# Abnormal Meiosis and/or Fertilization

4.4

Factors that interfere with meiosis and/or fertilization can contribute to genetic disorders and infertility. Random meiotic errors, disease, and environmental factors can result in either the inability to produce adequate numbers of viable gametes or gametes that do not carry the normal complement of genetic material.

## Abnormal Meiosis: Non-disjunction

On rare occasions, during meiosis, entire chromosomes are lost or gained from cells. When this occurs, it is usually a result of non-disjunction. **Non-disjunction** occurs when homologous chromosomes fail to separate during meiosis. The result is that one of the daughter cells will have an extra chromosome, while the other will be missing a chromosome (**Figure 1**). Cells that have an extra chromosome (extra genetic material) or that are missing a chromosome (missing genetic material) are not able to function normally.

**non-disjunction** the failure of homologous chromosomes to move to opposite poles of the cell during meiosis; results in an abnormal number of chromosomes in the daughter cells

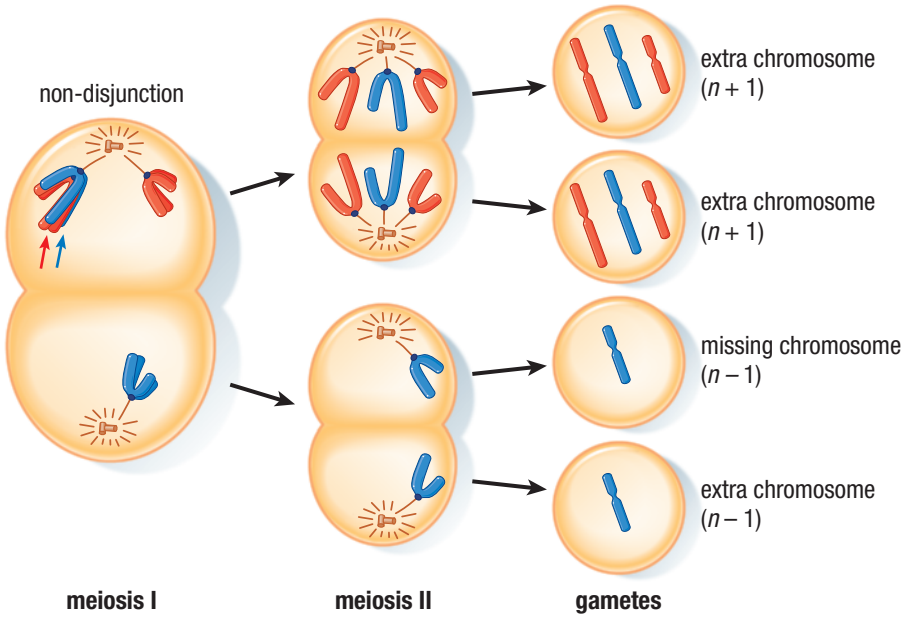


**Figure 1** Non-disjunction of homologous chromosomes during meiosis I results in two gametes with one extra chromosome ($n + 1$) and two gametes that are short one chromosome ($n - 1$).

In humans, non-disjunction results in gametes with 24 or 22 chromosomes. Consider the implications for the offspring. If a gamete with 24 chromosomes joins with a normal gamete (having 23 chromosomes) from the opposite sex, the resulting zygote will have 47 chromosomes instead of 46 (the normal chromosome number). The zygote will have 22 pairs of chromosomes and three copies of one chromosome, a chromosomal abnormality referred to as **trisomy**. However, if a gamete with 22 chromosomes joins with a normal gamete (having 23 chromosomes) from the opposite sex, the resulting zygote will have 45 chromosomes. Although the zygote will have 22 pairs of chromosomes, it will be missing one of its homologous chromosomes for the remaining pair, a genetic abnormality known as **monosomy**. If the zygote survives, each cell that it produces by mitosis as the embryo grows will retain this chromosomal abnormality.

