Was Mendel Wrong?

In 1872, a physician from Long Island, New York named George Huntington described a medical condition characterized by jerky, involuntary movements. Now known as Huntington disease, the condition typically appears in middle age. The initial symptoms are subtle, consisting of mild behavioral and neurological changes; but, as the disease progresses, speech is impaired, walking becomes difficult, and psychiatric problems develop that frequently lead to insanity. Most people who have Huntington disease live for 10 to 30 years after the disease begins; there is currently no cure or effective treatment.

Huntington disease appears with equal frequency in males and females, rarely skips generations and, when one parent has the disorder, approximately half of the children will be similarly affected. These are the hallmarks of an autosomal dominant trait— with one exception. The disorder occasionally arises before the age of 15 and, in these cases, progresses much more rapidly than it does when it arises in middle age. Among younger patients, the trait is almost always inherited from the father. According to Mendel’s principles of heredity (Chapter 3), males and females transmit autosomal traits with equal frequency, and reciprocal crosses should yield identical results; yet, for juvenile cases of Huntington...
disease, Mendel’s principles do not apply. Was Mendel wrong?

In 1983, a molecular geneticist at Massachusetts General Hospital named James Gusella determined that the gene causing Huntington disease is located near the tip of the short arm of chromosome 4. Gusella determined its location by analyzing DNA from members of the largest known family with Huntington disease, about 7000 people who live near Lake Maracaibo in Venezuela, more than 100 of whom have Huntington disease. Many experts predicted that, with the general location of the Huntington gene pinned down, the actual DNA sequence would be isolated within a few years. Despite intensive efforts, finding the gene took 10 years. When it was finally isolated in the spring of 1993 (Figure 5.1), the gene turned out to be quite different from any of those that code for the traits studied by Mendel.

The mutation that causes Huntington disease consists of an unstable region of DNA capable of expanding and contracting as it is passed from generation to generation. When the region expands, Huntington disease results. The degree of expansion affects the severity and age of onset of symptoms; the juvenile form of Huntington disease results from rapid expansion of the region, which occurs primarily when the gene is transmitted from father to offspring.

This genetic phenomenon — the earlier appearance of a trait as it is passed from generation to generation — is called anticipation. Like a number of other genetic phenomena, anticipation does not adhere to Mendel’s principles of heredity. This lack of adherence doesn’t mean that Mendel was wrong; rather, it means that Mendel’s principles are not, by themselves, sufficient to explain the inheritance of all genetic characteristics. Our modern understanding of genetics has been greatly enriched by the discovery of a number of modifications and extensions of Mendel’s basic principles, which are the focus of this chapter.

An important extension of Mendel’s principles of heredity — the inheritance of sex-linked characteristics — was introduced in Chapter 4. In this chapter, we will examine a number of additional refinements of Mendel’s basic tenets. We begin by reviewing the concept of dominance, emphasizing that dominance entails interactions between genes at one locus (allelic genes) and affects the way in which genes are expressed in the phenotype. Next, we consider lethal alleles and their effect on phenotypic ratios, followed by a discussion of multiple alleles. We then turn to interaction among genes at different loci (nonallelic genes). The phenotypic ratios produced by gene interaction are related to the ratios encountered in Chapter 3. In the latter part of the chapter, we will consider ways in which sex interacts with heredity. Our last stop will be a discussion of environmental influences on gene expression.

The modifications and extensions of hereditary principles discussed in this chapter do not invalidate Mendel’s important contributions; rather, they enlarge our understanding of heredity by building on the framework provided by his principles of segregation and independent assortment. These modifications rarely alter the way in which the genes are inherited; rather, they affect the ways in which the genes determine the phenotype.

Dominance Revisited

One of Mendel’s important contributions to the study of heredity is the concept of dominance — the idea that an individual possesses two different alleles for a characteristic, but the trait enclosed by only one of the alleles is observed in the phenotype. With dominance, the heterozygote possesses the same phenotype as one of the homozygotes. When biologists began to apply Mendel’s principles to organisms other than peas, it quickly became apparent that many characteristics do not exhibit this type of dominance. Indeed, Mendel
himself was aware that dominance is not universal, because he observed that a pea plant heterozygous for long and short flowering times had a flowering time that was intermediate between those of its homozygous parents. This situation, in which the heterozygote is intermediate in phenotype between the two homozygotes, is termed incomplete dominance.

Dominance can be understood in regard to how the phenotype of the heterozygote relates to the phenotypes of the homozygotes. In the example presented in Figure 5.2, flower color potentially ranges from red to white. One homozygous genotype, \(A^1A^1\), codes for red flowers, and another, \(A^2A^2\), codes for white flowers. Where the heterozygote falls on the range of phenotypes determines the type of dominance. If the heterozygote \((A^1A^2)\) has flowers that are the same color as those of the \(A^1A^1\) homozygote (red), then the \(A^1\) allele is completely dominant over the \(A^2\) allele; that is, red is dominant over white. If, on the other hand, the heterozygote has flowers that are a lighter shade of red or a slightly pink shade of white. As long as the heterozygote’s phenotype can be differentiated and falls within the range of the two homozygotes, dominance is incomplete. With incomplete dominance, the heterozygote need not be exactly intermediate (pink in our example) between the two homozygotes; it might be a slightly lighter shade of red or a slightly pink shade of white. As long as the heterozygote’s phenotype is not between those of its homozygous parents, this situation, in which the heterozygote is intermediate in phenotype between the two homozygotes, is termed incomplete dominance.

Another type of interaction between alleles is codominance, in which the phenotype of the heterozygote is not intermediate between the phenotypes of the homozygotes; rather, the heterozygote simultaneously expresses the phenotypes of both homozygotes. An example of codominance is seen in the MN blood types.

The MN locus codes for one of the types of antigens on the red blood cells. Unlike antigens foreign to the ABO and Rh blood groups (which also code for red-blood-cell antigens), foreign MN antigens do not elicit a strong immunological reaction, and therefore the MN blood types are not routinely considered in blood transfusions. At the MN locus, there are two alleles: the \(L^N\) allele, which codes for the \(M\) antigen; and the \(L^M\) allele, which codes for the \(N\) antigen. Homozygotes with genotype \(L^ML^M\) express the \(M\) antigen on their red blood cells and have the \(M\) blood type. Homozygotes with genotype \(L^NL^N\) express the \(N\) antigen and have the \(N\) blood type. Heterozygotes with genotype \(L^ML^N\) exhibit codominance and express both the \(M\) and the \(N\) antigens; they have blood type \(MN\). The differences between dominance, incomplete dominance, and codominance are summarized in Table 5.1.

The type of dominance that a character exhibits frequently depends on the level of the phenotype examined. An example is cystic fibrosis, one of the more common genetic disorders found in Caucasians and usually considered to be a recessive disease. People who have cystic fibrosis produce large quantities of thick, sticky mucus, which plugs up the airways of the lungs and clogs the ducts leading from the pancreas to the intestine, causing frequent respiratory infections and digestive problems. Even with medical treatment, patients with cystic fibrosis suffer chronic, life-threatening medical problems.

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**Table 5.1** Differences between dominance, incomplete dominance, and codominance

<table>
<thead>
<tr>
<th>Type of Dominance</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dominance</td>
<td>Phenotype of the heterozygote is the same as the phenotype of one of the homozygotes</td>
</tr>
<tr>
<td>Incomplete dominance</td>
<td>Phenotype of the heterozygote is intermediate (falls within the range) between the phenotypes of the two homozygotes</td>
</tr>
<tr>
<td>Codominance</td>
<td>Phenotype of the heterozygote includes the phenotypes of both homozygotes</td>
</tr>
</tbody>
</table>

---

**Figure 5.2** The type of dominance exhibited by a trait depends on how the phenotype of the heterozygote relates to the phenotypes of the homozygotes.
The gene responsible for cystic fibrosis resides on the long arm of chromosome 7. It encodes a protein termed cystic fibrosis transmembrane conductance regulator, mercifully abbreviated CFTR, which acts as a gate in the cell membrane and regulates the movement of chloride ions into and out of the cell. Patients with cystic fibrosis have a mutated, dysfunctional form of CFTR that causes the channel to stay closed, and so chloride ions build up in the cell. This buildup causes the formation of thick mucus and produces the symptoms of the disease.

Most people have two copies of the normal allele for CFTR, and produce only functional CFTR protein. Those with cystic fibrosis possess two copies of the mutated CFTR allele, and produce only the defective CFTR protein. Heterozygotes, with one normal and one defective CFTR allele, produce both functional and defective CFTR protein. Thus, at the molecular level, the alleles for normal and defective CFTR are codominant, because both alleles are expressed in the heterozygote. However, because one normal allele produces enough functional CFTR protein to allow normal chloride transport, the heterozygote exhibits no adverse effects, and the mutated CFTR allele appears to be recessive at the physiological level.

In summary, several important characteristics of dominance should be emphasized. First, dominance is a result of interactions between genes at the same locus; in other words, dominance is allelic interaction. Second, dominance does not alter the way in which the genes are inherited; it only influences the way in which they are expressed as a phenotype. The allelic interaction that characterizes dominance is therefore interaction between the products of the genes. Finally, dominance is frequently “in the eye of the beholder,” meaning that the classification of dominance depends on the level at which the phenotype is examined. As we saw with cystic fibrosis, an allele may exhibit codominance at one level and be recessive at another level.

**Lethal Alleles**

In 1905, Lucien Cuenot reported a peculiar pattern of inheritance in mice. When he mated two yellow mice, approximately $\frac{2}{3}$ of their offspring were yellow and $\frac{1}{3}$ were nonyellow. When he test-crossed the yellow mice, he found that all were heterozygous; he was never able to obtain a yellow mouse that bred true. There was a great deal of discussion about Cuenot’s results among his colleagues, but it was eventually realized that the yellow allele must be lethal when homozygous (Figure 5.3). A *lethal allele* is one that causes death at an early stage of development—often before birth—and so a some genotypes may not appear among the progeny.

Cuenot originally crossed two mice heterozygous for yellow: $Yy \times Yy$. Normally, this cross would be expected to produce $\frac{1}{4}$ YY, $\frac{1}{2}$ Yy, and $\frac{1}{4}$ yy (see Figure 5.3). The homozygous YY mice are conceived but never complete development, which leaves a 2:1 ratio of Yy (yellow) to yy (nonyellow) in the observed offspring; all yellow mice are heterozygous (Yy).

Another example of a lethal allele, originally described by Erwin Baur in 1907, is found in snapdragons. The aurea strain in these plants has yellow leaves. When two plants with yellow leaves are crossed, $\frac{2}{3}$ of the progeny have yellow leaves and $\frac{1}{3}$ have green leaves. When green is crossed with green, all the progeny have green leaves; however, when yellow is crossed with green, $\frac{2}{3}$ of the progeny are green and $\frac{1}{3}$ are yellow, confirming that all yellow-leaved snapdragons are heterozygous. A 2:1 ratio is almost always produced by a recessive lethal allele; so observing this ratio among the progeny of a cross between individuals with the same phenotype is a strong clue that one of the alleles is lethal.

In both of these examples, the lethal alleles are recessive because they cause death in homozygotes. Unlike its effect on survival, the effect of the allele on color is dominant; in both mice and snapdragons, a single copy of the allele in the heterozygote produces a yellow color. Lethal alleles also can be dominant; in this case, homozygotes and
heterozygotes for the allele die. Truly dominant lethal alleles cannot be transmitted unless they are expressed after the onset of reproduction, as in Huntington disease.

**Concepts**

A lethal allele causes death, frequently at an early developmental stage, and so one or more genotypes are missing from the progeny of a cross. Lethal alleles may modify the ratio of progeny resulting from a cross.

**Multiple Alleles**

Most of the genetic systems that we have examined so far consist of two alleles. In Mendel’s peas, for instance, one allele coded for round seeds and another for wrinkled seeds; in cats, one allele produced a black coat and another produced a gray coat. For some loci, more than two alleles are present within a group of individuals—the locus has multiple alleles. (Multiple alleles may also be referred to as an allelic series.) Although there may be more than two alleles present within a group, the genotype of each diploid individual still consists of only two alleles. The inheritance of characteristics encoded by multiple alleles is no different from the inheritance of characteristics encoded by two alleles, except that a greater variety of genotypes and phenotypes are possible.

