

Genetics

Patterns of Inheritance

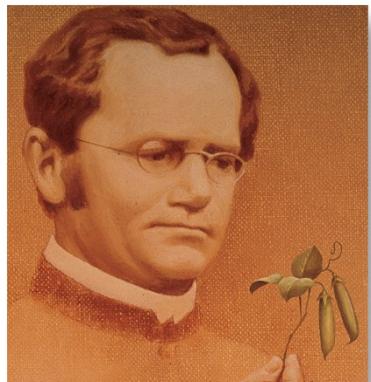
by

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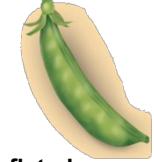
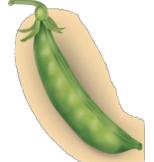
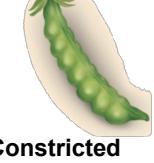
Mendel's Laws

- **Gregor Mendel**
 - Austrian monk
 - Worked with garden pea plants in 1860s
 - When he began his work, most acknowledged that both sexes contributed equally to a new individual.
 - Unable to account for presence of variations among members of a family over generations
 - Mendel's model compatible with evolution
 - Various combinations of traits are tested by the environment.
 - Combinations that lead to reproductive success are the ones that are passed on.

Figure 1 Mendel working in his garden.



a.

| | | Trait | | | | | | |
|-----------------|-----------|--|--|--|--|--|--|--|
| Characteristics | Dominant | Stem length | Pod shape | Seed shape | Seed color | Flower position | Flower color | Pod color |
| | Tall |  |  |  |  |  |  |  |
| | Recessive |  |  |  |  |  |  |  |

b.

(a): © Ned M. Seidler/National Geographic Image Collection

- Mendel's experimental procedure
 - Used garden pea, *Pisum sativa*
 - Easy to cultivate, short generation time
 - Normally self-pollinates but can be cross-pollinated by hand
 - Chose true-breeding varieties—offspring were like the parent plants and each other
 - Kept careful records of large number of experiments
 - His understanding of mathematical laws of probability helped interpret results.
 - Particulate theory of inheritance—based on the existence of minute particles (genes)

Figure 2a Garden pea anatomy and traits.

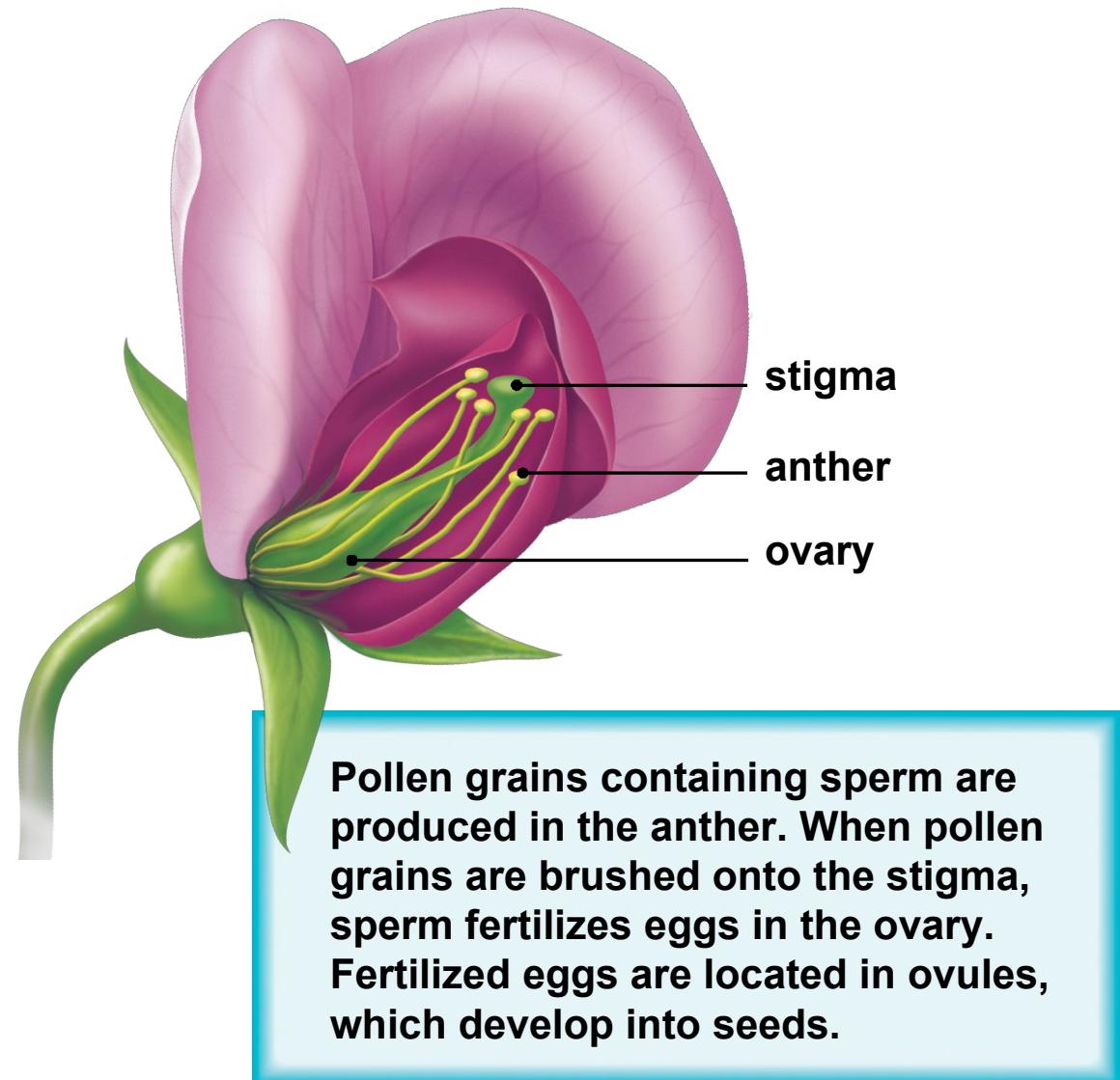


Figure 2b Garden pea anatomy and traits.

1 Cut away anthers.



2 Brush on pollen from another plant.



3 The results of cross from a parent that produces round, yellow seeds × parent that produces wrinkled yellow seeds.

Cross-pollination

• One-trait inheritance

- Original parents called P generation
 - First-generation offspring F₁ generation
 - Second-generation offspring F₂ generation
- Crossed green pod plants with yellow pod plants
 - All F₁ are green pods
 - Had yellow pods disappeared?

Figure 3 One-trait cross.

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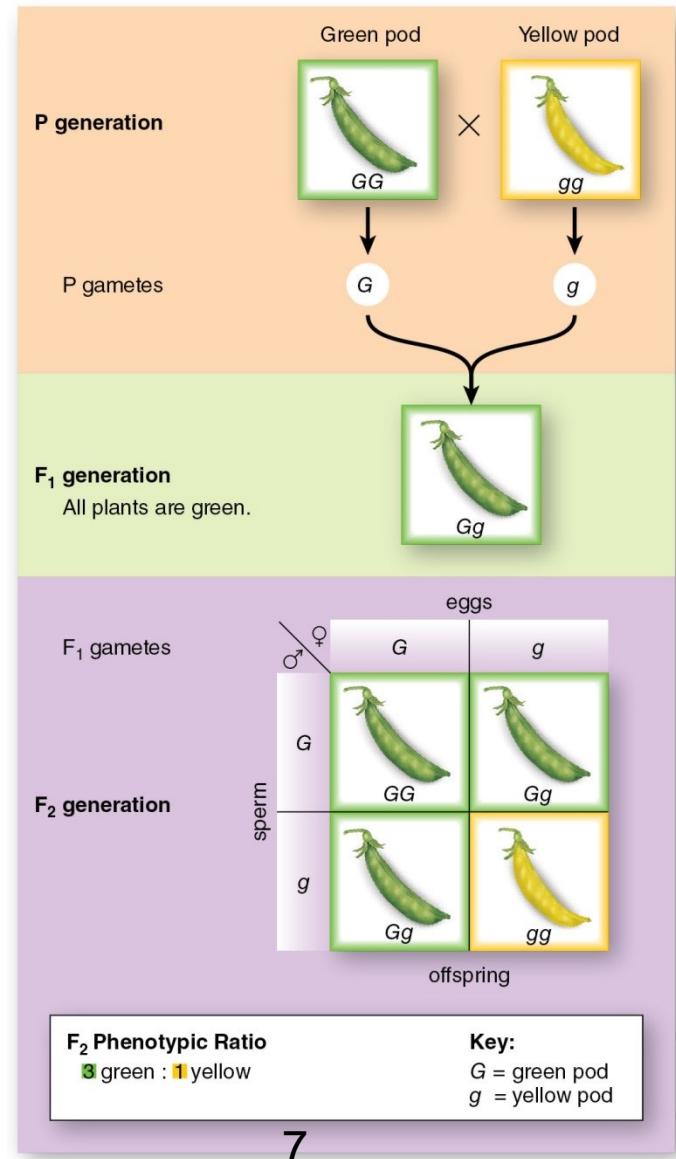
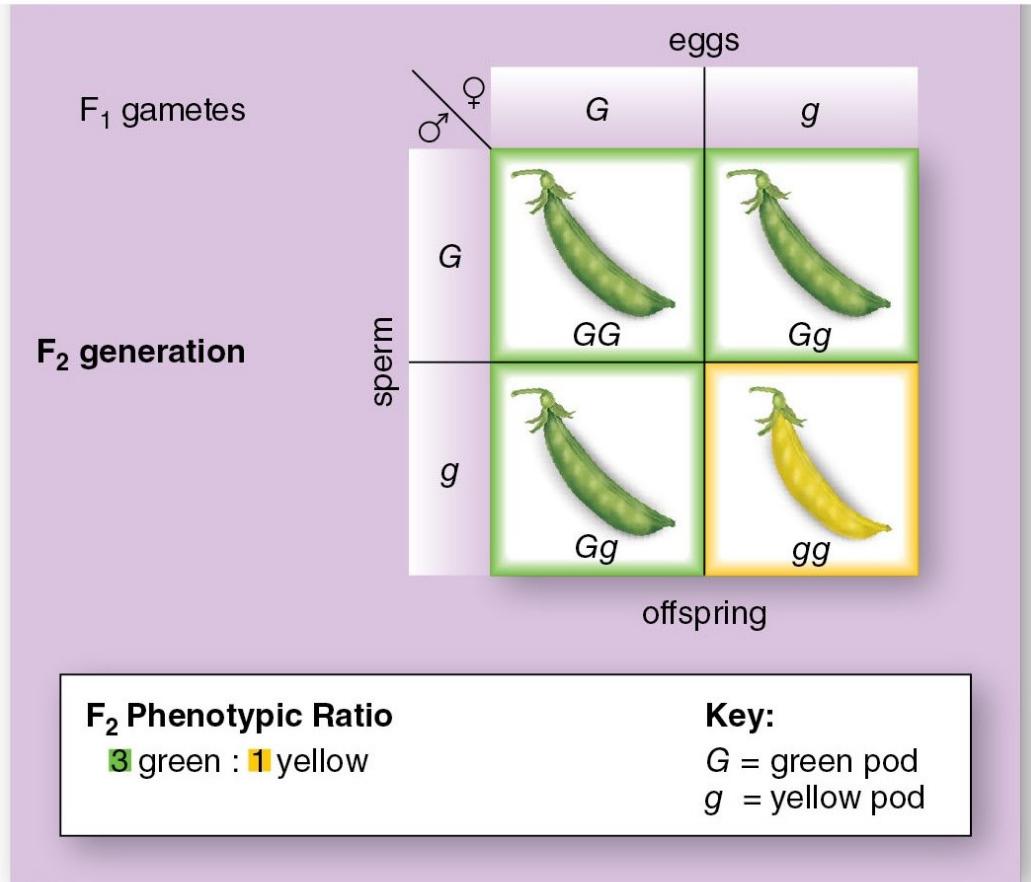