**trisomy** a chromosomal abnormality in which there are three homologous chromosomes in place of a homologous pair

**monosomy** a chromosomal abnormality in which there is a single chromosome in place of a homologous pair

## Non-disjunction Disorders

**Down syndrome** a chromosomal abnormality in which an individual has three copies of chromosome number 21; also referred to as trisomy 21

Non-disjunction is responsible for a variety of human genetic disorders, including Down syndrome, Turner syndrome, and Klinefelter syndrome. **Figure 2** compares the karyotype of a normal female with that of a female who has **Down syndrome**—a chromosomal abnormality in which there is an extra chromosome number 21. (Recall that autosomal chromosomes are numbered according to size.) For this reason, Down syndrome is also called trisomy 21.

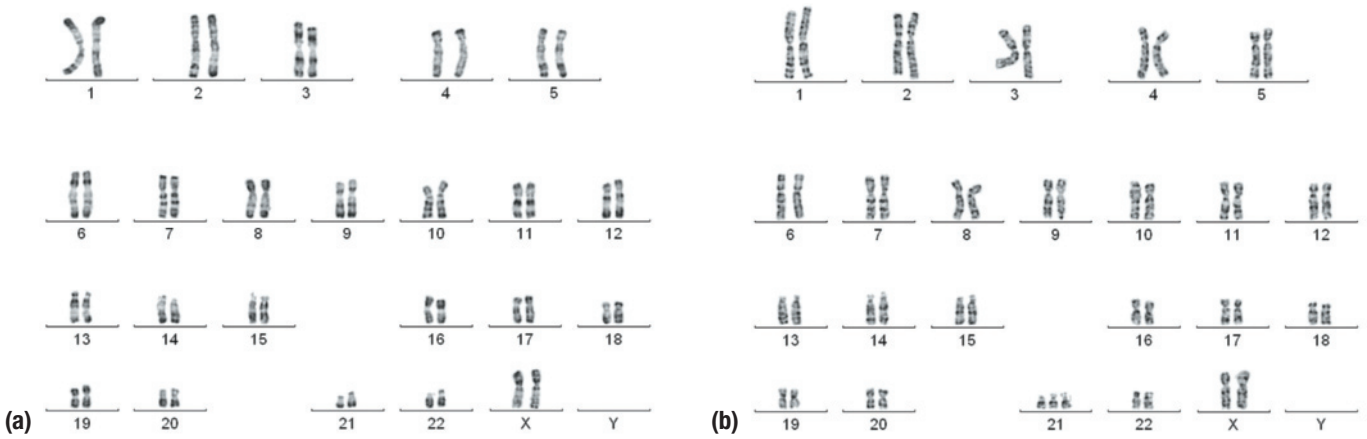


**Figure 2** A karyotype of (a) a normal female and (b) a female with Down syndrome (trisomy 21)

The extra chromosome means that there is excess genetic information and an unpaired chromosome in every cell. The complications cause individuals with Down syndrome to experience both physical and mental challenges. Common traits among people with Down syndrome may include a round, full face; short height; and a large forehead. Although Down syndrome is associated with developmental and intellectual disabilities, people with Down syndrome maintain a wide range of abilities and are generally able to carry out rich, fulfilling lives.

It is believed that approximately 1 in 800 live births produces a child with Down syndrome. The probability of having a baby with Down syndrome increases with age. For example, a woman in her forties has a 1 in 40 chance of having a child with Down syndrome, whereas a woman in her twenties has only a 1 in 1000 chance.

**Table 1** describes some additional human non-disjunction disorders.

**Table 1** Selected Human Non-disjunction Disorders

| Non-disjunction disorder | Chromosome abnormality | Characteristics of the disorder |
|---|---|---|
| Turner syndrome | one X and no Y sex chromosome | Approximately 1:2500 female births. Female in appearance but do not mature sexually and are sterile. Most Turner syndrome fetuses are miscarried before the 20th week of pregnancy. |
| Klinefelter syndrome | two X and one Y sex chromosome | Approximately 1:500 male births. Males are usually sterile and exhibit some feminine body characteristics, but severity varies. |
| Patau syndrome | trisomy of chromosome 13 | Approximately 1:25 000 live births. Many serious developmental problems, including brain, kidney, and heart defects. Children rarely live more than a few months. |
| Edwards syndrome | trisomy of chromosome 18 | Approximately 1:6000 live births. Many organ system defects. Very low survival rate. Most fetuses die before birth. Average life expectancy of live-born infants is less than one month. |

Investigation 4.4.1

**Interpreting Karyotypes (page 172)**
Now that you have read about karyotyping, you can complete Investigation 4.4.1.

In this observational study, you will prepare and analyze a karyotype using images of human chromosomes.

