Pedigrees—Tracking Inheritance

5.3

Thanks to the laws of heredity, revealed by Mendel, scientists can now do genetic analyses of heritable traits. Human genetics follow the same patterns of heredity seen in organisms such as the garden pea. For example, if we know that a child is born with a trait that neither parent has, then we can infer that the trait must not be controlled by a dominant allele and that the child must have inherited two recessive alleles.

Scientists are especially interested in determining the patterns of inheritance of genes that are beneficial or detrimental to human health. For obvious reasons, experimental genetic crosses cannot be conducted on humans. However, we can use what we know about heredity to investigate individuals and track the inheritance of a trait from generation to generation within a family.

Pedigree Charts

The simplest way to visually follow the inheritance of a gene is to construct a family tree known as a pedigree. A **pedigree** is a chart that traces the inheritance of a certain trait among members of a family. It shows the connections between parents and offspring, the sex of individuals in each generation, and the presence or absence of a trait. The chart is composed of symbols that identify sex and relationships between individuals (**Figure 1**).

pedigree a diagram of an individual's ancestors used in human genetics to analyze the Mendelian inheritance of a certain trait; also used for selective breeding of plants and animals

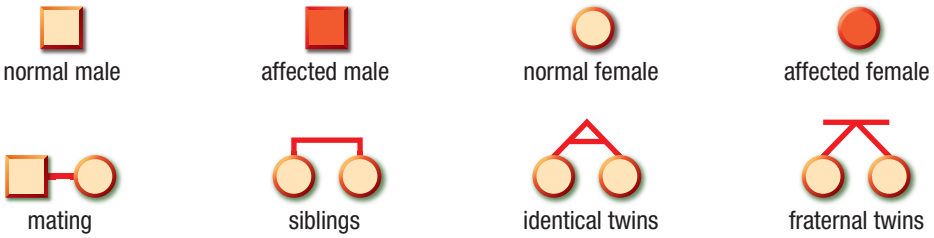

Figure 1 Squares represent males and circles represent females. Individuals who express a trait are shown in a shaded circle or square. Mating between two individuals is shown by a horizontal line, and children are connected to their parents with vertical lines.

Pedigree charts are very ordered within the constraints of the available information about the family. You will notice in **Figure 2** that each generation is identified by Roman numerals and that Arabic numerals symbolize individuals within a given generation. The birth order within each group of offspring is drawn from left to right, from oldest to youngest. Figure 2 shows a pedigree for a family with the trait of freckles.

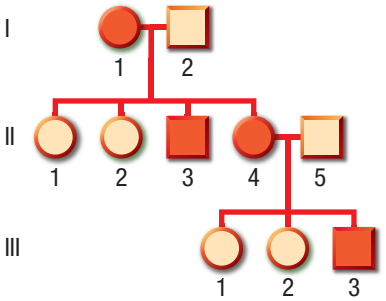

Figure 2 An example of a pedigree chart spanning three generations. In this pedigree, the grandmother (I-1), one of her sons (II-3), one of her daughters (II-4), and her grandson (III-3) have freckles. The allele for freckles (*F*) is dominant over the allele for no freckles (*f*).

Genetic counsellors construct and analyze pedigrees to help trace the genotypes and phenotypes in a family. They can determine if and how any particular trait runs in a family. For example, expectant parents might want to know how a recessive allele for hemophilia (a blood-clotting disorder) has been inherited in past generations. A genetic counsellor can help predict how that gene will be passed on to future generations.

Pedigree charts are also extremely useful for animal and plant breeders. Pedigrees can be used to track the inheritance of both desirable and undesirable traits and in some cases justify very high "stud fees" for prize animals. A farmer, for example, might ask for an opportunity to view a detailed pedigree of a bull before agreeing to pay for breeding with his prize cows. Similarly, a foal born to prize racehorse parents might be sold for millions of dollars based on their pedigrees—and long before its first race.

Tutorial 1 Interpreting Pedigree Charts

Figuring out genotypes from phenotypes on a pedigree chart requires you to use a process of elimination. You can often determine which genotypes are possible and which are not.

Sample Problem 1: Determining Genotypes of Individuals

Marfan syndrome is a genetic disorder that affects the body's connective tissue. When the dominant allele (*M*) is expressed, an individual will have Marfan syndrome. People with no defect in the Marfan allele are homozygous recessive (*mm*). Individuals with the syndrome are typically very tall, with disproportionately long limbs and fingers, and sometimes have problems with their hearts and eyes. Use the pedigree chart (**Figure 3**) to determine the genotypes of all individuals, if possible.