Figure 3 One-trait cross, continued.

- Punnett square
 - Shows all possible combinations of egg and sperm offspring may inherit
- When F_1 allowed to self-pollinate, F_2 were 3/4 green and 1/4 yellow
 - F_1 had passed on yellow pods

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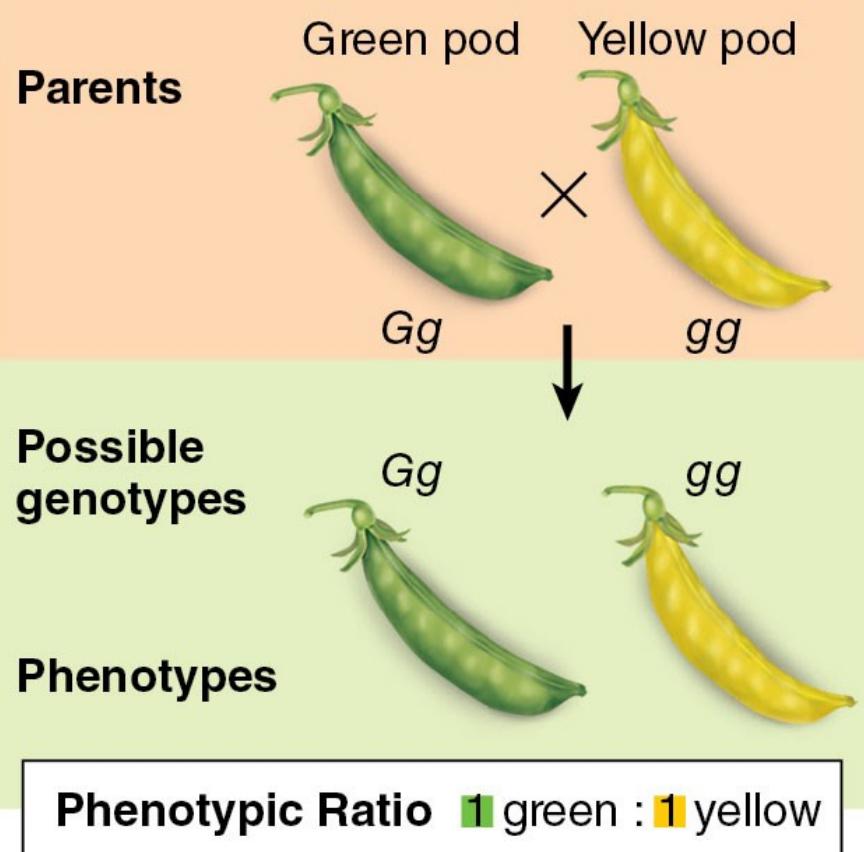
- Mendel reasoned 3:1 ratio only possible if
 - F_1 parents contained 2 separate copies of each heritable factor (1 dominant and 1 recessive)
 - Factors separated when gametes were formed, and each gamete carried only 1 copy of each factor
 - Random fusion of all possible gametes occurred at fertilization

- One-trait testcross
 - To see if the F_1 carries a recessive factor, Mendel crossed his F_1 generation green pod plants with true-breeding, yellow pod plants.
 - He reasoned that half the offspring would be green and half would be yellow.
 - His hypothesis that factors segregate when gametes are formed was supported.
 - Testcross
 - Used to determine whether or not an individual with the dominant trait has two dominant factors for a particular trait

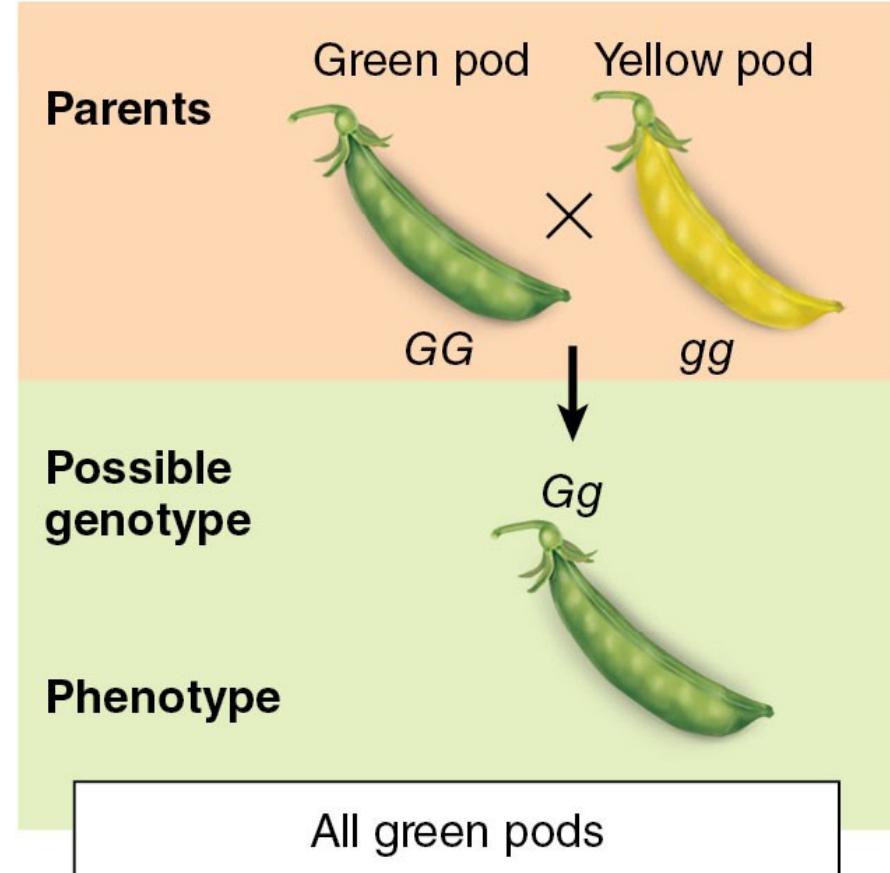
- One-trait testcross, continued
 - If a parent with the dominant phenotype has only one dominant factor, the results among the offspring are 1:1.
 - If a parent with the dominant phenotype has two dominant factors, all offspring have the dominant phenotype.

Figure 4 One-trait testcross.

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a.



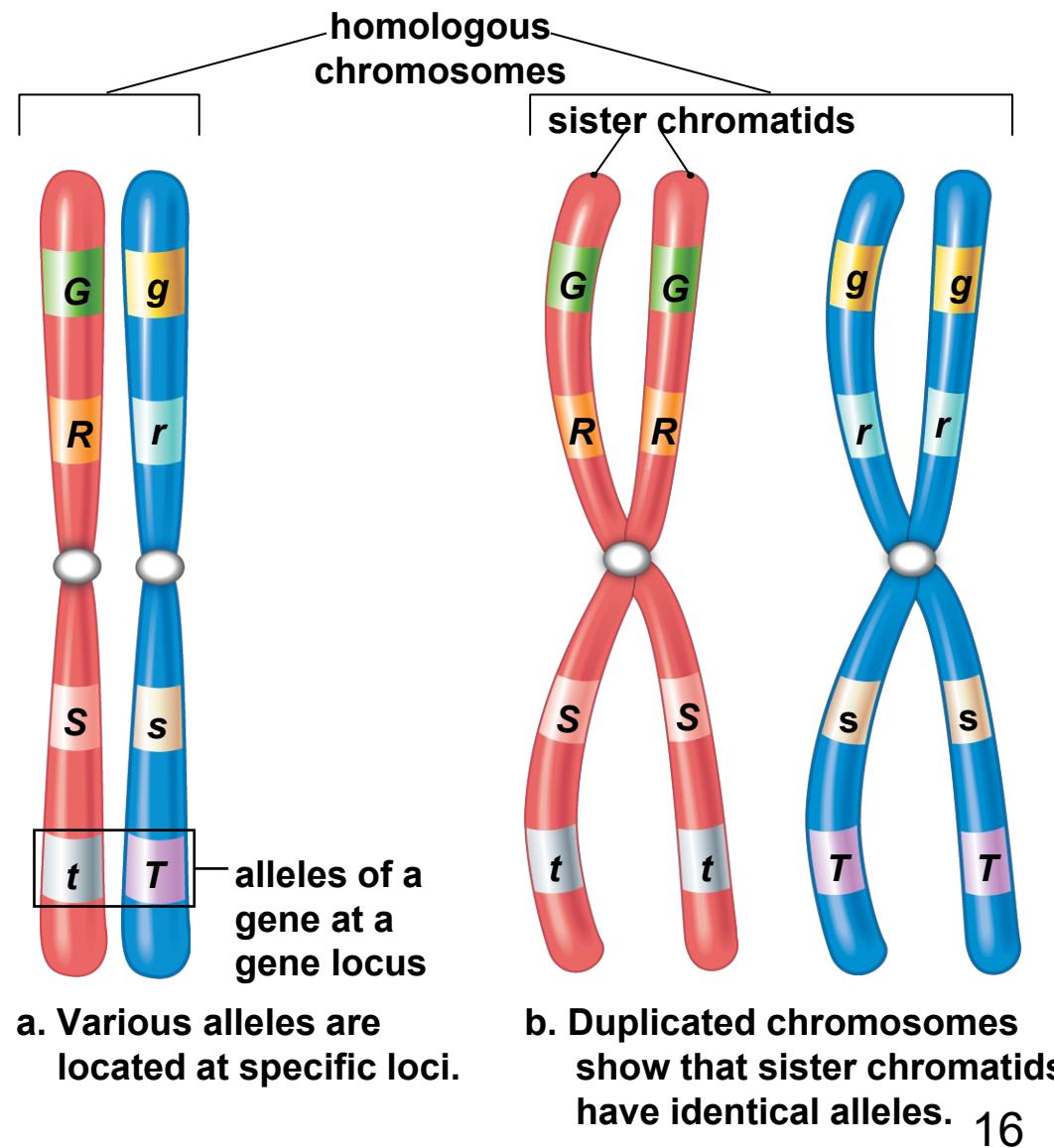
b.

