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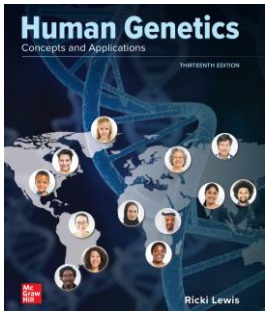



**Chapter 6**

Matters of Sex

**Thirteenth Edition**

**Ricki Lewis**



## Learning Outcomes 1

1. Describe the factors that contribute to whether we are and feel male or female.
2. Distinguish between the X and Y chromosomes.
3. Discuss how manipulating the sex ratio can affect societies.
4. Distinguish between Y linkage and X linkage.
5. Compare and contrast X-linked recessive inheritance and X-linked dominant inheritance.
6. Discuss the inheritance pattern of a trait that appears in only one sex.
7. Define *sex-influenced trait.*



## Learning Outcomes 2

8. Explain why X inactivation is necessary.
9. Explain how X inactivation is an epigenetic change.
10. Discuss how X inactivation affects the phenotype in female mammals.
11. Explain the chemical basis of silencing the genetic contribution from one parent.
12. Explain how differences in the timetables of sperm and oocyte formation can lead to parent-of-origin effects.



## Our Sexual Selves

Biological maleness or femaleness is determined at conception

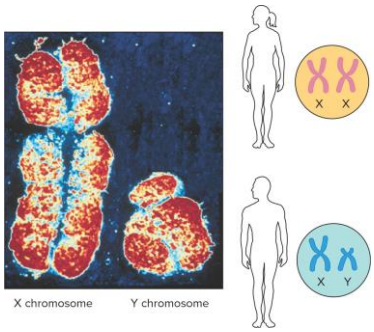
- When she inherits two X chromosomes or he inherits an X and a Y

Another level of sexual identity comes from the control that hormones exert on development of reproductive structures.

Biological factors and social cues influence sexual feelings.



## The Sex Chromosomes






## Sexual Development

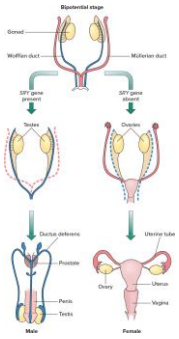
During the fifth week of prenatal development, all embryos develop two sets of:

- Unspecialized (indifferent) gonads
- Reproductive ducts—Müllerian (female-specific) and Wolffian (male-specific)

An embryo develops as a male or female based on the sex chromosome constitution and actions of certain genes

- Specifically the *SRY* gene (sex-determining region of the Y chromosome)

## Male or Female?

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## Sex Chromosomes Determine Gender 1

Human males are the **heterogametic sex** with different sex chromosomes (XY).

Human females are the **homogametic sex** (XX).

In other species sex can be determined in many ways.

- For example, in birds and snakes, males are homogametic (ZZ), while females are heterogametic (ZW).



## Sex Chromosomes Determine Gender 2

### X chromosome

- Contains > 1500 genes
- Much larger than the Y chromosome
- Acts as a homolog to Y in males

### Y chromosome

- Contains 231 genes
- Does not cross over along all of its length
- Many DNA segments are palindromes and may destabilize DNA replication



## Anatomy of the Y Chromosome 1

The Y chromosome has a very short arm and a long arm

**Pseudoautosomal regions** (**PAR1 and PAR2**)

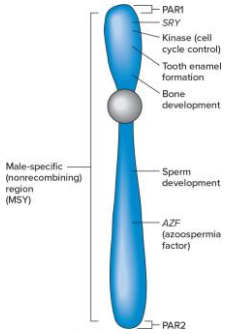
- 5% of the chromosome
- Contain 63 genes shared with X chromosome
  - Control bone growth, cell division, etc. in both sexes

### Male specific region (MSY)

- 95% of the chromosome
- Many of the genes are essential to fertility
  - Including *SRY* and *AZF* (needed for sperm production)



## Anatomy of the Y Chromosome 2

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## *SRY* Gene

Encodes a **transcription factor** protein

- Controls the expression of other genes, including *Sox9*
- Stimulates male development
- Sends signals to the indifferent gonads to destroy female structures
- Stimulates development of male structures

Testosterone and dihydrotestosterone (DHT) are secreted

- Stimulate development of male reproductive structures

## Disorders of Sex Development 1

- *Hermaphroditism* is an older and more general term for an individual with male and female sexual structures.
- *Intersex* refers to individuals whose internal structures are inconsistent with external structures, or whose genitalia are ambiguous.
- *Pseudohermaphroditism* refers to the presence of both female and male structures but at different life stages.

