# Genetic

## Mendel's law

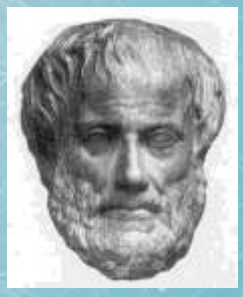
Patterns of Inheritance

- Mendel's Laws
- Variations on Mendel's Laws
- The Chromosomal Basis of Inheritance
- Sex Chromosomes and Sex-linked Genes

## The Field of Genetics has Ancient Roots

- Hippocrates (father of medicine): particles from every part of the body travel to eggs and sperm to be passed on
- Aristotle (philosopher): 'potential' rather than particles to produce body features
- 19th century biologists: blending- mom and dad's traits blend like blue and yellow paint

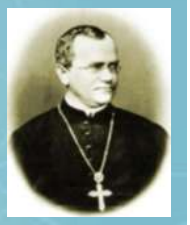
Hippocrates



Aristotle

## Experimental Genetics Began in an Abbey Garden

- Modern genetics began in 1860s
- Gregor Mendel (monk in what was then Austria- now Czech Republic)
- Parents pass on discrete, heritable factors (1866)
- Heritable factors retain their individuality for generations (no blending)
- Studied garden peas

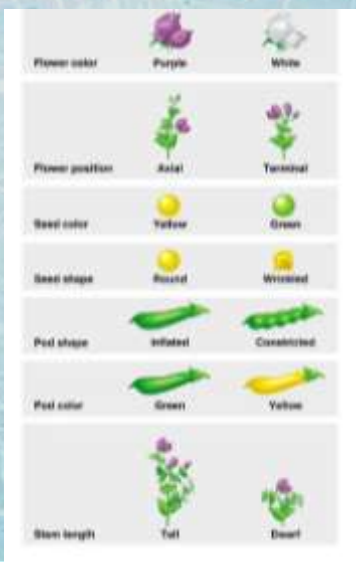


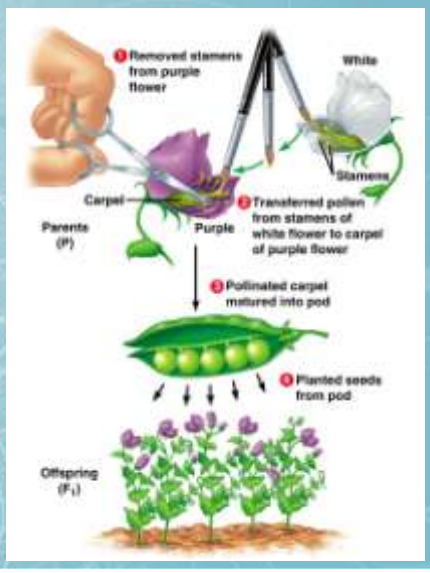
## Experimental Genetics Began in an Abbey Garden

- In a typical breeding experiment
  - Mendel mated two different, true-breeding varieties, a process called hybridization
- The true-breeding parents
  - Are called the P generation
- Cross: pollinating a flower of one variety with the pollen of another variety
- The hybrid offspring of the P generation
  - Are called the $F_1$ generation
  - F2 generation comes next

Mendel chose to work with peas:

- Because they are available in many varieties
- Because he could strictly control which plants mated with which
- Because he could easily start his experiments with varieties that were "true-breeding"



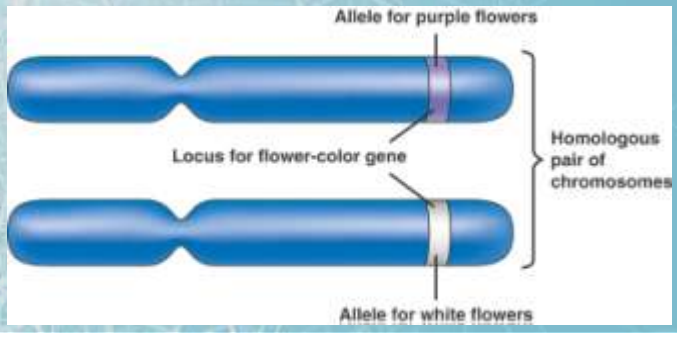
Some genetic vocabulary

Character: a heritable feature, such as flower color

Trait: a variant of a character, such as purple or white flowers

Gene: a discrete unit of hereditary information consisting of a specific DNA (nucleotide) sequence on a chromosome

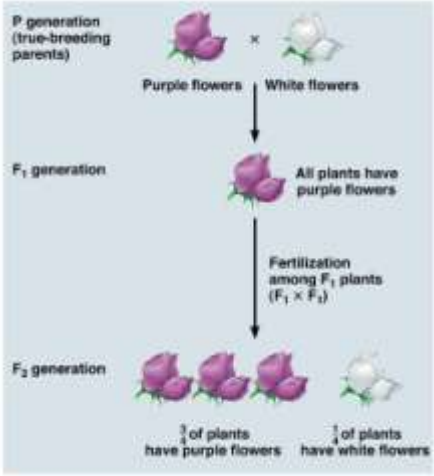
Allele: alternative version of a gene




Mendel's Law of Segregation Describes the Inheritance of a Single Characteristic

**Performed monohybrid crosses (only 1 trait differs between the varieties)**

- When Mendel crossed contrasting, true-breeding white and purple flowered pea plants
  - » *All of the offspring were purple!!!*




When Mendel crossed the F1 plants –

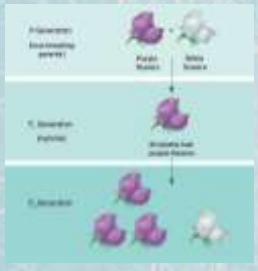
Many of the plants had purple flowers, but some had white flowers

Mendel discovered:

A ratio of about three to one (3:1) purple to white flowers, in the F2 generation

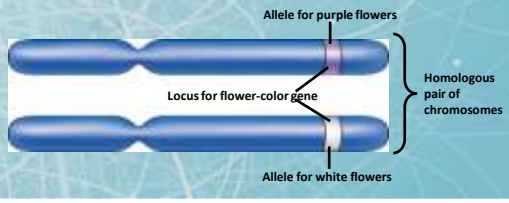
## Mendel's Law of Segregation Describes the Inheritance of a Single Characteristic

Mendel developed a hypothesis to explain the 3:1 inheritance pattern that he observed among the $F_2$ offspring



Four Parts:

1. First, alternative versions of genes account for variations in inherited characters which are now called alleles




## *Mendel's Model for Inheritance*

Four Parts:

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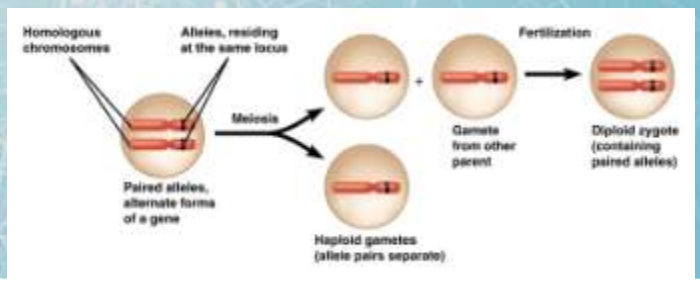
2. Second, for each character an organism inherits two alleles, one from each parent.
   *These alleles may be the same or different!*

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Four Parts:

1. First, alternative versions of genes account for variations in inherited characters which are now called alleles

2. Second, for each character an organism inherits two alleles, one from each parent.
*These alleles may be the same or different!*


3. Third, if the two alleles at a locus differ then one, the dominant allele, determines the organism's appearance.
*The other allele, the recessive allele, has no noticeable effect on the organism's appearance*

4. Fourth, A sperm or egg carries only one allele for each inherited trait because allele pairs separate (segregate) from each other during the production of gametes

Does Mendel's segregation model account for the 3:1 ratio he observed in the $F_2$ generation of his numerous crosses?

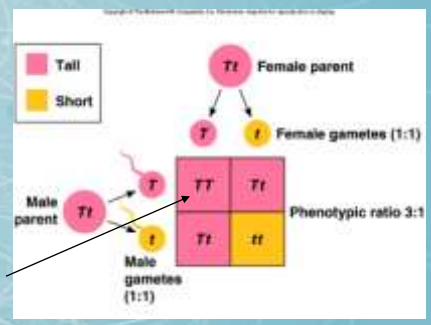
We can answer this question using a Punnett square

# The Punnet Square

- A very convenient tool used in genetics.
- Steps:
  - 1. Determine the parents gametes.
    - This may be the most important step.
  - 2. Match the gametes, and form possible offspring.
  - 3. Determine the chances of each type of offspring.

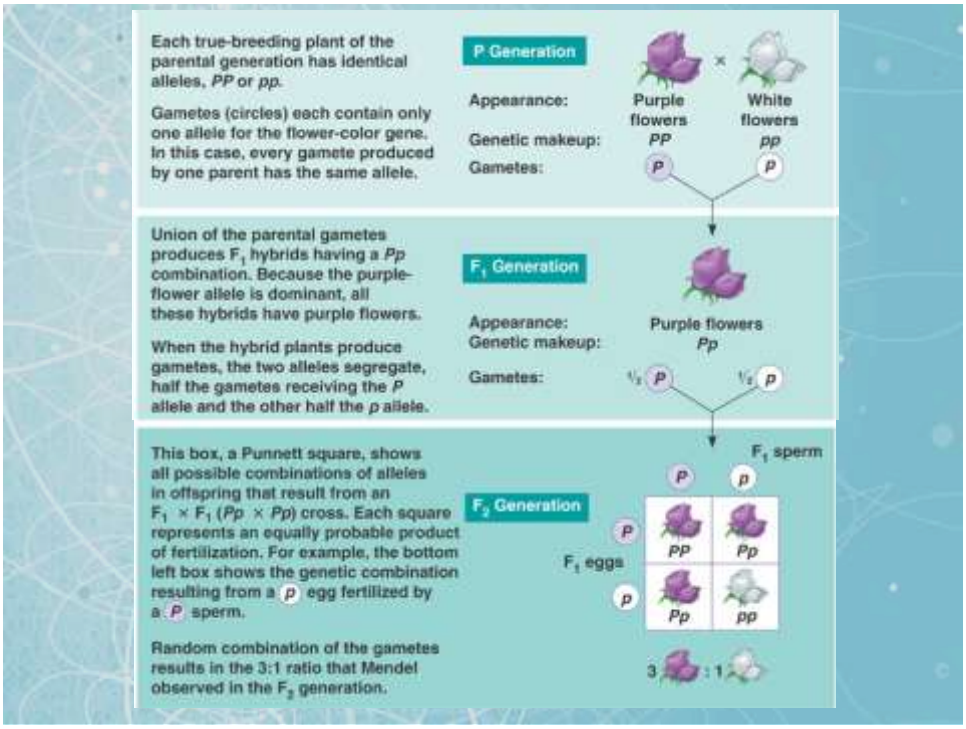
# A basic Punnet square:

- Notice that the mother and father are both heterozygous.
- If the dominant sperm fertilizes the dominant egg, then the offspring would be TT.
  - There is a 25% chance of this occurring.
  - 1 out of 4 will be this.



## Scientists use a “test cross” if they don’t know what the genotype of an individual is.

- What is the:
  - Phenotype of a purple pea plant?
  - Phenotype of a white pea plant?
  - Genotype of a white pea plant?
  - Genotype of a purple pea plant?
- How can you find out the unknown genotype of an individual?
- You would want to breed a “known” genotype against your “unknown.”
  - The offspring will tell you what the “unknown” is.



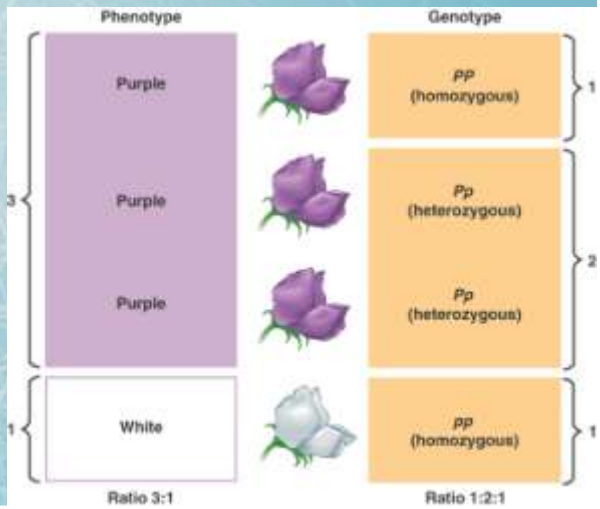
## Not Just Flower Color!

