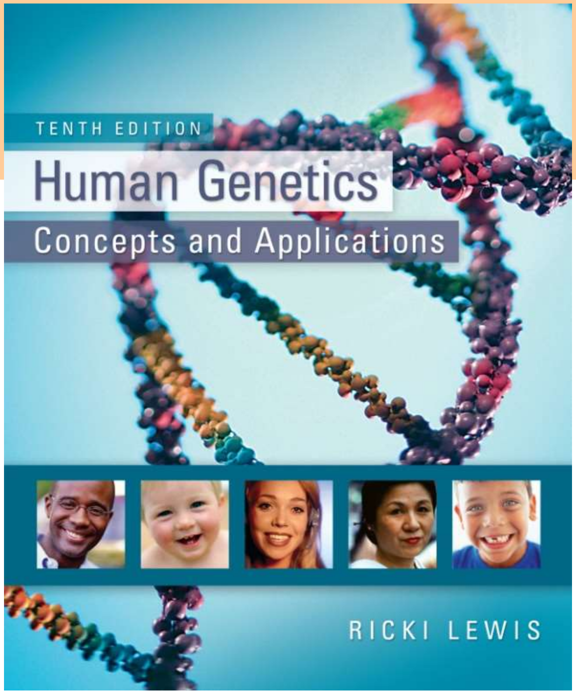
# Human Genetics
## Concepts and Applications
Tenth Edition

RICKI LEWIS




# 15 Changing Allele Frequencies

PowerPoint® Lecture Outlines
Prepared by Johnny El-Rady, University of South Florida

# Conditions that Change Allele Frequencies

Five conditions change allele frequencies (and ultimately phenotypic frequencies)

1) Nonrandom mating
2) Migration
3) Genetic drift
4) Mutation
5) Selection

# Nonrandom Mating

**Nonrandom mating** indicates that individuals of one genotype reproduce more often with each other

Indeed, we marry people similar to ourselves about 80% of the time

Traits that influence our mate choice include:

- Physical appearance
- Ethnic or religious preferences
- Intelligence and shared interests

# Nonrandom Mating Alters Allele Frequencies

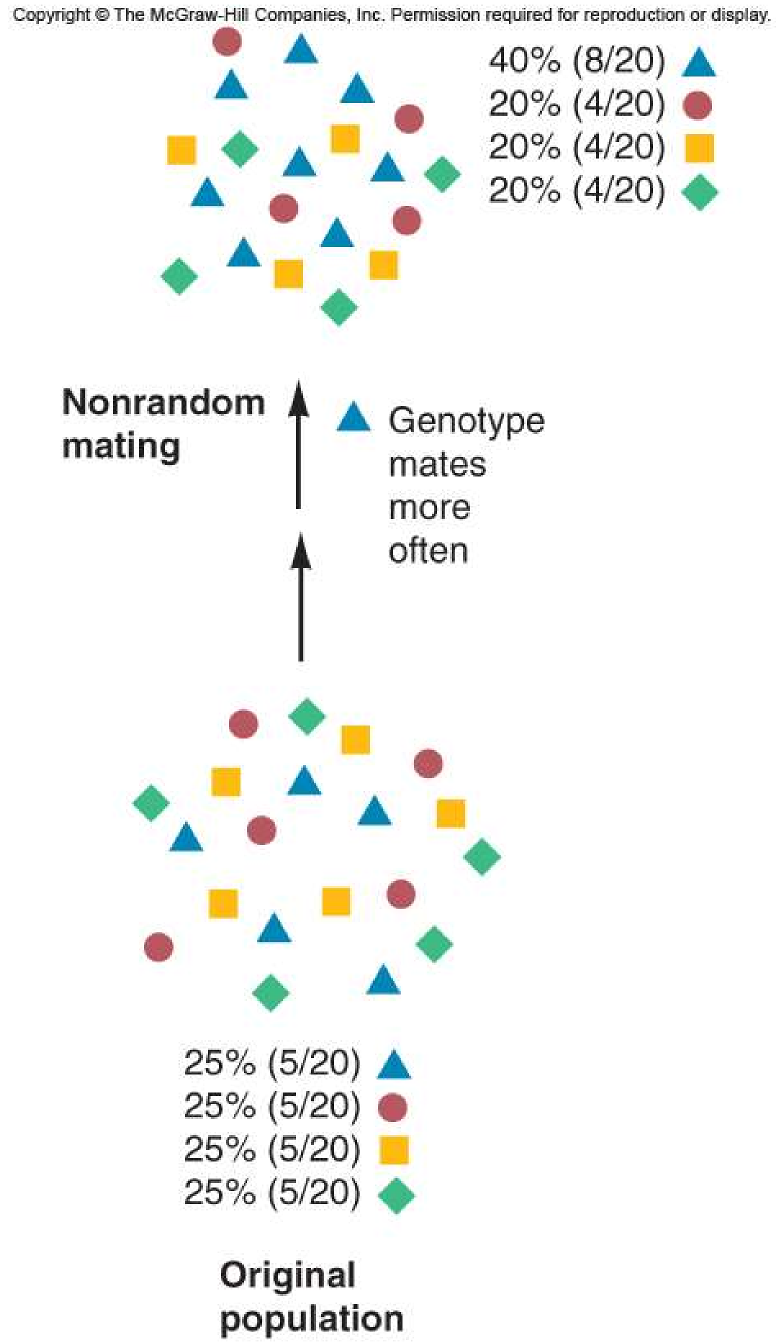



**Figure 15.1**

# Examples of Nonrandom Mating

Males fathering many children

- Arnold (South Africa)
  - Increase in frequency of a dominant dental disorder in the Cape population

- Genghis Khan (Asia)
  - 16 million men living today share his Y chromosome



Figure 15.2

# Examples of Nonrandom Mating

Hopi Indians – Albinism

Ashkenazi Jews – Tay-Sachs disease

**Consanguinity** – Marriage between blood relatives

**Endogamy** – Marriage within a community

# Migration

Individuals migrate and move genes from one area to another

- The addition or removal of alleles will alter the genotypic frequencies

Genetic effects of migration are reflected in current populations

Changes in allele frequency can be mapped across geographical or linguistic regions

