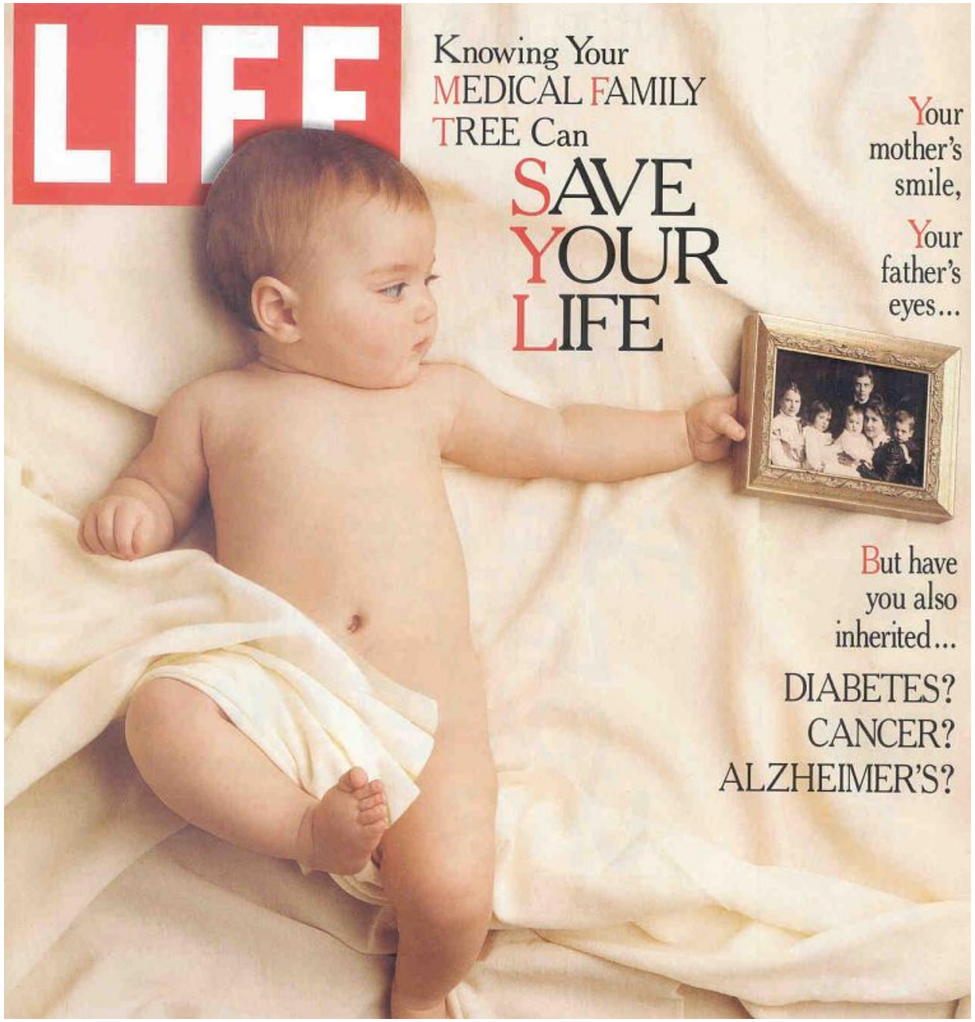
Single-Gene Inheritance

Importance of Family History



- Understanding the past is the key to predicting the future.

OBJECTIVES

- Construct and interpret pedigrees using standard nomenclature
- Describe the general features of Mendelian patterns of single gene inheritance.
- Identify the mode of inheritance of traits discussed in lecture.
- Describe aspects of phenotypic expression, using traits discussed in lecture as examples.
- Understand basic concepts of probability.
- Recognize the pattern of inheritance of a trait segregating in a family.
- Apply basic concepts of probability and principles of Mendelian inheritance to calculate the probabilities that offspring of specified mating types will be affected and unaffected.