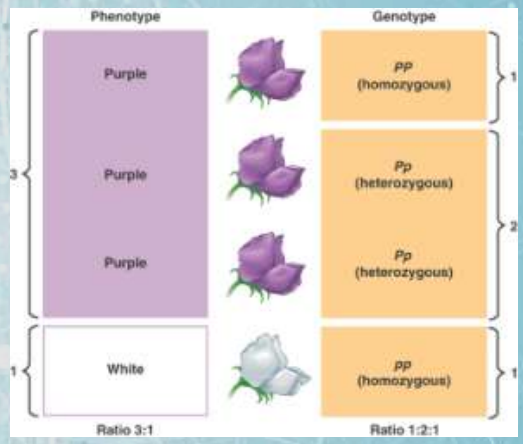
**Table 14.1 The Results of Mendel's $F_1$ Crosses for Seven Characters in Pea Plants**

| Character | Dominant Trait | × | Recessive Trait | $F_2$ Generation Dominant:Recessive | Ratio |
|---|---|---|---|---|---|
| Flower color | Purple | × | White | 705:224 | 3.15:1 |
| Flower position | Axial | × | Terminal | 651:207 | 3.14:1 |
| Seed color | Yellow | × | Green | 6022:2001 | 3.01:1 |
| Seed shape | Round | × | Wrinkled | 5474:1850 | 2.96:1 |
| Pod shape | Inflated | × | Constricted | 882:299 | 2.95:1 |
| Pod color | Green | × | Yellow | 428:152 | 2.82:1 |
| Stem length | Tall | × | Dwarf | 787:277 | 2.84:1 |

## Vocabulary – Enough Already!

- Punnett square: used to determine genotypic and phenotypic frequencies
- Phenotype: an organism's expressed traits (outward appearance)
- Genotype: an organism's genetic makeup (gene combinations)




An organism that is homozygous for a particular gene:

- Has a pair of identical alleles for that gene
- Exhibits true-breeding

An organism that is heterozygous for a particular gene:

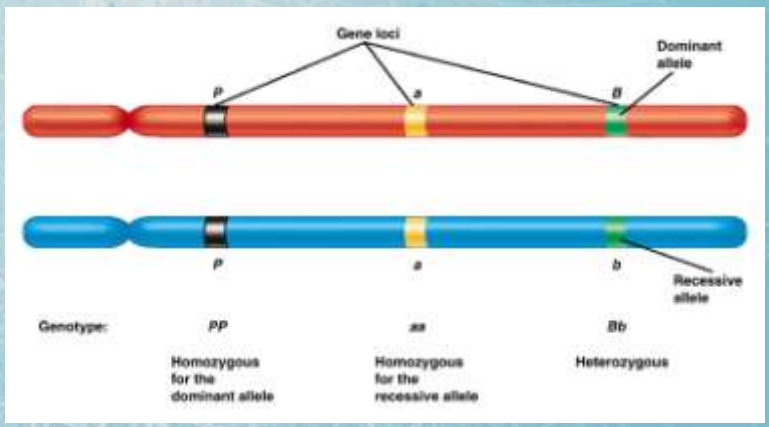
- Has a pair of alleles that are different for that gene

## Homologous Chromosomes Bear the Two Alleles for Each Characteristic

Remember:

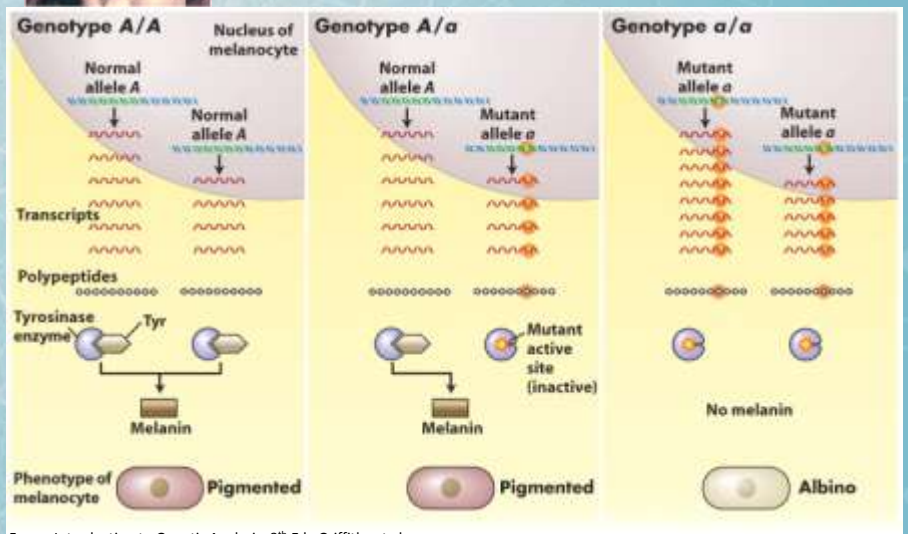
Alleles (alternative forms) of a gene reside at the same locus on homologous chromosomes

- Homozygous: both alleles match (either dominant or recessive)
- Heterozygous: one allele is dominant, one is recessive



Albinism

Failure to synthesize the pigment melanin




From: Introduction to Genetic Analysis, 8th Ed. Griffiths et al.

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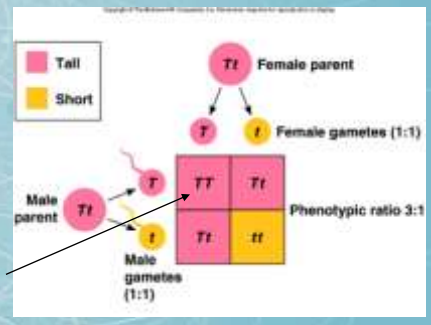