- Mendel's first law of inheritance—law of segregation
 - Cornerstone of his particulate theory of inheritance
- The law of segregation states the following:
 - Each individual has two factors for each trait
 - The factors segregate (separate) during the formation of the gametes
 - Each gamete contains only one factor from each pair of factors
 - Fertilization gives each new individual two factors for each trait

- The modern genetics view
 - Scientists note parallel between Mendel's particulate factors and chromosomes
 - Chromosomal theory of inheritance
 - Chromosomes are carriers of genetic information
 - Traits are controlled by discrete genes that occur on homologous pairs of chromosomes at a gene locus.
 - Each homologue holds one copy of each gene pair.
 - Meiosis explains Mendel's law of segregation and why only one gene for each trait is in a gamete.
 - When fertilization occurs, the resulting offspring again have two genes for each trait, one from each parent.

- Alleles—alternative forms of a gene
- Dominant allele masks the expression of the recessive allele
- For the most part, an individual's traits are determined by the alleles inherited.
- Alleles occur on homologous chromosomes at a particular location called the gene locus.

Figure 5 Homologous chromosomes.



- Genotype versus phenotype
 - Genotype—alleles individual receives at fertilization
 - Homozygous—two identical alleles
 - Homozygous dominant
 - Homozygous recessive
 - Heterozygous—two different alleles
 - Phenotype—physical appearance of individual
 - Mostly determined by genotype

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Table 10.1 Genotype Versus Phenotype

| Genotype | Genotype | Phenotype |
|----------|----------------------|---------------------|
| EE | Homozygous dominant | Unattached earlobes |
| Ee | Heterozygous | Unattached earlobes |
| ee | Homozygous recessive | Attached earlobes |

- Two-trait inheritance
 - Mendel crossed tall plants with green pods ($TTGG$) with short plants with yellow pods ($ttgg$).
 - F_1 plants showed both dominant characteristics—tall and green pods.
 - 2 possible results for F_2
 - If the dominant factors always go into gametes together, F_2 will have only 2 phenotypes.
 - Tall plants with green pods
 - Short plants with yellow pods
 - If four factors segregate into gametes independently, 4 phenotypes would result.

Figure 6 Two-trait cross done by Mendel.

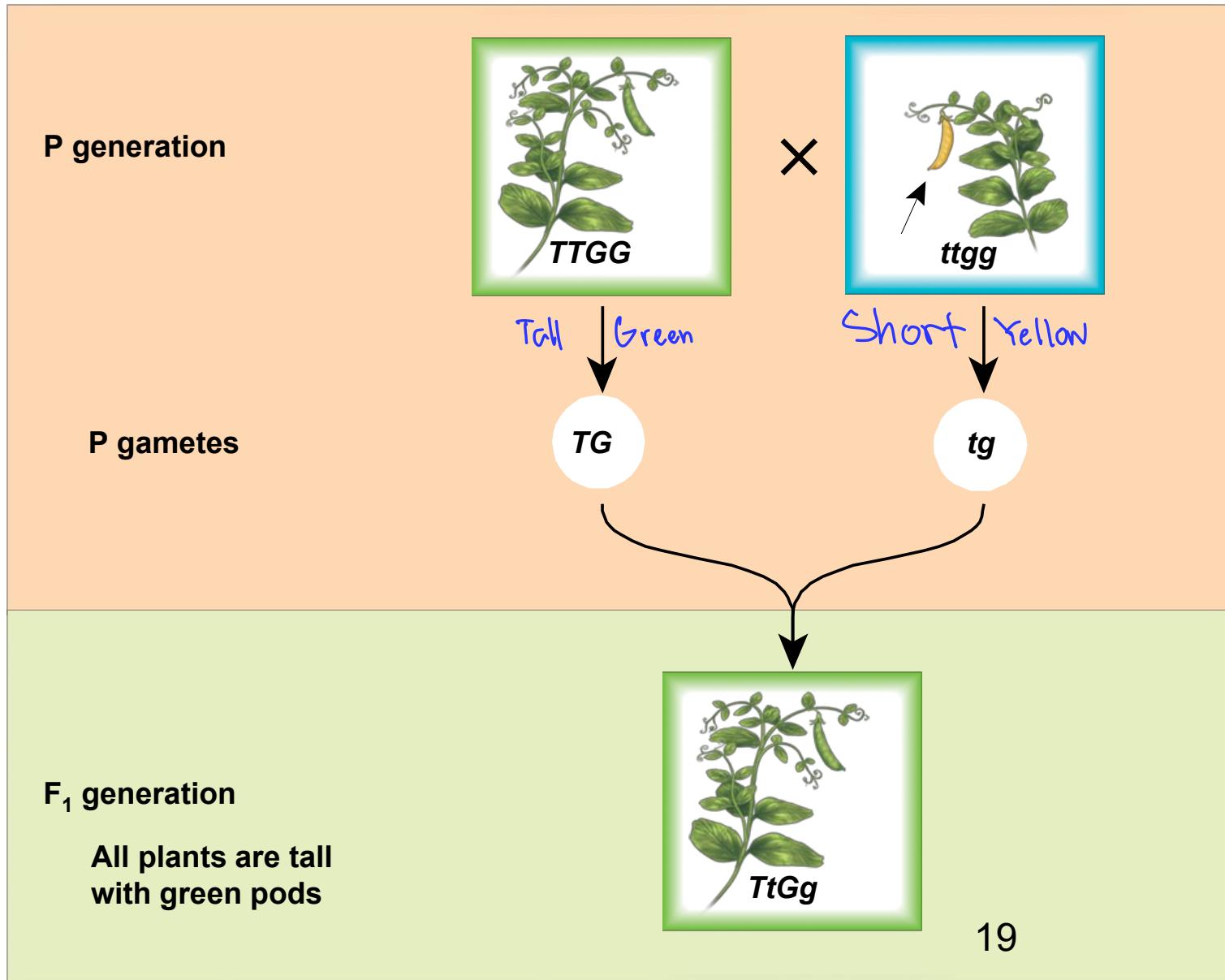
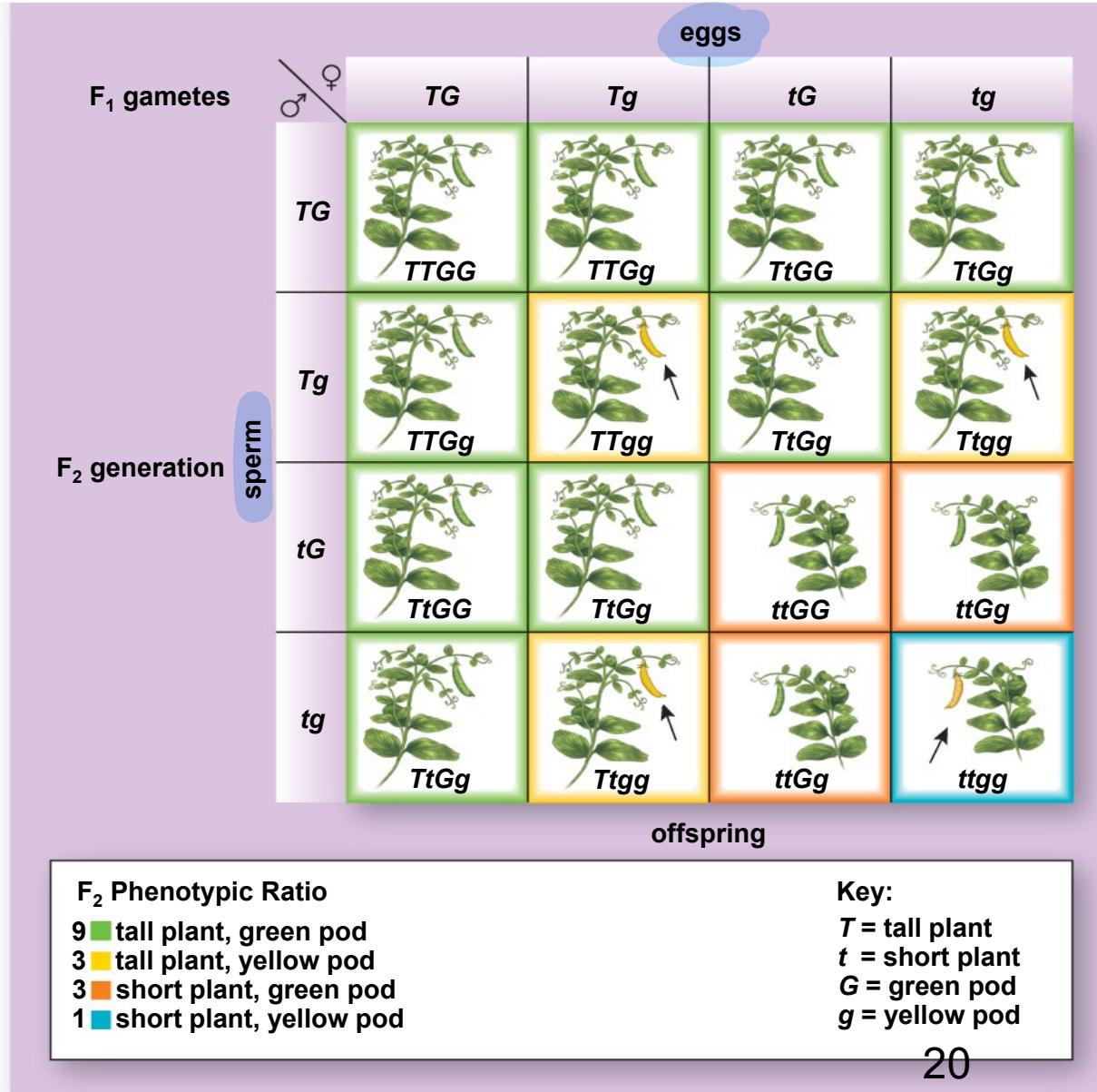


Figure 6 Two-trait cross done by Mendel, continued.