## Diagnosing Non-disjunction

Non-disjunction disorders are usually confirmed by preparing a karyotype. Technicians usually prepare a karyotype by obtaining and mixing a small sample of white blood cells with a solution that stimulates mitotic division. A different solution is added that stops division at metaphase, when the chromosomes are most condensed and can be photographed and sorted. The completed karyotype is then examined and the disorder is diagnosed.

### PRENATAL TESTING

A number of genetic disorders can be detected in a fetus or embryo prior to birth. Testing for a genetic disorder prior to birth is called **prenatal testing**. Testing for non-disjunction and other chromosomal abnormalities is often recommended for pregnant women over the age of 35 due to the increased risk associated with age. Prenatal testing for chromosome abnormalities often requires collecting and observing fetal cells, which can be obtained in a number of ways. As early as eight weeks into a pregnancy, the chorionic villus sampling (CVS) technique can be used to remove cells from the outer membrane (chorion) surrounding the embryo. Once the fetus is large enough, it becomes possible to obtain cells from the fluid-filled sac that surrounds the fetus, a technique called amniocentesis. Amniocentesis involves the use of a long syringe and an ultrasound machine (**Figure 3**). The collected cells are then used to prepare a karyotype chart.

Prenatal testing can also be accomplished without the need for obtaining fetal cells. Between the 15th and 20th weeks of pregnancy, women have the option of undergoing a blood test called multiple marker screening, which tests for hormone levels. Certain medical conditions correspond to a particular hormone, and performing a multiple marker screening test will identify if high levels of that particular hormone are present. If the woman's placenta has produced the hormone, it indicates an increased risk for that birth defect. Multiple marker screening can be used to test for Down syndrome and spina bifida (a malformation of the neural tube).

CAREER **LINK**

**Genetic Counsellor**

Genetic counsellors identify genetic patterns that can lead to disease and health problems for families and individuals. They help people to assess their options to make informed decisions about their future. To learn more about being a genetic counsellor,

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**prenatal testing** testing for a genetic disorder that occurs prior to birth

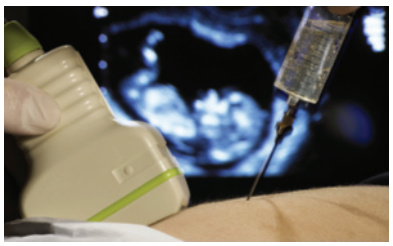

**Figure 3** During an amniocentesis, fluid from the amniotic sac is extracted with a large syringe. An ultrasound machine is used to guide the syringe away from the fetus.

# Problems with Fertilization

Much more common than a chromosome abnormality is the inability to conceive a child. In Ontario, approximately 10 % of couples who are trying to conceive experience problems. Of these cases, approximately one-third are attributed to the female and one-third to the male. The remaining one-third are ascribed to both individuals or are of an undetermined cause. There are many possible causes of infertility. They include poor or reduced egg and sperm quality and production, blocked fallopian tubes in women, and blockage in either the epididymis or vas deferens of the male.

## Assisted Reproductive Technologies (ARTs)

Assisted reproductive technologies (ARTs) are technologies used to enhance the chances of reproductive success. ARTs can be used to increase sperm and egg production, improve the chances of successful fertilization, and enhance the likelihood of implantation and development. An assisted reproduction program may involve the use of fertility drugs and the sourcing, selection, and manipulation of eggs, sperm, and/or embryos outside the human body.

