9.3 Mendel's law of segregation describes the inheritance of a single characteristic

Mendel performed many experiments in which he tracked the inheritance of characteristics that occur in two forms, such as flower color. The results led him to formulate several ideas about inheritance. Let's look at some of his experiments and follow the reasoning that led to his hypotheses.

Figure 9.3A starts with a cross between a pea plant with purple flowers and one with white flowers. This is called a **monohybrid cross** because the parent plants differ in only one characteristic. Mendel observed that F_1 plants produced by these two true-breeding parents all had purple flowers; they were not a lighter purple, as predicted by the blending hypothesis. Was the white-flowered plant's genetic contribution to the hybrids lost? By mating the F_1 plants, Mendel found the answer to be no. Out of 929 F_2 plants, Mendel found that 705 (about $\frac{3}{4}$) had purple flowers and 224 (about $\frac{1}{4}$) had white flowers, a ratio of about three plants with purple flowers to every one with white flowers in the F_2 generation. Mendel reasoned that the heritable factor for white flowers did not disappear in the F_1 plants, but that only the purple-flower factor was affecting F_1 flower color. He also deduced that the F_1 plants must have carried two factors for the flower-color characteristic, one for purple and one for white.

Mendel observed these same patterns of inheritance for six other pea plant characteristics (see Figure 9.2D). From these results, Mendel developed four hypotheses, which we describe here using modern terminology (such as "gene" instead of "heritable factor"):

1. *There are alternative forms of genes that account for variations in inherited characteristics.* For example, the gene for flower color in pea plants exists in two forms, one for purple and the other for white. The alternative versions of a gene are now called **alleles.**
2. *For each characteristic, an organism inherits two alleles, one from each parent. These alleles may be the same or different.* An organism that has two identical alleles for a gene is said to be **homozygous** for that gene (and is called a homozygote). An organism that has two different alleles for a gene is said to be **heterozygous** for that gene (and is called a heterozygote).
3. *If the two alleles of an inherited pair differ, then one determines the organism's appearance and is called the* ***dominant allele;*** *the other has no noticeable effect on the organism's appearance and is called the* ***recessive allele.*** We use uppercase letters to represent dominant alleles and lowercase letters to represent recessive alleles.
4. *A sperm or egg carries only one allele for each inherited trait because allele pairs separate (segregate) from each other during the production of gametes.* This statement is now known as the **law of segregation.** When sperm and egg unite at fertilization, each contributes its allele, restoring the paired condition in the offspring.

Figure 9.3B shows how Mendel explained the results given in Figure 9.3A. In this example, *P* represents the dominant

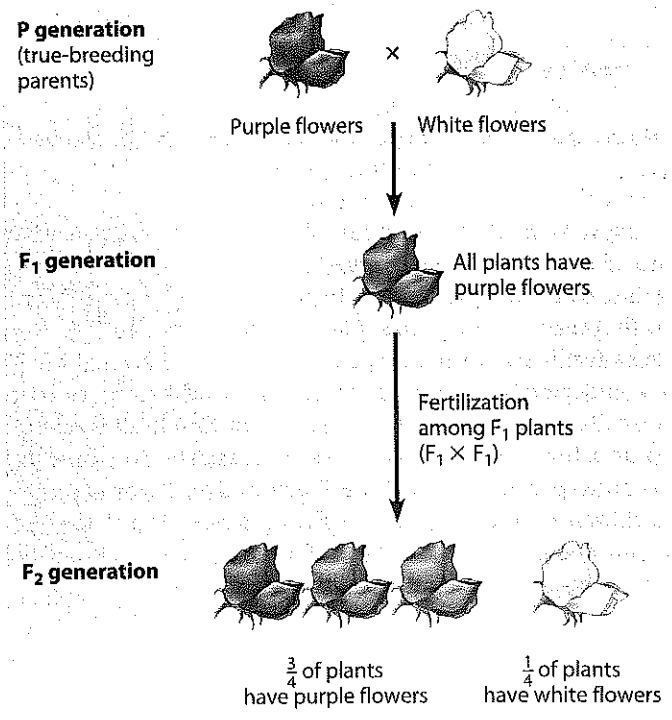

Figure 9.3A Crosses tracking one characteristic (flower color)

