Genetics 1 (Fundamental)
Food safety and Desert land Reclamation Programs
Level 1

Lecture 6 and 7

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Lecture 6

Types of Mendelian Inheritance Patterns Involving Single Genes

❑Simple Mendelian

- **Inheritance:** This term is commonly applied to the inheritance of alleles that obey Mendel's laws and follow a strict dominant/recessive relationship.
- some genes can be found in three or more alleles, making the relationship more complex.

- **Molecular:** 50% of the protein, produced by a single copy of the dominant (functional) allele in the heterozygote, is sufficient to produce the dominant trait.

- **Incomplete penetrance:**
- **Inheritance:** This pattern occurs when a dominant phenotype is not expressed even though an individual carries a dominant allele.
- An example is an individual who carries the polydactyly allele but has a normal number of fingers and toes.

- **Molecular:** Even though a dominant gene may be present, the protein encoded by the gene may not exert its effects. This can be due to environmental influences or due to other genes that may encode proteins that counteract the effects of the protein encoded by the dominant allele.

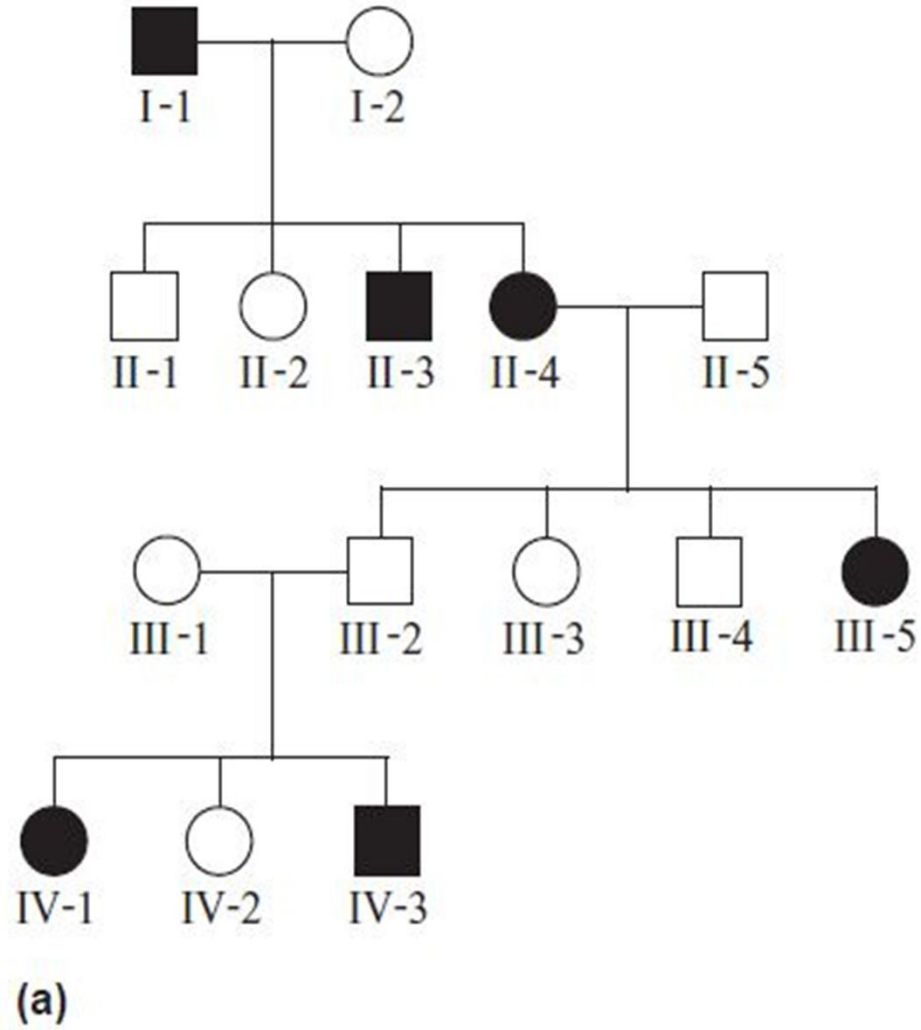
❑ Polydactyly, a dominant trait that shows incomplete penetrance.

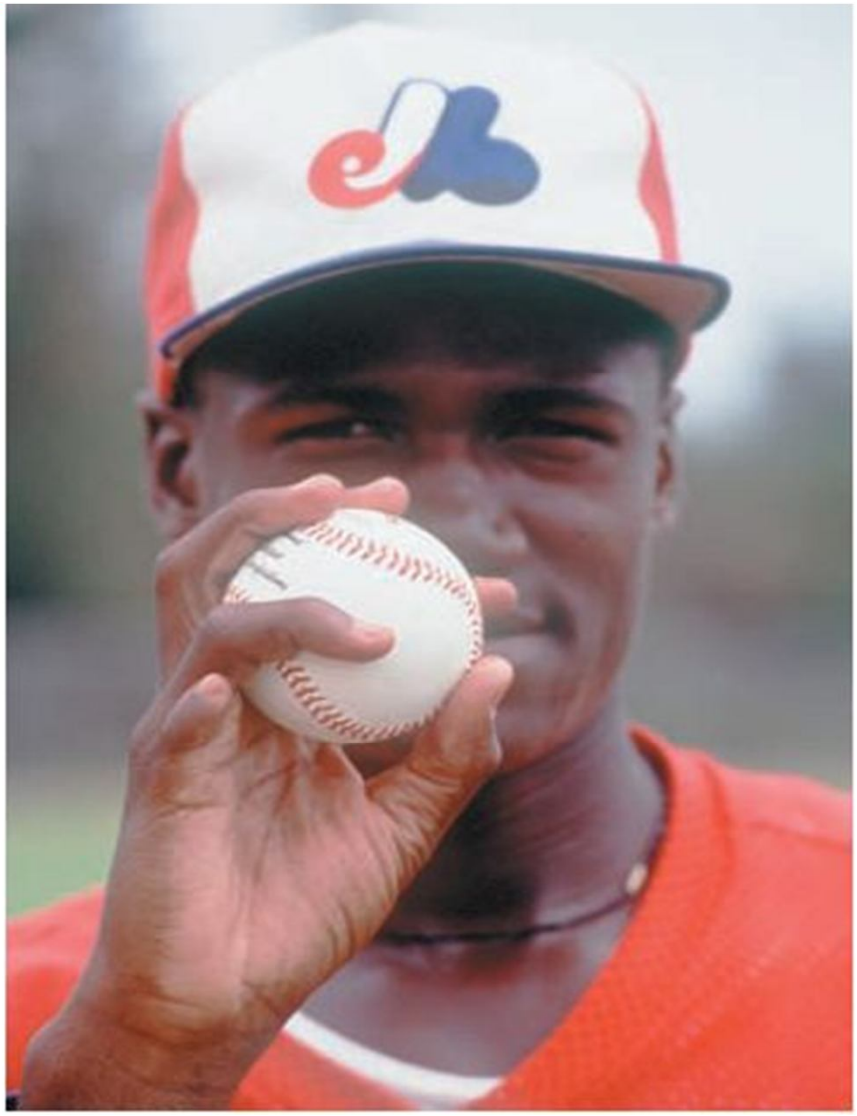
- Polydactyly is due to an autosomal dominant allele—the allele is found in a gene located on an autosome (not a sex chromosome) and a single copy of this allele is sufficient to cause this condition.