**Duck-Feather Patterns**

An example of multiple alleles is seen at a locus that determines the feather pattern of mallard ducks. One allele, M, produces the wild-type mallard pattern. A second allele, M<sup>r</sup>, produces a different pattern called restricted, and a third allele, M<sup>d</sup>, produces a pattern termed dusky. In this allelic series, restricted is dominant over mallard and dusky, and mallard is dominant over dusky: M<sup>r</sup> > M > M<sup>d</sup>. The six genotypes possible with these three alleles and their resulting phenotypes are:

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Phenotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>M&lt;sup&gt;r&lt;/sup&gt;M&lt;sup&gt;r&lt;/sup&gt;</td>
<td>restricted</td>
</tr>
<tr>
<td>M&lt;sup&gt;r&lt;/sup&gt;M</td>
<td>restricted</td>
</tr>
<tr>
<td>M&lt;sup&gt;r&lt;/sup&gt;M&lt;sup&gt;d&lt;/sup&gt;</td>
<td>restricted</td>
</tr>
<tr>
<td>M M</td>
<td>mallard</td>
</tr>
<tr>
<td>M M&lt;sup&gt;d&lt;/sup&gt;</td>
<td>mallard</td>
</tr>
<tr>
<td>M&lt;sup&gt;d&lt;/sup&gt;M&lt;sup&gt;d&lt;/sup&gt;</td>
<td>dusky</td>
</tr>
</tbody>
</table>

In general, the number of genotypes possible will be \( \frac{n(n+1)}{2} \), where \( n \) equals the number of different alleles at a locus. Working crosses with multiple alleles is no different from working crosses with two alleles; Mendel’s principle of segregation still holds, as shown in the cross between a restricted duck and a mallard duck (Figure 5.4).

**The ABO Blood Group**

Another multiple-allele system is at the locus for the ABO blood group. This locus determines your ABO blood type and, like the MN locus, codes for antigens on red blood cells. The three common alleles for the ABO blood group locus are: I<sup>A</sup>, which codes for the A antigen; I<sup>B</sup>, which codes for the B antigen; and i, which codes for no antigen (O). We can represent the dominance relations among the ABO alleles as follows: I<sup>A</sup> > i, I<sup>B</sup> > i, I<sup>A</sup> = I<sup>B</sup>. The I<sup>A</sup> and I<sup>B</sup> alleles are both dominant over i and are codominant with each other; the AB phenotype is due to the presence of an I<sup>A</sup> allele and an I<sup>B</sup> allele, which results in the production of A and B antigens on red blood cells. An individual with genotype II produces neither antigen and has blood type O. The six common genotypes at this locus and their phenotypes are shown in Figure 5.5a.

Antibodies are produced against any foreign antigens (see Figure 5.5a). For instance, a person having blood type A produces B antibodies, because the B antigen is foreign. A person having blood type B produces A antibodies, and someone having blood type AB produces neither A nor B antibodies, because neither A nor B antigen is foreign. A person having blood type O possesses no A or B antigens; consequently, that person produces both A antibodies and B antibodies. The presence of antibodies against foreign ABO antigens means...
that successful blood transfusions are possible only between persons with certain compatible blood types (Figure 5.5b).

The inheritance of alleles at the ABO locus can be illustrated by a paternity suit involving the famous movie actor Charlie Chaplin. In 1941, Chaplin met a young actress named Joan Barry, with whom he had an affair. The affair ended in February 1942 but, 20 months later, Barry gave birth to a baby girl and claimed that Chaplin was the father. Barry then sued for child support. At this time, blood typing had just come into widespread use, and Chaplin’s attorneys had Chaplin, Barry, and the child blood typed. Barry had blood type A, which can be produced by either genotype $I^A I^A$ or $I^A i$. Her baby possessed blood type B, which can be produced by either genotype $I^B I^B$ or $I^B i$. The baby could not have inherited the $I^B$ allele from Barry (Barry could not carry an $I^B$ allele if she were blood type A); therefore the baby must have inherited the $i$ allele from her. Barry must have had genotype $I^A i$, and the baby must have had genotype $I^B i$. Because the baby girl inherited her $i$ allele from Barry, she must have inherited the $I^B$ allele from her father. With blood type O, produced only by genotype $ii$, Chaplin could not have been the father of Barry’s child. In the course of

Your answer should be no. Joan Barry had blood type A, which can be produced by either genotype $I^A I^A$ or $I^A i$. Her baby possessed blood type B, which can be produced by either genotype $I^B I^B$ or $I^B i$. The baby could not have inherited the $I^B$ allele from Barry (Barry could not carry an $I^B$ allele if she were blood type A); therefore the baby must have inherited the $i$ allele from her. Barry must have had genotype $I^A i$, and the baby must have had genotype $I^B i$. Because the baby girl inherited her $i$ allele from Barry, she must have inherited the $I^B$ allele from her father. With blood type O, produced only by genotype $ii$, Chaplin could not have been the father of Barry’s child. In the course of

the trial to settle the paternity suit, three pathologists came to the witness stand and declared that it was genetically impossible for Chaplin to have fathered the child. Nevertheless, the jury ruled that Chaplin was the father and ordered him to pay child support and Barry’s legal expenses.

More than two alleles (multiple alleles) may be present within a group of individuals, although each diploid individual still has only two alleles at that locus.

### Gene Interaction

In the dihybrid crosses that we examined in Chapter 3, each locus had an independent effect on the phenotype. When Mendel crossed a homozygous round and yellow plant (RRYY) with a homozygous wrinkled and green plant (rryy) and then self-fertilized the F$_1$, he obtained F$_2$ progeny in the following proportions:

- $\frac{9}{16}$ R$_{Y_\_}$ round, yellow
- $\frac{3}{16}$ R$_{y_\_}$ round, green
- $\frac{3}{16}$ rR$_{Y_\_}$ wrinkled, yellow
- $\frac{1}{16}$ rR$_{y_\_}$ wrinkled, green
In this example, the genes showed two kinds of independence. First, the genes at each locus are independent in their assortment in meiosis, which is what produces the 9:3:3:1 ratio of phenotypes in the progeny, in accord with Mendel’s principle of independent assortment. Second, the genes are independent in their phenotypic expression; the $R$ and $r$ alleles affect only the shape of the seed and have no influence on the color of the endosperm; the $Y$ and $y$ alleles affect only color and have no influence on the shape of the seed.

Frequently, genes exhibit independent assortment but do not act independently in their phenotypic expression; instead, the effects of genes at one locus depend on the presence of genes at other loci. This type of interaction between the effects of genes at different loci (genes that are not allelic) is termed gene interaction. With gene interaction, the products of genes at different loci combine to produce new phenotypes that are not predictable from the single-locus effects alone. In our consideration of gene interaction, we’ll focus primarily on interaction between the effects of genes at two loci, although interactions among genes at three, four, or more loci are common.

**Concepts**

In gene interaction, genes at different loci contribute to the determination of a single phenotypic characteristic.

**Gene Interaction That Produces Novel Phenotypes**

Let’s first examine gene interaction in which genes at two loci interact to produce a single characteristic. Fruit color in the pepper Capsicum annuum is determined in this way. This plant produces peppers in one of four colors: red, brown, yellow, or green. If a homozygous plant with red peppers is crossed with a homozygous plant with green peppers, all the F$_1$ plants have red peppers (Fig. 5.6a). When the F$_1$ are crossed with one another, the F$_2$ are in a ratio of 9 red : 3 brown : 3 yellow : 1 green (Fig. 5.6b). This dihybrid ratio (Chapter 3) is produced by a cross between two plants that are both heterozygous for two loci (RrCc × RrCc). In peppers, a dominant allele $R$ at the first locus produces a red pigment; the recessive allele $r$ at this locus produces no red pigment. A dominant allele $C$ at the second locus causes decomposition of the green pigment chlorophyll; the recessive allele $c$ allows chlorophyll to persist. The genes at the two loci then interact to produce the colors seen in F$_2$ peppers:

<table>
<thead>
<tr>
<th>Genotype $\quad$ Phenotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>$R__C__$ $\quad$ red</td>
</tr>
<tr>
<td>$R__cc$ $\quad$ brown</td>
</tr>
<tr>
<td>$rrC__$ $\quad$ yellow</td>
</tr>
<tr>
<td>$rrcc$ $\quad$ green</td>
</tr>
</tbody>
</table>

To illustrate how Mendel’s rules of heredity can be used to understand the inheritance of characteristics determined by gene interaction, let’s consider a testcross between an F$_1$ plant from the cross in Figure 5.6 (RrCc) and a plant with green peppers (rrcc). As outlined in Chapter 3 (p. 000) for independent loci, we can work this cross by breaking it down into two simple crosses. At the first locus, the heterozygote $Rr$ is crossed with the homozygote $rr$; this cross produces $\frac{1}{2}$ $Rr$ and $\frac{1}{2}$ $rr$ progeny. Similarly, at the second locus, the heterozygous genotype $Cc$ is crossed with the homozygous genotype $cc$, producing $\frac{1}{2}$ $Cc$ and $\frac{1}{2}$ $cc$ progeny. In accord with Mendel’s principle of...
independent assortment, these single-locus ratios can be combined by using the multiplication rule: the probability of obtaining the genotype \( RrCc \) is the probability of \( Rr \) (\( 1/4 \)) multiplied by the probability of \( Cc \) (\( 1/4 \)), or \( 1/4 \). The probability of each progeny genotype resulting from the testcross is:

<table>
<thead>
<tr>
<th>Progeny genotype</th>
<th>Probability at each locus</th>
<th>Overall probability</th>
<th>Phenotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>RrCc</td>
<td>( 1/2 \times 1/2 = 1/4 )</td>
<td>( 1/4 )</td>
<td>red peppers</td>
</tr>
<tr>
<td>Rrcc</td>
<td>( 1/2 \times 1/2 = 1/4 )</td>
<td>( 1/4 )</td>
<td>brown peppers</td>
</tr>
<tr>
<td>rrCc</td>
<td>( 1/2 \times 1/2 = 1/4 )</td>
<td>( 1/4 )</td>
<td>yellow peppers</td>
</tr>
<tr>
<td>rrcC</td>
<td>( 1/2 \times 1/2 = 1/4 )</td>
<td>( 1/4 )</td>
<td>green peppers</td>
</tr>
</tbody>
</table>

When you work problems with gene interaction, it is especially important to determine the probabilities of single-locus genotypes and to multiply the probabilities of genotypes, not phenotypes, because the phenotypes cannot be determined without considering the effects of the genotypes at all the contributing loci.

Another example of gene interaction that produces novel phenotypes is seen in the genes that determine comb shape in chickens. The comb is the fleshy structure found on the head of a chicken. Genes at two loci (\( R, r \) and \( P, p \)) interact to determine the four types of combs shown in Figure 5.7. A walnut comb is produced when at least one dominant allele \( R \) is present at the first locus and at least one dominant allele \( P \) is present at the second locus (genotype \( R_P_ \)). A chicken with at least one dominant allele at the first locus and two recessive alleles at the second locus (genotype \( R_pp \)) possesses a rose comb. If two recessive alleles are present at the first locus and at least one dominant allele is present at the second (genotype \( rrP_ \)), the chicken has a pea comb. Finally, if two recessive alleles are present at both loci (\( rrpp \)), the bird has a single comb.

### Gene Interaction with Epistasis

Sometimes the effect of gene interaction is that one gene masks (hides) the effect of another gene at a different locus, a phenomenon known as **epistasis**. This phenomenon is similar to dominance, except that dominance entails the masking of genes at the same locus (allelic genes). In epistasis, the gene that does the masking is called the **epistatic gene**; the gene whose effect is masked is a **hypostatic gene**. Epistatic genes may be recessive or dominant in their effects.

Recessive epistasis. Recessive epistasis is seen in the genes that determine coat color in Labrador retrievers. These dogs may be black, brown, or yellow; their different coat colors are determined by interactions between genes at two loci (although a number of other loci also help to determine coat color; see p. 000). One locus determines the type of pigment produced by the skin cells: a dominant allele \( B \) codes for black pigment, whereas a recessive allele \( b \) codes for brown pigment. Alleles at a second locus affect the deposition of the pigment in the shaft of the hair; allele \( E \) allows dark pigment (black or brown) to be deposited, whereas a recessive allele \( e \) prevents the deposition of dark pigment, causing the hair to be yellow. The presence of genotype \( ee \) at the second locus therefore masks the expression of the black and brown alleles at the first locus. The
genotypes that determine coat color and their phenotypes are:

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Phenotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>B_E</td>
<td>black</td>
</tr>
<tr>
<td>bbE_</td>
<td>brown (frequently called chocolate)</td>
</tr>
<tr>
<td>B_ee</td>
<td>yellow</td>
</tr>
<tr>
<td>bbee</td>
<td>yellow</td>
</tr>
</tbody>
</table>

If we cross a black Labrador homozygous for the dominant alleles with a yellow Labrador homozygous for the recessive alleles and then intercross the F1, we obtain progeny in the F2 in a 9:3:4 ratio:

P: BBEE × bbee
black yellow

F1: BbEe
black

Intercross

F2: 9/16 B_E_ black
7/16 bbE_ brown
3/16 B_ee yellow
1/16 bbee yellow

Notice that yellow dogs can carry alleles for either black or brown pigment, but these alleles are not expressed in their coat color.

In this example of gene interaction, allele e is epistatic to B and b, because e masks the expression of the alleles for black and brown pigments, and alleles B and b are hypostatic to e. In this case, e is a recessive epistatic allele, because two copies of e must be present to mask the black and brown pigments.

Dominant epistasis Dominant epistasis is seen in the interaction of two loci that determine fruit color in summer squash, which is commonly found in one of three colors: yellow, white, or green. When a homozygous plant that produces white squash is crossed with a homozygous plant that produces green squash and the F1 plants are crossed with each other, the following results are obtained:

P: plants with white squash × plants with green squash

F1: plants with white squash

Intercross

F2: 12/16 plants with white squash
9/16 plants with yellow squash
3/16 plants with green squash

How can gene interaction explain these results?