# Migration Alters Allele Frequencies



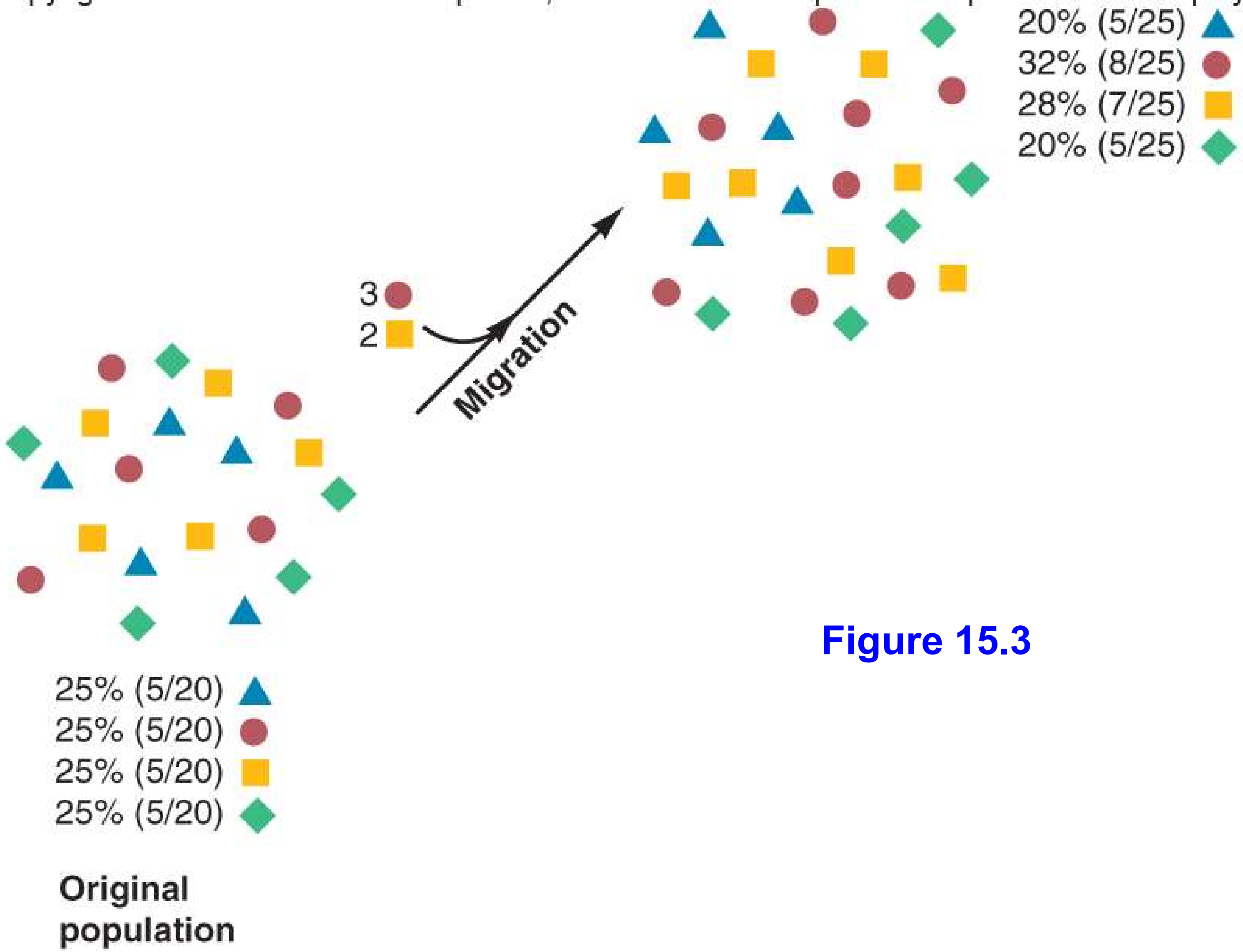



**Figure 15.3**

# Clines

**Clines** are gradients in allele frequencies between successive neighboring populations

Can suggest patterns of migration

Example

- Prevalence of galactokinase deficiency
  - An autosomal recessive disease that causes blindness

# Clines



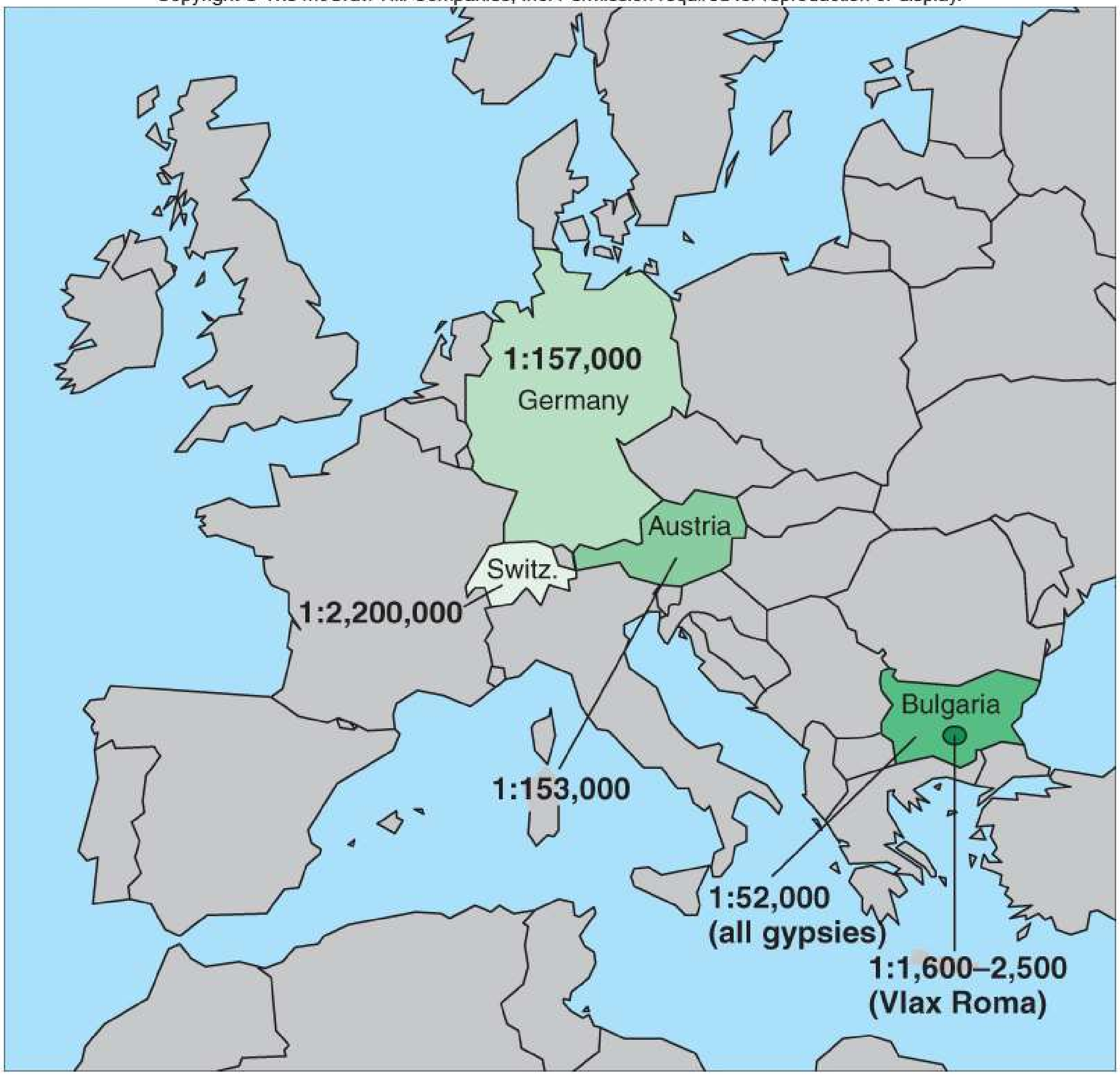



**Figure 15.4**

# Clines

**Clines** may be either abrupt or gradual

Cline boundaries may be correlated to:

- Historical events
- Cultural differences
- Geographical barriers
- Language differences
- Patterns of migration

