

# 4

## Sex Determination and Sex-Linked Characteristics



**Sex in the platypus is determined by sex chromosomes.** Females have 10 X chromosomes, whereas males have 5 X and 5 Y chromosomes.  
[Australian Geographic/Aflo Foto Agency/Photolibrary.]

### THE STRANGE CASE OF PLATYPUS SEX

The platypus, *Ornithorhynchus anatinus*, is clearly one of life's strangest animals. It possesses a furry coat and, like a mammal, is warm blooded and produces milk to nourish its young, but it lacks teeth, has a bill, and lays eggs like a bird. The feet are webbed like those of a duck, and females have no nipples (offspring suck milk directly from the abdominal skin); males have spurs on their hind legs that deliver a deadly, snakelike venom. The platypus has such a hodgepodge of mammalian, avian, and reptilian traits that the first scientists to examine a platypus skin specimen thought it might be an elaborate hoax, produced by attaching parts culled from several different organisms. In spite of its strange appearance, the platypus is genetically a monotreme mammal, a side branch that diverged from the rest of mammals some 166 million years ago.

The platypus lives in eastern and southern Australia and on the island of Tasmania. An excellent swimmer, it spends most of its time in small rivers and streams foraging for worms, frogs, insect larvae, shrimp, and crayfish. Among other oddities, it locates its prey by using electroreception.

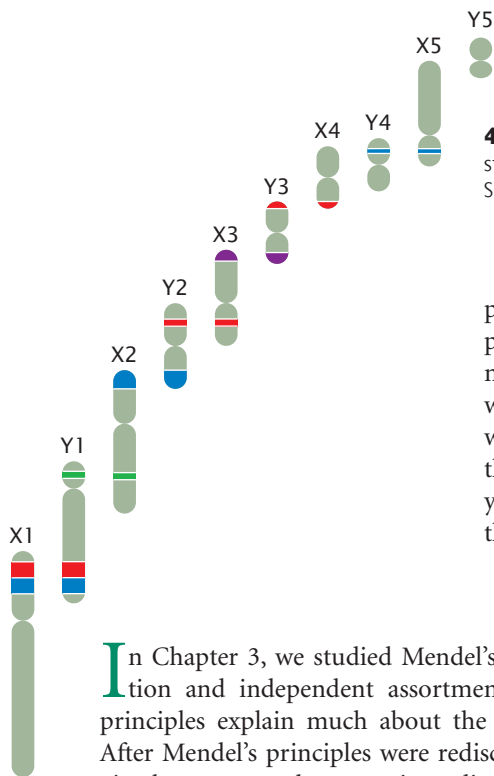
The platypus genome was sequenced in 2008, providing a detailed view of the genetic makeup of this strange animal. It has a relatively small genome for a mammal, with 2.3 billion base pairs of DNA and about 18,500 protein-encoding genes. Almost 10% of its genes encode proteins that take part in odor and chemical reception. The platypus genome is a blend of mammalian, reptilian, and unique characteristics.

Platypus sex also is unusual. For most mammals, whether an individual organism is male or female is determined by sex chromosomes. Most females possess two X chromosomes, whereas males have a single X chromosome and a smaller sex chromosome called Y. This is the usual type of sex determination in mammals, but how sex is determined in the platypus remained a mystery for many years. The platypus possesses 52 chromosomes, and early geneticists observed a confusing mix of different chromosomes in male and female platypuses, including an unusual chainlike group of chromosomes in meiosis (Figure 4.1).

In 2004, Frank Grutzner and a group of other scientists created fluorescent paints to mark the platypus chromosomes so that they could follow the behavior of individual chromosomes in the course of meiosis. What they discovered was remarkable: platypuses

fig 4.1





**4.1 Sex chromosomes of the duckbill platypus.** In meiosis, the sex chromosomes form chainlike structures. [Adapted from F. Veyrunes et al., *Genome Research* 18(6): 965–973, 2008. Copyright © 2008, Cold Spring Harbor Laboratory Press.]

possess ten sex chromosomes: female platypuses have ten X chromosomes, whereas male platypuses have five X chromosomes and five Y chromosomes. In meiosis, these sex chromosomes line up in a precise order, forming a long chain of sex chromosomes. In spite of what at first appears to be mass confusion, the platypus sex chromosomes pair and align with great precision so that each egg cell gets exactly five Xs; half the sperm get five Xs and the other half get five Ys. The mechanism that brings about this precise separation is not yet known. The complicated set of sex chromosomes in the platypus is just one example of the varied ways in which sex is determined and influences inheritance.

In Chapter 3, we studied Mendel's principles of segregation and independent assortment and saw how these principles explain much about the nature of inheritance. After Mendel's principles were rediscovered in 1900, biologists began to conduct genetic studies on a wide array of different organisms. As they applied Mendel's principles more widely, exceptions were observed, and it became necessary to devise extensions of his basic principles of heredity. In this chapter, we explore one of the major extensions of Mendel's principles: the inheritance of characteristics encoded by genes located on the sex chromosomes, which often differ in males and females (**Figure 4.2**). These characteristics and the genes that produce them are referred to as sex linked. To understand the inheritance of sex-linked characteristics, we must first know how sex is determined—why some members of a species are male and others are female. Sex determination is the focus of the first part of the chapter. The second part examines how characteristics encoded by genes on the sex chromosomes are inherited. In Chapter 5, we will explore some additional ways in which sex and inheritance interact.

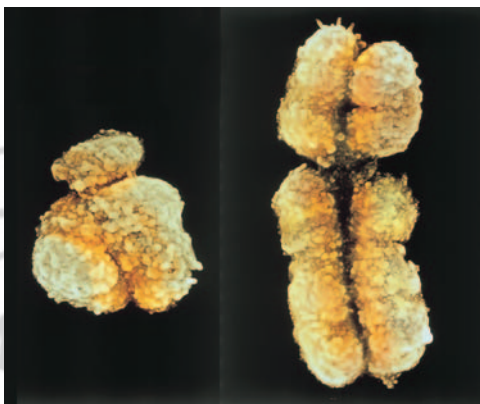
As we consider sex determination and sex-linked characteristics, it will be helpful to think about two important principles. First, there are several different mechanisms of sex determination and, ultimately, the mechanism of sex determination controls the inheritance of sex-linked characteristics. Second, like other pairs of chromosomes, the X and Y sex chromosomes pair in the course of meiosis and segregate, but, throughout most of their length, they are not homologous (their gene sequences do not encode the same characteristics): most genes on the X chromosome are different from genes on the Y chromosome. Consequently, males and females do not possess the same number of alleles at sex-linked loci. This difference in the number of sex-linked alleles produces distinct patterns of inheritance in males and females. **TRY PROBLEM 14**

## 4.1 Sex Is Determined by a Number of Different Mechanisms

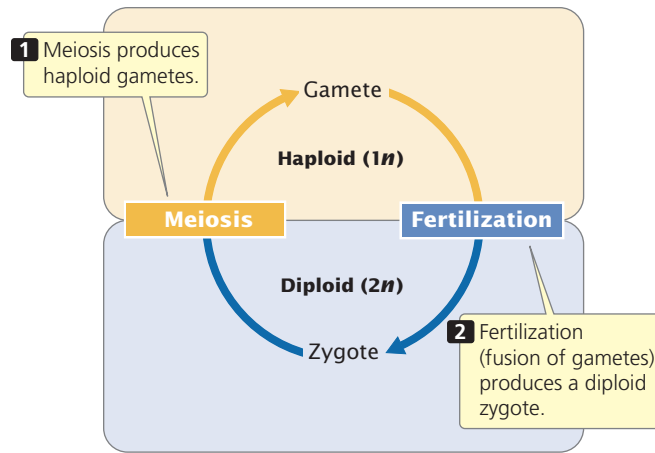
Sexual reproduction is the formation of offspring that are genetically distinct from their parents; most often, two parents contribute genes to their offspring and the genes are assorted into new combinations through meiosis. Among most eukaryotes, sexual reproduction consists of two processes that lead to an alternation of haploid and diploid cells: meiosis produces haploid gametes (spores in plants), and fertilization produces diploid zygotes (**Figure 4.3**).

The term **sex** refers to sexual phenotype. Most organisms have only two sexual phenotypes: male and female. The fundamental difference between males and females is gamete size: males produce small gametes; females produce relatively larger gametes (**Figure 4.4**).

The mechanism by which sex is established is termed **sex determination**. We define the sex of an individual organism in reference to its phenotype. Sometimes an individual organism has chromosomes or genes that are normally associated with one sex but a morphology corresponding to the opposite sex. For instance, the cells of female humans normally have two X chromosomes, and the cells



**4.2 The male sex chromosome (Y, at the left) differs from the female sex chromosome (X, at the right) in size and shape.** [Biophoto Associates/Photo Researchers.]



**4.3** In most eukaryotic organisms, sexual reproduction consists of an alternation of haploid ( $1n$ ) and diploid ( $2n$ ) cells.

of males have one X chromosome and one Y chromosome. A few rare persons have male anatomy, although their cells each contain two X chromosomes. Even though these people are genetically female, we refer to them as male because their sexual phenotype is male. (As we will see later in the chapter, these XX males usually have a small piece of the Y chromosome, which is attached to another chromosome.)

### CONCEPTS

In sexual reproduction, parents contribute genes to produce an offspring that is genetically distinct from both parents. In most eukaryotes, sexual reproduction consists of meiosis, which produces haploid gametes (or spores), and fertilization, which produces a diploid zygote.

#### ✓ CONCEPT CHECK 1

What process causes the genetic variation seen in offspring produced by sexual reproduction?



**4.4** Male and female gametes (sperm and egg, respectively) differ in size. In this photograph, a human sperm (with flagellum) penetrates a human egg cell. [Francis Leroy, Biocosmos/Science Photo Library/Photo Researchers.]

There are many ways in which sex differences arise. In some species, both sexes are present in the same organism, a condition termed **hermaphroditism**; organisms that bear both male and female reproductive structures are said to be **monoecious** (meaning “one house”). Species in which the organism has either male or female reproductive structures are said to be **dioecious** (meaning “two houses”). Humans are dioecious. Among dioecious species, sex may be determined chromosomally, genetically, or environmentally.

### Chromosomal Sex-Determining Systems

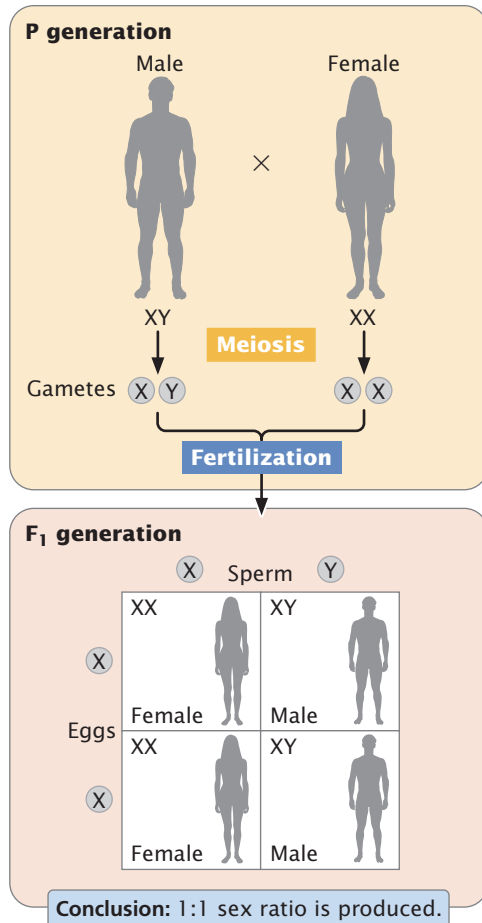
The chromosome theory of inheritance (discussed in Chapter 3) states that genes are located on chromosomes, which serve as vehicles for the segregation of genes in meiosis. Definitive proof of this theory was provided by the discovery that the sex of certain insects is determined by the presence or absence of particular chromosomes.

In 1891, Hermann Henking noticed a peculiar structure in the nuclei of cells from male insects. Understanding neither its function nor its relation to sex, he called this structure the X body. Later, Clarence E. McClung studied the X body in grasshoppers and recognized that it was a chromosome. McClung called it the accessory chromosome, but it eventually became known as the X chromosome, from Henking’s original designation. McClung observed that the cells of female grasshoppers had one more chromosome than the number of chromosomes in the cells of male grasshoppers, and he concluded that accessory chromosomes played a role in sex determination. In 1905, Nettie Stevens and Edmund Wilson demonstrated that, in grasshoppers and other insects, the cells of females have two X chromosomes, whereas the cells of males have a single X. In some insects, they counted the same number of chromosomes in the cells of males and females but saw that one chromosome pair was different: two X chromosomes were found in female cells, whereas a single X chromosome plus a smaller chromosome, which they called Y, was found in male cells.

Stevens and Wilson also showed that the X and Y chromosomes separate into different cells in sperm formation; half of the sperm receive an X chromosome and the other half receive a Y. All egg cells produced by the female in meiosis receive one X chromosome. A sperm containing a Y chromosome unites with an X-bearing egg to produce an XY male, whereas a sperm containing an X chromosome unites with an X-bearing egg to produce an XX female. This distribution of X and Y chromosomes in sperm accounts for the 1 : 1 sex ratio observed in most dioecious organisms (**Figure 4.5**). Because sex is inherited like other genetically determined characteristics, Stevens and Wilson’s discovery that sex is associated with the inheritance of a particular chromosome also demonstrated that genes are on chromosomes.

As Stevens and Wilson found for insects, sex in many organisms is determined by a pair of chromosomes, the **sex chromosomes**, which differ between males and females.

fig 4.5



**4.5 Inheritance of sex in organisms with X and Y chromosomes results in equal numbers of male and female offspring.**

The nonsex chromosomes, which are the same for males and females, are called **autosomes**. We think of sex in these organisms as being determined by the presence of the sex chromosomes, but, in fact, the individual genes located on the sex chromosomes are usually responsible for the sexual phenotypes.

**XX-XO sex determination** The mechanism of sex determination in the grasshoppers studied by McClung is one of the simplest mechanisms of chromosomal sex determination and is called the XX-XO system. In this system, females have two X chromosomes (XX), and males possess a single X chromosome (XO). There is no O chromosome; the letter O signifies the absence of a sex chromosome.