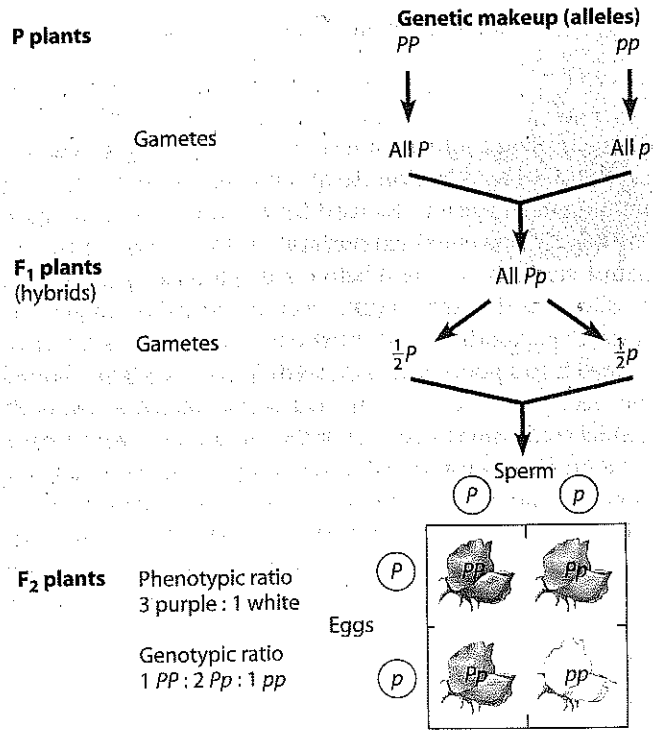

Figure 9.3B Explanation of the crosses in Figure 9.3A

9.5 The law of independent assortment is revealed by tracking two characteristics at once

Two of the seven characteristics Mendel studied were seed shape and seed color. Mendel's seeds were either round or wrinkled in shape, and they were either yellow or green in color. From monohybrid crosses, Mendel knew that the allele for round shape (designated *R*) was dominant to the allele for wrinkled shape (*r*) and that the allele for yellow seed color (*Y*) was dominant to the allele for green seed color (*y*). What would result from a mating of parental varieties differing in two characteristics—a **dihybrid cross**? Mendel crossed homozygous plants having round yellow seeds (genotype *RRYY*) with plants having wrinkled green seeds (*rryy*). As shown in Figure 9.5A, the union of *RY* and *ry* gametes yielded hybrids heterozygous for both characteristics (*RrYy*)—that is, *dihybrids*. As we would expect, all of these offspring, the F_1 generation, had round yellow seeds. But were the two characteristics transmitted from parents to offspring as a package, or was each characteristic inherited independently of the other?

The question was answered when Mendel allowed fertilization to occur among the F_1 plants. If the genes for the two characteristics were inherited together, as shown on the left in the figure, then the F_1 hybrids would produce only the same two kinds (genotypes) of gametes—*RY* and *ry*—that they received from their parents. This hypothesis predicts that the phenotypic ratio of the F_2 generation will be 3:1 (three plants with round yellow seeds for every one with wrinkled green seeds), as in the left Punnett square. If, however, the two seed characteristics segregated independently, then the F_1 generation would produce four gamete genotypes—*RY*, *rY*, *Ry*, and *ry*—in equal quantities. The Punnett square on the right shows all possible combinations of alleles that can result in the F_2 generation from the union of four kinds of sperm with four kinds of eggs. This Punnett square shows that there are nine different genotypes in the F_2. However, there are only four phenotypes, with a ratio of 9:3:3:1.

