990.*

ple, sometimes but not necessarily because one or both birth parents are unable to care for the child. The adoptee knows who the birth parents are, and some relationship between the birth parents and the child continues. This is an accepted part of many Aboriginal cultures and does not devalue the child — on the contrary, the cultural perception may be that the child "belongs" to the community more than to the individual who gave birth to or raises the child. In the Northwest Territories, such adoptions are recorded to ensure that the adoptive family is entitled to family and educational benefits for the child.

Given current efforts by many Aboriginal communities to gain control of child welfare services, as well as the work of the Royal Commission on Aboriginal Peoples, which has a comprehensive mandate in relation to Aboriginal child welfare and many other issues, we believe it would be inappropriate for this Commission to comment on this practice.

Access to Adoption

In private sessions with Commissioners, Canadians said that they had considered adoption; but some had not pursued it actively because of the low number of infants available for adoption, the complex and lengthy public adoption process, the length of waiting lists, or the prohibitive cost of private and international adoptions. Others had pursued adoption despite these difficulties.

Thus, the statistics discussed earlier in the chapter were given a human face in the Commission's private sessions; many people who had explored adoption after discovering their infertility saw adoption as a relatively undesirable or inaccessible option for them. Some rejected adoption because they wanted a genetically linked child or wanted to experience pregnancy and birth. For others, however, access to adoption was the more important issue. In addition to long waiting lists for public adoption and high costs

> If we prohibit pregnancy contracts and limit access to other technologies, then couples who wish to have children must have greater access to other courses of action. Adoption appears to be one solution that does not of course settle all the problems but which might be more feasible. At present, there are very great limitations to international adoption and adoption within Canada, and these need to be resolved. Those who cannot sort out the issues involved in international adoption should be given access to the psychosocial methods and resources to help them reconcile themselves to not having children. [Translation]
>
> *C. Coderre, Fédération des femmes du Québec, Public Hearings Transcripts, Montreal, Quebec, November 21, 1990.*

for private or international adoption, some thought they had been denied access to adoption because of personal characteristics such as their age, marital status, religion, or sexual orientation.

The Commission's research showed that some of these perceptions accurately reflect adoption agency policies. The criteria used by both private and public agencies to screen prospective parents generally reflect the traditional concept of the family — a relatively young married couple. Our research also showed that some adoption agencies have reservations about placing a child with single people, people of a different race or religion from the child, and couples over the age of 40. Gay and lesbian couples encounter the greatest difficulty when trying to adopt.

> What you have been hearing about the dramatic efforts of some to bear children should incline your Commission to come out as an ardent promoter of social policies to facilitate adoptions.
>
> In today's world, for every Canadian couple striving to have a child there are hundreds, even thousands, of children in need of parents. Many of them are not adopted because they are perceived to be imperfect. You can urge that it be a priority for all levels of government in this country to adopt measures to reduce the difficulties and delays that now frustrate many who want to adopt children. These measures should include educational efforts to help people overcome fears and prejudices about adoptions.
>
> They should also include international accords, to establish procedures that are respectful of the needs of children and would-be parents. It is inhumane not to have better programmes than today's to promote and facilitate adoptions.
>
> *Brief to the Commission from Action Famille, February 5, 1991.*

The age criterion is particularly relevant to people undergoing infertility treatment. By the time they discover their infertility and seek treatment for it, couples are usually in their early 30s. There may be a substantial waiting period before the couple is able to receive treatment. If treatment is unsuccessful (again requiring a year or more to find out), the couple may wish to adopt. They will discover, however, that the waiting period for a public adoption averages six years, bringing one or both of them perilously close to the age cut-off used by many adoption agencies to screen prospective parents.

This is among the reasons we have recommended elsewhere in this report that infertility treatment clinics improve their information and counselling services with respect to options and alternatives when a couple first seeks treatment (see Chapters 19 and 20). We believe that infertility treatment centres should not exclude people who are on an adoption

waiting list. In addition, adoption agencies should not screen out people waiting for or undergoing infertility treatment. Canadians told us that these practices are occurring, but our surveys of *in vitro* fertilization clinics and adoption agencies did not reveal the existence of such policies. Nevertheless, since people may withdraw from either waiting list for reasons such as spontaneous pregnancy, there is no good reason for such policies.

An Adoption System in the Best Interests of Children

The principle of the best interests of the child guided the development of adoption policies in Canada. The evolution of the adoption field over the last decade led us to question, however, whether this principle continues to be the basis of such policies or, in some cases, the lack of policy.

Children are important as individuals and as members of society; this should be reflected in all arrangements society makes for their care, including adoption systems. We question whether the current mix of private and public adoption systems is the best means of protecting children's interests and of supporting people's ability to form families through adoption. Many issues can arise — emotional, psychological, developmental, and social — in the period leading up to an adoption and as the parents raise the child, and we question whether current adoption policies and practices provide the necessary support for parents and children alike.

> Individual and cultural values play key roles in determining the acceptability of adoption as a viable alternative. Historical changes in the meaning of adoptive relationships have had an impact on the interpersonal experiences of adoption, the delivery of adoption services, and adoption legislation and policy. Recent social-psychological research has provided insight into some of the unique and predictable tasks that are encountered when becoming adoptive parents. Identity has emerged as a central focus in the adoption literature, with the accessibility of information about biological heritage being a key to healthy adoption adjustment.
>
> *K. Daly and M. Sobol. "Adoption as an Alternative for Infertile Couples: Prospects and Trends," in Research Volumes of the Commission, 1993.*

In addition to protecting the interests of children and meeting the needs of adoptive families, we also believe that adoption systems, including Canadian policies with respect to international adoption, should reflect concern for other principles that are part of our ethical prism, such as the non-commercialization of reproduction, equality or non-discrimination in

access, and scope for autonomy in decisions on the part of both birth parents and adoptive parents.

In the Commission's view, a comprehensive review of Canadian adoption systems is warranted at this time. The recently completed National Adoption Study, sponsored by Health Canada, was a step in this direction. The study gathered information on demographic trends (much of the information available for the first time in Canada), adoption law and policies in various jurisdictions across the country, and the policies and practices of public and private adoption providers. Although the study appeared too late in this Commission's mandate for us to address the issues it raises or evaluate its recommendations in detail, it is clear that its subject matter warrants continuing public policy attention from both federal and provincial/territorial governments. The Commission therefore recommends that

62. Federal and provincial/territorial governments undertake a joint review of adoption in Canada, with a view to addressing such issues as the relative merits of public and private adoption systems in promoting the best interests of the child and in meeting the needs of the other parties involved (including birth parents, adoptive parents, and siblings of the adopted child); access to adoption and barriers to access; cost; record keeping and disclosure; counselling and consent; the advantages and drawbacks of interprovincial harmonization of policies, services, and practices; and issues in relation to international adoptions.

Commissioners are of the view that the ethical and other issues raised by the existence of a private adoption system, as well as by the practice of international adoption, necessitate a thorough review and coordinated action in this regard. This could occur in the context of the continuing consultations suggested by the National Adoption Study or as a separate exercise.

In summary, the Commission found that adoption is not a feasible alternative for many Canadians who are involuntarily childless, mainly because the number of children, particularly infants, available for adoption has declined so markedly. As we have noted, fewer infants are adopted in Canada each year now than are born as a result of assisted conception techniques. In the next few chapters we examine these techniques, their role in treating infertility, and their place in Canada's response to the problem of involuntary childlessness.

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Infertility Treatments: Introduction and Social Context

There is no easy way for couples to discover they are infertile. Trying to have a child but not being able to conceive means hopes and plans for the future are dashed. Often, this happens after a couple has spent several years controlling their assumed fertility through contraception, which may make the discovery even more difficult. Also, it is quite common that by the time infertility is diagnosed, the couple may already be well into their reproductive years and have spent a significant amount of time trying to conceive naturally; they want to know what they can do before it is too late.

The three reproductive technologies covered in this section are separate but linked types of infertility treatment: fertility drugs; assisted insemination; and *in vitro* fertilization and its related techniques. These treatments can be seen as existing along a continuum. At one end there are fertility drugs, the most frequent and least invasive fertility treatment, often prescribed by family physicians or obstetricians and gynaecologists. For many couples, this is the only infertility treatment used. Others move on to increasingly invasive and complex treatments. Assisted insemination, the next treatment we consider in this section, used primarily for male infertility, is used less commonly than fertility drugs and is practised not only by family doctors and obstetricians but also in clinic-based fertility programs. The most invasive and most expensive technique is also the one most people associate with new reproductive technologies: *in vitro* fertilization. This is performed only in clinic-based fertility programs. A final chapter in this section looks at egg and embryo donation, rarely used in this country, examining the issues that arise because of the availability of IVF and the capacity to retrieve eggs, fertilize them for use in assisted conception, then preserve the remaining zygotes outside the human body.

Many individuals — the single largest group of those treated for infertility — are treated with fertility drugs prescribed by family physicians.

These are women who may never go any further with infertility treatment, never see specialists or enrol in a fertility program. For other patients, however, the initial treatment with fertility drugs is the start of a long and demanding journey of referrals to specialists and increasingly invasive treatments. The Commission examined all three areas — fertility drugs, assisted insemination, and *in vitro* fertilization — with equal rigour, using the principles of evidence-based medicine, discussed in Part One, as well as our ethical framework. One of our goals was to right the balance of attention, which has previously been weighted toward IVF. The research we carried out with respect to clinical effectiveness and safety, as well as practices and procedures, has not been done as comprehensively in Canada before. Our approach was innovative, and our findings, which will be presented in detail over the next three chapters, were unsettling. Commissioners were disturbed by the state of practice in this area.

We found, for instance, that little research has been done into the effectiveness or adverse outcomes of fertility drug use, with many practitioners accepting that they all work well, without necessarily having the evidence to support this view. We also found that IVF has been shown to be effective only for the one condition it was developed to treat — fallopian tube blockage — but that its use proliferated over the 1980s, so that it is now being used to treat a wider and wider range of conditions without evidence that it is effective for them. There is also marked variation in practices and procedures in fertility programs across the country, including some practices that are simply unsafe. Of particular concern was the fact that our 1991 survey of fertility programs across the country found that some programs were not quarantining donated sperm and retesting sperm donors for HIV six months after the donation before using the sperm for assisted insemination. At least three private practitioners surveyed were using fresh sperm for donor insemination, despite the existence of professional guidelines since 1988 requiring sperm to be frozen and quarantined to allow for testing of donors. We considered these findings so serious that we brought them to the attention of Canadians and the relevant professional bodies in releasing the survey findings in April 1993.

> A treatment cannot be assumed to be effective unless it has been demonstrated to be so through well-designed clinical research. Second, data must be collected to track long-term health outcomes to ensure that effective treatments are also safe treatments.

In the Commission's view, the joining of an egg and sperm *in vitro*, and transfer of the resulting zygote to a woman's body, are not unethical or inappropriate in and of themselves, provided they are carried out in circumstances that ensure ethical and responsible use of the technologies. However, our research in the field of infertility treatments led to one inescapable conclusion: Commissioners believe it is time to get back to

basics. First, a treatment cannot be assumed to be effective unless it has been demonstrated to be so through well-designed clinical research. Second, data must be collected to track long-term health outcomes to ensure that effective treatments are also safe treatments.

The question of whether there are safe and effective IVF treatments must be addressed by evaluating evidence. In our view, medical procedures should move from the realm of research to that of treatment only if they can be demonstrated to be effective and beneficial and if information on their risks and effects is available. With respect to IVF, information from this type of assessment facilitates decisions on two levels: societal decisions about the allocation of health care resources to provide IVF and related procedures; and specific decisions about treatment of individuals. We believe it is important, however, that this same evidence-based approach apply just as rigorously to the less invasive and less "high-tech" treatments (fertility drugs and assisted insemination) as it does to IVF. These treatments are provided to thousands of Canadian women each year, with potential implications for their health and that of their children and partners; these treatments should not be spared assessment simply because the technology they involve is not "high" technology. Decisive national leadership is needed to put the mechanisms in place to facilitate this more balanced approach, which would be spearheaded by the National Reproductive Technologies Commission we propose be established. Our specific recommendations for how this should be done are set out in the next four chapters.