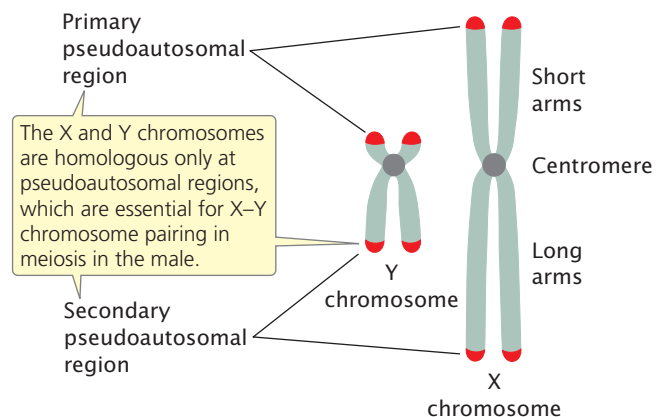
In meiosis in females, the two X chromosomes pair and then separate, with one X chromosome entering each haploid egg. In males, the single X chromosome segregates in meiosis to half the sperm cells; the other half receive no sex chromosome. Because males produce two different types of gametes with respect to the sex chromosomes, they are said to be the **heterogametic sex**. Females, which produce gametes that are all the same with respect to the sex chromosomes, are the

**homogametic sex**. In the XX-XO system, the sex of an individual organism is therefore determined by which type of male gamete fertilizes the egg. X-bearing sperm unite with X-bearing eggs to produce XX zygotes, which eventually develop as females. Sperm lacking an X chromosome unite with X-bearing eggs to produce XO zygotes, which develop into males.

**XX-XY sex determination** In many species, the cells of males and females have the same number of chromosomes, but the cells of females have two X chromosomes (XX) and the cells of males have a single X chromosome and a smaller sex chromosome, the Y chromosome (XY). In humans and many other organisms, the Y chromosome is acrocentric (Figure 4.6), not Y shaped as is commonly assumed. In this type of sex-determining system, the male is the heterogametic sex—half of his gametes have an X chromosome and half have a Y chromosome. The female is the homogametic sex—all her egg cells contain a single X chromosome. Many organisms, including some plants, insects, and reptiles, and all mammals (including humans), have the XX-XY sex-determining system. Other organisms have variations of the XX-XY system of sex determination, including the duck-billed platypus (discussed in the introduction to this chapter) in which females have five pairs of X chromosomes and males have five pairs of X and Y chromosomes.

Although the X and Y chromosomes are not generally homologous, they do pair and segregate into different cells in meiosis. They can pair because these chromosomes are homologous in small regions called the **pseudoautosomal regions** (see Figure 4.6), in which they carry the same genes. In humans, there are pseudoautosomal regions at both tips of the X and Y chromosomes.

**ZZ-ZW sex determination** In this system, the female is heterogametic and the male is homogametic. To prevent confusion with the XX-XY system, the sex chromosomes in this system are called Z and W, but the chromosomes do



**4.6 The X and Y chromosomes in humans differ in size and genetic content.** They are homologous only in the pseudoautosomal regions.

fig 4.6

not resemble Zs and Ws. Females in this system are ZW; after meiosis, half of the eggs have a Z chromosome and the other half have a W chromosome. Males are ZZ; all sperm contain a single Z chromosome. The ZZ-ZW system is found in birds, snakes, butterflies, some amphibians, and some fishes.

### CONCEPTS

The discovery that the presence or absence of particular chromosomes determines sex in insects provided evidence that genes are located on chromosomes. In XX-XO sex determination, the male is XO and heterogametic, and the female is XX and homogametic. In XX-XY sex determination, the male is XY and the female is XX; in this system, the male is heterogametic. In ZZ-ZW sex determination, the female is ZW and the male is ZZ; in this system, the female is the heterogametic sex.

#### ✓ CONCEPT CHECK 2

How does the heterogametic sex differ from the homogametic sex?

- The heterogametic sex is male; the homogametic sex is female.
- Gametes of the heterogametic sex have different sex chromosomes; gametes of homogametic sex have the same sex chromosome.
- Gametes of the heterogametic sex all contain a Y chromosome; gametes of the homogametic sex all contain an X chromosome.

### Genic Sex Determination

In some plants, fungi, and protozoans, sex is genetically determined, but there are no obvious differences in the chromosomes of males and females: there are no sex chromosomes. These organisms have **genic sex determination**; genotypes at one or more loci determine the sex of an individual plant, fungus, or protozoan.

It is important to understand that, even in chromosomal sex-determining systems, sex is actually determined

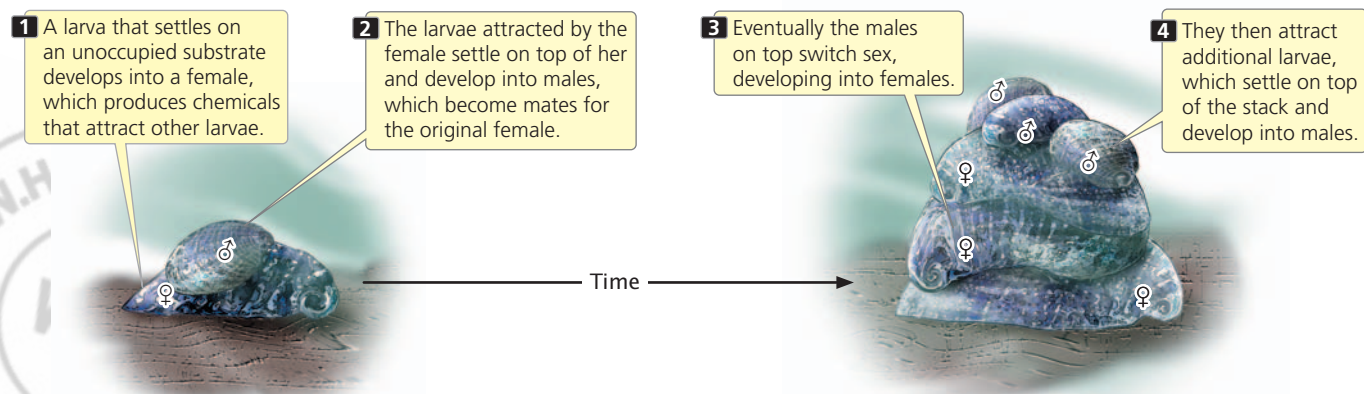
by individual genes. For example, in mammals, a gene (*SRY*, discussed later in this chapter) located on the Y chromosome determines the male phenotype. In both genic sex determination and chromosomal sex determination, sex is controlled by individual genes; the difference is that, with chromosomal sex determination, the chromosomes also look different in males and females.

### Environmental Sex Determination

Genes have had a role in all of the examples of sex determination discussed thus far. However, in a number of organisms, sex is determined fully or in part by environmental factors.

A fascinating example of environmental sex determination is seen in the marine mollusk *Crepidula fornicata*, also known as the common slipper limpet (**Figure 4.7**). Slipper limpets live in stacks, one on top of another. Each limpet begins life as a swimming larva. The first larva to settle on a solid, unoccupied substrate develops into a female limpet. It then produces chemicals that attract other larvae, which settle on top of it. These larvae develop into males, which then serve as mates for the limpet below. After a period of time, the males on top develop into females and, in turn, attract additional larvae that settle on top of the stack, develop into males, and serve as mates for the limpets under them. Limpets can form stacks of a dozen or more animals; the uppermost animals are always male. This type of sexual development is called **sequential hermaphroditism**; each individual animal can be both male and female, although not at the same time. In *Crepidula fornicata*, sex is determined environmentally by the limpet's position in the stack.

Environmental factors are also important in determining sex in many reptiles. Although most snakes and lizards have sex chromosomes, the sexual phenotype of many turtles, crocodiles, and alligators is affected by temperature during embryonic development. In turtles, for example,



**4.7** In *Crepidula fornicata*, the common slipper limpet, sex is determined by an environmental factor—the limpet's position in a stack of limpets.

**Table 4.1** Some sex-determining systems

System	Mechanism		Heterogametic Sex
XX-XO	Females XX	Males X	Male
XX-XY	Females XX	Males XY	Male
ZZ-ZW	Females ZW	Males ZZ	Female
Genic sex determination	No distinct sex chromosomes Sex determined by genes on undifferentiated chromosomes		Varies
Environmental sex determination	Sex determined by environmental factors		None

table 4.1

warm temperatures produce females during certain times of the year, whereas cool temperatures produce males. In alligators, the reverse is true. Some of the different types of sex determination are summarized in **Table 4.1**.

Now that we have surveyed some of the different ways in which sex can be determined, we will examine in detail one mechanism (the XX-XY system). Sex determination is XX-XY in both fruit flies and humans but, as we will see, the way in which the X and Y chromosomes determine sex in these two organisms is quite different. **TRY PROBLEMS 4 AND 20** →

**CONCEPTS**

In genic sex determination, sex is determined by genes at one or more loci, but there are no obvious differences in the chromosomes of males and females. In environmental sex determination, sex is determined fully or in part by environmental factors.

✓ **CONCEPT CHECK 3**

How do chromosomal, genic, and environmental sex determination differ?

**Sex Determination in *Drosophila melanogaster***

The fruit fly *Drosophila melanogaster* has eight chromosomes: three pairs of autosomes and one pair of sex chromosomes. Thus, it has inherited one haploid set of autosomes and one sex chromosome from each parent. Normally, females have two X chromosomes and males have an X chromosome and a Y chromosome. However, the presence of the Y chromosome does not determine maleness in *Drosophila*; instead, each fly's sex is determined by a balance between genes on the autosomes and genes on the X chromosome. This type of sex determination is called the **genic balance system**. In this system, a number of different genes influence sexual development. The X chromosome contains genes with female-producing effects, whereas the autosomes contain genes with male-producing effects. Consequently, a fly's sex is determined by the **X : A ratio**, the number of X chromosomes divided by the number of haploid sets of autosomal chromosomes.

An X : A ratio of 1.0 produces a female fly; an X : A ratio of 0.5 produces a male. If the X : A ratio is less than 0.5, a male phenotype is produced, but the fly is weak and sterile—such flies are sometimes called metamales. An X : A ratio between 1.0 and 0.5 produces an intersex fly, with a mixture of male and female characteristics. If the X : A ratio is greater than 1.0, a female phenotype is produced, but this fly (called a metafemale) has serious developmental problems and many never complete development. **Table 4.2** presents some different chromosome complements in *Drosophila* and their associated sexual phenotypes. Normal females have two X chromosomes and two sets of autosomes (XX, AA), and so their X : A ratio is 1.0. Males, on the other hand, normally have a single X and two sets of autosomes (XY, AA), and so their X : A ratio is 0.5. Flies with XXY sex chromosomes and two sets of autosomes (an X : A ratio of 1.0) develop as fully fertile females, in spite of the presence of a Y chromosome. Flies with only a single X and two sets of autosomes (XO, AA, for an X : A ratio of 0.5) develop as males, although they are sterile. These observations confirm that the Y chromosome does not determine sex in *Drosophila*. **TRY PROBLEM 15** →

table 4.2

**Table 4.2** Chromosome complements and sexual phenotypes in *Drosophila*

Sex-Chromosome Complement	Haploid Sets of Autosomes	X : A Ratio	Sexual Phenotype
XX	AA	1.0	Female
XY	AA	0.5	Male
XO	AA	0.5	Male
XXY	AA	1.0	Female
XXX	AA	1.5	Metafemale
XXXY	AA	1.5	Metafemale
XX	AAA	0.67	Intersex
XO	AAA	0.33	Metamale
XXXX	AAA	1.3	Metafemale

## CONCEPTS

The sexual phenotype of a fruit fly is determined by the ratio of the number of X chromosomes to the number of haploid sets of autosomal chromosomes (the X:A ratio).

## ✓ CONCEPT CHECK 4

What is the sexual phenotype of a fruit fly that has XXYYY sex chromosomes and two sets of autosomes?

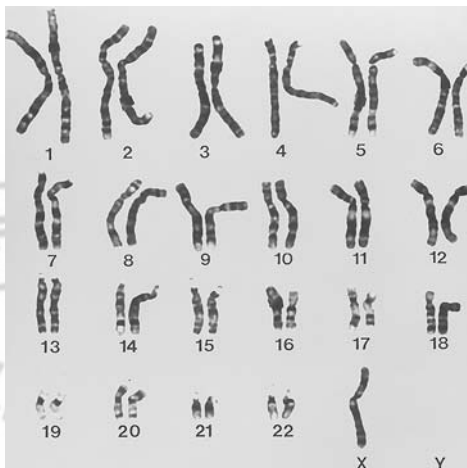
- |           |             |
|-----------|-------------|
| a. Male   | c. Intersex |
| b. Female | d. Metamale |

## Sex Determination in Humans

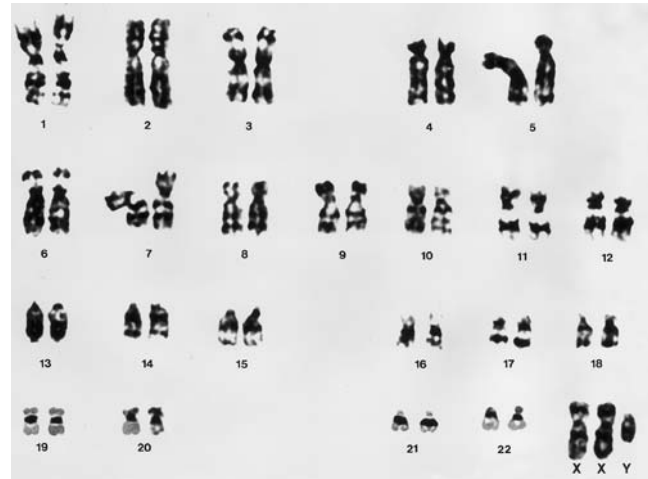
Humans, like *Drosophila*, have XX-XY sex determination, but, in humans, the presence of a gene (*SRY*) on the Y chromosome determines maleness. The phenotypes that result from abnormal numbers of sex chromosomes, which arise when the sex chromosomes do not segregate properly in meiosis or mitosis, illustrate the importance of the Y chromosome in human sex determination.

**Turner syndrome** Persons who have **Turner syndrome** are female and often have underdeveloped secondary sex characteristics. This syndrome is seen in 1 of 3000 female births. Affected women are frequently short and have a low hairline, a relatively broad chest, and folds of skin on the neck. Their intelligence is usually normal. Most women who have Turner syndrome are sterile. In 1959, Charles Ford used new techniques to study human chromosomes and discovered that cells from a 14-year-old girl with Turner syndrome had only a single X chromosome (**Figure 4.8**); this chromosome complement is usually referred to as XO.

There are no known cases in which a person is missing both X chromosomes, an indication that at least one X chromosome is necessary for human development. Presumably,



**4.8 Persons with Turner syndrome have a single X chromosome in their cells.** [Department of Clinical Cytogenetics, Addenbrookes Hospital/Science Photo Library/Photo Researchers.]