The Punnett square on the right also reveals that a dihybrid cross is equivalent to two monohybrid crosses occurring simultaneously. From the 9:3:3:1 ratio, we can see that there are 12 plants with round seeds to 4 with wrinkled seeds and 12 yellow-seeded plants to 4 green-seeded ones. These 12:4 ratios each reduce to 3:1, which is the F_2 ratio for a monohybrid cross. Mendel tried his seven pea characteristics in various dihybrid combinations and always obtained data close to the predicted 9:3:3:1 ratio. These results supported the hypothesis that *each pair of alleles segregates independently of the other pairs of alleles during gamete formation.* This is called Mendel's **law of independent assortment.**

Figure 9.5B shows how this law applies to the inheritance of two hereditary characteristics in Labrador retrievers: black versus chocolate coat color and normal vision versus the eye disorder called progressive retinal atrophy (PRA). As you

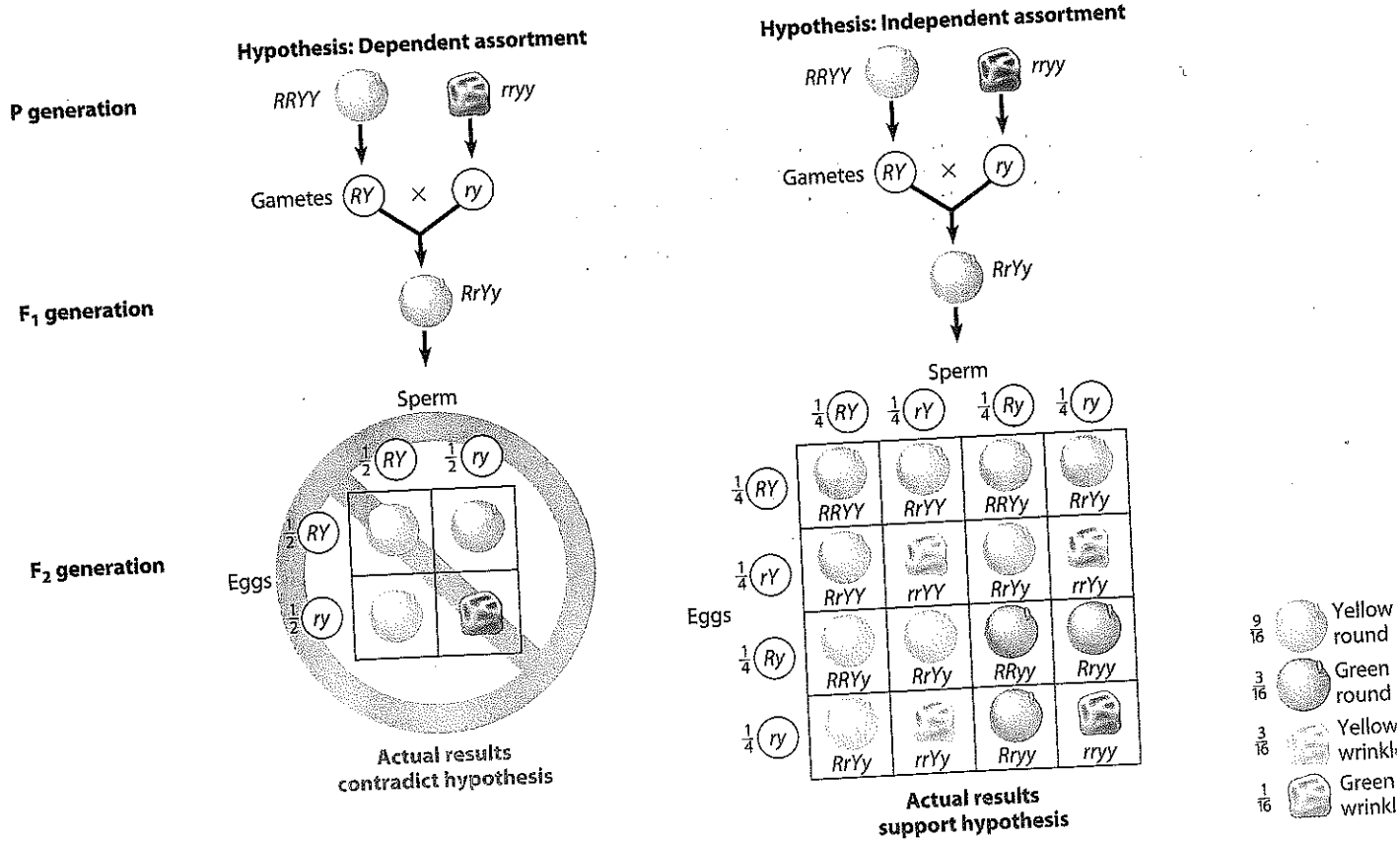

Figure 9.5A Two hypotheses for segregation in a dihybrid cross

9.14 A single gene may affect many phenotypic characteristics

All of our genetic examples to this point have been cases in which each gene specified only one hereditary characteristic. Most genes, however, influence multiple characteristics, a property called **pleiotropy** (from the Greek *pleion*, more).

An example of pleiotropy in humans is sickle-cell disease, a disorder characterized by the diverse symptoms shown in Figure 9.14. All of these possible phenotypic effects result from the action of a single kind of allele when it is present on both homologous chromosomes. The direct effect of the sickle-cell allele is to make red blood cells produce abnormal hemoglobin molecules. These molecules tend to link together and crystallize, especially when the oxygen content of the blood is lower than usual because of high altitude, overexertion, or respiratory ailments. As the hemoglobin crystallizes, the normally disk-shaped red blood cells deform to a sickle shape with jagged edges, as shown in the micrograph. Sickled cells are destroyed rapidly by the body, and the destruction of these cells may seriously lower the individual's red cell count, causing anemia and general weakening of the body. Also, because of their angular shape, sickled cells do not flow smoothly in the blood and tend to accumulate and clog tiny blood vessels. Blood flow to body parts is reduced, resulting in periodic fever, severe pain, and damage to various organs, including the heart, brain, and kidneys. Sickled cells also accumulate in the spleen, damaging it. Blood transfusions and certain drugs may relieve some of the symptoms, but there is no cure, and sickle-cell disease kills about 100,000 people in the world annually.

