Exam II Lectures and Text Pages

- I. Cell Cycles
  - Mitosis (218 – 228)
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- II. Mendelian Genetics (251 – 270)

- III. Chromosomal Genetics

- IV. Molecular Genetics
  - Replication
  - Transcription and Translation

- V. Microbial Models

- VI. DNA Technology

Beyond Mendel

- Mendelian characters are determined by one gene with two alleles, and complete dominance.

- The relationship between genotype and phenotype is rarely that simple.

- Segregation and independent assortment can still be extended to these more complex cases.

Single Locus Characters - Dominance

- Spectral of dominance – Dominance varies from complete dominance at one extreme with codominance at the other, with various degrees of incomplete dominance between.

- Complete dominance: One allele is fully expressed in the phenotype of a heterozygote, and it masks the phenotypic expression of the recessive.
  - The heterozygote and homozygous dominant are phenotypically indistinguishable.
Codominance

- Two dominant alleles affect the phenotype in separate, distinguishable ways. Both codominant alleles are fully expressed.
- Examples:
  - The human blood group MN (glycoproteins)
  - The A and B alleles of the ABO blood group

Incomplete Dominance

- The phenotype of F₁ hybrids is some intermediate between the phenotypes of the two parental varieties
- Heterozygotes can be distinguished from homozygotes by their phenotypes, the phenotypic and genotypic ratios in the F₂ of a monohybrid cross are the same—1:2:1.

The Relation Between Dominance and Phenotype

- Dominant and recessive alleles
  - Do not really “interact” at the level of the DNA
  - Lead to synthesis of different proteins that produce a phenotype
Frequency of Dominant Alleles

- Dominance does not determine the relative abundance of alleles
- Dominant alleles
  - Are not necessarily more common
  - Example: Polydactyly is rare in the U.S. (1 in 400 births).

Dominance? – At What Level?

- Tay-Sachs - only homozygous recessives for the T-S allele have the disease.
  - Brain cells of Tay-Sachs babies lack a lipid-metabolizing enzyme. Lipids accumulate in the brain, causing disease symptoms and death.
- 1. Organismal level: heterozygotes are symptom free, appears that the normal allele is completely dominant.
- 2. Biochemical level: Heterozygotes have enzyme activity levels that are intermediate between the two homozygotes. Inheritance seems to be incomplete dominance.
- 3. Molecular level: Heterozygotes produce equal amounts of normal and dysfunctional enzymes. The alleles are actually codominant.

Multiple Alleles

- The ABO blood group in humans has 3 alleles
  - a. Diploid combinations of the alleles produce four phenotypes: Blood type A, B, AB, or O.
  - b. A and B are polysaccharides (A and B antigens) on the surface of RBCs.
  - c. The three alleles are: IA, IB, and i.
    - IA codes for the production of A antigen, IB codes for B antigen, and i does not code for any antigen.
    - IA and IB are codominant
    - IA and IB are dominant to allele i.
  - d. There are six genotypes: IAIA, IAi, IAIB, IBIB, IBi, and ii.
  - e. Antigens are located on the cell and antibodies are in the serum.
    - Antibodies against foreign antigens react with foreign antigens on the foreign red cells.
    - In transfusions, the antigens of the donor must be compatible with the antibodies of the recipient. O is the universal donor.

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<thead>
<tr>
<th>Table 14.2</th>
<th>Determination of ABO Blood Group by Multiple Alleles</th>
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<tbody>
<tr>
<td>Genotype</td>
<td>Phenotype (Blood Group)</td>
</tr>
<tr>
<td>IAIA</td>
<td>A</td>
</tr>
<tr>
<td>IAi</td>
<td>A</td>
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<td>IAIB</td>
<td>AB</td>
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<td>IBIB</td>
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<td>IBi</td>
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<td>ii</td>
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**Pleiotropy**

- In pleiotropy
  - A single gene has multiple phenotypic effects

- **Example:** In many hereditary diseases, a single defective gene causes complex sets of symptoms.

- **Example:** One gene can also influence a combination of seemingly unrelated characteristics. In tigers and Siamese cats, the gene that controls fur pigmentation also influences the connections between a cat’s eyes and the brain. A defective gene causes abnormal pigmentation and crossed-eyes.

