Reproductive Technology, Gene Therapy, and Genetic Counseling

Infertility is a Common Problem

- In the US, about 13% of all couples are infertile
- Causes, include problems with gamete formation, and hormonal imbalances

Effectiveness of Various Methods of Birth Control

<table>
<thead>
<tr>
<th>Method</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total ablation</td>
<td>100%</td>
<td>10%</td>
</tr>
<tr>
<td>Total hysterectomy</td>
<td>100%</td>
<td>10%</td>
</tr>
<tr>
<td>Hormonal therapy (interval)</td>
<td>100%</td>
<td>10%</td>
</tr>
<tr>
<td>Highly effective</td>
<td>90%</td>
<td>90%</td>
</tr>
<tr>
<td>Highly effective but need to be used continuously</td>
<td>90%</td>
<td>90%</td>
</tr>
<tr>
<td>Moderately effective</td>
<td>70%</td>
<td>70%</td>
</tr>
<tr>
<td>Spermicides</td>
<td>60%</td>
<td>60%</td>
</tr>
<tr>
<td>Barrier method</td>
<td>50%</td>
<td>50%</td>
</tr>
<tr>
<td>Soft cervical cap</td>
<td>40%</td>
<td>40%</td>
</tr>
<tr>
<td>Diaphragm</td>
<td>30%</td>
<td>30%</td>
</tr>
<tr>
<td>Spermicidal jellies</td>
<td>20%</td>
<td>20%</td>
</tr>
</tbody>
</table>
| Table 16.1 Some Causes of Fertility Problems

<table>
<thead>
<tr>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Problems with ovulation (27%)</td>
<td>Testes vein enlargement (38%)</td>
</tr>
<tr>
<td>Pelvic adhesions (12%)</td>
<td>Unknown causes (23%)</td>
</tr>
<tr>
<td>Oviduct problems (22%)</td>
<td>Duct obstructions (13%)</td>
</tr>
<tr>
<td>Endometriosis (5%–15%)</td>
<td>Testicular failure (3%)</td>
</tr>
<tr>
<td>Pituitary malfunctions (7%)</td>
<td>Ejaculatory dysfunction (2%)</td>
</tr>
</tbody>
</table>
Assisted Reproductive Technologies (ART) Expand Childbearing Options

- Assisted reproductive technologies (ART)
  - A collection of techniques used to help infertile couples have children
  
- Techniques have developed ahead of legal and social consensus about their use

Collecting Gametes

- 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

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

- Intracytoplasmic sperm injection (ICSI)
  - An egg is fertilized by microinjection of a single sperm (for defects in sperm count or motility)

Intracytoplasmic Sperm Injection (ICSI)
Some Ways Gametes Can Be Combined

- Father is sterile, mother is fertilized by donor and carries child
- Father is sterile but able to carry child. Donor egg is fertilized by father via IVF. Embryo is transferred and mother carries child
- Father is sterile but able to carry child. Donor egg is fertilized by father and transferred to mother
- Father is sterile but carries child. Egg from donor is fertilized with sperm from father and implanted in mother
- Both parents are sterile. Egg from donor is fertilized with sperm from donor

LEGEND
- Sperm from donor
- Egg from donor
- Egg from mother
- Baby born of donor
- Baby born of mother

In Vitro Fertilization in Women Over 40

- Use of ART raises unresolved ethical issues
  - Health risks to both parents and their offspring resulting from ART
  - Use of preimplantation genetic diagnosis to select siblings who are suitable tissue or organ donors for other members of the family
Use of ART Carries Risks to Parents and Children

- 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 (in ICSI)

Preimplantation Genetic Diagnosis (PGD) Has Several Uses

- 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 or leukemia to serve as transplant donors

Preimplantation Genetic Diagnosis (PGD)

- Removing a cell from a day 3 embryo

Selecting a Sibling as a Stem Cell Donor

Sibling for a cure? (Fanconi Anemia, Molly Nash and brother Adam)
Genetic Journeys: Saving Cord Blood

- Umbilical cord blood contains stem cells used to treat immune disorders
- 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

Genetics in Society: The Business of Making Babies

- IVF and ART have become a profitable business with revenues up to $3 billion per year
- This business has little or no government or industry oversight, and there is little consistency in state regulations or insurance coverage

Gene Therapy Promises to Correct Many Disorders

- Gene therapy transfers a normal gene copy into target cells of individuals carrying a mutant allele

**Gene therapy**
- The transfer of cloned genes into somatic cells as a means of treating a genetic disorder

What Are the Strategies for Gene Transfer?

- There are several 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

Gene Therapy Showed Early Promise

- Ashanti de Silva remains the only success for severe combined immunodeficiency disease (SCID) gene therapy

David Vetter (Bubble Boy 1971-1984)

Gene Therapy Trials
Gene Therapy Trials

- Cancer diseases 66.5% (n = 871)
- Cardiovascular diseases 9.1% (n = 119)
- Monogenic diseases 8.3% (n = 109)
- Infectious diseases 6.5% (n = 85)
- Neurological diseases 1.5% (n = 20)
- Ocular diseases 0.9% (n = 12)
- Other diseases 1.6% (n = 21)
- Gene marking 3.8% (n = 50)
- Healthy volunteers 1.7% (n = 22)

Some Gene Therapy Involves Stem Cells, Gene Targeting, and Therapeutic Cloning

- A blastocyst begins to implant in the uterine wall

Therapeutic Cloning

- Stem cells can also be created by transferring a somatic cell nucleus into an enucleated egg

Somatic cell nuclear transfer

- A cloning technique that transfers a somatic cell nucleus to an enucleated egg, which is stimulated to develop into an embryo
- Inner cell mass cells collected from the embryo are grown to form a population of stem cells

Stem Cells are Classified by their Potential

- **Totipotent**
  - The ability of a stem cell to form every cell type in the body; characteristic of embryonic stem cells (e.g. embryonic stem cells)

- **Pluripotent**
  - The ability of a stem cell to form most of the cell types in the body (e.g. umbilical cord stem cells)

- **Multipotent**
  - The restricted ability of a stem cell to form only one or a few different cell types (bone marrow stem cells)
Gene Transfer

- Adult stem cells modified by gene transfer are being developed to treat genetic disorders
- Viral vectors were used to insert normal genes into cells with mutant genes

Gene Doping: Athletics and Enhancement Gene Therapy

- Athletes have been suspended from competitions for using erythropoietin (EPO), a hormone that increases production of red blood cells to enhance athletic performance
- Repoxygen, a form of gene therapy which results in increased synthesis and release of erythropoietin, may be impossible to detect

Genetic Counseling

Genetic Counseling Assesses Reproductive Risks

- 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
  - Those concerned that they may have an inherited disorder or birth defect

How Does Genetic Counseling Work?

- Prenatal screening and cytogenetic or biochemical tests can be used along with pedigree analysis to determine risk

- Decisions about whether to have additional children, to undergo abortion, or even to marry are always left to those being counseled