Chapter 16
Reproductive Technology, Genetic Testing, and Gene Therapy
16.1 Infertility Is a Common Problem

- In the US, about 13% of all couples are infertile & this number has been increasing since 2000.

- Infertility is a complex problem and has many causes, including physical and physiological problems with gamete formation and hormonal imbalances.
The Major Causes of Female Infertility

- **Oviduct blockage**
- **Uterine problems**
- **Damaged or absent ovaries**
- **Infection, surgery, inflammation, autoimmune disease, STDs, viral infections**
- **Hormone-related ovulation problems**
- **Estrogen is too low**

Cervical problems: \( \leq 10\% \)

- **30–50\%**
The Major Causes of Male Infertility

- Semen disorders: 37%
- Unknown: 25%
- Varicocele: 9%
- Varicose vein in scrotum: 10%
- Testicular failure: 7%
- Other: 6%
- Obstruction: 6%
- Undescended testes: 6%
Other Causes of Infertility

- **Personal behavior and health…**
- Smoking or any use of tobacco lowers the chance of conceiving by 1/3

- Women who are significantly overweight or underweight can have problems becoming pregnant.
Infertility Increases with Age

![Graph showing the percentage likelihood of infertility with age. The graph includes points for ages 20-24, 25-29, 30-34, 35-39, 40-44, 45-49, and 50+. The percentages of infertility are 3%, 5%, 8%, 15%, 32%, 69%, and 100%, respectively.](image-url)
16.2 Assisted Reproductive Technologies (ART) Expand Childbearing Options

1) **Intrauterine insemination** - see next slide

2) **Assisted reproductive technologies (ART)**
   - A series of methods used to help infertile couples have children
     - Hormones can induce ovaries to produce many oocytes which can be collected, sorted, and frozen for future use
     - Sperm can be pooled, or retrieved through microsurgery and frozen in sperm banks
Intrauterine Insemination (IUI)

Sperm injected into uterus
Methods of Assisted Reproduction

- **In vitro fertilization (IVF)**
  Gametes are collected and fertilized in a dish.
  The resulting zygote is implanted in the uterus.

- **Gamete intrafallopian transfer (GIFT)**
  Gametes are collected and placed into a woman’s oviduct where fertilization occurs.

- **Zygote intrafallopian transfer (GIFT)**
  Gametes are collected and fertilized by *in vitro* fertilization before transfer to the oviduct.

- **Intracytoplasmic sperm injection (ICSI)**
  An egg is fertilized by microinjection of a single sperm (for defects in sperm count or motility).
In Vitro Fertilization
Gamete Intrafallopian Transfer (GIFT)

- Eggs and sperm placed into the oviduct
- ovary
- uterus
Zygote Intrafallopian Transfer (ZIFT)

IVF zygotes placed into the oviduct

ovary

— uterus
Intracytoplasmic Sperm Injection (ICSI)
Artificial Insemination and Embryo Transfer

This shows the many ways gametes can be combined in ARTs.

1. Father is infertile. Mother is inseminated by donor and carries child.

2. Mother is infertile but able to carry child. Donor egg is inseminated by father via IVF. Embryo is transferred and mother carries child.

3. Mother is infertile and unable to carry child. Donor of egg is inseminated by father and carries child.

4. Both parents are infertile, but mother is able to carry child. Donor egg is inseminated by sperm donor via IVF. Embryo is transferred and mother carries child.

KEY

- Sperm from father
- Egg from mother
- Baby born of mother
- Sperm from donor
- Egg from donor
- Baby born of donor (Surrogate)
In Vitro Fertilization (IVF)
INFO NOT ON EXAM;
Shows the various ways to combine gametes in IVF.

1. Mother is fertile but unable to conceive. Egg from mother and sperm from father are combined in laboratory. Embryo is placed in mother’s uterus.

2. Mother is infertile but able to carry child. Egg from donor is combined with sperm from father and implanted in mother.