Concept 14.3: Inheritance patterns are often more complex than predicted by simple Mendelian genetics

- The relationship between genotype and phenotype is rarely as simple as in the pea plant characters Mendel studied
- Many heritable characters are not determined by only one gene with two alleles
- However, the basic principles of segregation and independent assortment apply even to more complex patterns of inheritance

Extending Mendelian Genetics for a Single Gene

- Inheritance of characters by a single gene may deviate from simple Mendelian patterns in the following situations:
  - When alleles are not completely dominant or recessive
  - When a gene has more than two alleles
  - When a gene produces multiple phenotypes

Degrees of Dominance

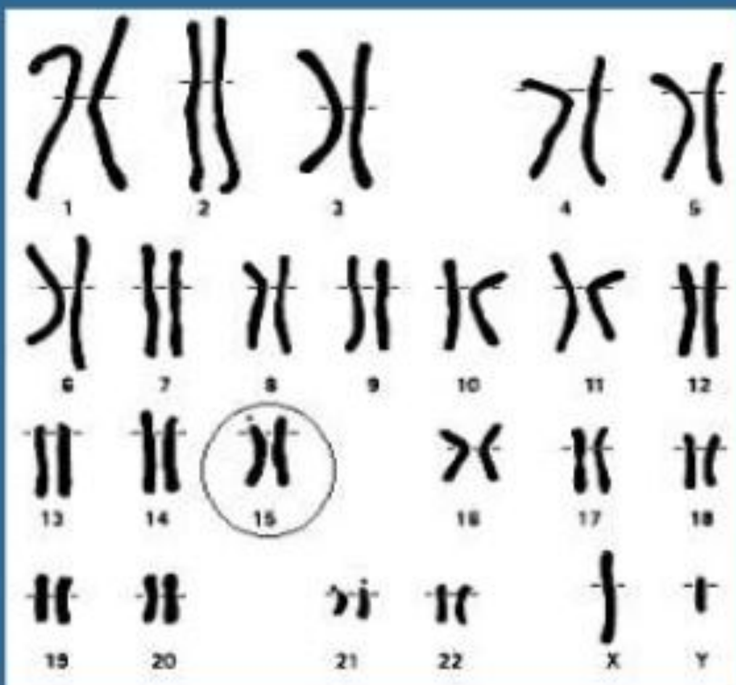
- **Complete dominance** occurs when phenotypes of the heterozygote and dominant homozygote are identical
- In **incomplete dominance**, the phenotype of F_1 hybrids is somewhere between the phenotypes of the two parental varieties
- In **codominance**, two dominant alleles affect the phenotype in separate, distinguishable ways

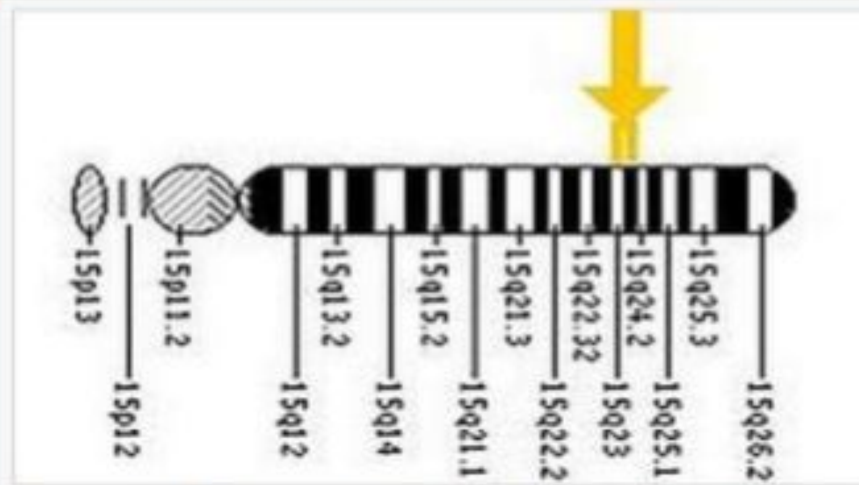
The Relation Between Dominance and Phenotype

- A dominant allele does not subdue a recessive allele; alleles don’t interact that way
- Alleles are simply variations in a gene’s nucleotide sequence
- For any character, dominance/recessiveness relationships of alleles depend on the level at which we examine the phenotype

Causes of Tay-Sachs

The disease is caused **by mutations on chromosome 15 in the HEX A gene,** which produces a lack of hexosaminidase A.





The HEXA gene is located on the long (q) arm of chromosome 15 between positions 23 and 24.