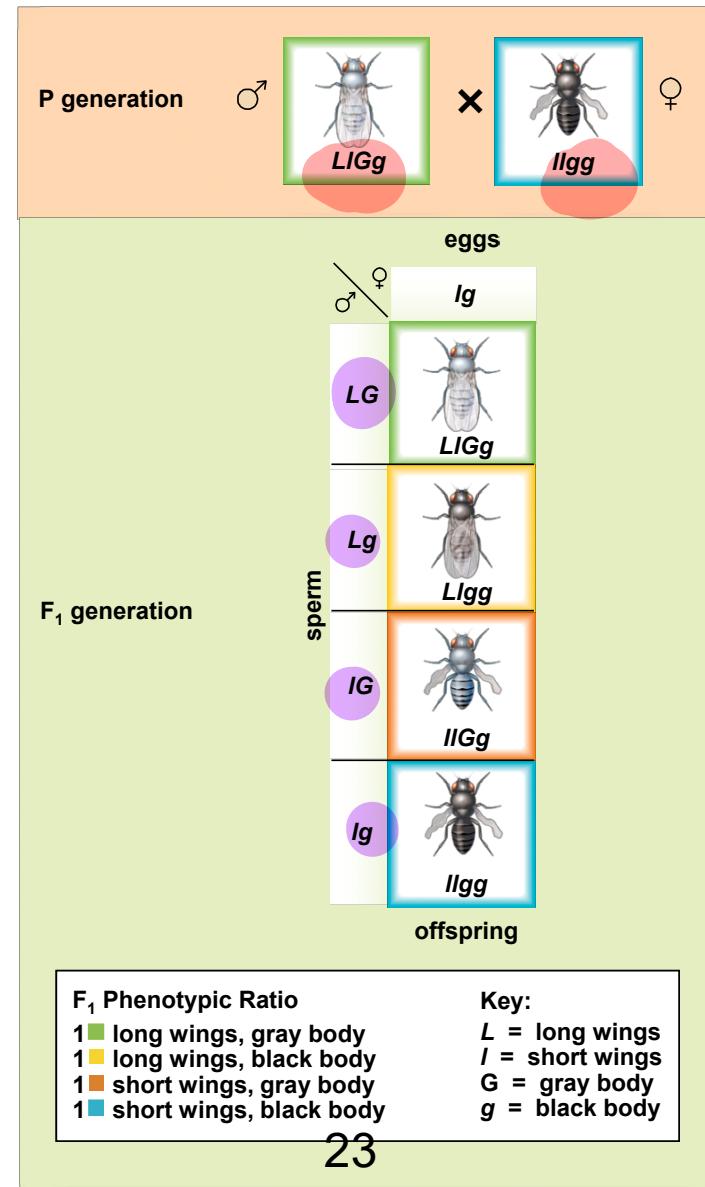


- Based on the results, Mendel formulated his second law of heredity.
- Law of independent assortment
 - Each pair of factors segregates (assorts) independently of the other pairs.
 - All possible combinations of factors can occur in the gametes.
- When all possible sperm have an opportunity to fertilize all possible eggs, the expected phenotypic results of a two-trait cross are always 9:3:3:1.

- Two-trait testcross *Mutation*
 - Fruit fly *Drosophila melanogaster*
 - Used in genetics research
 - Wild-type fly has long wings and gray body
 - Some mutants have vestigial wings and ebony bodies
 - $L = \text{long}$, $l = \text{short}$, $G = \text{gray}$, $g = \text{black}$
 - Can't determine genotype of long-winged gray-bodied fly ($L_\underline{G}_$) $\text{o}=\check{\text{k}}\check{\text{r}}\check{\text{t}}\check{\text{o}}$
 - Cross with short-winged black-bodied fly ($llgg$)

Figure 7 Two-trait testcross.

- In this example, 1:1:1:1 ratio of offspring indicates $L_\underline{G}_$ fly was $LIGg$ (dihybrid).



- Mendel's laws and probability
 - Punnet square assumes
 - Each gamete contains one allele for each trait
 - Law of segregation
 - Collectively the gametes have all possible combinations of alleles
 - Law of independent assortment
 - Male and female gametes combine at random
 - Use rules of probability to calculate expected phenotype ratios
 - Rule of multiplication—chance of two (or more) independent events occurring together is the product of their chances of occurring separately
 - Coin flips—odd of getting tails is $\frac{1}{2}$, odds of getting tails when you flip 2 coins $\frac{1}{2} \times \frac{1}{2} = \frac{1}{4}$

- Mendel's laws and meiosis - မြန်စာတော်မြန်

- ព្រោះទាំង នៅវាតាម កម្ពស់សប្តាហាត់
Dominant

- Gene for earlobes and hairline on different chromosomes
 - Gametes have all possible combinations of alleles

Figure 8 Mendel's laws and meiosis.

សំណើជាតិ

sperm
egg **Recessive**



Unattached earlobes: EE or Ee



Attached earlobes: ee



Widow's peak: WW or Ww

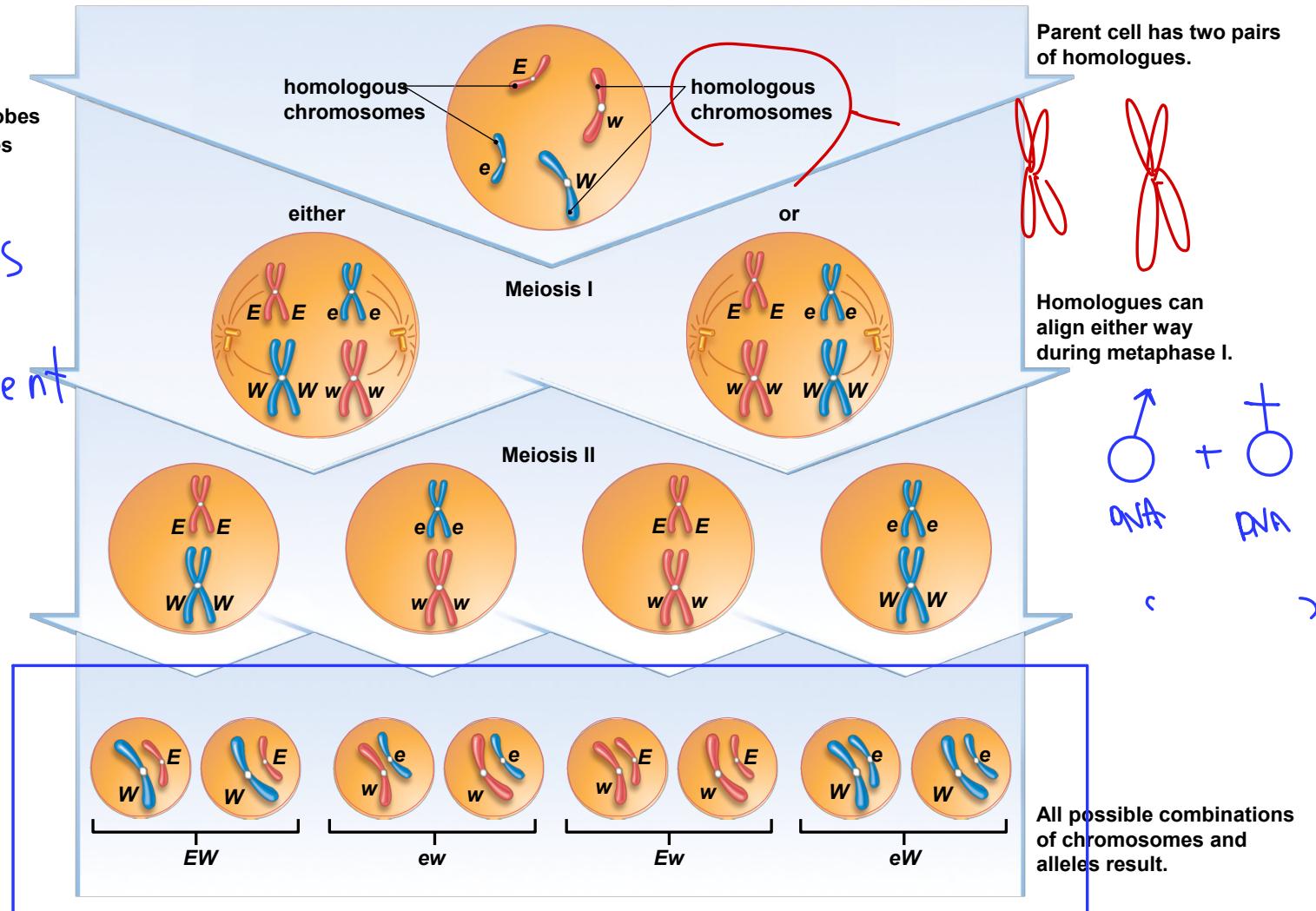


Straight hairline: `ww`

Figure 8 Mendel's laws and meiosis, continued.

