

Chapter 12

Reading: Chapter 12

Topic: X-linkage, pedigrees, genetic disorders

Main concepts:

- Genetic counselors and researchers often use pedigree charts to track the inheritance of a genetic disorder in a family.
- Analysis of a pedigree chart can reveal whether a trait is the result of a dominant allele, a recessive allele, or other pattern of inheritance.
- Different genetic disorders may show different patterns of inheritance. Some are caused by a single gene. Some single gene disorders are the result of a recessive allele, others by a dominant allele. Some are carried on the sex chromosomes (X or Y), others are carried on the somatic chromosomes (all chromosomes except X or Y).
- A person who is heterozygous for a recessive genetic disorder, such as cystic fibrosis or albinism, is a carrier. That person does not show the disorder, but can pass the recessive allele on to the next generation.
- A person who has at least one dominant allele in a disorder that is caused by a dominant allele will have that disorder.
- Some single-gene disorders show incomplete dominance. A heterozygous person would show only mild symptoms. This is true of sickle-cell anemia, and in this case, having one sickle-cell allele makes a person more resistant to malaria, so there is actually an advantage to the allele.
- Sex-linked alleles show a unique pattern of inheritance because they are on the sex chromosomes. For X-linked traits, women still need to inherit two copies of a recessive allele to show the trait, because women have two X chromosomes. Men have an X and a Y chromosome, and the Y does not carry the same genes as the X does. Men only need to inherit one X-linked recessive allele to show the recessive trait, because there is no complimentary allele on a second X chromosome.
- (this is not in the book, but you will need to know it): To make a Punnett square to show inheritance of X-linked traits, we must draw a Punnett square that shows not just the symbols for the alleles, but also for the chromosomes that carry them. The example below shows the sex chromosomes and alleles for a disorder called Duchenne Muscular Dystrophy (DMD), a devastating form of muscular dystrophy that is usually fatal in early childhood:

X^D = X chromosome carrying a dominant allele for Duchenne Muscular Dystrophy
 X^d = X chromosome carrying a recessive (disease) allele for Duchenne Muscular Dystrophy
 Y = normal Y chromosome

$X^D X^D$ = woman who is normal and not a carrier
 $X^D X^d$ = woman who is normal and heterozygous (carrier)
 $X^d X^d$ = woman who has DMD (actually impossible - why?)
 $X^D Y$ = man who is normal
 $X^d Y$ = male with DMD (fatal in childhood)

	X^D	X^d
X^D	$X^D X^D$	$X^D X^d$
Y	$X^D Y$	$X^d Y$

The Punnett square for an X-linked trait looks like this. Again, we're not just tracking the traits, we're tracking how the chromosomes themselves are inherited. This carrier mother and normal father have a 1 in 4 chance of having a child with DMD, and that child will always be a boy. Their sons have a 1 in 2 chance of being born with DMD. All girls will be normal, but each girl has a 1 in 2 chance of being a carrier.

Common misconceptions:

- Once students start doing problems involving X-linked traits, they sometimes have a hard time going back to simple monohybrid crosses. They may try to put all traits on X chromosomes. Only X-linked traits involve the X chromosome, and only the sex chromosomes have these unusual patterns of inheritance.
- Students often get the idea that all disease-causing alleles are recessive, and may talk about someone being a carrier of a disease caused by a dominant allele. Remember that a dominant allele is one whose trait is expressed in the phenotype even if only one allele is inherited.

Reading notes:

- Explain what a pedigree chart is. Note which symbols are used to represent different people on the chart.
- List several genetic disorders caused by single-gene, recessive alleles. Explain what a carrier is.
- Name at least one disorder caused by a dominant allele.
- Name the two sex chromosomes in humans. Name at least one disorder carried on the X chromosome.