Tay Sach's features:

TAY SACHS

- **T**esting recommended
- **A**utosomal recessive
- **Y**oung death (<4 yrs.)
- **S**pot in macula (cherry red spots)
- **A**shkenazi Jews
- **C**NS degeneration
- **H**ex A deficiency
- **S**torage disease

MENDELIAN GENETICS AND HUMANS

Human genetic disorders

Tay Sachs Disease

Inheritance Pattern:

-Autosomal recessive

Physical Effects:

-Nerve cells destroyed in brain and spinal cord

-Symptoms appear 3-6 months after birth

-Loss of motor control and atrophy of muscles, seizures

-Death

Autosomal Recessive Disorders

- Tay-Sachs Disease
  - Usually occurs in Jewish people
  - Symptoms
    - Development slows at age 4 to 8 months
    - Neurological and Psychomotor impairment
    - Child gradually becomes blind and helpless, seizures, paralyzed, death by age 3 – 4 years old
  - Caused by gene on chromosome 15 → caused buildup of nonfunctional lysosomes in neurons

- **Tay-Sachs disease** is fatal; a dysfunctional enzyme causes an accumulation of lipids in the brain
  - At the *organismal* level, the allele is recessive
  - At the *biochemical* level, the phenotype (i.e., the enzyme activity level) is incompletely dominant