# Genetic Drift

**Genetic drift** is the change in allele frequency when a small group separates from the larger whole

Caused by random sampling errors

Allele frequency changes are unpredictable

More pronounced in small populations

# Genetic Drift Alters Allele Frequencies



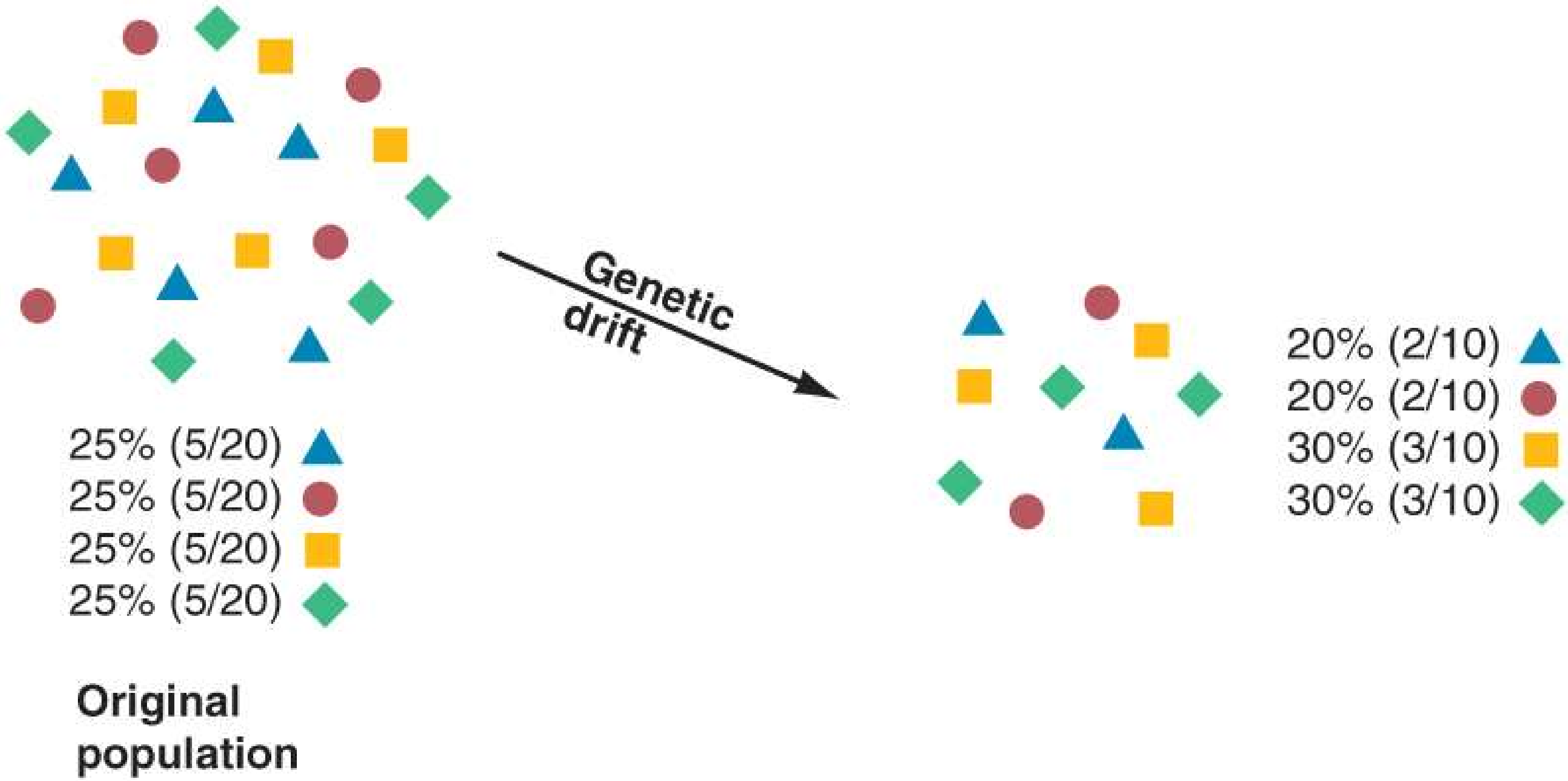



**Figure 15.5**

# Genetic Drift

Events that create small populations enhance the effect of genetic drift

- Founding a new population
- Bottlenecks (natural disaster, famine)
- Geographic separation (islands)
- Cultural separation

# Founder Effect

Occurs when a small group leaves home to found new settlements

The new colony may have different allele frequencies than the original population

- It may, by chance, either lack some alleles or have high frequency of others

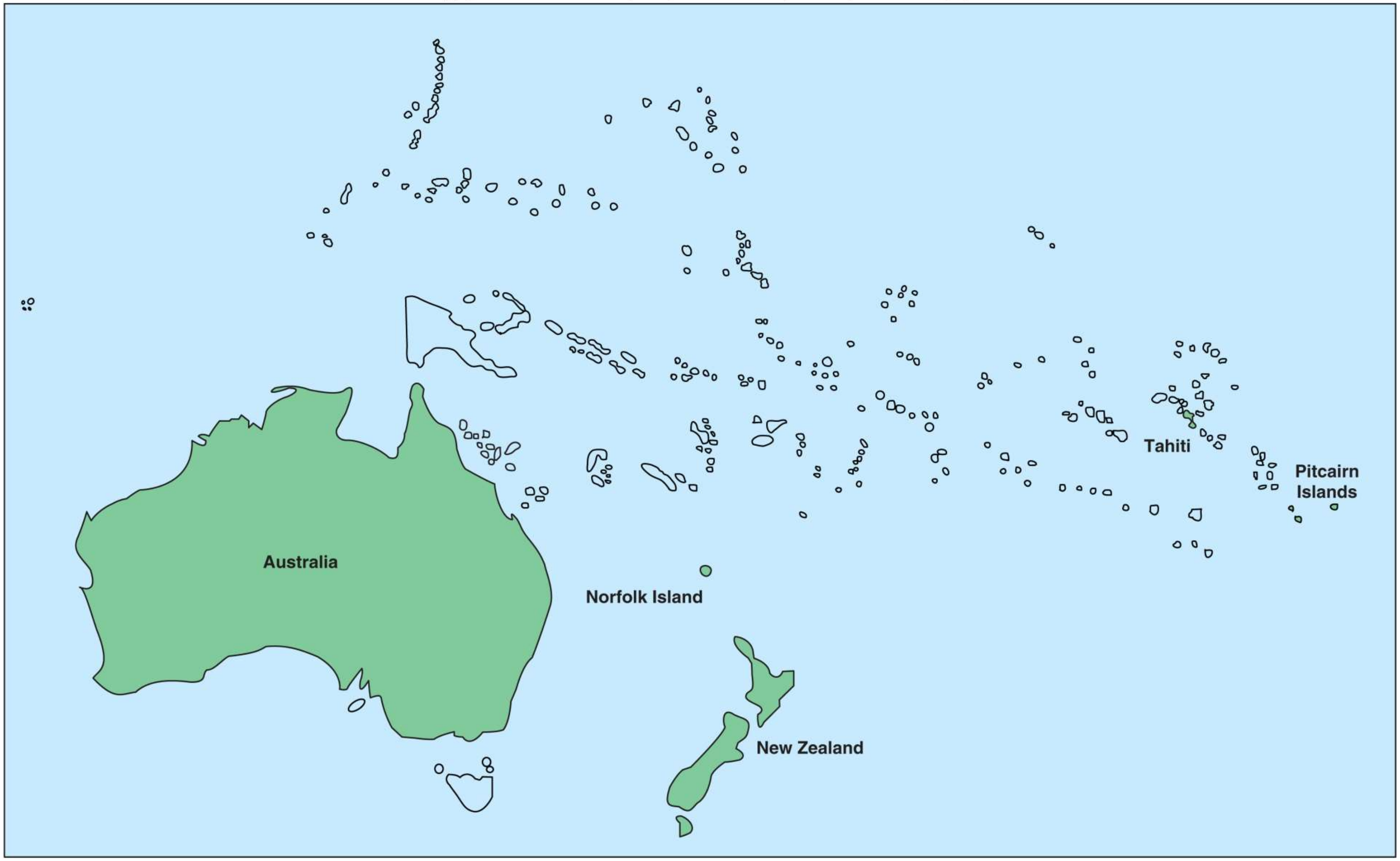

Australia
Norfolk Island
New Zealand
Tahiti
Pitcairn
Islands

**Figure 15.6**

## Table 15.1 Founder Populations

| Population | Number of Founders | Number of Generations | Population Size Today |
|---|---|---|---|
| Costa Rica | 4,000 | 12 | 2,500,000 |
| Finland | 500 | 80–100 | 5,000,000 |
| Hutterites | 80 | 14 | 36,000 |
| Japan | 1,000 | 80–100 | 120,000,000 |
| Iceland | 25,000 | 40 | 300,000 |
| Newfoundland | 25,000 | 16 | 500,000 |
| Quebec | 2,500 | 12–16 | 6,000,000 |
| Sardinia | 500 | 400 | 1,660,000 |

# Examples of Founder Effect

French Canadians of Quebec

- Have only 4/500 alleles for *BRCA1* gene

Dunker community of Germantown, Penn.

- Descendants of German immigrants who came between 1719 and 1729
- Have different distribution of blood types than the German native and non-Dunker neighbor populations

# Genetic Drift and Nonrandom Mating

Small population size increases the probability of homozygosity

Increases recessive phenotypes in population

Example

- Amish and Mennonite populations of Penn. marry predominantly within their religious groups
- Maintain their original small genetic pool
- Increased incidence of otherwise rare traits

Figure 15.7

Dr. Victor McKusick/Johns Hopkins University School of Medicine

Ellis-van Creveld syndrome

# Population Bottlenecks

Occurs when a large population is drastically reduced in size

Rebounds in population size occur with descendants of limited number of survivors

- Therefore, new population has a much more restricted gene pool than the large ancestral population