3. Father is infertile and mother is fertile but unable to conceive. Egg from mother is combined with sperm from donor.

4. Both parents are infertile, but mother is able to carry child. Egg and sperm from donors are combined in laboratory (also see number 4, column at left).

5. Mother is infertile and unable to carry child. Egg of donor is combined with sperm from father. Embryo is transferred to donor (also see number 3, column at left).

6. Both parents are fertile, but mother is unable to carry child. Egg from mother and sperm from father are combined. Embryo is transferred to donor.

7. Father is infertile. Mother is fertile but unable to carry child. Egg from mother is combined with sperm from donor. Embryo is transferred to surrogate mother.

KEY
- Sperm from father
- Egg from mother
- Baby born of mother
- Sperm from donor
- Egg from donor
- Baby born of donor (Surrogate)
IVF has Resulted in the Birth of Millions of Children

Fig. 16-7, p. 359
16.3 Ethical Issues in Reproductive Technology

- Use of ART raises unresolved ethical issues
  - Health risks to both parents and their offspring resulting from ART
  - Use of preimplantation genetic diagnosis (PGD) to select embryos that are suitable tissue or organ donors for other members of the family

- Risks of ART
  - Threefold increase in ectopic pregnancies
  - Multiple births (35% in IVF)
  - Increased risk of low birth weight
  - Increased risk of transmitting genetic defects to male children when ICSI is performed
Several types of testing and screening

- Newborn screening – done 24-72 hours after birth
- Carrier testing - done on family members and usually involves sickle cell disease or cystic fibrosis allele
- Pre-natal testing – cystic fibrosis or chromosome abnormalities
- Pre-symptomatic or predictive testing – late onset diseases such as Huntington disease
### Table 16.1  Some Metabolic Diseases and Birth Defects That Can Be Diagnosed by Prenatal Testing

<table>
<thead>
<tr>
<th>Disease</th>
<th>Disease</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acatalasemia</td>
<td>Gaucher disease</td>
<td>Niemann-Pick disease</td>
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<tr>
<td>Adrenogenital syndrome</td>
<td>G6PD deficiency</td>
<td>Oroticaciduria</td>
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<tr>
<td>Chediak-Higashi syndrome</td>
<td>Homocystinuria</td>
<td>Progeria</td>
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<tr>
<td>Citrullinemia</td>
<td>I-Cell disease</td>
<td>Sandhoff disease</td>
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<tr>
<td>Cystathioninuria</td>
<td>Lesch-Nyhan syndrome</td>
<td>Spina bifida</td>
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<tr>
<td>Cystic fibrosis</td>
<td>Mannosidosis</td>
<td>Tay-Sachs disease</td>
</tr>
<tr>
<td>Fabry disease</td>
<td>Maple syrup urine disease</td>
<td>Thalassemia</td>
</tr>
<tr>
<td>Fucosidosis</td>
<td>Marfan syndrome</td>
<td>Werner syndrome</td>
</tr>
<tr>
<td>Galactosemia</td>
<td>Muscular dystrophy, X-linked</td>
<td>Xeroderma pigmentosum</td>
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Preimplantation Genetic Diagnosis (PGD)

- **Preimplantation genetic diagnosis (PGD)**
  - Removal and genetic analysis of a single cell from a 3- to 5-day old embryo
  - Used to select embryos free of genetic disorders for implantation and development
  - Has been used to select embryos tissue-matched to siblings with Fanconi anemia (fatal bone marrow disease) or leukemia to serve as transplant donors
Preimplantation Genetic Diagnosis (PGD)

- Removing a cell from a day 3 embryo
Reasons Cited for PGD in the US

- Aneuploidy: 93%
- Autosomal disorders: 82%
- Chromosomal rearrangement: 67%
- X-linked diseases: 58%
- Non-medical sex selection: 42%
- To avoid an adult-onset disease: 28%
- HLA typing with single gene test: 24%
- HLA typing w/o single gene test: 6%
- To select for a disability: 3%
First successful IVF in the world was in 1978

The first successful IVF in the US was carried out in 1981

Since that time more than 40 hospitals and clinics have opened

Charges for services can run as high as $60,000

IVF is estimated to be a $3-billion-per-year industry

These businesses have little government oversight

*State who has been most successful is Maryland.*
Umbilical cord blood contains stem cells used to treat various immune disorders and neurological problems.