  - At the *molecular* level, the alleles are codominant

Frequency of Dominant Alleles

- Dominant alleles are not necessarily more common in populations than recessive alleles
- For example, Polydactyly one baby out of 400 in the United States is born with extra fingers or toes

- The allele for this unusual trait is dominant to the allele for the more common trait of five digits per appendage
- In this example, the recessive allele is far more prevalent than the population’s dominant allele

Multiple Alleles

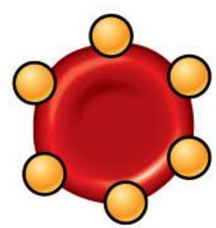
- Most genes exist in populations in more than two allelic forms
- For example, the four phenotypes of the ABO blood group in humans are determined by three alleles for the enzyme (I) that attaches A or B carbohydrates to red blood cells: I^A, I^B, and *i*.
- The enzyme encoded by the I^A allele adds the A carbohydrate, whereas the enzyme encoded by the I^B allele adds the B carbohydrate; the enzyme encoded by the *i* allele adds neither

Figure 14.11

(a) The three alleles for the ABO blood groups and their carbohydrates

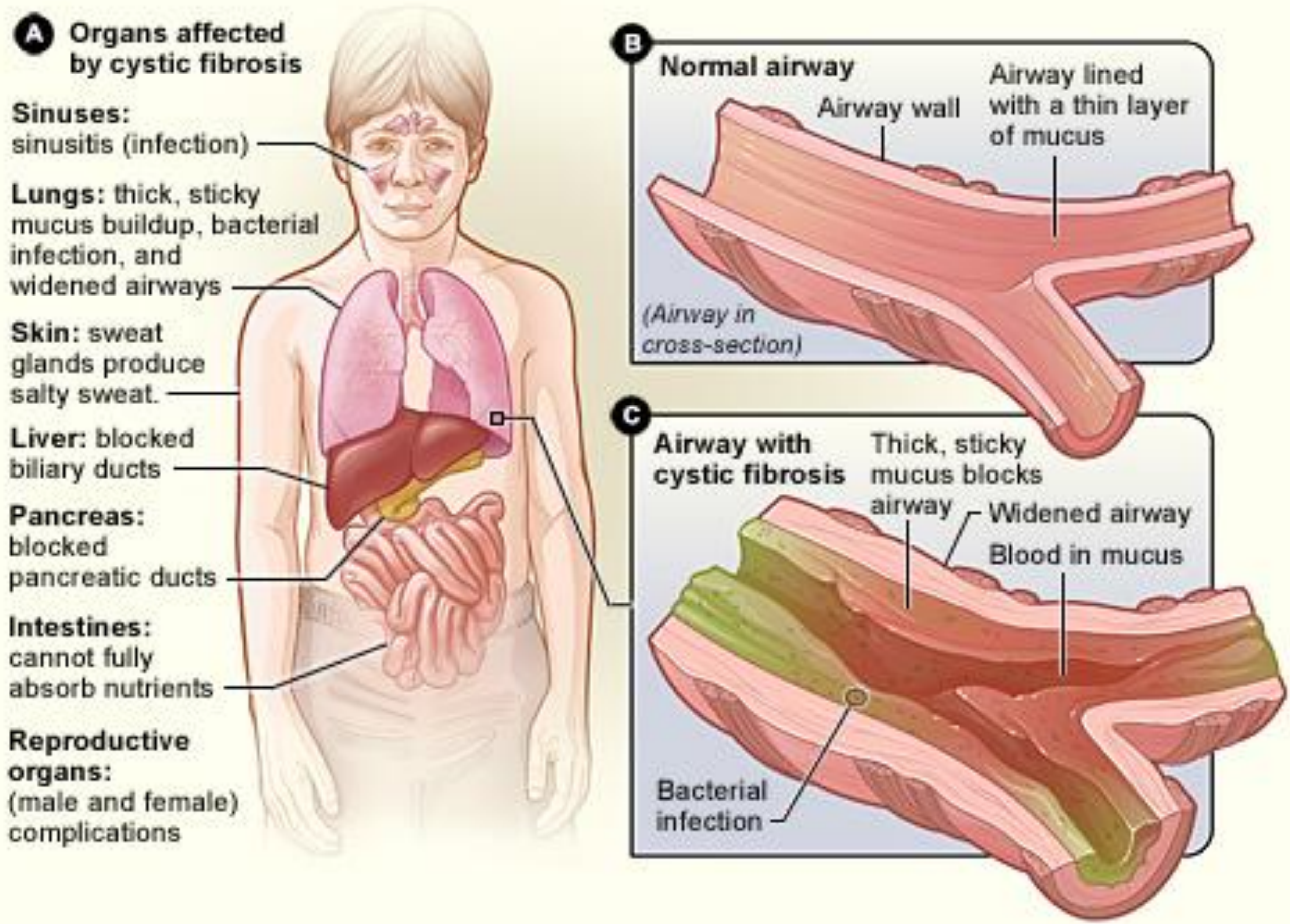
Allele	I^A	I^B	i
Carbohydrate	A △	B ○	none