We did not arrive at our conclusions lightly. We came to them, rather, as a logical outgrowth of our ethical foundation and guiding principles and our commitment to evidence-based medicine. Commissioners believe that demanding safe and effective treatment is not patronizing of individuals who are infertile; rather, it is the prudent approach based on society's responsibility to defend vulnerable interests — both those of individuals and those of the wider community. Adherence to the ethic of care makes it imperative to reduce risk to minimum acceptable levels, but this is not invariably the situation with infertility treatment in Canada today. We recognize that adoption of our proposals may mean that some couples will not have access to treatments they, and indeed some physicians, may have come to consider necessary. The statement of one woman who is infertile appearing before the Commission exemplifies what others also told us; she said that infertile people want treatment, but they do not want unsafe or ineffective treatment.

Infertile people want treatment, but they do not want unsafe or ineffective treatment.

We also recognize that the standards we propose place greater demands for evidence on this area of medical care than is currently the case in other areas of medicine. But we believe that setting high standards

of quality here is appropriate because we are dealing with human reproduction, an area that must be approached with caution and an eye to future generations, and because such standards are within our reach as a society and within the reach of the health care system through which infertility treatments are provided. Infertility treatment involves both individual and collective aspects, combining complex diagnosis and treatment procedures with socially significant and far-reaching implications for others as well. This combination of factors means it is even more important to approach infertility treatment responsibly. There is the potential to provide a model of how evidence-based medicine should work, an example that may be valuable for other areas of medical care. The approach we propose will also provide the needed evidence upon which governments will be able to base rational and accountable resource allocation decisions about providing coverage under provincial/territorial health insurance plans for infertility treatments that have been demonstrated effective and safe.

Although infertility treatments are provided in a medical context, they have profound social significance as well. The remainder of this introductory section examines the social context for infertility treatment.

The Social Context for Infertility Treatments: What We Heard

Decisions about infertility treatment take place at two levels. At the personal level, individuals and couples who are infertile must decide whether they want to undergo treatment to attempt to have a child, basing the decision on their individual circumstances, values, and knowledge. These decisions are not made in a vacuum, however, but in a context of societal values and attitudes and previous societal decisions. Issues such as how society views technology and the medicalization of women's health, particularly their reproductive health, and decisions about which procedures qualify as medical treatments, what kinds of resources to allocate to them, and who has access to them, form the social context for understanding infertility treatments. Some of these issues were discussed in a more general sense in Part One of this report but will be touched upon again because of their immediate relevance to infertility treatment.

The values, opinions, and behaviours of Canadians, and their attitudes toward reproduction and IVF in particular, also form part of the social context for IVF and the background to our discussion of how society should address the issues raised by use of the technology at the collective level. *In vitro* fertilization was one of the most extensively debated technologies in the Commission's mandate; this is reflected in the amount of attention it received from the media and from individuals and groups that participated in the Commission's work, through public hearings, private sessions,

roundtables, panel discussions, letters, and submissions. In addition, the Commission sought further understanding through national surveys and a survey of people enrolled in fertility programs across the country. The findings of these surveys will be discussed throughout the next few chapters. These consultation activities were complemented by extensive research projects examining not only the medical, but also the psychological and social aspects of infertility treatment.

> Thus, although we support the use of *in vitro* fertilization techniques for childless couples, the use of donor sperm and ova and surrogacy breaks, or, at least, severely strains the bond of mutuality between partners as well as between parents and children. The issue, in other words, is about the use of technology in relationships, not just about setting the limits to technology.
>
> *J. Olthuis, Citizens for Public Justice, Public Hearings Transcripts, Toronto, Ontario, October 29, 1990.*

The national dialogue on infertility treatment that resulted from the Commission's work in this area gave Commissioners a rich and multifaceted basis from which to consider the issues. This multidimensional perspective was necessary because no single vantage point can provide a comprehensive overview of the personal, medical, social, ethical, economic, and legal dimensions of the issues surrounding infertility treatment.

Despite the issues and concerns they raise, most Canadians see infertility treatments as valuable reproductive options. For example, we found from our survey that the majority (58 percent) support donor insemination for couples in which the male partner has a sperm problem that affects his fertility, whereas almost 80 percent approve of IVF, a much more complex and high-tech procedure, when it involves the use of the couple's own eggs and sperm. Many women and couples impressed upon the Commission that these treatments have given them the chance to experience parenthood and have children and urged the Commission to ensure that they remain a reproductive option. The Commission also heard concerns, however, about how the treatments are provided and how records about the treatments and their results are kept. These concerns, many of which were borne out by the Commission's research, are discussed in greater detail in the following sections.

How Society Views Technology

The ambivalence with which many in society view technology is clearly illustrated by attitudes toward *in vitro* fertilization. A cursory examination of media coverage demonstrates the contradictory images of, on one hand, bouncing babies and their overjoyed parents and, on the other hand, complex technology, gleaming laboratories, and the power of medical scientists who can manipulate human zygotes.

In fact, society's attitudes toward the whole field of infertility treatment reflects such an ambivalence. Heartfelt calls for solutions to infertility co-exist with a sense of suspicion and scepticism about the solutions now being offered. For instance, experiences with some drugs (such as thalidomide and DES) have made many people wary of the effects of fertility drugs on the women taking them and on their children.

> Like all other medical techniques, NRTs are used in a growing number of pregnancies, and are evolving from their original foundations of therapy and prevention to involve the rationalized management of human reproduction.
>
> This has major consequences, such as women's relinquishment of the maternity experience, and increased dependence of individuals on the priorities set by the medical staff and NRT accessibility criteria. What will become of couples' freedom to make their own decisions about fecundity if NRTs continue to develop at the current rate? [Translation]
>
> *Brief to the Commission from Confédération des organismes familiaux du Québec, February 2, 1991.*

Women's Reproductive Health and Well-Being

While understanding people's desire to have children and to have access to treatment that may make this possible, many Canadians have strong reservations about infertility treatment as it is now provided. Many of these reservations focus on IVF because of its highly technological nature, but the concerns the Commission heard reflect the hesitancy with which many people view other infertility treatments as well.

Individuals and groups, among them the major women's groups in Canada, are concerned that, just as the movement to de-medicalize women's reproductive health, through services such as midwifery, is making strides, infertility treatment may encourage a return to a medicalized model of women's reproductive health. They are concerned that women are socialized to believe they must be mothers, and that they are being pressured to seek medical solutions to social dilemmas. Further, the Commission heard, this re-medicalization has been carried out irresponsibly, endangering women's health in the process, and experimental procedures, primarily IVF, are being used as treatment without any evidence of effectiveness or safety. Intervenors were also concerned that women are treated as the patients in assisted insemination programs, with any risks that entails, when, in fact, assisted insemination is a treatment for the male partner's infertility.

There is also a wider public perception that infertility treatments, because they take place in clinics or doctors' offices, are "safe." This belief explains in part the sense of betrayal experienced when the perception is shown to be unfounded, as was the case with the Commission's survey of

fertility programs, which found that some physicians and programs were not taking the necessary precautions to prevent the transmission of HIV, the virus thought to cause AIDS.

Concerns about safety were why some groups and individuals called for a moratorium on infertility treatments. Some groups would like to see a halt to the expansion of all services until the necessary evidence on effectiveness and safety can be gathered. In particular, they think more information is needed on whether infertility drugs work and whether they have long-term health effects for women and children.

Other groups focussed on IVF, opposing any provision of this procedure, regardless of evidence of its effectiveness, because of the ethical issues surrounding the creation and storage of zygotes outside the human body. The fact that zygotes created but not needed for IVF treatment are sometimes discarded or used for research offends their beliefs about the status of the embryo/zygote.

> I ... want to express my views to you today as a wife, an infertile woman, a feminist and a recipient of in vitro fertilization.
>
> My concern is that too many others, mainly parents and those who are childless by choice, portray people with infertility problems as mindless guinea pigs, obsessed by [an] unnatural desire to procreate at any cost regardless of any risk to the health of the child which we might have or risk to our own health. Infertile women especially seem to be pictured as victims of a male-dominated medical profession and/or dominated by a husband's need to produce progeny to secure his immortality, or some such version ... others speak for us assuming that somehow we are not capable of rational decision-making when managing our infertility ... This stereotypical view of infertile people is false.
>
> *J. McDonald, Kingston Infertility Network, Public Hearings Transcripts, Ottawa, Ontario, September 20, 1990.*

These views were juxtaposed to those of individuals and couples who are infertile and who told the Commission that having a child is very important to them and who saw infertility treatment as their only chance to achieve this. They felt strongly that they were capable of making their own decisions about their use of the technologies, provided information was available to them.

Contrary to what some observers have said about external pressure, our survey of 1 395 women who participated in infertility programs across the country showed that women's own desire for children was the strongest motive for seeking help at an infertility clinic. We discussed in Chapter 2 how social construction has a part to play in shaping people's attitudes about having children, but the women we surveyed felt their own desire was much more important than any other motivating factor, including a spouse's desire for children, and very few reported pressure.

Many intervenors in the Commission's public consultations were also disturbed by the links between the use of new reproductive technologies in animals and in human beings. For instance, IVF is used to help people have children, but it is used in animals to improve genetic traits, and there were fears expressed that this use could be transferred to human beings. These issues are discussed in greater detail in Chapter 22.

Decision Making About Infertility Treatments

Canadians told the Commission that they want more opportunities to influence decisions about the use of technologies and the allocation of public resources to them; they do not want to leave decisions about how the technologies are practised and who has access to them solely in the hands of medical practitioners and researchers. Although we heard the view that society should look to the medical profession as both the repository of knowledge about new reproductive technologies and the best source of decisions regarding their use, more often we heard the view that practitioners and researchers should not be making moral and ethical judgements for individual patients or for the community at large. In fact, many physicians told the Commission that they do not want to be placed in that position, yet they have been placed there unwillingly because of the absence of other forms of societal ethical decision making.

> I have worked with several couples who are infertile and have gone through the use of new reproductive technologies and some of the anguish they have gone through in trying to get pregnant and not succeeding ... I have also worked at the other end of [the] spectrum for many years ... with very poor women who have had extremely premature births because they don't get adequate nutrition throughout their pregnancy, and their babies don't survive ... And the discrepancy of those two things ... in one culture like ours, just continues to flabbergast me ... this is money that we have to choose how we are going to spend in the society.
>
> *D. Marshall, Citizens for Public Justice, Public Hearings Transcripts, Toronto, Ontario, October 29, 1990.*

Need for Informed Choice

The controversy about whether infertility treatments, especially IVF, amount to experiments on women or valid treatments was often presented as a polarized debate, but in reality the Commission found that there was more common ground than confrontation. One of the key areas of agreement was on the need for more information about all technologies, not just IVF, and about their effectiveness and safety, so that individuals and couples considering using the technologies can exercise informed choice.

There was also agreement that this information must be accessible to a wide range of prospective patients, reflecting the pluralistic nature of Canadian society.

Women and couples felt that they did not have enough information about the short- and long-term effects of undergoing treatment. The Commission's survey of patients in fertility programs across Canada found that the issues about which they wanted most information were those on which the material provided by programs placed least emphasis and was least helpful. These included the psychosocial aspects of treatment, their chances of having a child, the short- and long-term effects of treatment, and treatment alternatives.

Individual attitudes and choices about infertility treatments are often conditioned by underlying assumptions or beliefs about the role of technology, the determinants of women's reproductive health and well-being, and the need for informed choice. Several other more explicit issues can also affect an individual's or couple's decisions about whether to accept infertility treatment and, if so, which one.

Funding for Infertility Treatments

Public funding for infertility treatments is a major determinant of how much they are used. The Commission's study of fertility programs found that 70 percent of IVF treatments are carried out in Ontario, which has 37 percent of Canada's population. Ontario is the only province that covers the procedure under its health insurance plan.