- This trait causes the affected individual to have additional fingers or toes (or both).

- Sometimes, however, individuals carry the dominant allele but do not exhibit the trait.

Polydactyly, a dominant trait that shows incomplete penetrance.





❑Incomplete dominance:

- **Inheritance:** This pattern occurs when the heterozygote has a phenotype that is intermediate between either corresponding homozygote.
- For example, a cross between homozygous red-flowered and homozygous white-flowered parents will have heterozygous offspring with pink flowers.

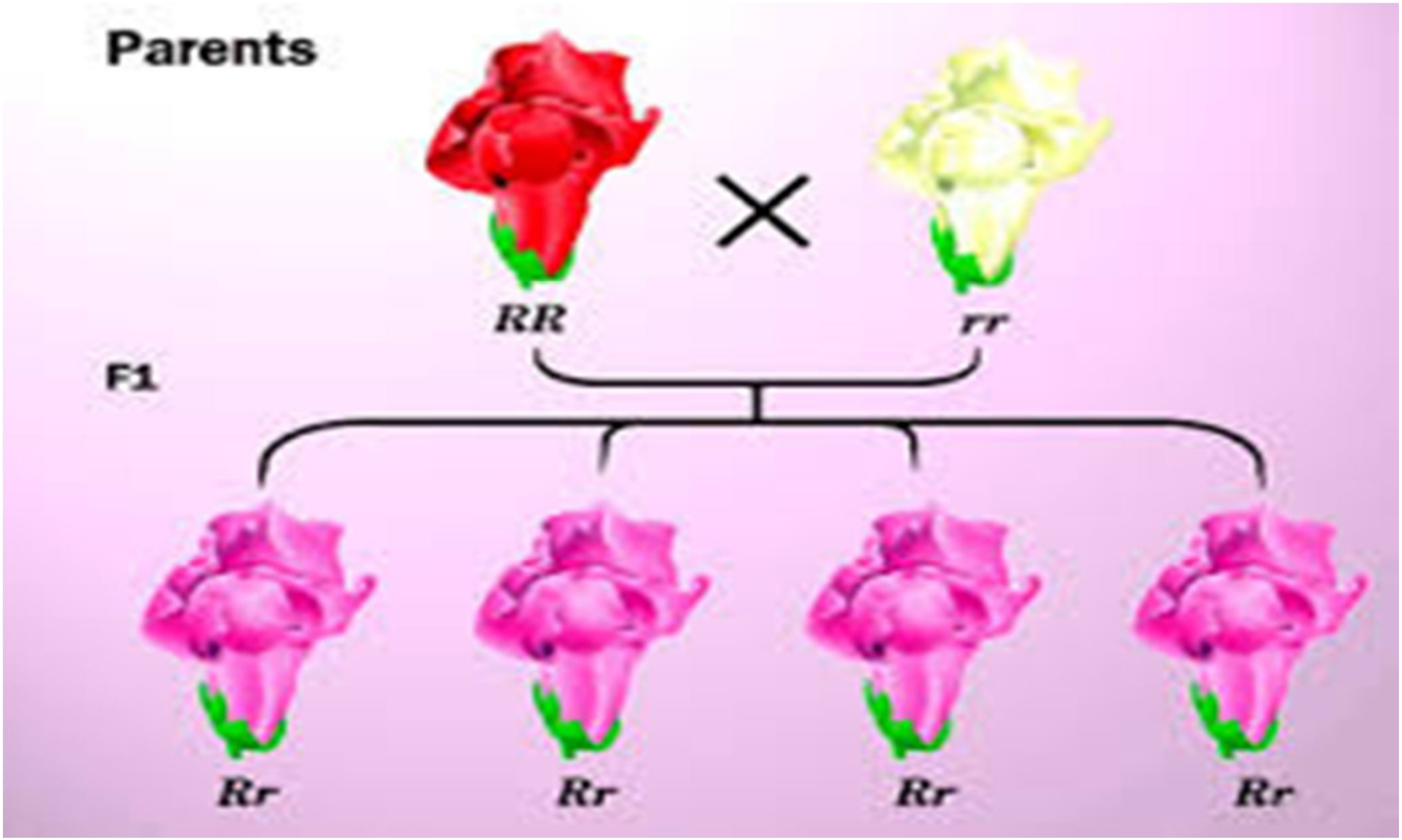
- **Molecular:** 50% of the protein, produced by a single copy of the functional allele in the heterozygote, is not sufficient to produce the same trait as the homozygote making 100%.

Incomplete dominance

- Incomplete dominance (also called partial dominance or semi-dominance) occurs when the phenotype of the heterozygous phenotype is distinct from and often intermediate to the phenotypes of the homozygous phenotypes.