# Population Bottlenecks



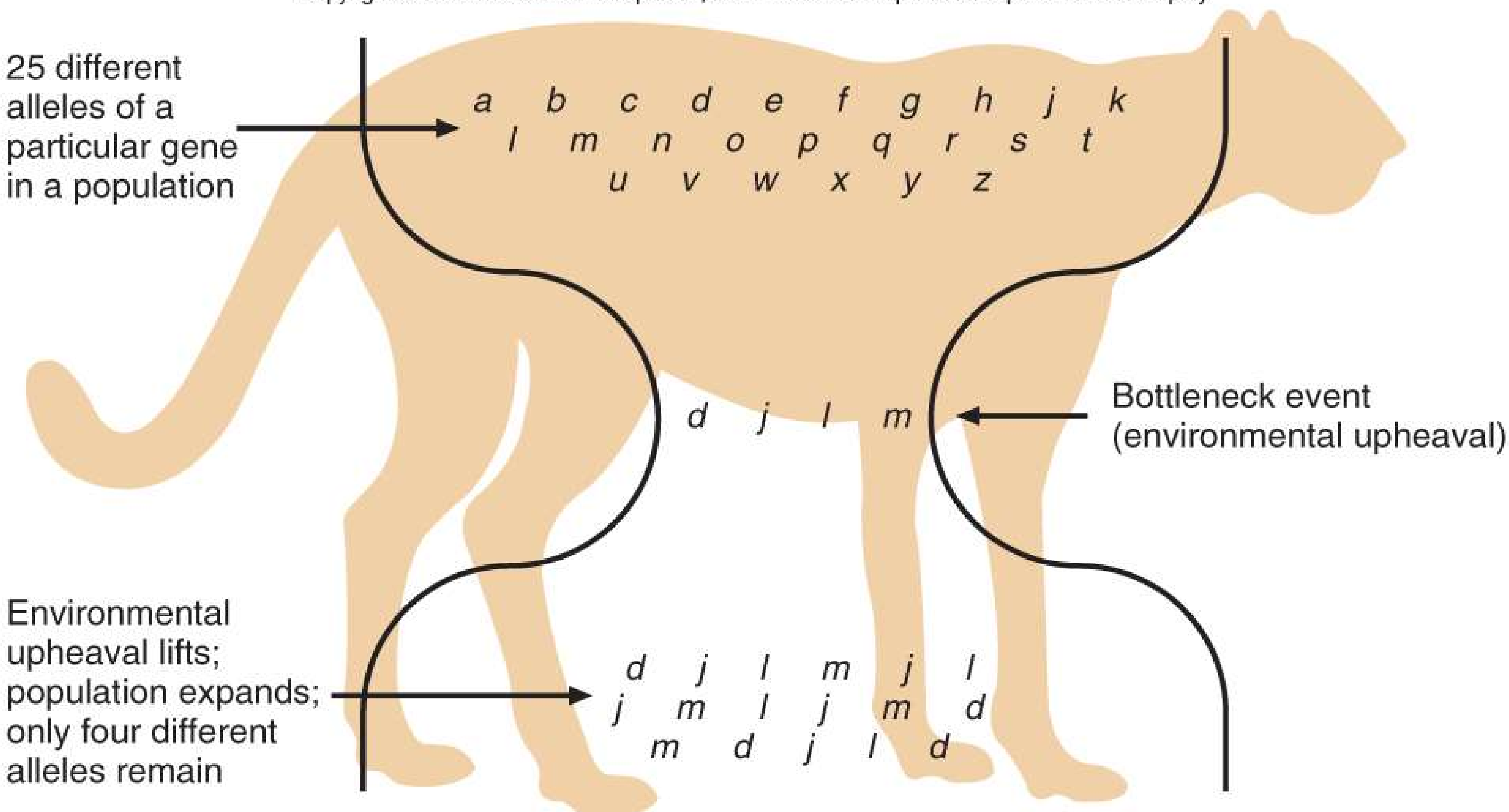



**Figure 15.8**

# Examples of Population Bottlenecks

Pingelapese people of Micronesia

- Bottleneck created by a typhoon

Cheetahs in S. and E. Africa

- Bottleneck created by changing habitats (after the most recent ice age) and mass slaughter by humans in the $19^{th}$ century

Ashkenazi Jews

- Massacres and nonrandom mating between survivors contributed to high incidence of certain disorders

# Examples of Population Bottlenecks

Table 15.2



**Table 15.2 Autosomal Recessive Genetic Diseases Prevalent Among Ashkenazi Jewish Populations**

| Disorder | MIM | Signs and Symptoms (Phenotype) | Carrier Frequency |
|---|---|---|---|
| Bloom syndrome | 210900 | Sun sensitivity, short stature, poor immunity, impaired fertility, increased cancer risk | 1/110 |
| Breast cancer | 113705, 600185 | Malignant breast tumor caused by mutant *BRCA1* or *BRCA2* genes | 3/100 |
| Canavan disease | 271900 | Brain degeneration, seizures, developmental delay, early death | 1/40 |
| Familial dysautonomia | 223900 | No tears, cold hands and feet, skin blotching, drooling, difficulty swallowing, excess sweating | 1/32 |
| Gaucher disease | 231000 | Enlarged liver and spleen, bone degeneration, nervous system impairment | 1/12 |
| Niemann-Pick disease type A | 257200 | Lipid accumulation in cells, particularly in the brain; intellectual and physical disability, death by age 3 | 1/90 |
| Tay-Sachs disease | 272800 | Brain degeneration causing intellectual disability, paralysis, blindness, death by age 4 | 1/26 |
| Fanconi anemia type C | 227650 | Deficiencies of all blood cell types, poor growth, increased cancer risk | 1/89 |

# Mutation

**Mutations** are a major and continual source of genetic variation in populations

- Can introduce new alleles
- Can convert one allele to another

Mutation has a minor impact (most are silent) unless coupled with another effect such as small population size or selection

# Mutations Alter Allele Frequencies



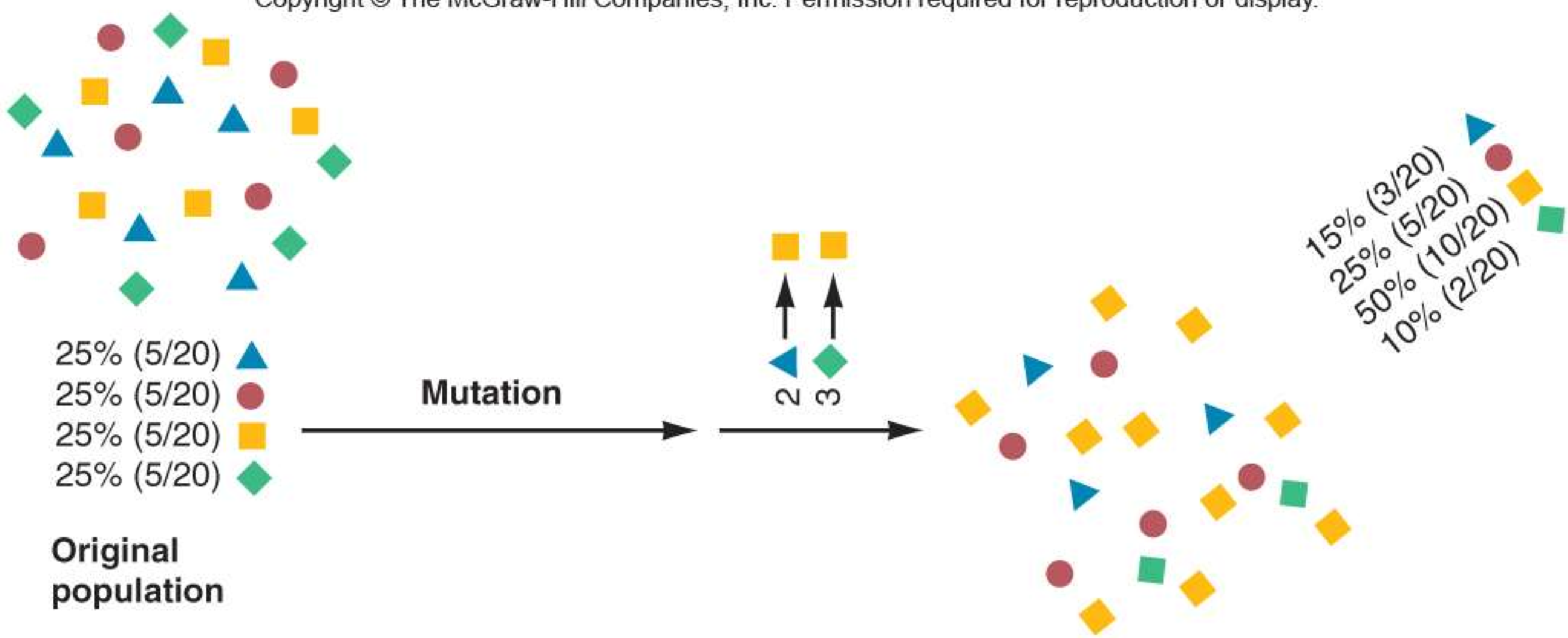



**Figure 15.9**

# Mutation

Selection eliminates deleterious alleles

However, harmful recessive alleles are maintained in heterozygotes and are reintroduced by mutations