**4.9 Persons with Klinefelter syndrome have a Y chromosome and two or more X chromosomes in their cells.** [Biophoto Associates/Science Source/Photo Researchers.]

embryos missing both Xs spontaneously abort in the early stages of development.

**Klinefelter syndrome** Persons who have **Klinefelter syndrome**, which occurs with a frequency of about 1 in 1000 male births, have cells with one or more Y chromosomes and multiple X chromosomes. The cells of most males having this condition are XXY (**Figure 4.9**), but the cells of a few Klinefelter males are XXXY, XXXXY, or XXYY. Men with this condition frequently have small testes and reduced facial and pubic hair. They are often taller than normal and sterile; most have normal intelligence.

**Poly-X females** In about 1 in 1000 female births, the infant's cells possess three X chromosomes, a condition often referred to as **triplo-X syndrome**. These persons have no distinctive features other than a tendency to be tall and thin. Although a few are sterile, many menstruate regularly and are fertile. The incidence of mental retardation among triple-X females is slightly greater than that in the general population, but most XXX females have normal intelligence. Much rarer are females whose cells contain four or five X chromosomes. These females usually have normal female anatomy but are mentally retarded and have a number of physical problems. The severity of mental retardation increases as the number of X chromosomes increases beyond three.

**The role of sex chromosomes** The phenotypes associated with sex-chromosome anomalies allow us to make several inferences about the role of sex chromosomes in human sex determination.

1. The X chromosome contains genetic information essential for both sexes; at least one copy of an X chromosome is required for human development.

2. The male-determining gene is located on the Y chromosome. A single copy of this chromosome, even in the presence of several X chromosomes, produces a male phenotype.
3. The absence of the Y chromosome results in a female phenotype.
4. Genes affecting fertility are located on the X and Y chromosomes. A female usually needs at least two copies of the X chromosome to be fertile.
5. Additional copies of the X chromosome may upset normal development in both males and females, producing physical and mental problems that increase as the number of extra X chromosomes increases.

**The male-determining gene in humans** The Y chromosome in humans and all other mammals is of paramount importance in producing a male phenotype. However, scientists discovered a few rare XX males whose cells apparently lack a Y chromosome. For many years, these males presented an enigma: How could a male phenotype exist without a Y chromosome? Close examination eventually revealed a small part of the Y chromosome attached to another chromosome. This finding indicates that it is not the entire Y chromosome that determines maleness in humans; rather, it is a gene on the Y chromosome.

Early in development, all humans possess undifferentiated gonads and both male and female reproductive ducts. Then, about 6 weeks after fertilization, a gene on the Y chromosome becomes active. By an unknown mechanism, this gene causes the neutral gonads to develop into testes, which begin to secrete two hormones: testosterone and Mullerian-inhibiting substance. Testosterone induces the development of male characteristics, and Mullerian-inhibiting substance causes the degeneration of the female reproductive ducts. In the absence of this male-determining gene, the neutral gonads become ovaries, and female features develop.

The male-determining gene in humans, called the **sex-determining region Y (SRY) gene**, was discovered in 1990 (Figure 4.10). This gene is found in XX males and is missing from XY females; it is also found on the Y chromosome of other mammals. Definitive proof that SRY is the male-

determining gene came when scientists placed a copy of this gene into XX mice by means of genetic engineering. The XX mice that received this gene, although sterile, developed into anatomical males.

The SRY gene encodes a protein called a transcription factor (see Chapter 13) that binds to DNA and stimulates the transcription of other genes that promote the differentiation of the testes. Although SRY is the primary determinant of maleness in humans, other genes (some X linked, others Y linked, and still others autosomal) also have roles in fertility and the development of sex differences.

### CONCEPTS

The presence of the SRY gene on the Y chromosome causes a human embryo to develop as a male. In the absence of this gene, a human embryo develops as a female.

### ✓ CONCEPT CHECK 5

What is the phenotype of a person who has XXXY sex chromosomes?

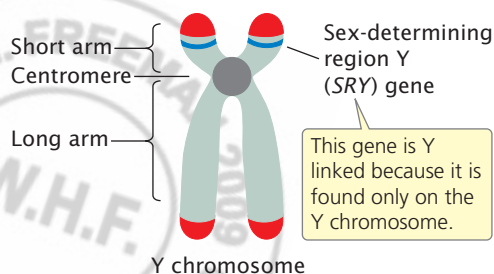
- a. Klinefelter syndrome
- b. Turner syndrome
- c. Poly-X female

**Androgen-insensitivity syndrome** Although the SRY gene is the primary determinant of sex in human embryos, several other genes influence sexual development, as illustrated by women with androgen-insensitivity syndrome. These persons have female external sexual characteristics and think of themselves as female. Indeed, most are unaware of their condition until they reach puberty and fail to menstruate. Examination by a gynecologist reveals that the vagina ends blindly and that the uterus, oviducts, and ovaries are absent. Inside the abdominal cavity, a pair of testes produce levels of testosterone normally seen in males. The cells of a woman with androgen-insensitivity syndrome contain an X and a Y chromosome.

How can a person be female in appearance when her cells contain a Y chromosome and she has testes that produce testosterone? The answer lies in the complex relation between genes and sex in humans. In a human embryo with a Y chromosome, the SRY gene causes the gonads to develop into testes, which produce testosterone. Testosterone stimulates embryonic tissues to develop male characteristics. But, for testosterone to have its effects, it must bind to an androgen receptor. This receptor is defective in females with androgen-insensitivity syndrome; consequently, their cells are insensitive to testosterone, and female characteristics develop. The gene for the androgen receptor is located on the X chromosome; so persons with this condition always inherit it from their mothers. (All XY persons inherit the X chromosome from their mothers.)

Androgen-insensitivity syndrome illustrates several important points about the influence of genes on a person's

fig 4.10



**4.10** The SRY gene is on the Y chromosome and causes the development of male characteristics.

sex. First, this condition demonstrates that human sexual development is a complex process, influenced not only by the *SRY* gene on the Y chromosome, but also by other genes found elsewhere. Second, it shows that most people carry genes for both male and female characteristics, as illustrated by the fact that those with androgen-insensitivity syndrome have the capacity to produce female characteristics, even though they have male chromosomes. Indeed, the genes for most male and female secondary sex characteristics are present not on the sex chromosomes but on autosomes. The key to maleness and femaleness lies not in the genes but in the control of their expression. **TRY PROBLEM 16** →

## 4.2 Sex-Linked Characteristics Are Determined by Genes on the Sex Chromosomes

In Chapter 3, we learned several basic principles of heredity that Mendel discovered from his crosses among pea plants. A major extension of these Mendelian principles is the pattern of inheritance exhibited by **sex-linked characteristics**, characteristics determined by genes located on the sex chromosomes. Genes on the X chromosome determine **X-linked characteristics**; those on the Y chromosome determine **Y-linked characteristics**. Because the Y chromosome of many organisms contains little genetic information, most sex-linked characteristics are X linked. Males and females differ in their sex chromosomes; so the pattern of inheritance for sex-linked characteristics differs from that exhibited by genes located on autosomal chromosomes.

### X-Linked White Eyes in *Drosophila*

The first person to explain sex-linked inheritance was American biologist Thomas Hunt Morgan (**Figure 4.11**). Morgan began his career as an embryologist, but the discovery

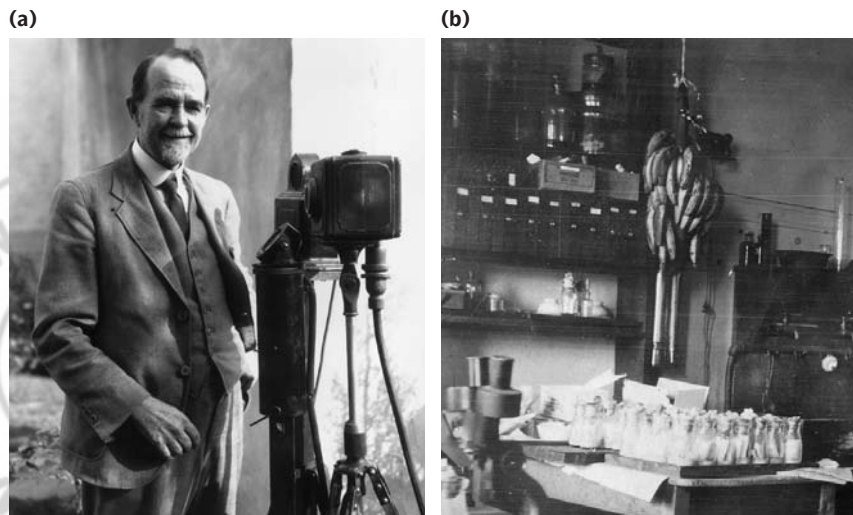
of Mendel's principles inspired him to begin conducting genetic experiments, initially on mice and rats. In 1909, Morgan switched to *Drosophila melanogaster*; a year later, he discovered among the flies of his laboratory colony a single male that possessed white eyes, in stark contrast with the red eyes of normal fruit flies. This fly had a tremendous effect on the future of genetics and on Morgan's career as a biologist.

To investigate the inheritance of the white-eyed characteristic in fruit flies, Morgan systematically carried out a series of genetic crosses. First, he crossed pure-breeding, red-eyed females with his white-eyed male, producing  $F_1$  progeny of which all had red eyes (**Figure 4.12a**). (In fact, Morgan found 3 white-eyed males among the 1237 progeny, but he assumed that the white eyes were due to new mutations.) Morgan's results from this initial cross were consistent with Mendel's principles: a cross between a homozygous dominant individual and a homozygous recessive individual produces heterozygous offspring exhibiting the dominant trait. His results suggested that white eyes are a simple recessive trait. However, when Morgan crossed the  $F_1$  flies with one another, he found that all the female  $F_2$  flies possessed red eyes but that half the male  $F_2$  flies had red eyes and the other half had white eyes. This finding was clearly not the expected result for a simple recessive trait, which should appear in  $1/4$  of both male and female  $F_2$  offspring.

To explain this unexpected result, Morgan proposed that the locus affecting eye color is on the X chromosome (i.e., eye color is X linked). He recognized that the eye-color alleles are present only on the X chromosome; no homologous allele is present on the Y chromosome. Because the cells of females possess two X chromosomes, females can be homozygous or heterozygous for the eye-color alleles. The cells of males, on the other hand, possess only a single X chromosome and can carry only a single eye-color allele. Males therefore cannot be either homozygous or heterozygous but are said to be **hemizygous** for X-linked loci.

fig 4.12

fig 4.11



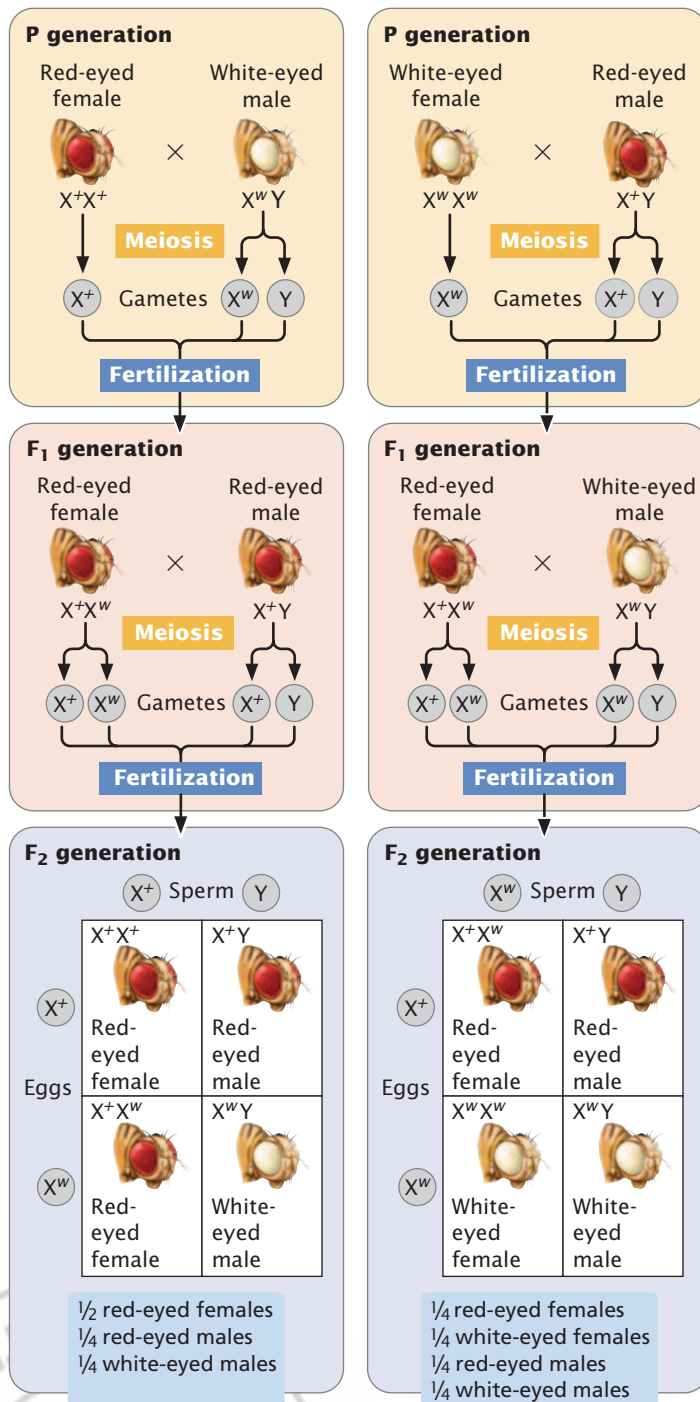
**4.11 Thomas Hunt Morgan's work with *Drosophila* helped unravel many basic principles of genetics, including X-linked inheritance.** (a) Morgan. (b) The Fly Room, where Morgan and his students conducted genetic research. [Part a: AP/Wide World Photos. Part b: American Philosophical Society.]

## Experiment

**Question:** Are white eyes in fruit flies inherited as an autosomal recessive trait?

**Methods** Perform reciprocal crosses.

(a) Red-eyed female crossed with white-eyed male (b) White-eyed female crossed with red-eyed male



**Conclusion:** No. The results of reciprocal crosses are consistent with X-linked inheritance.

To verify his hypothesis that the white-eye trait is X linked, Morgan conducted additional crosses. He predicted that a cross between a white-eyed female and a red-eyed male would produce all red-eyed females and all white-eyed males (Figure 4.12b). When Morgan performed this cross, the results were exactly as predicted. Note that this cross is the reciprocal of the original cross and that the two reciprocal crosses produced different results in the F<sub>1</sub> and F<sub>2</sub> generations. Morgan also crossed the F<sub>1</sub> heterozygous females with their white-eyed father, the red-eyed F<sub>2</sub> females with white-eyed males, and white-eyed females with white-eyed males. In all of these crosses, the results were consistent with Morgan's conclusion that white eyes are an X-linked characteristic.