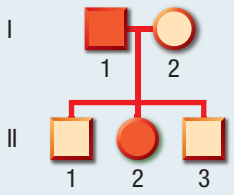

Figure 3 A family's pedigree showing the inheritance of Marfan syndrome

Step 1. Determine which individuals carry a dominant Marfan allele.

The shapes for the father (I-1) and the daughter (II-2) are shaded, indicating that they have Marfan syndrome. The Marfan allele is dominant, so all individuals expressing this trait must be either *MM* or *Mm*. So the father and daughter must be either heterozygous (*Mm*) or homozygous dominant (*MM*). I-1 and II-2 have a dominant allele (*M*) and either another dominant allele (*M*) or a recessive one (*m*) (**Figure 4**).

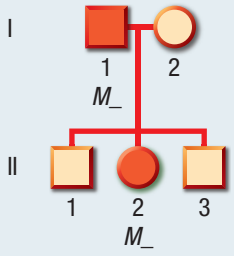

Figure 4

Step 2. Determine which individuals *do not* carry a dominant Marfan allele.

The shapes for the mother (I-2) and the two sons (II-1 and II-3) are not shaded, indicating that they do not have Marfan syndrome. Therefore, they are all homozygous recessive (*mm*) (**Figure 5**).

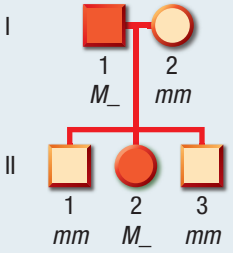

Figure 5

Step 3. Determine which individuals are heterozygous or homozygous for the Marfan allele.

The mother is *mm*, so she can pass on only a normal allele to her offspring. The daughter must be heterozygous (*Mm*). The two sons do not have Marfan syndrome, so they must both have inherited a normal allele (*m*) from the father. The father must be heterozygous (*Mm*). The completed pedigree chart is shown in **Figure 6**.

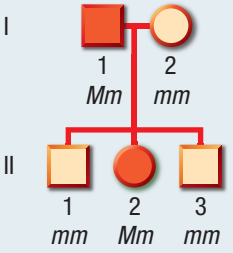

Figure 6 Individuals with Marfan syndrome must have at least one *M*, and recessive individuals must be *mm*.

Sample Problem 2: Determining Modes of Inheritance

Individuals with albinism have a defect in an enzyme that is involved in the production of melanin, a pigment normally found in the skin. These individuals have little or no pigment in their skin, hair, and eyes. The characteristic is governed by only two alleles: the normal allele and the albinism allele. Analyze the pedigree chart at right (**Figure 7**) to determine whether the albinism allele is a dominant or a recessive allele. Then determine the genotypes of each individual. Use *P* and *p* to represent the dominant and recessive alleles, respectively.

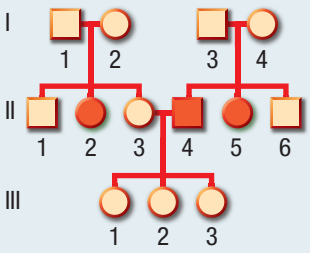

Figure 7 A family's pedigree chart for albinism

Step 1. Determine if albinism is dominant or recessive.

Individuals II-2, II-4, and II-5 have albinism, but none of their parents exhibit this trait. It is not possible to inherit a dominant trait from a parent who is not also dominant. Therefore, the trait must be caused by a recessive allele. The F_1 offspring who have albinism (II-2, II-4, II-5) have inherited two copies of the *p* allele, making them homozygous recessive (*pp*) for the characteristic. The genotypes of II-2, II-4, and II-5 are labelled *pp* (**Figure 8**).

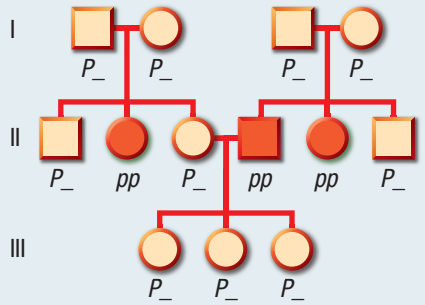

Figure 8 All individuals can be labelled *P* or *pp* based on their expressed traits.

Step 2. Determine which individuals carry one copy of the dominant normal allele.

Individuals who do not have albinism must have at least one *P* allele. All dominant individuals are labelled with one *P*, as shown in Figure 8.

Step 3. Determine the genotypes of non-albino individuals.