Key:
W = widow's peak
w = straight hairline
E = unattached earlobes
e = attached earlobes

- genetics
- environment

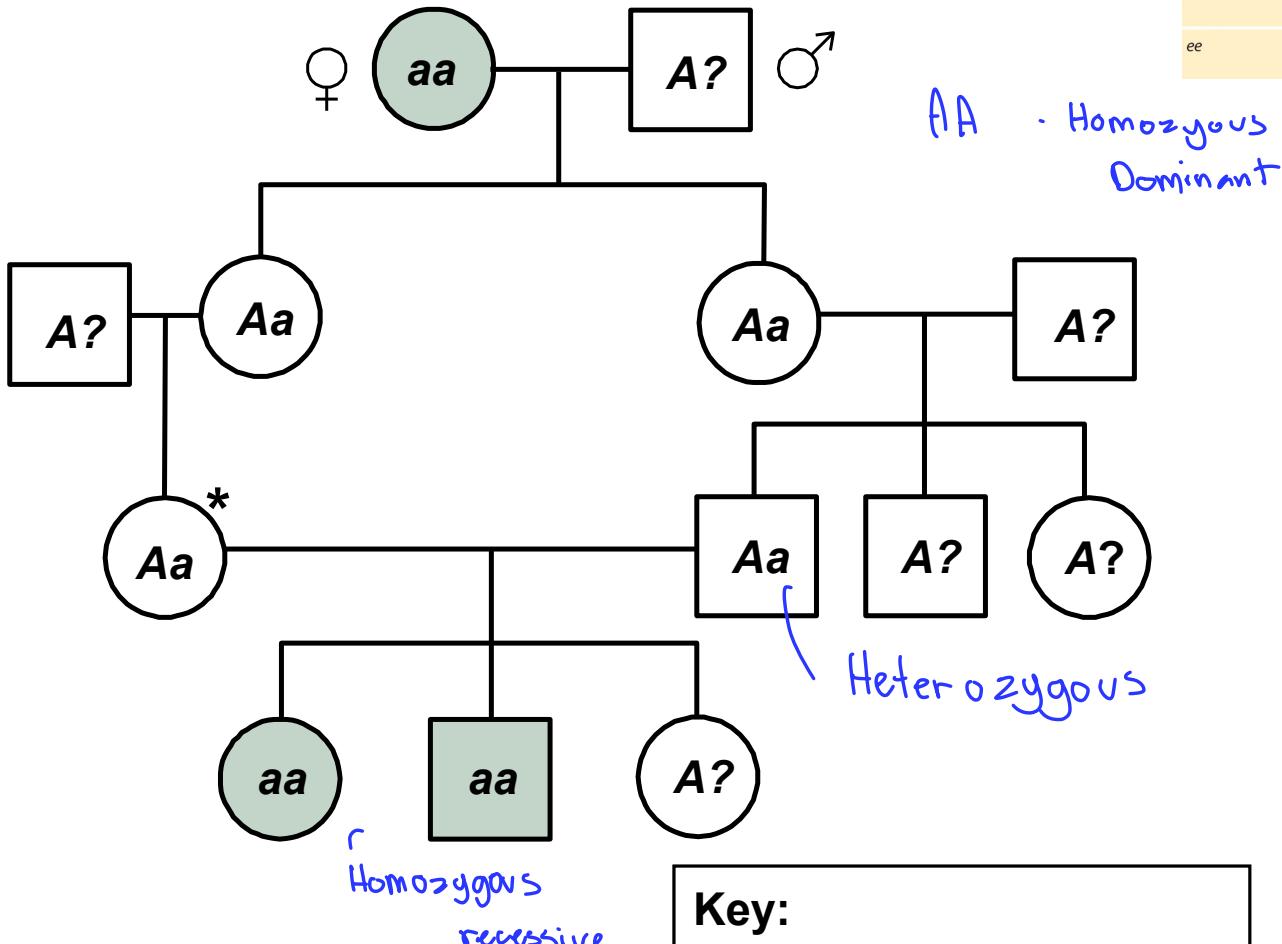


Mendel's Laws Apply to Humans

- Pedigree
 - Chart of a family's history in regard to a particular genetic trait
 - Males are squares
 - Females are circles
 - Shading represents individuals expressing disorder
 - Horizontal line between circle and square is a union
 - Vertical line down represents children of that union
 - Counselor may already know pattern of inheritance and then can predict chance that child born to a couple would have the abnormal phenotype

- Pedigrees for autosomal disorders
 - Autosomal recessive disorder
 - Child can be affected when neither parent is affected
 - Heterozygous parents are carriers.
 - Parents can be tested before having children.

Figure 9 Autosomal recessive pedigree.

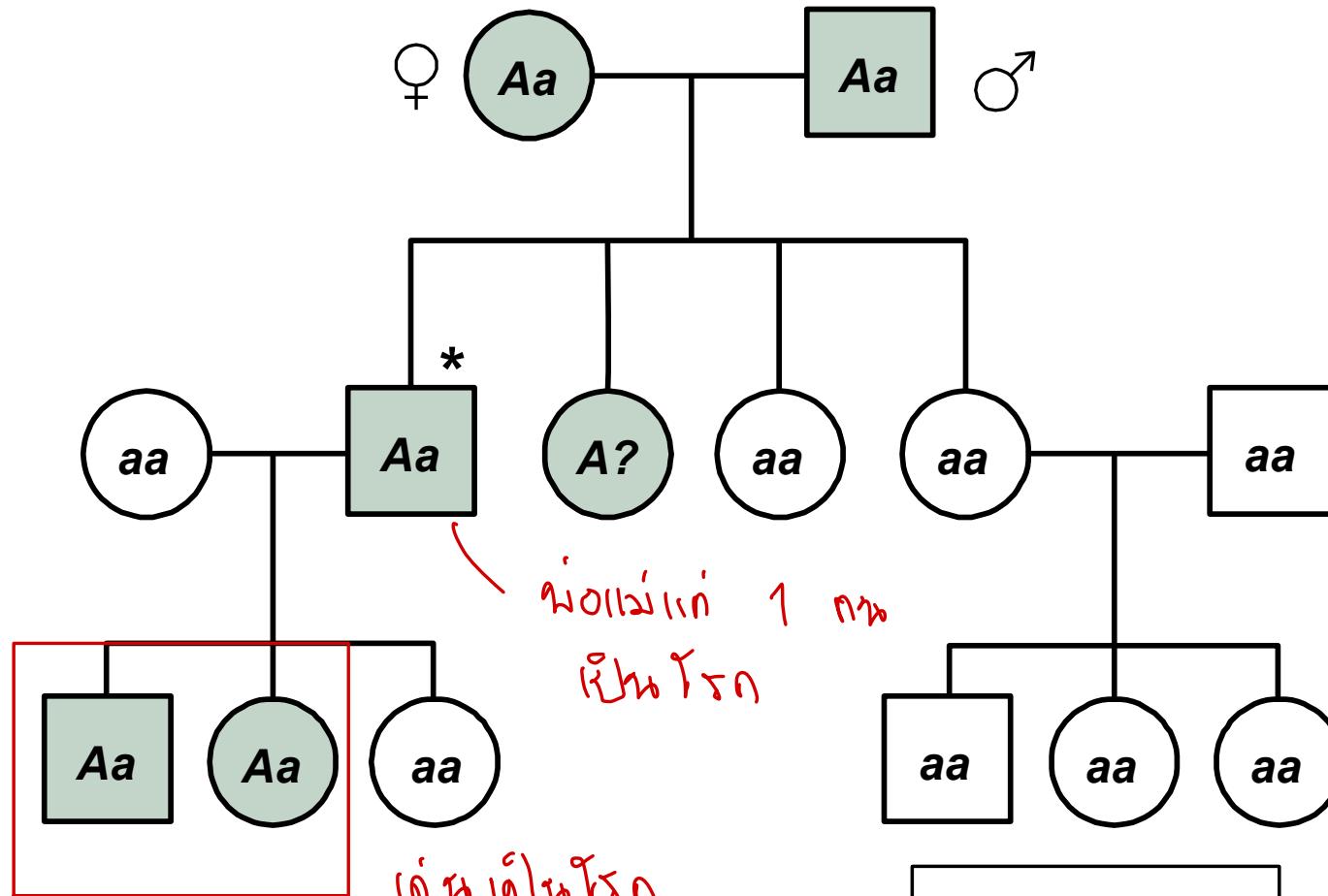


- Affected children can have unaffected parents.
- Heterozygotes (Aa) have a normal phenotype. *1 in 4 chance*
- Both males and females are affected with equal frequency.

| | |
|------|----------------------|
| EE | Homozygous dominant |
| Ee | Heterozygous |
| ee | Homozygous recessive |

- Autosomal dominant disorder
 - Child can be unaffected even when parents are heterozygous and therefore affected
 - When both parents are unaffected, none of their children will have the condition.
 - No dominant gene to pass on

Figure 10 Autosomal dominant pedigree.



- Affected children will have at least one affected parent.
- Heterozygotes (**Aa**) are affected.
- Both males and females are affected with equal frequency.

Key:
AA = affected
Aa = affected
A? = affected
aa = normal

Figure 11 Methemoglobinemia.

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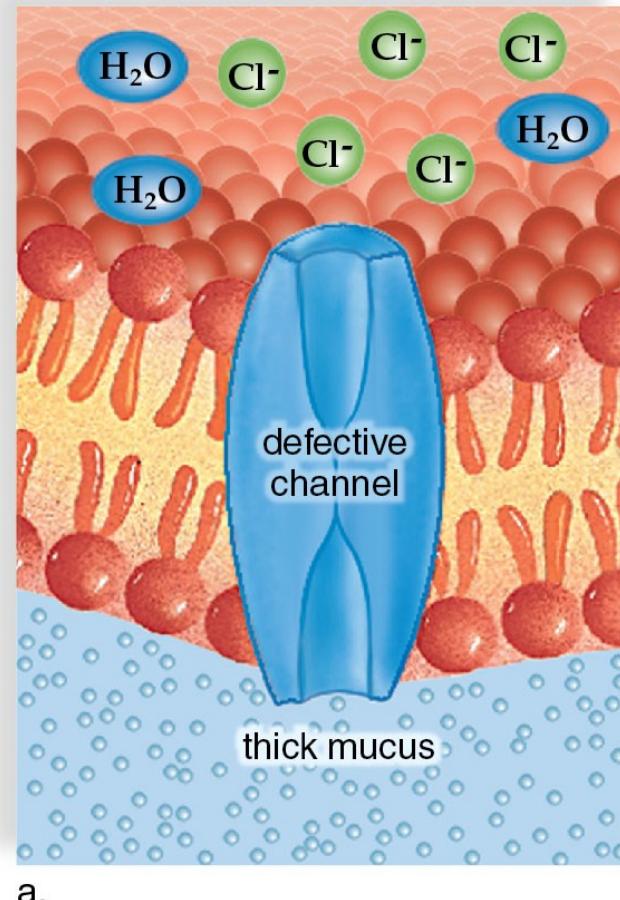
Courtesy of Division of Medical Toxicology, University of Virginia

- Genetic disorders of interest
 - Autosomal disorders
 - Methemoglobinemia—lack enzyme to convert methemoglobin back to hemoglobin
 - Relatively harmless, bluish-purplish skin

- Cystic fibrosis—autosomal recessive disorder
 - Most common lethal genetic disorder among Caucasians in U.S.
 - Chloride ion channel defect causes abnormally thick mucus

Figure 12 Cystic fibrosis.