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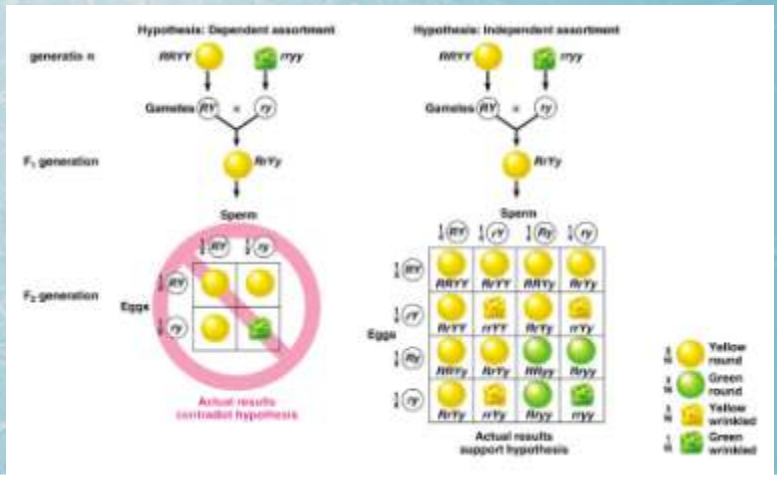
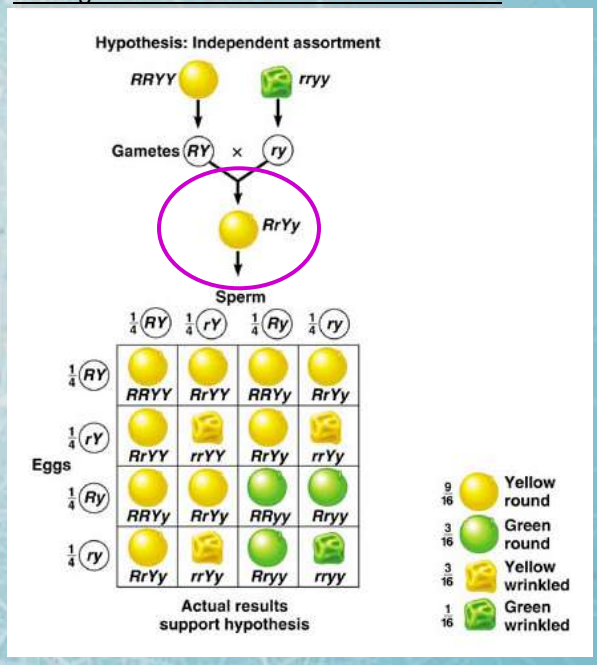
## Independent Assortment is Revealed by Tracking Two Characteristics at Once

- Dihybrid cross: cross individuals differing in two characteristics
- Mendel crossed peas with round, yellow seeds (dominant traits) and peas with wrinkled, green seeds (recessive traits)
- Determined that traits were passed independent of each other (got yellow, wrinkled offspring, for example)
- Law of independent assortment: each pair of alleles segregates independently of the other pairs of alleles during gamete formation




## Putting Mendel's Laws on the Chromosomes!



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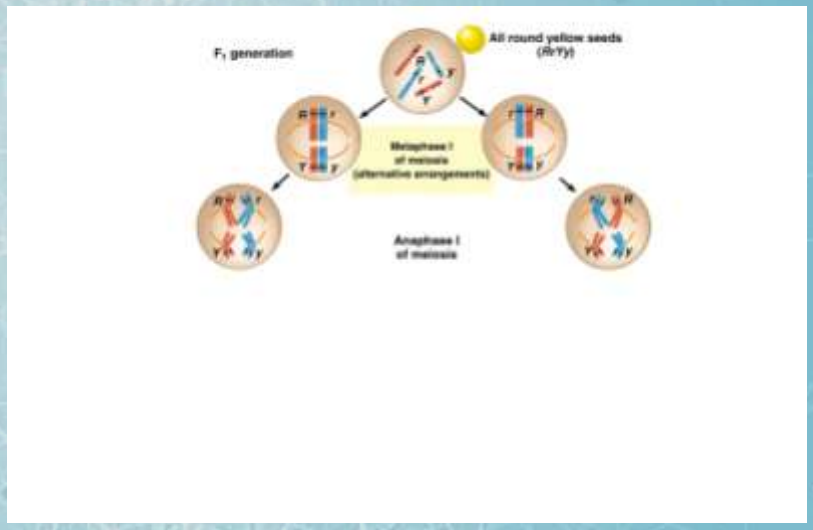


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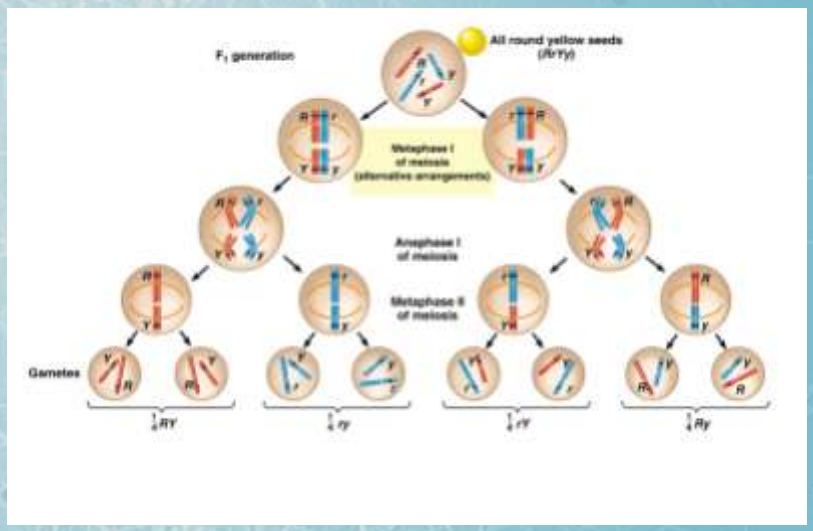

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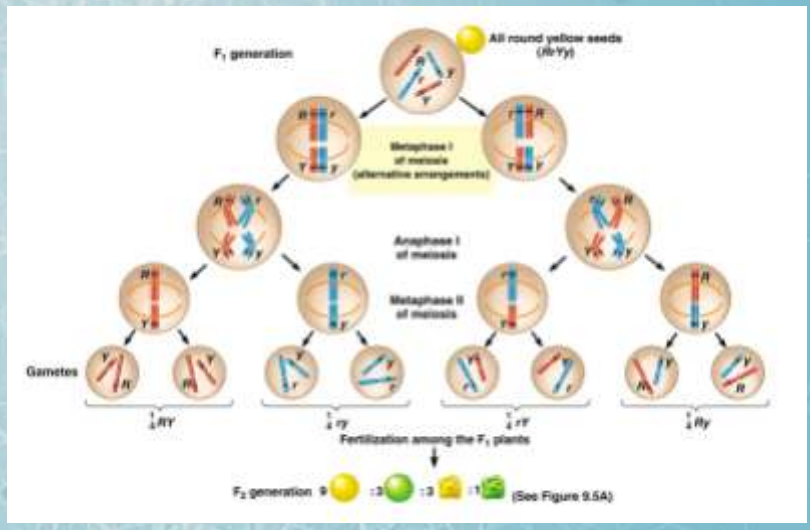