Every parent of an albino child must have at least one *p* allele. Every albino parent passes on a *p* allele to each of their children. Some but not all of the missing alleles can be filled in by looking at the parents and offspring of recessive individuals (**Figure 9**).

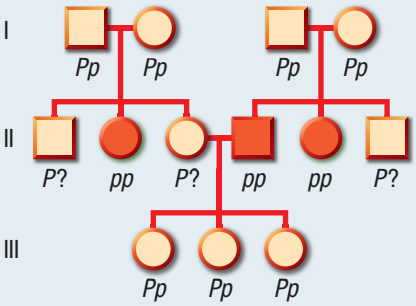

Figure 9 The second allele of *P?* individuals is unknown.

Practice

1. Phenylketonuria (PKU) is a genetic disorder caused by a recessive allele. Individuals with PKU accumulate phenylalanine in their body. High amounts of phenylalanine lead to delayed mental development. **Figure 10** is a pedigree chart that shows the inheritance of the defective PKU allele in one family.
   (a) How many generations are shown in the pedigree chart? [ans: 3]
   (b) Determine the genotypes of the individuals in Figure 10. Let *p* represent the recessive PKU allele.

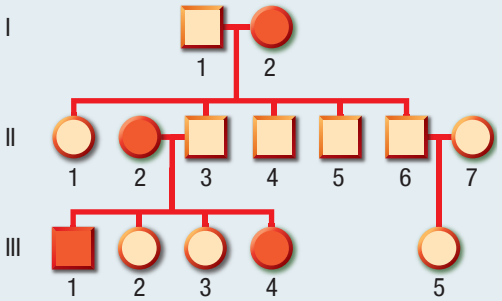

Figure 10

2. Not all humans react strongly to poison ivy. This trait is thought to be controlled by a single allele. The following pedigree (**Figure 11,** next page) shows the inheritance of sensitivity to poison ivy in one family.
   (a) Analyze the pedigree chart and determine whether the disorder is inherited as a result of a dominant or a recessive trait.

(b) Determine the genotype for each individual if possible.

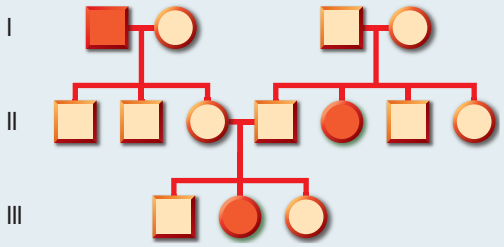

Figure 11 A family's pedigree chart for sensitivity to poison ivy

Sex Linkage—Following the X and Y Chromosomes

autosomal inheritance inheritance of alleles located on autosomal (non-sex) chromosomes

sex-linked describes an allele that is found on one of the sex chromosomes, X or Y, and when passed on to offspring is expressed

X-linked phenotypic expression of an allele that is found on the X chromosome

Different organisms have different numbers of chromosomes. Humans have 23 pairs of chromosomes. One set of chromosomes consists of the sex chromosomes, while the other 22 sets are autosomes, the non-sex chromosomes. If an allele is found on an autosome, it is said to be under the control of **autosomal inheritance**. With autosomal inheritance, both males and females are affected equally, since there is no difference between the autosomes of males and the autosomes of females.

However, some alleles that cause genetic disorders are found on the X chromosome. Females (XX) have two copies of the gene, but males (XY), with only one X chromosome, have only a single copy. Since the allele with the disorder is found on the X chromosome and is recessive, this type of inheritance is called **sex-linked** and, more specifically, **X-linked**. If a male inherits the X chromosome from a mother who carries the recessive allele, he will express the disorder because the Y chromosome cannot mask the effects of that allele. The male cannot inherit an X-linked disorder from his father, since a father passes on a Y chromosome to a son. A female must inherit two copies of the recessive gene—one on each X chromosome—in order to express the disorder.

WEB LINK

Royal Genes

Queen Victoria and her descendants constitute one of the most famous pedigree charts. To explore this pedigree in a case study and learn more about X-linked inheritance,

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Some examples of X-linked inheritance are red–green colour blindness, hemophilia A, and male-pattern baldness. Individuals who have hemophilia A are not able to form a clot when they are cut and may bleed for a lengthy period of time. In **Figure 12** the mother is a carrier of the hemophilia allele (X^h), and the father does not have hemophilia. The probability of this couple producing a son who has hemophilia (X^hY) is 25 %, and the probability of their producing a daughter who is a carrier (X^HX^h) is 25 %. There is a 50 % chance that the couple will produce a daughter or son who does not inherit the hemophilia allele (X^HX^H and X^HY).

