**Overview: Drawing from the Deck of Genes**

- What genetic principles account for the passing of traits from parents to offspring?
- The "blending" hypothesis is the idea that genetic material from the two parents blends together (like blue and yellow paint blend to make green)
- The "particulate" hypothesis is the idea that parents pass on discrete heritable units (genes)
- This hypothesis can explain the reappearance of traits after several generations
- Mendel documented a particulate mechanism through his experiments with garden peas

**Concept 14.1: Mendel used the scientific approach to identify two laws of inheritance**

- Mendel discovered the basic principles of heredity by breeding garden peas in carefully planned experiments

**Mendel's Experimental, Quantitative Approach**

- Advantages of pea plants for genetic study
  - There are many varieties with distinct heritable features, or **characters** (such as flower color); character variants (such as purple or white flowers) are called **traits**
  - Mating can be controlled
  - Each flower has sperm-producing organs (stamens) and an egg-producing organ (carpel)
  - Cross-pollination (fertilization between different plants) involves dusting one plant with pollen from another
- Mendel chose to track only those characters that occurred in two distinct alternative forms
- He also used varieties that were **true-breeding** (plants that produce offspring of the same variety when they self-pollinate)
- In a typical experiment, Mendel mated two contrasting, true-breeding varieties, a process called **hybridization**
- The true-breeding parents are the **P generation**
- The hybrid offspring of the P generation are called the **$F_1$ generation**
- When $F_1$ individuals self-pollinate or cross- pollinate with other $F_1$ hybrids, the **$F_2$ generation** is produced

**The Law of Segregation**

- When Mendel crossed contrasting, true-breeding white- and purple-flowered pea plants, all of the $F_1$ hybrids were purple
- When Mendel crossed the $F_1$ hybrids, many of the $F_2$ plants had purple flowers, but some had white
- Mendel discovered a ratio of about three to one, purple to white flowers, in the $F_2$ generation
- Mendel reasoned that only the purple flower factor was affecting flower color in the $F_1$ hybrids
- Mendel called the purple flower color a dominant trait and the white flower color a

recessive trait
- The factor for white flowers was not diluted or destroyed because it reappeared in the $F_2$ generation
- Mendel observed the same pattern of inheritance in six other pea plant characters, each represented by two traits
- What Mendel called a "heritable factor" is what we now call a gene

***Mendel's Model***
- Mendel developed a hypothesis to explain the 3:1 inheritance pattern he observed in $F_2$ offspring
- Four related concepts make up this model
- These concepts can be related to what we now know about genes and chromosomes

- First: alternative versions of genes account for variations in inherited characters
- For example, the gene for flower color in pea plants exists in two versions, one for purple flowers and the other for white flowers
- These alternative versions of a gene are now called **alleles**
- Each gene resides at a specific locus on a specific chromosome

- Second: for each character, an organism inherits two alleles, one from each parent
- Mendel made this deduction without knowing about the role of chromosomes
- The two alleles at a particular locus may be identical, as in the true-breeding plants of Mendel's P generation
- Alternatively, the two alleles at a locus may differ, as in the $F_1$ hybrids

- Third: if the two alleles at a locus differ, then one (the **dominant allele**) determines the organism's appearance, and the other (the **recessive allele**) has no noticeable effect on appearance
- In the flower-color example, the $F_1$ plants had purple flowers because the allele for that trait is dominant

- Fourth (now known as the **law of segregation**): the two alleles for a heritable character separate (segregate) during gamete formation and end up in different gametes
- Thus, an egg or a sperm gets only one of the two alleles that are present in the organism
- This segregation of alleles corresponds to the distribution of homologous chromosomes to different gametes in meiosis

- Mendel's segregation model accounts for the 3:1 ratio he observed in the $F_2$ generation of his numerous crosses
- The possible combinations of sperm and egg can be shown using a **Punnett square**, a diagram for predicting the results of a genetic cross between individuals of known genetic makeup
- A capital letter represents a dominant allele, and a lowercase letter represents a recessive allele

***Useful Genetic Vocabulary***

- An organism with two identical alleles for a character is said to be **homozygous** for the gene controlling that character
- An organism that has two different alleles for a gene is said to be **heterozygous** for the gene controlling that character
- Unlike homozygotes, heterozygotes are not true-breeding
- Because of the different effects of dominant and recessive alleles, an organism's traits do not always reveal its genetic composition
- Therefore, we distinguish between an organism's **phenotype**, or physical appearance, and its **genotype**, or genetic makeup
- In the example of flower color in pea plants, *PP* and *Pp* plants have the same phenotype (purple) but different genotypes

***The Testcross***

- How can we tell the genotype of an individual with the dominant phenotype?
- Such an individual could be either homozygous dominant or heterozygous
- The answer is to carry out a **testcross**: breeding the mystery individual with a homozygous recessive individual
- If any offspring display the recessive phenotype, the mystery parent must be heterozygous

**The Law of Independent Assortment**

- Mendel derived the law of segregation by following a single character
- The $F_1$ offspring produced in this cross were **monohybrids**, individuals that are heterozygous for one character
- A cross between such heterozygotes is called a **monohybrid cross**

- Mendel identified his second law of inheritance by following two characters at the same time
- Crossing two true-breeding parents differing in two characters produces **dihybrids** in the $F_1$ generation, heterozygous for both characters
- A **dihybrid cross**, a cross between $F_1$ dihybrids, can determine whether two characters are transmitted to offspring as a package or independently