- For example, the snapdragon flower color is homozygous for either red or white. When the red homozygous flower is paired with the white homozygous flower, the result yields a pink snapdragon flower. The pink snapdragon is the result of incomplete dominance.

When plants of the F1 generation are self-pollinated, the phenotypic and genotypic ratio of the F2 generation will be 1:2:1 (Red:Pink:White).



F2 generation

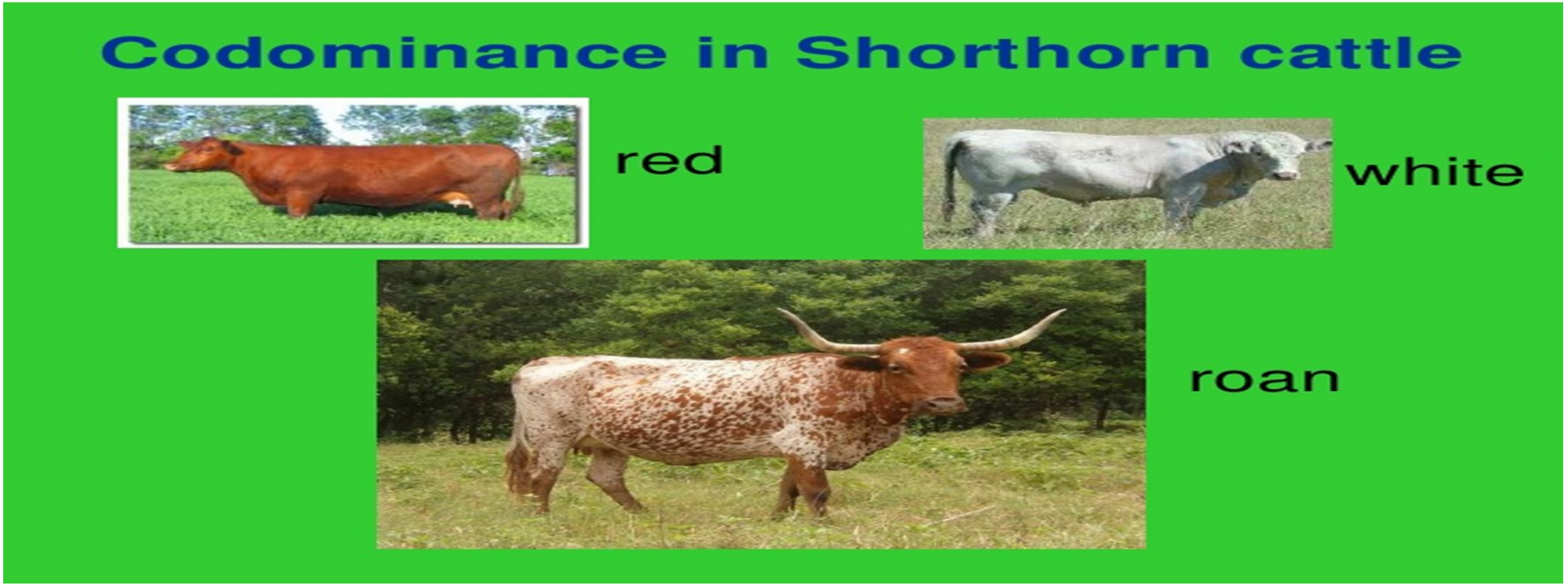
❑Codominance:

- **Inheritance:** This pattern occurs when the heterozygote expresses both alleles simultaneously.
- For example, in blood typing, an individual carrying the *A* and *B* alleles will have an AB blood type.

- **Molecular:** The codominant alleles encode proteins that function slightly differently from each other, and the function of each protein in the heterozygote affects the phenotype uniquely.

Co-dominance

- Co-dominance occurs when the both of the allele, dominant or recessive ones are fully expressed but do not overlay each other in compare to the complete dominance. They do not interfere, but they act together so the contributions of both alleles are visible in the phenotype.



P RR (Red color) x rr (white color)

G (R) (r)

F1 Rr (roan) %100 x Rr

G (R) (r) x (R) (r)

F2 RR (red) Rr Rr (Roan) rr (white)

1 : 2 : 1

❑Overdominance:

- **Inheritance:** This pattern occurs when the heterozygote has a trait that is more beneficial than either homozygote.

- **Molecular:** Three common ways that heterozygotes gain benefits: (1) Their cells may have increased resistance to infection by microorganisms; (2) they may produce more forms of protein dimers, with enhanced function; or (3) they may produce proteins that function under a wider range of conditions.

❑ Overdominance Occurs When Heterozygotes Have Superior Traits

- The environment plays a key role in the outcome of traits. For certain genes, heterozygotes may display characteristics that are more beneficial for their survival in a particular environment. Such heterozygotes may be more likely to survive and reproduce.

- Overdominance is usually due to two alleles that produce proteins with slightly different amino acid sequences.

- For example, a heterozygote may be larger, disease-resistant, or better able to withstand harsh environmental conditions. The phenomenon in which a heterozygote has greater reproductive success compared with either of the corresponding homozygotes is called **overdominance** or **heterozygote advantage.**

Sickle cell disease
autosomal recessive disorder

- A well-documented example involves a human allele that causes sickle cell disease in homozygous individuals.
- This disease is an autosomal recessive disorder in which the affected individual produces an altered form of the protein hemoglobin, which carries oxygen within red blood cells.
- Most people carry the Hb^A allele and make hemoglobin A. Individuals affected with sickle cell anemia are homozygous for the Hb^S allele and produce only hemoglobin S. This causes their red blood cells to deform into a sickle shape under conditions of low oxygen concentration.