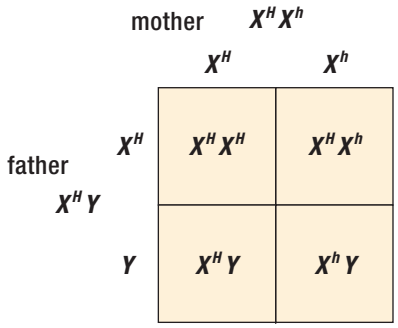

Figure 12 Hemophilia A is X-linked. A female carrier can pass on the hemophilia allele to her sons and daughters. Males cannot pass on hemophilia to their sons.

Y-linked phenotypic expression of an allele that is found on the Y chromosome

Y-linked disorders also exist and are passed on from father to son. One reason there are fewer Y-linked disorders than X-linked ones is that the Y chromosome is small and does not carry as much genetic information as the X-chromosome. Reduced fertility in males can be caused by a Y-linked disorder. Males who possess this disorder can have children using medical intervention.

5.3 Summary

- Pedigree charts are visual representations of a family tree that can be used to follow the inheritance of a trait.
- If an allele is located on an autosome, or a non-sex chromosome, it is transmitted through autosomal inheritance.
- Sex-linked inheritance occurs when a recessive allele is found on the X or Y chromosome and that chromosome is passed on to the offspring.
- In X-linked inheritance, the sexes exhibit different phenotypic ratios. More males than females will express the recessive phenotype, but more females are carriers of the recessive X-linked allele.
- In Y-linked inheritance, traits are controlled by single alleles passed on from fathers to sons on the Y chromosome.

5.3 Questions

1. Sickle-cell anemia is a condition in which the red blood cells of an individual can become shaped like the letter "C." This shape prevents the red blood cells from moving easily through blood vessels. It can result in the cells clumping, blocking blood flow and causing pain, infection, and organ damage. The allele that causes sickle-cell anemia is autosomal recessive (*s*), and the dominant allele can be represented by *S*.
   (a) For the following families, determine the genotypes of the parents and offspring. When it is not possible to decide which genotype an individual is, list both. T/I C
      (i) Two normal parents have four normal children and one with sickle-cell anemia.
      (ii) A normal male and a female with sickle-cell anemia have six children, all normal.
      (iii) A normal male and a female with sickle-cell anemia have six children; three are normal, and three have sickle-cell anemia.
   (b) Construct a pedigree chart for the families in (ii) and (iii).
2. Distinguish between autosomal inheritance and sex-linked inheritance. K/U
3. A male with hemophilia (X^hY) mates with a woman who does not carry the hemophiliac gene (X^HX^H). Use a Punnett square to answer (a) and (b). T/I
   (a) What is the probability of producing sons or daughters who have hemophilia?
   (b) What is the probability of producing daughters who are carriers of the hemophiliac allele?
4. Examine the pedigree charts in **Figures 13** and **14**. T/I
   (a) Determine whether the mode of inheritance for the traits is autosomal dominant or autosomal recessive.

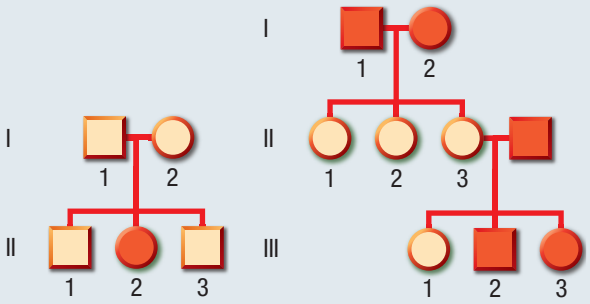

Figure 13

Figure 14

   (b) Copy each pedigree chart. Then label the genotype of each individual in the pedigree chart. Assume that the dominant allele is *A* and the recessive allele is *a*.
5. Hairy ears is a rare condition that is sex linked. Let *H* be the dominant allele (non-hairy ears) and *h* be the recessive allele (hairy ears). T/I
   (a) Examine the pedigree chart in **Figure 15**. Determine if the condition is X-linked or Y-linked.
   (b) Label all possible genotypes.

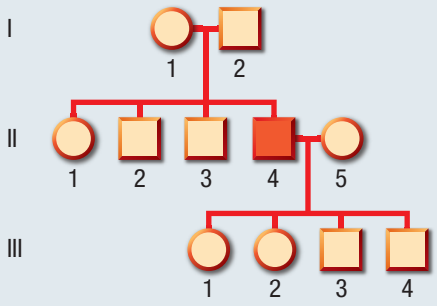

Figure 15