In the F2, 12/16 or 3/4 of the plants produce white squash and 3/16 + 1/16 = 4/16 = 1/4 of the plants produce squash having color. This outcome is the familiar 3:1 ratio produced by a cross between two heterozygous individuals, which suggests that a dominant allele at one locus inhibits the production of pigment, resulting in white progeny. If we use the symbol W to represent the dominant allele that inhibits pigment production, then genotype W does not produce white squash, whereas WW allows pigment and results in colored squash.

Among those WW F2 plants with pigmented fruit, we observe 3/16 yellow and 1/16 green (a 3:1 ratio). This outcome is because a second locus determines the type of pigment produced in the squash, with yellow (Y) dominant over green (y). This locus is expressed only in wW plants, which lack the dominant inhibitory allele W. We can assign the genotype W_Y_ to plants that produce yellow squash and the genotype WW_yy to plants that produce green squash. The genotypes and their associated phenotypes are:

- W_Y_ white squash
- W_yy white squash
- WW_Y_ yellow squash
- WW_yy green squash

Allele W is epistatic to Y and y—it suppresses the expression of these pigment-producing genes. W is a dominant epistatic allele because, in contrast with e in Labrador retriever coat color, a single copy of the allele is sufficient to inhibit pigment production.

Summer squash provides us with a good opportunity for considering how epistasis often arises when genes affect a series of steps in a biochemical pathway. Yellow pigment in the squash is most likely produced in a two-step biochemical pathway (Figure 5.8). A colorless (white) compound (designated A in Figure 5.8) is converted by enzyme I into green compound B, which is then converted into yellow squash C by enzyme II. Compound C is the yellow pigment in the fruit.

Plants with the genotype wW produce enzyme I and may be green or yellow, depending on whether enzyme II is present. When allele Y is present at a second locus, enzyme II is produced and compound B is converted into compound C, producing a yellow fruit. When two copies of y, which does not encode a functional form of enzyme II, are present, squash remain green. The presence of W at the first locus inhibits the conversion of compound A into compound B; plants with genotype W_y do not make compound B and their fruit remains white, regardless of which alleles are present at the second locus.

Many cases of epistasis arise in this way. A gene (such as W) that has an effect on an early step in a biochemical pathway will be epistatic to genes (such as Y and y) that affect subsequent steps, because the effect of the enzyme in the later step depends on the product of the earlier reaction.
Duplicate recessive epistasis. Let’s consider one more detailed example of epistasis. Albinism is the absence of pigment and is a common genetic trait in many plants and animals. Pigment is almost always produced through a multistep biochemical pathway; thus, albinism may entail gene interaction. Robert T. Dillon and Amy R. Wethington found that albinism in the common freshwater snail *Physa heterostrhoa* can result from the presence of either of two recessive alleles at two different loci. Inseminated snails were collected from a natural population and placed in cups of water, where they laid eggs. Some of the eggs hatched into albino snails. When two albino snails were crossed, all of the F1 were pigmented. On intercrossing the F1, the F2 consisted of pigmented snails and albino snails. How did this 9:7 ratio arise?

The 9:7 ratio seen in the F2 snails can be understood as a modification of the 9:3:3:1 dihybrid ratio obtained when two individuals heterozygous for two loci are crossed. The 9:7 ratio arises when dominant alleles at both loci (A_B_) produce pigmented snails; any other genotype produces albino snails:

\[
P \quad \begin{align*} &aabb \quad AA.bb \\ &\quad \downarrow \\ &F_1 \quad \begin{align*} &AaBb \\ &\quad \downarrow \text{pigmented} \\ &F_2 \quad \begin{align*} &\frac{9}{16} A_\_B_ \quad \text{pigmented} \\ &\frac{3}{16} aA\_B \quad \text{albino} \\ &\frac{3}{16} A_\_bb \quad \text{albino} \\ &\frac{1}{16} aabb \quad \text{albino} \\ \end{align*} \end{align*}
\]

The 9:7 ratio in these snails is probably produced by a two-step pathway of pigment production (Figure 5.9). Pigment (compound C) is produced only after compound A has been converted into compound B by enzyme I and after compound B has been converted into compound C by enzyme II. At least one dominant allele A at the first locus is required to produce enzyme I; similarly, at least one dominant allele B at the second locus is required to produce enzyme II. Albinism arises from the absence of compound C, which may happen in three ways. First, two recessive alleles at the first locus (genotype aaB_) may prevent the production of enzyme I, and so compound B is never produced. Second, two recessive alleles at the second locus (genotype A_bb) may prevent the production of enzyme II. In this case, compound B is never converted into compound C. Third, two recessive alleles may be present at both loci (aabb), causing the absence of both enzyme I and enzyme II. In this example of gene interaction, a is epistatic to B, and b is epistatic to A; both are recessive epistatic alleles because the presence of two copies of either allele a or b is necessary to suppress pigment production. This example differs from the suppression of coat color in Labrador retrievers in that recessive alleles at either of two loci are capable of suppressing pigment production in the snails, whereas recessive alleles at a single locus suppress pigment expression in Labs.

**Concepts**

Epistasis is the masking of the expression of one gene by another gene at a different locus. The epistatic gene does the masking; the hypostatic gene is masked. Epistatic genes can be dominant or recessive.

**Connecting Concepts**

Interpreting Ratios Produced by Gene Interaction

A number of modified ratios that result from gene interaction are shown in Table 5.2. Each of these examples represents a modification of the basic 9:3:3:1 dihybrid ratio.

---

**Figure 5.9**

Yellow pigment in summer squash is produced in a two-step pathway.
A dominant allele at the A locus is required to produce enzyme I, which converts compound A into compound B.

A dominant allele at the B locus is required to produce enzyme II, which converts compound B into compound C (pigment).

Albinism arises from the absence of enzyme I (aaB_), so compound B is never produced...

...or from the absence of enzyme II (A_bb), so compound C is never produced, or from the absence of both enzymes (aa bb).

Pigmented snails must produce enzymes I and II, which requires genotype A_B_.

---

5.9 Pigment is produced in a two-step pathway in snails.

In interpreting the genetic basis of modified ratios, we should keep several points in mind. First, the inheritance of the genes producing these characteristics is no different from the inheritance of genes coding for simple genetic characters. Mendel’s principles of segregation and independent assortment still apply; each individual possesses two alleles at each locus, which separate in meiosis, and genes at the different loci assort independently. The only difference is in how the products of the genotypes interact to produce the phenotype. Thus, we cannot consider the expression of genes at each locus separately, but must take into consideration how the genes at different loci interact.

A second point is that in the examples that we have considered, the phenotypic proportions were always in sixteenths because, in all the crosses, pairs of alleles segregated at two independently assorting loci. The probability of inheriting one of the two alleles at a locus is \( \frac{1}{2} \). Because there are two loci, each with two alleles, the probability of inheriting any particular combination of genes is \( \left( \frac{1}{2} \right)^4 = \frac{1}{16} \). For a trihybrid cross, the progeny proportions should be in sixty-fourths, because \( \left( \frac{1}{2} \right)^6 = \frac{1}{64} \). In general, the progeny proportions should be in fractions of \( \left( \frac{1}{2} \right)^n \), where \( n \) equals the number of loci with two alleles segregating in the cross.

---

### Table 5.2 Modified dihybrid — phenotypic ratios due to gene interaction

<table>
<thead>
<tr>
<th>Ratio</th>
<th>Genotype</th>
<th>Type of Interaction</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>A_B_</td>
<td>A_bb</td>
<td>aab_</td>
<td>aabb</td>
</tr>
<tr>
<td>9:3:3:1</td>
<td>9</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>None</td>
<td></td>
<td>Seed shape and endosperm color in peas</td>
</tr>
<tr>
<td>9:3:4</td>
<td>9</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Recessive epistasis</td>
<td></td>
<td>Coat color in Labrador retrievers</td>
</tr>
<tr>
<td>12:3:1</td>
<td>12</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Dominant epistasis</td>
<td></td>
<td>Color in squash</td>
</tr>
<tr>
<td>9:7</td>
<td>9</td>
<td>12</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Duplicate recessive epistasis</td>
<td></td>
<td>Albinism in snails</td>
</tr>
<tr>
<td>9:6:1</td>
<td>9</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Duplicate interaction</td>
<td></td>
<td>—</td>
</tr>
<tr>
<td>15:1</td>
<td>15</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Duplicate dominant epistasis</td>
<td></td>
<td>—</td>
</tr>
<tr>
<td>13:3</td>
<td>13</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>

*Reading across, each row gives the phenotypic ratios of progeny from a dihybrid cross (AaBb × AaBb).*
Crosses rarely produce exactly 16 progeny; therefore, modifications of a dihybrid ratio are not always obvious. Modified dihybrid ratios are more easily seen if the number of individuals of each phenotype is expressed in sixteenths:

\[
x = \frac{\text{number of progeny with a phenotype}}{16}
\]

where \( x \) equals the proportion of progeny with a particular phenotype. If we solve for \( x \) (the proportion of the particular phenotype in sixteenths), we have:

\[
x = \frac{\text{number of progeny with a phenotype} \times 16}{\text{total number of progeny}}
\]

For example, suppose we cross two homozygous individuals, interbreed the F₁ and obtain 63 red, 21 brown, and 28 white F₂ individuals. Using the preceding formula, the phenotypic ratio in the F₂ is: red = \((63 \times 16)/112 = 9\); brown = \((21 \times 16)/112 = 3\); and white = \((28 \times 16)/112 = 4\). The phenotypic ratio is 9:3:4.

A final point to consider is how to assign genotypes to the phenotypes in modified ratios owing to gene interaction. Don’t try to memorize the genotypes associated with all the modified ratios in Table 5.2. Instead, practice relating modified ratios to known ratios, such as the 9:3:3:1 dihybrid ratio. Suppose we obtain \( \frac{15}{16} \) green progeny and \( \frac{1}{16} \) white progeny in a cross between two plants. If we compare this 15:1 ratio with the standard 9:3:3:1 dihybrid ratio, we see that \( \frac{9}{16} + \frac{3}{16} + \frac{1}{16} = \frac{15}{16} \). All the genotypes associated with these proportions in the dihybrid cross (\( A_B \), \( A_bb \), and \( aaB_\)) must give the same phenotype, the green progeny. Genotype \( aabb \) makes up \( \frac{1}{16} \) of the progeny in a dihybrid cross, the white progeny in this cross.

In assigning genotypes to phenotypes in modified ratios, students sometimes become confused about which letters to assign to which phenotype. Suppose we obtain the following phenotypic ratio: \( \frac{9}{16} \) black : \( \frac{3}{16} \) brown : \( \frac{2}{16} \) white. Which genotype do we assign to the brown progeny, \( A_bb \) or \( aaB_\)? Either answer is correct, because the letters are just arbitrary symbols for the genetic information. The important thing to realize about this ratio is that the brown phenotype arises when both recessive alleles are present at one locus.

**Concepts**

Gene interaction frequently produces modified phenotypic ratios. These modified ratios can be understood by relating them to other known ratios.

The Complex Genetics of Coat Color in Dogs

Coat color in dogs is an excellent example of how complex interactions between genes may take part in the determination of a phenotype. Domestic dogs come in an amazing variety of shapes, sizes, and colors. For thousands of years, humans have been breeding dogs for particular traits, producing the large number of types that we see today. Each breed of dog carries a selection of genes from the ancestral dog gene pool; these genes define the features of a particular breed.

One of the most obvious differences between dogs is coat color. The genetics of coat color in dogs is quite complex; many genes participate, and there are numerous interactions between genes at different loci. We will consider seven loci (in the list that follows) that are important in producing many of the noticeable differences in color and pattern among breeds of dogs. In interpreting the genetic basis of differences in coat color of dogs, consider how the expression of a particular gene is modified by the effects of other genes. Keep in mind that additional loci not listed here can modify the colors produced by these seven loci and that not all geneticists agree on the genetics of color variation in some breeds.

1. **Agouti (A) locus**—This locus has five common alleles that determine the depth and distribution of color in a dog’s coat:
   - \( A^S \) Solid black pigment.
   - \( a^w \) Agouti, or wolffish gray. Hair encoded by this allele have a “salt and pepper” appearance, produced by a band of yellow pigment on a black hair.
   - \( a^f \) Yellow. The black pigment is markedly reduced; so the entire hair is yellow.
   - \( a^s \) Saddle markings (dark color on the back, with extensive tan markings on the head and legs).
   - \( a^t \) Bicolor (dark color over most of the body, with tan markings on the feet and eyebrows).

\( A^S \) and \( a^f \) are generally dominant over the other alleles, but the dominance relations are complex and not yet completely understood.

2. **Black (B) locus**—This locus determines whether black pigment can be formed. The actual color of a dog’s fur depends on the effects of genes at other loci (such as the A, C, D, and E loci). Two alleles are common:
   - \( B \) Allows black pigment to be produced; the dog will be black if it also possesses certain alleles at the A, C, D, and E loci.
   - \( b \) Black pigment cannot be produced; pigmented dogs can be chocolate, liver, tan, or red.