Problems

1. Is it possible for there to be a lethal, dominant allele? Why or why not?
2. Can a person be a carrier for a disease caused by a dominant allele? Why or why not?
3. Where do boys get their X chromosomes from: their mothers or their fathers?
4. If an X-linked recessive disorder (such as DMD) is fatal in childhood, can a girl ever be born with the disorder? What if the disorder is not fatal, such as red-green color blindness?
5. Red-green color blindness is a recessive disorder carried on the X chromosome. Write out the genotypes (be sure to include the sex chromosomes as shown above) for: a normal woman, a carrier woman, a color-blind woman, a normal man, a color-blind man. Use R to represent the normal allele and r for the recessive allele. Can a man be a carrier for color blindness?
6. Give the odds of having a color blind girl or a color-blind boy for a) a color-blind woman who marries a normal man, b) a color-blind man who marries a normal (homozygous dominant) woman, and c) a carrier woman who marries a normal man.

Useful websites:

- "Sex-linked Inheritance Problem Set" http://www.biology.arizona.edu/mendelian_genetics/problem_sets/sex_linked_inheritance/sex_linked_inheritance.html is a series of problems that will help you understand X-linked traits.
 - "Interpreting a Pedigree Chart" http://www.biology.arizona.edu/human_bio/problem_sets/human_genetics/05t.html has further instructions in how to read and construct pedigrees.
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Answers:

Problems:

1. Yes — but not, as some students think, because the allele can be passed on by carriers. Remember, you only need one dominant allele to show a dominant trait, so if you have just one allele, you die. So how does it get passed on to the next generation? The dominant lethal alleles that we know of, such as Huntington's chorea, don't cause any symptoms until adulthood, after the age of reproduction. If people died of them in childhood, they would never get passed on.
2. No. If you have the dominant allele, you have the trait. You can be heterozygous, yes, but you would not be a carrier, since a carrier is someone who has one allele but does not show the trait. That only works for recessive disorders.
3. A boy always gets his X chromosome from his mother and his Y chromosome from his father. His mother can't give him a Y, and if he got an X from Dad, he'd be a girl.
4. If the recessive X-linked trait is fatal in childhood, a girl will never be born with it. She would have to get one allele from her mother and one from her father. Since the allele is on the X chromosome, a male who inherits the allele on his X chromosome would have the disease, and if he dies in childhood, he would never pass the allele on to a daughter. If the X-linked trait is not fatal, then a girl could be born with the trait, but only if her father has the trait. She must get one X from her mother and one from her father, and her father only has one X to give.
5. A man can never be a carrier of any X-linked trait, including color-blindness. He either has the allele (and thus shows the trait) or he does not:

$X^R X^R$ = woman who is normal and not a carrier

$X^R X^r$ = woman who is normal and heterozygous (carrier)

$X^r X^r$ = woman who has red-green color blindness

$X^R Y$ = man who is normal

$X^r Y$ = man who has red-green color blindness

6. Punnett squares for the crosses:

- a. Mom is color blind ($X^r X^r$), Dad is normal ($X^R Y$):

	X^r
X^R	$X^R X^r$
Y	$X^r Y$

There is a 1 in 2 chance of any one child being color blind — but those who are color blind will always be boys. All daughters will be carriers, all sons will be color-blind.

- b. Mom is normal ($X^R X^R$), Dad is color-blind ($X^r Y$):

Notes

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	X^R
X^r	$X^R X^r$
Y	$X^R Y$

All children will have normal vision (since boys all get the normal X from Mom), but all daughters will be carriers (since they get the affected X from Dad).

c. Mom is normal but a carrier ($X^R X^r$), Dad is normal ($X^R Y$):

	X^R	X^r
X^R	$X^R X^R$	$X^R X^r$
Y	$X^R Y$	$X^r Y$

There is a 1 in 4 chance of any one child being color blind. All daughters will be normal, because each gets a normal X from Dad, but each has a 1 in 2 chance of being a carrier, because they can get either the normal X or the affected X from Mom. Sons have a 1 in 2 chance of being color blind, since they can get either the affected X or the normal X from Mom.