(b) Blood group genotypes and phenotypes

Genotype	I^AI^A or I^Ai	I^BI^B or I^Bi	I^AI^B	ii
Red blood cell appearance				
Phenotype (blood group)	A	B	AB	O

Pleiotropy

- Most genes have multiple phenotypic effects, a property called **pleiotropy**
- For example, pleiotropic alleles are responsible for the multiple symptoms of certain hereditary diseases, such as cystic fibrosis and sickle-cell disease



A Organs affected by cystic fibrosis
Sinuses: sinusitis (infection)
Lungs: thick, sticky mucus buildup, bacterial infection, and widened airways
Skin: sweat glands produce salty sweat.
Liver: blocked biliary ducts
Pancreas: blocked pancreatic ducts
Intestines: cannot fully absorb nutrients
Reproductive organs: (male and female) complications
B
Normal airway
Airway wall
Airway lined with a thin layer of mucus
(Airway in cross-section)
C
Airway with cystic fibrosis
Thick, sticky mucus blocks airway
Widened airway
Blood in mucus
Bacterial infection

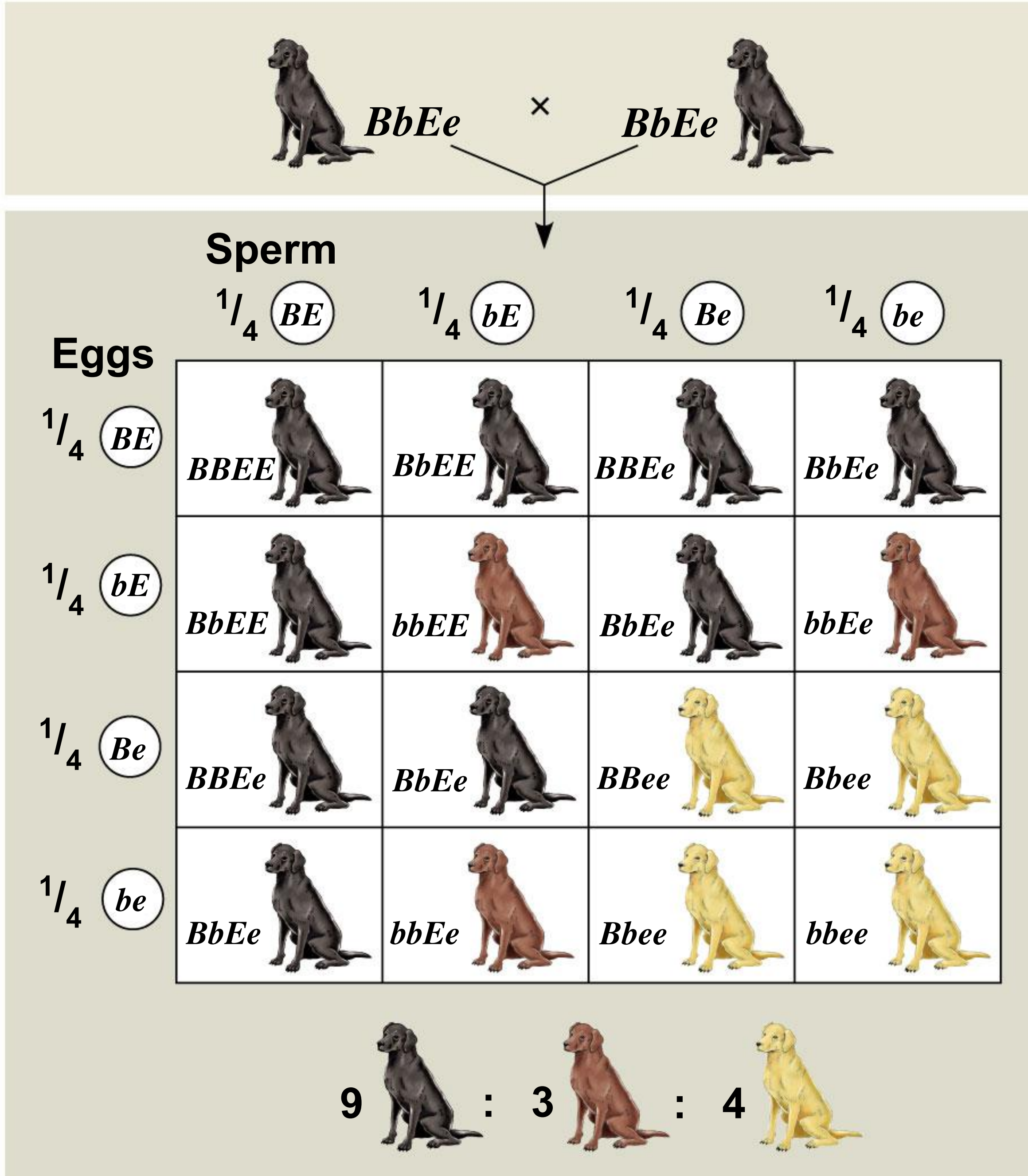
Extending Mendelian Genetics for Two or More Genes

- Some traits may be determined by two or more genes

Epistasis

- In **epistasis**, a gene at one locus alters the phenotypic expression of a gene at a second locus
- For example, in Labrador retrievers and many other mammals, coat color depends on two genes
- One gene determines the pigment color (with alleles *B* for black and *b* for brown)
- The other gene (with alleles *C* for color and *c* for no color) determines whether the pigment will be deposited in the hair