\( B \) is dominant over \( b \).

3. **Albino (C) locus**—This locus determines whether full color will be expressed. There are five alleles at this locus:
   - \( C \) Color fully expressed.
   - \( c^{Ch} \) Chinchilla. Less color is expressed, and pigment is completely absent from the base of the long hairs, producing a pale coat.
   - \( c^d \) All white coat with dark nose and dark eyes.
   - \( c^b \) All white coat with blue eyes.
   - \( c \) Fully albino. The dogs have an all-white coat with pink eyes and nose.
5.10 Coat color in dogs is determined by interactions between genes at a number of loci. (a) Most Labrador retrievers are genotype $A^aA^cCCDDSStt$, varying only at the $B$ and $E$ loci. (b) Most beares are genotype $a^aB^bBCCDDSs^ps^tt$. (c) Dalmations are genotype $A^aA^cCCDEEs^ssTT$, varying at the $B$ locus so that the dogs are black ($B_-$) or brown ($bb$). (Part a, Robert Maier/Animals Animals; part b, Ralph Reinhold/Animals Animals; part c, Robert Percy/ Animals Animals.)

The dominance relations among these alleles is presumed to be $C > c^h > c^i > c^h > c$; but the $c^h$ and $c$ alleles are rare, and crosses including all possible genotypes have not been completed.

4. Dilution (D) locus — This locus, with two alleles, determines whether the color will be diluted. For example, diluted black pigment appears bluish, and diluted yellow appears cream. The diluted effect is produced by an uneven distribution of pigment in the hair shaft:

- $D$ Intense pigmentation.
- $d$ Dilution of pigment.
- $D$ is dominant over $d$.

5. Extension (E) locus — Four alleles at this locus determine where the genotype at the $A$ locus is expressed. For example, if a dog has the $A^s$ allele (solid black) at the $A$ locus, then black pigment will either be extended throughout the coat or be restricted to some areas, depending on the alleles present at the $E$ locus. Areas where the $A$ locus is not expressed may appear as yellow, red, or tan, depending on the presence of particular genes at other loci. When $A^s$ is present at the $A$ locus, the four alleles at the $E$ locus have the following effects:

- $E^m$ Black mask with a tan coat.
- $E$ The $A$ locus expressed throughout (solid black).
- $E^b$ Brindle, in which black and yellow are in layers to give a tiger-striped appearance.
- $E^r$ No black in the coat, but the nose and eyes may be black.

The dominance relations among these alleles are poorly known.

6. Spotting (S) locus — Alleles at this locus determine whether white spots will be present. There are four common alleles:

- $S$ No spots.
- $s$ Irish spotting; numerous white spots.
- $s^p$ Piebald spotting; various amounts of white.
- $s^w$ Extreme white piebald; almost all white.

$S$ is completely dominant over $s$, $s^p$, and $s^w$; $s$ and $s^p$ are dominant over $s^w$ ($S > s$, $s > s^p$). The relation between $s$ and $s^p$ is poorly defined; indeed, they may not be separate alleles. Genes at other poorly known loci also modify spotting patterns.

7. Ticking (T) locus — This locus determines the presence of small colored spots on the white areas, which is called ticking:

- $T$ Ticking; small colored spots on the areas of white.
- $t$ No ticking.

$T$ is dominant over $t$. Ticking cannot be expressed if a dog has a solid coat ($S_-$).

To illustrate how genes at these loci interact in determining a dog's coat color, let's consider a few examples:

**Labrador retriever** — Labrador retrievers (Figure 5.10a) may be black, brown, or yellow. Most are homozygous $A^aA^cCCDDSStt$; thus, they vary only at the $B$ and $E$ loci. The $A^s$, $C$, and $D$ alleles allow dark pigment to be expressed; whether a dog is black depends on which genes are present at the $B$ and $E$ loci. As discussed earlier in the chapter, all black Labradors must carry at least one $B$ allele and one $E$ allele ($B_E$). Brown dogs are homozygous $bb$ and have at least one $E$ allele ($bbE_-$). Yellow dogs are a result of the presence of $ee$ ($B_ee$ or $bb$). Labrador retrievers are homozygous for the $S$ allele, which produces a solid color; the few white spots that appear in some dogs of this breed are due to other modifying genes. The allele for ticking, $T$, is presumed not to exist in Labradors; however, Labrador retrievers have solid coats and ticking is expressed only in spotted dogs; so its absence is uncertain.

**Beagle** — Most beagles are homozygous $a^aB^bBCCDDSs^ps^tt$, although other alleles at these loci are occasionally present. The $a^a$ allele produces the saddle markings — dark back and sides, with tan head
and legs— that are characteristic of the breed ( FIGURE 5.10b). Alleles B, C, and D allow black to be produced, but its distribution is limited by the a\(^s\) allele. Genotype ee does occasionally arise, leading to a few all-tan beagles. White spotting in beagles is due to the s\(^p\) allele. Ticking can appear, but most beagles are tt.

**Dalmatian**— Dalmatians ( FIGURE 5.10c) have an interesting genetic makeup. Most are homozygous A\(^s\)A\(^s\)CCDDEEs\(^w\)s\(^w\)TT; so they vary only at the B locus. Notice that these dogs possess genotype A\(^s\)A\(^s\)CCDDEE, which allows for a solid coat that would be black, if genotype B\(_-\) is present, or brown (called liver), if genotype bb is present. However, the presence of the s\(^w\) allele produces a white coat, masking the expression of the solid color. The dog’s color appears only in the pigmented spots, which are due to the presence of the ticking allele T. Table 5.3 gives the common genotypes of other breeds of dogs.

**Complementation: Determining Whether Mutations Are at the Same or Different Loci**

How do we know whether different mutations that affect a characteristic occur at the same locus (are allelic) or at different loci? In fruit flies, for example, white is an X-linked mutation that produces white eyes instead of the red eyes found in wild-type flies. Apricot is an X-linked recessive mutation that produces light orange-colored eyes. Do the white and apricot mutations occur at the same locus or at different loci? We can use the complementation test to answer this question.

To carry out a **complementation test**, parents that are homozygous for different mutations are crossed, producing offspring that are heterozygous. If the mutations are allelic (occur at the same locus), then the heterozygous offspring have only mutant alleles (ab) and exhibit a mutant phenotype:

<table>
<thead>
<tr>
<th>a</th>
<th>×</th>
<th>b</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td></td>
<td>b</td>
</tr>
</tbody>
</table>

If, on the other hand, the mutations occur at different loci, each of the homozygous parents possesses wild-type genes at the other locus (aa b\(^+\)b\(^+\) and a\(^+\)a\(^+\) bb); so the heterozygous offspring inherit a mutant and a wild-type allele at each locus. In this case, the mutations complement each other and the heterozygous offspring have the wild-type phenotype.

<table>
<thead>
<tr>
<th>Table 5.3</th>
<th>Common genotypes in different breeds of dogs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Breed</strong></td>
<td><strong>Usual Homozygous Genes</strong></td>
</tr>
<tr>
<td>Basset hound</td>
<td>BBCCDDDEett</td>
</tr>
<tr>
<td>Beagle</td>
<td>a(^a)a(^a)BBCCDDssTT</td>
</tr>
<tr>
<td>English bulldog</td>
<td>BBCDDtt</td>
</tr>
<tr>
<td>Chihuahua</td>
<td>tt</td>
</tr>
<tr>
<td>Collie</td>
<td>BBCCEEtt</td>
</tr>
<tr>
<td>Dalmatian</td>
<td>A(^s)A(^s)CCDDEEs(^w)s(^w)TT</td>
</tr>
<tr>
<td>Doberman</td>
<td>a(^a)d(^a)CCEESStt</td>
</tr>
<tr>
<td>German shepherd</td>
<td>BBDDSStt</td>
</tr>
<tr>
<td>Golden retriever</td>
<td>A(^a)A(^a)BBDDSStt</td>
</tr>
<tr>
<td>Greyhound</td>
<td>BBtt</td>
</tr>
<tr>
<td>Irish setter</td>
<td>BBCCDDeeSStt</td>
</tr>
<tr>
<td>Labrador retriever</td>
<td>A(^a)A(^a)CCDDeSSStt</td>
</tr>
<tr>
<td>Poodle</td>
<td>SSStt</td>
</tr>
<tr>
<td>Rottweiler</td>
<td>a(^a)d(^a)BBCCDDEESStt</td>
</tr>
</tbody>
</table>

*Most dogs in the breed are homozygous for these genes; a few individual dogs may possess other alleles at these loci. Source: Data from M. B. Willis, *Genetics of the Dog* (London: Witherby, 1989).*
Complementation occurs when an individual possessing two mutant genes has a wild-type phenotype and is an indicator that the mutations are nonallelic genes.

When the complementation test is applied to white and apricot mutations, all of the heterozygous offspring have light-colored eyes, demonstrating that white and apricot are produced by mutations that occur at the same locus and are allelic.

Interaction Between Sex and Heredity

In Chapter 4, we considered characteristics encoded by genes located on the sex chromosomes and how their inheritance differs from the inheritance of traits encoded by autosomal genes. Now we will examine additional influences of sex, including the effect of the sex of an individual on the expression of genes on autosomal chromosomes, characteristics determined by genes located in the cytoplasm, and characteristics for which the genotype of only the maternal parent determines the phenotype of the offspring. Finally, we’ll look at situations in which the expression of genes on autosomal chromosomes is affected by the sex of the parent from whom they are inherited.

Sex-Influenced and Sex-Limited Characteristics

Sex influenced characteristics are determined by autosomal genes and are inherited according to Mendel’s principles, but they are expressed differently in males and females. In this case, a particular trait is more readily expressed in one sex; in other words, the trait has higher penetrance (see p. 000 in Chapter 3) in one of the sexes.

For example, the presence of a beard on some goats is determined by an autosomal gene ($B^b$) that is dominant in males and recessive in females. In males, a single allele is required for the expression of this trait: both the homozygote ($B^bB^b$) and the heterozygote ($B^bB^+$) have beards, whereas the $B^+B^+$ male is beardless. In contrast, females require two alleles in order for this trait to be expressed: the homozygote $B^bB^b$ has a beard, whereas the heterozygote ($B^bB^+$) and the other homozygote ($B^+B^+$) are beardless. The key to understanding the expression of the bearded gene is to look at the heterozygote. In males (for which the presence of a beard is dominant), the heterozygous genotype produces a beard but, in females (for which the presence of a beard is recessive and its absence is dominant), the heterozygous genotype produces a goat without a beard.

Figure 5.11a illustrates a cross between a beardless male ($B^+B^+$) and a bearded female ($B^bB^+$). The alleles
separate into gametes according to Mendel’s principle of segregation, and all the F₁ are heterozygous (B⁻B⁺). Because the trait is dominant in males and recessive in females, all the F₁ males will be bearded, and all the F₁ females will be beardless. When the F₁ are crossed with one another, ¾ of the F₂ progeny are B⁺B⁻, ¼ are B⁺B⁺, and ¼ are B⁻B⁻ (Figure 5.11b). Because male heterozygotes are bearded, ¾ of the males in the F₂ possess beards; because female heterozygotes are beardless, only ¼ of the females in F₂ are bearded.

An example of a sex-influenced characteristic in humans is pattern baldness, in which hair is lost prematurely from the front and the top of the head (Figure 5.12). Pattern baldness is an autosomal character believed to be dominant in males and recessive in females, just like beards in goats. Contrary to a popular misconception, a man does not inherit pattern baldness from his mother’s side of the family (which would be the case if the character were X linked, but it isn’t). Pattern baldness is autosomal; men and women can inherit baldness from either their mothers or their fathers. Men require only a single allele for baldness to become bald, whereas women require two alleles for baldness, and so pattern baldness is much more common among men. Furthermore, pattern baldness is expressed weakly in women; those with the trait usually have only a mild thinning of the hair, whereas men frequently lose all the hair on the top of the head. The expression of the allele for pattern baldness is clearly enhanced by the presence of male sex hormones; males who are castrated at an early age rarely become bald (but castration is not a recommended method for preventing baldness).

An extreme form of sex-influenced inheritance, a sex-limited characteristic is encoded by autosomal genes that are expressed in only one sex — the trait has zero penetrance in the other sex. In domestic chickens, some males display a plumage pattern called cock feathering (Figure 5.13a). Other males and all females display a pattern called hen feathering (Figure 5.13b and c). Cock feathering is an autosomal recessive trait that is sex limited to males. Because the trait is autosomal, the genotypes of males and females are the same, but the phenotypes produced by these genotypes differ in males and females:

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Male phenotype</th>
<th>Female phenotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>HH</td>
<td>hen feathering</td>
<td>hen feathering</td>
</tr>
<tr>
<td>Hh</td>
<td>hen feathering</td>
<td>hen feathering</td>
</tr>
<tr>
<td>hh</td>
<td>cock feathering</td>
<td>hen feathering</td>
</tr>
</tbody>
</table>

An example of a sex-limited characteristic in humans is male-limited precocious puberty. There are several types of precocious puberty in humans, most of which are not genetic. Male-limited precocious puberty, however, results from an autosomal dominant allele (P) that is expressed only in males; females with the gene are normal in phenotype. Males with precocious puberty undergo puberty at an early age, usually before the age of 4. At this time, the penis enlarges, the voice deepens, and pubic hair develops. There is no impairment of sexual function; affected males are fully fertile. Most are short as adults, because the long bones stop growing after puberty.