### IN VITRO FERTILIZATION (IVF)

Conventional in vitro fertilization (IVF) treatment involves the stimulation of the ovaries using hormonal medications (in order to increase egg production), the retrieval of ova (eggs) from the ovaries, the fertilization of the eggs outside the body, and the transfer of the resulting embryo into the uterus, where, it is hoped, the embryo will implant and mature.

As science and technology advance, more and more techniques are being made available to increase the success rates associated with in vitro fertilization. Two of these are intracytoplasmic sperm injection (ICSI) and laser-assisted hatching (LAH).

Intracytoplasmic sperm injection is a form of IVF that involves the injection of a single sperm directly into the cytoplasm of an egg (**Figure 4(a)**).

IVF procedures result in disorders that cause the zona pellucida to be stiffer than normal. When sperm and eggs are combined using IVF procedures, the zona pellucida (the shell surrounding the fertilized egg) hardens, which can make it more difficult for the embryo to implant. Laser-assisted hatching is a technology designed to improve the efficiency of reproductive technologies such as ICSI. Using a precision laser, an opening is made in the zona pellucida. This weakens the wall of the embryo and helps the embryo hatch from the zona pellucida so that it can implant correctly (**Figure 4(b)**).

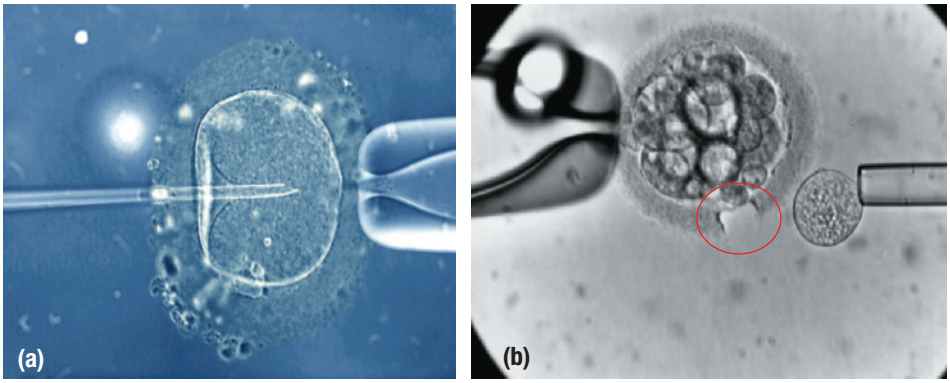


**Figure 4** (a) An egg cell is being directly fertilized by the injection of a single sperm using a micropipette. (b) The relatively thick zona pellucida is being reduced on the bottom right side of the embryo. A laser targeting circle is used to precisely aim before firing a high-energy laser pulse.

### ARTIFICIAL INSEMINATION

Artificial insemination (AI) is the placement of sperm into the reproductive tract of a female. In humans, this process is referred to as intrauterine insemination. A sperm sample from the donor male is "washed' to concentrate the sperm, which are then inserted directly into the uterus. Fresh or previously frozen sperm can be used.

## Research This

### Possible Causes of Infertility

**Skills:** Researching, Identifying Alternatives, Analyzing, Communicating, Evaluating

SKILLS HANDBOOK A2.1, A5.1

There is growing concern about increasing levels of infertility in many otherwise healthy populations. There are many possible factors contributing to the problem. These include environmental contaminants, undiagnosed transmitted diseases, smoking, and cultural factors, such as waiting to have children later in life. The subject is an area of active research.

In this activity you will research the current understanding of these contributing factors.

1. Use the Internet to research probable and/or suspected causes of male and female infertility.
2. Include government health agencies in your search.
3. Research information regarding the trends in infertility in the Ontario population.
4. Summarize your findings and tabulate them in an appropriate format, such as a table.

A. Which causes are of the greatest concern? T/I A

B. Which of the suspected causes are most readily treated or avoided? T/I A

C. In small groups, discuss your findings. How serious an issue do you think this is? T/I C A

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## Implications of Reproductive Technologies

Advances in science and technology are providing insights into the underlying causes of human reproductive disorders and new methods of treating and overcoming them. Many of these same advances are being applied to non-human organisms.