- Using a dihybrid cross, Mendel developed the **law of independent assortment**
- The law of independent assortment states that each pair of alleles segregates independently of each other pair of alleles during gamete formation
- Strictly speaking, this law applies only to genes on different, nonhomologous chromosomes or those far apart on the same chromosome
- Genes located near each other on the same chromosome tend to be inherited together

**Concept 14.2: The laws of probability govern Mendelian inheritance**

- Mendel's laws of segregation and independent assortment reflect the rules of probability

- When tossing a coin, the outcome of one toss has no impact on the outcome of the next toss
- In the same way, the alleles of one gene segregate into gametes independently of another gene's alleles

**The Multiplication and Addition Rules Applied to Monohybrid Crosses**

- The **multiplication rule** states that the probability that two or more independent events will occur together is the product of their individual probabilities
- Probability in an $F_1$ monohybrid cross can be determined using the multiplication rule
- Segregation in a heterozygous plant is like flipping a coin: Each gamete has a 50% chance of carrying the dominant allele and a 50% chance of carrying the recessive allele

- The **addition rule** states that the probability that any one of two or more exclusive events will occur is calculated by adding together their individual probabilities
- The rule of addition can be used to figure out the probability that an $F_2$ plant from a monohybrid cross will be heterozygous rather than homozygous

**Solving Complex Genetics Problems with the Rules of Probability**

- We can apply the multiplication and addition rules to predict the outcome of crosses involving multiple characters
- A dihybrid or other multicharacter cross is equivalent to two or more independent monohybrid crosses occurring simultaneously
- In calculating the chances for various genotypes, each character is considered separately, and then the individual probabilities are multiplied

**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

- 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

- **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, 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

***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

**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

***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

**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

**Concept 14.4: Many human traits follow Mendelian patterns of inheritance**
- Humans are not good subjects for genetic research
  - Generation time is too long
  - Parents produce relatively few offspring
  - Breeding experiments are unacceptable
- However, basic Mendelian genetics endures as the foundation of human genetics

**Pedigree Analysis**
- A **pedigree** is a family tree that describes the interrelationships of parents and children across generations
- Inheritance patterns of particular traits can be traced and described using pedigrees

- Pedigrees can also be used to make predictions about future offspring
- We can use the multiplication and addition rules to predict the probability of specific phenotypes

**Recessively Inherited Disorders**

- Many genetic disorders are inherited in a recessive manner
- These range from relatively mild to life-threatening

***The Behavior of Recessive Alleles***

- Recessively inherited disorders show up only in individuals homozygous for the allele
- **Carriers** are heterozygous individuals who carry the recessive allele but are phenotypically normal; most individuals with recessive disorders are born to carrier parents
- Albinism is a recessive condition characterized by a lack of pigmentation in skin and hair

- If a recessive allele that causes a disease is rare, then the chance of two carriers meeting and mating is low
- Consanguineous matings (i.e., matings between close relatives) increase the chance of mating between two carriers of the same rare allele
- Most societies and cultures have laws or taboos against marriages between close relatives

***Cystic Fibrosis***

- **Cystic fibrosis** is the most common lethal genetic disease in the United States,striking one out of every 2,500 people of European descent
- The cystic fibrosis allele results in defective or absent chloride transport channels in plasma membranes leading to a buildup of chloride ions outside the cell
- Symptoms include mucus buildup in some internal organs and abnormal absorption of nutrients in the small intestine

***Sickle-Cell Disease: A Genetic Disorder with Evolutionary Implications***

- **Sickle-cell disease** affects one out of 400 African-Americans
- The disease is caused by the substitution of a single amino acid in the hemoglobin protein in red blood cells
- In homozygous individuals, all hemoglobin is abnormal (sickle-cell)
- Symptoms include physical weakness, pain, organ damage, and even paralysis

- Heterozygotes (said to have sickle-cell trait) are usually healthy but may suffer some symptoms
- About one out of ten African Americans has sickle cell trait, an unusually high frequency of an allele with detrimental effects in homozygotes
- Heterozygotes are less susceptible to the malaria parasite, so there is an advantage to being heterozygous

**Dominantly Inherited Disorders**

- Some human disorders are caused by dominant alleles
- Dominant alleles that cause a lethal disease are rare and arise by mutation

- *Achondroplasia* is a form of dwarfism caused by a rare dominant allele

***Huntington's Disease: A Late-Onset Lethal Disease***

- The timing of onset of a disease significantly affects its inheritance
- **Huntington's disease** is a degenerative disease of the nervous system
- The disease has no obvious phenotypic effects until the individual is about 35 to 40 years of age
- Once the deterioration of the nervous system begins the condition is irreversible and fatal

**Multifactorial Disorders**

- Many diseases, such as heart disease, diabetes, alcoholism, mental illnesses, and cancer have both genetic and environmental components
- Little is understood about the genetic contribution to most multifactorial diseases

**Genetic Testing and Counseling**

- Genetic counselors can provide information to prospective parents concerned about a family history for a specific disease

***Counseling Based on Mendelian Genetics and Probability Rules***

- Using family histories, genetic counselors help couples determine the odds that their children will have genetic disorders
- Probabilities are predicted on the most accurate information at the time; predicted probabilities may change as new information is available

***Tests for Identifying Carriers***

- For a growing number of diseases, tests are available that identify carriers and help define the odds more accurately

***Fetal Testing***

- In **amniocentesis**, the liquid that bathes the fetus is removed and tested
- In **chorionic villus sampling (CVS)**, a sample of the placenta is removed and tested
- Other techniques, such as *ultrasound* and *fetoscopy*, allow fetal health to be assessed visually in utero

***Newborn Screening***

- Some genetic disorders can be detected at birth by simple tests that are now routinely performed in most hospitals in the United States