Because the trait is rare, affected males are usually heterozygous (Pp). A male with precocious puberty who mates...
with a woman who has no family history of this condition will transmit the allele for precocious puberty to of the children (FIGURE 5.14a), but it will be expressed only in the sons. If one of the heterozygous daughters (Pp) mates with a male who has normal puberty (pp), ½ of the sons will exhibit precocious puberty (FIGURE 5.14b). Thus a sex-limited characteristic can be inherited from either parent, although the trait appears in only one sex.

The results of molecular studies reveal that the underlying genetic defect in male-limited precocious puberty affects the receptor for luteinizing hormone (LH). This hormone normally attaches to receptors found on certain cells of the testes and stimulates these cells to produce testosterone. During normal puberty in males, high levels of LH stimulate the increased production of testosterone, which, in turn, stimulates the anatomical and physiological changes associated with puberty. The P allele for precocious puberty codes for a defective LH receptor, which stimulates testosterone production even in the absence of LH. Boys with this allele produce high levels of testosterone at an early age, when levels of LH are low. Defective LH receptors are also found in females who carry the precocious-puberty gene, but their presence does not result in precocious puberty, because additional hormones are required along with LH to induce puberty in girls.

Concepts

Sex-influenced characteristics are traits encoded by autosomal genes that are more readily expressed in one sex. Sex-limited characteristics are encoded by autosomal genes whose expression is limited to one sex.

5.14 Sex-limited characteristics are inherited according to Mendel’s principles. Precocious puberty is an autosomal dominant trait that is limited to males.
Cytoplasmic Inheritance

Mendel's principles of segregation and independent assortment are based on the assumption that genes are located on chromosomes in the nucleus of the cell. For the majority of genetic characteristics, this assumption is valid, and Mendel's principles allow us to predict the types of offspring that will be produced in a genetic cross. However, not all the genetic material of a cell is found in the nucleus; some characteristics are encoded by genes located in the cytoplasm. These characteristics exhibit cytoplasmic inheritance.

A few organelles, notably chloroplasts and mitochondria, contain DNA. Each human mitochondrion contains about 15,000 nucleotides of DNA, encoding 37 genes. Compared with that of nuclear DNA, which contains some 3 billion nucleotides encoding perhaps 35,000 genes, the amount of mitochondrial DNA (mtDNA) is very small; nevertheless, mitochondrial and chloroplast genes encode some important characteristics. The molecular details of this extranuclear DNA are discussed in Chapter 20; here, we will focus on patterns of cytoplasmic inheritance.

Cytoplasmic inheritance differs from the inheritance of characteristics encoded by nuclear genes in several important respects. A zygote inherits nuclear genes from both parents, but typically all of its cytoplasmic organelles, and thus all its cytoplasmic genes, come from only one of the gametes, usually the egg. Sperm generally contributes only a set of nuclear genes from the male parent. In a few organisms, cytoplasmic genes are inherited from the male parent, or from both parents; however, for most organisms, all the cytoplasm is inherited from the egg. In this case, cytoplasmically inherited traits are present in both males and females and are passed from mother to offspring, never from father to offspring. Reciprocal crosses, therefore, give different results when cytoplasmic genes encode a trait.

Cytoplasmically inherited characteristics frequently exhibit extensive phenotypic variation, because there is no mechanism analogous to mitosis or meiosis to ensure that cytoplasmic genes are evenly distributed in cell division. Thus, different cells and individuals will contain various proportions of cytoplasmic genes.

Consider mitochondrial genes. There are thousands of mitochondria in each cell, and each mitochondrion contains from 2 to 10 copies of mtDNA. Suppose that half of the mitochondria in a cell contain a normal wild-type copy of mtDNA and the other half contain a mutated copy (Figure 5.15). In cell division, the mitochondria segregate into progeny cells at random. Just by chance, one cell may receive mostly mutated mtDNA and another cell may receive mostly wild-type mtDNA (Figure 5.15). In this way, different progeny from the same mother and even cells within an individual offspring may vary in their phenotype. Traits encoded by chloroplast DNA (cpDNA) are similarly variable.

In 1909, cytoplasmic inheritance was recognized by Carl Correns as one of the first exceptions to Mendel's principles. Correns, one of the biologists who rediscovered Mendel's work, studied the inheritance of leaf variegation in the four-o'clock plant, Mirabilis jalapa. Correns found that the leaves and shoots of one variety of four-o'clock were variegated, displaying a mixture of green and white splotches. He also noted that some branches of the variegated strain had all-green leaves; other branches had all-white leaves. Each branch produced flowers; so Correns was able to cross flowers from variegated, green, and white branches in all combinations (Figure 5.16). The seeds from green branches always gave rise to green progeny, no matter whether the pollen was from a green, white, or variegated branch. Similarly, flowers on white branches always produced white progeny. Flowers on the variegated branches gave rise to green, white, and variegated progeny, in no particular ratio.

5.15 Cytoplasmically inherited characteristics frequently exhibit extensive phenotypic variation because cells and individual offspring contain various proportions of cytoplasmic genes. Mitochondria that have wild-type mtDNA are shown in red; those having mutant mtDNA are shown in blue.
The production of all three phenotypes by
never by the paternal parent (the source of the pollen). Fur-
offspring were determined entirely by the maternal parent,
of variegation in the four-o'clocks illustrate cytoplasmic inheritance.

mal chloroplasts. In the
variegated branches contain a mixture of normal and abnor-
by a defective gene in the cpDNA, which results in a failure
cytoplasmic inheritance. Variegation in these plants is caused

Genetic Maternal Effect
A genetic phenomenon that is sometimes confused with
cytoplasmic inheritance is genetic maternal effect, in which
the phenotype of the offspring is determined by the genotype
of the mother. In cytoplasmic inheritance, the genes for a
characteristic are inherited from only one parent, usually the
mother. In genetic maternal effect, the genes are inherited from
both parents, but the offspring’s phenotype is determined not by its own genotype but by the genotype of its mother.

Genetic maternal effect frequently arises when sub-
stances present in the cytoplasm of an egg (encoded by the
mother’s genes) are pivotal in early development. An excel-
ent example is shell coiling of the snail Limnaea peregra. In
most snails of this species, the shell coils to the right, which
is termed dextral coiling. However, some snails possess
a left-coiling shell, exhibiting sinistral coiling. The direction
of coiling is determined by a pair of alleles; the allele for dex-
tral (s') is dominant over the allele for sinistral (s). However,
the direction of coiling is determined not by that snail’s own
phenotype is determined not by the genotype, but by the genotype of its mother. The direction of coiling is affected by the way in which the cytoplasm divides
soon after fertilization, which in turn is determined by a
substance produced by the mother and passed to the off-
spring in the cytoplasm of the egg.

If a male homozygous for dextral alleles (s's') is
crossed with a female homozygous for sinistral alleles (ss),
all of the F1 are heterozygous (s's) and have a sinistral shell,
because the genotype of the mother (ss) codes for sinistral
(Figure 5.17). If these F1 snails are self-fertilized, the
genotypic ratio of the F2 is 1 s's' : 2 s's : 1 ss. The phenotype
of all F2 snails will be dextral regardless of their genotypes,
because the genotype of their mother (s's') encodes a right-
coiling shell and determines their phenotype.

5.16 Crosses for leaf type in four o'clocks illustrate cytoplasmic inheritance.

Corren’s crosses demonstrated cytoplasmic inheritance
of variegation in the four-o’clocks. The phenotypes of the
offspring were determined entirely by the maternal parent,
ever by the paternal parent (the source of the pollen). Fur-
thermore, the production of all three phenotypes by flowers
on variegated branches is consistent with the occurrence of
cytoplasmic inheritance. Variegation in these plants is caused
by a defective gene in the cpDNA, which results in a failure
to produce the green pigment chlorophyll. Cells from green
branches contain normal chloroplasts only, cells from white
branches contain abnormal chloroplasts only, and cells from
variegated branches contain a mixture of normal and abnor-
amal chloroplasts. In the flowers from variegated branches,
One of the basic tenets of Mendelian genetics is that the parental origin of a gene does not affect its expression—reciprocal crosses give identical results. We have seen that there are some genetic characteristics—those encoded by X-linked genes and cytoplasmic genes—for which reciprocal crosses do not give the same results. In these cases, males and females do not contribute the same genetic material to the offspring. With regard to autosomal genes, males and females contribute the same number of genes, and paternal and maternal genes have long been assumed to have equal effects. The results of recent studies, however, have identified several mammalian genes whose expression is significantly affected by their parental origin. This phenomenon, the differential expression of genetic material depending on whether it is inherited from the male or female parent, is called genomic imprinting.

Genomic imprinting has been observed in mice in which a particular gene has been artificially inserted into a mouse’s DNA (to create a transgenic mouse). In these mice, the inserted gene is faithfully passed from generation to generation, but its expression may depend on which parent transmitted the gene. For example, when a transgenic male passes an imprinted gene to his offspring, they express the gene; but, when his daughter transmits the same gene to her offspring, they don’t express it. In turn, her son’s offspring express it, but her daughter’s offspring don’t. Both male and female offspring possess the gene for the trait; the key to whether the gene is expressed is the sex of the parent transmitting the gene. In the present example, the gene is expressed only when it is transmitted by a male parent. The reverse situation, expression of a trait when the gene is transmitted by the female parent, also occurs.

Genomic imprinting has been implicated in several human disorders, including Prader-Willi and Angelman syndromes. Children with Prader-Willi syndrome have small hands and feet, short stature, poor sexual development, and mental retardation; they develop voracious appetites and frequently become obese. Many persons with Prader-Willi syndrome are missing a small region of chromosome 15 called q11–13. The deletion of this region is always inherited from the father in persons with Prader-Willi syndrome.

The deletions of q11–13 on chromosome 15 can also be inherited from the mother, but this inheritance results in a completely different set of symptoms, producing Angelman syndrome.
syndrome. Children with Angelman syndrome exhibit frequent laughter, uncontrolled muscle movement, a large mouth, and unusual seizures. The deletion of segment q11–13 from chromosome 15 has severe effects on the human phenotype, but the specific effects depend on which parent contributes the deletion. For normal development to take place, copies of segment q11–13 of chromosome 15 from both male and female parents are apparently required.

Several other human diseases also appear to exhibit genomic imprinting. Although the precise mechanism of this phenomenon is unknown, methylation of DNA — the addition of methyl (CH₃) groups to DNA nucleotides (see Chapters 10 and 16) — is essential to the process of genomic imprinting, as demonstrated by the observation that mice deficient in DNA methylation do not exhibit imprinting. Some of the ways in which sex interacts with heredity are summarized in Table 5.4.

### Table 5.4 Sex influences on heredity

<table>
<thead>
<tr>
<th>Genetic Phenomenon</th>
<th>Phenotype Determined by</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex-linked characteristic</td>
<td>genes located on the sex chromosome</td>
</tr>
<tr>
<td>Sex-influenced characteristic</td>
<td>genes on autosomal chromosomes that are more readily expressed in one sex</td>
</tr>
<tr>
<td>Sex-limited characteristic</td>
<td>autosomal genes whose expression is limited to one sex</td>
</tr>
<tr>
<td>Genetic maternal effect</td>
<td>nuclear genotype of the maternal parent</td>
</tr>
<tr>
<td>Cytoplasmic inheritance</td>
<td>cytoplasmic genes, which are usually inherited entirely from only one parent</td>
</tr>
<tr>
<td>Genomic imprinting</td>
<td>genes whose expression is affected by the sex of the transmitting parent</td>
</tr>
</tbody>
</table>

Anticipation

Another genetic phenomenon that is not explained by Mendel's principles is **anticipation**, in which a genetic trait becomes more strongly expressed or is expressed at an earlier age as it is passed from generation to generation. In the early 1900s, several physicians observed that patients with moderate to severe myotonic dystrophy — an autosomal dominant muscle disorder — frequently had ancestors who were only mildly affected by the disease. These observations led to the concept of anticipation. However, the concept quickly fell out of favor with geneticists because there was no obvious mechanism to explain it; traditional genetics held that genes are passed unaltered from parents to offspring. Geneticists tended to attribute anticipation to observational bias.

The results of recent research have reestablished anticipation as a legitimate genetic phenomenon. The mutation causing myotonic dystrophy consists of an unstable region of DNA that can increase or decrease in size as the gene is passed from generation to generation, much like the gene that causes Huntington disease. The age of onset and the severity of the disease are correlated with the size of the unstable region; an increase in the size of the region through generations produces anticipation. The phenomenon has now been implicated in several genetic diseases. We will examine these interesting types of mutations in more detail in Chapter 17.

**Concepts**

Anticipation is the stronger or earlier expression of a genetic trait through succeeding generations. It is caused by an unstable region of DNA that increases or decreases in size.