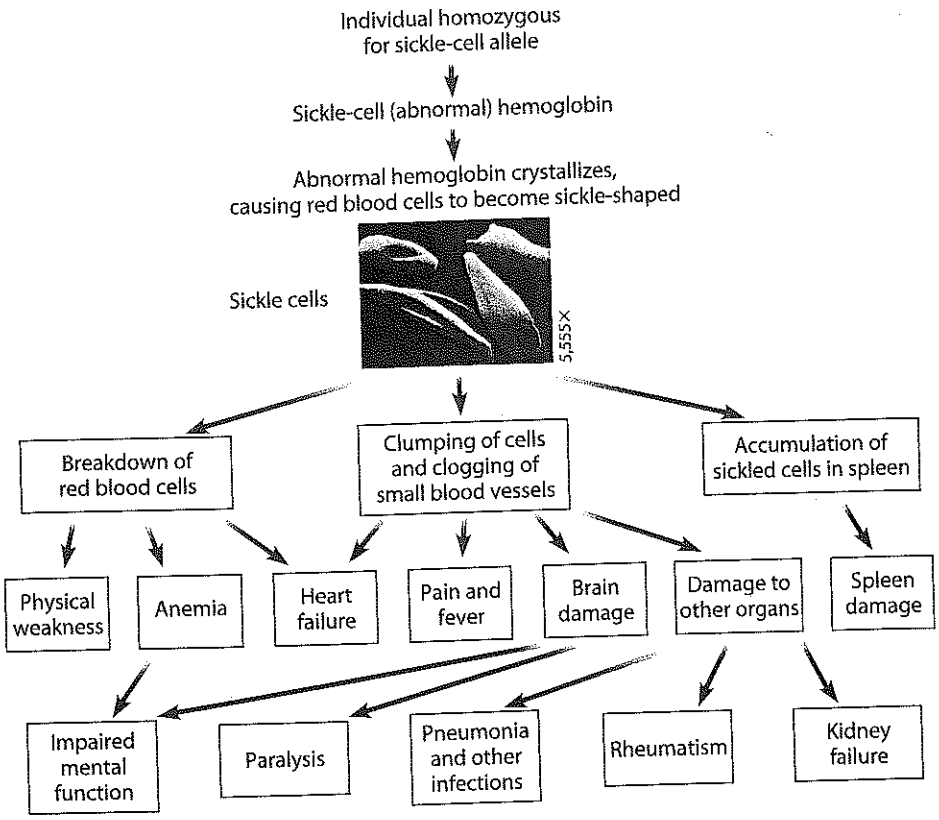

Figure 9.14 Sickle-cell disease, multiple effects of a single human gene

In most cases, only people who are homozygous for the sickle-cell allele suffer from the disease. Heterozygotes, who have one sickle-cell allele and one nonsickle allele, are usually healthy, although in rare cases they may experience some pleiotropic effects when oxygen in the blood is severely reduced, such as at very high altitudes. These effects may occur because the nonsickle and sickle-cell alleles are codominant: Both alleles are expressed in heterozygous individuals, and their red blood cells contain both normal and abnormal hemoglobin. Heterozygotes are said to have "sickle-cell trait."

Sickle-cell disease is the most common inherited disorder among people of African descent, striking one in 400 African-Americans. About one in ten African-Americans is a carrier—a heterozygote. Among Americans of other ancestry, the sickle-cell allele is extremely rare.

One in ten is an unusually high frequency of carriers for an allele with such harmful effects in homozygotes. We might expect that the frequency of the sickle-cell allele in the population would be much lower because many homozygotes die before passing their genes to the next generation. The high frequency appears to be a vestige of the roots of African-Americans. Sickle-cell disease is most common in tropical Africa, where the deadly disease malaria is also prevalent. The protistan parasite that causes malaria spends part of its life cycle inside red blood cells. When it enters those of a person with the sickle-cell allele, it triggers sickling. The body destroys most of the sickled cells, and the parasite does not grow well in those that remain. Consequently, sickle-cell carriers are resistant to malaria, and in many parts of Africa, they live longer and have more offspring than noncarriers who are exposed to malaria. In this way, malaria has kept the frequency of the sickle-cell allele relatively high in much of the African continent. To put it in evolutionary terms, as long as malaria is a danger, individuals with the sickle-cell allele have a selective advantage.

? How does sickle-cell disease exemplify the concept of pleiotropy?

■ Homozygosity for the sickle-cell allele causes abnormal hemoglobin, and the impact of the abnormal hemoglobin on the shape of red blood cells leads to a cascade of symptoms in multiple organs of the body.

9.24 Sex-linked disorders affect mostly males

Fruit fly genetics has taught us much about human inheritance. A number of human conditions result from sex-linked (X-linked) recessive alleles that are inherited in the same way as the white-eye trait in fruit flies. The fruit fly model also shows us why recessive sex-linked traits are expressed much more frequently in men than in women. Like a male fruit fly, if a man inherits only one sex-linked recessive allele—from his mother—the allele will be expressed. In contrast, a woman has to inherit two such alleles—one from each parent—in order to exhibit the trait.

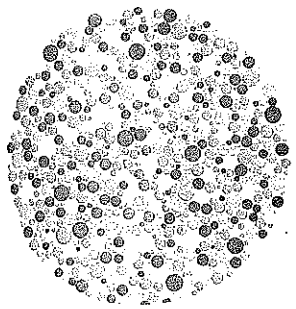

Figure 9.24A A test for red-green color blindness

Red-green color blindness is a common sex-linked disorder characterized by a malfunction of light-sensitive cells in the eyes. It is actually a class of disorders, involving several X-linked genes. A person with normal color vision can see more than 150 colors. In contrast, someone with red-green color blindness can see fewer than 25. For some affected people, red hues appear gray; others see gray instead of green; still others are green-weak or red-weak, tending to confuse shades of these colors. Mostly males are affected, but heterozygous females have some defects. (If you have red-green color blindness, you probably cannot see the numeral 7 in Figure 9.24A.)