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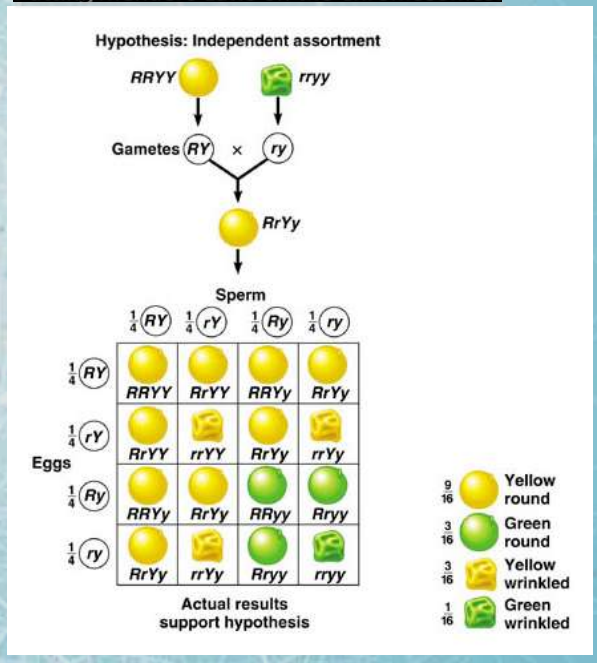

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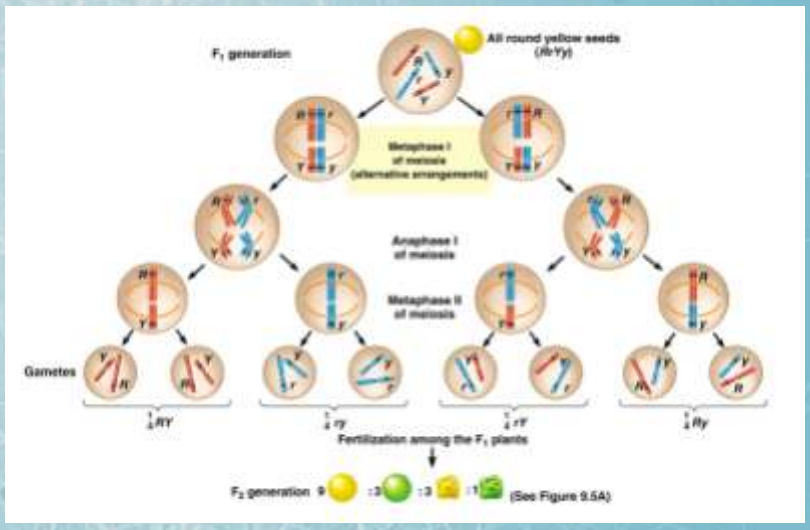
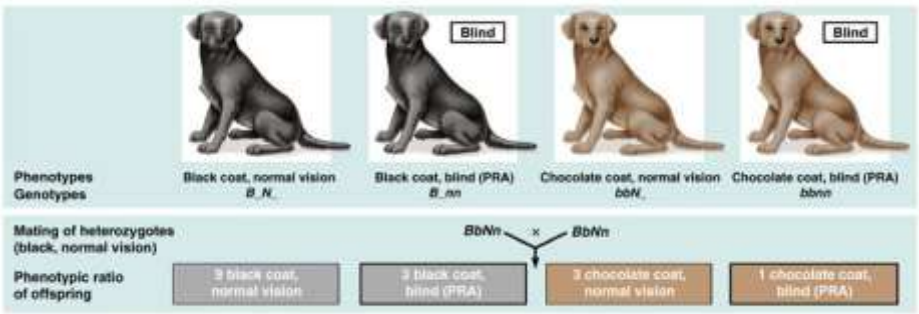



## Independent Assortment of Two Genes in the Labrador Retriever

- Coat color and 'normal' vision controlled by separate genes
- Blanks in the figure can represent either dominate **or** recessive alleles
- Yellow labs have coat color controlled by different gene altogether!

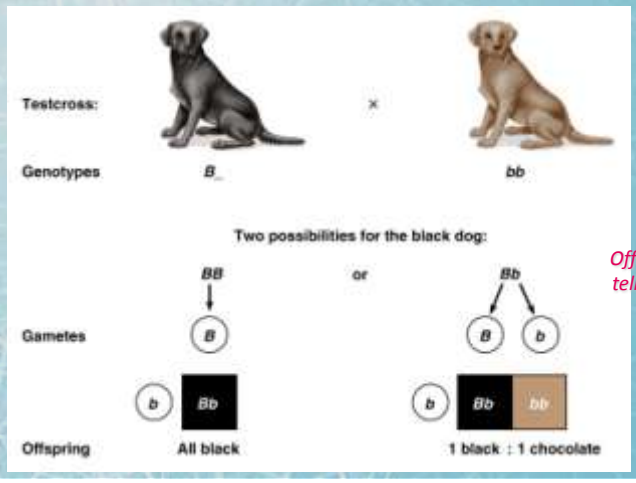



PRA = Progressive Retinal Atrophy

## Geneticists Use The Testcross to Determine Unknown Genotypes

In many cases, the genotype is not immediately obvious

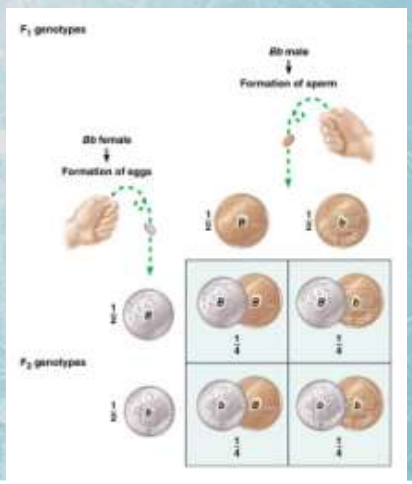
- A testcross allows one to determine the genotype of an organism with the dominant phenotype but unknown genotype
- Crosses an individual with the dominant phenotype with an individual that is homozygous recessive for a trait

