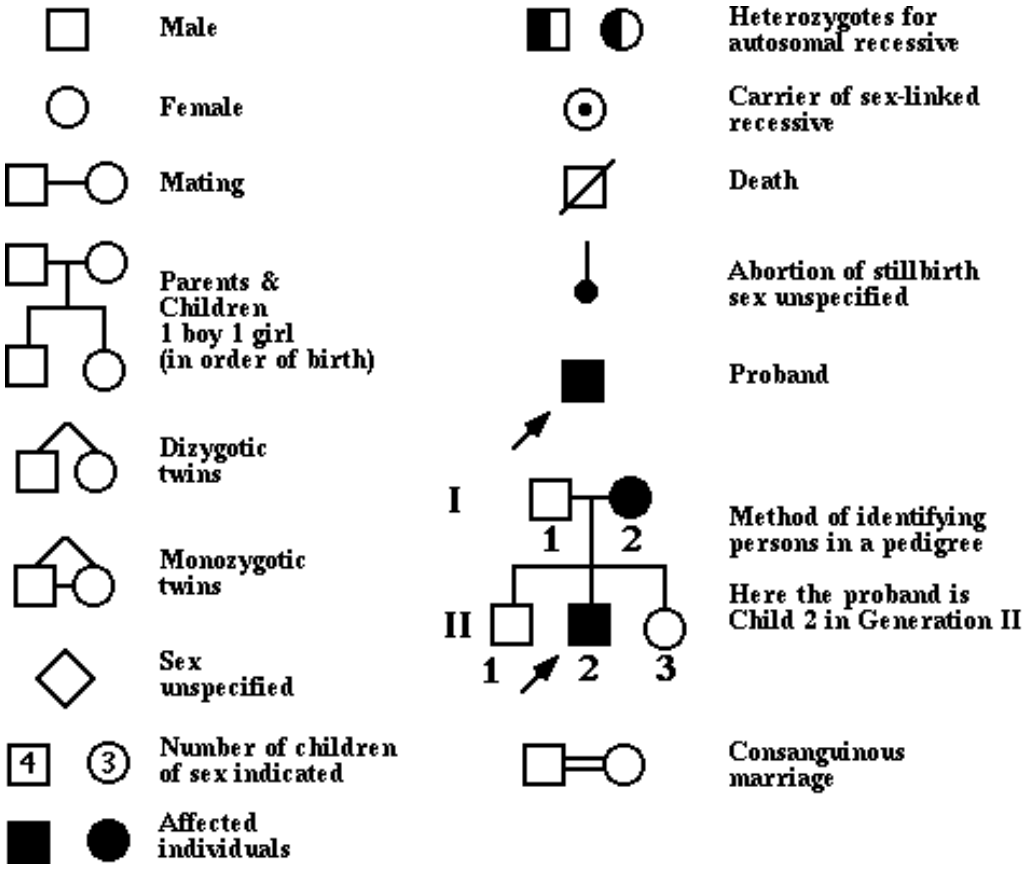
Name _____ Date _____

Pedigree Construction Notes

GO TO → Mendelian Inheritance (http://www.uic.edu/classes/bms/bms655/lesson3.html)

When human geneticists first began to publish family studies, they used a variety of symbols and conventions. Now there are agreed upon standards for the construction of pedigrees.



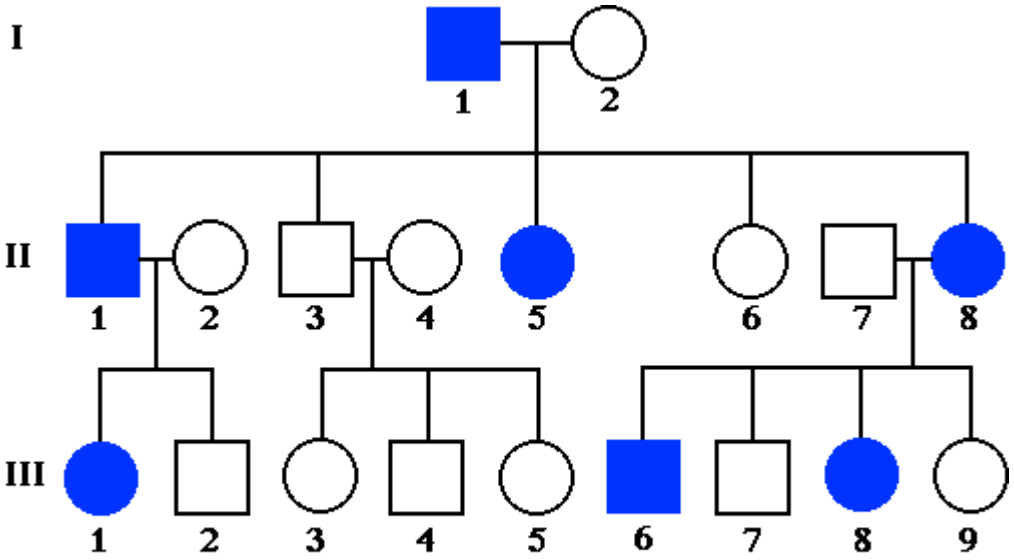
Remember:

1. Males are always represented by square symbols, females with circular symbols.
2. A line drawn between a square and a circle represents a mating of that male and female.
3. Two lines drawn between a square and a circle indicate a consanguineous mating, the two individuals are related, usually second cousins or closer relatives.
4. When possible, the square should be placed on the left and the circle on the right of the mating line.
5. Generations are connected by a vertical line extending down from the mating line to the next generation.
6. Children of a mating are connected to a horizontal line, called the **sibship** line, by short vertical lines.
7. The children of a sibship are always listed in order of birth, the oldest being on the left.
8. Sometimes to simplify a pedigree only one parent is shown, the other is omitted. This neither signifies parthenogenic development nor does it signify divinely inspired conception, it

merely means the parent left out is not from the family being studied and is genotypically homozygous normal for the trait being studied.

9. Normal individuals are represented by an open square or circle, depending upon the gender, and affected individuals by a solid square or circle.
10. Each generation is numbered to the left of the **sibship** line with Roman Numerals.
11. Individuals in each generation are numbered sequentially, beginning on the left, with Arabic Numerals. For example the third individual in the second generation would be identified as individual II-3.

SCROLL DOWN TO "**AUTOSOMAL DOMINANT INHERITANCE**"
Read the short passage, shade the appropriate boxes and fill in the blanks below



Pedigree 1. An idealized pedigree of a family with hypercholesterolemia, an autosomal dominant disease where the heterozygote has a reduced number of functional low density lipoprotein receptors.

The family represented by Pedigree 1 is a good example of how autosomal dominant diseases appear in a pedigree. Each of the four hallmarks of autosomal dominant inheritance are fulfilled.

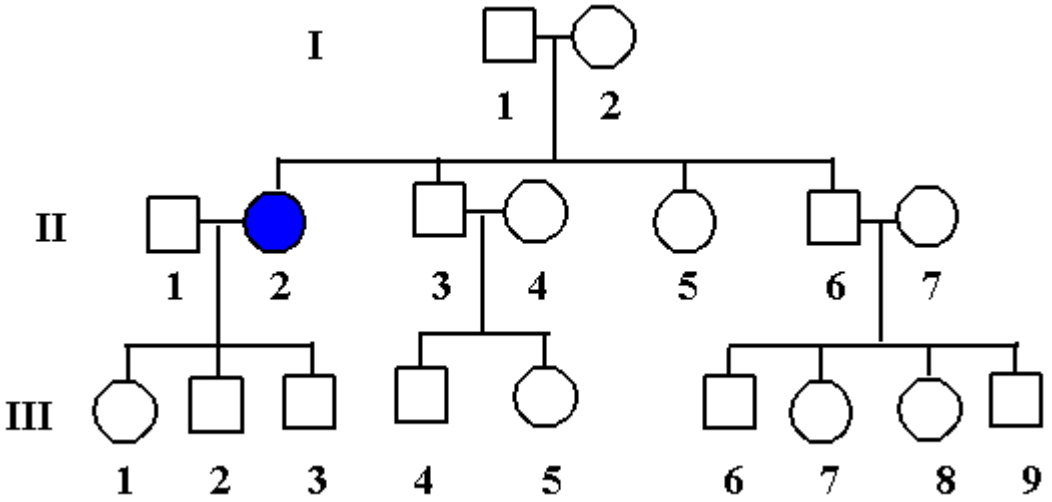
- Each affected individual has an affected parent; there is no skipping of generations.
- Males and females are equally likely to be affected.
- About 1/2 of the offspring of an affected individual are affected (the recurrence risk is 1/2).
- Normal siblings (II-3) of affected individuals have all normal offspring. Low density lipoprotein receptors are structural proteins or polypeptides, not enzymes.
- If III-1, an affected female, were to produce a child that child would have a 1/2 chance of being normal and a 1/2 chance of being affected. If her normal brother, III-2, were to produce a child that child would have a nearly 0 chance of being affected.