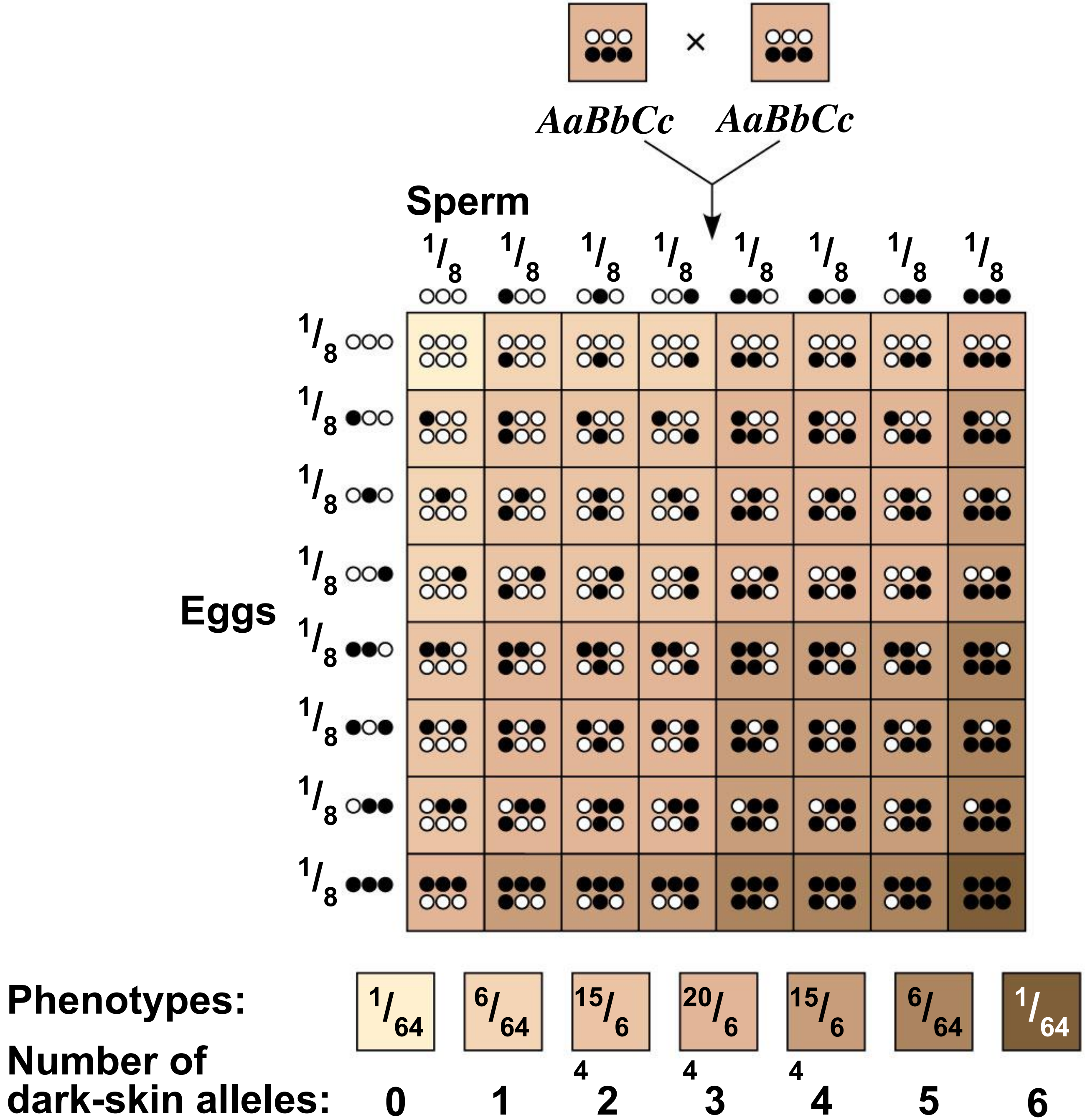
Figure 14.12


BbEe
×
BbEe
Sperm
1/4 BE
1/4 bE
1/4 Be
1/4 be
Eggs
1/4 BE
1/4 bE
1/4 Be
1/4 be
BBEE
BbEE
BBEe
BbEe
BbEE
bbEE
BbEe
bbEe
BBEe
BbEe
BBee
Bbee
BbEe
bbEe
Bbee
bbee
9 : 3 : 4

Polygenic Inheritance

- **Quantitative characters** are those that vary in the population along a continuum
- Quantitative variation usually indicates **polygenic inheritance**, an additive effect of two or more genes on a single phenotype
- Skin color in humans is an example of polygenic inheritance

Figure 14.13


×
AaBbCc
AaBbCc
Sperm
Eggs
1/8
Phenotypes:
1/64
6/64
15/64
20/64
15/64
6/64
1/64
Number of dark-skin alleles:
0
1
2
3
4
5
6

Nature and Nurture: The Environmental Impact on Phenotype

- Another departure from Mendelian genetics arises when the phenotype for a character depends on environment as well as genotype
- The **norm of reaction** is the phenotypic range of a genotype influenced by the environment
- For example, hydrangea flowers of the same genotype range from blue-violet to pink, depending on soil acidity

- Norms of reaction are generally broadest for polygenic characters
- Such characters are called **multifactorial** because genetic and environmental factors collectively influence phenotype

Integrating a Mendelian View of Heredity and Variation

- An organism's phenotype includes its physical appearance, internal anatomy, physiology, and behavior
- An organism's phenotype reflects its overall genotype and unique environmental history