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**Characters Controlled by Two or More Loci**

- Some traits may be determined by two or more genes

- **In epistasis,** a gene at one locus alters the phenotypic expression of a gene at a second locus
  - If one gene suppresses the expression of another, the first gene is said to be **epistatic** to the second.
  - If epistasis occurs between two non-linked genes, the phenotypic ratio resulting from a dihybrid cross will deviate from 9:3:3:1.

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**An Example of Epistasis**

- In rodents, the gene for pigment deposition (C) is epistatic to the gene for pigment production. Homozygous recessive for deposition (cc) will result in an albino regardless of the genotype at the production locus. Both genes affect the same character, but they are inherited separately and will assort independently.

- A cross between black mice that are heterozygous for both genes results in a 9:3:4 phenotypic ratio:
  - 9 Black (B_C_); 3 Brown (bcC_); 4 Albino (___cc)

![Figure 14.11](image-url)
Polygenic Inheritance

- Mendel's characters were discrete and could be classified on an either-or basis.
- Many characters are quantitative characters that vary by degree along a continuum within a population.
  - Continuous variation is usually determined by many loci or polygenic inheritance = Mode of inheritance in which the additive effect of two or more genes determines a single phenotypic character.

Quantitative Variation

- Quantitative variation usually indicates polygenic inheritance

A simplified model for the inheritance of skin color:
Three genes with the dark-skin allele (A, B, C) contribute one "unit" of darkness to the phenotype. These alleles are incompletely dominant over the other alleles (a, b, c).
- AABBCC is very dark and aabbcc is very light.
- AaBbCc has skin of an intermediate shade.
- The alleles have a cumulative effect, genotypes AaBbCc and AaBbcc make the same contribution to skin darkness.

Environmental factors, such as sun exposure, could also affect the phenotype.

Nature vs. Nurture – Environmental Impact

- Environmental conditions can influence the phenotypic expression of a gene, so a single genotype may produce a range of phenotypes. This environmentally-induced phenotypic range is the norm of reaction for the genotype.
Norm of Reaction for a Genotype

- The phenotypic range of a particular genotype that is influenced by the environment
  - May be limited, so a genotype only produces a specific phenotype, (ABO blood type)
  - May include a wide range of possibilities. Example: blood cell count varies with environmental factors such as altitude, activity level, or infections.
  - Are generally broadest for polygenic characters. The expression of most polygenic characters, is multifactorial; depends upon many factors – a variety of possible genotypes, and a variety of environmental influences.

Figure 14.13

Integrating a Mendelian View of Heredity and Variation

- Patterns of inheritance that are departures from simple Mendelian characters, can be integrated into a comprehensive theory of Mendelian genetics.
  1. Holistically, an organism's entire phenotype reflects its overall genotype and unique environmental history.
  2. Extending Mendel's principles of segregation and independent assortment can help explain more complex hereditary patterns such as epistasis and quantitative characters.

Mendelian Inheritance in Humans

- Many human traits follow Mendelian patterns of inheritance
- Humans are not convenient subjects for genetic research
  1. Generation time is about 20 years.
  2. Produce comparatively few offspring.
  3. Well-planned breeding experiments are impossible.
**Pedigree Analysis**

- A pedigree
  - Is a family tree that shows the results of matings that have already occurred
  - Shows the inheritance pattern of a particular character

Squares = males and circles = females

A horizontal line connecting a male and female indicates mating; offspring are listed below in birth order, left to right.

Shaded symbols are individuals showing the trait being traced.

**Inheritance patterns**

- Often, we can look at pedigrees and determine if a trait is dominant or recessive, and you should be able to deduce the genotype of most individuals. We can also make predictions about future offspring.

**Recessive Disorders**

- Recessive alleles that cause disorders are usually defective versions of normal alleles.
  - Defective alleles code a malfunctioning protein or no protein.
  - Heterozygotes can be phenotypically normal, if one copy of the normal allele can produce sufficient quantities of the normal protein.

- Recessive disorders range in severity: from nonlethal traits to lethal diseases.
  - Because these disorders are caused by recessive alleles:
    - They are expressed only in homozygotes (aa) who inherit one recessive from each parent.
    - Heterozygotes (Aa) can be phenotypically normal and act as carriers.
  - Most people with recessive disorders are born to normal parents, both of whom are carriers.
    - The probability is 1/4 that a mating of two carriers (Aa X Aa) will produce a homozygous recessive.
    - The probability is 2/3 that a normal child from such a mating will be a heterozygote, or carrier.
Cystic Fibrosis

- The most common lethal genetic disease in the United States, strikes 1 in every 2,500 Caucasians (much rarer in other races).
- Four percent of the Caucasian population are carriers.
- Symptoms include
  - Mucus buildup in some internal organs
  - Abnormal absorption of nutrients in the small intestine

Tay-Sachs Disease

- Occurs in 1 out of 3,600 Ashkenazic births.
- This incidence is about 100 times higher than among Sephardic (Mediterranean) groups and people of non-Jewish descent.
- Disease symptoms are caused by the buildup of lipids in the brain.