Cord blood is better for transplants than marrow; it has not been exposed to pathogens and is less likely to carry antibodies.

Mothers should consider donating cord blood to a cord blood bank to save lives.
16.5 Gene Therapy Promises to Correct Many Disorders

- Gene therapy transfers a normal gene copy into target cells of individuals carrying a mutant allele
- Methods for transferring cloned genes into human cells
  - Viral vectors
  - Chemical methods used to transfer genes across cell membranes
  - Physical methods such as microinjection or fusion of cells with vesicles carrying cloned DNA
Using Viral Vectors for Gene Therapy

1. Clone normal gene into viral vector.
2. Infect patient's white blood cells with virus.
3. In some cells, viral DNA inserts into chromosome.
4. Inject cells into patient.
Gene Therapy Showed Early Promise

- The only successful gene therapy has been in a very few cases of severe combined immunodeficiency disease (SCID)

- There have been a number of recent failures and at least two deaths that has resulted in a loss of confidence for gene therapy
Numbers of Gene Therapy Trials

<table>
<thead>
<tr>
<th>Key Category</th>
<th>Percentage</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer diseases</td>
<td>66.5%</td>
<td>n = 871</td>
</tr>
<tr>
<td>Cardiovascular diseases</td>
<td>9.1%</td>
<td>n = 119</td>
</tr>
<tr>
<td>Monogenic diseases</td>
<td>8.3%</td>
<td>n = 109</td>
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<tr>
<td>Infectious diseases</td>
<td>6.5%</td>
<td>n = 85</td>
</tr>
<tr>
<td>Neurological diseases</td>
<td>1.5%</td>
<td>n = 20</td>
</tr>
<tr>
<td>Ocular diseases</td>
<td>0.9%</td>
<td>n = 12</td>
</tr>
<tr>
<td>Other diseases</td>
<td>1.6%</td>
<td>n = 21</td>
</tr>
<tr>
<td>Gene marking</td>
<td>3.8%</td>
<td>n = 50</td>
</tr>
<tr>
<td>Healthy volunteers</td>
<td>1.7%</td>
<td>n = 22</td>
</tr>
</tbody>
</table>
Ethical Issues Related to Gene Therapy

- **Somatic gene therapy**
  - The only form of gene therapy used to date
  - Gene transfer to somatic target cells
  - Involves a single target tissue treating only one person
  - Done to correct a genetic disorder, using established ethical and medical guidelines
Ethical Issues Related to Gene Therapy

- These types of gene therapy are not yet in use mainly due to unresolved ethical issues.

- **Germ-line gene therapy**
  - Gene transfer to gametes or the cells that produce them.
  - Transfers a gene to all cells in the next generation, including germ cells (*Every cell in the new individual would contain the transferred gene.*)

- **Enhancement gene therapy**
  - Gene transfer to enhance traits such as intelligence and athletic ability rather than to treat a genetic disorder.
16.6 Genetic Counseling
Assesses Reproductive Risks

- Genetic counseling involves developing an accurate assessment of a family history to determine the risk of genetic disease.

- Counselors help people understand:
  - Medical facts, diagnosis, and treatment
  - How heredity contributes to the disorder and risk of having children with the disorder
  - Alternatives for dealing with the risk of recurrence
  - Ways to adjust to the disorder
Who are Genetic Counselors?

- Genetic counselors have specialized graduate training in medical genetics, psychology, and counseling.
Why Do People Seek Genetic Counseling?

- Counseling is recommended for
  - Women who are or may be pregnant after age 35
  - Couples who have a child with a genetic defect
  - Couples seeking information about genetic defects that are common in their ethnic group
  - Couples who are close blood relatives
  - Individuals at risk through jobs or lifestyle
  - Women who have had multiple miscarriages
  - Those concerned that they may have an inherited disorder or birth defect