

Chapter Six: Pedigree Analysis and Applications

COMPREHENSION QUESTIONS

Section 6.1

- *1. What three factors complicate the task of studying the inheritance of human characteristics?
- (1) *Mating cannot be controlled. It is not ethical or feasible to set up controlled mating experiments.*
 - (2) *Humans have a long generation time, so it takes a long time to track inheritance of traits over more than one generation.*
 - (3) *The number of progeny per mating is limited, so phenotypic ratios are uncertain.*

Section 6.2

2. Who is the proband in a pedigree? Is the proband always found in the last generation of the pedigree? Why or why not?
- The proband is the person of interest for whom the pedigree chart has been drawn. The proband is not necessarily found in the last generation because the proband's children, or the children of the proband's siblings, often provide information about the genotype of the proband.*

Section 6.3

- *3. For each of the following modes of inheritance, describe the features that will be exhibited in a pedigree in which the trait is present: autosomal recessive, autosomal dominant, X-linked recessive, X-linked dominant, and Y-linked inheritance.
- Pedigrees with autosomal recessive traits will show affected males and females arising with equal frequency from unaffected parents. The trait often appears to skip generations. Unaffected people with an affected parent will be carriers.*
- Pedigrees with autosomal dominant traits will show affected males and females arising with equal frequency from a single affected parent. The trait does not usually skip generations.*
- X-linked recessive traits will affect males predominantly and will be passed from an affected male through his unaffected daughter to his grandson. X-linked recessive traits are not passed from father to son.*
- X-linked dominant traits will affect males and females and will be passed from an affected male to all his daughters, but not to his sons. An affected woman (usually heterozygous for a rare dominant trait) will pass on the trait equally to half her daughters and half her sons.*
- Y-linked traits will show up exclusively in males, passed from father to son.*
4. How does the pedigree of an autosomal recessive trait differ from the pedigree of an X-linked recessive trait?

Pedigrees of autosomal recessive traits will have equal frequencies of affected males and females, whereas pedigrees of X-linked recessive traits will show mostly affected males. Also, both parents must be carriers to have children with autosomal recessive traits, whereas a mother carrying an X-linked trait can have affected sons regardless of the genotype of the father. Finally, an X-linked trait is never passed from the father to his sons.

5. Other than the fact that a Y-linked trait appears only in males, how does the pedigree of a Y-linked trait differ from the pedigree of an autosomal dominant trait?
A Y-linked dominant trait is passed from a father to all of his sons, whereas an autosomal dominant trait would be passed to only half of his sons.

Section 6.4

- *6. What are the two types of twins and how do they arise?
The two types of twins are monozygotic and dizygotic. Monozygotic twins arise when a single fertilized egg splits into two embryos in early embryonic cleavage divisions. They are genetically identical. Dizygotic twins arise from two different eggs fertilized at the same time by two different sperm. They share, on the average, 50% of the same genes.
7. Explain how a comparison of concordance in monozygotic and dizygotic twins can be used to determine the extent to which the expression of a trait is influenced by genes or environmental factors.
Monozygotic twins have 100% genetic identity, whereas dizygotic twins have 50% genetic identity. Any trait that is completely genetically determined will therefore be 100% concordant in monozygotic twins and 50% concordant in dizygotic twins. Conversely, any trait that is completely environmentally determined will have the same degree of concordance in monozygotic and dizygotic twins. To the extent that a trait has greater concordance in monozygotic twins than in dizygotic twins, the trait is genetically influenced. Environmental influences will reduce the concordance in monozygotic twins below 100%.

Section 6.5

8. How are adoption studies used to separate the effects of genes and environment in the study of human characteristics?
Studies of adoptees, their biological parents, and their adoptive parents separate environmental and genetic influences on traits. Adoptees share similar environments with their adoptive parents (because they live in the same house and eat similar foods), but they share 50% of their genes with each of their biological parents. If adoptees have greater similarity for a trait with their adoptive parents, then the trait is environmentally influenced. If the adoptees have greater similarity for the trait with their biological parents, then the trait is genetically influenced.

Section 6.6

- *9. What is genetic counseling?

Genetic counseling provides assistance to clients by interpreting results of genetic testing and diagnosis; providing information about relevant disease symptoms, treatment, and progression; assessing and calculating the various genetic risks that the person or couple faces; and helping clients and family members cope with the stress of decision-making and facing up to the drastic changes in their lives that may be precipitated by a genetic condition.

10. Give at least four different reasons that a person might seek genetic counseling.
 - (1) *The person may be aware of a genetic disease or risk factor in the person's family.*
 - (2) *An older woman may be pregnant or contemplating pregnancy and may need information about risks and options for prenatal genetic testing.*
 - (3) *A person may have tested positive for a genetic disease or risk factor and may need help with interpretation.*
 - (4) *A person or couple may have a child with a genetic disease, or may be caregivers for a person with a genetic disease, and require counseling on treatment options and management of the disease.*
 - (5) *A married couple may be closely related (e.g., first cousins) and may need advice about pedigree analysis and genetic testing options.*
 - (6) *A couple has difficulty achieving pregnancy or carrying a pregnancy to term.*
 - (7) *A person has been exposed to mutagens or chemicals that cause a higher risk of birth defects.*
 - (8) *A couple contemplating starting a family may both be carriers of a recessive genetic condition.*
 - (9) *A couple needs advice on interpretation of results of a prenatal test.*

Section 6.7

11. Briefly define newborn screening, heterozygote screening, presymptomatic testing, and prenatal diagnosis.

Newborn screening: Newborn infants are tested for various treatable genetic disorders by sampling a few drops of their blood soon after birth.

Heterozygote screening: Normal or asymptomatic individuals in a population or community are tested for recessive disease alleles to determine the frequency of the disease allele in the population and to identify carriers, particularly if there is a relatively high incidence of the disease in the population or community.

Presymptomatic testing: People known to be at higher risk for a disease that occurs later in life are tested before symptoms appear.