> Canada's health care system does not take infertility seriously. Nowhere has the prevention, diagnosis or treatment of infertility been acknowledged as a priority ... infertility is marginalized as a health care issue through excessive waiting lists, restrictions on access to treatment, and a constant threat of funding cutbacks. Those who seek access to treatment are demoralized by their exclusion from a health care system which claims to be universal but repeatedly tells them that infertility is an insignificant health care issue.
>
> *Brief to the Commission from the Infertility Awareness Association of Canada, April 30, 1992.*

Canadians communicated a range of views on whether infertility treatments should be part of the publicly financed medical care system. Some people believed that infertility is a physical condition that should be treated through the health care system, and others believed that the health care system is already too overburdened to provide high-tech solutions to infertility, regardless of whether they are effective and safe. We also heard testimony that safe and effective procedures that could help those who are infertile should be included in the health care system on the grounds that infertility is just as important in the lives of those affected as

many other conditions now treated in the health care system. We heard many people talk about the importance of children in the lives of individuals, couples, and society in general. Because of this importance, many people believe that if safe, ethical, and effective medical procedures are available to assist people who are infertile to have children, a caring society should provide them through the health care system. Others, however, have no objection to funding some treatments, such as assisted insemination, if they are effective, but believe that extending funding to expensive and high-tech procedures such as IVF diverts attention and resources from other reproductive health services, including preventing infertility in the first place.

Access

For many Canadians, the decision about whether to use one of these technologies has been removed from them, because of lack of access. These include people who live in isolated or rural areas and who do not have the resources to travel to fertility programs; those who are not part of stable, heterosexual relationships; and those who cannot afford the procedures if they are not covered by their provincial/territorial medical insurance plan. In addition, those who do not speak English or French may be less likely to have access to information on programs or procedures, and so have less access to them.

> The gap between women's access to the knowledge about NRT's and the rapid advancements in the field is increasingly adding to the power of the professionals over the consumers ... The lack of communication between immigrant women and health professionals increases immigrant women's vulnerability to be exploited ... thus further reducing this group of women's power. The NRT's have enormous potential to further add to sexism and racism.
>
> *Brief to the Commission from the Immigrant Women of Saskatchewan, October 25, 1990.*

Some intervenors stated that physicians control access to fertility clinics and that access to treatment is easier for highly educated, high-income, married, heterosexual couples. We heard that the route to the use of reproductive technologies is currently unclear and complex, and people with less education are less likely to find access to it. It is expensive, and, in many provinces, the cost has to be borne directly by the users. This means level of income may determine access.

Some of these people give up their hopes of having a child. Others seek alternative routes to conception, such as single women or lesbians who use self-insemination using donor sperm. This process, which is discussed in the section on assisted insemination, redresses part of the

problem of access (by removing the necessity for medical involvement), but it also raises issues about safety.

Commissioners heard specifically from single women and lesbians who described how they had been discriminated against in the traditional medical setting. Some witnesses told the Commission that the over-medicalization of assisted insemination using donor sperm has created a situation in which medical practitioners have become gatekeepers, enforcing what they perceive to be community standards about family formation by establishing access criteria that exclude single or lesbian women.

Impact on the Family and Its Biological Relationships

Infertility treatments have direct effects on familial relationships, because they can be carried out using donated gametes (donated sperm for assisted insemination, or donated eggs, sperm, or both for IVF). Our surveys showed that Canadians hold strong opinions about breaking the ties between biological and social parenthood. For instance, when asked about assisted insemination using the partner's sperm, almost all survey respondents found this acceptable; fewer approved of using donor sperm. When asked questions about using donated sperm, 58 percent of Canadians approved of DI in general. Forty-seven percent said they would use DI personally, but 22 percent were opposed to the use of DI (see research volume, *Social Values and Attitudes Surrounding New Reproductive Technologies*).

Views about the acceptability of separating the biological and the social aspects of parenthood differ among individual Canadians and among specific groups that make up Canadian society. We deliberately reached out to solicit the views of Aboriginal people and Canadians who are members of racial or ethnic minorities in roundtable discussions and focus groups. From these we gained insights into cultural values that affect how people see donor insemination — we learned, for example, that many Aboriginal cultures emphasize passing on one's spirit to the next generation through one's children. We also heard from people in these groups who spoke about the importance of continuing their "family line." Groups representing ethnic minorities told the Commission that children are a priority in part because they enable a community to pass on its cultural and ethnic heritage.

This social context of infertility treatments provides a backdrop for our more detailed discussion of these aspects with regard to each treatment. The remaining chapters in this section on infertility treatments present our findings on fertility drugs, assisted insemination, *in vitro* fertilization, and egg and embryo donation. It is important to remember, however, that the treatments are not discrete, but intertwined: fertility drugs are often used in both assisted insemination and *in vitro* fertilization; IVF is sometimes used as a diagnostic test of male fertility before making the decision to use

donor sperm rather than the sperm of the male partner; and patients often progress from one treatment to another.

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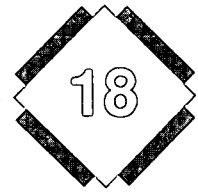

Infertility Treatments: Fertility Drugs

Fertility drugs are hormones that affect the reproductive system. They are the most common treatment for infertility — general practitioners and gynaecologists often prescribe them alone, and some are also used at infertility clinics in support of more complex treatments, such as *in vitro* fertilization. A review of current fertility drug treatment practices must take account of the two quite distinct contexts in which fertility drugs are prescribed: in the offices of family practitioners and obstetricians/gynaecologists consulted by women or couples having difficulties conceiving, and in specialized clinics where drugs are used to promote the maturation of multiple eggs for *in vitro* fertilization procedures. The number of women treated in each sector is difficult to estimate accurately on the basis of available data. Nevertheless, a rough comparison of annual Canadian sales of fertility drugs (excluding those for endometriosis) to the use of such drugs by IVF clinics would suggest that about three-quarters of the fertility drugs prescribed each year in Canada are prescribed by family practitioners and obstetricians/gynaecologists practising outside the specialized clinics. The existence of these two practice areas, as well as the different concerns brought before the Commission with respect to them, necessitates a two-pronged approach. The issues and the options for dealing with them (mechanisms available for ensuring appropriate use of the drugs) are different in each sector.

About three-quarters of the fertility drugs prescribed each year in Canada are prescribed by family practitioners and obstetricians/gynaecologists practising outside the specialized clinics.

Of particular concern are variations in the expertise and facilities available in the two sectors to deal with any adverse consequences of

fertility drug use. Ovulation induction drugs and other drugs used to treat infertility can have powerful effects on the body, especially if used in high doses. As a result, complications can occur, making it necessary for women taking the drugs to be monitored closely for side effects. This can be difficult to do without the specialized knowledge and laboratory facilities (needed to detect side effects biochemically even before other symptoms appear) that are available at specialized clinics.

Because these drugs play such an important role in the treatment of infertility, Commissioners needed information on several aspects of them. This chapter therefore begins with a description of the concerns we heard from Canadians. We go on to review briefly the development of fertility drugs and the purposes for which they are used in treating infertility. Then we present our analysis of the effectiveness and risks of the fertility drugs prescribed most commonly, based on our review of the limited available evidence, and we examine the current regulatory environment for the development and introduction of new drugs; we then review current practices in the prescription and use of these drugs in the two sectors just identified — infertility treatment clinics and the broader practitioner community. Finally, we present our conclusions and recommendations for ensuring that fertility drugs are used only in ethically responsible ways that take into account protection of the health of women and their children, respect for women's autonomy in making decisions about their reproductive health, and the need to generate the information necessary to ensure that policies and practices with respect to fertility drug use evolve in appropriate and beneficial ways.

The Views of Canadians

During our public hearings and through our surveys of fertility clinics and patients, the Commission heard many concerns about the way fertility drugs are currently used in practice. Many groups and individuals made representations relevant to the use of fertility drugs; the Commission heard from infertility patients and practitioners and those involved with the women's health movement; and we obtained information from pharmaceutical

> Most of what I know today I wish I had known 10 years ago, and it comes about directly as a result of my having read everything I could get my hands on ... the doctors never volunteered that information ... but, you know, I came into this process reasonably well educated, middle class, knowing how to ... go about finding things out. What happens to people who don't have those advantages?
>
> *D. Allen, private citizen, Public Hearings Transcripts, Toronto, Ontario, October 29, 1990.*

manufacturers and regulators, and many others. One category of concerns brought before the Commission related to the development and regulation of fertility drugs in Canada today. Commissioners agreed that a full understanding of the issues surrounding fertility drugs required an examination of both the commercial context for the development and marketing of these products and the regulatory environment governing their introduction and use. The conclusions arising from our review of the commercial context for the development and marketing of drugs are presented in Chapter 24, while the regulatory environment is examined later in this chapter.

Many groups and individuals who appeared at the public hearings or made submissions to the Commission expressed concern that commercial motives may be inappropriately driving the development of reproductive technologies (including fertility drugs), that these motives may promote high-tech approaches to the treatment of infertility to the detriment of other alternatives, and that industry research funding policies are emphasizing drugs and other infertility treatments at the expense of prevention. Many intervenors expressed concern about the activities of the pharmaceutical industry in developing and marketing fertility drugs and raised issues regarding drug safety, efficacy, and regulation. The Commission also heard views that pharmaceutical companies do not consider ethical aspects sufficiently when developing drugs. It was suggested to the Commission that some pharmaceutical companies avoid Canadian safety standards by testing drugs on women in developing countries, where standards of safety and informed consent are less stringent than in the developed world. This, they say, amounts to exploitation, with negative consequences for the lives and health of women and their families in the developing world.

Pharmaceutical companies told the Commission that the drugs they market were tested and monitored extensively according to Canadian regulations before being introduced into practice. Many Canadians expressed a belief, however, that manufacturers are insufficiently concerned with safety and that the government does not demand rigorous enough testing of fertility drugs before they are made available for general use. Not all individuals feel this way: some couples who were undergoing infertility treatment told the Commission they feared that too stringent

> Medical questions that need to be researched include, are there any effects of taking fertility drugs that do not become apparent until later life? ...
>
> And for the women who have taken fertility drugs, I would think they would have to be watched for perhaps 20 years afterwards to see if they differ statistically from any other group.
>
> *D. Ellis, The Canadian Federation of Business and Professional Women's Clubs, Public Hearings Transcripts, Toronto, Ontario, October 29, 1990.*

testing of fertility drugs in Canada is driving up prices and delaying development of new techniques.

A second category of concerns brought before us related to treatment and prescription practices. Commissioners learned through public consultations that many Canadians believe that fertility drugs are being overused or used too routinely, sometimes without the benefit of complete diagnoses of the infertility problems they are intended to treat. Women who had been treated for infertility told the Commission that doctors prescribing drugs for unapproved indications or at excessive dosages had put their health at risk, yet they felt they had not been adequately informed about the nature, effectiveness, and risks of the drugs they had been prescribed.[1] Medical professionals and many women's groups were concerned that there is little follow-up to identify the health effects of drug use, so that if there are short- or long-term harmful consequences, these may not be identified. Intervenors were also concerned that women were not being adequately informed about the known side effects.

> Also we are concerned about the health risks posed to women, medication which is given to women as fertility drugs ... The emotional cost and then translated into physical health cost do become phenomenal.
>
> *N. Javed, Immigrant Women of Saskatchewan, Public Hearings Transcripts, Saskatoon, Saskatchewan, October 25, 1990.*

For example, some women who had taken clomiphene citrate (a drug used to induce ovulation) told the Commission they had experienced side effects such as hot flushes, bloating, abdominal pain, dizziness, and insomnia. Some said they had not been told enough about what to expect; others said that their doctors had downplayed the seriousness of some of the symptoms (blurred vision, for example, though not life-threatening, could be alarming or create serious situations). Some women reported increased anxiety, depression, and mood swings — psychological effects that are considered mild and are not usually recorded by medical professionals. We

> When I asked the specialist about the side effects of Pergonal®, her attitude was distinctly unfriendly, like there was something wrong with me that I chose to ask a question about whether or not multiple births would happen as a result of taking Pergonal®, and she looked at me like I was being totally ungrateful and that I should just be very grateful that they were doing anything for me. And when I said that I want to know more about Pergonal®, she dismissed my concerns by giving me a leaflet on Clomid®, which I already had read.
>
> *D. Flanagan, private citizen, Public Hearings Transcripts, Toronto, Ontario, November 19, 1990.*

also heard testimony that insufficient attention is paid to a side effect that can have lifelong consequences for couples and their children — the higher incidence of multiple births following fertility drug use.