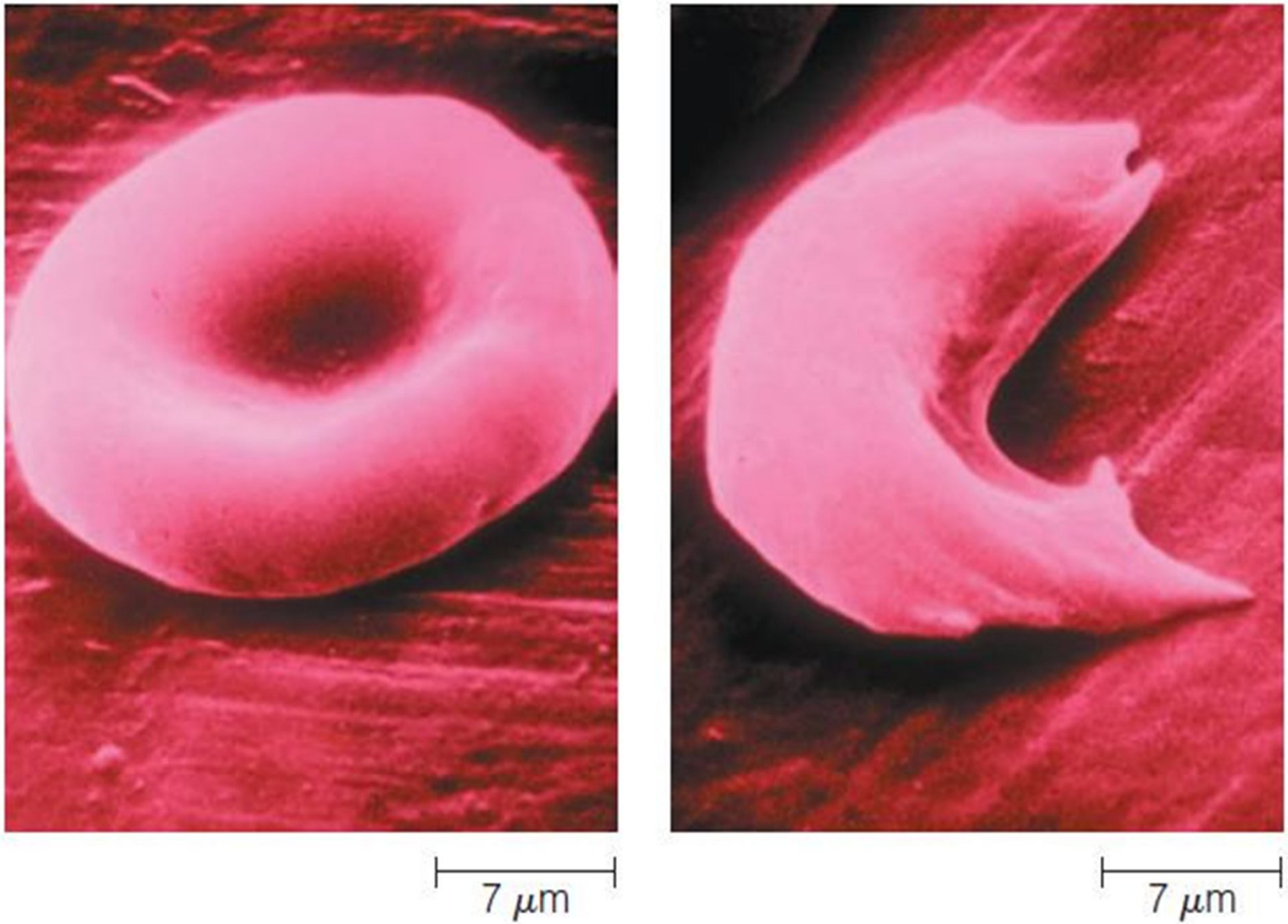
- The sickling phenomenon causes the life span of these cells to be greatly shortened to only a few weeks compared with a normal span of four months, and therefore, anemia results. In addition, abnormal sickled cells can become clogged in the capillaries throughout the body, leading to localized areas of oxygen depletion.

- Such an event, called a crisis, causes pain and sometimes tissue and organ damage. For these reasons, the homozygous Hb^SHb^S individual usually has a shortened life span relative to an individual producing hemoglobin A. In spite of the harmful consequences to homozygotes, the sickle cell allele has been found at a fairly high frequency among human populations that are exposed to malaria. The protozoan genus that causes malaria, *Plasmodium*, spends part of its life cycle within the *Anopheles* mosquito and another part within the red blood cells of humans who have been bitten by an infected mosquito.

- However, red blood cells of heterozygotes, Hb^AHb^S, are likely to rupture when infected by this parasite, thereby preventing the parasite from propagating. People who are heterozygous have better resistance to malaria than do Hb^AHb^A homozygotes, while not incurring the ill effects of sickle cell disease.