Prenatal diagnosis: Results from prenatal testing for any of a number of genetic conditions. Techniques, such as amniocentesis or chorionic villus sampling, are used to obtain tissue samples of the still developing fetus, or fetal protein or cells in the maternal circulation are characterized.
12. Compare the advantages and disadvantages of amniocentesis versus chorionic villus sampling for prenatal diagnosis.

Amniocentesis samples the amniotic fluid by inserting a needle into the amniotic sac, usually performed at about 16 weeks of pregnancy, and requires culturing the fetal cells. Chorionic villus sampling can be performed several weeks earlier (10th or 11th week of pregnancy) and samples a small piece of the chorion by inserting a catheter

through the vagina. Amniocentesis is relatively safe, but results are not available until week 17 or 18 of pregnancy. Chorionic villus sampling has a slightly higher risk of complication, including fetal injury, but results are available several weeks earlier.

13. What is preimplantation genetic diagnosis?
Preimplantation genetic diagnosis may be performed on embryos created through in vitro fertilization. The embryos are cultured until they reach the 8–16 cell stage, and one cell is removed from each embryo for genetic testing.
14. How does heterozygote screening differ from presymptomatic genetic testing?
Both involve testing healthy individuals, but heterozygote screening refers to testing randomly selected individuals in populations to determine carrier frequency for recessive genetic disorders. Presymptomatic genetic testing refers to testing apparently healthy members of families to determine whether they have inherited a disease allele for diseases that manifest symptoms later in life.

Section 6.8

15. Briefly describe some of the recently discovered genes that contribute to human uniqueness and the importance that they may have had in human evolution.
Comparative genomic approaches aim to identify genes that are either unique to humans or have undergone changes that are unique to humans, and that may help to explain human evolution. Two questions of fundamental interest are the evolution of the large human brain and the evolution of language abilities. Mutations at six loci, named microcephalins (MCPH) 1–6, can cause severely reduced brain size. These loci may have undergone strong selection for alleles that promote large brain size. Another gene, the FOXP2 gene, was identified by mutations that cause speech and language disabilities. The human variant of FOXP2 appears to have emerged only about 200,000 years ago, coinciding with the emergence of modern humans.

APPLICATION QUESTIONS AND PROBLEMS

Section 6.1

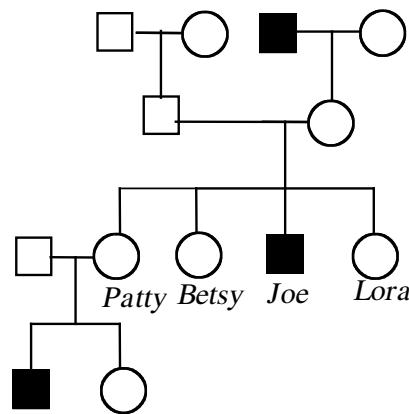
16. If humans have characteristics that make them unsuitable for genetic analysis, such as long generation time, small family size, and uncontrolled crosses, why do geneticists study humans? Give several reasons why humans have been the focus of so much genetic study.
Study of human genetics is necessary to understand and overcome human genetic diseases. Because of the long life span, relatively large body size, and uniquely human lifestyle and behaviors, animal models are nonexistent or insufficient for many genetic disorders. The careful preservation of marriage, birth, death, and health records in many societies provide a wealth of data for genetic analysis. The completion of the human genome project now facilitates mapping and identifying human genes. We humans have a strong sense of identity and worth as individuals,

and wish to understand how an individual's genetic profile contributes to our health, our behavior, our abilities and disabilities, and our individual future prospects.

Section 6.2

- *17. Joe is color blind. His mother and father have normal vision, but his mother's father (Joe's maternal grandfather) is color blind. All Joe's other grandparents have normal color vision. Joe has three sisters—Patty, Betsy, and Lora, all with normal color vision. Joe's oldest sister, Patty, is married to a man with normal color vision; they have two children, a 9-year-old color-blind boy and a 4-year-old girl with normal color vision.

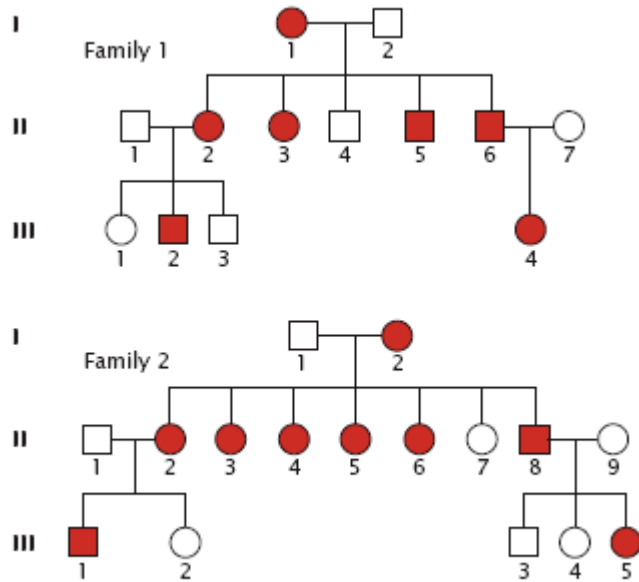
- a. Using correct symbols and labels, draw a pedigree of Joe's family.



- b. What is the most likely mode of inheritance for color blindness in Joe's family?
X-linked recessive. Only males have the trait, and they inherit the trait from their mothers, who are carriers. It cannot be a Y-linked trait because it is not passed from father to son. It is unlikely to be an autosomal recessive trait, because we would not expect two unrelated males marrying into the pedigree (Joe's father and Patty's husband) to be both carriers for a relatively rare trait.
- c. If Joe marries a woman who has no family history of color blindness, what is the probability that their first child will be a color-blind boy?
Barring a new mutation or nondisjunction, zero. Joe cannot pass his color-blind X chromosome to his son.
- d. If Joe marries a woman who is a carrier of the color-blind allele, what is the probability that their first child will be a color-blind boy?
The probability is 1/4. There is 1/2 probability that their first child will be a boy, and there is an independent 1/2 probability that the first child will inherit the color-blind X chromosome from the carrier mother. 1/2(1/2) = 1/4.
- e. If Patty and her husband have another child, what is the probability that it will be a color-blind boy?
Again, 1/4. Patty is a carrier because she had a color-blind son. The same reasoning applies as in part (d). Each child is an independent event.