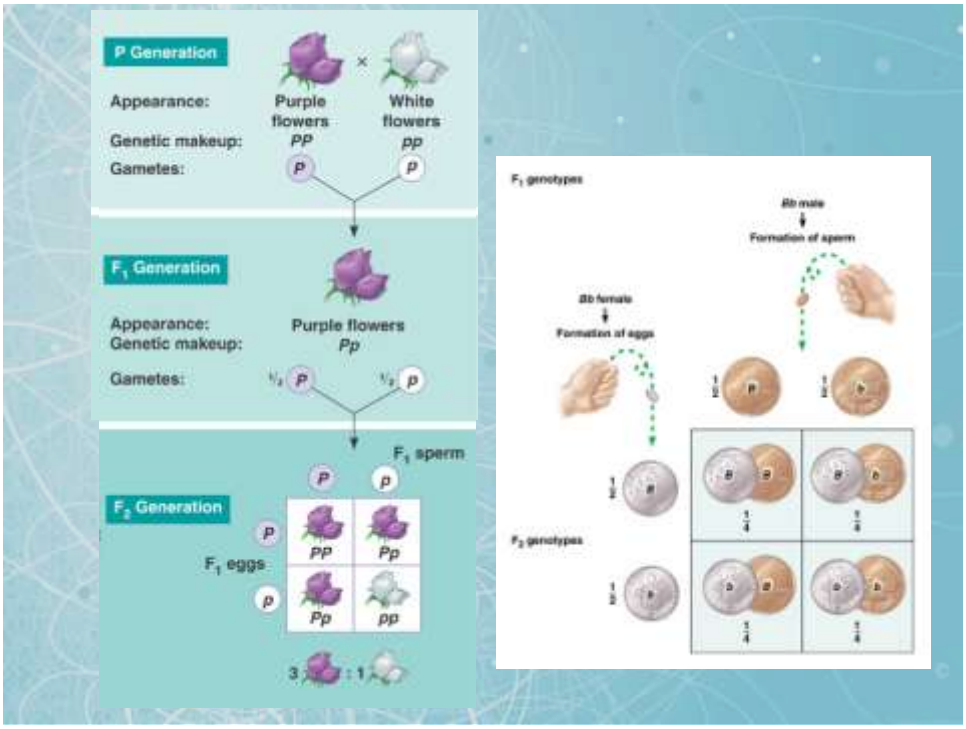



*Offspring phenotypes tell you the unknown genotype*

## Mendel's Laws Reflect the Rules of Probability

- Probability scale: 0 → 1
- Event certain to take place: 1; event certain NOT to take place: 0
- Probabilities of all outcomes must add to 1
- Rule of multiplication: multiply probability of two independent events happening (flipping a coin twice, for example)





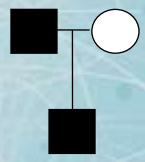

## Mendel's Laws Reflect the Rules of Probability

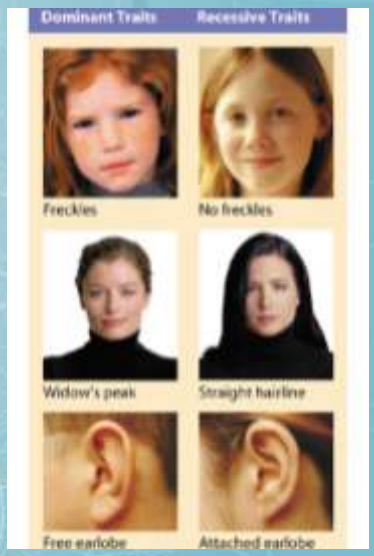
- What about genetics?
- Trihybrid cross: what's the probability of getting homozygous recessive at all 3 locations (AaBbCc x AaBbCc)?
  - Probability aa: ¼
  - Probability bb: ¼
  - Probability cc: ¼

**Probability aabbcc: ¼ x ¼ x ¼ = 1/64**

## Genetics Traits in Humans Can be Tracked Through Family Pedigrees

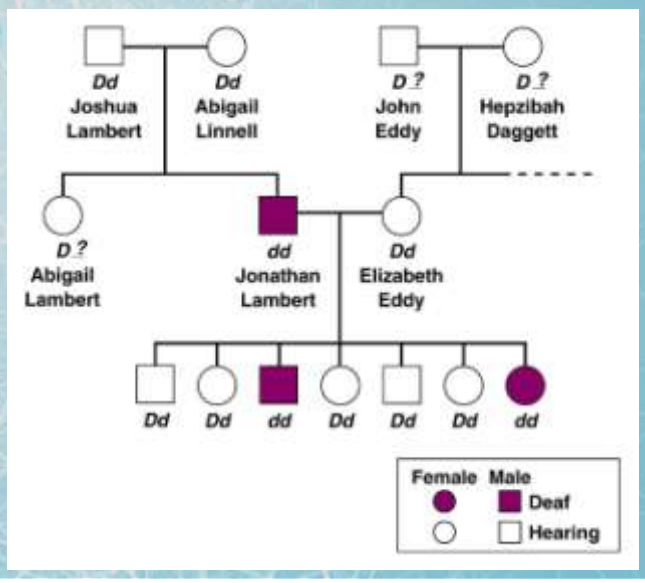
- Many traits simple Mendelian traits:
  - Freckles
  - Widow's peak
  - Free earlobes
- Pedigree: family tree
- Square: male, circle: female



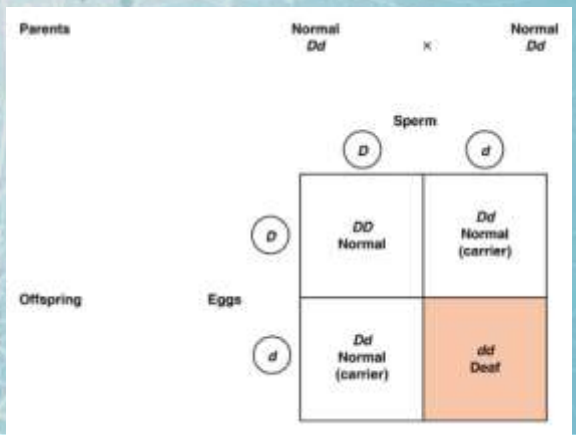

## Genetics Traits in Humans Can be Tracked Through Family Pedigrees

Pedigree showing the inheritance of deafness in a family from Martha's Vineyard



## Many Inherited Disorders in Humans are Controlled by a Single Gene

- Recessive disorders:
  - Most human genetic disorders
  - Most common lethal disorder: cystic fibrosis (most common among Caucasians)
  - Rate of disorders increases with inbreeding
- Dominant disorders:
  - Most are non-lethal (dwarfism, webbed fingers and toes, extra fingers and toes)
  - Lethal examples: Huntington's Diesase

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  - Lethal examples: Huntington's Diesase