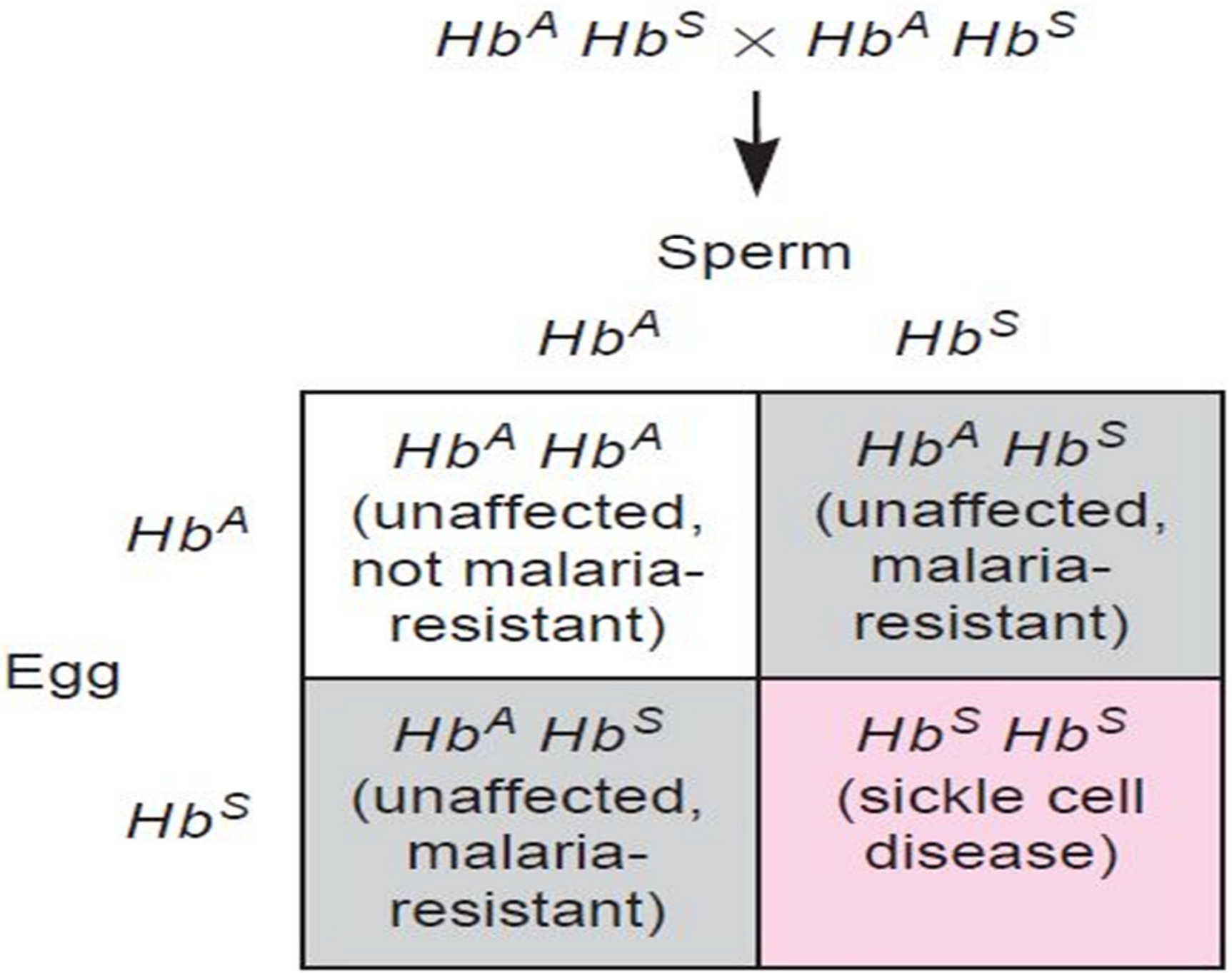
- Therefore, even though the homozygous Hb^SHb^S condition is detrimental, the greater survival of the heterozygote has selected for the presence of the Hb^S allele within populations where malaria is prevalent.

- When viewing survival in such a region, overdominance explains the prevalence of the sickle cell allele.
- In this example, 1/4 of the offspring are Hb^AHb^A (unaffected, not malaria-resistant), ½ are Hb^AHb^S (unaffected, malaria-resistant) and 1/4 are Hb^SHb^S (sickle cell disease). This 1:2:1 ratio deviates from a simple Mendelian 3:1 phenotypic ratio.
- **The role that natural selection plays in maintaining alleles that are beneficial to the heterozygote but harmful to the homozygote explain ????.**



(a) Normal red blood cell

(b) Sickled red blood cell


$Hb^A\ Hb^S \times Hb^A\ Hb^S$
Sperm
Hb^A
Hb^S
Egg
Hb^A
Hb^S
$Hb^A\ Hb^A$ (unaffected, not malaria-resistant)
$Hb^A\ Hb^S$ (unaffected, malaria-resistant)
$Hb^A\ Hb^S$ (unaffected, malaria-resistant)
$Hb^S\ Hb^S$ (sickle cell disease)

❑X-linked inheritance:

- **Inheritance:** This pattern involves the inheritance of genes that are located on the X chromosome. In mammals and fruit flies, males are hemizygous for X-linked genes, whereas females have two copies.

- **Molecular:** If a pair of X-linked alleles shows a simple dominant/recessive relationship, 50% of the protein, produced by a single copy of the dominant allele in a heterozygous female, is sufficient to produce the dominant trait (in the female).

❑Sex-influenced inheritance:

- **Inheritance:** This pattern refers to the effect of sex on the phenotype of the individual. Some alleles are recessive in one sex and dominant in the opposite sex.
- An example is pattern baldness in humans.

- **Molecular:** Sex hormones may regulate the molecular expression of genes. This can influence the phenotypic effects of alleles.

Sex-influenced inheritance

- Sex-influenced inheritance refers to the phenomenon in which an allele is dominant in one sex but recessive in the opposite sex. Therefore, sex influence is a phenomenon of heterozygotes.

- The genes that govern sex-influenced traits are almost always autosomal, not on the X or Y chromosome.

- In humans, the common form of pattern baldness provides an example of sex-influenced inheritance.

- The balding pattern is characterized by hair loss on the front and top of the head but not on the sides. This type of pattern baldness is inherited as an autosomal trait.

- When a male is heterozygous for the baldness allele, he will become bald.

Genotype	Phenotype	
	Males	Females
BB	Bald	Bald
Bb	Bald	Nonbald
bb	Nonbald	Nonbald

- The sex-influenced nature of pattern baldness is related to the production of the male sex hormone testosterone.

- The gene that affects pattern baldness encodes an enzyme called 5-α-reductase, which converts testosterone to 5-α-dihydrotestosterone (DHT).

- DHT binds to cellular receptors and affects the expression of many genes, including those in the cells of the scalp.

- The allele that causes pattern baldness results in an overexpression of this enzyme. Because mature males normally make more testosterone than females, this allele has a greater phenotypic effect in males.

- **Sex-limited inheritance:**
- **Inheritance:** This refers to traits that occur in only one of the two sexes. An example is breast development in mammals.

- **Molecular:** Sex hormones may regulate the molecular expression of genes. This can influence the phenotypic effects of alleles.
- In this case, sex hormones that are primarily produced in only one sex are essential to produce a particular phenotype.

- The genes that influence sex limited traits may be autosomal or X-linked.

- In humans, examples of sex-limited traits are the presence of ovaries in females and the presence of testes in males.

- Due to these two sex-limited traits, mature females can only produce eggs, whereas mature males can only produce sperm.