## Nondisjunction and the Chromosome Theory of Inheritance

When Morgan crossed his original white-eyed male with homozygous red-eyed females, all 1237 of the progeny had red eyes, except for 3 white-eyed males. As already mentioned, Morgan attributed these white-eyed F<sub>1</sub> males to the occurrence of further random mutations. However, flies with these unexpected phenotypes continued to appear in his crosses. Although uncommon, they appeared far too often to be due to spontaneous mutation. Calvin Bridges, who was one of Morgan's students, set out to investigate the genetic basis of these exceptions.

Bridges found that the exceptions arose only in certain strains of white-eyed flies. When he crossed one of these exceptional white-eyed females with a red-eyed male, about 5% of the male offspring had red eyes and about 5% of the female offspring had white eyes. In this cross, the expected result is that every male fly should inherit its mother's X chromosome and should have the genotype  $X^wY$  and white eyes (see the F<sub>1</sub> progeny in Figure 4.12b). Every female fly should inherit a dominant red-eye allele on its father's X chromosome, along with a white-eye allele on its mother's X chromosome; thus, all the female progeny should be  $X^+X^w$  and have red eyes (see F<sub>1</sub> progeny in Figure 4.12b). The continual appearance of red-eyed males and white-eyed females in this cross was therefore unexpected.

**Bridges's explanation** To explain the appearance of red-eyed males and white-eyed females in his cross, Bridges hypothesized that the exceptional white-eyed females of this strain actually possessed

**4.12 Morgan's X-linked crosses for white eyes in fruit flies.** (a) Original and F<sub>1</sub> crosses. (b) Reciprocal crosses.



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The results of Morgan's crosses are illustrated in Animation 4.1.

two X chromosomes and a Y chromosome ( $X^wX^wY$ ). Sex in *Drosophila* is determined by the X:A ratio (see Table 4.2); for XXY females, the X:A ratio is 1.0, and so these flies developed as females in spite of possessing a Y chromosome.

About 90% of the time, the two X chromosomes of the  $X^wX^wY$  females separate from each other in anaphase I of meiosis, with an X and a Y chromosome going into one gamete and a single X going into another gamete (Figure 4.13). When these gametes are fertilized by sperm from a normal red-eyed male, white-eyed males and red-eyed females are produced. About 10% of the time, the two X chromosomes in the females fail to separate in anaphase I of meiosis, a phenomenon known as **nondisjunction**. When nondisjunction of the Xs occurs, half of the eggs receive two copies of the X chromosome and the other half receive only a Y chromosome (see Figure 4.13). When these eggs are fertilized by sperm from a normal red-eyed male, four combinations of sex chromosomes are produced. An egg with two X chromosomes that is fertilized by an X-bearing sperm produces an  $X^+X^wX^w$  zygote, which usually dies. When an egg carrying two X chromosomes is fertilized by a Y-bearing sperm, the resulting zygote is  $X^wX^wY$ , which develops into a white-eyed female. An egg with only a Y chromosome that is fertilized by an X-bearing sperm produces an  $X^+Y$  zygote, which develops into a normal red-eyed male. If the egg with only a Y chromosome is fertilized by a Y-bearing sperm, the resulting zygote has two Y chromosomes and no X chromosome and dies. Nondisjunction of the X chromosomes among  $X^wX^wY$  white-eyed females therefore produces a few white-eyed females and red-eyed males, which is exactly what Bridges found in his crosses.

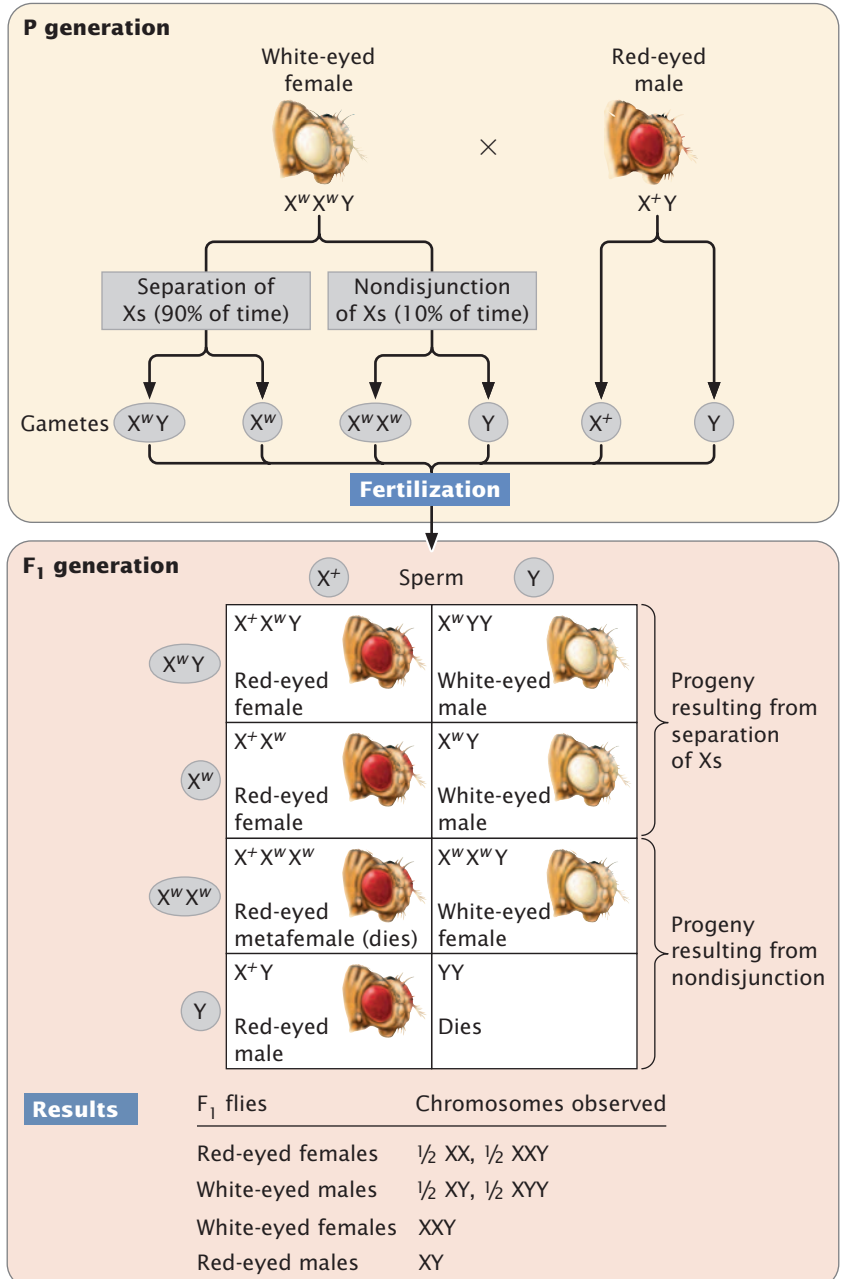
**Confirmation of Bridges's hypothesis** Bridges's hypothesis predicted that the white-eyed females from these crosses would possess two X chromosomes and one Y chromosome and that the red-eyed males would possess a single X chromosome. To verify his hypothesis, Bridges examined the chromosomes of his flies and found precisely what he had predicted. The significance of Bridges's study is not that it explained the appearance of an occasional odd fly in his culture but that he was able link the inheritance of a specific gene ( $w$ ) to the presence of a specific chromosome (X). This association between genotype and chromosomes gave unequivocal evidence that sex-linked genes are located on the X chromosome and confirmed the chromosome theory of inheritance. **TRY PROBLEM 21**

## Experiment

**Question:** In a cross between a white-eyed female and a red-eyed male, why are a few white-eyed females and red-eyed males produced?

## Methods

**Hypothesis:** White-eyed females and red-eyed males in  $F_1$  result from nondisjunction in an XXY female.



**Conclusion:** The white-eyed females and red-eyed males in the  $F_1$  result from nondisjunction of the X chromosomes in an XXY female.

**4.13 Bridges conducted experiments that proved that the gene for white eyes is located on the X chromosome.**

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The results of Bridges's crosses are further explained in Animation 4.1.

## CONCEPTS

By showing that the appearance of rare phenotypes is associated with the inheritance of particular chromosomes, Bridges proved that sex-linked genes are located on the X chromosome and that the chromosome theory of inheritance is correct.

## ✓ CONCEPT CHECK 6

What was the genotype of the few  $F_1$  red-eyed males obtained by Bridges when he crossed a white-eyed female with a red-eyed male?

- a.  $X^+$                       c.  $X^+Y$   
b.  $X^wX^+Y$               d.  $X^+X^+Y$

## X-Linked Color Blindness in Humans

To further examine X-linked inheritance, let's consider another X-linked characteristic: red-green color blindness in humans. Within the human eye, color is perceived in light-sensing cone cells that line the retina. Each cone cell contains one of three pigments capable of absorbing light of a particular wavelength; one absorbs blue light, a second absorbs red light, and a third absorbs green light. The human eye actually detects only three colors—red, green, and blue—but the brain mixes the signals from different cone cells to create the wide spectrum of colors that we perceive. Each of the three pigments is encoded by a separate locus; the locus for the blue pigment is found on chromo-

some 7, and those for the green and the red pigments lie close together on the X chromosome.

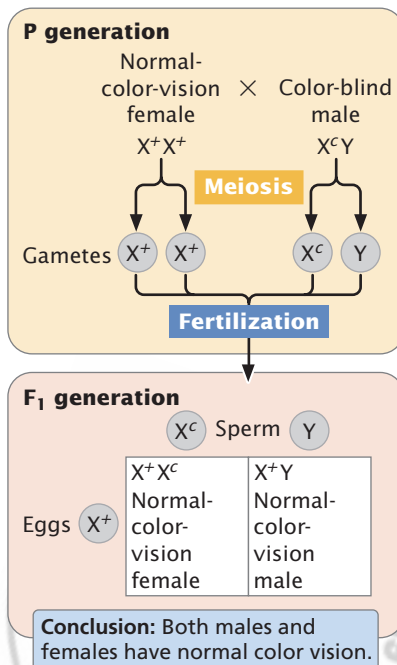
The most common types of human color blindness are caused by defects of the red and green pigments; we will refer to these conditions as red-green color blindness. Mutations that produce defective color vision are generally recessive and, because the genes encoding the red and the green pigments are located on the X chromosome, red-green color blindness is inherited as an X-linked recessive characteristic.

We will use the symbol  $X^c$  to represent an allele for red-green color blindness and the symbol  $X^+$  to represent an allele for normal color vision. Females possess two X chromosomes; so there are three possible genotypes among females:  $X^+X^+$  and  $X^+X^c$ , which produce normal vision, and  $X^cX^c$ , which produces color blindness. Males have only a single X chromosome and two possible genotypes:  $X^+Y$ , which produces normal vision, and  $X^cY$  which produces color blindness.

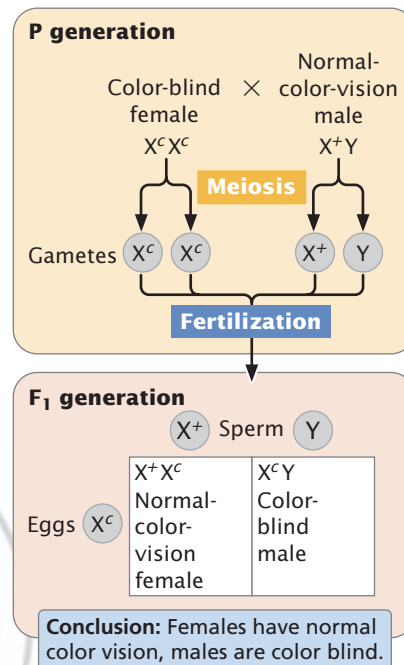
If a woman homozygous for normal color vision mates with a color-blind man (Figure 4.14a), all of the gametes produced by the woman will contain an allele for normal color vision. Half of the man's gametes will receive the X chromosome with the color-blind allele, and the other half will receive the Y chromosome, which carries no alleles affecting color vision. When an  $X^c$ -bearing sperm unites with the  $X^+$ -bearing egg, a heterozygous female with normal vision ( $X^+X^c$ ) is produced. When a Y-bearing sperm unites with the X-bearing egg, a hemizygous male with normal vision ( $X^+Y$ ) is produced.

fig 4.14

## (a) Normal female and color-blind male



## (b) Reciprocal cross



4.14 Red-green color blindness is inherited as an X-linked recessive trait in humans.

In the reciprocal cross between a color-blind woman and a man with normal color vision (Figure 4.14b), the woman produces only  $X^c$ -bearing gametes. The man produces some gametes that contain the X chromosome and others that contain the Y chromosome. Males inherit the X chromosome from their mothers; because both of the mother's X chromosomes bear the  $X^c$  allele in this case, all the male offspring will be color blind. In contrast, females inherit an X chromosome from both parents; thus all the female offspring of this reciprocal cross will be heterozygous with normal vision. Females are color blind only when color-blind alleles have been inherited from both parents, whereas a color-blind male need inherit a color-blind allele from his mother only; for this reason, color blindness and most other rare X-linked recessive characteristics are more common in males.

In these crosses for color blindness, notice that an affected woman passes the X-linked recessive trait to her sons but not to her daughters, whereas an affected man passes the trait to his grandsons through his daughters but never to his sons. X-linked recessive characteristics may therefore appear to alternate

between the sexes, appearing in females one generation and in males the next generation.

Recall that the X and Y chromosomes pair in meiosis because they are homologous at the small pseudoautosomal regions. Genes in these regions of the X and Y chromosome are homologous, just like those on autosomes, and they exhibit autosomal patterns of inheritance rather than the sex-linked inheritance seen for most genes on the X and Y chromosomes.

## Worked Problem

Now that we understand the pattern of X-linked inheritance, let's apply our knowledge to answer a specific question in regard to X-linked inheritance of color blindness in humans.

Betty has normal vision, but her mother is color blind. Bill is color blind. If Bill and Betty marry and have a child together, what is the probability that the child will be color blind?