GO TO → AUTOSOMAL RECESSIVE INHERITANCE
(http://www.uic.edu/classes/bms/bms655/lesson5.html)

The first, and most important, thing to remember about autosomal recessive inheritance is that most, if not all, affected individuals have parents with normal phenotypes.

There are five hallmarks of autosomal recessive inheritance:

1. **Males and females are equally likely to be affected.**
2. **On average, the recurrence risk to the unborn sibling of an affected individual is 1/4.**
3. **The trait is characteristically found in siblings, not parents of affected or the offspring of affected.**
4. **Parents of affected children may be related. The rarer the trait in the general population, the more likely a consanguineous mating is involved.**
5. **The trait may appear as an isolated (sporadic) event in small sibships.**



- The above pedigree illustrates four of the five hallmarks of autosomal recessive inheritance. I-1 and I-2 are unrelated, yet they produced an affected offspring (**affected offspring have normal parents)**.
- By chance, they both must have been carriers. Even though II-2 is affected, she produced no affected offspring (**trait appears in siblings, not parents or offspring)**.
- By far the most probable genotype for an individual from outside the family (II-1) is homozygous normal. III-1, III-2 and III-3 are all obligate carriers (heterozygotes), since they are not affected but could only have inherited the recessive gene from II-2 II-3, II-5, and II-6 each have a 2/3 chance of being a carrier and a 1/3 chance of being homozygous normal. They are not affected, but they come from a carrier x carrier mating.
- II-4 and II-7 have a high probability of being homozygous normal since they are from outside the family. III-4, III-5, III-6, III-7, III-8, and III-9 all have a 1/3 chance of being carriers and a 2/3 chance of being homozygous normal.
- One parent of each is probably homozygous normal, the other has a 2/3 chance of being a carrier and a 1 in 2 chance of passing on the recessive allele if they were a carrier.

GO TO → **X-LINKED INHERITANCE**
(http://www.uic.edu/classes/bms/bms655/lesson6.html)

When the locus for a gene for a particular trait or disease lies on the X chromosome, the disease is said to be X-linked. The inheritance pattern for X-linked inheritance differs from autosomal inheritance only because the X chromosome has no homologous chromosome in the male, the male has an X and a Y chromosome. Very few genes have been discovered on the Y chromosome.

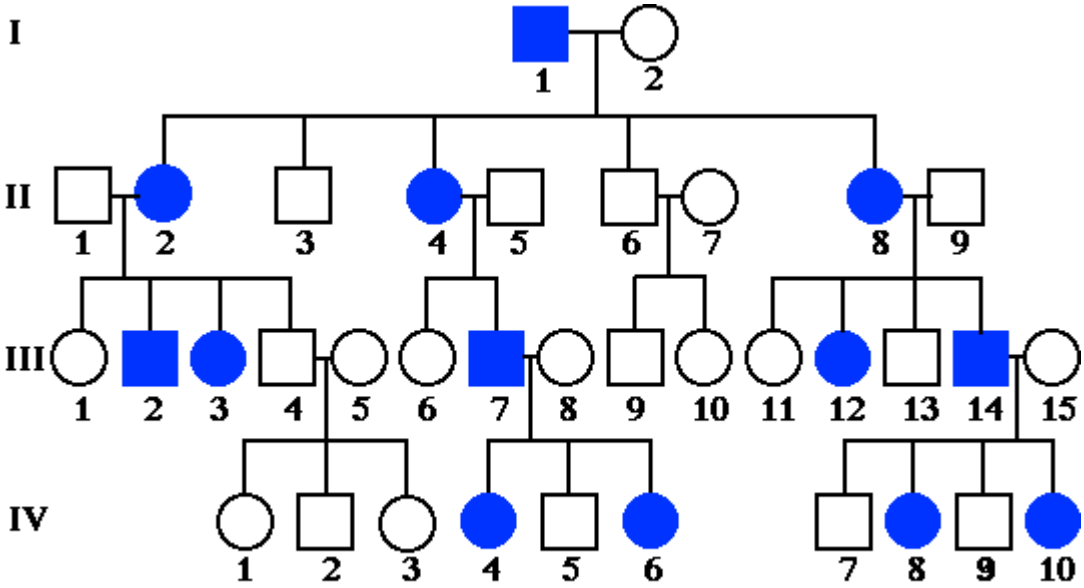
The inheritance pattern follows the pattern of segregation of the X and Y chromosomes in meiosis and fertilization. A male child always gets his X from one of his mother's two X's and his Y chromosome from his father. **X-linked genes are never passed from father to son.** A female child always gets the father's X chromosome and one of the two X's of the mother. **An affected female must have an affected father.** Males are always hemizygous for X linked traits, that is, they can never be heterozygoses or homozygotes. **They are never carriers. A single dose of a mutant allele will produce a mutant phenotype in the male, whether the mutation is dominant or recessive.** On the other hand, females must be either homozygous for the normal allele, heterozygous, or homozygous for the mutant allele, just as they are for autosomal loci.