- **Sex-limited traits are responsible for sexual dimorphism** in which members of the opposite sex have different morphological features. This phenomenon is common among many animals species and is often striking among various species of birds in which the male has more ornate plumage than the female.

- Roosters have a larger comb and longer neck and tail feathers than do hens. These sex-limited features may be found in roosters but never in normal hens.

(a) Hen (b) Rooster

Differences in the feathering pattern in female and male chickens, an example of sex-limited inheritance.

Lecture 7

➢Lethal alleles:

- **Inheritance:** An allele that has the potential of causing the death of an organism.

- **Molecular:** Lethal alleles are most commonly loss-of-function alleles that encode proteins that are necessary for survival. In some cases, the allele may be due to a mutation in a nonessential gene that changes a protein to function with abnormal and detrimental consequences.

Mutations in an Essential Gene May Result in a Lethal Phenotype

- **A lethal allele** is an allele that has the potential to cause the death of an organism.

- These are usually inherited in a recessive manner. When the absence of a specific protein results in a lethal phenotype, the gene that encodes the protein is considered an **essential gene** for survival. Though it varies according to species, researchers estimate that approximately 1/3 of all genes are essential genes.

- By comparison, **nonessential genes** are not absolutely required for survival, although they are likely to be beneficial to the organism.
- A loss-of-function mutation in a nonessential gene will not usually cause death.

- On rare occasions, however, a nonessential gene may acquire a mutation that causes the gene product to be abnormally expressed in a way that may interfere with normal cell function and lead to a lethal phenotype. Therefore, not all lethal mutations occur in essential genes, although the great majority do.

- Many lethal alleles prevent cell division and thereby cause an organism to die at a very early stage. Others, however, may only exert their effects later in life, or under certain environmental conditions.

Huntington disease (dominant allele)

- For example, a human genetic disease known as **Huntington disease** is caused by a dominant allele.

- The disease is characterized by a progressive degeneration of the nervous system, dementia, and early death. The age when these symptoms appear, or the **age of onset,** is usually between 30 and 50.

- Other lethal alleles may kill an organism only when certain environmental conditions prevail. Such **conditional lethal alleles** have been extensively studied in experimental organisms.

- For example, some conditional lethals will cause an organ ism to die only in a particular temperature range. These alleles, called **temperature- sensitive (ts) lethal alleles** **,** have been observed in many organisms, including *Drosophila.* A ts lethal allele may be fatal for a developing larva at a high temperature (30°C), but the larva will survive if grown at a lower temperature (22°C).

- Temperature sensitive lethal alleles are typically caused by mutations that alter the structure of the encoded protein so it does not function correctly at the nonpermissive temperature or becomes unfolded and is rapidly degraded.

Lethal alleles & the environment

- Conditional lethal alleles may also be identified when an individual is exposed to a particular agent in the environment. For example, people with a defect in the gene that encodes the enzyme glucose-6-phosphate dehydrogenase (G6PD) have a negative reaction to the ingestion of fava beans. This can lead to an acute hemolytic syndrome with 10% mortality if not treated properly.

Semilethal alleles

- A semilethal allele will cause some individuals to die but not all of them. The reasons for semilethality are not always understood, but environmental conditions and the actions of other genes within the organism may help to prevent the detrimental effects of certain semilethal alleles.

- An example of a semilethal allele is the X-linked white-eyed allele in Drosophila melanogaster . Depending on the growth conditions, approximately 1/4 to 1/3 of the flies that would be expected to exhibit this white-eyed trait die prematurely.

➢ Dominant lethal alleles:

1- Manx cat

- In some cases, a lethal allele may produce ratios that seemingly deviate from Mendelian ratios. An example is an allele in a breed of cats known as **Manx, which originated on the Isle of Man.**

- The Manx cat carries a dominant mutation that affects the spine. This mutation shortens the tail, resulting in a range of tail lengths from normal to tailless.

- When two Manx cats are crossed to each other, the ratio of offspring is 1 normal to 2 Manx. How do we explain the 1:2 ratio? The answer is that about 1/4 of the offspring die during early embryonic development. In this case, the Manx phenotype is dominant, whereas the lethal phenotype occurs only in the homozygous condition.

Mm (Manx) × *Mm* (Manx)

Sperm

Egg	*M*	*m*
M	*MM* (early embryonic death)	*Mm* (Manx)
m	*Mm* (Manx)	*mm* (non-Manx)

1:2 ratio of kittens that are born

(b) Example of a Manx inheritance pattern

2- Creeper condition in chickens

- "Creeper" allele in chickens, which causes the legs to be short and stunted.
- Creeper is a dominant gene, heteroyzous chickens display the creeper phenotype.

- If two creeper chickens are crossed, one would expect to have (from mendelian genetics) 3/4 of the offspring to be creeper and 1/4 to be normal.

- Instead the ratio obtained is 2/3 creeper and 1/3 normal.
- This occurs because homozygous creeper chickens die.