However, intervening in natural reproductive processes is highly controversial. Many people and organizations have significant ethical and moral concerns regarding some, or any, reproductive technologies. Many of these concerns are most strongly held with regard to applying these technologies to humans rather than other species. Regardless of your own position on these important questions, it is valuable to have an understanding of the science behind such technologies and their applications.

## Non-human Applications of Reproductive Technology

Many reproductive technologies are being applied to animal breeding and wildlife conservation efforts. Artificial insemination (AI), for example, is used in the breeding of livestock, pets, captive wild animals, and even honeybees. In fact, artificial insemination has been used extensively in agriculture for many decades.

The primary purpose of using AI in non-human applications is to enhance genetic diversity and reduce the costs involved. The genetic diversity of a herd can easily be enhanced using artificial insemination. A breeder can select the frozen sperm from a catalogue of thousands of available male donors. It is much less costly to ship a canister of frozen semen around the world than it is to ship a prize stallion for stud.

Artificial insemination is also a valuable tool in efforts to save endangered species. Giant pandas are one of the world's most critically endangered species. Unfortunately, reproductive rates are low, even in the wild, and in captivity, males and females often show little or no interest in breeding. To date, Chinese scientists have produced over 100 baby pandas using artificial insemination (**Figure 5**).

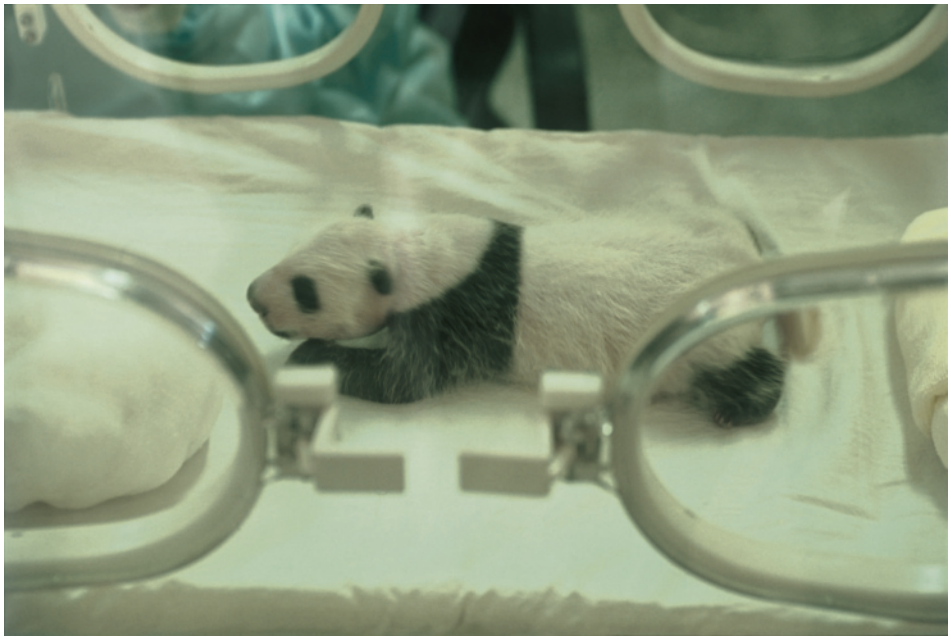

**Figure 5** A baby giant panda born at the Chengdu research facility in China

The benefits of artificial insemination include the following:

- Semen can be frozen and stored for extended periods of time.
- By obtaining semen from many different animals, a "bank" of genetic information can be preserved.
- Transportation costs are low compared to moving live animals for breeding.
- It permits the breeding of animals that do not breed successfully in captivity.