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- Alkaptonuria—autosomal recessive disorder
 - Lack functional *homogentisate oxygenase* gene
 - Accumulation of homogentisic acid turns urine black when exposed to air

Figure 13 Alkaptonuria.

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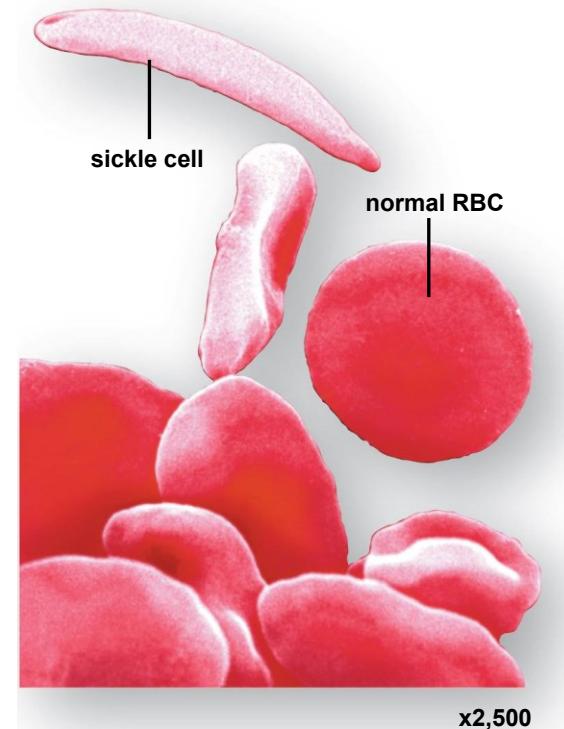
Normal

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Alkaptonuria

- Sickle cell disease—
autosomal recessive
disorder
 - Single base change in globin gene changes 1 amino acid in hemoglobin
 - Makes red blood cells sickle-shaped
 - Leads to poor circulation, anemia, low resistance to infection

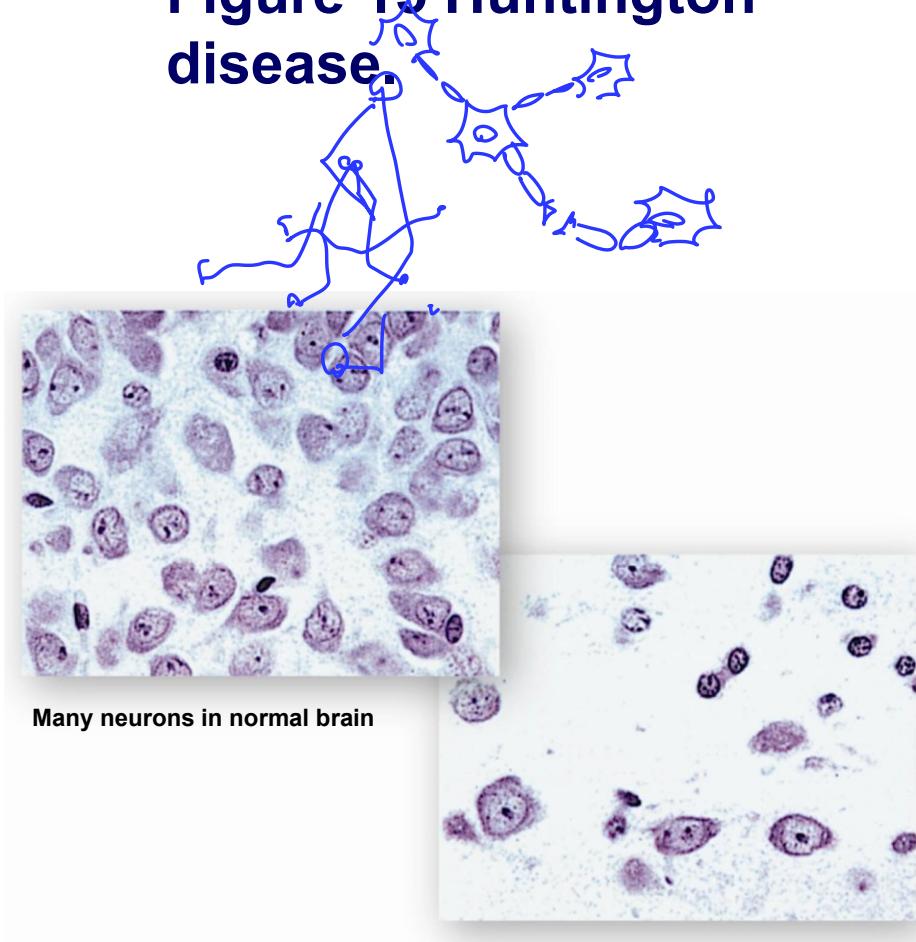
Figure 14 Sickle-cell disease.



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- Huntington disease—autosomal dominant disorder
 - Progressive degeneration of neurons in brain
 - Mutation for huntingtin protein
 - Patients appear normal until middle-aged—usually after having children
 - Test for presence of gene

Figure 15 Huntington disease.



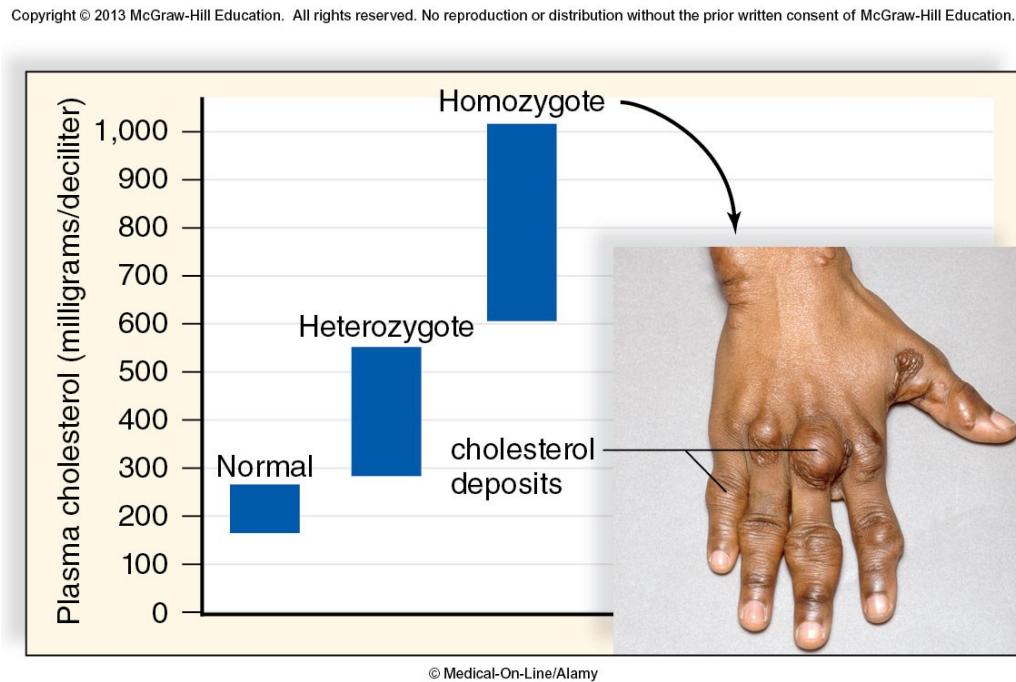
(both): Courtesy Dr. Hemachandra Reddy

Beyond Mendel's Laws

- Incomplete dominance

- Heterozygote has intermediate phenotype
- Familial hypercholesterolemia is an example in humans. Persons with one mutated allele have an abnormally high level of cholesterol in the blood, and those with two mutated alleles have a higher level still.
- Human wavy hair is intermediate between curly and straight hair.

Figure 16 Incomplete dominance.