### • Solution

Because color blindness is an X-linked recessive characteristic, Betty's color-blind mother must be homozygous for the color-blind allele ( $X^cX^c$ ). Females inherit one X chromosome from each of their parents; so Betty must have inherited a color-blind allele from her mother. Because Betty has normal color vision, she must have inherited an allele for normal vision ( $X^+$ ) from her father; thus Betty is heterozygous ( $X^+X^c$ ). Bill is color blind. Because males are hemizygous for X-linked alleles, he must be ( $X^cY$ ). A mating between Betty and Bill is represented as:

	Betty $X^+X^c$	×	Bill $X^cY$	
	↓		↓	
Gametes	$X^+$ $X^c$		$X^c$ $Y$	
	$X^+$		$X^c$	
$X^c$	$X^+X^c$ Normal female		$X^cX^c$ Color-blind female	
$Y$	$X^+Y$ Normal male		$X^cY$ Color-blind male	

Thus,  $\frac{1}{4}$  of the children are expected to be female with normal color vision,  $\frac{1}{4}$  female with color blindness,  $\frac{1}{4}$  male with normal color vision, and  $\frac{1}{4}$  male with color blindness.

→ Get some additional practice with X-linked inheritance by working Problem 23 at the end of this chapter.

## CONCEPTS

Characteristics determined by genes on the sex chromosomes are called sex-linked characteristics. Diploid females have two alleles at each X-linked locus, whereas diploid males possess a single allele at each X-linked locus. Females inherit X-linked alleles from both parents, but males inherit a single X-linked allele from their mothers.

### ✓ CONCEPT CHECK 7

Hemophilia (reduced blood clotting) is an X-linked recessive disease in humans. A woman with hemophilia mates with a man who exhibits normal blood clotting. What is the probability that their child will have hemophilia?

## Symbols for X-Linked Genes

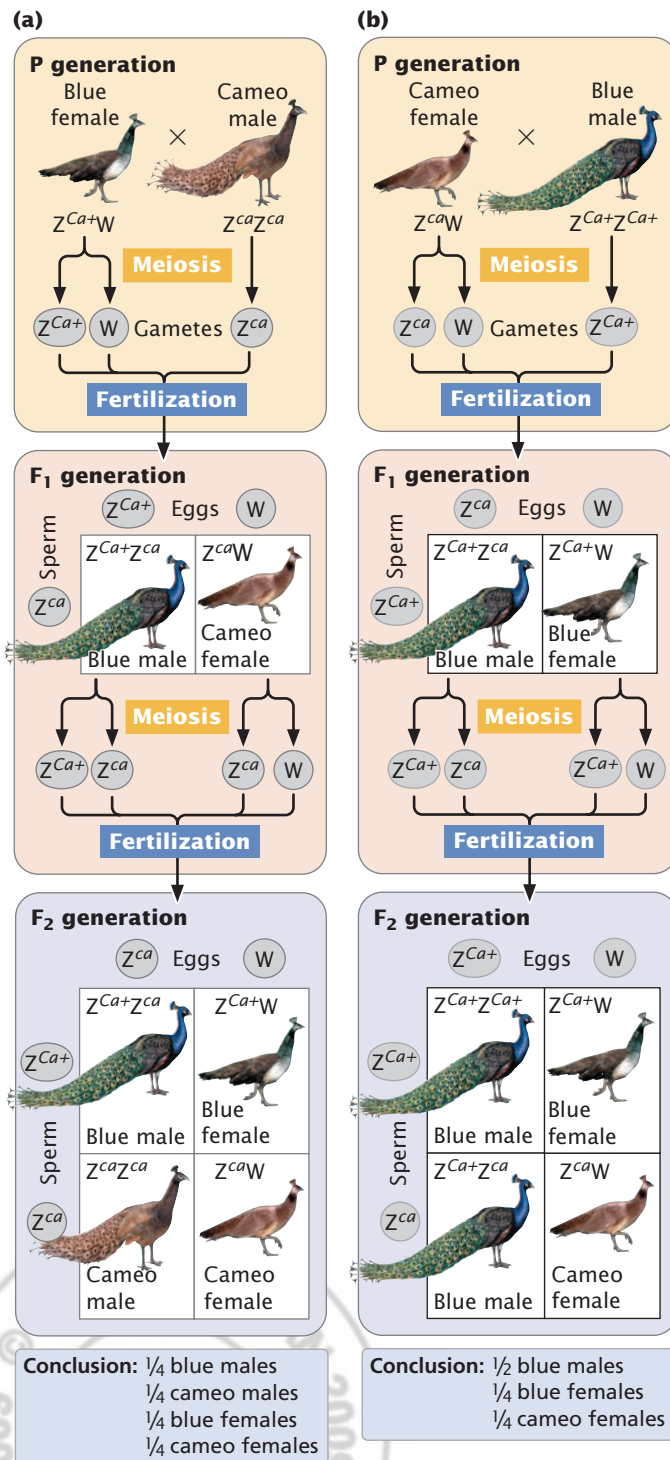
There are several different ways to record genotypes for X-linked traits. Sometimes the genotypes are recorded in the same fashion as they are for autosomal characteristics. In this case, the hemizygous males are simply given a single allele: the genotype of a female *Drosophila* with white eyes is  $ww$ , and the genotype of a white-eyed hemizygous male is  $w$ . Another method is to include the Y chromosome, designating it with a diagonal slash (/). With this method, the white-eyed female's genotype is still  $ww$  and the white-eyed male's genotype is  $w/$ . Perhaps the most useful method is to write the X and Y chromosomes in the genotype, designating the X-linked alleles with superscripts, as is done in this chapter. With this method, a white-eyed female is  $X^wX^w$  and a white-eyed male is  $X^wY$ . The use of Xs and Ys in the genotype has the advantage of reminding us that the genes are X linked and that the male must always have a single allele, inherited from the mother.

## Z-Linked Characteristics

In organisms with ZZ-ZW sex determination, the males are the homogametic sex (ZZ) and carry two sex-linked (usually referred to as Z-linked) alleles; thus males may be homozygous or heterozygous. Females are the heterogametic sex (ZW) and possess only a single Z-linked allele. The inheritance of Z-linked characteristics is the same as that of X-linked characteristics, except that the pattern of inheritance in males and females is reversed.

An example of a Z-linked characteristic is the cameo phenotype in Indian blue peafowl (*Pavo cristatus*). In these birds, the wild-type plumage is a glossy metallic blue. The female peafowl is ZW and the male is ZZ. Cameo plumage,

which produces brown feathers, results from a Z-linked allele ( $Z^{ca}$ ) that is recessive to the wild-type blue allele ( $Z^{Ca+}$ ). If a blue-colored female ( $Z^{Ca+}W$ ) is crossed with a cameo male ( $Z^{ca}Z^{ca}$ ), all the  $F_1$  females are cameo ( $Z^{ca}W$ ) and all the



**4.15** The cameo phenotype in Indian blue peafowl is inherited as a Z-linked recessive trait. (a) Blue female crossed with cameo male. (b) Reciprocal cross of cameo female crossed with homozygous blue male.

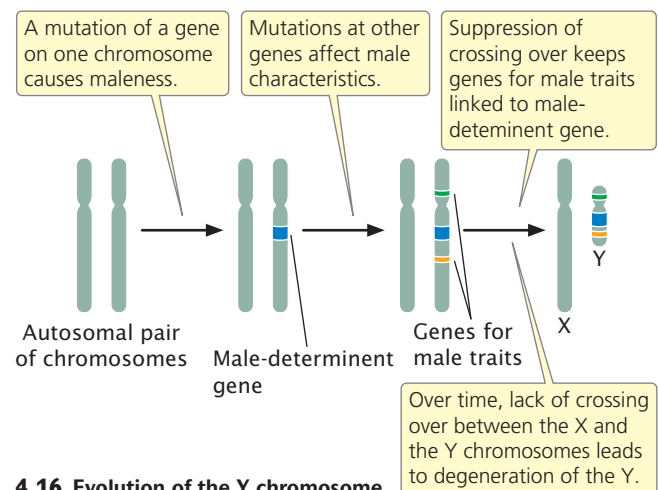
$F_1$  males are blue ( $Z^{Ca+}Z^{ca}$ ), as shown in **Figure 4.15**. When the  $F_1$  are interbred, 1/4 of the  $F_2$  are blue males ( $Z^{Ca+}Z^{ca}$ ), 1/4 are blue females ( $Z^{Ca+}W$ ), 1/4 are cameo males ( $Z^{ca}Z^{ca}$ ), and 1/4 are cameo females ( $Z^{ca}W$ ). The reciprocal cross of a cameo female with a homozygous blue male produces an  $F_1$  generation in which all offspring are blue and an  $F_2$  generation consisting of 1/2 blue males ( $Z^{Ca+}Z^{Ca+}$  and  $Z^{Ca+}Z^{ca}$ ), 1/4 blue females ( $Z^{Ca+}W$ ), and 1/4 cameo females ( $Z^{ca}W$ ).

In organisms with ZZ-ZW sex determination, the female always inherits her W chromosome from her mother, and she inherits her Z chromosome, along with any Z-linked alleles, from her father. In this system, the male inherits Z chromosomes, along with any Z-linked alleles, from both his mother and his father. This pattern of inheritance is the reverse of that of X-linked alleles in organisms with XX-XY sex determination. **TRY PROBLEM 32** →

## Y-Linked Characteristics

Y-linked traits exhibit a distinct pattern of inheritance and are present only in males because only males possess a Y chromosome. All male offspring of a male with a Y-linked trait will display the trait, because every male inherits the Y chromosome from his father. **TRY PROBLEM 42** →

**Evolution of the Y chromosome** Research on sex chromosomes has led to the conclusion the X and Y chromosomes in many organisms evolved from a pair of autosomes. The first step in this evolutionary process took place when one member of a pair of autosomes acquired a gene that determines maleness, such as the *SRY* gene found in humans today (**Figure 4.16**). This step took place in mammals about 250 millions years ago. Any individual organism with a copy of the chromosome containing this gene then became male. Additional mutations occurred on the proto-Y chromosome affecting traits that are beneficial only in males, such as the bright coloration used by male birds to attract females and the antlers used by a male elk in competition with other males. The genes that encode these types of traits are advantageous only if they are present in males. To prevent genes



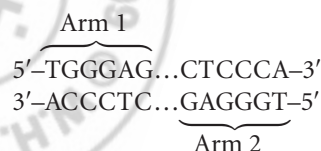
**4.16** Evolution of the Y chromosome.

that encode male traits from appearing in females, crossing over was suppressed for most of the length of the X and Y chromosomes in meiosis. Crossing over can still take place between the two X chromosomes in females, but there is little crossing over between the X and the Y chromosomes, except for small pseudoautosomal regions in which the X and the Y chromosomes continue to pair and segregate in meiosis, as stated earlier.

For reasons that are beyond the discussion here, the lack of crossing over led to (and continues to lead to) an accumulation of mutations and the loss of genetic material from the Y chromosome (see Figure 4.16). Over millions of years, the Y chromosome slowly degenerated, losing DNA and genes until it became greatly reduced in size and contained little genetic information. This degeneration produced the Y chromosome found in males today. Indeed, the Y chromosomes of humans and many other organisms are usually small and contain little genetic information; therefore, few characteristics exhibit Y-linked inheritance. Some researchers have predicted that the human Y chromosome will continue to lose genetic information in the future and will completely disappear from the species in about 10 million years, a disheartening prospect for those of us with a Y chromosome. However, internal recombination within the Y chromosome (see next section) may prevent the ultimate demise of the human Y chromosome.

**Characteristics of the human Y chromosome** The genetic sequence of most of the human Y chromosome has now been determined as part of the Human Genome Project (see Chapter 19). This work reveals that about two-thirds of the Y chromosome consists of short DNA sequences that are repeated many times and contain no active genes. The other third consists of just a few genes. Only about 350 genes have been identified on the human Y chromosome, compared with thousands on most chromosomes, and only about half of those identified on the Y chromosome encode proteins. The function of most Y-linked genes is poorly understood; many appear to influence male sexual development and fertility. Some are expressed throughout the body, but many are expressed predominately or exclusively in the testes. Although the Y chromosome has relatively few genes, recent research in *Drosophila* suggests that the Y chromosome carries genetic elements that affect the expression of numerous genes on autosomal and X chromosomes.

A surprising feature revealed by sequencing is the presence of eight massive palindromic sequences on the Y chromosome. A palindrome is defined as a word, such as “rotator,” or sentence that reads the same backward and forward. A palindromic sequence in DNA reads the same on both strands of the double helix, creating two nearly identical copies stretching out from a central point, such as:



Thus, a palindromic sequence in DNA appears twice, very much like the two copies of a DNA sequence that are found on two homologous chromosomes. Indeed, recombination takes place between the two palindromic sequences on the Y chromosome. As already mentioned, the X and the Y chromosomes are not homologous at almost all of their sequences, and most of the Y chromosome does not undergo crossing over with the X chromosome. This lack of interchromosomal recombination leads to an accumulation of deleterious mutations on the Y chromosome and the loss of genetic material. Evidence suggests that the two arms of the Y chromosome recombine with each other, which partly compensates for the absence of recombination between the X and the Y chromosomes. This internal recombination may help to maintain some sequences and functions of genes on the Y chromosome and prevent its total degeneration.

Although the palindromes afford opportunities for recombination, which helps prevent the decay of the Y chromosome over evolutionary time, they occasionally have harmful effects. Recent research has revealed that recombination between the palindromes can lead to rearrangements of the Y chromosome that cause anomalies of sexual development. In some cases, recombination between the palindromes leads to deletion of the *SRY* gene, producing an XY female. In other cases, recombination deletes other Y-chromosome genes that take part in sperm production. Sometimes, recombination produces a Y chromosome with two centromeres, which may break as the centromeres are pulled in opposite directions in mitosis. The broken Y chromosomes may be lost in mitosis, resulting in XO cells and Turner syndrome.

## CONCEPTS

Y-linked characteristics exhibit a distinct pattern of inheritance: they are present only in males, and all male offspring of a male with a Y-linked trait inherit the trait. Palindromic sequences within the Y chromosome can undergo internal recombination, but such recombination may lead to chromosome anomalies.

### ✓ CONCEPT CHECK 8

What unusual feature of the Y chromosome allows some recombination among the genes found on it?

**The use of Y-linked genetic markers** DNA sequences in the Y chromosome undergo mutation with the passage of time and vary among individual males. These mutations create variations in DNA sequence—called genetic markers—that are passed from father to son like Y-linked traits and can be used to study male ancestry. Although the markers themselves do not encode any physical traits, they can be detected with the use of molecular methods. Much of the Y chromosome is nonfunctional; so mutations readily accumulate. Many of these mutations are unique; they

arise only once and are passed down through the generations. Individual males possessing the same set of mutations are therefore related, and the distribution of these genetic markers on Y chromosomes provides clues about the genetic relationships of present-day people.