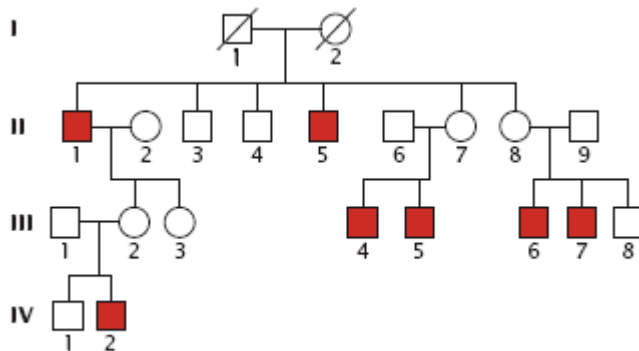
Section 6.3

18. Many studies have suggested a strong genetic predisposition to migraine headaches, but the mode of inheritance is not clear. L. Russo and colleagues examined migraine headaches in several families, two of which are shown below (L. Russo et al. 2005. *American Journal of Human Genetics* 76:327–333). What is the most likely mode of inheritance for migraine headaches in these families? Explain your reasoning.



In both families, the trait is most likely dominant because it does not skip generations, and affected individuals have one affected parent. In family 2, it is not X-linked because the affected male II-8 has an unaffected daughter. For X-linked loci, an affected male would transmit the trait to all his daughters. It could be either X-linked or autosomal in family 1.

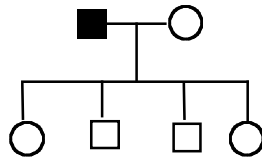
19. Dent disease is a rare disorder of the kidney in which there is impaired reabsorption of filtered solutes and progressive renal failure. R. R. Hoopes and colleagues studied mutations associated with Dent disease in the following family (R. R. Hoopes et al. 2005. *American Journal of Human Genetics* 76:260–267).



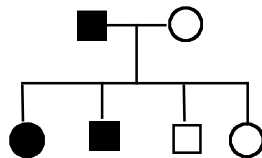
- a. On the basis of this pedigree, what is the most likely mode of inheritance for the disease? Explain your reasoning.
Only males have the disease, it skips generations, and unaffected female carriers have both affected and unaffected sons. These observations are consistent with a recessive X-linked trait. Y-linked traits are transmitted directly from father to son, and do not skip generations.
- b. From your answer to part a., give the most likely genotypes for all persons in the pedigree.
We will use X^+ to denote the normal X allele and X^d to denote the Dent allele.
I: 1 – $X^+ Y$; 2 – $X^+ X^d$
II: 1 and 5 are $X^d Y$, 7 and 8 are $X^+ X^d$, the rest do not have the disease allele
III: 2 and 3 are carriers $X^+ X^d$, 4–7 are $X^d Y$, and the rest do not have the disease allele
IV: 2 is $X^d Y$, 1 is $X^+ Y$

20. A man with a specific unusual genetic trait marries an unaffected woman and they have four children. Pedigrees of this family are shown in parts (a) through (e), but the presence or absence of the trait in the children is not indicated. For each type of inheritance, indicate how many children of each sex are expected to express the trait by filling in the appropriate circles and squares. Assume that the trait is rare and fully penetrant.

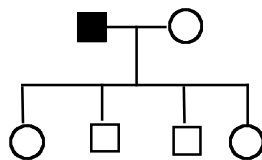
- a. Autosomal recessive trait—*none*



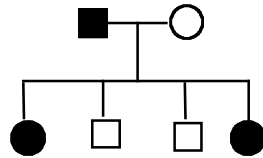
- b. Autosomal dominant trait— $\frac{1}{2}$ of each sex