Interaction Between Genes and Environment

In Chapter 3, we learned that each phenotype is the result of a genotype developing within a specific environment; the genotype sets the potential for development, but how the phenotype actually develops within the limits imposed by the genotype depends on environmental effects. Stated another way, each genotype may produce several different phenotypes, depending on the environmental conditions in which development occurs. For example, genotype GG may produce a plant that is 10 cm high when raised at 20°C, but the same genotype may produce a plant that is 18 cm high when raised at 25°C. The range of phenotypes produced by a genotype in different environments (in this case, plant height) is called the **norm of reaction** (Figure 5.18).

For most of the characteristics discussed so far, the effect of the environment on the phenotype has been slight.
Mendel’s peas with genotype yy, for example, developed yellow endosperm regardless of the environment in which they were raised. Similarly, persons with genotype $I^A I^A$ have the A antigen on their red blood cells regardless of their diet, socioeconomic status, or family environment. For other phenotypes, however, environmental effects play a more important role.

Environmental Effects on Gene Expression

The expression of some genotypes is critically dependent on the presence of a specific environment. For example, the himalayan allele in rabbits produces dark fur at the extremities of the body — on the nose, ears, and feet (Figure 5.19). The dark pigment develops, however, only when the rabbit is reared at 25°C or less; if a Himalayan rabbit is reared at 30°C, no dark patches develop. The expression of the himalayan allele is thus temperature dependent — an enzyme necessary for the production of dark pigment is inactivated at higher temperatures. The pigment is normally restricted to the nose, feet, and ears of Himalayan rabbits because the animal’s core body temperature is normally above 25°C and the enzyme is functional only in the cells of the relatively cool extremities. The himalayan allele is an example of a temperature-sensitive allele, an allele whose product is functional only at certain temperatures.

Some types of albinism in plants are temperature dependent. In barley, an autosomal recessive allele inhibits chlorophyll production, producing albinism when the plant is grown below 7°C. At temperatures above 18°C, a plant homozygous for the albino allele develops normal chlorophyll and is green. Similarly, among Drosophila melanogaster homozygous for the autosomal mutation vestigial, greatly reduced wings develop at 25°C, but wings near normal size develop at higher temperatures (see Figure 5.18).

Environmental factors also play an important role in the expression of a number of human genetic diseases. Glucose-6-phosphate dehydrogenase is an enzyme taking part in supplying energy to the cell. In humans, there are a number of genetic variants of glucose-6-phosphate dehydrogenase, some of which destroy red blood cells when the body is stressed by infection or by the ingestion of certain drugs or foods. The symptoms of the genetic disease appear only in the presence of these specific environmental factors.

Another genetic disease, phenylketonuria (PKU), is due to an autosomal recessive allele that causes mental retardation. The disorder arises from a defect in an enzyme that normally metabolizes the amino acid phenylalanine. When this enzyme is defective, phenylalanine is not metabolized, and its buildup causes brain damage in children. A simple
environmental change, putting an affected child on a low-phenylalanine diet, prevents retardation.

These examples illustrate the point that genes and their products do not act in isolation; rather, they frequently interact with environmental factors. Occasionally, environmental factors alone can produce a phenotype that is the same as the phenotype produced by a genotype; this phenotype is called a phenocopy. In fruit flies, for example, the autosomal recessive mutation eyeless produces greatly reduced eyes. The eyeless phenotype can also be produced by exposing the larvae of normal flies to sodium metaborate.

Concepts

The expression of many genes is modified by the environment. The range of phenotypes produced by a genotype in different environments is called the norm of reaction. A phenocopy is a trait produced by environmental effects that mimics the phenotype produced by a genotype.

The Inheritance of Continuous Characteristics

So far, we've dealt primarily with characteristics that have only a few distinct phenotypes. In Mendel's peas, for example, the seeds were either smooth or wrinkled, yellow or green; the coats of dogs were black, brown, or yellow; blood types were of four distinct types, A, B, AB, or O. Characteristics such as these, which have a few easily distinguished phenotypes, are called discontinuous characteristics.

Not all characteristics exhibit discontinuous phenotypes. Human height is an example of such a character; people do not come in just a few distinct heights but, rather, display a continuum of heights. Indeed, there are so many possible phenotypes of human height that we must use a measurement to describe a person's height. Characteristics that exhibit a continuous distribution of phenotypes are termed continuous characteristics. Because such characteristics have many possible phenotypes and must be described in quantitative terms, continuous characteristics are also called quantitative characteristics.

Continuous characteristics frequently arise because genes at many loci interact to produce the phenotypes. When a single locus with two alleles codes for a characteristic, there are three genotypes possible: AA, Aa, and aa. With two loci, each with two alleles, there are $3^2 = 9$ genotypes possible. The number of genotypes coding for characteristic is $3^n$, where $n$ equals the number of loci with two alleles that influence the characteristic. For example, when a characteristic is determined by eight loci, each with two alleles, there are $3^8 = 6561$ different genotypes possible for this character. If each genotype produces a different phenotype, many phenotypes will be possible. The slight differences between the phenotypes will be indistinguishable, and the characteristic will appear continuous. Characteristics encoded by genes at many loci are called polygenic characteristics.

The converse of polygeny is pleiotropy, in which one gene affects multiple characteristics. Many genes exhibit pleiotropy. PKU, mentioned earlier, results from a recessive allele; persons homozygous for this allele, if untreated, exhibit mental retardation, blue eyes, and light skin color.

Frequently the phenotypes of continuous characteristics are also influenced by environmental factors. Each genotype is capable of producing a range of phenotypes— it has a relatively broad norm of reaction. In this situation, the particular phenotype that results depends on both the genotype and the environmental conditions in which the genotype develops. For example, there may be only three genotypes coding for a characteristic, but, because each genotype has a broad norm of reaction, the phenotype of the character exhibits a continuous distribution. Many continuous characteristics are both polygenic and influenced by environmental factors; such characteristics are called multifactorial because many factors help determine the phenotype.

The inheritance of continuous characteristics may appear to be complex, but the alleles at each locus follow Mendel's principles and are inherited in the same way as alleles coding for simple, discontinuous characteristics. However, because many genes participate, environmental factors influence the phenotype, and the phenotypes do not sort out into a few distinct types, we cannot observe the distinct ratios that have allowed us to interpret the genetic basis of discontinuous characteristics. To analyze continuous characteristics, we must employ special statistical tools, as will be discussed in Chapter 22.

Concepts

Discontinuous characteristics exhibit a few distinct phenotypes; continuous characteristics exhibit a range of phenotypes. A continuous characteristic is frequently produced when genes at many loci and environmental factors combine to determine a phenotype.

Connecting Concepts Across Chapters

This chapter introduced a number of modifications and extensions of the basic concepts of heredity that we learned in Chapter 3. A major theme has been gene expression: how interactions between genes, interactions between genes and sex, and interactions between genes and the environment affect the phenotypic expression of genes. The modifications and extensions discussed in this chapter do not alter the way that genes are inherited, but they do modify the way in which the genes determine the phenotype.
A number of topics introduced in this chapter will be explored further in other chapters of the book. Here we have purposefully ignored many aspects of the nature of gene expression because our focus has been on the “big picture” of how these interactions affect phenotypic ratios in genetic crosses. In subsequent chapters, we will explore the molecular details of gene expression, including transcription (Chapter 13), translation (Chapter 15), and the control of gene expression (Chapter 16). The molecular nature of anticipation will be examined in more detail in Chapter 17, and DNA methylation, the basis of genomic imprinting, will be discussed in Chapter 10. Complementation testing will be revisited in Chapter 8, and the role of multiple genes and environmental factors in the inheritance of continuous characteristics will be studied more thoroughly in Chapter 22.

**CONCEPTS SUMMARY**

- Dominance always refers to genes at the same locus (allelic genes) and can be understood in regard to how the phenotype of the heterozygote relates to the phenotypes of the homozygotes.
- Dominance is complete when a heterozygote has the same phenotype as a homozygote. Dominance is incomplete when the heterozygote has a phenotype intermediate between those of two parental homozygotes. Codominance is the result when the heterozygote exhibits traits of both parental homozygotes.
- The type of dominance does not affect the inheritance of an allele; it does affect the phenotypic expression of the allele. The classification of dominance may depend on the level of the phenotype examined.
- Lethal alleles cause the death of an individual possessing them, usually at an early stage of development, and may alter phenotypic ratios.
- Multiple alleles refer to the presence of more than two alleles at a locus within a group. Their presence increases the number of genotypes and phenotypes possible.
- Gene interaction refers to interaction between genes at different loci to produce a single phenotype. An epistatic gene at one locus suppresses or masks the expression of hypostatic genes at different loci. Gene interaction frequently produces phenotypic ratios that are modifications of dihybrid ratios.
- A complementation test, in which individuals homozygous for different mutations are crossed, can be used to determine if the mutations occur at the same locus or at different loci.

- Sex-influenced characteristics are encoded by autosomal genes that are expressed more readily in one sex.
- Sex-limited characteristics are encoded by autosomal genes expressed in only one sex. Both males and females possess sex-limited genes and transmit them to their offspring.
- In cytoplasmic inheritance, the genes for the characteristic are found in the cytoplasm and are usually inherited from a single (usually maternal parent).
- Genetic maternal effect is present when an offspring inherits genes from both parents, but the nuclear genes of the mother determine the offspring’s phenotype.
- Genomic imprinting refers to characteristics encoded by autosomal genes whose expression is affected by the sex of the parent transmitting the genes.
- Anticipation refers to a genetic trait that is more strongly expressed or is expressed at an earlier age in succeeding generations.
- Phenotypes are often modified by environmental effects. The range of phenotypes that a genotype is capable of producing in different environments is the norm of reaction. A phenocopy is a phenotype produced by an environmental effect that mimics a phenotype produced by a genotype.
- Discontinuous characteristics are characteristics with a few distinct phenotypes; continuous characteristics are those that exhibit a wide range of phenotypes. Continuous characteristics are frequently produced by the combined effects of many genes and environmental effects.

**IMPORTANT TERMS**

- codominance (p. 103)
- lethal allele (p. 104)
- multiple alleles (p. 105)
- gene interaction (p. 107)
- epistasis (p. 108)
- epistatic gene (p. 108)
- hypostatic gene (p. 108)
- complementation test (p. 114)
- complementation (p. 115)
- sex-influenced characteristic (p. 115)
- sex-limited characteristic (p. 116)
- cytoplasmic inheritance (p. 118)
- genetic maternal effect (p. 119)
- genomic imprinting (p. 120)
- anticipation (p. 121)
- norm of reaction (p. 121)
- temperature-sensitive allele (p. 122)
- phenocopy (p. 123)
- discontinuous characteristic (p. 123)
- continuous characteristic (p. 123)
- quantitative characteristic (p. 123)
- polygenic characteristic (p. 123)
- pleiotropy (p. 123)
- multifactorial characteristic (p. 123)
Worked Problems

1. The type of plumage found in mallard ducks is determined by three alleles at a single locus: \( M^R \), which codes for restricted plumage; \( M \), which codes for mallard plumage; and \( m^d \), which codes for dusky plumage. The restricted phenotype is dominant over mallard and dusky; mallard is dominant over dusky (\( M^R > M > m^d \)). Give the expected phenotypes and proportions of offspring produced by the following crosses.

(a) \( M^R M \times m^d m^d \)
(b) \( M^R m^d \times M m^d \)
(c) \( M^R m^d \times M^R M \)
(d) \( M^R M \times M m^d \)

**Solution**

We can determine the phenotypes and proportions of offspring by (1) determining the types of gametes produced by each parent and (2) combining the gametes of the two parents with the use of a Punnett square.

(a) Parents

<table>
<thead>
<tr>
<th>Gametes</th>
<th>Restricted</th>
<th>Mallard</th>
</tr>
</thead>
<tbody>
<tr>
<td>( M^R )</td>
<td>( m^d )</td>
<td></td>
</tr>
<tr>
<td>( m^d )</td>
<td>( M )</td>
<td></td>
</tr>
</tbody>
</table>

\( \frac{1}{2} \) restricted, \( \frac{1}{2} \) mallard

(b) Parents

<table>
<thead>
<tr>
<th>Gametes</th>
<th>Restricted</th>
<th>Mallard</th>
</tr>
</thead>
<tbody>
<tr>
<td>( M^R )</td>
<td>( m^d )</td>
<td></td>
</tr>
<tr>
<td>( m^d )</td>
<td>( M )</td>
<td></td>
</tr>
</tbody>
</table>

\( \frac{1}{2} \) restricted, \( \frac{1}{2} \) mallard

(c) Parents

<table>
<thead>
<tr>
<th>Gametes</th>
<th>Restricted</th>
<th>Mallard</th>
</tr>
</thead>
<tbody>
<tr>
<td>( M^R )</td>
<td>( M^R )</td>
<td></td>
</tr>
<tr>
<td>( m^d )</td>
<td>( m^d )</td>
<td></td>
</tr>
</tbody>
</table>

\( \frac{3}{4} \) restricted, \( \frac{1}{4} \) mallard

(d) Parents

<table>
<thead>
<tr>
<th>Gametes</th>
<th>Restricted</th>
<th>Mallard</th>
</tr>
</thead>
<tbody>
<tr>
<td>( M^R )</td>
<td>( M )</td>
<td></td>
</tr>
<tr>
<td>( M )</td>
<td>( m^d )</td>
<td></td>
</tr>
</tbody>
</table>

\( \frac{1}{2} \) restricted, \( \frac{1}{2} \) mallard

2. A homozygous strain of yellow corn is crossed with a homozygous strain of purple corn. The \( F_1 \) are intercrossed, producing an ear of corn with 119 purple kernels and 89 yellow kernels (the progeny).