Y-linked markers have been used to study the offspring of Thomas Jefferson, principal author of the Declaration of Independence and third president of the United States. In 1802, Jefferson was accused by a political enemy of fathering a child by his slave Sally Hemings, but the evidence was circumstantial. Hemings, who worked in the Jefferson household and accompanied Jefferson on a trip to Paris, had five children. Jefferson was accused of fathering the first child, Tom, but rumors about the paternity of the other children circulated as well. Hemings's last child, Eston, bore a striking resemblance to Jefferson, and her fourth child, Madison, testified late in life that Jefferson was the father of all of Hemings's children. Ancestors of Hemings's children maintained that they were descendants of the Jefferson line, but some Jefferson descendants refused to recognize their claim.

To resolve this long-standing controversy, geneticists examined markers from the Y chromosomes of male-line descendants of Hemings's first son (Thomas Woodson), her last son (Eston Hemings), and a paternal uncle of Thomas Jefferson with whom Jefferson had Y chromosomes in common. (Descendants of Jefferson's uncle were used because Jefferson himself had no verified male descendants.) Geneticists determined that Jefferson possessed a rare and distinctive set of genetic markers on his Y chromosome. The same markers were also found on the Y chromosomes of the male-line descendants of Eston Hemings. The probability of such a match arising by chance is less than 1%. (The markers were not found on the Y chromosomes of the descendants of Thomas Woodson.) Together with the circumstantial historical evidence, these matching markers strongly suggest that Jefferson fathered Eston Hemings but not Thomas Woodson.

Y-chromosome sequences have also been used extensively to examine past patterns of human migration and the genetic relationships among different human populations.

### CONNECTING CONCEPTS

#### Recognizing Sex-Linked Inheritance

What features should we look for to identify a trait as sex linked? A common misconception is that any genetic characteristic in which the phenotypes of males and females differ must be sex linked. In fact, the expression of many *autosomal* characteristics differs between males and females. The genes that encode these characteristics are the same in both sexes, but their expression is influenced by sex hormones. The different sex hormones of males and females

cause the same genes to generate different phenotypes in males and females.

Another misconception is that any characteristic that is found more frequently in one sex is sex linked. A number of autosomal traits are expressed more commonly in one sex than in the other. These traits are said to be sex influenced. Some autosomal traits are expressed in only one sex; these traits are said to be sex limited. Both sex-influenced and sex-limited characteristics will be considered in more detail in Chapter 5.

Several features of sex-linked characteristics make them easy to recognize. Y-linked traits are found only in males, but this fact does not guarantee that a trait is Y linked, because some autosomal characteristics are expressed only in males. A Y-linked trait is unique, however, in that all the male offspring of an affected male will express the father's phenotype, and a Y-linked trait can be inherited only from the father's side of the family. Thus, a Y-linked trait can be inherited only from the paternal grandfather (the father's father), never from the maternal grandfather (the mother's father).

X-linked characteristics also exhibit a distinctive pattern of inheritance. X linkage is a possible explanation when reciprocal crosses give different results. If a characteristic is X-linked, a cross between an affected male and an unaffected female will not give the same results as a cross between an affected female and an unaffected male. For almost all autosomal characteristics, reciprocal crosses give the same result. We should not conclude, however, that, when the reciprocal crosses give different results, the characteristic is X linked. Other sex-associated forms of inheritance, considered in Chapter 5, also produce different results in reciprocal crosses. The key to recognizing X-linked inheritance is to remember that a male always inherits his X chromosome from his mother, not from his father. Thus, an X-linked characteristic is not passed directly from father to son; if a male clearly inherits a characteristic from his father—and the mother is not heterozygous—it cannot be X linked.

## 4.3 Dosage Compensation Equalizes the Amount of Protein Produced by X-Linked Genes in Males and Females

In species with XX-XY sex determination, the difference in the number of X chromosomes possessed by males and females presents a special problem in development. Because females have two copies of every X-linked gene and males have only one copy, the amount of gene product (protein) encoded by X-linked genes would differ in the two sexes: females would produce twice as much gene product as that produced by males. This difference could be highly detrimental because protein concentration plays a critical role in development. Animals overcome this potential problem through **dosage compensation**, which equalizes the amount of protein produced by X-linked genes in the two sexes. In fruit flies, dosage compensation is achieved by a doubling of the activity of the genes on the X chromosome of the male.

**Table 4.3** Number of Barr bodies in human cells with different complements of sex chromosomes

Sex Chromosomes	Syndrome	Number of Barr Bodies
XX	None	1
XY	None	0
XO	Turner	0
XXY	Klinefelter	1
XXYY	Klinefelter	1
XXX	Klinefelter	2
XXXX	Klinefelter	3
XXXY	Triplo-X	2
XXXX	Poly-X female	3
XXXXX	Poly-X female	4

In the worm *Caenorhabditis elegans*, it is achieved by a halving of the activity of genes on both of the X chromosomes in the female. Placental mammals use yet another mechanism of dosage compensation: genes on one of the X chromosomes in the female are inactivated, as described later in this section.

### Lyon Hypothesis

In 1949, Murray Barr observed condensed, darkly staining bodies in the nuclei of cells from female cats (**Figure 4.17**); this darkly staining structure became known as a **Barr body**. Mary Lyon proposed in 1961 that the Barr body was an inactive X chromosome; her hypothesis has become known as the **Lyon hypothesis**. She suggested that, within each female cell, one of the two X chromosomes becomes inactive; which

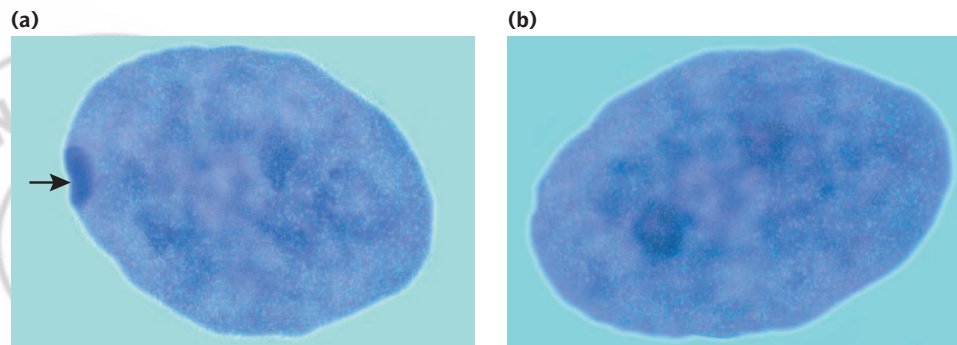
X chromosome is inactivated is random. If a cell contains more than two X chromosomes, all but one of them are inactivated. The number of Barr bodies present in human cells with different complements of sex chromosomes is shown in **Table 4.3**.

As a result of X inactivation, females are functionally hemizygous at the cellular level for X-linked genes. In females that are heterozygous at an X-linked locus, approximately 50% of the cells will express one allele and 50% will express the other allele; thus, in heterozygous females, proteins encoded by both alleles are produced, although not within the same cell. This functional hemizygosity means that cells in females are not identical with respect to the expression of the genes on the X chromosome; females are mosaics for the expression of X-linked genes.

Random X inactivation takes place early in development—in humans, within the first few weeks of development. After an X chromosome has become inactive in a cell, it remains inactive and is inactive in all somatic cells that descend from the cell. Thus, neighboring cells tend to have the same X chromosome inactivated, producing a patchy pattern (mosaic) for the expression of an X-linked characteristic in heterozygous females.

This patchy distribution can be seen in tortoiseshell and calico cats (**Figure 4.18**). Although many genes contribute to coat color and pattern in domestic cats, a single X-linked locus determines the presence of orange color. There are two possible alleles at this locus:  $X^+$ , which produces nonorange (usually black) fur, and  $X^o$ , which produces orange fur. Males are hemizygous and thus may be black ( $X^+Y$ ) or orange ( $X^oY$ ) but not black and orange. (Rare tortoiseshell males can arise from the presence of two X chromosomes,  $X^+X^oY$ .) Females may be black ( $X^+X^+$ ), orange ( $X^oX^o$ ), or tortoiseshell ( $X^+X^o$ ), the tortoiseshell pattern arising from a patchy mixture of black and orange fur. Each orange patch is a clone of cells derived from an original cell in which the black allele is inactivated, and each black patch is a clone of cells derived from an original cell in which the orange allele is inactivated.

fig 4.17



**4.17 A Barr body is an inactivated X chromosome.** (a) Female cell with a Barr body (indicated by arrow). (b) Male cell without a Barr body. [Chris Bjornberg/Photo Researchers.]

table 4.3

fig 4.18



**4.18** The patchy distribution of color on tortoiseshell cats results from the random inactivation of one X chromosome in females. [Chanan Photography.]

The Lyon hypothesis suggests that the presence of variable numbers of X chromosomes should not affect the phenotype in mammals, because any X chromosomes in excess of one X chromosome should be inactivated. However, persons with Turner syndrome (XO) differ from normal females, and those with Klinefelter syndrome (XXY) differ from normal males. How do these conditions arise in the face of dosage compensation?

These disorders probably arise because some X-linked genes escape inactivation. Indeed, the nature of X inactivation is more complex than originally envisioned. Studies of individual genes now reveal that only about 75% of X-linked human genes are permanently inactivated. About 15% completely escape X inactivation, meaning that these genes produce twice as much protein in females as they do in males. The remaining 10% are inactivated in some females but not in others. The reason for this variation among females in the activation of some X-linked genes is not known.

### Mechanism of Random X Inactivation

Random inactivation of X chromosomes requires two steps. In the first step, the cell somehow assesses, or counts, how many X chromosomes are present. In the second step, one X chromosome is selected to become the active X chromosome and all others are silenced.

Although many details of X-chromosome inactivation remain unknown, several genes and sequences that participate in the process have been identified. Foremost among them is a gene called *Xist* (for X-inactivation-specific transcript). On the X chromosomes destined to become inactivated, the *Xist* gene is active, producing an RNA molecule that coats the X chromosome and inactivates the genes on it, probably by altering chromatin structure. On the X chromosome destined to become active, other genes repress the activity of *Xist* so that the *Xist* RNA never coats the X chromosome and genes on this chromosome remain active.

### Dosage Imbalance Between X-Linked Genes and Autosomal Genes

X inactivation compensates for the difference in the number of X chromosomes in male and female mammals, but it creates another type of dosage problem. With X inactivation, males and females have a single active copy of each X-linked gene but possess two active copies of each autosomal gene, leading to different doses (amount) of proteins encoded by X-linked genes relative to proteins encoded by autosomal genes. Proteins often interact with one another and unbalanced dosage frequently leads to problems in development. Recent studies have shown that mammalian cells compensate for this imbalance by increasing the expression of (upregulating) genes on the single active X chromosome so that the total amount of protein produced by genes on the X chromosome is similar to that produced by genes on two copies of autosomal chromosomes. How genes on the single active X chromosome are upregulated is unknown at present. **TRY PROBLEM 41** →

### CONCEPTS

In mammals, dosage compensation ensures that the same amount of X-linked gene product will be produced in the cells of both males and females. All but one X chromosome are inactivated in each cell; which of the X chromosomes is inactivated is random and varies from cell to cell.

### ✓ CONCEPT CHECK 9

How many Barr bodies will a male with XXXYY chromosomes have in each of his cells? What are these Barr bodies?

## CONCEPTS SUMMARY

- Sexual reproduction is the production of offspring that are genetically distinct from their parents. Most organisms have two sexual phenotypes—males and females. Males produce small gametes; females produce large gametes.
- The mechanism by which sex is specified is termed sex determination. Sex may be determined by differences in specific chromosomes, genotypes, or environment.
- The sex chromosomes of males and females differ in number and appearance. The homogametic sex produces gametes that are all identical with regard to sex chromosomes; the heterogametic sex produces gametes that differ in their sex-chromosome composition.
- In the XX-XO system of sex determination, females possess two X chromosomes, whereas males possess a single X chromosome. In the XX-XY system, females possess two X chromosomes, whereas males possess a single X chromosome and a single Y chromosome. In the ZZ-ZW system, males possess two Z chromosomes, whereas females possess a Z chromosome and a W chromosome.
- Some organisms have genic sex determination, in which genotypes at one or more loci determine the sex of an individual organism. Still others have environmental sex determination.
- In *Drosophila melanogaster*, sex is determined by a balance between genes on the X chromosomes and genes on the autosomes, the X : A ratio.
- In humans, sex is ultimately determined by the presence or absence of the SRY gene located on the Y chromosome.
- Sex-linked characteristics are determined by genes on the sex chromosomes; X-linked characteristics are encoded by genes on the X chromosome, and Y-linked characteristics are encoded by genes on the Y chromosome.
- A female inherits X-linked alleles from both parents; a male inherits X-linked alleles from his female parent only.
- The sex chromosomes evolved from autosomes. Crossing over between the X and the Y chromosomes has been suppressed, but palindromic sequences within the Y chromosome allow for internal recombination on the Y chromosome. This internal recombination sometimes leads to chromosome rearrangements that can adversely affect sexual development.
- Y-linked characteristics are found only in males and are passed from father to all sons.
- Dosage compensation equalizes the amount of protein produced by X-linked genes in males and females. In placental mammals, one of the two X chromosomes in females normally becomes inactivated. Which X chromosome is inactivated is random and varies from cell to cell. Some X-linked genes escape X inactivation, and other X-linked genes may be inactivated in some females but not in others. X inactivation is controlled by the *Xist* gene.

## IMPORTANT TERMS

sex (p. 74)	genic sex determination (p. 77)	X-linked characteristic (p. 81)
sex determination (p. 74)	sequential hermaphroditism (p. 77)	Y-linked characteristic (p. 81)
hermaphroditism (p. 75)	genic balance system (p. 78)	hemizyosity (p. 81)
monoecious organism (p. 75)	X : A ratio (p. 78)	nondisjunction (p. 83)
dioecious organism (p. 75)	Turner syndrome (p. 79)	dosage compensation (p. 88)
sex chromosome (p. 75)	Klinefelter syndrome (p. 79)	Barr body (p. 89)
autosome (p. 76)	triplo-X syndrome (p. 79)	Lyon hypothesis (p. 89)
heterogametic sex (p. 76)	sex-determining region Y (SRY) gene (p. 80)	
homogametic sex (p. 76)	sex-linked characteristic (p. 81)	
pseudoautosomal region (p. 76)		

## ANSWERS TO CONCEPT CHECKS

- Meiosis
- b
- In chromosomal sex determination, males and females have chromosomes that are distinguishable. In genic sex determination, sex is determined by genes, but the chromosomes of males and females are indistinguishable. In environmental sex determination, sex is determined fully or in part by environmental effects.
- b
- a
- c
- All male offspring will have hemophilia, and all female offspring will not have hemophilia; so the overall probability of hemophilia in the offspring is  $\frac{1}{2}$ .
- Eight large palindromes that allow crossing over within the Y chromosome.
- Two Barr bodies. A Barr body is an inactivated X chromosome.