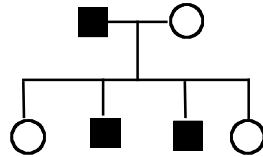
- c. X-linked recessive trait—*none*



- d. X-linked dominant trait—*all the female children*

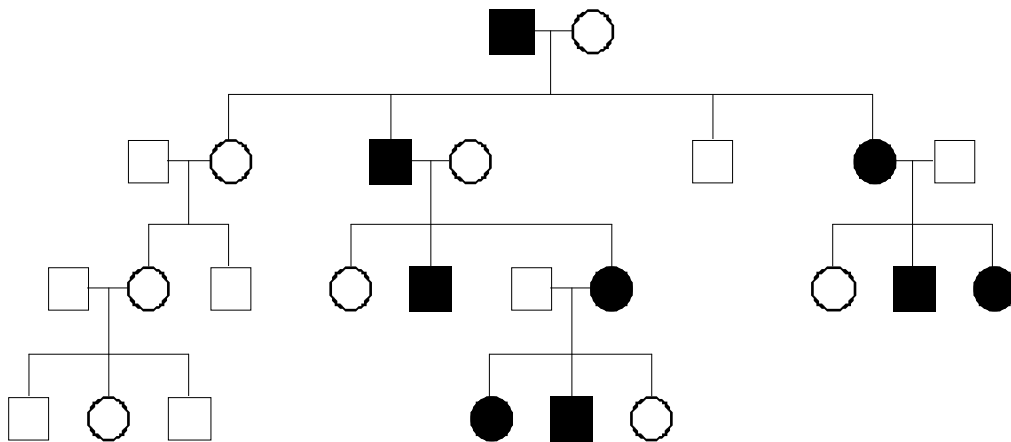


e. Y-linked trait—*all the male children*



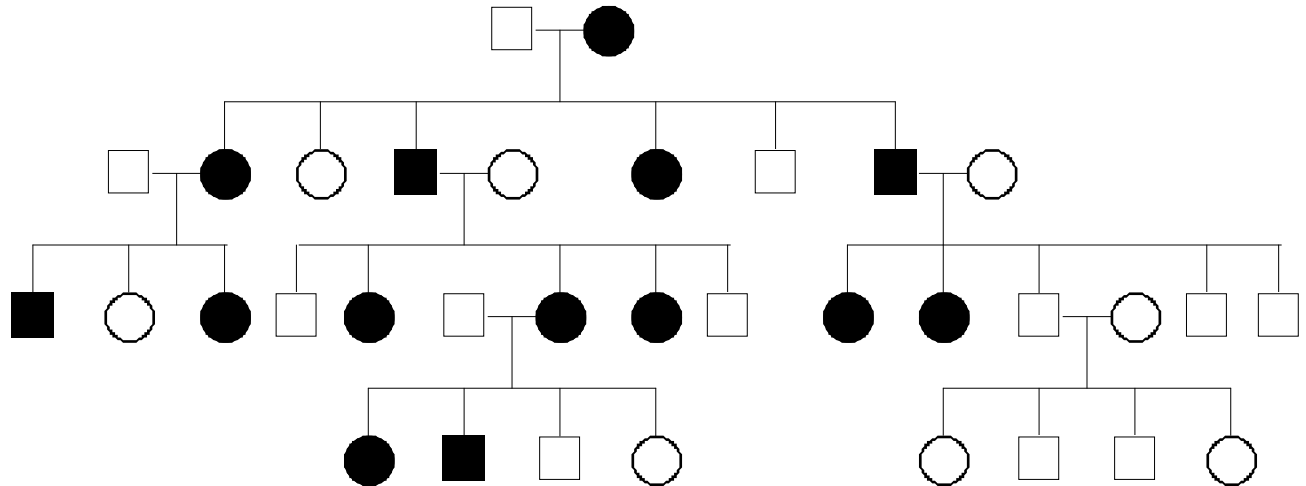
*21. For each of the following pedigrees, give the most likely mode of inheritance, assuming that the trait is rare. Carefully explain your reasoning.

a.



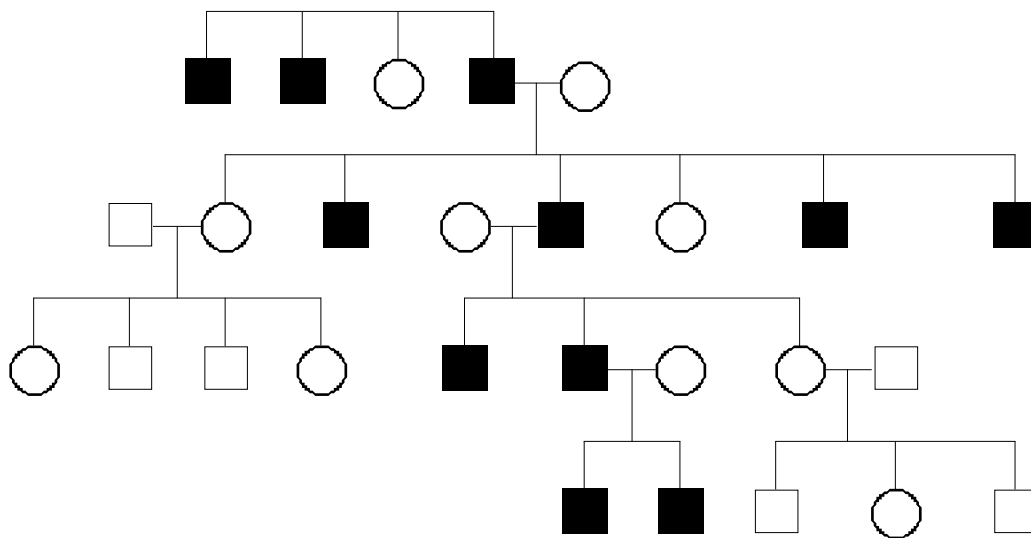
Autosomal dominant. The trait must be autosomal because affected males pass on the trait to both sons and daughters. It is dominant because it does not skip generations, all affected individuals have affected parents, and it is extremely unlikely that multiple unrelated individuals mating into the pedigree would be carriers for a rare trait.

b.



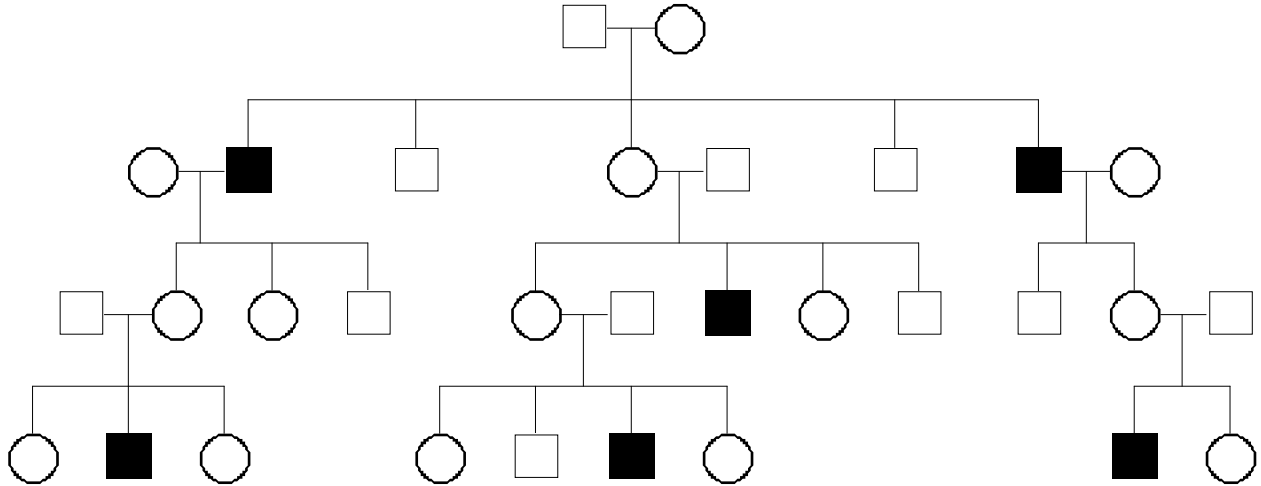
X-linked dominant. Superficially this pedigree appears similar to the pedigree in part (a) in that both males and females are affected, and it appears to be a dominant trait. However, closer inspection reveals that, whereas affected females can pass on the trait to either sons or daughters, affected males pass on the trait only to all daughters.

c.