**Genetic load** is the collection of recessive deleterious alleles present in a population

# Natural Selection

Is the differential survival and reproduction of individuals with a particular genotype/phenotype

**Negative selection** = Banishment of a dangerous trait

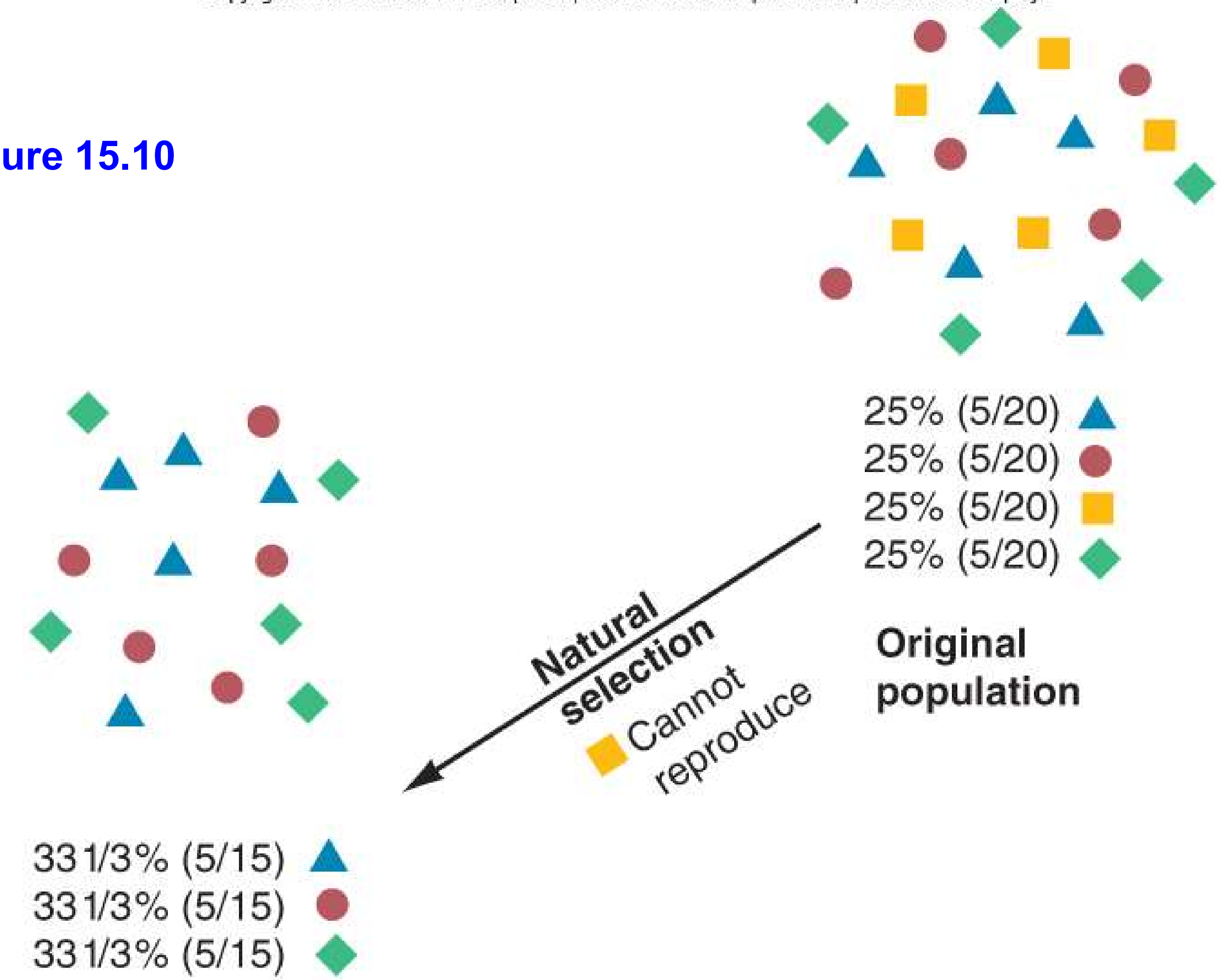
**Positive selection** = Retaining an advantageous trait

Both lead to changes in allele frequencies

# Natural Selection Alters Allele Frequencies



**Figure 15.10**



© Goodshoot/Alamy RF

**Figure 15.11**

# Artificial Selection

Controlled breeding with the intent of perpetuating individuals with a particular phenotype

Examples:

- Crop plants
- Pets





**Figure 15.12**



**Figure 15.13**

# Natural Selection and Tuberculosis

TB infections have historically swept across susceptible populations killing many

Natural selection operating on both the bacterial and human population has lessened the virulence of the infection

Recent resurgence reflects AIDS and increasing bacterial resistance to antibiotics

# Bacterial Antibiotic-Resistance

Bacteria become resistant in two ways:

1) Mutation passed from one bacterial generation to another by cell division

2) Groups of resistant genes are passed on transposons; they are transmitted from cell to cell by plasmids

A particularly dangerous strain is methicillin-resistant *Staphylococcus aureus* (MRSA)

# Natural Selection in HIV

RNA or DNA viruses replicate often and errors are not repaired

Viral mutations accumulate rapidly

In HIV infection, natural selection controls the diversity of HIV variants within the human body as the disease progresses

The human immune system and drugs to slow infection become selective agents

Combinations of drugs that act in different ways are more effective

Initially the immune system identifies and eliminates many cells infected with HIV

Mutations occur in the virus

Viral mutations allowing increased replication or immune system evasion are favored

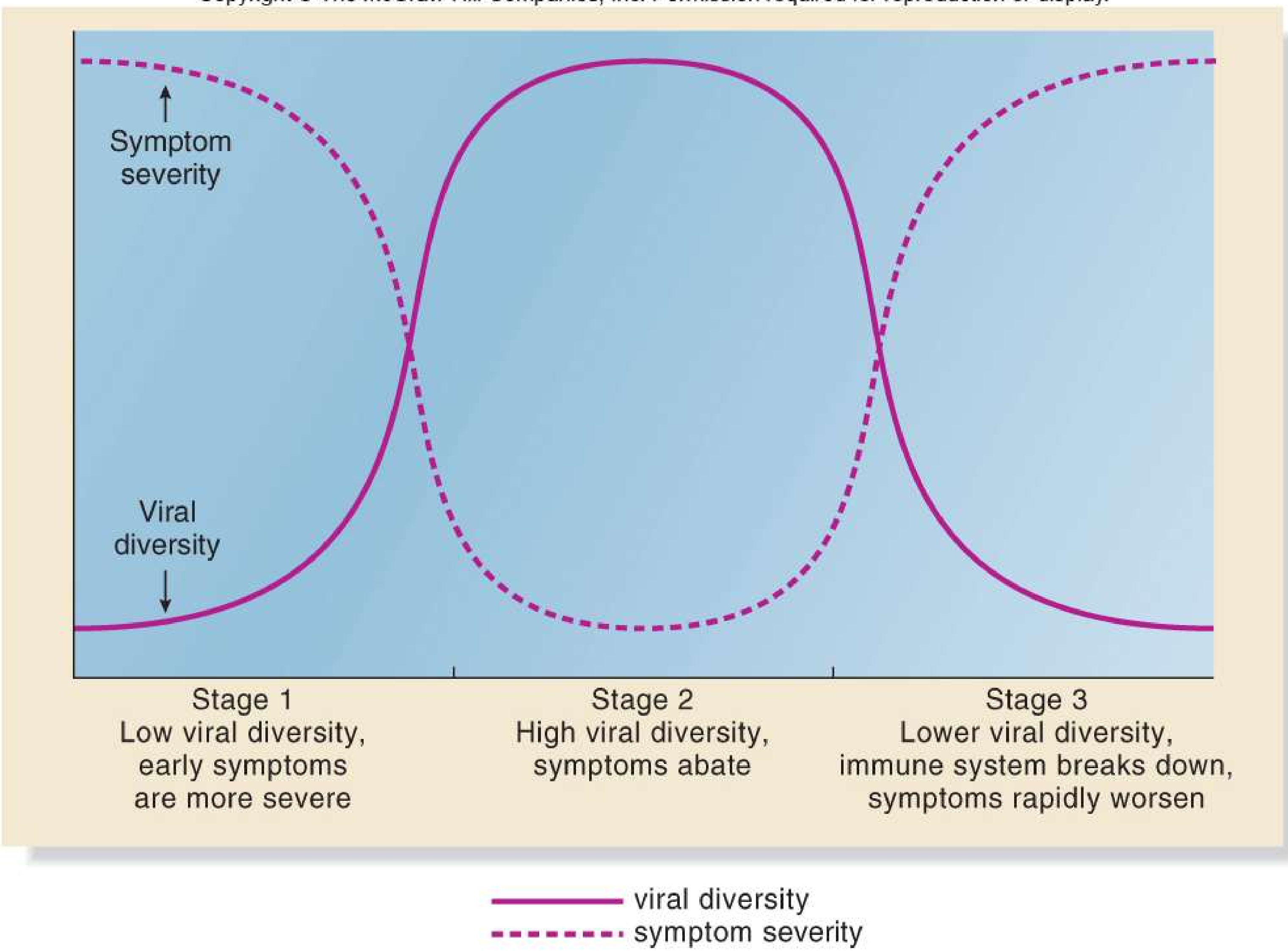
Gradually the immune system of the infected person can no longer fight off the HIV infection