Hemophilia is a sex-linked recessive trait with a long, well-documented history. Hemophiliacs bleed excessively when injured because they lack one or more of the proteins required for blood clotting. The most seriously affected individuals may bleed to death after relatively minor bruises or cuts.

A high incidence of hemophilia has plagued the royal families of Europe. The first royal hemophiliac seems to have been a son of Queen Victoria (1819–1901) of England. It is likely that the hemophilia allele arose through a mutation in one of the gametes of Victoria's mother or father, making Victoria a carrier of the deadly allele. Hemophilia was eventually introduced into the royal families of Prussia, Russia, and Spain through the marriages of two of Victoria's daughters who were carriers. Thus, the age-old practice of strengthening international alliances by marriage effectively spread hemophilia through the royal families of several nations. The photograph in Figure 9.24B shows Queen Victoria's granddaughter Alexandra, her husband Nicholas, who was the last czar of Russia, their daughters, and their son Alexis. The pedigree uses half-colored symbols to represent heterozygous carriers of the hemophilia allele. As you can see in the pedigree, Alexandra, like her mother and grandmother, was a carrier, and Alexis had the disease.

Another sex-linked recessive disorder is **Duchenne muscular dystrophy**, a condition characterized by a progressive weakening of the muscles and loss of coordination. Almost

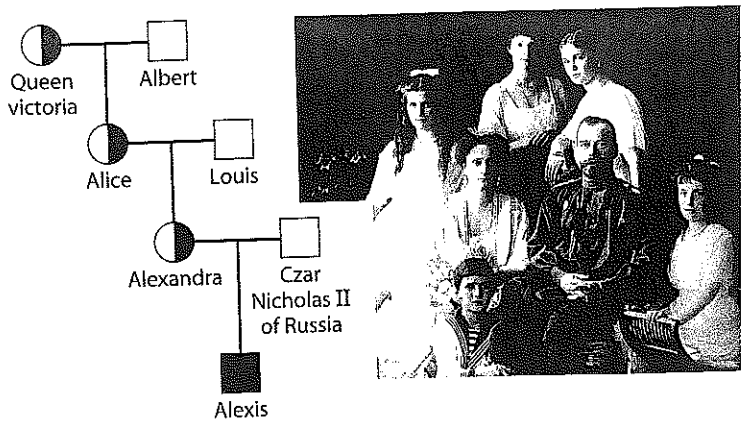

Figure 9.24B Hemophilia in the royal family of Russia

all cases are males, and the first symptoms appear in early childhood, when the child begins to have difficulty standing up. He is inevitably wheelchair-bound by age 12. Eventually, he becomes severely wasted, and normal breathing becomes difficult. Affected individuals rarely live past their early 20s.

For such a severe disease, Duchenne muscular dystrophy is relatively common. In the general U.S. population, about one in 3,500 male babies is affected, and the disease is even more common in some inbred populations. In one Amish community in Indiana, for instance, one out of every 100 males is born with the disease.

With the help of DNA technology (discussed in Chapter 12), the defective gene that causes Duchenne muscular dystrophy has been mapped at a particular point on the X chromosome. The gene's wild-type allele codes for a protein called dystrophin, which is present in normal muscle but missing in Duchenne patients.

The discovery of sex-linked genes and their pattern of inheritance in fruit flies and humans was one of many breakthroughs in understanding how genes are passed from one generation to the next. During the first half of the 20th century, geneticists rediscovered Mendel's work, reinterpreted his laws in light of chromosomal behavior during meiosis, and firmly established the chromosome theory of inheritance. The chromosome theory set the stage for another explosion of experimental work in the second half of the 20th century. This work was in molecular genetics, an area we explore in the next three chapters.

? Neither Tom nor Sue has Duchenne muscular dystrophy, but their first son does. If the couple has a second child, what is the probability that he or she will also have the disease?

■ $\frac{1}{4}$ ($\frac{1}{2}$ chance of a male child × $\frac{1}{2}$ chance that he will inherit the mutant X)