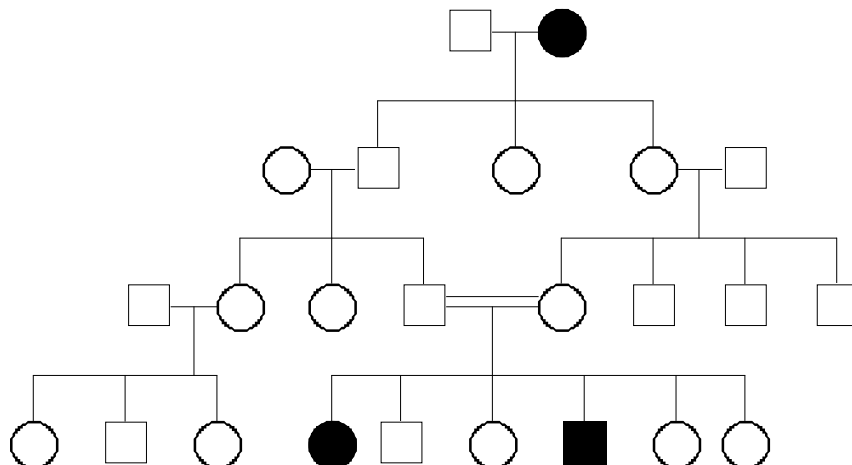
Y-linked. The trait affects only males and is passed from father to son. All sons of an affected male are affected.

d.



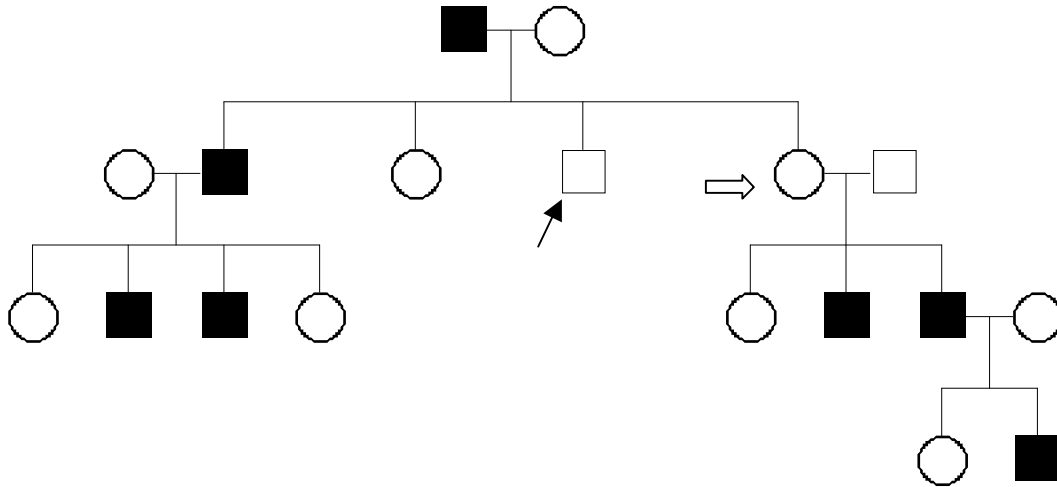
X-linked recessive or sex-limited autosomal dominant. Because only males show the trait, the trait could be X-linked recessive, Y-linked, or sex-limited. We can eliminate Y-linkage because affected males do not pass on the trait to their sons. X-linked recessive inheritance is consistent with the pattern of unaffected female carriers producing both affected and unaffected sons and affected males producing unaffected female carriers but no affected sons. Sex-limited autosomal dominant inheritance is also consistent with unaffected heterozygous females producing affected heterozygous sons, unaffected homozygous recessive sons, and unaffected heterozygous or homozygous recessive daughters. The two remaining possibilities of X-linked recessive versus sex-limited autosomal dominant could be distinguished if we had enough data to determine whether affected males could have both affected and unaffected sons, as expected from autosomal dominant inheritance, or whether affected males can have only unaffected sons, as expected from X-linked recessive inheritance. Unfortunately, this pedigree shows only two sons from affected males. In both cases, the sons are unaffected, consistent with X-linked recessive inheritance, but two instances are not enough to conclude that affected males cannot produce affected sons.

e.



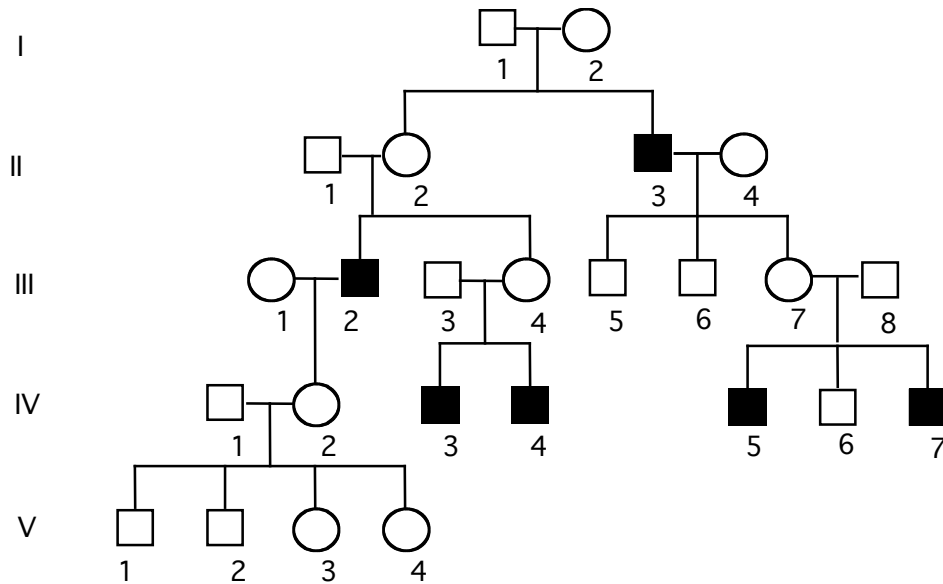
Autosomal recessive. Unaffected parents produced affected progeny, so the trait is recessive. The affected daughter must have inherited recessive alleles from both her unaffected parents, so it must be autosomal. If it were X-linked, her father would have shown the trait.