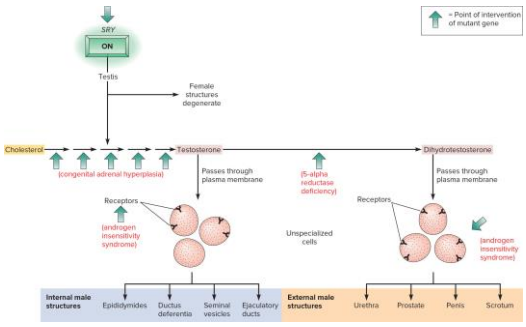
## Disorders of Sex Development 2

Pseudohermaphroditism includes:

- Androgen insensitivity syndrome
  - Mutation on the X-chromosome blocks formation of androgen receptors
- 5-alpha reductase deficiency
  - Unable to convert testosterone to DHT
  - Child has inside male anatomy but looks like a girl on the exterior
- Congenital adrenal hyperplasia
  - Enzyme block causes androgens to accumulate
  - Cause precocious puberty in males or male secondary sex characteristics to develop in females.

## Mutations That Affect Male Sexual Development

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## Homosexuality 1

Person's phenotype and genotype are consistent

- Physical attraction is toward members of the same sex

Homosexuality has been seen in all cultures for thousands of years

- Documented in over 1500 animal species

## Homosexuality 2

Evidence suggests a complex input from both genes and the environment.

- Identical twins are more likely to be homosexual than members of fraternal twin pairs.
- Genetic markers were identified on the X chromosome more often identical among pairs of homosexual brothers.

One study has concluded that "many tiny genetic effects" may contribute to homosexuality.

- So, there is no one specific gene that determines attraction to the same or opposite sex.

## Components of Sexual Identity

**Table 6.1 Sexual Identity**

| Level | Events | Timing |
|---|---|---|
| Chromosomal/ genetic sex | XY = male<br>XX = female | Fertilization |
| Gonadal sex | Undifferentiated structure begins to develop as testis or ovary | 6 weeks after fertilization |
| Phenotypic sex | Development of external and internal reproductive structures continues as male or female in response to Hormones | 8 weeks after fertilization, at puberty |
| Gender identity | Strong feelings of being male or female develop | From childhood, possibly earlier |
| Sexual Orientation | Attraction to same or opposite sex | From childhood |

 Source: Courtesy Professor Jennifer A. Marshall-Graves, Australian National University 

## Sex Ratios

The proportion of males to females in a human population

- Calculated by # of males/# of females multiplied by 1000
- **Primary sex ratio—**At conception
- **Secondary sex ratio—**At birth
- **Tertiary sex ratio—**At maturity

Sex ratios can change markedly with age

- Reflects medical conditions and environment factors

## Y-Linked Traits

Genes on the Y chromosome are said to be **Y-linked**

Y-linked traits are very rare

Transmitted from male to male

- A female does not have a Y chromosome

Currently, identified Y-linked traits involve infertility and are not transmitted

## X-Linked Traits

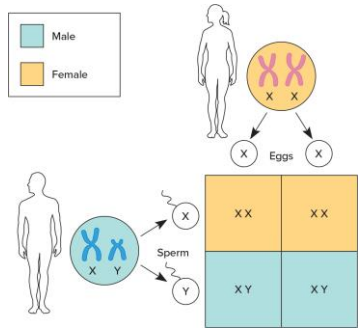
Patterns of expression on the X chromosome differ in females and males.

- Females—X-linked traits are passed like autosomal traits.
- Males—A single copy of an X-linked allele causes expression of the trait or illness.

Human male is considered **hemizygous** for X-linked traits.

## Sex Determination in Humans

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## Introducing Cells 2

**Table 6.2 Comparison of X-Linked Recessive and X-Linked Dominant Inheritance**

| X-Linked Recessive Trait | X-Linked Dominant Trait |
|---|---|
| Always expressed in the male | Expressed in females in one copy |
| Expressed in a female homozygote and very rarely in a female heterozygote | Much more severe effects in males |
| Affected male inherits trait from heterozygote or homozygote Mother | High rates of miscarriage due to early lethality in males |
| Affected female inherits trait from affected father and affected or heterozygote mother | Passed from male to all daughters but to no sons |

## X-Linked Recessive Traits 1

An X-linked recessive trait is expressed in females if the causative allele is present in two copies.