Commissioners also heard testimony from Canadians who fear that those who develop, approve, and prescribe fertility drugs have forgotten the lessons of the past. The harmful consequences of drugs such as DES and thalidomide have led Canadians to question whether fertility drugs on the market today are truly safe. Many believe that the possibility of unanticipated harm means there is a clear need for more information about the long-term effects of drugs used to treat infertility. Again, we heard concerns that women considering fertility drug use are not being adequately informed of the fact that little is known about the long-term effects of fertility drug use on women and their children.

> The experimental nature of procedures, drugs used, and risks involved must be clearly explained to potential users of new reproductive technologies. Informed consent must be stringently enforced. The use of the drugs Clomid® and Pergonal® to stimulate women's ovaries in *in vitro* fertilization comes with a number of disturbing side effects and little long-term follow-up studies. The use of DES in the '50s and '60s had long-range consequences that were not anticipated at that time and that children of that generation are dealing with now.
>
> *J. Hutchinson, Social Issues Committee, YWCA, Calgary, Public Hearings Transcripts, Calgary, Alberta, September 14, 1990.*

The Development of Fertility Drugs

Estrogen, a naturally occurring hormone that is responsible in part for regulating the female reproductive system, was first synthesized in the 1930s. This made possible many treatments that are now an accepted part of medical care. Hormones are used to treat menstrual disorders, to prevent pregnancy, and to prevent miscarriage when hormone insufficiency has been diagnosed. They are also used to alleviate the discomforts of menopause and prevent consequent complications. Progesterone, another hormone of the reproductive cycle, was also discovered and extracted during the same decade. Also, discovery of these two key hormones enabled researchers to influence menstruation and ovulation in mammals and thus to understand the reproductive process more fully.

These discoveries led to synthesis of the first fertility drugs — those that induce ovulation. The first of these was clomiphene citrate, which was developed and tested initially for its potential as a contraceptive in the 1950s. In 1961 it was shown to stimulate the ovaries when ovulation was

not occurring, and by 1967 it was being used to treat this condition. The development and use of clomiphene were followed closely by the introduction of human menopausal gonadotropin or hMG, a purified preparation of naturally occurring hormones produced by the pituitary gland. It induces ovulation by stimulating the development and maturation of the follicle and corpus luteum, the structures in the ovaries in which eggs develop and mature, leading to ovulation (see Chapter 7). Human menopausal gonadotropin was first used in 1958, but because it was expensive and difficult to extract (from human urine), it was not marketed widely until the 1960s, when a less expensive and easier method of extraction was discovered.

Once drugs were developed that could affect the various phases of ovulation, it became feasible to develop other techniques of assisted reproduction. The control over ovulation and the production of multiple eggs made possible by these drugs thus supported the development of assisted reproduction procedures during the last two decades. For example, *in vitro* fertilization is feasible largely because fertility drugs can be used to induce the ovaries to produce more than one egg — without these additional eggs the chances of fertilization, implantation, and development would be lower. At the same time, as discussed in Chapter 20, the use of these drugs in the context of assisted reproduction raises its own concerns.

> We have met women who have been given a trial of drugs like Clomid® or Pergonal® "just to see if it would help," before they have even learned the rudimentaries of charting their own cycles. In fact a recent article in the *Medical Post* suggests clomiphene citrate is the first step to solving the frustration of treating unexplained infertility. I'm sure there will be other intervenors who will address the risks of such medication or the concerns.
>
> *M. MacDonald, Fertility Management Services, Public Hearings Transcripts, Toronto, Ontario, October 31, 1990.*

There are about a dozen fertility drugs on the market in Canada; clomiphene and hMG are the most commonly used fertility drugs at present. Neither was ever fully evaluated before it was introduced — in fact, the exact metabolic pathway by which clomiphene acts is still not known. When these drugs were introduced into clinical practice in the 1960s, the need for rigorous standards in assessing the safety and effectiveness of drugs was not as clear as it is now. Today this need is evident, as is the need to follow up on drug use and to gather information on adverse effects that, if infrequent, can be gained only from studies of their use by large numbers of people over many years.

Effectiveness and Risks of Fertility Drugs

In keeping with our evidence-based approach, the Commission reviewed the available evidence on the drugs now used to treat infertility, looking for information that could be used as the basis for judgements about their effectiveness, side effects, and risks. This field is not static, however, and the many different clinical situations involved make it difficult to establish and apply general rules; in this evolving field, it would not be appropriate to make detailed recommendations about every drug that currently is used or may be used. It is nevertheless useful to outline our findings with respect to some of the most commonly used drugs. An initial assessment does not, however, preclude the need for continuing follow-up to monitor the effects of drug use and to adjust policies and guidelines in light of the knowledge gained.

> In fact, we know that incredible amounts of money go into trying to ensure that the drugs on the market are innocuous, and for all that, mistakes are made, such as thalidomide, something that everyone remembers. I am not referring to the malformations that still occur today due to the ingestion during pregnancy of drugs that are damaging to the fetus. These days, however, we no longer see such malformations, as they are eliminated as soon as they are detected in the mother using another new medical breakthrough — ultrasound. [Translation]
>
> *C. Bouchard, Campagne Québec-Vie, Public Hearings Transcripts, Quebec City, Quebec, September 26, 1990.*

A formal meta-analysis of the effectiveness of most fertility drugs is not possible because of the deficiency of data from a sufficient number of well-designed, large-scale studies. The Commission therefore used two criteria to determine whether a drug could be categorized as a treatment that is of benefit. First, the drug had to have been tested and been shown to be of benefit in appropriately designed randomized control trials with at least 200 subjects in each of the control and treatment groups. Alternatively, the drug had to be shown clearly to affect a specific pathway or factor known to cause infertility — there had to be a clear and plausible biological reason for the drug to "work." Unless the evidence showed that the drug fell into one of these two categories, we judged it unproven — that is, we found that the evidence is insufficient to say whether use of the drug is either better or worse than receiving no treatment.

The fertility drugs available today, when used alone, attempt to restore fertility by acting on various biological mechanisms in reproduction. They do not bypass any of the vital steps in the process that culminates in fertilization of an egg; instead, they attempt to correct disorders in women

and men that can cause hormonal imbalance, or to reverse the effects of an illness that blocks fertility. Most fertility drugs on the market today fall into one of three broad categories: ovulation induction drugs, ovulation suppression drugs, and those used to treat male infertility. We begin by describing their present use and our assessment of their effectiveness for these uses, given the limited data available, then go on to examine the risks identified to date.

Ovulation Induction Drugs

The most common use of fertility drugs is to correct ovulatory defects. If a woman is not ovulating, she cannot conceive — no egg is released to be fertilized. Disturbances in the hypothalamus — leading to either high or low hormone levels in the blood — or problems in the ovary, such as polycystic ovary disease, may be associated with irregular or absent ovulation. In these conditions the delicate balance of hormones has been upset, with the result that ovulation, if it occurs at all, does not occur regularly. As well, a small proportion of women (estimated at between 1 and 5 percent) who stop taking birth control pills after using them for a number of years do not resume normal cycles with ovulation for six months or longer,[2] and these drugs may be used by such women.

Ovulation Induction Drugs

Ovulation induction drugs are used for women who are anovulatory and also to promote regular menstrual cycles for women who have never had periods or who subsequently stop having them. They may also be used for women with oligomenorrhea, irregular cycles, ovarian failure (due to abnormal development, premature menopause, or damage to the ovaries by chemicals or radiation), or other hormonal dysfunctions that may cause a problem in ovulation, including those caused by polycystic ovary disease.

The drugs are also used in association with other infertility treatments, such as IVF, GIFT, and some assisted inseminations to maximize their effectiveness. They do this by stimulating production of multiple eggs per cycle — even if the woman was ovulating normally. Having more eggs to fertilize in a cycle increases the likelihood of a live birth.

The three main fertility drugs used to induce ovulation are clomiphene citrate, human menopausal gonadotropin, and bromocriptine. A fourth — gonadotropin-releasing hormone — is used in treatment of a specific syndrome.

Clomiphene Citrate

Clomiphene citrate (brand names Clomid®, Serophene®) is usually the first choice for treatment of women with irregular or absent ovulation. If

used in appropriate doses, it is considered by practitioners and experts in the field to be a relatively mild, safe drug with only a few adverse health effects. Although it carries a small risk of some potentially life-threatening side effects, these are much less frequent with clomiphene than with other ovulation induction drugs (see section on Risks of Ovulation Induction).

Clomiphene is generally accepted to be an effective treatment for all ovulation disorders and has become a standard treatment for them (see research volume, *Treatment of Infertility: Current Practices and Psychosocial Implications*). Even though there have been few randomized clinical trials on clomiphene citrate for ovulation disorders, several studies have demonstrated that clomiphene is effective in inducing ovulation in women who are anovulatory, and the biological mechanism makes sense. In addition, physicians who have had extensive experience with the drug have observed that women who have not been having periods are likely to resume normal cycles when they use this drug.

It is estimated in the literature that when used to treat infertility resulting from anovulation, clomiphene use results in pregnancy in 30 to 40 percent of cases, although a Commission study found that practitioners often overestimate clomiphene success rates (see research volume, *New Reproductive Technologies and the Health Care System: The Case for Evidence-Based Medicine*). In the Commission's assessment, then, clomiphene citrate has been proven effective and is of low risk when used at the proper dosage to treat lack of ovulation resulting from primary amenorrhea, secondary amenorrhea, and oligomenorrhea. When prescribed at approved doses when these disorders have been diagnosed, clomiphene citrate should be considered an accepted treatment. Because of the lack of definitive data from large-scale studies, however, continuing data collection on the results of clomiphene use is essential. In addition, women contemplating the use of clomiphene for an ovulation problem should be informed about the limited availability of reliable data on its use, and the effects of the dosages used should be monitored closely.

When prescribed at approved doses when these disorders have been diagnosed, clomiphene citrate should be considered an accepted treatment.

Clomiphene has also been used in the treatment of unexplained infertility, which is the diagnosis for about one-quarter of couples seeking treatment at Canadian infertility clinics. When no reason or condition can be found in either partner to explain their infertility, it is the judgement of practitioners and experts in the field that clomiphene is a low-risk, fairly simple treatment that could help rectify a hormone imbalance not detected by current methods.

Couples who have been trying to conceive for some time (particularly if they are at the age when they feel their reproductive time is running out) often feel a sense of urgency about treatment, especially the need to feel

that they are "doing something" to increase their chances of becoming pregnant. Physicians may conclude in these situations that prescribing clomiphene represents a compassionate response to a couple whose infertility cannot be explained, and there is always the hope that the drug might increase their chance of pregnancy, perhaps by correcting an undetected hormonal imbalance that may be affecting the couple's fertility. In fact, our survey of infertility clinics showed that 29 percent of women in couples with unexplained infertility are treated first with clomiphene, and there is some evidence to suggest that clomiphene citrate is effective when used in this way, although the mechanism is not understood.

Based on our assessment of the current data, clomiphene citrate may be an effective treatment for couples who have had unexplained infertility for a minimum of three years.[3] We therefore see a need to evaluate short-term treatment with clomiphene for this purpose in the context of a clinical trial, with stringent requirements for informed participation. Our review of the available evidence also showed, however, that the use of clomiphene citrate by women in couples with unexplained infertility of *less* than three years' duration is not justified. There is a greater probability that such couples will be able to conceive without treatment, and physicians should counsel these couples accordingly. The possible risks associated with clomiphene citrate, together with the likelihood of conception occurring naturally, mean it is not justified to prescribe clomiphene in these cases. However, if a woman's older age indicates that she has little chance of conceiving naturally before the three-year time period, she should be considered for inclusion in a clinical trial investigating clomiphene as treatment for unexplained infertility in older women.