HIV infection progresses to AIDS when lack of an intact immune system leads to opportunistic infections

Now becoming chronic rather than lethal

# Figure 15.14




Symptom severity
Viral diversity
Stage 1
Low viral diversity, early symptoms are more severe
Stage 2
High viral diversity, symptoms abate
Stage 3
Lower viral diversity, immune system breaks down, symptoms rapidly worsen
viral diversity
symptom severity

# Balanced Polymorphism

Persistence of harmful recessive alleles due to heterozygotes

When two or more forces (environmental threat vs. harmful allele) act in different directions on alleles of a gene

Also called **heterozygote advantage**

- Have a reproductive advantage under certain conditions

# Balanced Polymorphism

Table 15.3



**Table 15.3** **Balanced Polymorphism**

| Disease 1 (inherited, carrier) | Protects against → Disease 2 | Because → Mechanism | References |
|---|---|---|---|
| Sickle cell disease | Malaria | Atypical red blood cells cannot retain parasites | Section 12.2 |
| G6PD deficiency | Malaria | Parasite cannot reproduce in atypical red blood cells | Section 12.5 |
| PKU | Fungal infection in fetuses | Elevated phenylalanine inactivates fungal toxin | Sections 5.2, 10.4, 14.1, 15.6 |
| Prion protein mutation | Transmissible spongiform encephalopathy | Prion protein cannot misfold in presence of infectious prion protein | Figure 10.22, section 12.5, Reading 10.1 |
| CF | Diarrheal disease (cholera, typhoid fever) | Fewer chloride channels in intestinal cells prevent water loss | Sections 14.1, 14.3, Readings 2.2, 4.2 |
| Smith-Lemli-Opitz syndrome | Cardiovascular disease | Lowered serum cholesterol | MIM 270400 (multiple birth defects, intellectual disability) |

# Sickle Cell Disease and Malaria

The beta hemoglobin gene exhibits balanced polymorphism

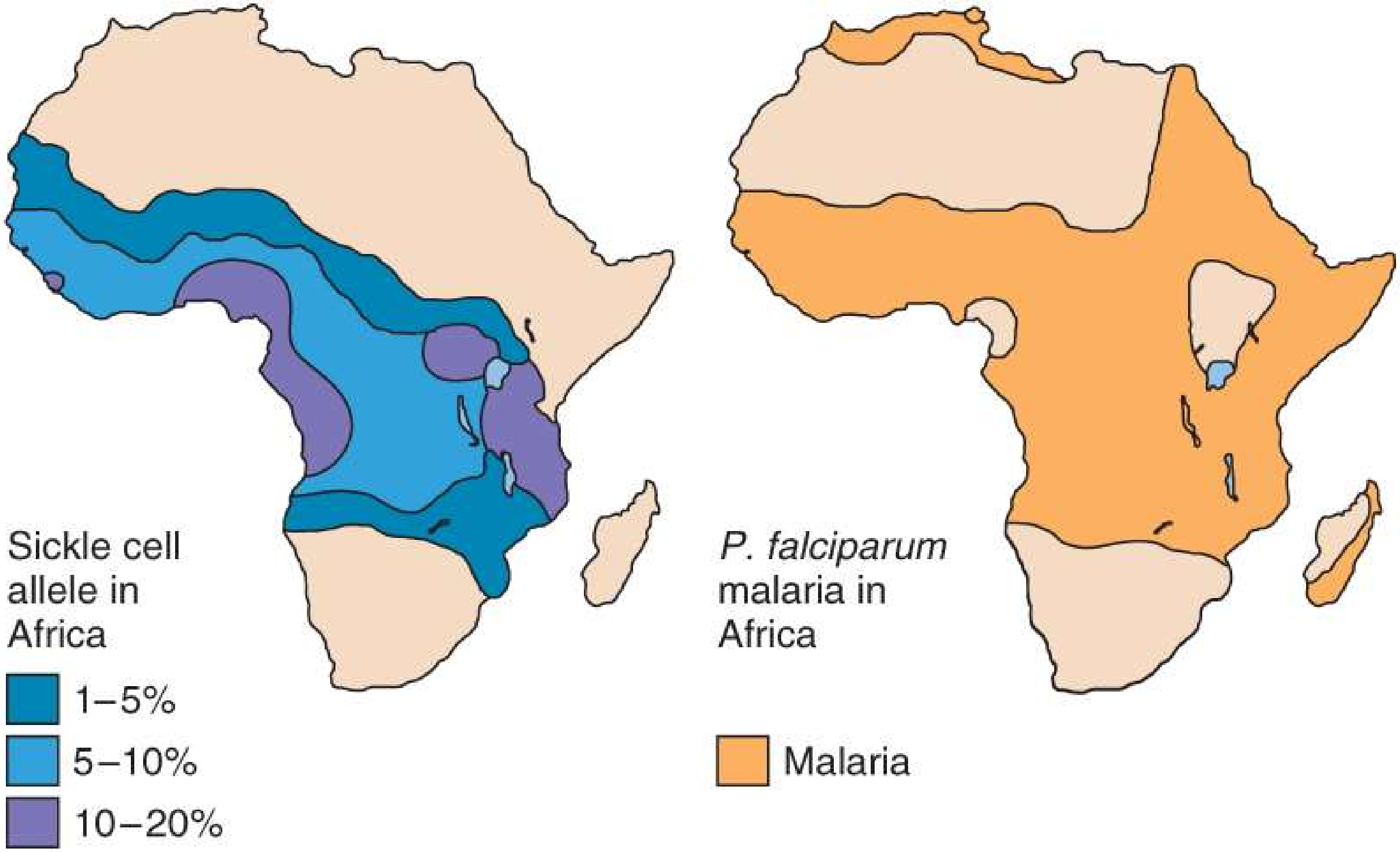
Sickle cell allele causes the recessive sickle cell anemia trait (when homozygous) and is therefore under negative selection

Sickle cell allele helps protect heterozygotes from malaria therefore under positive selection

# Sickle Cell Disease and Malaria

**Figure 15.15**





# Prion Disease and Cannibalism

Kuru is an illness causing brain degeneration in the Foré people in New Guinea

The tribe practiced ritual cannibalism

Heterozygotes for a protein folding gene may protect from transmissible spongiform encephalopathies

# Cystic Fibrosis and Diarrheal Disease

Diarrheal diseases can be major killers

CFTR protein affects chloride channels

Cholera toxin causes chloride channels to open producing severe dehydration

Typhoid fever requires a functional CFTR for bacteria to enter the cell

Heterozygotes have some protection from these two bacterial diseases

Table 15.4

**Table 15.4** **Forces that Change Allele Frequencies**

| Mechanism of Allele Frequency Change | Examples |
|---|---|
| Nonrandom mating | Agriculture<br>Cape population and Arnold<br>Hopi Indians with albinism<br>Genghis Khan's Y chromosome |
| Migration | Consanguinity<br>Galactokinase deficiency in Europe<br>ABO blood type distribution<br>Clines along the Nile and in Italy |
| Genetic drift | |
| Founder effect | Norfolk Island mutineer descendants and migraine<br>Disorders among Old Order Amish and Mennonites<br>Afrikaners and porphyria variegata |
| Population bottleneck | Pingelapese blindness<br>Cheetahs<br>Pogroms against Ashkenazi Jews |
| Mutation | Chapters 12 and 13 |
| Natural selection | Lactose intolerance<br>Tibetan adaptation to high altitude<br>TB incidence and virulence<br>HIV infection<br>Antibiotic resistance in bacteria<br>Sickle cell disease and malaria<br>Prion disease and cannibalism<br>CF and diarrheal disease<br>PKU and protection against fungal infection |