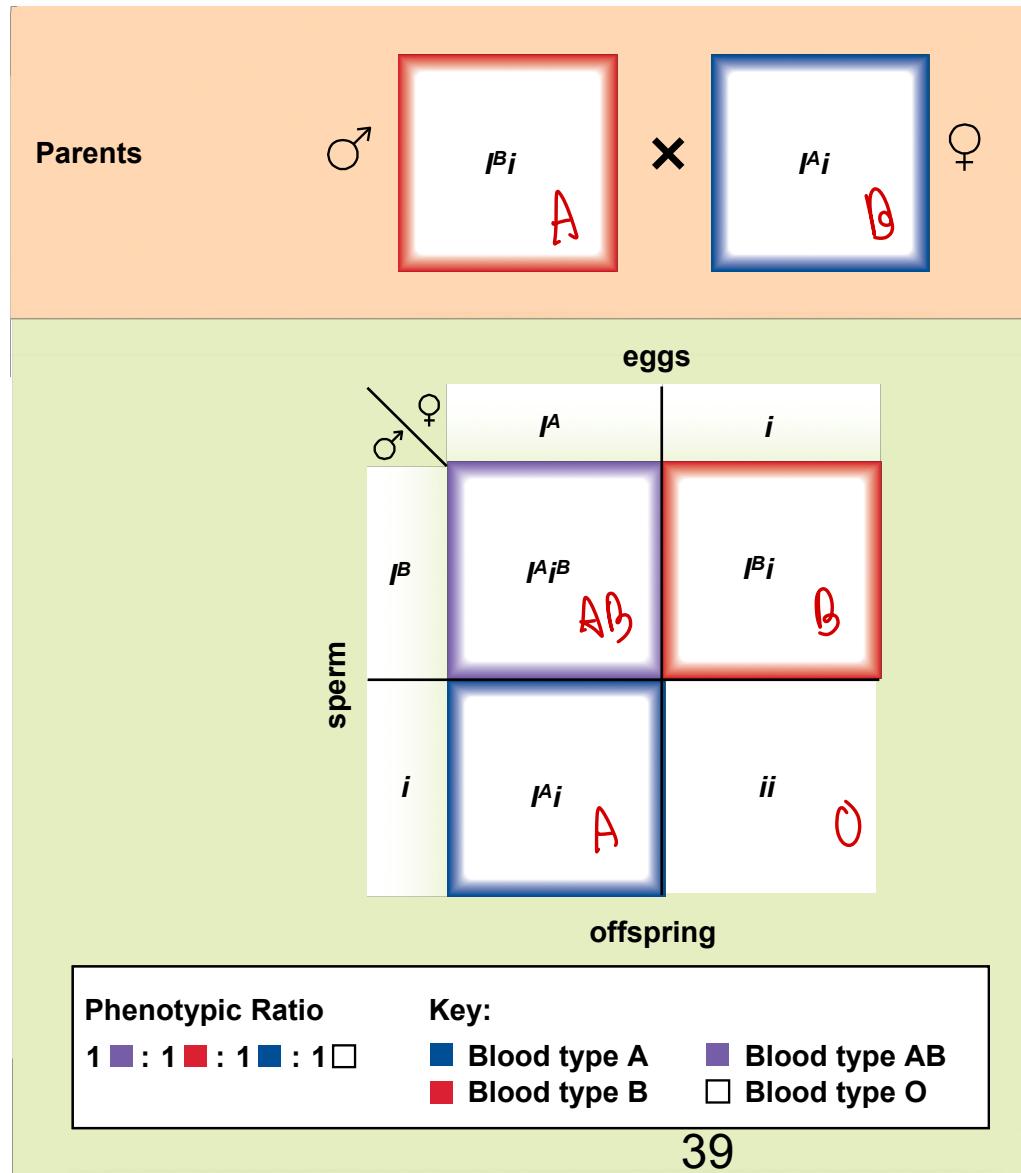
HDL

LDL

- Multiple-allele traits
 - ABO blood group inheritance has 3 alleles
 - I^A = A antigen on red blood cells
 - I^B = B antigen on red blood cells
 - i = neither A nor B antigen on red blood cells
 - Each person has only 2 of the 3 alleles
 - Both I^A and I^B are dominant to i
 - I^A and I^B are codominant—both will be expressed equally in the heterozygote

Figure 17 Inheritance of ABO blood type.

- Type A = I^A/I^A , I^A/i
- Type B = I^B/I^B , I^B/i
- Type AB = I^A/I^B
- Type O = ii

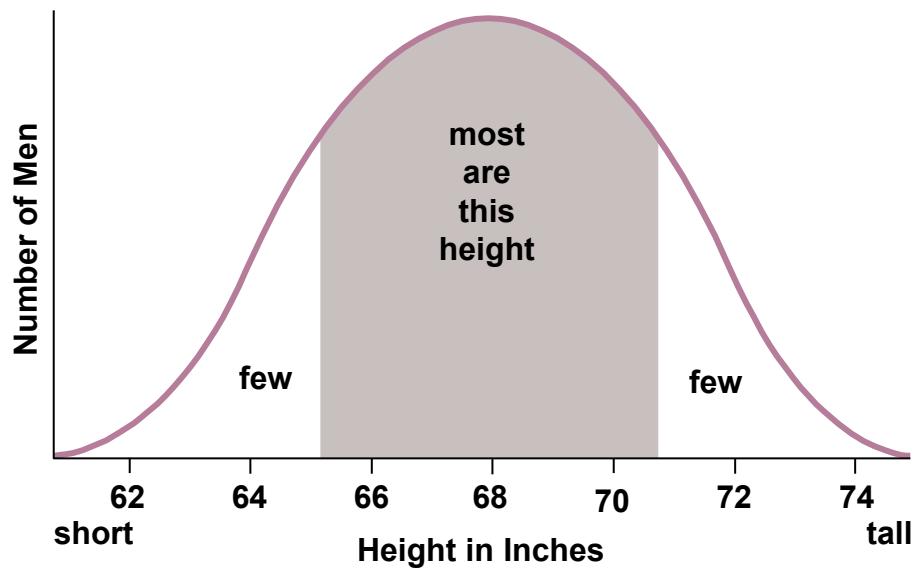


Poly - many

- Polygenic inheritance

- Trait is governed by 2 or more sets of alleles
- Each dominant allele has a quantitative effect on phenotype and effects are additive
- Result in continuous variation—bell-shaped curve
- Multifactorial traits—polygenic traits subject to environmental effects
 - Cleft lip, diabetes, schizophrenia, allergies, cancer
 - Due to combined action of many genes plus environmental influences

Figure 18 Height in humans, a polygenic trait.



- Environmental influences
- Relative importance of each can vary
 - Temperature can effect coat color.
 - Rabbits homozygous for *ch* have black fur where the skin temperature is low.
 - Enzyme encoded by gene is active only at low temperatures

Figure 20 Coat color in Himalayan rabbits.

The dark color on the ears, nose, and feet of these rabbits is believed to be due to lower body temperature in these areas.



- Pleiotropy
 - Single genes have more than one effect.
 - Marfan syndrome is due to production of abnormal connective tissue

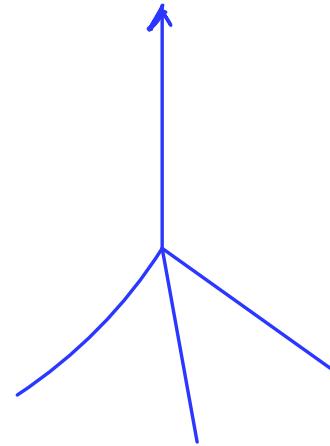
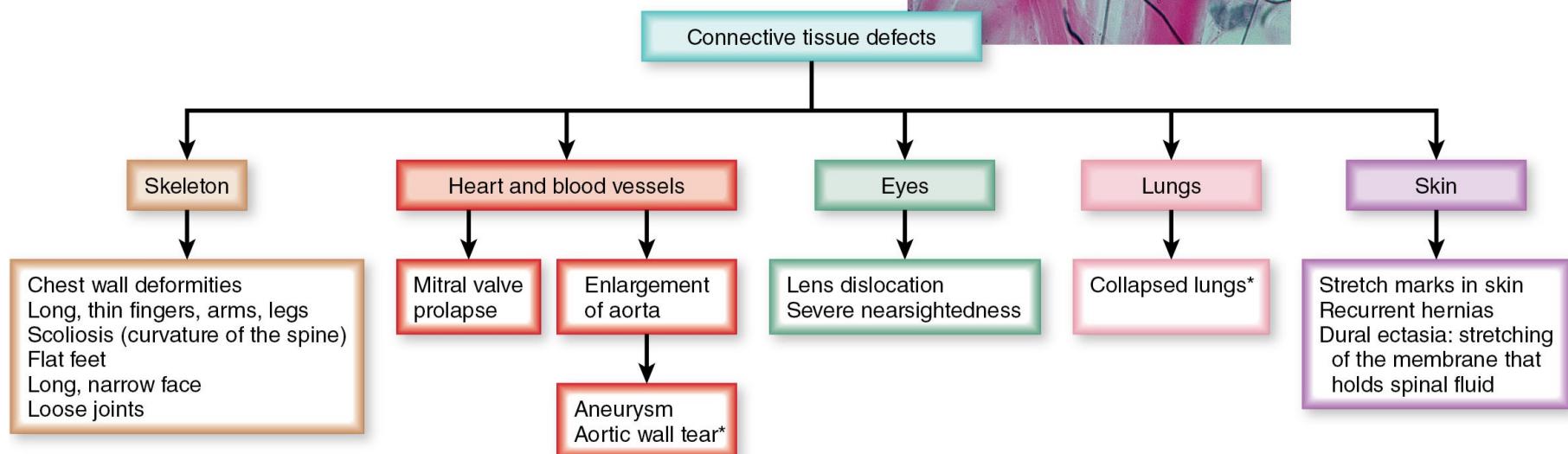
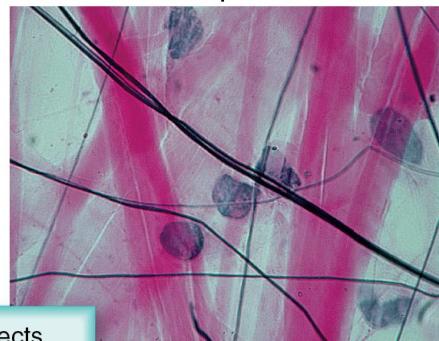


Figure 21 Marfan syndrome, multiple effects of a single human gene.

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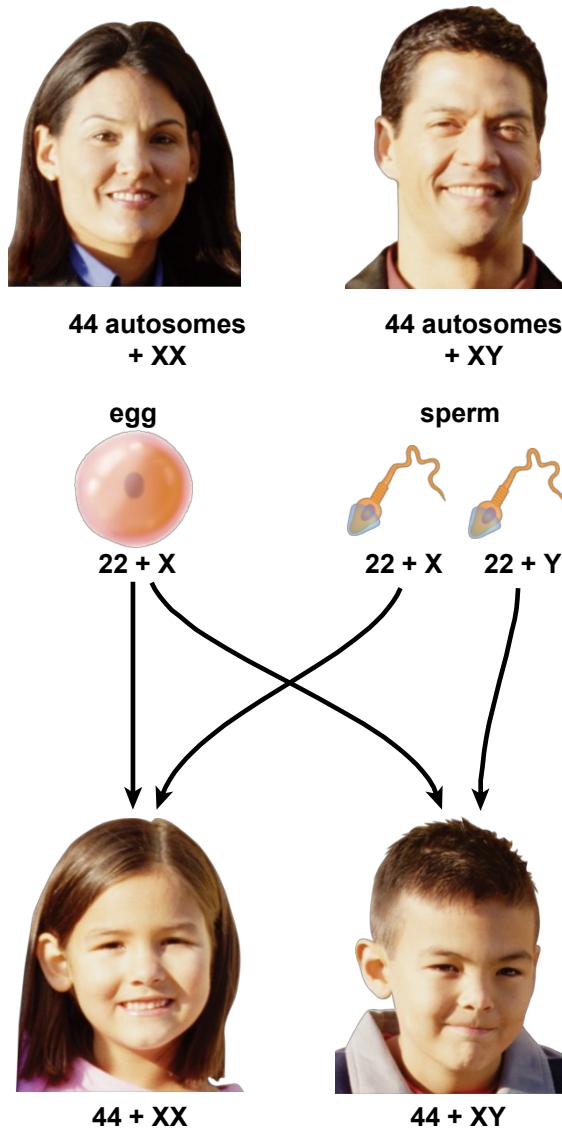
Linkage