- If condition is not lethal, a man may be healthy enough to transmit it to offspring

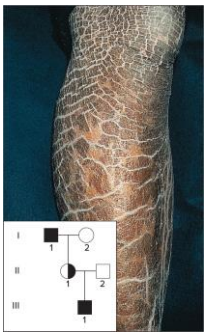
Examples:

- Ichthyosis = Enzyme deficiency blocks removal of cholesterol from skin cells
- Colorblindness = About 8% of males of European ancestry have the condition
- Hemophilia = Disorder of blood-clotting

## X-Linked Recessive Traits 2

Ichthyosis



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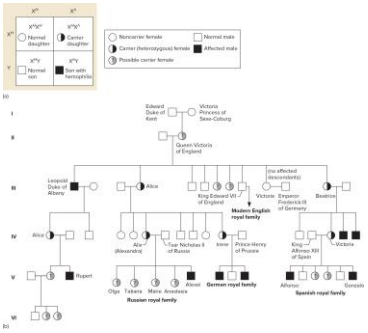
## X-Linked Recessive Traits 3

Hemophilia B



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## X-Linked Dominant Traits 1

Dominant X-linked traits are rare.

Gene expression differs between the sexes

- A female who inherits a dominant X-linked allele or in whom the mutation originates has the associated trait
- But a male who inherits the allele is usually more severely affected because he has no other allele to mask its effect.

Most cases are the result of new mutations, rather than transmission from a parent

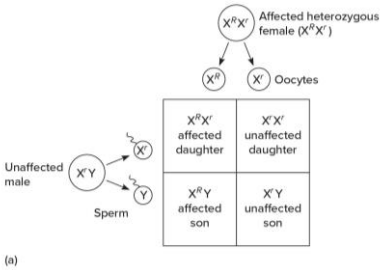
Examples:

- Rett syndrome (Refer to Chapter 2 opener)
- Incontinentia pigmenti



## X-Linked Dominant Traits 2

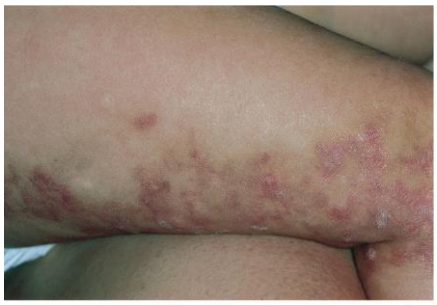
Incontinentia pigmenti




(a)



## X-Linked Dominant Traits 3



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## Solving Genetic Problems

Steps to follow:

1. Look at the inheritance pattern.
2. Draw a pedigree.
3. List genotypes and phenotypes and their probabilities.
4. Assign genotypes and phenotypes to parents.
5. Determine how alleles separate into gametes.
6. Unite the gametes in a Punnett square.
7. Determine the phenotypic and genotypic ratios for the $F_1$ generation.
8. To predict further generations, use the genotypes of the $F_1$ and repeat steps 4 to 6.

## Sex-Limited Traits

Traits that affect a structure or function that is present in only one sex

The gene may be autosomal or X-linked

Examples:

- Beard growth
- Milk production
- Preeclampsia in pregnancy
  - A gene from the father may affect the placenta in a way that elevates the pregnant woman's blood pressure.

## Sex-Influenced Traits

- Allele is dominant in one sex but recessive in the other
- The gene may be autosomal or X-linked
- Difference in expression can be caused by hormonal differences between sexes

Examples:

- Pattern baldness in humans
  - A heterozygous male is bald, but a heterozygous female is not
- Response to treatment for glioblastoma
  - Female patients live longer than male patients after surgery, radiation, and use of a drug, temozolomide.

## X Inactivation 1

Females have two alleles for X chromosome genes but males have only one.

In mammals, **X inactivation** balances this inequality in the expression of genes on the X chromosome.

- A female mammal is a mosaic for expression of most genes on the X chromosome.

*XIST* gene encodes an RNA that binds to and inactivates the X chromosome.