Clomiphene citrate is also a common form of first treatment for infertile women with minimal or mild endometriosis. The evidence to date, however, is insufficient to draw any conclusions. This question should also be addressed through well-designed clinical trials.

Human Menopausal Gonadotropin

The second most common fertility drug prescribed to induce ovulation is hMG (brand names Pergonal®, Humegon®). Human menopausal gonadotropin is a much stronger drug than clomiphene citrate and it may induce ovulation in some women who do not respond to clomiphene. Its most common use is therefore to induce ovulation in women with amenorrhea, oligomenorrhea, or irregular cycles when clomiphene has not worked. It has more risks, however, and its side effects are quite severe (see section on Risks of

> hMG can be an appropriate treatment for women who are anovulatory and who have not responded to clomiphene citrate.

Ovulation Induction). To help avoid more serious side effects, hMG is often prescribed in conjunction with gonadotropin-releasing hormone (Gn-RH).[4]

There is a clear and plausible biological mechanism by which hMG works, and physicians have observed that the drug is effective in producing ovulation in many women with amenorrhea. Although side effects are more common than with clomiphene and may be severe, the Commission believes that fully informed women may wish to take this risk. In the Commission's assessment, then, hMG can be an appropriate treatment for women who are anovulatory and who have not responded to clomiphene citrate.

We did not find enough evidence, however, to state that treatment with hMG is effective for cases of oligomenorrhea and irregular cycles or for unexplained infertility. Women with these conditions still ovulate, albeit irregularly, so in theory they still have a chance of becoming pregnant. There is no convincing evidence that hMG corrects a specific biological pathway in this situation, and as the side effects are considerably more serious than those of clomiphene citrate, Commissioners believe that hMG is not an appropriate treatment for these conditions. There is not enough evidence to categorize hMG as effective, there is no pathway that would logically be corrected by hMG in this situation, and there is risk to the patient. Human menopausal gonadotropin is of unproven value for these diagnoses and should not be offered as treatment, nor should this use of hMG be a priority for research.

Bromocriptine

The effectiveness of bromocriptine (brand name Parlodel®) has not been proven in randomized control trials, but its mechanism of action is specific, and it has been shown to correct the high blood prolactin occurring in some women experiencing infertility. Based on what we currently know about how it works, its use is justified only to treat women who have documented high levels of prolactin, and it should not be used without this documentation.

Gonadotropin-Releasing Hormone

Gn-RH is prescribed for women in whom Kallman syndrome has lowered the level of Gn-RH to abnormal levels, causing amenorrhea. It is an effective treatment for this specific condition, and it works through a precise and convincing biological mechanism by restoring Gn-RH to normal levels. The Commission therefore concludes that the use of Gn-RH to treat amenorrhea caused by Kallman syndrome is effective and should be considered medically necessary.

Risks of Ovulation Induction

To determine what is known about the adverse effects of ovulation induction drugs, Commission researchers searched 15 computerized data

bases, looking at more than 500 journals from 1955 to the present. They found 4 840 references to research studies in this area. By the time they eliminated duplicates and studies that were unobtainable, they were down to 1 651 studies, 937 of which met the criteria for meta-analysis, allowing their results to be compared with each other. The complete results of this review are available in the research volumes accompanying this report (see research volume, *New Reproductive Technologies and the Health Care System: The Case for Evidence-Based Medicine*).

To determine what is known about the adverse effects of ovulation induction drugs, Commission researchers searched 15 computerized data bases, looking at more than 500 journals from 1955 to the present. They found 4 840 references to research studies in this area.

This comprehensive review showed that there has been a lack of systematic research on adverse side effects of ovulation induction drugs. Perhaps the most striking fact about the review is that it was the first comprehensive attempt ever in Canada to compile evidence on the adverse effects of ovulation induction drugs. The review showed that although these are immensely powerful drugs, there has been a relative vacuum in research attention directed to examining the results of their use; by contrast, drugs used for chemotherapy and cardiac arrhythmias are extensively reviewed. A commitment to the tenets of evidence-based medicine requires that this deficiency be remedied.

As with any medication, side effects occur in some women treated with ovulation induction drugs; in a small proportion of cases, serious health problems occur. The most serious side effect is a condition called ovarian hyperstimulation syndrome, which can be mild, moderate, or severe. Depending on the drug used, some women experience hot flushes, ovarian enlargement resulting in abdominal discomfort or pain, breast tenderness, dizziness, headache, nervousness, nausea or vomiting, fatigue, and visual disturbances. Women experiencing mild or moderate symptoms can be treated with rest, medication, and monitoring. However, the complications associated with severe cases (which occur in between 0.4 and 4 percent of cycles), though rare, can be life-threatening.[5] The highest risk of severe ovarian hyperstimulation syndrome is with the use of hMG. Women receiving ovulation induction drugs must therefore be monitored closely for signs of the syndrome, with careful attention paid to dosages, and steps must be taken to counteract the syndrome if it occurs.

Women receiving ovulation induction drugs must therefore be monitored closely.

Another of the adverse effects that has been shown clearly to result from ovulation induction drug use is an increased rate of multiple birth.

The use of hMG carries the greatest risk, with multiple pregnancies reported in as many as 32 percent of women in some studies. The rate of multiple births in Canada has increased dramatically since the advent of fertility drug use. The statistics show a dramatic increase in the multiple-birth set rate in the 1980s and early 1990s as fertility drug and IVF use became more common. Recently published data for Canada between 1974 and 1990 show that the multiple-birth set rate rose from 912.8 in 1974 to 1 058.9 per 100 000 confinements in 1990. During this same period, the birth rate for triplets, quadruplets, and quintuplets rose from 8.3 to 21.7 per 100 000 confinements.[6]

Canada is not alone in showing such an increase in multiple births. For example, in 1985 in Wales and England, there were 14 sets of triplets per 100 000 births; by 1989, it had risen to 27 sets per 100 000, and, since then, it has increased even more dramatically. An American study, too, has shown similar recent marked increases in the frequency of high-order multiple births. Interestingly, the increases there have occurred primarily among white women in their late 20s and early 30s who are of higher socioeconomic status. The explanation for all these rises is almost certainly the use of fertility drugs and techniques such as *in vitro* fertilization. In fact, the Statistics Canada study found that the increase in rate of multiple births of three or more children was highest in Ontario, which also has the greatest number of fertility clinics and is the only province where IVF is covered under the provincial health care plan.

Further evidence that infertility treatment is the cause of the increase in multiple births is found in a study in Britain in the early to mid-1980s, which found that 70 percent of mothers of quadruplets and 36 percent of mothers of triplets had been prescribed ovulation-stimulating drugs. A decade later, with increasing use of these drugs and other techniques, it is likely that an even greater proportion is attributable to this.

Another of the adverse effects that has been shown clearly to result from ovulation induction drug use is an increased rate of multiple birth.

It is logical to assume that fertility drug use is largely responsible for the increase in the multiple birth rate. Although a substantial percentage (38 percent) of all individuals born following *in vitro* fertilization in Canada are from a multiple pregnancy, the absolute number of IVF births for the Canadian population is still small; thus, fertility drug use, particularly ovulation induction drugs, must have made a greater contribution to the marked rise. As discussed in Chapter 20, multiple pregnancies pose significant risks for pregnant women, for the fetuses, and for the eventual children, as well as costs for the health care system and society generally as these children grow up.

The possibility has also been raised that fertility drug use could be associated with subsequent ovarian cancer. A large recent study for the

National Institute of Child Health and Human Development found that the data available at that time (January 1993) were inadequate to estimate whether there is an increased risk and, if so, its magnitude. However, this possibility is a cause for concern, pointing to the need for further research.

In general terms, further research is needed to provide full information on the long-term health effects of fertility drug use on women and their children. Although clomiphene has been in use since the late 1960s, for example, only recently have any data been available on its longer-term health effects. There has been considerable conjecture about the effects of clomiphene on the health of children; in particular, an Australian study raised the possibility of an increase in the occurrence of neural tube defects, but this has not been confirmed in other studies or in a large recent case-control study on this topic.[7] Overall, studies of children at birth have shown that the incidence of congenital anomalies among the children of women who took fertility drugs has been similar to that in the general population.[8]

Studies of children at birth have shown that the incidence of congenital anomalies among the children of women who took fertility drugs has been similar to that in the general population.

Ovulation Suppression Drugs

The second group of drugs used to treat infertility, ovulation suppression drugs, are used primarily to treat women with endometriosis, one of the risk factors associated with infertility. Ovulation suppression is a highly invasive step, yet it is used, with no evidence that it is effective, to treat a condition whose cause and pathogenesis are not even understood, simply in the hope that treatment will have an effect on the woman's fertility. The drugs are used to suppress her menstrual cycle for at least six months, in the hope that the symptoms affecting fertility will subside and conception will be more likely to occur once drug use is discontinued and menstrual cycles resume.

The Commission analyzed the data available in the worldwide literature on three types of common ovulation suppression drugs — danazol, norethindrone, and Gn-RH analogues — and their effect on endometriosis-related infertility. Based on this analysis, it is the Commission's assessment that the use of danazol, norethindrone, Gn-RH analogues, or any ovulation suppression drug is ineffective in treating infertility thought to result from endometriosis or unexplained infertility. Their use should be discontinued, as they have moderate to severe side effects; moreover, they eliminate the possibility of conceiving naturally for the duration of treatment. Such risks should not be undertaken when there is evidence that the use of these drugs is ineffective.

Drugs to Treat Male Infertility

The Commission evaluated data on the drugs used most often to treat male infertility; they include clomiphene citrate, gonadotropin-releasing hormone, oral kallikrein, bromocriptine, and androgens (male hormones).

Seminal Defects

Since it is usual for a man's sperm count to vary, an accurate diagnosis of a seminal defect can be made only if several sperm samples are collected over a period of time. Data collected from Canadian academic infertility clinics show that in couples where the man had a seminal defect, 74 percent had oligospermia (reduced sperm count) and 26 percent had azoospermia (no sperm).

Azoospermia clearly results in infertility, but the relationship between low sperm count and male infertility is less clear. The partners of men with oligospermia have a live birth rate of 2 percent per month of unprotected intercourse, compared to about 20 to 25 percent for the population at large. Although 20 million sperm per millilitre is regarded as the dividing line between oligospermia and a normal sperm count, men with lower sperm counts (less than 5 million) have been known to conceive. Many physicians believe that as-yet-undetectable subfertility in the female partner adds to the problem in cases where a couple in which the man has oligospermia cannot conceive. This would help to explain why the partners of some men with low sperm counts are able to conceive while the partners of others cannot.

Clomiphene Citrate

The Commission found that there is not enough evidence to determine whether clomiphene citrate is an effective treatment for men with oligospermia. It is inappropriate to continue to expose men to the risks of clomiphene use without collecting the data that would allow evidence-based decisions about whether its use constitutes appropriate medical practice; this drug should therefore be a priority for investigation in the context of a well-designed clinical trial, but it should not be used as an accepted treatment.

Gonadotropin-Releasing Hormone

Gn-RH is prescribed for men in whom Kallman syndrome has lowered the level of Gn-RH to abnormal levels, causing azoospermia. It is an effective treatment for this specific condition, and it works through a precise and convincing biological mechanism by restoring Gn-RH to normal levels. The Commission therefore concludes that the use of Gn-RH to treat azoospermia caused by Kallman syndrome is effective and should be considered medically necessary.

Oral Kallikrein

The Commission found no evidence that oral kallikrein is an effective treatment for oligospermia, and as there is no biologically plausible way it would work we conclude that it should not be used for this treatment purpose. Nor should it be a research priority.

Bromocriptine

Bromocriptine is prescribed for oligospermia with the aim of reducing estrogen levels. The Commission's analysis of international data revealed insufficient evidence to categorize bromocriptine as effective or ineffective.[9] However, there is a potential mechanism by which it could work, so we conclude that its effectiveness should be investigated in a clinical trial.