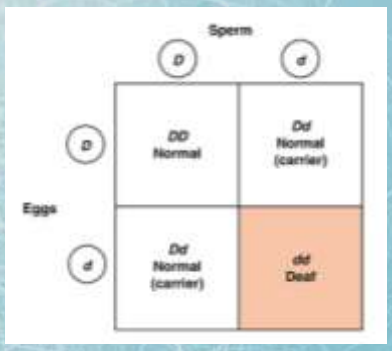
**TABLE 9.9 SOME AUTOSOMAL DISORDERS IN HUMANS**

| Disorder | Major Symptoms | Incidence | Comments |
|---|---|---|---|
| **Recessive disorders** | | | |
| Albinism | Lack of pigment in skin, hair, and eyes | 1/17,000 | Prone to skin cancer |
| Cystic fibrosis | Excess mucus in lungs, digestive tract, liver; increased susceptibility to infections; death in early childhood unless treated | 1/2,500 Caucasians | See Modules 9.9 and 12.11 |
| Galactosemia | Accumulation of galactose in tissues; mental retardation; eye and liver damage | 1/60,000 | Treated by eliminating galactose from diet |
| Phenylketonuria (PKU) | Accumulation of phenylalanine in blood; lack of normal skin pigment; mental retardation | 1/10,000 in U.S. and Europe | See Module 9.10 |
| Sickle-cell disease (homozygous) | Sickled red blood cells; damage to many tissues | 1/400 African Americans | Alleles are codominant; see Modules 9.13 and 9.14 |
| Tay-Sachs disease | Lipid accumulation in brain cells; mental deficiency; blindness; death in childhood | 1/3,600 Jews from central Europe | See Module 4.11 |
| **Dominant disorders** | | | |
| Achondroplasia | Dwarfism | 1/15,000 | See Module 9.9 |
| Alzheimer's disease (one type) | Mental deterioration, usually strikes late in life | Rare | |
| Huntington's disease | Mental deterioration and uncontrollable movements; strikes in middle age | 1/10,000 | See Modules 9.9 and 12.11 |
| Hypercholesterolemia | Excess cholesterol in blood; heart disease | 1/500 are heterozygous | Incomplete dominance; see Module 9.12 |

## Concept Check

A man and a woman who are both carriers of the Martha's Vineyard deafness allele have had three children who are not deaf. If the couple has a fourth child, what is the probability that the child will be deaf?

1/4



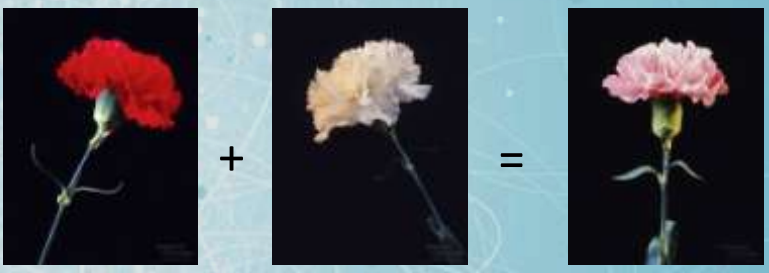

## Variations on Mendel's Laws – i.e. Complications, Complications!

(Non-Mendelian Genetics)

1. Incomplete Dominance
2. Multiple Alleles for a single gene
3. Pleiotropy – *some genes have multiple phenotypic characteristics*
4. Polygenic Inheritance – *additive effects of 2 or more genes*

## Incomplete Dominance in Snapdragons and Carnations

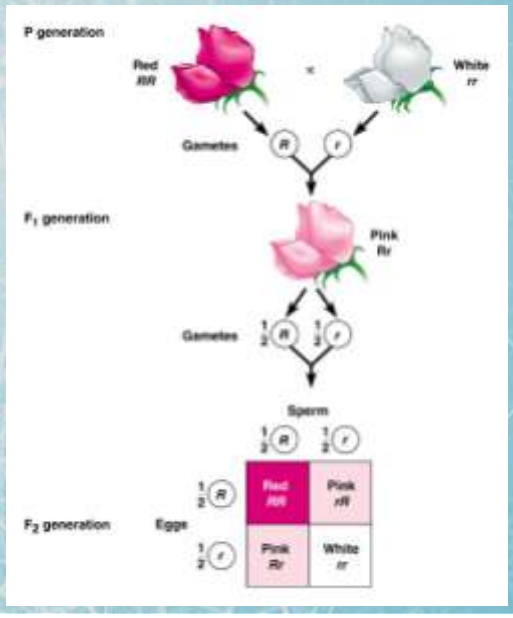
Or, what if Mendel had studied snapdragons?!



Incomplete dominance results in intermediate phenotypes

- Complete dominance: dominant allele always expressed, recessive allele expressed in homozygous condition
- Incomplete dominance: heterozygote is intermediate to dominant and recessive alleles
- Classic example: snapdragons/carnations

## Incomplete Dominance in Snapdragons and Carnations



Nobel Prize (1985)
Physiology or Medicine

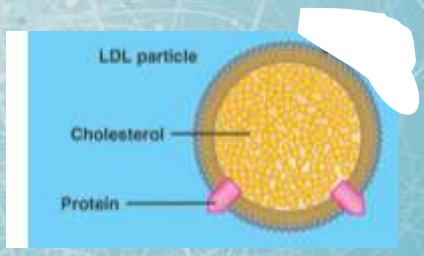
Michael Brown

Cholesterol uptake lead to the discovery of Receptor Mediated Endocytosis

Joseph Goldstein

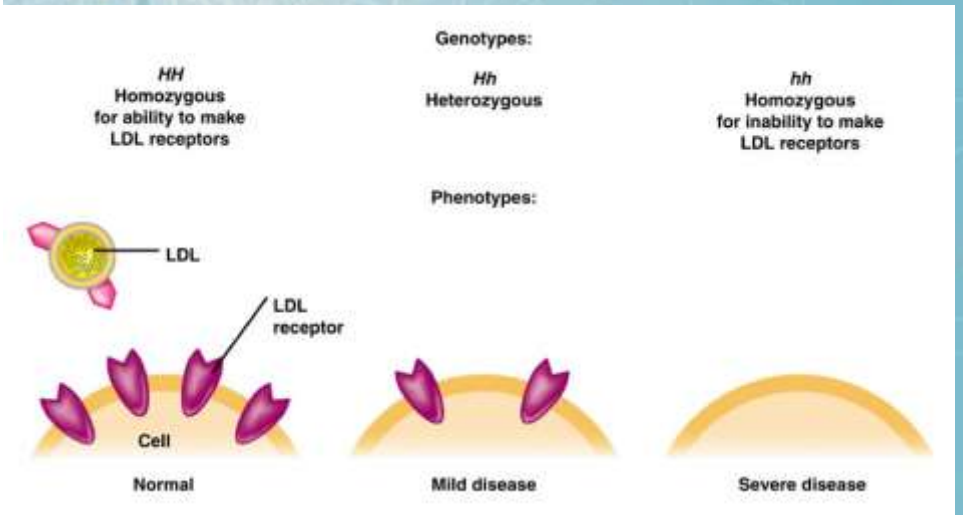
Famial Hypercholesterolemia: Genetic Disorder

| | Death |
|---|---|
| homozygotes | ~ 10 to teens |
| heterozygotes | < 50 |




**Exceptions to Mendel's Laws - Incomplete Dominance**

Familial Hypercholesterolemia



## Variations on Mendel's Laws – i.e. Complications, Complications!

(Non-Mendelian Genetics)