## WORKED PROBLEMS

1. A fruit fly has XXXYY sex chromosomes; all the autosomal chromosomes are normal. What sexual phenotype does this fly have?

## • Solution

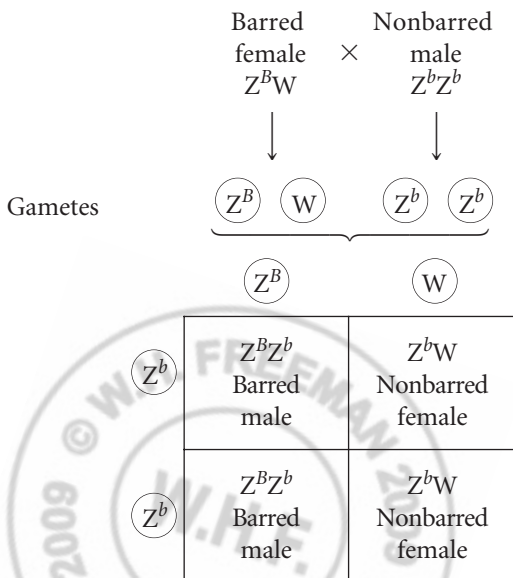
Sex in fruit flies is determined by the X : A ratio—the ratio of the number of X chromosomes to the number of haploid autosomal sets. An X : A ratio of 1.0 produces a female fly; an X : A ratio of 0.5 produces a male. If the X : A ratio is greater than 1.0, the fly is a metafemale; if it is less than 0.5, the fly is a metamale; if the X : A ratio is between 1.0 and 0.5, the fly is an intersex.

This fly has three X chromosomes and normal autosomes. Normal diploid flies have two autosomal sets of chromosomes; so the X : A ratio in this case is  $\frac{3}{2}$ , or 1.5. Thus, this fly is a metafemale.

2. Chickens, like all birds, have ZZ-ZW sex determination. The bar-feathered phenotype in chickens results from a Z-linked allele that is dominant over the allele for nonbar feathers. A barred female is crossed with a nonbarred male. The  $F_1$  from this cross are intercrossed to produce the  $F_2$ . What are the phenotypes and their proportions in the  $F_1$  and  $F_2$  progeny?

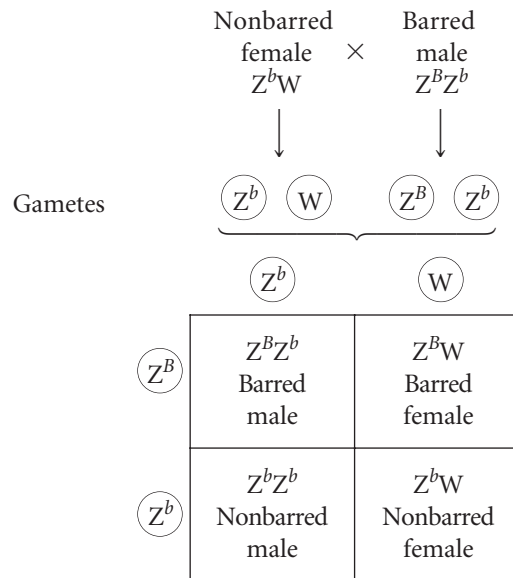
## • Solution

With the ZZ-ZW system of sex determination, females are the heterogametic sex, possessing a Z chromosome and a W chromosome; males are the homogametic sex, with two Z chromosomes. In this problem, the barred female is hemizygous for the bar phenotype ( $Z^B W$ ). Because bar is dominant over nonbar, the nonbarred male must be homozygous for nonbar ( $Z^b Z^b$ ). Crossing these two chickens, we obtain:



Thus, all the males in the  $F_1$  are barred ( $Z^B Z^b$ ), and all the females are nonbarred ( $Z^b W$ ).

We now cross the  $F_1$  to produce the  $F_2$ :



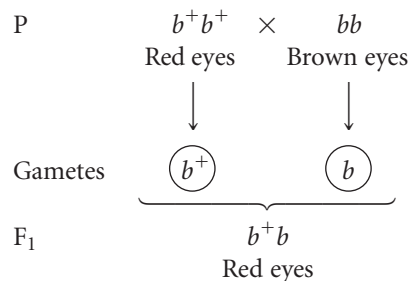
So,  $\frac{1}{4}$  of the  $F_2$  are barred males,  $\frac{1}{4}$  are nonbarred males,  $\frac{1}{4}$  are barred females, and  $\frac{1}{4}$  are nonbarred females.

3. In *Drosophila melanogaster*, forked bristles are caused by an allele ( $X^f$ ) that is X linked and recessive to an allele for normal bristles ( $X^+$ ). Brown eyes are caused by an allele ( $b$ ) that is autosomal and recessive to an allele for red eyes ( $b^+$ ). A female fly that is homozygous for normal bristles and red eyes mates with a male fly that has forked bristles and brown eyes. The  $F_1$  are intercrossed to produce the  $F_2$ . What will the phenotypes and proportions of the  $F_2$  flies be from this cross?

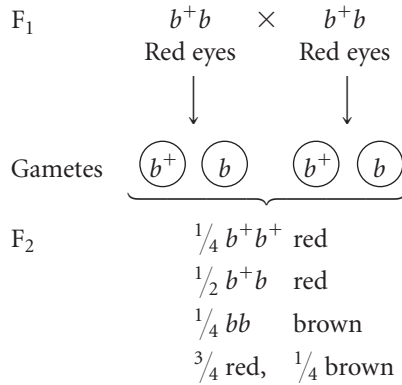
## • Solution

This problem is best worked by breaking the cross down into two separate crosses, one for the X-linked genes that determine the type of bristles and one for the autosomal genes that determine eye color.

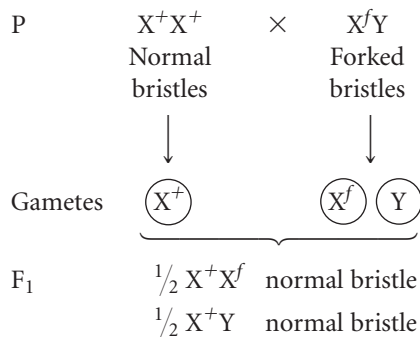
Let's begin with the autosomal characteristics. A female fly that is homozygous for red eyes ( $b^+ b^+$ ) is crossed with a male with brown eyes. Because brown eyes are recessive, the male fly must be homozygous for the brown-eye allele ( $bb$ ). All of the offspring of this cross will be heterozygous ( $b^+ b$ ) and will have red eyes:



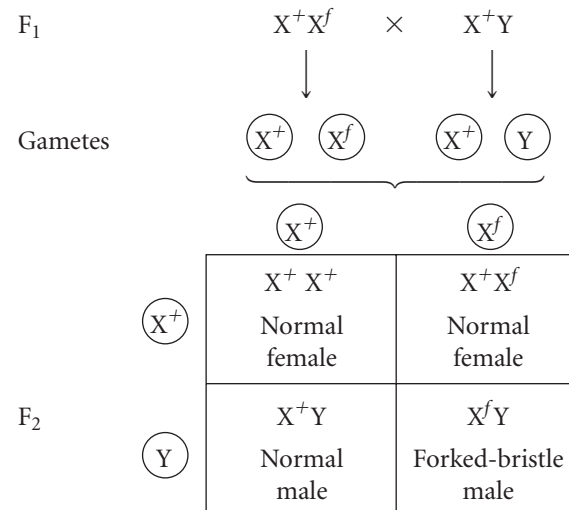
The  $F_1$  are then intercrossed to produce the  $F_2$ . Whenever two individual organisms heterozygous for an autosomal recessive characteristic are crossed,  $\frac{3}{4}$  of the offspring will have the dominant trait and  $\frac{1}{4}$  will have the recessive trait; thus,  $\frac{3}{4}$  of the  $F_2$  flies will have red eyes and  $\frac{1}{4}$  will have brown eyes:



Next, we work out the results for the X-linked characteristic. A female that is homozygous for normal bristles ( $X^+X^+$ ) is crossed with a male that has forked bristles ( $X^fY$ ). The female  $F_1$  from this cross are heterozygous ( $X^+X^f$ ), receiving an X chromosome with a normal-bristle allele from their mother ( $X^+$ ) and an X chromosome with a forked-bristle allele ( $X^f$ ) from their father. The male  $F_1$  are hemizygous ( $X^+Y$ ), receiving an X chromosome with a normal-bristle allele from their mother ( $X^+$ ) and a Y chromosome from their father:

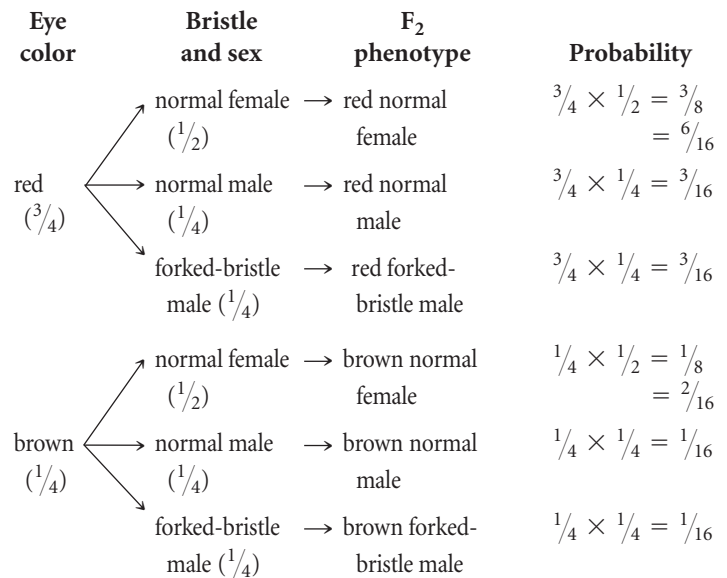


When these  $F_1$  are intercrossed,  $\frac{1}{2}$  of the  $F_2$  will be normal-bristle females,  $\frac{1}{4}$  will be normal-bristle males, and  $\frac{1}{4}$  will be forked-bristle males:



$\frac{1}{2}$  normal female,  $\frac{1}{4}$  normal male,  $\frac{1}{4}$  forked-bristle male

To obtain the phenotypic ratio in the  $F_2$ , we now combine these two crosses by using the multiplication rule of probability and the branch diagram:



## COMPREHENSION QUESTIONS

### Section 4.1

1. What is the most defining difference between the males and the females of any organism?
2. How do monoecious organisms differ from dioecious organisms?
3. Describe the XX-XO system of sex determination. In this system, which is the heterogametic sex and which is the homogametic sex?
4. How does sex determination in the XX-XY system differ from sex determination in the ZZ-ZW system?

5. What is the pseudoautosomal region? How does the inheritance of genes in this region differ from the inheritance of other Y-linked characteristics?
6. What is meant by genic sex determination?
7. How does sex determination in *Drosophila* differ from sex determination in humans?
8. Give the typical sex-chromosome complement found in the cells of people with Turner syndrome, with Klinefelter syndrome, and with androgen-insensitivity syndrome. What is the sex-chromosome complement of triplo-X females?

Section 4.2

- \*9. What characteristics are exhibited by an X-linked trait?
- 10. Explain how Bridges’s study of nondisjunction in *Drosophila* helped prove the chromosome theory of inheritance.
- \*11. What characteristics are exhibited by a Y-linked trait?

APPLICATION QUESTIONS AND PROBLEMS

Introduction

- 14. As described in the introduction to this chapter, platypuses possess 10 sex chromosomes. Females have five pairs of X chromosomes ( $X_1X_1X_2X_2X_3X_3X_4X_4X_5X_5$ ) and males have five pairs of X and Y chromosomes ( $X_1Y_1X_2Y_2X_3Y_3X_4Y_4X_5Y_5$ ). Do each of the XY chromosome pairs in males assort independently in meiosis? Why or why not?

Section 4.1

- \*15. What is the sexual phenotype of fruit flies having the following chromosomes?

	Sex chromosomes	Autosomal chromosomes
a.	XX	all normal
b.	XY	all normal
c.	XO	all normal
d.	XXY	all normal
e.	XXY	all normal
f.	XXYY	all normal
g.	XXX	all normal
h.	XX	four haploid sets
i.	XXX	four haploid sets
j.	XXX	three haploid sets
k.	X	three haploid sets
l.	XY	three haploid sets
m.	XX	three haploid sets

- 16. For each of the following sex-chromosome complements, what is the phenotypic sex of a person who has
  - a. XY with the *SRY* gene deleted?
  - b. XY with the *SRY* gene located on an autosomal chromosome?
  - c. XX with a copy of the *SRY* gene on an autosomal chromosome?
  - d. XO with a copy of the *SRY* gene on an autosomal chromosome?
  - e. XXY with the *SRY* gene deleted?
  - f. XXYY with one copy of the *SRY* gene deleted?
- 17. A normal female *Drosophila* produces abnormal eggs that contain all (a complete diploid set) of her chromosomes. She mates with a normal male *Drosophila* that produces normal sperm. What will the sex of the progeny from this cross be?
- 18. In certain salamanders, the sex of a genetic female can be altered, changing her into a functional male; these

Section 4.3

- 12. Explain why tortoiseshell cats are almost always female and why they have a patchy distribution of orange and black fur.
- 13. What is a Barr body? How is it related to the Lyon hypothesis?

- salamanders are called sex-reversed males. When a sex-reversed male is mated with a normal female, approximately  $\frac{2}{3}$  of the offspring are female and  $\frac{1}{3}$  are male. How is sex determined in these salamanders? Explain the results of this cross.
- 19. In some mites, males pass genes to their grandsons, but they never pass genes to their sons. Explain.
- \*20. In organisms with the ZZ-ZW sex-determining system, from which of the following possibilities can a female inherit her Z chromosome?

	Yes	No
Her mother’s mother	_____	_____
Her mother’s father	_____	_____
Her father’s mother	_____	_____
Her father’s father	_____	_____

Section 4.2

- 21. When Bridges crossed white-eyed females with red-eyed males, he obtained a few red-eyed males and white-eyed females (see Figure 4.13). What types of offspring would be produced if these red-eyed males and white-eyed females were crossed with each other?
- \*22. Joe has classic hemophilia, an X-linked recessive disease. Could Joe have inherited the gene for this disease from the following persons?