22. The trait represented in the following pedigree is expressed only in the males of the family. Is the trait Y-linked? Why or why not? If you believe the trait is not Y-linked, propose an alternate explanation for its inheritance.



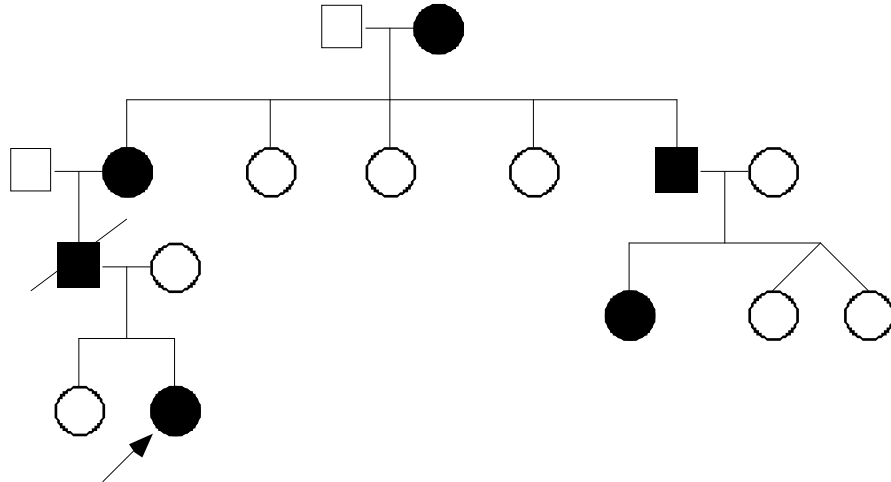
Y-linked traits are passed from father to son. This trait cannot be Y-linked because an affected father can have an unaffected son (indicated by a solid arrow) and also because we see sons inheriting the trait from their mother (indicated by an open arrow). Moreover, this trait cannot be X-linked because it is often passed from father to son, whereas X-linked traits are passed from father to daughter. The most probable mode of inheritance for this trait is sex-limited (only in males) autosomal dominant.

- *23. The following pedigree illustrates the inheritance of Nance–Horan syndrome, a rare genetic condition in which affected persons have cataracts and abnormally shaped teeth.



(Pedigree adapted from D. Stambolian, R. A. Lewis, K. Buetow, A. Bond, and R. Nussbaum. *American Journal of Human Genetics* 47[1990]:15.)

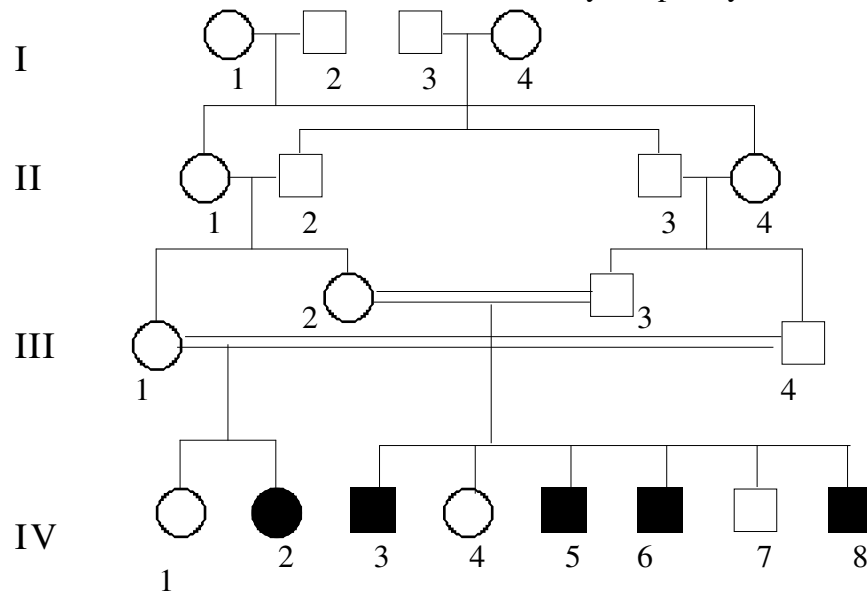
- a. On the basis of this pedigree, what do you think is the most likely mode of inheritance for Nance–Horan syndrome?
X-linked recessive. Only males have the condition, and unaffected female carriers have affected sons.
 - b. If couple III-7 and III-8 have another child, what is the probability that the child will have Nance–Horan syndrome?
The probability is 1/4. The female III-7 is a carrier, so there is a 1/2 probability that the child will inherit her X chromosome with the Nance–Horan allele and another 1/2 probability that the child will be a boy.
 - c. If III-2 and III-7 mated, what is the probability that one of their children would have Nance–Horan syndrome?
The probability is 1/2 because half the boys will inherit the Nance–Horan allele from the III-7 carrier female. All the girls will inherit one Nance–Horan allele from the III-2 affected male, and half of them will get a second Nance–Horan allele from the III-2 female, so half the girls will also have Nance–Horan syndrome.
24. The following pedigree illustrates the inheritance of ringed hair, a condition in which each hair is differentiated into light and dark zones. What mode or modes of inheritance are possible for the ringed hair trait in this family?



(Pedigree adapted from L. M. Ashley and R. S. Jacques, *Journal of Heredity* 41[1950]:83.)