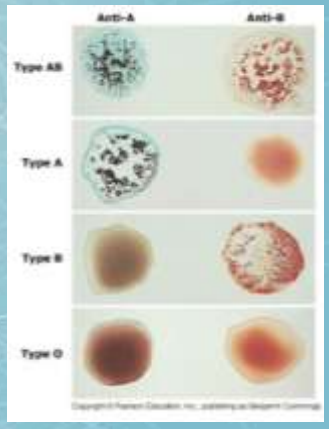
1. Incomplete Dominance
2. Multiple Alleles for a single gene
3. Pleiotropy – *some genes have multiple phenotypic characteristics*
4. Polygenic Inheritance – *additive effects of 2 or more genes*

## Many Genes Have More Than Two Alleles in the Population

- Why only two alleles? Many genes have more
- Example: blood types
- A and B dominant, O recessive

**Table 14.2 Determination of ABO Blood Group by Multiple Alleles**

| Genotype | Phenotype (Blood Group) | Red Blood Cells |
|---|---|---|
| $I^AI^A$ or $I^Ai$ | A | |
| $I^BI^B$ or $I^Bi$ | B | |
| $I^AI^B$ | AB | |
| $ii$ | O | |



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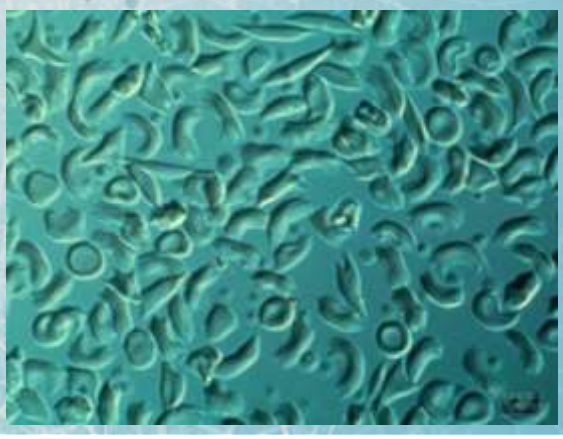
## A Single Gene May Affect Many Phenotypic Characteristics

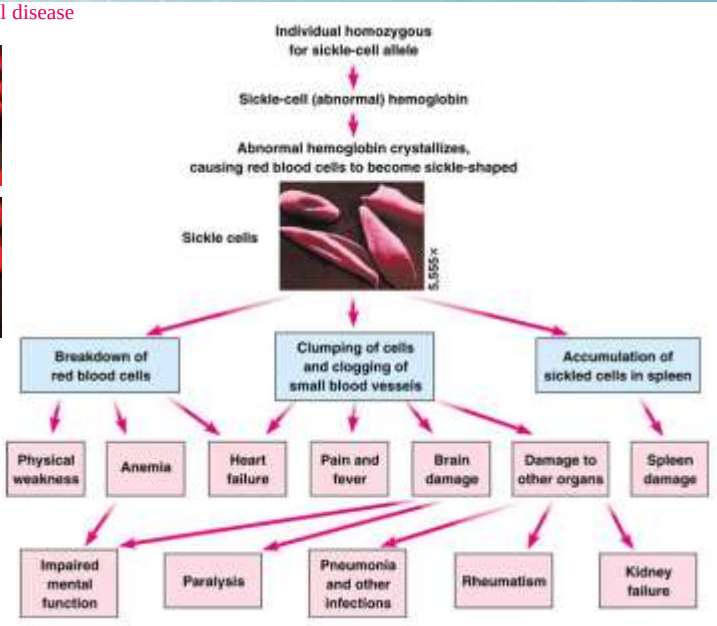
Pleiotropy: gene influences multiple characteristics

- Example: sickle-cell disease
- Causes red blood cells to become misshapen (sickle shaped) in low oxygen environments
- Heterozygote usually doesn't suffer much, but has resistance to malaria (homozygous recessive is sensitive to malaria)



## Pleiotropy: gene influences multiple characteristics

- Example: sickle-cell disease

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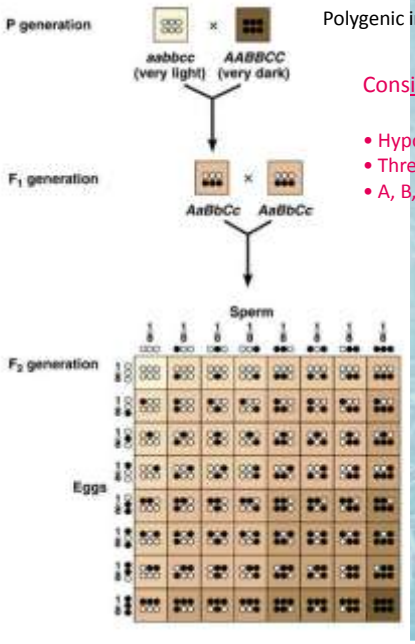
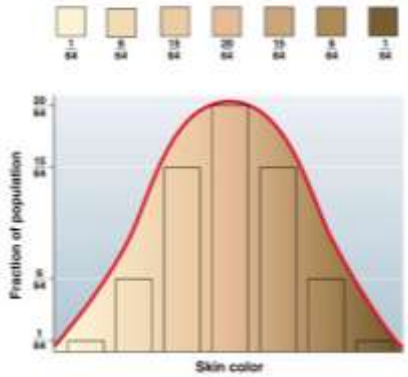
## Polygenic Inheritance of Skin Color




Polygenic inheritance: Two or more genes influence a single phenotype

Consider:

- Hypothetical example (at least three genes for skin color)
- Three (at least!) 'dark' skin alleles for each gene
- A, B, C incompletely dominant to a, b, c



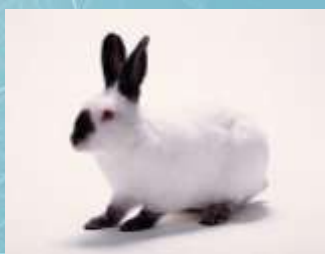

## Genes and the Environment

'Nature vs Nurture'

Soil pH

*Acid* *Neutral/Alkaline*

Temperature



## Genes and the Environment

'Nature vs Nurture'

- Many human phenotypes are influenced by both genes and environment:
  - Risk of heart disease
  - Risk of cancer
  - Susceptibility to alcoholism and schizophrenia
  - In addition to genes, sun affects skin color