All “creeper” birds are heterozygous

- Creeper x Normal

  1:1 phenotypic ratio

  – Creeper phenotype is dominant

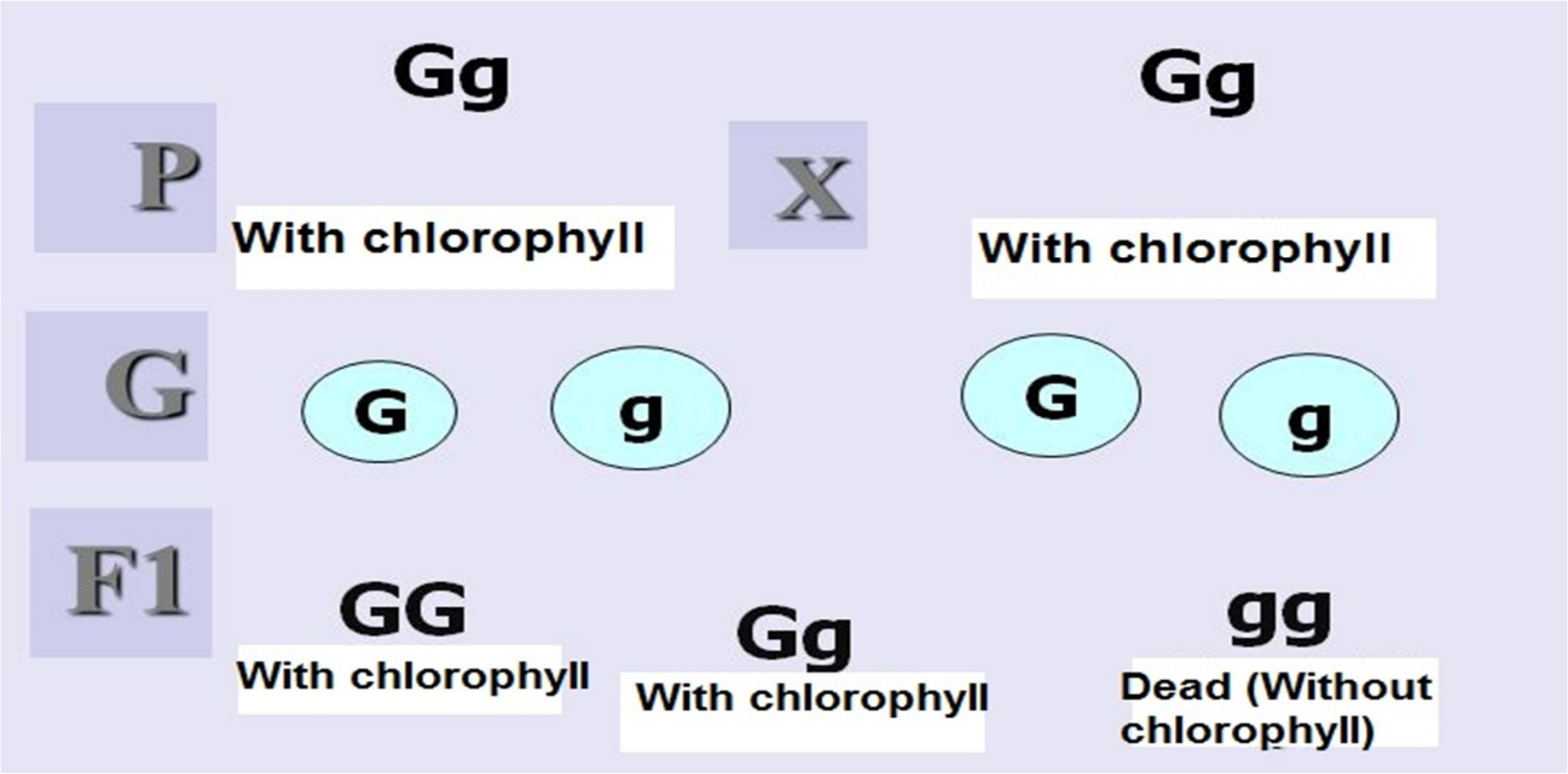
♀ \ ♂	C	c
c	Cc Creeper	cc Normal
c	Cc Creeper	cc Normal

- Creeper x creeper → 2:1
- Creeper allele is a recessive lethal

  – Creeper homozygotes are dead

♀ \ ♂	C	c
C	CC Dead	Cc Creeper
c	Cc Creeper	cc Normal

Recessive allele in plants
The white color of Seedlings in Maize



Many Genes Exist as Three or More Different Alleles

- As researchers have probed genes at the molecular level within natural populations of organisms, they have discovered that most genes exist in **multiple alleles .**

- Within a population, genes are typically found in three or more alleles.

- An interesting example of multiple alleles involves coat color in rabbits.

The coat color in rabbits

- The relationship between genotype and phenotype for a combination of four different alleles, which are designated *C* (full coat color), c^{ch} (chinchilla pattern of coat color), c^{h} (himalayan pattern of coat color), and *c* (albino).

- In this case, the gene encodes an enzyme called tyrosinase, which is the first enzyme in a metabolic pathway that leads to the synthesis of melanin from the amino acid tyrosine.

- This pathway results in the formation of two forms of melanin.
- Eumelanin, a black pigment, is made first, and then phaeomelanin, an orange/yellow pigment, is made from eumelanin.
- Alleles of other genes can also influence the relative amounts of eumelanin and phaeomelanin.
- Differences in the various alleles are related to the function of tyrosinase.
- The *C* allele encodes a fully functional tyrosinase that allows the synthesis of both eumelanin and phaeomelanin, resulting in a full brown coat color.

- The *C* allele is dominant to the other three alleles.

- The chinchilla allele (c^{ch}) is a partial defect in tyrosinase that leads to a slight reduction in black pigment and a greatly diminished amount of orange/yellow pigment, which makes the animal look gray.

- The albino allele, designated *c*, is a complete loss of tyrosinase, resulting in white color.

- The himalayan pattern of coat color, determined by the *ch* allele, is an example of a **temperature-sensitive allele.**

- The mutation in this gene has caused a change in the structure of tyrosinase, so it works enzymatically only at low temperature. Because of this property, the enzyme functions only in cooler regions of the body, primarily the tail, the paws, and the tips of the nose and ears.

- **The expression of a temperature-sensitive conditional allele produces a Siamese pattern of coat color.**
- **Genes →Traits** The allele affecting fur pigmentation encodes a pigment producing protein that functions only at lower temperatures. For this reason, the dark fur is produced only in the cooler parts of the animal, including the tips of the ears, nose, paws, and tail.

(a) Full coat color CC, Cc^h, Cc^{ch}, or Cc.

(b) Chinchilla coat color $c^{ch}c^{ch}$, $c^{ch}c^h$, or $c^{ch}c$.

(c) Himalayan coat color c^hc^h or c^hc.

(d) Albino coat color cc.

Genes Located on Mammalian Sex Chromosomes Can Be Transmitted in an X-Linked, a Y-Linked, or a Pseudoautosomal Pattern

- The term **sex-linked gene** refers to a gene that is found on one of the two types of sex chromosomes but not on both.