## X Inactivation 2

X inactivation occurs early in prenatal development

- The adult female has patches of tissue that differ in their expression of X-linked genes

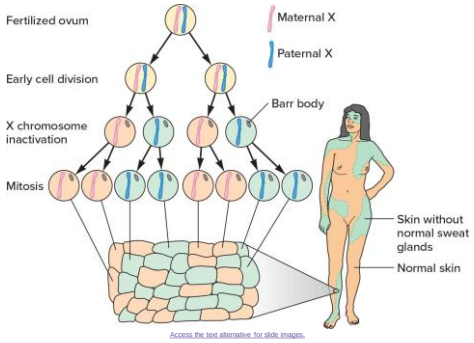
Alters the phenotype and not the genotype

It is an example of an **epigenetic change**

- An inherited change that does not alter the DNA base sequence
- Inactivated DNA has chemical methyl ($CH_3$) groups bound to it that prevent it from being transcribed into RNA

## X Inactivation 3

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## Effect of X Inactivation on the Phenotype 1

X inactivation can be used to check the sex of an individual

- Nucleus of a cell of a female, during interphase, contains a **Barr body**

The consequences of X inactivation on the phenotype can be interesting

- Homozygous X-linked genotypes—No effect
- Heterozygotes—Leads to expression of one allele or the other

## Effect of X Inactivation on the Phenotype 2

- A female that expresses the phenotype corresponding to an X-linked gene is a **manifesting heterozygote.**
- X inactivation is obvious in calico cats.





## Effect of X Inactivation on the Phenotype 3

In humans, X inactivation can be used to identify carriers of some X-linked disorders

- Hunter syndrome (mucopolysaccharidosis II)
- Lesch-Nyhan syndrome
- Affects the severity of Rett syndrome

Unequal X inactivation pattern can occur if the two X chromosomes have different alleles for a gene that controls cell division

- Gives certain cells a survival advantage




## Parent-of-Origin Effects

In Mendel's experiments, it didn't matter whether a trait came from the male or female parent

For some genes, parental origin influences phenotype

- Age of onset
- Symptom severity

Mechanisms of parent-of-origin effects

- Genomic imprinting
- Differences between developmental timetables of sperm and oocytes

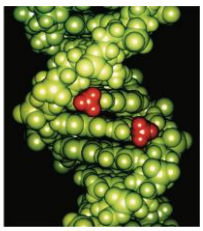



## Genomic Imprinting 1

In **genomic imprinting,** methyl ($CH_3$) groups bind a gene or several linked genes

- Prevent them from being expressed


For an imprinted gene, the copy inherited from either the father or the mother is always covered with methyls, even in different individuals.







## Genomic Imprinting 2

Parental effect on gene expression is seen as diseases inherited from a parent

- For example, central precocious puberty is always inherited from the father.
  - A gene called *MKRN3* from the father is covered in methyls, and therefore imprinted.
  - In this condition, girls reach puberty before age 8 and boys before age 9.

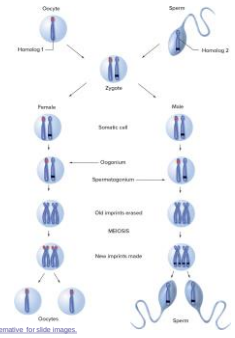
Epigenetic alteration—Layer of meaning stamped upon a gene without changing its DNA sequence




## Genomic Imprinting 3

Imprints are erased during meiosis.

- Then reassigned based on instituted according to the sex of the individual

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## Importance of Genomic Imprinting 1

Function of imprinting isn't well understood, may be a way to regulate abundance of key proteins in the embryo.

Imprinted genes are in clusters along a chromosome, controlled by imprinting centers.

- One gene in a cluster could be essential for early development.
  - Others become imprinted due to bystander effect.



## Importance of Genomic Imprinting 2

Research suggests that it takes two opposite sex parents to produce a healthy embryo

- Male genome controls placenta development
- Female genome controls embryo development

Genomic imprinting may also explain incomplete penetrance

May be a concern in assisted reproductive technologies



## Imprinting and Human Disease 1

Humans have 150+ imprinted genes, and at least 60 of them affect health if abnormally expressed

Two distinct syndromes result from a small deletion in chromosome 15

- Prader-Willi syndrome
  - Deletion inherited from father
- Angelman syndrome
  - Deletion inherited from mother

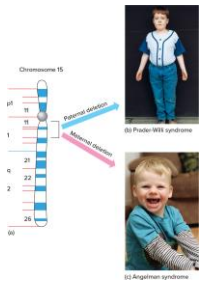
Abnormal imprinting is associated with:

- Diabetes mellitus; Autism; Alzheimer disease
- Schizophrenia; Male homosexuality



## Imprinting and Human Disease 2

Deletion on chromosome 15 reveals imprinting.




 (W. Carla D. Kinser; (c): Dan James/Caters News Agency) 

## Different Timetables in Sperm and Oocyte Formation

Differences in development of sperm and oocytes explain some parent-of-origin effects.

- Huntington disease
  - Has younger age of onset, with faster and more severe symptoms, if inherited from the father
- Noonan syndrome
  - Children of older fathers have an increased risk



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