	Yes	No
a. His mother’s mother	_____	_____
b. His mother’s father	_____	_____
c. His father’s mother	_____	_____
d. His father’s father	_____	_____

- \*23. In *Drosophila*, yellow body is due to an X-linked gene that is recessive to the gene for gray body.
  - a. A homozygous gray female is crossed with a yellow male. The  $F_1$  are intercrossed to produce  $F_2$ . Give the genotypes and phenotypes, along with the expected proportions, of the  $F_1$  and  $F_2$  progeny.
  - b. A yellow female is crossed with a gray male. The  $F_1$  are intercrossed to produce the  $F_2$ . Give the genotypes and phenotypes, along with the expected proportions, of the  $F_1$  and  $F_2$  progeny.
  - c. A yellow female is crossed with a gray male. The  $F_1$  females are backcrossed with gray males. Give the genotypes and phenotypes, along with the expected proportions, of the  $F_2$  progeny.

- d. If the  $F_2$  flies in part *b* mate randomly, what are the expected phenotypic proportions of flies in the  $F_3$ ?



[Courtesy Masa-Toshi Yamamoto, Drosophila Genetic Resource Center, Kyoto Institute of Technology.]

24. Coat color in cats is determined by genes at several different loci. At one locus on the X chromosome, one allele ( $X^+$ ) encodes black fur; another allele ( $X^o$ ) encodes orange fur. Females can be black ( $X^+X^+$ ), orange ( $X^oX^o$ ), or a mixture of orange and black called tortoiseshell ( $X^+X^o$ ). Males are either black ( $X^+Y$ ) or orange ( $X^oY$ ). Bill has a female tortoiseshell cat named Patches. One night Patches escapes from Bill's house, spends the night out, and mates with a stray male. Patches later gives birth to the following kittens: one orange male, one black male, two tortoiseshell females, and one orange female. Give the genotypes of Patches, her kittens, and the stray male with which Patches mated.
- \*25. Red–green color blindness in humans is due to an X-linked recessive gene. Both John and Cathy have normal color vision. After 10 years of marriage to John, Cathy gave birth to a color-blind daughter. John filed for divorce, claiming that he is not the father of the child. Is John justified in his claim of nonpaternity? Explain why. If Cathy had given birth to a color-blind son, would John be justified in claiming nonpaternity?
26. Red–green color blindness in humans is due to an X-linked recessive gene. A woman whose father is color blind possesses one eye with normal color vision and one eye with color blindness.
- Propose an explanation for this woman's vision pattern. Assume that no new mutations have spontaneously arisen.
  - Would it be possible for a man to have one eye with normal color vision and one eye with color blindness?
- \*27. Bob has XXY chromosomes (Klinefelter syndrome) and is color blind. His mother and father have normal color vision, but his maternal grandfather is color blind. Assume that Bob's chromosome abnormality arose from nondisjunction in meiosis. In which parent and in which meiotic division did nondisjunction take place? Explain your answer.
28. Xg is an antigen found on red blood cells. This antigen is caused by an X-linked allele ( $X^g$ ) that is dominant over an

allele for the absence of the antigen ( $X^-$ ). The inheritance of these X-linked alleles was studied in children with chromosome abnormalities to determine where nondisjunction of the sex chromosomes took place. For each type of mating in parts *a* through *d*, indicate whether nondisjunction took place in the mother or in the father and, if possible, whether it took place in meiosis I or meiosis II.

- $X^gY \times X^-X^- \rightarrow X^g$  (Turner syndrome)
- $X^gY \times X^gX^- \rightarrow X^-$  (Turner syndrome)
- $X^gY \times X^-X^- \rightarrow X^gX^-Y$  (Klinefelter syndrome)
- $X^gY \times X^gX^- \rightarrow X^-X^-Y$  (Klinefelter syndrome)

29. The Talmud, an ancient book of Jewish civil and religious laws, states that, if a woman bears two sons who die of bleeding after circumcision (removal of the foreskin from the penis), any additional sons that she has should not be circumcised. (The bleeding is most likely due to the X-linked disorder hemophilia.) Furthermore, the Talmud states that the sons of her sisters must not be circumcised, whereas the sons of her brothers should be. Is this religious law consistent with sound genetic principles? Explain your answer.

30. Craniofrontonasal syndrome (CFNS) is a birth defect in which premature fusion of the cranial sutures leads to abnormal head shape, widely spaced eyes, nasal clefts, and various other skeletal abnormalities. George Feldman and his colleagues, looked at several families in which offspring had CFNS and recorded the results shown in the following table (G. J. Feldman. 1997. *Human Molecular Genetics* 6:1937–1941).

Family number	Parents		Offspring			
			Normal		CFNS	
	Father	Mother	Male	Female	Male	Female
1	normal	CFNS	1	0	2	1
5	normal	CFNS	0	2	1	2
6	normal	CFNS	0	0	1	2
8	normal	CFNS	1	1	1	0
10a	CFNS	normal	3	0	0	2
10b	normal	CFNS	1	1	2	0
12	CFNS	normal	0	0	0	1
13a	normal	CFNS	0	1	2	1
13b	CFNS	normal	0	0	0	2
7b	CFNS	normal	0	0	0	2

- On the basis of these results, what is the most likely mode of inheritance for CFNS?
- Give the most likely genotypes of the parents in family 1 and in family 10a.

- \*31. Miniature wings ( $X^m$ ) in *Drosophila* result from an X-linked allele that is recessive to the allele for long wings ( $X^+$ ). Give the genotypes of the parents in each of the following crosses.

Male parent	Female parent	Male offspring	Female offspring
a. long	long	231 long, 250 miniature	560 long
b. miniature	long	610 long	632 long
c. miniature	long	410 long, 417 miniature	412 long, 415 miniature
d. long	miniature	753 miniature	761 long
e. long	long	625 long	630 long

- \*32. In chickens, congenital baldness is due to a Z-linked recessive gene. A bald rooster is mated with a normal hen. The  $F_1$  from this cross are interbred to produce the  $F_2$ . Give the genotypes and phenotypes, along with their expected proportions, among the  $F_1$  and  $F_2$  progeny.
33. Red–green color blindness is an X-linked recessive trait in humans. Polydactyly (extra fingers and toes) is an autosomal dominant trait. Martha has normal fingers and toes and normal color vision. Her mother is normal in all respects, but her father is color blind and polydactylous. Bill is color blind and polydactylous. His mother has normal color vision and normal fingers and toes. If Bill and Martha marry, what types and proportions of children can they produce?
34. A *Drosophila* mutation called *singed* ( $s$ ) causes the bristles to be bent and misshapen. A mutation called *purple* ( $p$ ) causes the fly's eyes to be purple in color instead of the normal red. Flies homozygous for *singed* and *purple* were crossed with flies that were homozygous for normal bristles and red eyes. The  $F_1$  were intercrossed to produce the  $F_2$ , and the following results were obtained.

#### Cross 1

P	male, singed bristles, purple eyes × female, normal bristles, red eyes
$F_1$	420 female, normal bristles, red eyes 426 male, normal bristles, red eyes
$F_2$	337 female, normal bristles, red eyes 113 female, normal bristles, purple eyes 168 male, normal bristles, red eyes 170 male, singed bristles, red eyes 56 male, normal bristles, purple eyes 58 male, singed bristles, purple eyes

#### Cross 2

P	female, singed bristles, purple eyes × male, normal bristles, red eyes
$F_1$	504 female, normal bristles, red eyes 498 male, singed bristles, red eyes

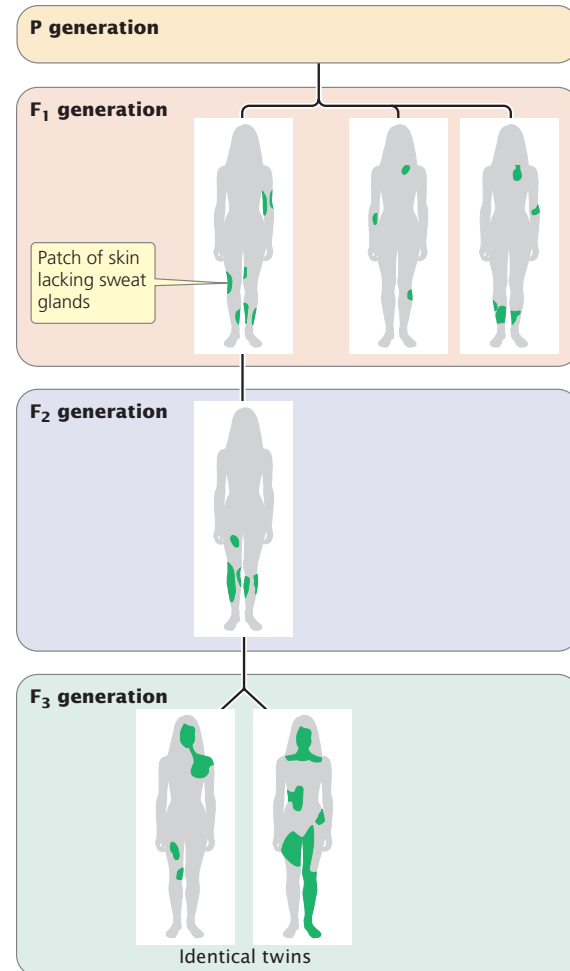
$F_2$	227 female, normal bristles, red eyes 223 female, singed bristles, red eyes 225 male, normal bristles, red eyes 225 male, singed bristles, red eyes 78 female, normal bristles, purple eyes 76 female, singed bristles, purple eyes 74 male, normal bristles, purple eyes 72 male, singed bristles, purple eyes
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- a. What are the modes of inheritance of *singed* and *purple*? Explain your reasoning.
- b. Give genotypes for the parents and offspring in the P,  $F_1$ , and  $F_2$  generations of Cross 1 and Cross 2.
35. The following two genotypes are crossed:  $Aa Bb Cc X^+X^r \times Aa BB cc X^+Y$ , where  $a$ ,  $b$ , and  $c$  represent alleles of autosomal genes and  $X^+$  and  $X^r$  represent X-linked alleles in an organism with XX-XY sex determination. What is the probability of obtaining genotype  $aa Bb Cc X^+X^+$  in the progeny?
- \*36. Miniature wings in *Drosophila melanogaster* are due to an X-linked gene ( $X^m$ ) that is recessive to an allele for long wings ( $X^+$ ). Sepia eyes are produced by an autosomal gene ( $s$ ) that is recessive to an allele for red eyes ( $s^+$ ).
- a. A female fly that has miniature wings and sepia eyes is crossed with a male that has normal wings and is homozygous for red eyes. The  $F_1$  flies are intercrossed to produce the  $F_2$ . Give the phenotypes, as well as their expected proportions, of the  $F_1$  and  $F_2$  flies.
- b. A female fly that is homozygous for normal wings and has sepia eyes is crossed with a male that has miniature wings and is homozygous for red eyes. The  $F_1$  flies are intercrossed to produce the  $F_2$ . Give the phenotypes, as well as their expected proportions, of the  $F_1$  and  $F_2$  flies.
37. Suppose that a recessive gene that produces a short tail in mice is located in the pseudoautosomal region. A short-tailed male mouse is mated with a female mouse that is homozygous for a normal tail. The  $F_1$  mice from this cross are intercrossed to produce the  $F_2$ . Give the phenotypes, as well as their proportions, of the  $F_1$  and  $F_2$  mice?
- \*38. A color-blind woman and a man with normal vision have three sons and six daughters. All the sons are color blind. Five of the daughters have normal vision, but one of them is color blind. The color-blind daughter is 16 years old, is short for her age, and has not undergone puberty. Explain how this girl inherited her color blindness.

### Section 4.3

- \*39. How many Barr bodies would you expect to see in a human cell containing the following chromosomes?
- |       |         |         |
|-------|---------|---------|
| a. XX | d. XXY  | g. XYY  |
| b. XY | e. XYY  | h. XXX  |
| c. XO | f. XXXY | i. XXXX |

40. A woman with normal chromosomes mates with a man who also has normal chromosomes.
- Suppose that, in the course of oogenesis, the woman's sex chromosomes undergo nondisjunction in meiosis I; the man's chromosomes separate normally. Give all possible combinations of sex chromosomes that this couple's children might inherit and the number of Barr bodies that you would expect to see in each of the cells of each child.
  - What chromosome combinations and numbers of Barr bodies would you expect to see if the chromosomes separate normally in oogenesis, but nondisjunction of the sex chromosomes takes place in meiosis I of spermatogenesis?
41. Anhidrotic ectodermal dysplasia is an X-linked recessive disorder in humans characterized by small teeth, no sweat glands, and sparse body hair. The trait is usually seen in men, but women who are heterozygous carriers of the trait often have irregular patches of skin with few or no sweat glands (see the illustration on the right).
- Explain why women who are heterozygous carriers of a recessive gene for anhidrotic ectodermal dysplasia have irregular patches of skin lacking sweat glands.
  - Why does the distribution of the patches of skin lacking sweat glands differ among the females depicted in the illustration, even between the identical twins?



[After A. P. Mance and J. Mance, *Genetics: Human Aspects* (Sinauer, 1990), p. 133.]

## CHALLENGE QUESTIONS

### Section 4.2

42. A geneticist discovers a male mouse with greatly enlarged testes in his laboratory colony. He suspects that this trait results from a new mutation that is either Y linked or autosomal dominant. How could he determine whether the trait is autosomal dominant or Y linked?

### Section 4.3

43. Female humans who are heterozygous for X-linked recessive genes sometimes exhibit mild expression of the trait. However, such mild expression of X-linked traits in females who are heterozygous for X-linked alleles is not seen in *Drosophila*. What might cause this difference in the expression of X-linked genes in female humans and female *Drosophila*? (Hint: In *Drosophila*, dosage compensation is accomplished by doubling the activity of genes on the X chromosome of males.)
44. Identical twins (also called monozygotic twins) are derived from a single egg fertilized by a single sperm, creating a zygote that later divides into two (see Chapter 6). Because

identical twins originate from a single zygote, they are genetically identical.

Caroline Loat and her colleagues examined 9 measures of social, behavioral, and cognitive ability in 1000 pairs of identical male twins and 1000 pairs of identical female twins (C. S. Loat et al. 2004. *Twin Research* 7:54–61). They found that, for three of the measures (prosocial behavior, peer problems, and verbal ability), the two male twins of a pair tended to be more alike in their scores than were two female twins of a pair. Propose a possible explanation for this observation. What might this observation indicate about the location of genes that influence prosocial behavior, peer problems, and verbal ability?

45. Occasionally, a mouse X chromosome is broken into two pieces and each piece becomes attached to a different autosomal chromosome. In this event, the genes on only one of the two pieces undergo X inactivation. What does this observation indicate about the mechanism of X-chromosome inactivation?