- Hundreds of X-linked genes have been identified in humans and other mammals.

- The inheritance pattern of X-linked genes shows certain distinctive features. For example, males transmit X-linked genes only to their daughters, and sons receive their X-linked genes from their mothers.

- The term **hemizygous** is used to describe the single copy of an X-linked gene in the male. A male mammal is said to be hemizygous for X-linked genes. Because males of certain species, such as humans, have a single copy of the X chromosome, another distinctive feature of X-linked inheritance is that males are more likely to be affected by rare, recessive X-linked disorders.

- By comparison, relatively few genes are located only on the Y chromosome. These few genes are called **holandric genes.**

- An example of a holandric gene is the *Sry* gene found in mammals. Its expression is necessary for proper male development.

- A Y-linked inheritance pattern is very distinctive—the gene is transmitted only from fathers to sons. Besides sex-linked genes, the X and Y chromosomes also contain short regions of homology where the X and Y chromosomes carry the same genes. In addition to several smaller regions, the human sex chromosomes have three homologous Regions.

- These regions, which are evolutionarily related, promote the necessary pairing of the X and Y chromosomes that occurs during meiosis I of spermatogenesis.
- Relatively few genes are located in these homologous regions. One example is a human gene called *Mic2*, which encodes a cell surface antigen.

- **A comparison of the homologous and non homologous regions of the X and Y chromosome in humans.** The brackets show three regions of homology between the X and Y chromosome.

- A few pseudoautosomal genes, such as *Mic2*, are found on both the X and Y chromosomes in these small regions of homology.

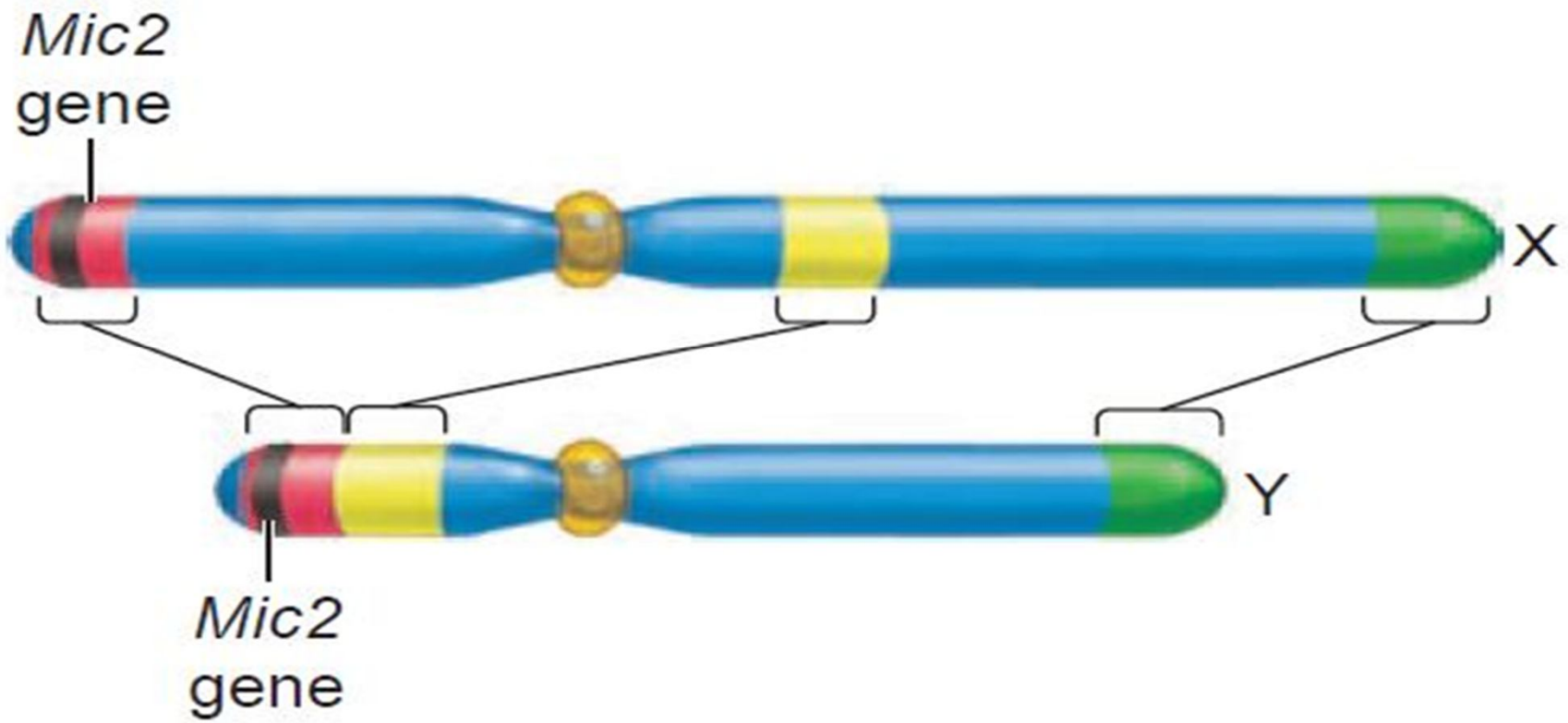
- Researchers estimate that the X chromosome contains between 900 and 1200 genes and the Y chromosome has between 70 and 300 genes.

Pseudoautosomal inheritance

- The *Mic2* gene is found on both the X and Y chromosomes. It follows a pattern of inheritance called **pseudoautosomal inheritance.**

- The term pseudoautosomal refers to the idea that the inheritance pattern of the *Mic2* gene is the same as the inheritance pattern of a gene located on an autosome even though the *Mic2* gene is actually located on the sex chromosomes. As in autosomal inheritance, males have two copies of pseudoautosomally inherited genes, and they can transmit the genes to both daughters and sons.

- The brackets show three regions of homology between the X and Y chromosome. A few pseudoautosomal genes, such as Mic2, are found on both the X and Y chromosomes in these small regions of homology.



Reference

- Color Atlas of Genetics 2nd edition Eberhard Passarge @2001.

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