- 2 traits on same chromosome—gene linkage
- 2 traits on same chromosome do NOT segregate independently
- Recombination between linked genes
 - Linked alleles stay together—heterozygote forms only 2 types of gametes, produces offspring only with 2 phenotypes

Sex-Linked Inheritance

- Females are XX
 - All eggs contain an X
- Males are XY
 - Sperm contain either an X or a Y
- Y carries SRY gene—determines maleness
- X is much larger and carries more genes
 - X-linked—gene on X chromosome

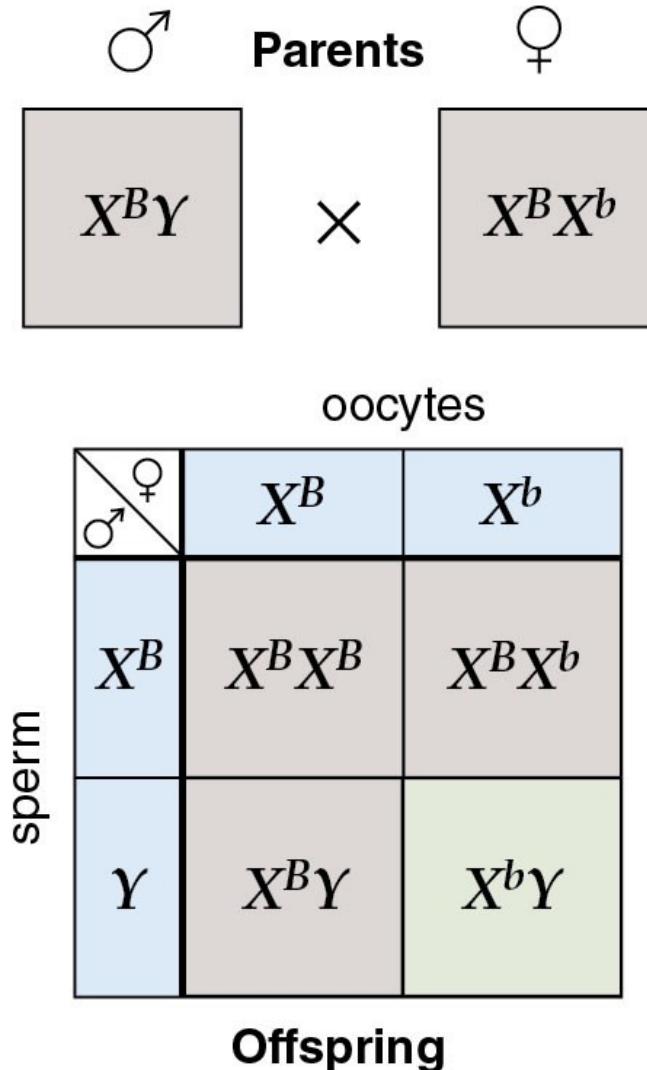
Figure 23 Sex determination in human beings.



- Sex-linked alleles
 - Fruit flies have same sex chromosome pattern as humans
 - When red-eyed female mated white mutant white-eyed male, all offspring were red-eyed
 - In the F_2 , the 3:1 ratio was found but all of the white-eyed flies were males
 - Y chromosome does not carry alleles for X-linked traits
 - Males always receive X from female parent, Y from male parent
 - Carrier—female who carries an X-linked trait but does not express it

Figure 24 X-linked inheritance.

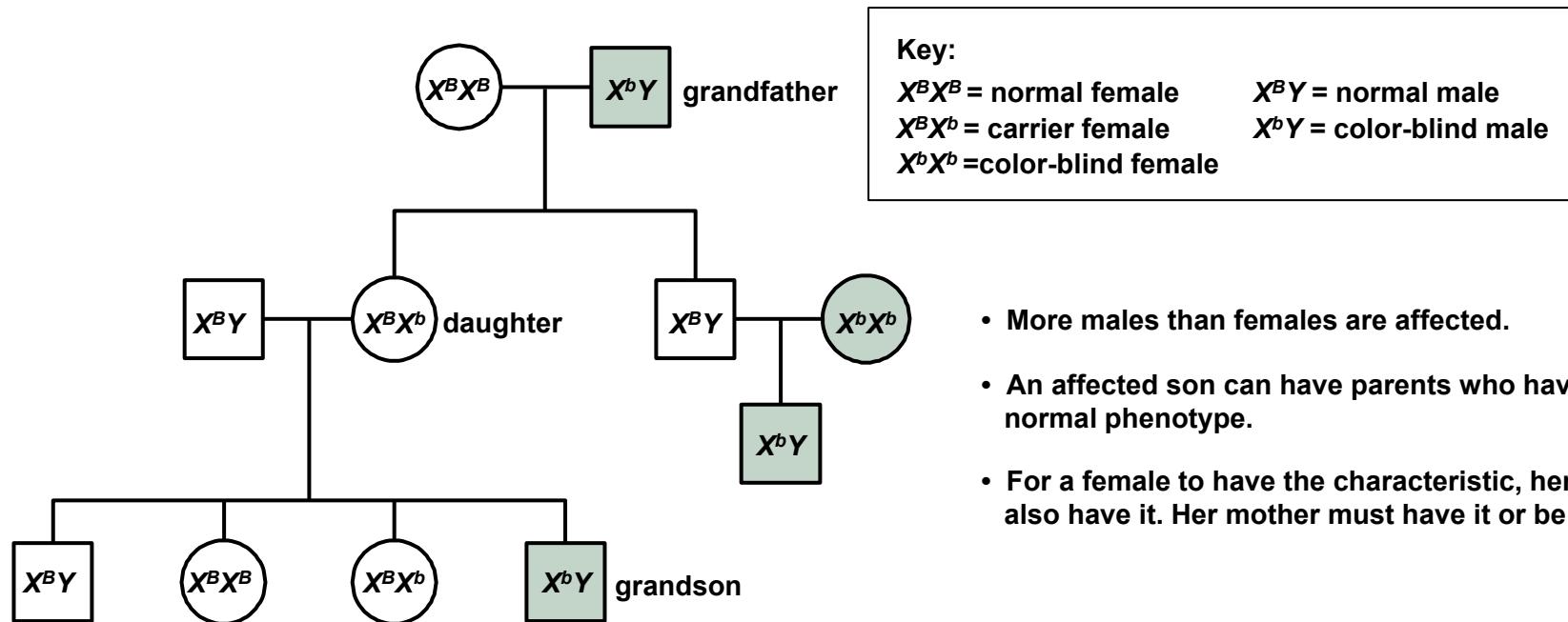
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| Key | |
|------------------|---------------|
| X^B | Normal vision |
| X^b | Color blind |
| Normal vision | |
| Color blind | |
| Phenotypic Ratio | |
| Females | All |
| Males | 1 |
| | 1 |

- Pedigree for sex-linked disorder
 - X-linked recessive disorder
 - Sons inherit trait from mothers—son's X comes from mother
 - More males than females have disorder—allele on X is always expressed in males
 - Females who have the condition inherited the mutant allele from both their mother and their father
 - Conditions appear to pass from grandfather to grandson

Figure 25 X-linked recessive pedigree.



- More males than females are affected.
- An affected son can have parents who have the normal phenotype.
- For a female to have the characteristic, her father must also have it. Her mother must have it or be a carrier.

- X-linked dominant
 - Only a few traits
 - Daughters of affected males have the condition
 - Affected females can pass condition to daughters and sons
 - Depends on which X inherited from a carrier mother if father is normal
- Y chromosome
 - Only a few disorders
 - Present only in males and are passed to all sons but not daughters

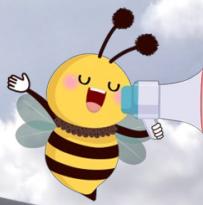
- X-linked recessive disorders

- Color blindness
 - About 8% of Caucasian men have red-green color blindness
- Duchenne muscular dystrophy
 - Absence of protein dystrophin causes wasting away of muscles
 - Therapy—immature muscle cells injected into muscles

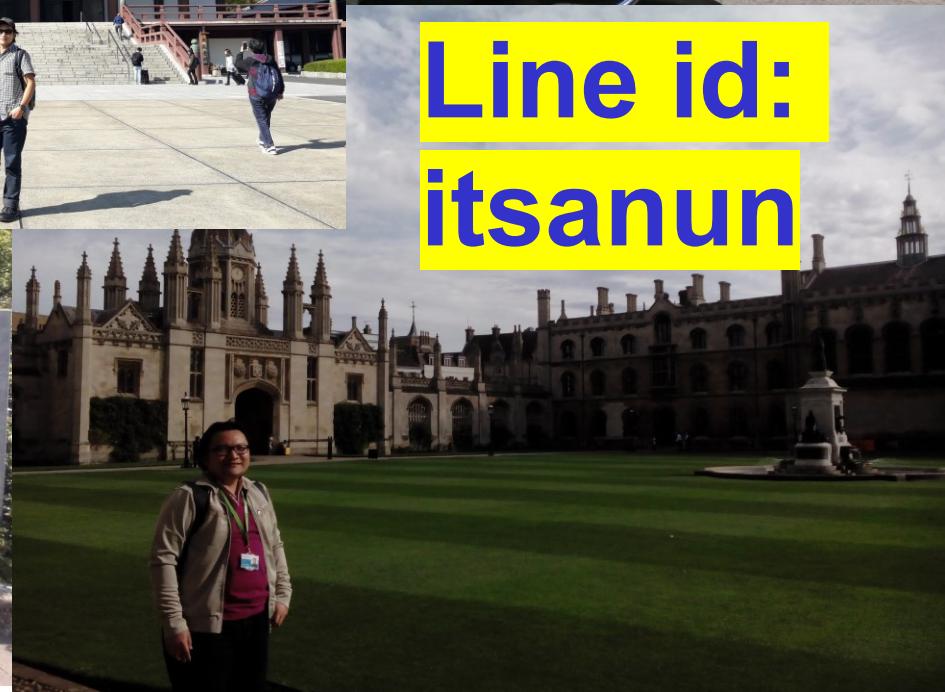
Figure 26 Muscular dystrophy.



(left, right): Courtesy Dr. Rabi Tawil; (center): Courtesy Muscular Dystrophy



Thank you very much for your
attention



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