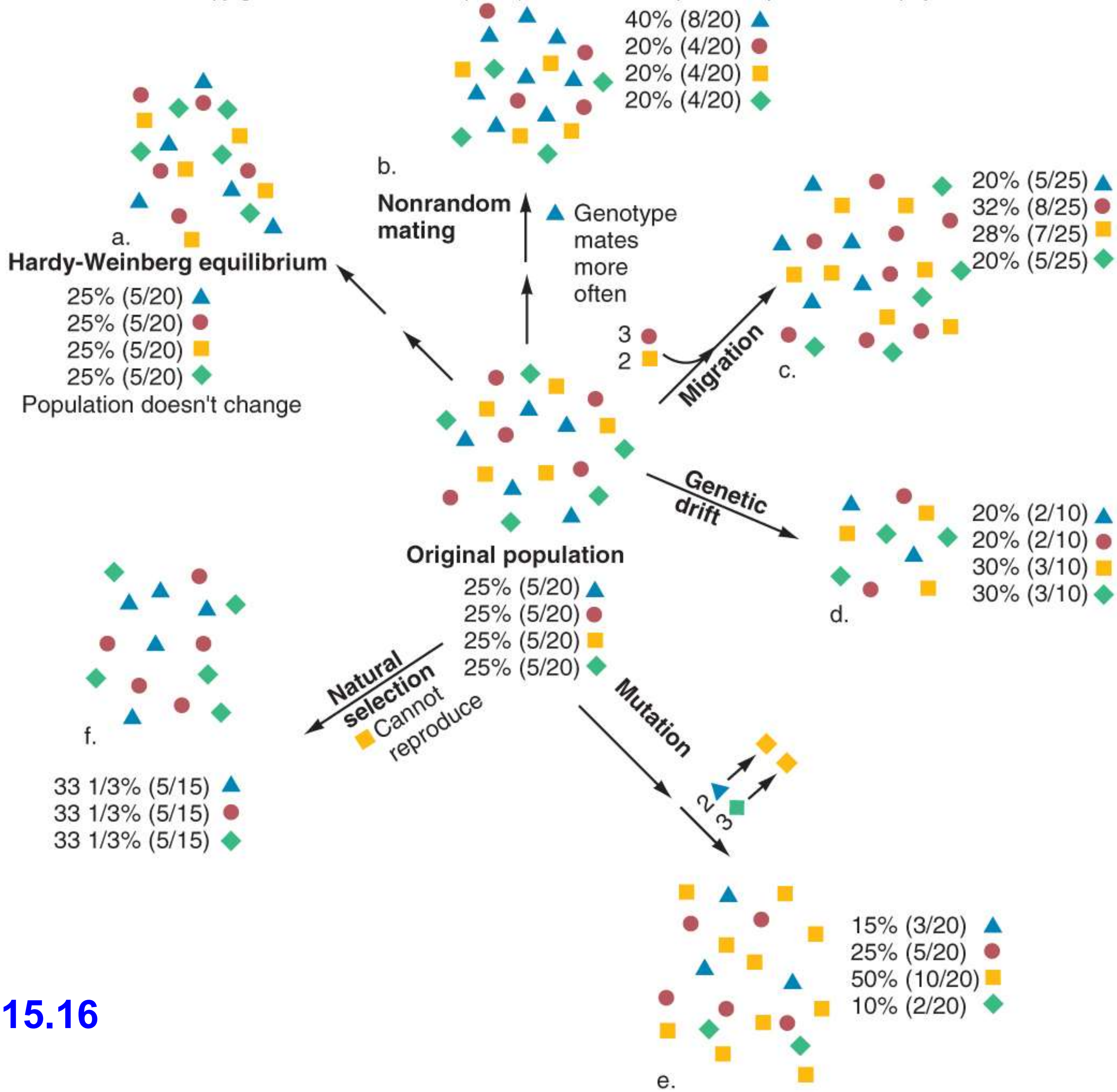

40% (8/20)
20% (4/20)
20% (4/20)
20% (4/20)
b.
Nonrandom mating
Genotype mates more often
a.
Hardy-Weinberg equilibrium
25% (5/20)
25% (5/20)
25% (5/20)
25% (5/20)
Population doesn't change
20% (5/25)
32% (8/25)
28% (7/25)
20% (5/25)
3
2
Migration
c.
Genetic drift
20% (2/10)
20% (2/10)
30% (3/10)
30% (3/10)
d.
Original population
25% (5/20)
25% (5/20)
25% (5/20)
25% (5/20)
f.
Natural selection
Cannot reproduce
Mutation
2
3
33 1/3% (5/15)
33 1/3% (5/15)
33 1/3% (5/15)
15% (3/20)
25% (5/20)
50% (10/20)
10% (2/20)
e.

**Figure 15.16**

# Phenylketonuria (PKU)

The diversity of PKU mutations suggests that the disease has arisen more than once

In most populations, point mutations in the PAH gene cause PKU

However, all Yemeni Jews in Israel with PKU have a large deletion

Records indicate that the deletion arose in San'a (the capital of Yemen)

- It then spread among Yemenite Jews

# Phenylketonuria (PKU)



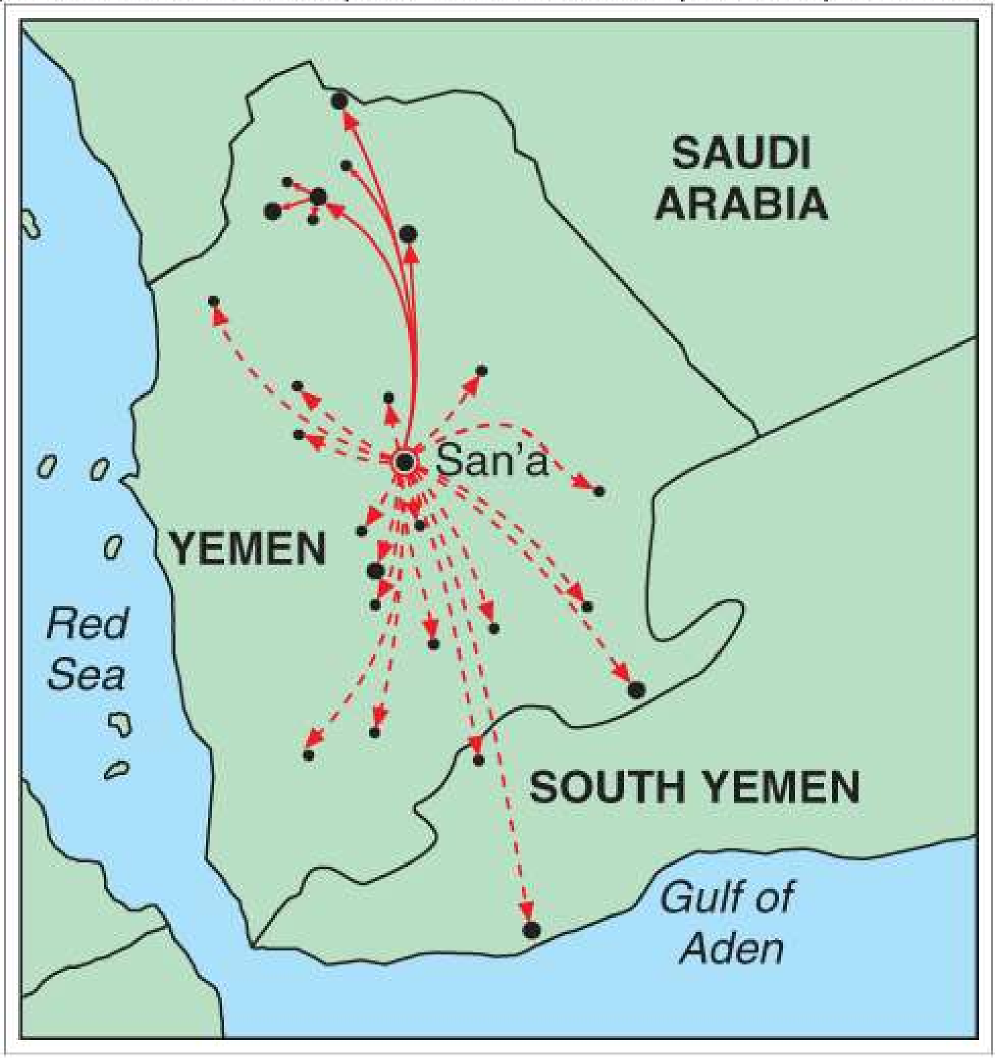



**Figure 15.17**

# Eugenics

The word **eugenics** was coined in 1883 by Sir Francis Galton to mean "good in birth"