This pedigree is consistent with autosomal dominant inheritance. Affected individuals marrying unaffected individuals have affected children, so the trait is dominant. Males do not pass the trait to all their daughters, so it cannot be X-linked dominant.

25. Ectodactyly is a rare condition in which the fingers are absent and the hand is split. This condition is usually inherited as an autosomal dominant trait. Ademar Freire-Maia reported the appearance of ectodactyly in a family in São Paulo, Brazil, whose pedigree is shown here. Is this pedigree consistent with autosomal dominant inheritance? If not, what mode of inheritance is most likely? Explain your reasoning.

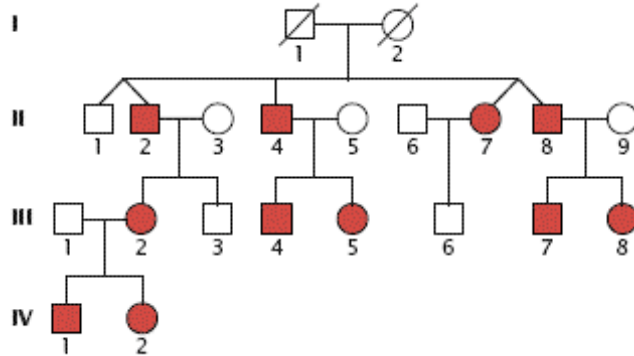


(Pedigree adapted from A. Freire-Maia, *Journal of Heredity* 62[1971]:53.)

This pedigree shows autosomal recessive inheritance, not autosomal dominant inheritance. It cannot be dominant because unaffected individuals have affected children. In generation II, two brothers married two sisters, so the members of generation III in the two families are as closely related as full siblings. A single recessive allele in one of the members of generation I was inherited by all four members of generation III. The consanguineous matings in generation III then

produced children homozygous for the recessive ectodactyly allele. X-linkage is ruled out because the father of female IV-2 is unaffected; he has to be heterozygous.

26. The complete absence of one or more teeth (tooth agenesis) is a common trait in humans—indeed, more than 20% of humans lack one or more of their third molars. However, more severe absence of teeth, defined as missing six or more teeth, is less common and frequently an inherited condition. L. Lammi and colleagues examined tooth agenesis in the Finnish family shown here (L. Lammi. 2004. *American Journal of Human Genetics* 74:1043–1050).



- What is the most likely mode of inheritance for tooth agenesis in this family? Explain your reasoning.
Both males and females have the trait, and affected males and females transmit to either sons or daughters. The trait is most likely autosomal dominant.
- Are the two sets of twins in this family monozygotic or dizygotic twins? What is the basis of your answer?
They are dizygotic, because they differ in either genotype (the first set of twin boys) or gender (the boy and girl).
- If IV-2 married a man who has a full set of teeth, what is the probability that their child would have tooth agenesis?
People with full teeth are homozygous for the recessive allele for full teeth, and IV-2 must be heterozygous. Therefore, the probability of a child with tooth agenesis is 50%.
- If III-2 and III-7 married and had a child, what is the probability that their child would have tooth agenesis?
They are both heterozygotes, so the probability would be $\frac{3}{4}$ for a child to have the dominant tooth agenesis phenotype, assuming that homozygotes for tooth agenesis are viable.

Section 6.4

- *27. A geneticist studies a series of characteristics in monozygotic twins and dizygotic twins, obtaining the following concordances. For each characteristic, indicate whether the rates of concordance suggest genetic influences, environmental influences, or both. Explain your reasoning.

Characteristic	Monozygotic concordance (%)	Dizygotic concordance (%)
Migraine headaches	60	30
Eye color	100	40
Measles	90	90
Clubfoot	30	10
High blood pressure	70	40
Handedness	70	70
Tuberculosis	5	5

Migraine headaches appear to be influenced by genetic and environmental factors. Markedly greater concordance in monozygotic twins, who share 100% genetic identity, than in dizygotic twins, who share 50% genetic identity, is indicative of a genetic influence. However, the fact that monozygotic twins show only 60% concordance despite sharing 100% genetic identity indicates that environmental factors also play a role.

Eye color appears to be purely genetically determined because the concordance is greater in monozygotic twins than in dizygotic twins. Moreover, the monozygotic twins have 100% concordance for this trait, indicating that environment has no detectable influence.

Measles appears to have no detectable genetic influence because there is no difference in concordance between monozygotic and dizygotic twins. Some environmental influence can be detected because monozygotic twins show less than 100% concordance.

Clubfoot appears to have genetic and environmental influences, by the same reasoning as for migraine headaches. A strong environmental influence is indicated by the high discordance in monozygotic twins.

High blood pressure has genetic and environmental influences, similar to clubfoot.

Handedness, like measles, appears to have no genetic influence because the concordance is the same in monozygotic and dizygotic twins. Environmental influence is indicated by the less than 100% concordance in monozygotic twins.

Tuberculosis similarly lacks indication of genetic influence, with the same degree of concordance in monozygotic and dizygotic twins. The primacy of environmental influence is indicated by the very low concordance in monozygotic twins.

28. M. T. Tsuang and colleagues studied drug dependence in male twin pairs (M. T. Tsuang et al. 1996. *American Journal of Medical Genetics* 67:473–477). They found that 4 out of 30 monozygotic twins were concordant for dependence on opioid drugs, whereas 1 out of 34 dizygotic twins were concordant for the same trait. Calculate the concordance rates for opioid dependence in these monozygotic and dizygotic twins. On the basis of these data, what conclusion can you make concerning the roles of genetic and environmental factors in opioid dependence?
The concordance rate for monozygotic twins is 4/30 or 13%. For dizygotic twins, the concordance rate is 1/34 or 3%. Since the monozygotic twins have a higher concordance rate than dizygotic twins, these data could suggest a genetic influence. However, these rates are low and the actual numbers so few that the difference in

concordance rates may not be significant. Thus, these data are somewhat suggestive of a small genetic influence, but not conclusive. The low concordance in monozygotic twins indicates a significant environmental influence.