Androgens

The male hormones (androgens) mesterolone and testosterone are sometimes prescribed for men with oligospermia in the hope that sperm production will be stimulated. As a group, androgens have been shown to be ineffective in treating oligospermia. They should therefore not be offered as treatment and should be considered a low priority for research.

Need for Research

Male infertility has been a neglected area in research, despite the fact that 24 percent of couples seen at Canadian infertility clinics are infertile because of a diagnosed problem in the male partner (see research volume, *Treatment of Infertility: Current Practices and Psychosocial Implications*). Medical science is unable to identify a specific cause for 30 to 40 percent of cases of male infertility, and researchers have estimated that only 11 percent of infertile men are potentially treatable at present. As we pointed out earlier, the area of male infertility warrants much greater research emphasis. Assigning a higher research priority to investigating male infertility would promote greater understanding of the causes, diagnoses, and treatments of seminal disorders and might enable a reduced use of treatments in female partners who are fertile because of male infertility.

Ensuring Safe and Effective Fertility Drug Treatment in the Future

In summary, the Commission concludes that ensuring the effectiveness of fertility drug treatment requires that clinical trials on the uses of drugs we identified as requiring more research be carried out in licensed clinics and approved by the National Reproductive Technologies Commission. While it is not current practice for provincial/territorial ministries to be involved in funding clinical trials, provincial departments

do have a responsibility to ensure efficient management of the health care system. Therefore, as discussed in Chapter 4, funding should be provided in part by provincial/territorial health ministries, in part by arm's-length contributions from the pharmaceutical manufacturers of the fertility drugs used, and in part by federal research funding bodies. The Commission therefore recommends that

63. Randomized controlled trials of fertility drugs already on the Canadian market be designed and carried out by licensed clinics providing assisted conception services, in conjunction with the National Reproductive Technologies Commission and the Health Protection Branch, Health Canada. Participation of women and men in these trials should involve their fully informed consent, and research proposals should obtain prior approval of both the Assisted Conception Sub-Committee of the National Commission and local research ethics boards.

and that

64. Funding for well-designed clinical trials of fertility drugs be made available by pharmaceutical companies (with arm's-length administration of the funding), medical research funding bodies such as the Medical Research Council, provincial/territorial ministries of health, and Health Canada through the National Health Research and Development Program.

The Drug Regulatory System

The legacy of harm caused by two drugs formerly prescribed during pregnancy, thalidomide and DES, raises questions for many Canadians about whether the drug regulatory system is as well designed as it could be to screen drugs for safety and effectiveness before they reach the market. No scheme can offer absolute assurances of safety; it is only when a drug is used by thousands of people over a significant period of time that uncommon or longer-term effects on health can be identified and assessed. It is possible, nevertheless, to design the initial screening process and post-marketing surveillance procedures in such a way as to ensure that any

unforeseen harmful consequences are identified, assessed, and dealt with quickly and appropriately.

The Current System

We reviewed the process by which drugs are approved in Canada before they go on the market and the mechanisms in place to monitor the safety of drugs following their approval. The production and marketing of drugs used to treat infertility, like all other human prescription drugs, are heavily regulated in Canada. Canada's drug laws were changed in 1963 after the harmful effects of thalidomide were identified, to require that companies submit evidence of effectiveness of a new drug before they can be licensed. From their initial development to the approval for sale to consumers, drugs are subject to a lengthy process of testing and evaluation. The research leading to the marketing of a safe, effective drug can take decades and cost a pharmaceutical company millions of dollars.

The process begins with the manufacturer conducting animal and laboratory studies (pre-clinical trials) to identify the therapeutic uses and risks of a new compound, to determine new uses of an existing compound, or to test the use of an existing compound produced in a new way. This research may take place in Canada or another country where the pharmaceutical company has research facilities. If the laboratory and animal research demonstrates that the drug has the desired therapeutic effect and has an acceptable level of safety, the next step is to conduct research using human subjects. If the research is to be conducted in Canada, the company must first obtain permission from the Drugs Directorate, Health Protection Branch, Health Canada, to begin clinical trials with human subjects. Companies must then submit data from three phases of clinical research to gain approval to market a new drug. In phase I clinical trials, designed to assess safety, a small number of healthy volunteers receive the drug. In phase II trials, small numbers of selected patients receive the drug to see whether it affects the condition it is intended to treat. If both phases show appropriate results, several hundred or even thousands of patients participate in formal, randomized double-

> Improvements are needed to the existing process of regulating the use of pharmaceutical products. IVF involves the use of a number of substances and technologies the long-term effects of which on the health of women and children are not yet known. D.E.S. Action proposes that the regulations governing the use of pharmaceutical products and medical procedures include a criterion which takes into consideration the current "social need" for any new product and procedure. [Translation]
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> *Brief to the Commission from D.E.S. Action Canada, June 1991.*

blind trials (phase III). (Neither patients nor researchers know what drug is being administered or whether it is a placebo.) The purpose of phase III trials is to assess the therapeutic and adverse effects of the drug at the recommended dosage and also to identify other medications with which the new drug may interact.

If the three phases of clinical trials demonstrate that the drug is effective and safe, the pharmaceutical company files a New Drug Submission (NDS) with the Drugs Directorate, indicating trial results, dosage strengths and the form in which the drug will be marketed, and details about known side effects and efficacy. The Drugs Directorate conducts a detailed review of the NDS to assess whether the drug should be approved for the Canadian market. Foreign research results are accepted if the research is judged to be of sufficient quality. If the drug is approved, it receives a Notice of Compliance, and the recommended dosage ("approved dosage") and uses for the drug ("approved indications") are set. If a company subsequently wants to promote the drug for additional uses or at different dosages, it must submit additional evidence that the drug is proven effective and low-risk at those dosages and for those uses.

Drugs are also subject to post-marketing surveillance for seven years following their introduction, but as we discuss later in this chapter, this system, known as the Adverse Drug Reaction Reporting Program, has several shortcomings.

Changes in the Drug Approval System

Although our country is considered to have one of the most stringent and rigorous drug regulatory systems in the world, concerns have arisen regarding its capacity to ensure that drugs used in Canada are effective and safe over the longer term. We heard criticisms that Canada's system is too isolated from drug regulatory systems in place in other industrialized countries and that, once drugs are approved for sale in Canada, there is negligible follow-up and limited monitoring to identify harmful side effects. Many critics of the current system also argue that Canada's slow approval process prevents Canadians from obtaining access to new or improved drugs in a timely fashion.

Several reports have evaluated the current regulatory system and made recommendations to address various of these concerns. The most recent of these include *Working in Partnerships: Drug Review for the Future*, by Denis Gagnon (1992); *Developing a National Postmarketing Pharmaceutical Surveillance Program*, by J.N. Hlynka (1991); *Towards an Improved Drug Regulatory System: Progress Since Stein*, by the Drugs Directorate, Health and Welfare Canada (1992); and *Benefit, Risk and Cost Management of Drugs*, report of the Canadian Public Health Association National Advisory Panel on Risk/Benefit Management of Drugs (1993). Other reports, such as *Breast Cancer: Unanswered Questions*, by the

Parliamentary Sub-Committee on the Status of Women, have also addressed issues related to drug regulation.

A common theme of these reports, and a recurring one heard from the Health Protection Branch, industry, health care professionals, and consumer groups, is the need to change the drug regulatory system. The proposed reforms include streamlining the approval process, making the regulatory system more accountable to decision makers outside the system, and in particular strengthening follow-up on monitoring procedures for drugs already on the market.

Among the reforms being considered to speed up the drug approval process is aligning it with internationally accepted standards such as those of the European Community or the U.S. National Institutes of Health.[10] This would involve, for example, taking foreign reviews of drugs into account during the review process; becoming more involved in cooperative drug reviews with comparable countries such as Australia and Sweden; and adopting the European Community criteria for drug evaluation, which have become the standards in many industrialized countries.

In the Commissioners' view, however, different countries could well have varying views on what constitutes an acceptable level of drug safety. In some cases, Canadians may be unwilling to accept a level of risk or a side effect associated with a drug that another country finds acceptable, and vice versa. International data and studies will continue to be useful to Canadian regulators, but we believe that fertility drugs in particular should be approved or rejected according to standards of safety and efficacy that are acceptable to Canadians. We conclude that Canada should maintain sovereignty over the review process leading to approval or disapproval of fertility drugs, as the drugs used are powerful and have the potential to do harm. The Commission therefore recommends that

We conclude that Canada should maintain sovereignty over the review process leading to approval or disapproval of fertility drugs, as the drugs used are powerful and have the potential to do harm.

65. The evaluation of drugs used in assisted conception be considered an area where Canadian specifications for evaluation are required, in recognition of the potential long-term health effects of these drugs on women, men, and children.

A second way to streamline the system would be to make greater use of external reviewers (outside the Drugs Directorate) to evaluate drug submissions and provide expert advice in specific areas. We agree that this is appropriate, provided the external reviewers are objective (their

objectivity would be compromised, for example, if they performed contract work for both the Drugs Directorate and pharmaceutical companies) and they have the appropriate training and expertise in regulatory matters if asked to conduct complete drug reviews. Drug evaluations require two distinct types of expertise: clinical assessment of a drug and regulatory analysis. External reviewers may be well qualified to give a medical analysis of a drug, but they may lack the knowledge about regulation necessary to conduct a complete drug review.

In investigating the effectiveness and safety of existing fertility drugs, the Commission found that there is a small network of physicians in Canada who have both practical experience prescribing fertility drugs and extensive experience conducting clinical trials and evaluating existing research on effects of the drugs. We believe that these individuals would be highly qualified to assist the Drugs Directorate in clinical assessments of new fertility drugs and in addressing issues that arise with respect to the safety or effectiveness of existing drugs. The Commission recommends that

66. When assessing new fertility drugs for approval, the Drugs Directorate consult with experts who have clinical and research experience with fertility drugs, to ensure that the benefits and risks have been evaluated comprehensively. Consideration should be given to forming permanent advisory committees of individuals qualified to assess specific categories of drugs, such as those used in treating infertility.

Recombinant Fertility Drugs

The active ingredients of many fertility drugs are natural hormones; for example, in the past, gonadotropins were extracted from the urine of women who were post-menopausal — a complex, time-consuming, and inefficient process. In the future, genetic engineering will enable production of large quantities of gonadotropins using human genes spliced into microbial or other non-human cells. Because recombinant drugs will be produced by genetically altered organisms, they must be assessed to determine whether the organism used in the production process has also left behind significant impurities.

The Drugs Directorate has developed broad guidelines for the safety and testing of biotechnology products. Some observers believe, however, that the guidelines should be more comprehensive and specific and should have the capacity to evolve as the science develops. While assessing the appropriateness of the guidelines for safety testing of recombinant drugs is beyond the mandate of this report, we believe that this issue should be

addressed by the federal government. The Commission therefore recommends that

> **67. The federal government develop up-to-date criteria, to be used in the approval process, appropriate for screening the safety and efficacy of new biotechnology products, including recombinant fertility drugs.**

Ethical Review of Trials

Finally, the Commission notes that some fertility drug research trials are not conducted in hospitals and universities, where they are subject to review by institutional ethics review boards, but in the offices of individual physicians under the auspices of pharmaceutical companies. Because of the potential for serious effects on the health of users and their children, we believe that all such trials should be reviewed by research ethics boards, regardless of the setting in which they are conducted. This would ensure that the research is conducted in accordance with existing guidelines for medical research involving human subjects, including the requirement that participants be fully informed before consenting to participate, and that they are not charged for any drugs used in the trial. There may be costs involved in this ethical review, and these costs should be recoverable from the pharmaceutical company by the institution conducting the review. We recommend that

> **68. The federal drug approval process include a requirement that any proposed trial of a fertility drug be reviewed by the research ethics board of a major hospital or university.**

Current Treatment and Prescription Practices

The Commission identified three issues of particular relevance here: the practices surrounding how drugs are prescribed and used; the information available to women and couples about the drugs they are considering taking; and the information available on short- and long-term health effects of drug use.