On a societal level, eugenics is the control of human reproduction with the intent of changing a population's genetic structure

Positive eugenics = Promotes reproduction among those considered superior

Negative eugenics = Interferes with reproduction of those judged inferior

| Table 15.5 | A Chronology of Eugenics-Related Events |
| --- | --- |
| **1883** | Sir Francis Galton coins the term *eugenics*. |
| **1889** | Sir Francis Galton's writings are published in the book *Natural Inheritance*. |
| **1896** | Connecticut enacts law forbidding sex with a person who has epilepsy or is "feebleminded" or an "imbecile." |
| **1904** | Galton establishes the Eugenics Record Office at the University of London to keep family records. |
| **1907** | First eugenic law in the United States orders sterilization of institutionalized intellectually disabled males and criminal males when experts recommend it. |
| **1910** | Eugenics Record Office founded in Cold Spring Harbor, New York, to collect family and institutional data. |
| **1924** | Immigration Act limits entry into the United States of "idiots, imbeciles, feebleminded, epileptics, insane persons," and restricts immigration to 7 percent of the U.S. population from a particular country according to the 1890 census—keeping out those from southern and eastern Europe. |
| **1927** | Supreme Court (*Buck vs. Bell*) upholds compulsory sterilization of the intellectually disabled by a vote of 8 to 1, leading to many state laws. |
| **1934** | Eugenic sterilization law of Nazi Germany orders sterilization of individuals with conditions thought to be inherited, including epilepsy, schizophrenia, and blindness, depending upon rulings in Genetic Health Courts. |
| **1939** | Nazis begin killing 5,000 children with birth defects or intellectual disability, then 70,000 "unfit" adults. |
| **1956** | U.S. state eugenic sterilization laws are repealed, but 58,000 people have already been sterilized. |
| **1965** | U.S. immigration laws reformed, lifting many restrictions. |
| **1980s** | California's Center for Germinal Choice established, where Nobel Prize winners can deposit sperm to inseminate selected women. |
| **1990s** | In the U.S., state laws passed to prevent health insurance or employment discrimination based on genotype. |
| **2003** | Many governments recommend certain genetic tests, and enact legislation to prevent genetic discrimination. |
| **2004** | Genocide of black Africans in Sudan. |
| **2009** | U.S. Genetic Information Nondiscrimination Act enacted, but is limited in scope. |

**Table 15.5**

# Eugenics

Eugenics extends the concept of natural selection and Mendel's laws but does not translate well into practice

Some people consider modern genetic screening practices eugenic

- However, genetic testing typically aims to prevent or alleviate human suffering

Wars may have eugenic consequences

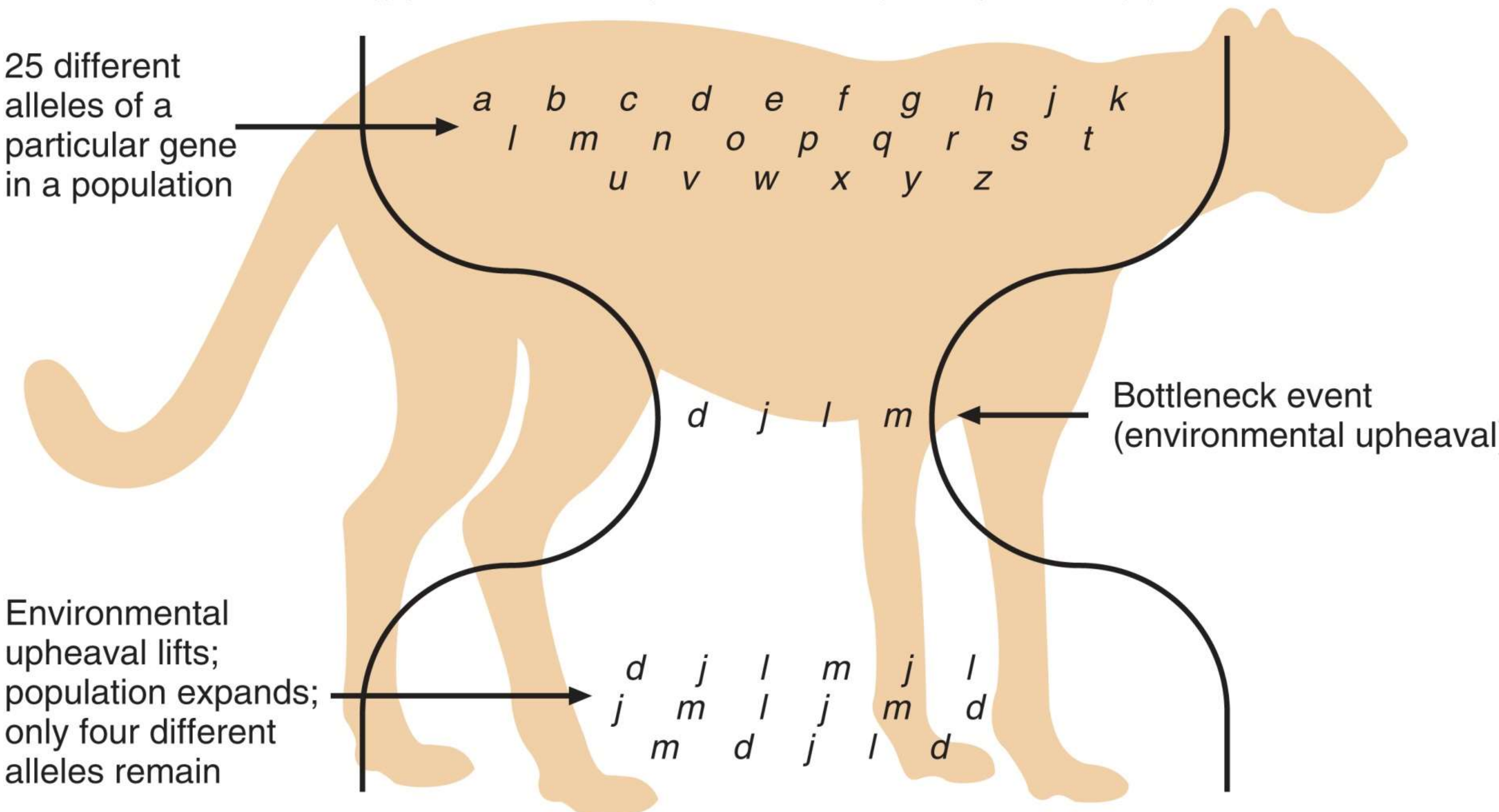

25 different alleles of a particular gene in a population
a b c d e f g h j k
l m n o p q r s t
u v w x y z
d j l m
Bottleneck event (environmental upheaval)
Environmental upheaval lifts; population expands; only four different alleles remain
d j l m j l
j m l j m d
m d j l d

**Figure 15.8**

| Table 15.7 | A Chronology of Eugenics-Related Events |
|---|---|
| **1883** | Sir Francis Galton coins the term *eugenics*. |
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| **1990s** | In the U.S., state laws passed to prevent health insurance or employment discrimination based on genotype. |
| **2003** | Many governments recommend certain genetic tests, and have legislation to prevent genetic discrimination. In the U.S., protective legislation is still in discussion. |
| **2004** | Genocide of black Africans occurs in Sudan. |
| **2008** | Federal genetic anti-discrimination legislation finalized in U.S. |
| **2009** | Genetic information nondiscrimination act enacted. |