CAREER **LINK**

**Careers in Reproductive Technology**

Advances in reproductive technologies and their application provide many fascinating career opportunities in agriculture, forestry, conservation biology, and veterinary medicine. To learn more about specific careers in these fields,

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One serious concern is that efforts to preserve the genetic diversity of endangered species in frozen "banks" may undermine efforts being made to preserve the species in the wild. Creating gene banks and related technologies, such as cloning, can be extremely expensive. Many people feel that the money spent on these efforts could be put to better use by helping to protect wild populations and their natural habitat.

## 4.4 Summary

- Errors in meiosis, including non-disjunction, can result in abnormal numbers of chromosomes and can cause serious genetic disorders.
- Karyotypes can be used to evaluate chromosome numbers and diagnose genetic disorders.
- Prenatal testing can be used to determine the likelihood of certain genetic disorders.
- Assisted reproductive technologies may be used when a couple is infertile in order to enhance their chances of conceiving a child.
- There are many applications of reproductive technologies in agriculture, industry, and wildlife conservation.
- The use of many reproductive technologies is highly controversial.

**UNIT TASK BOOKMARK**

Is there any evidence that the genetic disorder you are investigating is associated with a major chromosome abnormality? What information about prenatal testing should you include in your consultation report?

## 4.4 Questions

1. What is non-disjunction? How can it lead to both trisomy and monosomy? K/U
2. Why do you think there are more types of trisomy disorders than monosomy disorders? K/U T/I A
3. Amniocentesis, chorionic villus sampling, and multiple marker screening provide important information about the health of the fetus to the parents. This knowledge can help parents prepare for the possible birth of a child with a genetic disorder. A
   (a) Why are older women more likely to have these tests performed?
   (b) Do you think there should be any restrictions on their use?
4. Outline the benefits of using artificial insemination in wildlife conservation efforts. K/U A
5. How might the use of ART detract from efforts to protect natural habitats and populations living in the wild? K/U A
6. Describe the following types of assisted reproductive technology: K/U
   (a) conventional in vitro fertilization
   (b) intracytoplasmic sperm injection
   (c) laser-assisted hatching
   (d) artificial insemination
7. Describe the scale of the infertility problem in Ontario. K/U
8. Go online to learn more about the research conducted by Dr. Uchida and other Canadian geneticists. How have their findings contributed to our understanding of genetic disorders? T/I A
9. Examine the karyotype shown in **Figure 6**. K/U T/I

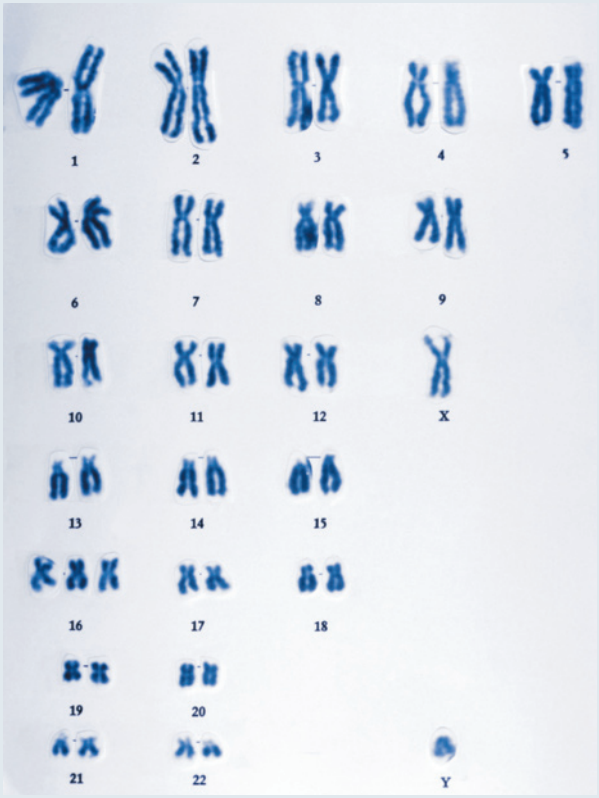


**Figure 6**

   (a) What is the gender of the individual?
   (b) Could this be the karyotype of a human sperm cell? Explain your reasoning.
   (c) What evidence is there of non-disjunction?

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