Prescription Practices

Drugs are tested and government-approved for certain uses and at certain doses, but once they reach the market doctors can prescribe them as they see fit. Doctors often hear of alternative unapproved uses of drugs from medical journals, at conferences, and from colleagues in other countries where drugs may be approved for different indications. Many fertility drugs are therefore commonly used for unapproved indications, and they are also used at unapproved dosages. In this context "unapproved" does not mean the drugs have been assessed and refused approval: it means that this particular use or dosage has not been assessed and approved in Canada. Some of the unapproved uses are in conjunction with new and emerging technologies that themselves have yet to be evaluated adequately.

There are often good reasons why physicians prescribe drugs for unapproved uses; certain drugs that are valuable in treating rare medical conditions could not be used if physicians were limited only to approved uses in their prescription decisions (see research volume, *New Reproductive Technologies and the Science, Industry, Education, and Social Welfare Systems in Canada*). This is because pharmaceutical companies do not wish to absorb the cost of the additional testing that would be required to gain government approval for uncommon indications where the market return would be small.

Nevertheless, the Commission sees no benefit in allowing fertility drugs to be prescribed at unproven doses and for new indications outside the context of clinical trials. The risks of prescribing fertility drugs for unproven uses and at unproven doses should not be taken unless the drugs are administered in such a way that the information gained can be used to decide whether they work and are of acceptable risk. A woman taking high doses of an unproven fertility drug may be putting her health at risk without good evidence that she is any more likely to have a child.

Without the comparisons made possible by well-designed trials — in which results can be compared between those who did and those who did not take the drug — risk is undertaken without even resulting in an increase in knowledge in the field, knowledge that is needed to minimize the number of women exposed to potential harm. Doctors should be cognizant of the fact that prescribing drugs in this manner is experimentation and should therefore be governed by the checks and balances of any research involving human subjects. The Commission therefore concludes that clear protocols and guidelines for the use of

fertility drugs by practitioners, both in licensed clinics and practising outside them, are needed. In particular, the Commission recommends that

69. The Assisted Conception Sub-Committee of the National Reproductive Technologies Commission develop, with input from the relevant professional bodies, standards and guidelines for use by practitioners prescribing fertility drugs in licensed clinics providing assisted conception services.

and that

70. The College of Family Practitioners of Canada and the Society of Obstetricians and Gynaecologists of Canada develop and disseminate similar guidelines for use by practitioners prescribing fertility drugs outside the context of licensed clinics. In particular, these guidelines should recommend against the prescribing of drugs where safe use requires specialized expertise and hormonal monitoring of women taking the drugs.

In addition, physicians need an objective source of information on these drugs. At present, the most widely used source is the *Compendium of Pharmaceuticals and Specialties* (CPS). The CPS is published and distributed by the Canadian Pharmaceutical Association and lists the names, uses, and side effects of drugs on the Canadian market. The information in the CPS is supplied by drug manufacturers, who also subsidize the Canadian Pharmaceutical Association. Thus, the CPS is not an objective source of drug information. One study found that 46.9 percent of drugs listed in the 1977 edition of CPS could be classified as "probably useless," "obsolete," or "irrational mixtures," and that more than 60 percent did not list well-known risks, dangers, or adverse effects.[11] The Commission was troubled to find research showing that many doctors rely solely on CPS information for their drug data. If this is a doctor's only source of information about prescription drugs, the health of patients could be jeopardized. The Commission therefore believes that

Government, as the guardian of the public interest, should take a role in facilitating the provision of objective sources of drug information independent of pharmaceutical manufacturers so that doctors have a practical alternative to the CPS.

government, as the guardian of the public interest, should take a role in facilitating the provision of objective sources of drug information independent of pharmaceutical manufacturers so that doctors have a practical alternative to the CPS. This is not an issue that is going to be resolved in the short term; it is one faced by all developed countries and will need the ongoing cooperation of several sectors. If the interests of Canadians are to be protected, however, physicians must have better access to practical, useful, and objective information on drugs.

We therefore conclude that the federal government should identify mechanisms to meet the need for development and dissemination of comparative, objective assessments of drugs, including fertility drugs. In the meantime, our recommendations with regard to fertility drug use in clinics and in the broader medical community, together with our recommendations regarding collection and dissemination of information on drugs, will help meet this need with regard to fertility drugs in particular.

Monitoring is already done by several bodies, but the Commission is of the view that the promotional activities of companies marketing fertility drugs in particular in Canada should be monitored on a continuing basis and therefore recommends that

71. The promotional activities of companies marketing fertility drugs in Canada be monitored on a continuing basis by the Assisted Conception Sub-Committee of the National Reproductive Technologies Commission and that any inappropriate activity be publicly identified.

Informed Consent

As we have noted, most women who take fertility drugs obtain them from their general practitioner or gynaecologist. The Commission was contacted by some patients who were prescribed fertility drugs by physicians practising outside clinics. Their information, though valuable, is not likely to be representative, and in fact there is no practical way at present to identify or obtain representative information concerning use of fertility drugs prescribed by general practitioners or gynaecologists.

The Commission did, however, survey 1 395 clinic patients, and their views can be used to draw conclusions about patient perceptions of fertility drug treatment as practised at clinics. About half the women had already had some kind of fertility drug treatment before coming to the clinic. At the clinics, a majority of patients were prescribed fertility drugs, either alone or in conjunction with other treatments. Patients receiving only fertility drugs reported receiving much less information or counselling than those

undergoing other treatments — fewer than half those taking fertility drugs said they received counselling or took part in discussions about their treatment, compared to 89 percent of patients who had IVF (see research volume, *Treatment of Infertility: Current Practices and Psychosocial Implications*).

The data collected for the Commission on the practices of fertility clinics and attitudes of patients showed that counselling, information provision, and support for informed decision making do not measure up to patients' expectations with respect to informed choice or indeed to the standards set by physicians' professional organizations. The Commission also found that this information deficit seriously limits patients' ability to make decisions about their health. Without sufficient information about fertility drug treatment and its attendant risks, benefits, costs, and possible outcomes, patients must cope with added physical and psychological stresses. The Commission therefore recommends that

72. Fertility drug treatment provided in licensed clinics offering assisted conception services be administered in a context of informed choice for patients. Standard protocols should include the availability of professional, non-directive counselling, and full, unbiased information on what is known about the side effects and long-term outcomes of the drug(s) to be used.

and that

73. The Assisted Conception Sub-Committee of the National Commission develop, with input from relevant professional bodies, unbiased and readily understandable information materials on fertility drugs for distribution to patients by physicians and clinics providing assisted conception services.

Identifying Short-Term Effects

Neither the government nor pharmaceutical companies have effective systems in place to monitor the results of fertility drug use after a drug has been approved for sale. There is a need for more data on both the short-term risks associated with their use and, especially, any long-term health effects on women or their children.

As we have discussed, no drug approval process, no matter how rigorous, can guarantee that a drug is safe when it is approved for market.

Only after a large number of people have used a drug over a long enough period of time does it become possible to predict all the potential adverse effects of a drug with any accuracy. Clinical trials generally involve 2 000 to 3 000 patients who have used the drug. With a sample of this size, rare adverse effects, or effects that occur many years after the end of the trial, cannot be identified. For these reasons, monitoring drugs after they come on the market (called post-market surveillance) is essential for physicians, consumers, and regulators alike.

The current system for collecting and analyzing data on the adverse effects of drugs has several important shortcomings. Under the Adverse Drug Reaction Reporting Program, doctors submit a report of observed adverse drug reactions (ADRs) to the pharmaceutical company that manufactures the drug or directly to the Drugs Directorate's Bureau of Pharmaceutical Surveillance. But the ADR Reporting Program is little used. There are two basic problems. There is no meaningful system by which ADR report events are gathered, collated, analyzed, and published. Also, physician compliance with reporting is low. The reporting system is inadequate. It lacks criteria telling physicians what the Drugs Directorate wants them to report. Health care professionals are not well informed about ADR reporting procedures. Moreover, there is lack of feedback to health care professionals when an ADR report is filed.

The rate of reporting ADRs by physicians is low. One industry representative told the Commission that only 10 percent of all adverse reactions are reported by doctors. Two factors contribute to the low reporting rate. Without a clearly defined system, there is little incentive for physicians to participate. As one expert told the Commission, "Physicians are very pragmatic people. They won't report adverse drug reactions unless they can see results." At the same time, the reporting system is strictly voluntary, and physicians are offered no compensation, despite the time required to complete the necessary paperwork, to follow up on patients, and to participate in any further investigation.

Regulatory requirements for adverse drug reactions do not cover all drugs; after a drug has been on the market for seven years, for example, it is no longer considered necessary to monitor for adverse reactions. Another weakness is poor analysis and follow-up on adverse drug reactions. As a result, reports of adverse drug reactions constitute anecdotal and unstandardized evidence that has not been collected following a rigorous scientific approach; as such, they are valuable only in indicating a potential problem and the need for appropriately rigorous study of it.

A recent proposal by the Drugs Directorate would require health care practitioners to report adverse drug reactions to five regional ADR reporting centres or to the manufacturer. The regional centres would transmit the reports to the national ADR reporting centre, which would compile the reports and distribute them to manufacturers, the regional centres, and the WHO Collaborating Centre in Sweden. The national centre would then evaluate the data to identify drugs requiring further study. The federal

government has committed funding to a regional pilot project using this approach but has not committed funds to implement the national program.

We strongly agree that the post-market surveillance system should be improved, but we believe that further steps are needed as well. The financial burden of follow-up on preliminary indications of adverse side effects or outcomes should not fall solely on the federal government. We believe that drug companies should be required to help fund investigations into problems identified through analysis of ADR data. Pharmaceutical companies have a lot to gain or lose, depending on the findings of researchers: profits increase if a drug is found to be safe, and costly legal action can be avoided if findings show at an early stage that a drug is dangerous. Therefore, the Commission believes companies should not do the investigations themselves but should be required to provide arm's-length financial support for investigations on the adverse effects of their products emerging from ADR data. We also believe that pharmaceutical companies that market fertility drugs should be required to help fund studies on fertility drugs done by the National Reproductive Technologies Commission using its data base to link with other health data bases to assess long-term outcomes of drug use, as discussed below. This funding should have no conditions attached other than it is to be used to study outcomes of fertility drug use. To minimize the possibility of influencing the Commission in any way, an intermediary body should receive the funding and administer it. The Commission therefore recommends that

Companies should not do the investigations themselves but should be required to provide arm's-length financial support for investigations on the adverse effects of their products emerging from ADR data.

74. The federal government require pharmaceutical companies marketing fertility drugs to contribute funding for studies found by Health Canada to be required based on incoming adverse drug reaction data. This funding should be administered by national research funding agencies, but the studies should be facilitated and overseen by the National Reproductive Technologies Commission.

Appropriate data collection and recording are necessary to permit assessments of the effects and outcomes of fertility drug use. The Commission believes that the data base established within the National Reproductive Technologies Commission must be structured and maintained so as to make possible evaluation of the short- and long-term health effects

of fertility drugs. Submission of data to enable this would be required from every licensed fertility clinic.

Analysis of outcome information on fertility drugs, facilitated by the collection of standardized data by the National Reproductive Technologies Commission, will make possible the establishment of appropriate clinical standards; will inform policy decisions about drug treatment and its place in reproductive medicine; and will encourage priority setting for research in this field. Harmful drug effects identified by the NRTC through this data collection and analysis could also be made available to the ADR regional centres for distribution to practitioners, as well as to the public generally. The Commission recommends that

75. Categories of data established by the National Reproductive Technologies Commission on the use of fertility drugs, information on individuals receiving them, and data on adverse effects and outcomes be reported annually by infertility clinics to the National Reproductive Technologies Commission as a condition of licensing. Data collected in this manner should be analyzed and evaluated regularly by the National Reproductive Technologies Commission.