Sickle-Cell Disease

- Sickle-cell disease
  - Affects 1/400 African-Americans, most common inherited disease in this group
  - Is caused by the substitution of a single amino acid in the hemoglobin
- Symptoms include
  - Physical weakness, pain, organ damage, and even paralysis
- About 1/10 African Americans are heterozygous for sickle-cell and are said to have the sickle-cell trait.
  - Carriers are usually healthy, although some suffer symptoms after extended periods of low blood oxygen.
  - Carriers can function normally because the alleles are codominant; heterozygotes produce both types of hemoglobin.
- The high incidence of carriers is due to heterozygote advantage.
Mating of Close Relatives

• The probability of inheriting the same rare harmful allele from both parents, is greater if the parents are closely related.
  - **Consanguinity**: A genetic relationship that results from shared ancestry
  - Parents with recently shared ancestry are more likely to inherit the same recessive alleles. The probability is higher that these matings will result in homozygotes for harmful recessives.

• It is difficult to accurately assess the extent to which consanguinity increases the incidence of inherited diseases. Embryos homozygous for deleterious mutations often spontaneously abort.
  - **Incest taboos**: Most cultures forbid marriage between close relatives. This may be the result of observations that stillbirths and birth defects are more common when parents are closely related.

Dominantly Inherited Disorders

• Lethal dominant alleles are rarer than lethal recessives, because:
  - They are always expressed, the effects are not masked in heterozygotes.
  - They usually result from new genetic mutations that occur in gametes and later kill the developing embryo.

• Late-acting lethal dominants can escape elimination if the disorder does not appear until after afflicted individuals have transmitted the gene to their children.

Achondroplasia

• A form of dwarfism (lethal when homozygous for the dominant allele)
  - Affects 1/10,000 people who are heterozygous for the gene.

• Homozygous recessives are normal (99.9% of the population).
Huntington’s Disease

- Degenerative disease of the nervous system
- No obvious effects until about 35 to 40 years of age. Irreversible and lethal once degeneration begins
- Molecular geneticists located the allele near the tip of chromosome #4.
- Children of an afflicted parent have a 50% chance of inheriting the lethal dominant. A newly developed test can detect the allele before symptoms appear.

Figure 14.16

Multifactorial Disorders

- Not all hereditary diseases are simple Mendelian traits.
- Many diseases have genetic AND environmental components
- Examples include:
  - Heart disease, diabetes, alcoholism, cancer and some forms of mental illness
- The hereditary component is often polygenic and poorly understood.
- Health may be maximized by optimizing the factors that can be controlled: the role of environmental and behavioral factors that influence the development of these diseases.

Genetic Testing and Counseling

- Genetic counselors
  - Can provide information to prospective parents concerned about a family history for a specific disease
- Risk assessment includes studying the family history for a disease using Mendel's law of segregation and probability to deduce risk.
Example

- A couple is planning to have a child, and both the man and woman had siblings who died from the same recessively inherited disorder. A genetic counselor could deduce the risk of their first child inheriting the disease by using the laws of probability:

  - Question: What is the probability that the husband and wife are each carriers?
  - Question: The chance of two carriers having a child with the disease?
  - Question: Probability that this couple’s firstborn will have the disorder?
  - Question: If the first child is born with the disease, what is the probability that the second child will inherit the disease?

The conception of each child is an independent random event. The genotype of one child does not influence the genotype of the other children.

Carrier Testing

- Several tests are available to determine if prospective parents are carriers of genetic disorders.
  - Tests are available that can determine heterozygous carriers for Tay-Sachs, cystic fibrosis, and sickle-cell.
  - Tests enable people to make informed decisions about having children.

Fetal Testing and Newborn Screening

- Other techniques such as ultrasound and fetoscopy allow examination of a fetus for major abnormalities.

- Newborn Screening - In most U.S. hospitals, simple tests are routinely performed at birth to detect genetic disorders such as PKU.