Section 6.5

29. In a study of schizophrenia (a mental disorder including disorganization of thought and withdrawal from reality), researchers looked at the prevalence of the disorder in the biological and adoptive parents of people who were adopted as children; they found the following results:

Adopted persons	Prevalence of schizophrenia (%)	
	Biological parents	Adoptive parents
With schizophrenia	12	2
Without schizophrenia	6	4

Source: S. S. Kety et al., The biological and adoptive families of adopted individuals who become schizophrenic: prevalence of mental illness and other characteristics, *The Nature of Schizophrenia: New Approaches to Research and Treatment*, L. C. Wynne, R. L. Cromwell, and S. Matthysse, Eds. (New York: Wiley, 1978), pp. 25–37.)

What can you conclude from these results concerning the role of genetics in schizophrenia? Explain your reasoning.

These data suggest that schizophrenia has a strong genetic component. The biological parents of schizophrenic adoptees are far more likely to be schizophrenic than genetically unrelated individuals (the adoptive parents), despite the fact that the schizophrenic adoptees share the same environment as the adoptive parents. If environmental variables (such as chemicals in the water or food or power lines) were a major factor, then one would expect to see a higher frequency of schizophrenia in the adoptive parents. Another possibility is that this increased frequency of schizophrenia in the biological parents simply reflects a greater likelihood that schizophrenic parents give up their children for adoption. This latter possibility is ruled out by the data that the biological parents of nonschizophrenic adoptees do not show a similar increased frequency of schizophrenia compared to adoptive parents.

Section 6.7

30. What, if any, ethical issues might arise from the widespread use of noninvasive fetal diagnosis, which can be carried out much earlier than amniocentesis or CVS? *An issue that is common to all prenatal testing, but may be exacerbated by this new procedure, is the question of what genetic conditions should be tested. Because of the early diagnosis, mothers will have the ability to terminate the pregnancy during the first trimester, with less risk and fewer complications than at more advanced stages. To what extent should regulations determine what types of tests are offered, fearing that some mothers or couples may make decisions based on such factors as the sex of the fetus or other conditions that do not have serious health consequences?*

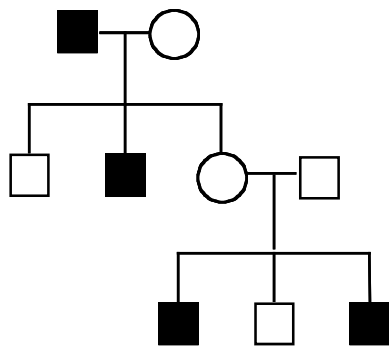
CHALLENGE QUESTIONS

Section 6.1

31. Many genetic studies, particularly those of recessive traits, have focused on small isolated human populations, such as those on islands. Suggest one or more advantages that isolated populations might have for the study of recessive traits. *Isolated populations become inbred, so recessive phenotypes arise more frequently. Some recessive traits that are rare in other, large human populations may be more frequent in isolated populations, facilitating pedigree analysis.*

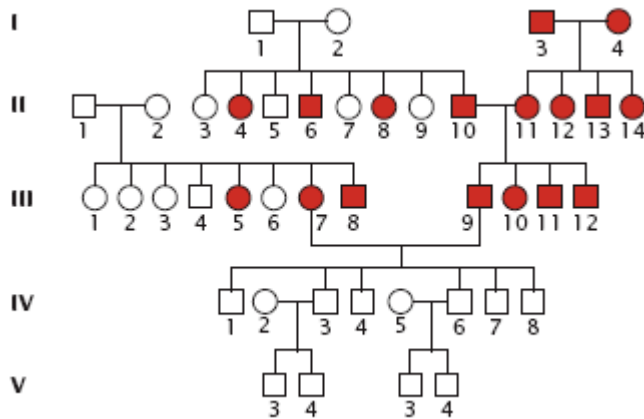
Section 6.3

32. Draw a pedigree that represents an autosomal dominant trait, sex-limited to males, and that excludes the possibility that the trait is Y-linked.



This pedigree excludes Y-linkage because not all the sons of an affected male are affected, an unaffected male has affected sons, and also because it is transmitted through an unaffected female to her sons.

33. A. C. Stevenson and E. A. Cheeseman studied deafness in a family in Northern Ireland and recorded the following pedigree (A. C. Stevenson and E. A. Cheeseman. 1956. *Annals of Human Genetics* 20:177–231).



- a. If you consider only generations I through III, what is the most likely mode of inheritance for this type of deafness?

Autosomal recessive. Affected children of both sexes arise from unaffected parents. Affected parents, being homozygous recessive, have all affected children.

- b. Provide a possible explanation for the cross between III-7 and III-9 and the results for generations IV through V.

One possible explanation is that this deafness may be caused by recessive alleles at two different loci. If we use A and a for the alleles at one locus and B and b for the alleles at the second locus, III-7 could be aa BB and III-9 could be AA bb. All their children (generation IV) would then be Aa Bb, and have normal hearing, having dominant alleles at both loci. Generation 5 are children of marriages with spouses from outside the pedigree, presumably being homozygous dominant for one or both loci.

A second possibility is allelic complementation: two different recessive alleles at the same locus interact in such a way as to produce the dominant phenotype.

Section 6.4

34. Dizygotic twinning often runs in families and its frequency varies among ethnic groups, whereas monozygotic twinning rarely runs in families and its frequency is quite constant among ethnic groups. These observations have been interpreted as evidence for a genetic basis for variation in dizygotic twinning but for little genetic basis for variation in monozygotic twinning. Can you suggest a possible reason for these differences in the genetic tendencies of dizygotic and monozygotic twinning? *The tendency for women to ovulate multiple eggs could be influenced by the mother's genotype. A woman's genotype would determine such factors as hormonal levels important for ovulation. In contrast, the tendency for a fertilized zygote to split into two embryos may be an entirely random event not dependent on the genetic composition of either the embryo or the mother.*