76. The National Reproductive Technologies Commission issue an annual report giving significant findings resulting from data collection and analysis, and that aggregate data be used in the development of written information materials on the drugs used most commonly to treat infertility, to be distributed to clinics, regulators, and people contemplating the use of fertility drugs.

and that

77. General practitioners and obstetricians/gynaecologists prescribing fertility drugs should continue to report adverse effects from the use of fertility drugs through the Adverse Drug Reaction Reporting Program or the proposed regional system if it is implemented.

Tracking Long-Term Outcomes

A major problem in assessing the long-term health effects of ovulation induction drugs (and many other drugs) is that no mechanism is in place to track long-term consequences. Provincial and federal bodies that have studied the current situation with regard to the long-term effects of prescription drugs have found it lacking. Concerns about long-term tracking of outcomes of fertility drug use are particularly important, and the Commission took this issue very seriously.

The Commission found no Canadian data available on these drugs because of the absence of a mechanism to gather and assess data on long-term outcomes. There are, however, innovative ways of using data already being collected by the health care system (such as hospital admission and discharge records), to determine whether women who took fertility drugs subsequently had health problems requiring treatment. Computerized record linkage using existing data bases could drastically reduce costs and widen the scope of study by using health and vital statistics data already being collected by governments or institutions for other reasons and linking it to data — for example, on drug use — collected by other facilities.[12] This kind of data linkage is possible without violating people's privacy and would allow evaluation of any long-term effects of taking medications, including ovulation induction drugs. What is required is a uniform method of collecting information on people who have taken the drugs, so that record linkage studies of this type can be carried out.

Rational decision making in health care — whether by patients, practitioners, or policy makers — must be based on sound evidence, which can be provided only by collecting appropriate follow-up information over time ... Monitoring mechanisms are necessary to evaluate data in an ongoing way to inform decisions at many levels.

Rational decision making in health care — whether by patients, practitioners, or policy makers — must be based on sound evidence, which can be provided only by collecting appropriate follow-up information over time. The Commission finds it disturbing that no mechanism is in place to allow the long-term health effects of fertility drugs (or, indeed, other drugs) to be assessed, particularly because those effects could have implications for women and men taking the drugs today as well as for their children. Current systems set up to store health and hospital records often do not provide for a mechanism to pull those data together into groupings that would permit analysts to assess the effects of past treatments. Moreover, after drugs are approved for use, little is done to ensure they are used appropriately or to track their use and effects. Monitoring mechanisms are necessary to evaluate data in an ongoing way to inform

decisions at many levels. In the field of fertility drugs, this information would allow assessment of new and existing drug treatments, would make possible the establishment of clinical standards, and would inform policy decisions about drug treatment and its place in reproductive medicine. It would allow decisions to be made more quickly about the appropriateness of treatments and would encourage priority setting for research in this field.

Health-related data are accumulated across the country in a variety of forms: in hospital records, physician billing data for health insurance plans, death and birth records, and a host of other data bases. Using the example of the province of Saskatchewan (which has data available on hospital, medical, and prescription drug use — see research volume, *New Reproductive Technologies and the Health Care System: The Case for Evidence-Based Medicine*), researchers for the Commission investigated the feasibility of linking information from different data bases through time and across health sectors, to see whether outcomes of treatments could be assessed. This is a specific example of the kind of valuable study that could be carried out in the field of human reproduction, and we conclude on the basis of our investigation that such approaches would be feasible.

For example, clomiphene citrate use would be a good subject for a pilot record linkage study in Saskatchewan, where appropriately structured data bases exist. Health care data amassed since 1967 (the period during which clomiphene has been in use) could be accessed to answer outstanding questions and contribute useful information and analysis to the field of infertility research without involving the added major expense of primary data collection. Such a study could link data on clomiphene use with data from health and vital statistics data bases to assess its effectiveness, the factors associated with successful and unsuccessful outcomes, and any later negative impacts of the drug during the study period. Such studies could also provide data on the direct costs to the health care system. Not only could such studies link ovulation induction using clomiphene with outcomes, it could also compare outcomes in the children of women who took the drugs with outcomes in the children of similar women who conceived without them. Women could be matched by age, socioeconomic status, and place of residence, as such data are contained in the existing data bases. For example, it would be possible theoretically to assess whether prematurity, low birth weight, neonatal death, or hospitalizations were more common in the children of women who took clomiphene citrate.

One of the aspects essential to address in any record linkage study is stringent protection of any personally identifying data. If coded identifiers are assigned to each individual covered by a province's health programs and these identifiers are used when information about individuals is recorded in various data bases, it is possible to link the use of services over time by a given individual without researchers knowing the identity of the individuals involved. Fortunately, then, there are proven ways to meet the critical need to protect privacy while also allowing the evaluation of health consequences that is needed for appropriate policy and decision making.

Record linkage studies would also overcome the problems associated with following up individually in direct studies of patients who have used fertility drugs. Research has shown that the majority of infertility patients do not wish to participate directly in follow-up studies; they express a desire to put the experience behind them, regardless of whether the outcome was positive or negative. This too is a reason for developing alternative means of obtaining data on outcomes without intruding on patients' privacy. Using record linkage and data that are already collected for other purposes removes the necessity to contact patients.

Other useful "piggybacking" approaches on existing data bases may also be feasible. For example, it may be possible to structure pharmacists' data bases to make them amenable to linkage and to collect information when certain kinds of prescriptions are being filled, or to incorporate a data collection method into the system physicians use to bill provincial health insurance plans. The feasibility and practicality of these approaches would naturally vary from province to province and the territories given their different systems, but the benefits would be considerable in terms of gathering sufficient country-wide data — within a relatively short period of several years and at much less cost than primary data collection — to draw reliable conclusions about outcomes. In the Commission's view, provincial/territorial ministries of health could collaborate with each other to apply such approaches not only in reproductive health care but also in other areas to support rational decision making and appropriate use of public resources.

There are proven ways to meet the critical need to protect privacy while also allowing the evaluation of health consequences that is needed for appropriate policy and decision making ... Using record linkage and data that are already collected for other purposes removes the necessity to contact patients.

The Commission's research indicates that, with appropriate development of data bases on patients undergoing infertility treatment, it would be feasible to evaluate the long-term health effects of drug treatments on patients and their children. We believe that federal research funding agencies and provincial/territorial ministries of health should fund appropriate research proposals in this area. The Commission therefore recommends that

78. The licensing requirements for facilities providing assisted conception services ensure that data collected on use of infertility treatments (including fertility drugs) contain sufficient standardized information on individuals to permit linkage with other data

bases on health outcomes, so that approved research can be conducted into possible long-term health effects of new reproductive technologies and into the effect of treatments on fertility.

and that

79. Pharmaceutical companies marketing fertility drugs be required by the federal government to contribute funding to be used for studies sponsored by the National Reproductive Technologies Commission linking data in its data base to data on longer-term health outcomes of individuals who have taken fertility drugs.

To safeguard the interests of patients in this process, the Commission recommends that

80. Patients be informed that non-identifying data on them will be used for studies on long-term outcomes; that this will not involve any contact with them; that only coded data will be used; that no named identifying information on any individual will be released to researchers; and that any published data will be in sufficient aggregation that individuals could not be identified.

and that

81. Access to data collected by the National Reproductive Technologies Commission be restricted to use of coded data by researchers conducting research projects that have been evaluated and approved by the National Reproductive Technologies Commission.

Conclusion

Fertility drugs occupy a unique place in the infertility treatment spectrum. Many do not consider fertility drugs to be a "new reproductive technology," yet fertility drugs are developed and used to act on the same

biological processes as new reproductive technologies, with the aim of correcting some of the same disorders, and they have the same far-reaching implications — they could potentially affect not only the women who use them but also their children.

Fertility drugs are the most prevalent infertility treatment and are used in most other assisted conception techniques. The prevalence of fertility drug use makes it important to collect information on their short- and long-term outcomes. The side effects and long-term outcomes of fertility drug use have implications for society that are just as great as those of drugs used to treat heart disease or cancer. The evaluation of long-term outcomes is not easy, however, in part because the use of some drugs (especially clomiphene citrate) occurs most frequently outside the context of specialized treatment facilities, and in part because information on both the individuals receiving treatment and their children is relevant to this assessment.

It is not in society's interests that the use of these drugs continue without thorough and ongoing evaluation of their risks and effectiveness. Present federal regulatory bodies are not equipped to be solely responsible for appropriate and adequate evaluation of the safety and effectiveness of fertility drugs. The Commission's findings in this area suggest that data collected by the National Reproductive Technologies Commission are needed to allow evaluation of fertility drugs. The evidence gathered through analysis must be fed back continuously into shaping appropriate and safe practice.

The Commission's research and consultations with patients and clinics indicate that some of the concerns about fertility drugs raised at the Commission's hearings and private meetings are valid. We have identified the problems we found with existing systems and mechanisms, as well as the gaps in the research and evaluation of these drugs. The current process for approving and regulating drugs that come onto the market and for monitoring the side effects and long-term health effects of fertility drugs is inadequate. Although the Canadian drug evaluation and approval system is now being overhauled, the Commission believes that further steps are necessary. The existing system of post-marketing surveillance of drugs in Canada is seriously deficient in providing good data on the short- and long-term effects of fertility drugs on women and their children. The involvement and interaction of the proposed National Reproductive Technologies Commission with the emerging drug approval system would be beneficial in this area. Additional post-marketing mechanisms are called for; data on treatments provided at infertility clinics should be

> Adopting the approach we propose will provide Canadians with the assurance they seek that governments and professional bodies are fulfilling their responsibilities to protect citizens from unethical, unproven, or unsafe practices and treatments.

collected in a standardized way, as a condition of licensing, to facilitate post-marketing surveillance. In addition, research using record linkage to assess long-term health outcomes should be pursued and facilitated by the NRTC.

The Commission also found that some treatment practices with regard to fertility drugs are putting the health of patients at risk without the prospect of benefit. It is clear from the evidence before the Commission that there is a need to protect patients from unproven or experimental drug therapies and that guidelines for appropriate use of these drugs should be developed and disseminated widely. The Commission believes that our proposed system for licensing assisted conception clinics, including compliance with professional guidelines on drug use as a condition of licensing, will be a major step in the right direction. Moreover, it is essential — and the Commission has recommended — that the College of Family Physicians of Canada and the Society of Obstetricians and Gynaecologists of Canada develop the guidelines for the use of such drugs by practitioners outside clinics and that these be disseminated by the two organizations to their membership.

The Commission recommends that, apart from clomiphene citrate (which should be used only according to guidelines developed by the College of Family Physicians of Canada and the Society of Obstetricians and Gynaecologists of Canada), all other drugs should be used only if the patient can be closely monitored with appropriate specialized clinical and laboratory expertise. Thus, it will usually be inappropriate to use them outside infertility treatment clinics. Furthermore, only drugs that meet the standards of effectiveness we have established should be included in guidelines for practice used by licensed clinics. Use of fertility drugs in clinics other than in this way would be conditional on participation in clinical research trials designed to evaluate outcomes, so that the interests of patients can be protected while still allowing progress in knowledge and improvement of practice.

Many patients are receiving inadequate information about drug treatment. Full, understandable, and unbiased information should be available to patients before they take fertility drugs; this is why we have recommended that such information be developed by the Assisted Conception Sub-Committee of the NRTC and be made available for distribution by physicians and clinics. Data collected by the NRTC should be made available in a timely fashion to practitioners through annual aggregate reports and should be passed on to patients in accessible and useful form. Appropriate information and counselling to

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facilitate informed choice should be available to patients in licensed clinics as a condition of licensing. All experimental treatments should be identified as such to the patients participating in them in the context of clinical trials.

In summary, the Commission believes that only the drug treatments that have been demonstrated effective at acceptable levels of risk should be offered. Others should be offered only in the context of multicentre clinical trials, in which standards of ethical research are adhered to. Yet others should be discontinued altogether. Adopting the approach we propose will provide Canadians with the assurance they seek that governments and professional bodies are fulfilling their responsibilities to protect citizens from unethical, unproven, or unsafe practices and treatments.

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