(a) What is the genotype of the yellow kernels?
(b) Give a genetic explanation for the differences in kernel color in this cross.

**Solution**

(a) We should first consider whether the cross between yellow and purple strains might be a monohybrid cross for a simple dominant trait, which would produce a 3:1 ratio in the \( F_2 \) (\( Aa \times Aa \rightarrow \frac{3}{4} A_\_ \) and \( \frac{1}{4} aa \)). Under this hypothesis, we would expect \( 156 \) purple progeny and \( 52 \) yellow progeny:

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Genotype</th>
<th>Observed number</th>
<th>Expected number</th>
</tr>
</thead>
<tbody>
<tr>
<td>purple</td>
<td>( A__ )</td>
<td>119</td>
<td>( \frac{3}{4} \times 208 = 156 )</td>
</tr>
<tr>
<td>yellow</td>
<td>( aa )</td>
<td>89</td>
<td>( \frac{1}{4} \times 208 = 52 )</td>
</tr>
<tr>
<td>total</td>
<td></td>
<td>208</td>
<td></td>
</tr>
</tbody>
</table>
We see that the expected numbers do not closely fit the observed numbers. If we performed a chi-square test (see Chapter 3), we would obtain a calculated chi-square value of 35.08, which has a probability much less than .05, indicating that it is extremely unlikely that, when we expect a 3:1 ratio, we would obtain 119 purple progeny and 89 yellow progeny. Therefore, we can reject the hypothesis that these results were produced by a monohybrid cross.

Another possible hypothesis is that the observed F2 progeny are in a 1:1 ratio. However, we learned in Chapter 3 that a 1:1 ratio is produced by a cross between a heterozygote and a homozygote (Aa × aa) and, from the information given, the cross was not between a heterozygote and a homozygote, because the original parental strains were both homozygous. Furthermore, a chi-square test comparing the observed numbers with an expected 1:1 ratio yields a calculated chi-square value of 4.32, which has a probability of less than .05.

Next, we should look to see if the results can be explained by a dihybrid cross (AaBb × AaBb). A dihybrid cross results in phenotypic proportions that are in sixteenths. We can apply the formula given earlier in the chapter to determine the number of sixteenths for each phenotype:

\[ x = \frac{\text{number of progeny with a phenotype}}{\text{total number of progeny}} \times 16 \]

\[ x_{\text{purple}} = \frac{119 \times 16}{208} = 9.15 \]

\[ x_{\text{yellow}} = \frac{89 \times 16}{208} = 6.85 \]

Thus, purple and yellow appear approximately a 9:7 ratio. We can test this hypothesis with a chi-square test:

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Genotype</th>
<th>Observed number</th>
<th>Expected number</th>
</tr>
</thead>
<tbody>
<tr>
<td>purple</td>
<td>?</td>
<td>119</td>
<td>( \frac{9}{16} \times 208 = 117 )</td>
</tr>
<tr>
<td>yellow</td>
<td>?</td>
<td>89</td>
<td>( \frac{3}{16} \times 208 = 91 )</td>
</tr>
<tr>
<td>total</td>
<td></td>
<td>208</td>
<td></td>
</tr>
</tbody>
</table>

\[ \chi^2 = \sum \frac{(\text{observed} - \text{expected})^2}{\text{expected}} = \frac{(119 - 117)^2}{117} + \frac{(89 - 91)^2}{91} = 0.034 + 0.44 = 0.078 \]

Degree of freedom = \( n - 1 = 2 - 1 = 1 \)

\[ P > 0.05 \]

The probability associated with the chi-square value is greater than .05, indicating that there is a relatively good fit between the observed results and a 9:7 ratio.

We now need to determine how a dihybrid cross can produce a 9:7 ratio and what genotypes correspond to the two phenotypes. A dihybrid cross without epistasis produces a 9:3:3:1 ratio:

\[ AaBb \times AaBb \]

\[ \downarrow \]

\[ A_B_ : \frac{9}{16} \]

\[ A_bb : \frac{3}{16} \]

\[ aAB_ : \frac{3}{16} \]

\[ aabb : \frac{1}{16} \]

Because \( \frac{9}{16} \) of the progeny from the corn cross are purple, purple must be produced by genotypes \( A_B_ \); in other words, individual kernels that have at least one dominant allele at the first locus and at least one dominant allele at the second locus are purple. The proportions of all the other genotypes \( A_bb, aAB_, \) and \( aabb \) sum to \( \frac{7}{16} \), which is the proportion of the progeny in the corn cross that are yellow, so any individual kernel that does not have a dominant allele at both the first and the second locus is yellow.

(b) Kernel color is an example of duplicate recessive epistasis, where the presence of two recessive alleles at either the first locus or the second locus or both suppresses the production of purple pigment.

3. A geneticist crosses two yellow mice with straight hair and obtains the following progeny:

\[ \frac{1}{2} \text{ yellow, straight} \]

\[ \frac{1}{4} \text{ yellow, fuzzy} \]

\[ \frac{1}{4} \text{ gray, straight} \]

\[ \frac{1}{12} \text{ gray, fuzzy} \]

(a) Provide a genetic explanation for the results and assign genotypes to the parents and progeny of this cross.

(b) What additional crosses might be carried out to determine if your explanation is correct?

**Solution**

(a) This cross concerns two separate characteristics—color and type of hair; so we should begin by examining the results for each characteristic separately. First, let’s look at the inheritance of color. Two yellow mice are crossed producing \( \frac{1}{2} \text{ yellow, straight} \) and \( \frac{1}{4} \text{ yellow, fuzzy} \). We learned in this chapter that a 2:1 ratio is often produced when a recessive lethal gene is present:

\[ Yy \times Yy \]

\[ \downarrow \]

\[ YY \quad \frac{1}{4} \text{ die} \]

\[ Yy \quad \frac{1}{2} \text{ yellow, becomes} \quad \frac{2}{3} \]

\[ yy \quad \frac{1}{4} \text{ gray, becomes} \quad \frac{1}{3} \]

Now, let’s examine the inheritance of the hair type. Two mice with straight hair are crossed, producing \( \frac{1}{2} \text{ straight} \) and \( \frac{1}{4} \text{ fuzzy} \). We learned in Chapter 3 that a
3:1 ratio is usually produced by a cross between two individuals heterozygous for a simple dominant allele:

\[ \text{Ss} \times \text{Ss} \]

\[ \text{SS} \quad \frac{1}{4} \text{straight} \]

\[ \text{Ss} \quad \frac{1}{2} \text{straight} \]

\[ \text{ss} \quad \frac{1}{4} \text{fuzzy} \]

We can now combine both loci and assign genotypes to all the individuals in the cross:

\[ P \quad \text{yellow, straight} \times \text{yellow, straight} \]

\[ YySs \]

\[ \text{F1} \]

\[ H^+H^+ \times \text{H} \]

\[ \frac{1}{2} \text{H}^+ \text{H}^+ \]

\[ \frac{1}{2} \text{H} \text{H} \]

\[ \text{Males} \]

\[ \frac{1}{2} \text{H}^+ \text{H}^+ \quad \text{horned} \]

\[ \frac{1}{2} \text{H} \text{H} \quad \text{hornless} \]

\[ \text{Females} \]

\[ \frac{1}{2} \text{H}^+ \text{H}^+ \quad \text{horned} \]

\[ \frac{1}{2} \text{H} \text{H} \quad \text{hornless} \]

\[ \text{F1 females will be hornless, as shown below:} \]

\[ \text{P} \quad \text{H}^+\text{H}^+ \times \text{H} \]

\[ \text{F1} \]

\[ \frac{1}{2} \text{H}^+ \text{H}^+ \]

\[ \frac{1}{2} \text{H} \text{H} \]

\[ \text{horned males and hornless females} \]

A heterozygous hornless F1 female (H+H) is then crossed with a hornless male (H+H+):

\[ \frac{1}{2} \text{H}^+ \text{H}^+ \]

\[ \frac{1}{2} \text{H} \text{H} \]

\[ \text{Males} \]

\[ \frac{1}{2} \text{H}^+ \text{H}^+ \quad \text{hornless} \]

\[ \frac{1}{2} \text{H} \text{H} \quad \text{horned} \]

\[ \text{Females} \]

\[ \frac{1}{2} \text{H}^+ \text{H}^+ \quad \text{hornless} \]

\[ \frac{1}{2} \text{H} \text{H} \quad \text{hornless} \]

Therefore, \( \frac{1}{2} \) of the male progeny will be horned but none of the female progeny will be horned.

**COMPREHENSION QUESTIONS**

1. How do incomplete dominance and codominance differ?
2. Explain how dominance and epistasis differ.
3. What is a recessive epistatic gene?
4. What is a complementation test and what is it used for?
5. What is genomic imprinting?
6. What characteristics do you expect to see in a trait that exhibits anticipation?

**Solution**

The presence of horns in these sheep is an example of a sex-influenced characteristic. Because the phenotypes associated with the genotypes differ for the two sexes, let's begin this problem by writing out the genotypes and phenotypes for each sex. We will let \( H \) represent the allele that codes for horns and \( H^+ \) represent the allele for hornless. In males, the allele for horns is dominant over the allele for hornless, which means that males homzygous (HH) and heterozygous (H+H) for this gene are horned. Only males homzygous for the recessive hornless allele (H+H) will be hornless. In females, the allele for horns is recessive, which means that only females homozygous for this allele (HH) will be horned; females heterozygous (H+H) and heterozygous (H+H+) for the hornless allele will be hornless. The following table summarizes genotypes and associated phenotypes:

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Male phenotype</th>
<th>Female phenotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>HH</td>
<td>horned</td>
<td>horned</td>
</tr>
<tr>
<td>H+H</td>
<td>horned</td>
<td>hornless</td>
</tr>
<tr>
<td>H+H+</td>
<td>hornless</td>
<td>hornless</td>
</tr>
</tbody>
</table>

In the problem, a horned female is crossed with a hornless male. From the preceding table, we see that a horned female must be homozygous for the allele for horns (HH) and a hornless male must be homozygous for the allele for hornless (H+H+); so all the F1 will be heterozygous; the F1 males will be horned and the F1 females will be hornless, as shown below:

\[ \text{P} \quad \text{H}^+\text{H}^+ \times \text{H} \]

\[ \text{F1} \]

\[ \frac{1}{2} \text{H}^+ \text{H}^+ \]

\[ \frac{1}{2} \text{H} \text{H} \]

\[ \text{horned males and hornless females} \]

Therefore, \( \frac{1}{2} \) of the male progeny will be horned but none of the female progeny will be horned.

7. What characteristics are exhibited by a cytoplasmically inherited trait?
8. What is the difference between genetic maternal effect and genomic imprinting?
9. What is the difference between a sex-influenced gene and a gene that exhibits genomic imprinting?
10. What are continuous characteristics and how do they arise?
*11. Palomino horses have a golden yellow coat, chestnut horses have a brown coat, and cremello horses have a coat that is almost white. A series of crosses between the three different types of horses produced the following offspring:

<table>
<thead>
<tr>
<th>Cross</th>
<th>Offspring</th>
</tr>
</thead>
<tbody>
<tr>
<td>palomino × palomino</td>
<td>13 palomino, 6 chestnut, 5 cremello</td>
</tr>
<tr>
<td>chestnut × chestnut</td>
<td>16 chestnut</td>
</tr>
<tr>
<td>cremello × cremello</td>
<td>13 cremello</td>
</tr>
<tr>
<td>palomino × chestnut</td>
<td>8 palomino, 9 chestnut</td>
</tr>
<tr>
<td>palomino × cremello</td>
<td>11 palomino, 11 cremello</td>
</tr>
<tr>
<td>chestnut × cremello</td>
<td>23 palomino</td>
</tr>
</tbody>
</table>

(a) Explain the inheritance of the palomino, chestnut, and cremello phenotypes in horses.
(b) Assign symbols for the alleles that determine these phenotypes, and list the genotypes of all parents and offspring given in the preceding table.

*12. The $L^M$ and $L^N$ alleles at the MN blood group locus exhibit codominance. Give the expected genotypes and phenotypes and their ratios in progeny resulting from the following crosses.

(a) $L^M L^M \times L^M L^N$
(b) $L^M L^N \times L^N L^N$
(c) $L^M L^N \times L^N L^N$
(d) $L^M L^N \times L^N L^N$
(e) $L^M L^M \times L^M L^N$

13. In the pearl millet plant, color is determined by three alleles at a single locus: $R^p_1$ (red), $R^p_2$ (purple), and $r$ (green). Red is dominant over purple and green, and purple is dominant over green ($R^p_1 > R^p_2 > r$). Give the expected phenotypes and ratios of offspring produced by the following crosses.