When an X-linked gene is said to express dominant inheritance, it means that a single dose of the mutant allele will affect the phenotype of the female. A recessive X-linked gene requires two doses of the mutant allele to affect the female phenotype. The following are the hallmarks of X-linked dominant inheritance:

- **The trait is never passed from father to son.**
- **All daughters of an affected male and a normal female are affected. All sons of an affected male and a normal female are normal.**
- **Matings of affected females and normal males produce 1/2 the sons affected and 1/2 the daughters affected.**
- **Males are usually more severely affected than females. The trait may be lethal in males.**
- **In the general population, females are more likely to be affected than males, even if the disease is not lethal in males.**

Males are usually more severely affected than females because in each affected female there is one normal allele producing a normal gene product and one mutant allele producing the non-functioning product, while in each affected male there is only the mutant allele with its non-functioning product and the Y chromosome, no normal gene product at all. Affected females are more prevalent in the general population because the female has two X chromosomes, either of which could carry the mutant allele, while the male only has one X chromosome as a target for

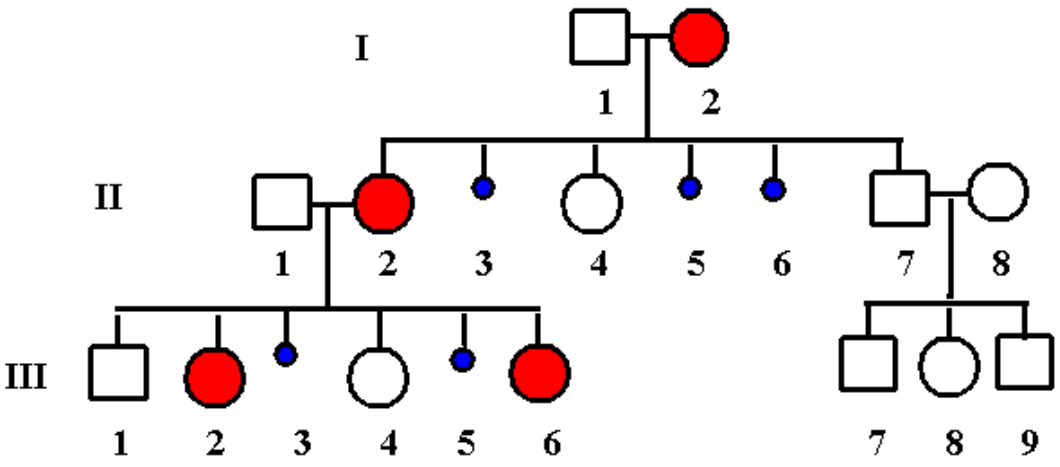
the mutant allele. When the disease is no more deleterious in males than it is in females, females are about twice as likely to be affected as males. As shown in Pedigree 5 below, X-linked dominant inheritance has a unique heritability pattern.



Pedigree 5. X-linked dominant inheritance.

The key for determining if a dominant trait is X-linked or autosomal is to look at the offspring of the mating of an affected male and a normal female. If the affected male has an affected son, then the disease is not X-linked. All of his daughters must also be affected if the disease is X-linked. In Pedigree 5, both of these conditions are met.

What happens when males are so severely affected that they can't reproduce? Suppose they are so severely affected they never survive to term, then what happens? This is not uncommon in X-linked dominant diseases. There are no affected males to test for X-linked dominant inheritance to see if the produce all affected daughters and no affected sons. Pedigree 6 shows the effects of such a disease in a family. There are no affected males, only affected females, in the population. Living females outnumber living males two to one when the mother is affected. The ratio in the offspring of affected females is: 1 affected female: 1 normal female: 1 normal male.



Pedigree 6.

You will note that in Pedigree 6 there have also been several spontaneous abortions in the offspring of affected females. Normally, in the general population of us normal couples, one in six recognized pregnancies results in a spontaneous abortion. Here the ratio is much higher. Presumably many of the spontaneous abortions shown in Pedigree 6 are males that would have been affected had they survived to term.