(a) $R^p_1/rp \times R^p_2/rp$
(b) $R^p_1/rp \times R^p_2/rp$
(c) $R^p_1/rp \times R^p_2/rp$
(d) $R^p_1/rp \times R^p_2/rp$
(e) $r/\times r/\times r/$

*14. Give the expected genotypic and phenotypic ratios for the following crosses for ABO blood types.

(a) $I^A i \times I^A i$
(b) $I^A B \times I^A i$
(c) $I^A B \times I^A B$
(d) $i i \times I^A i$
(e) $I^A B \times i i$

15. If there are five alleles at a locus, how many genotypes may there be at this locus? How many different kinds of homozygotes will there be? How many genotypes and homozygotes would there be with eight alleles?

16. Turkeys have black, bronze, or black-bronze plumage. Examine the results of the following crosses:

<table>
<thead>
<tr>
<th>Parents</th>
<th>Offspring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cross 1: black and bronze</td>
<td>all black</td>
</tr>
<tr>
<td>Cross 2: black and black</td>
<td>$\frac{3}{4}$ black, $\frac{1}{4}$ bronze</td>
</tr>
<tr>
<td>Cross 3: black-bronze and black-bronze</td>
<td>all black-bronze</td>
</tr>
<tr>
<td>Cross 4: black and bronze</td>
<td>$\frac{1}{2}$ black, $\frac{1}{4}$ bronze, $\frac{1}{4}$ black-bronze</td>
</tr>
<tr>
<td>Cross 5: bronze and black-bronze</td>
<td>$\frac{1}{2}$ bronze, $\frac{1}{4}$ black-bronze</td>
</tr>
<tr>
<td>Cross 6: bronze and bronze</td>
<td>$\frac{3}{4}$ bronze, $\frac{1}{4}$ black-bronze</td>
</tr>
</tbody>
</table>

Do you think these differences in plumage arise from incomplete dominance between two alleles at a single locus? If yes, support your conclusion by assigning symbols to each allele and providing genotypes for all turkeys in the crosses. If your answer is no, provide an alternative explanation and assign genotypes to all turkeys in the crosses.

17. In rabbits, an allelic series helps to determine coat color: $C$ (full color), $c^h$ (chinchilla, gray color), $c^h$ (himalayan, white with black extremities), and $c$ (albino, all white). The $C$ allele is dominant over all others, $c^h$ is dominant over $c$, and $c^h$ is dominant over $c$, and $c$ is recessive to all the other alleles. This dominance hierarchy can be summarized as $C > c^h > c^h > c$. The rabbits in the following list are crossed and produce the progeny shown. Give the genotypes of the parents for each cross.

<table>
<thead>
<tr>
<th>Phenotypes of parents</th>
<th>Phenotypes of offspring</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) full color × albino</td>
<td>$\frac{1}{2}$ full color, $\frac{1}{2}$ albino</td>
</tr>
<tr>
<td>(b) himalayan × albino</td>
<td>$\frac{1}{2}$ himalayan, $\frac{1}{2}$ albino</td>
</tr>
<tr>
<td>(c) full color × albino</td>
<td>$\frac{1}{2}$ full color, $\frac{1}{2}$ chinchilla</td>
</tr>
<tr>
<td>(d) full color × himalayan</td>
<td>$\frac{1}{2}$ full color, $\frac{1}{4}$ himalayan, $\frac{1}{4}$ albino</td>
</tr>
<tr>
<td>(e) full color × full color</td>
<td>$\frac{3}{4}$ full color, $\frac{1}{4}$ albino</td>
</tr>
</tbody>
</table>

18. In this chapter we considered Joan Barry’s paternity suit against Charlie Chaplin and how, on the basis of blood types, Chaplin could not have been the father of her child.

(a) What blood types are possible for the father of Barry’s child?
(b) If Chaplin had possessed one of these blood types, would that prove that he fathered Barry’s child?
22. Eye color of the Oriental fruit fly (Bactrocera dorsalis) is determined by a number of genes. A fly having wild-type eyes is crossed with a fly having yellow eyes. All the F₁ flies from this cross have wild-type eyes. When the F₁ are interbred, 9/16 of the F₂ progeny have wild-type eyes, 3/16 have amethyst eyes (a bright, sparkling blue color), and 4/16 have yellow eyes.

(a) Give genotypes for all the flies in the P, F₁, and F₂ generations.

(b) Does epistasis account for eye color in Oriental fruit flies? If so, which gene is epistatic and which gene is hypostatic?

23. A variety of opium poppy (Papaver somniferum L.) having lacerate leaves was crossed with a variety that has normal leaves. All the F₁ had lacerate leaves. Two F₁ plants were interbred to produce the F₂. Of the F₂, 249 had lacerate leaves and 16 had normal leaves. Give genotypes for all the plants in the P, F₁, and F₂ generations. Explain how lacerate leaves are determined in the opium poppy.

24. A dog breeder liked yellow and brown Labrador retrievers. In an attempt to produce yellow and brown puppies, he bought a yellow Labrador male and a brown Labrador female and mated them. Unfortunately, all the puppies produced in this cross were black. (See p. 000 for a discussion of the genetic basis of coat color in Labrador retrievers.)

(a) Explain this result.

(b) How might the breeder go about producing yellow and brown Labradors?

25. When a yellow female Labrador retriever was mated with a brown male, half of the puppies were brown and half were yellow. The same female, when mated with a different brown male, produced all brown males. Explain these results.

26. In summer squash, a plant that produces disc-shaped fruit is crossed with a plant that produces long fruit. All the F₁ have disc-shaped fruit. When the F₁ are intercrossed, F₂ progeny are produced in the following ratio: 9/16 disc-shaped fruit: 3/16 spherical fruit: 1/16 long fruit. Give the genotypes of the F₂ progeny.

27. In sweet peas, some plants have purple flowers and other plants have white flowers. A homozygous variety of pea that has purple flowers is crossed with a homozygous variety that has white flowers. All the F₁ have purple flowers. When these F₁ are self-fertilized, the F₂ appear in a ratio of 9/16 purple to 1/16 white.

(a) Give genotypes for the purple and white flowers in these crosses.

(b) Draw a hypothetical biochemical pathway to explain the production of purple and white flowers in sweet peas.

28. For the following questions, refer to p. 000 for a discussion of how coat color and pattern are determined in dogs.

(a) Explain why Irish setters are reddish in color.

(b) Will a cross between a beagle and a Dalmatian produce puppies with ticking? Why or why not?

(c) Can a poodle crossed with any other breed produce spotted puppies? Why or why not?

(d) If a St. Bernard is crossed with a Doberman, will the offspring have solid, yellow, saddle, or bicolor coats?

(e) If a Rottweiler is crossed with a Labrador retriever, will the offspring have solid, yellow, saddle, or bicolor coats?
*29. When a Chinese hamster with white spots is crossed with another hamster that has no spots, approximately $\frac{1}{2}$ of the offspring have white spots and $\frac{1}{2}$ have no spots. When two hamsters with white spots are crossed, $\frac{2}{3}$ of the offspring possess white spots and $\frac{1}{3}$ have no spots.

(a) What is the genetic basis of white spotting in Chinese hamsters?
(b) How might you go about producing Chinese hamsters that breed true for white spotting?

30. Male-limited precocious puberty results from a rare, sex-limited autosomal allele (P) that is dominant over the allele for normal puberty (p) and is expressed only in males. Bill undergoes precocious puberty, but his brother Jack and his sister Beth underwent puberty at the usual time, between the ages of 10 and 14. Although Bill's mother and father underwent normal puberty, two of his maternal uncles (his mother's brothers) underwent precocious puberty. All of Bill's grandparents underwent normal puberty. Give the most likely genotypes for all the relatives mentioned in this family.

31. Pattern baldness in humans is a sex-influenced trait that is autosomal dominant in males and recessive in females. Jack has a full head of hair. JoAnn also has a full head of hair, but her mother is bald. (In women, pattern baldness is usually expressed as a thinning of the hair.) If Jack and JoAnn marry, what proportion of their children are expected to be bald?

32. In goats, a beard is produced by an autosomal allele that is dominant in males and recessive in females. We'll use the symbol $B^o$ for the beard allele and $B^+$ for the beardless allele. Another independently assorting autosomal allele that produces a black coat ($W$) is dominant over the allele for white coat ($w$). Give the phenotypes and their expected proportions for the following crosses.

(a) $B^+B^o$ Ww male $\times$ $B^+B^o$ Ww female
(b) $B^+B^o$ Ww male $\times$ $B^+B^o$ Ww female
(c) $B^+B^+$ Ww male $\times$ $B^+B^+$ Ww female
(d) $B^+B^+$ Ww male $\times$ $B^+B^+$ Ww female

33. In the snail Limnaea peregra, shell coiling results from a genetic maternal effect. An autosomal allele for a right-handed shell ($s^+$), called dextral, is dominant over the allele for a left-handed shell ($s$), called sinistral. A pet snail called Martha is sinistral and reproduces only as a female (the snails are hermaphroditic). Indicate which of the following statements are true and which are false. Explain your reasoning in each case.

(a) Martha's genotype must be $ss$.
(b) Martha's genotype cannot be $s^+s^-$.
(c) All the offspring produced by Martha must be sinistral.
(d) At least some of the offspring produced by Martha must be sinistral.
(e) Martha's mother must have been sinistral.
(f) All Martha's brothers must be sinistral.

34. In unicorns, two autosomal loci interact to determine the type of tail. One locus controls whether a tail is present at all; the allele for a tail (T) is dominant over the allele for tailless (t). If a unicorn has a tail, then alleles at a second locus determine whether the tail is curly or straight. Farmer Baldridge has two unicorns with curly tails. When he crosses these two unicorns, $\frac{1}{2}$ of the progeny have curly tails, $\frac{3}{4}$ have straight tails, and $\frac{1}{4}$ do not have a tail. Give the genotypes of the parents and progeny in Farmer Baldridge's cross. Explain how he obtained the 2:1:1 phenotypic ratio in his cross.

*35. Phenylketonuria (PKU) is an autosomal recessive disease that results from a defect in an enzyme that normally metabolizes the amino acid phenylalanine. When this enzyme is defective, high levels of phenylalanine cause brain damage. In the past, most children with PKU became mentally retarded. Fortunately, mental retardation can be prevented in these children today by carefully controlling the amount of phenylalanine in the diet. As a result of this treatment, many people with PKU are now reaching reproductive age with no mental retardation. By the end of the teen years, when brain development is complete, many people with PKU go off the restrictive diet. Children born to women with PKU (who are no longer on a phenylalanine-restricted diet) frequently have low birth weight, developmental abnormalities, and mental retardation, even though they are heterozygous for the recessive PKU allele. However, children of men with PKU do not have these problems. Provide an explanation for these observations.

36. In 1983, a sheep farmer in Oklahoma noticed a ram in his flock that possessed increased muscle mass in his hindquarters. Many of the offspring of this ram possessed the same trait, which became known as the callipyge mutant (callipyge is Greek for "beautiful buttocks"). The mutation that caused the callipyge phenotype was eventually mapped to a position on the sheep chromosome 18.

When the male callipyge offspring of the original mutant ram were crossed with normal females, they produced the following progeny: $\frac{1}{4}$ male callipyge, $\frac{1}{4}$ female callipyge, $\frac{1}{4}$ male normal, and $\frac{1}{4}$ female normal. When female callipyge offspring of the original mutant ram were crossed with normal males, all of the offspring were normal. Analysis of the chromosomes of these offspring of callipyge females showed that half of them received a chromosome 18 with the callipyge gene from their mother. Propose an explanation for the inheritance of the callipyge gene. How might you test your explanation?
37. Suppose that you are tending a mouse colony at a genetics research institute and one day you discover a mouse with twisted ears. You breed this mouse with twisted ears and find that the trait is inherited. Both male and female mice have twisted ears, but when you cross a twisted-eared male with a normal-eared female, you obtain different results from those obtained when you cross a twisted-eared female with normal-eared male—the reciprocal crosses give different results. Describe how you would go about determining whether this trait results from a sex-linked gene, a sex-influenced gene, a genetic maternal effect, a cytoplasmically inherited gene, or genomic imprinting. What crosses would you conduct and what results would be expected with these different types of inheritance?

SUGGESTED READINGS

Discusses the phenomenon of genomic imprinting.

A nice review of the history of anticipation.

Reviews some of the evidence that DNA methylation is implicated in genomic imprinting.

Report on the discovery of the gene that causes Huntington disease.

Review of the use of dog genetics for understanding human genetic diseases.

Discusses some of the possible evolutionary reasons for genomic imprinting.

Another review of genomic imprinting.

Discusses the characteristics of cytoplasmically inherited mitochondrial mutations.


Discussion of human multifactorial diseases and the effect of the Human Genome Project on the identification of genes influencing these diseases.

More discussion of cytoplasmically inherited mitochondrial mutations.

A comprehensive review of canine genetics.