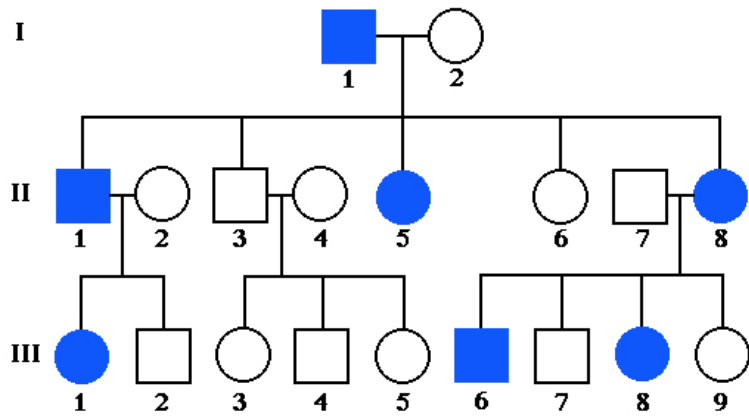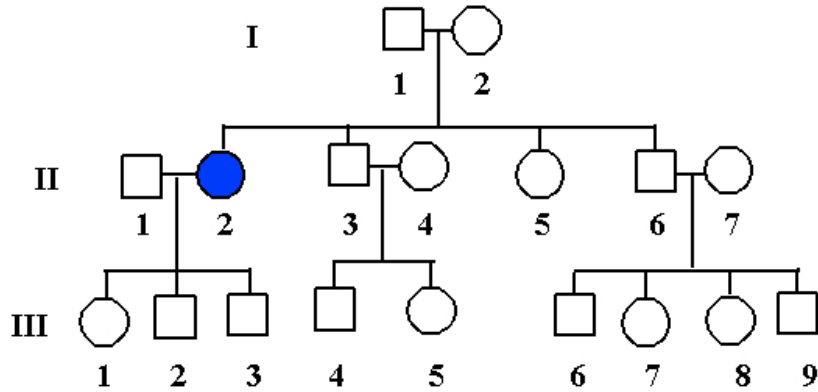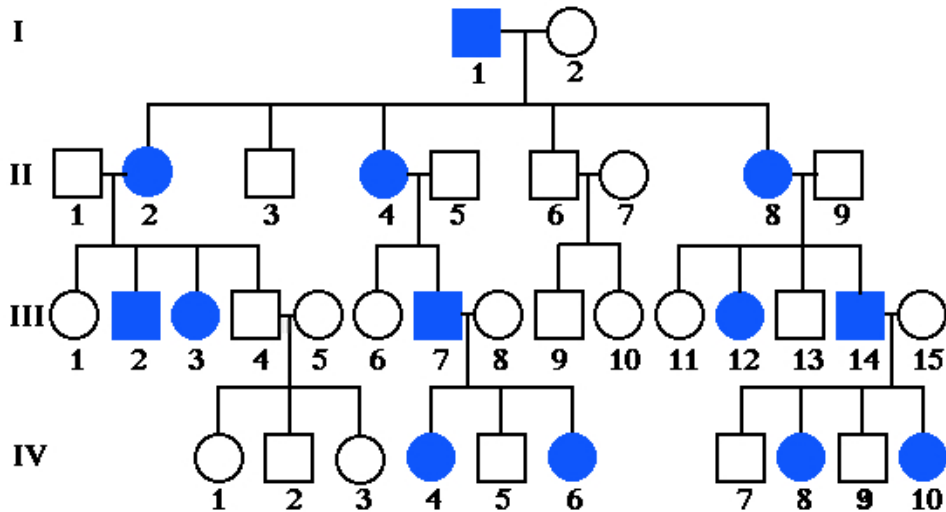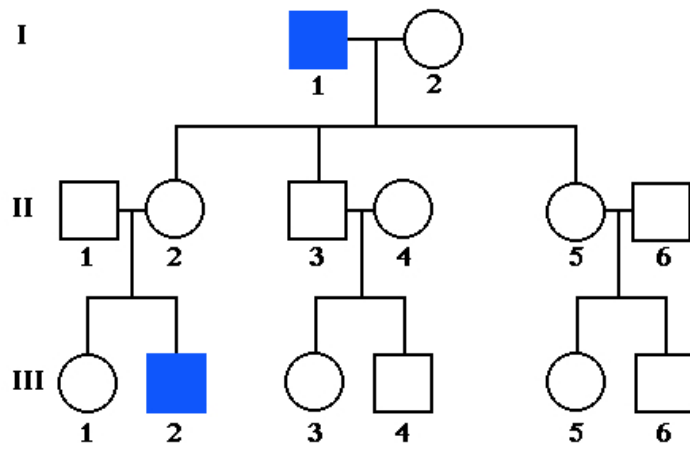Name _____

1. What kind of inheritance pattern?

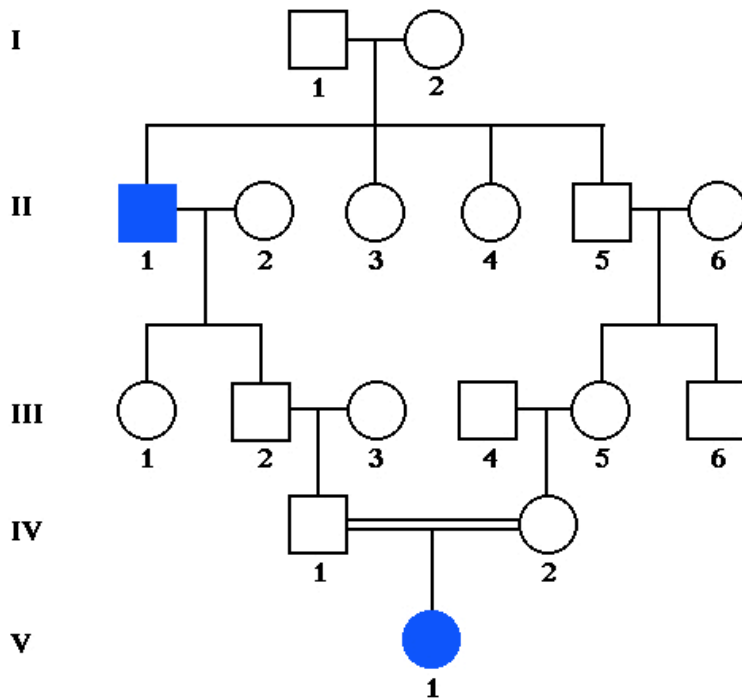2. What kind of inheritance pattern?

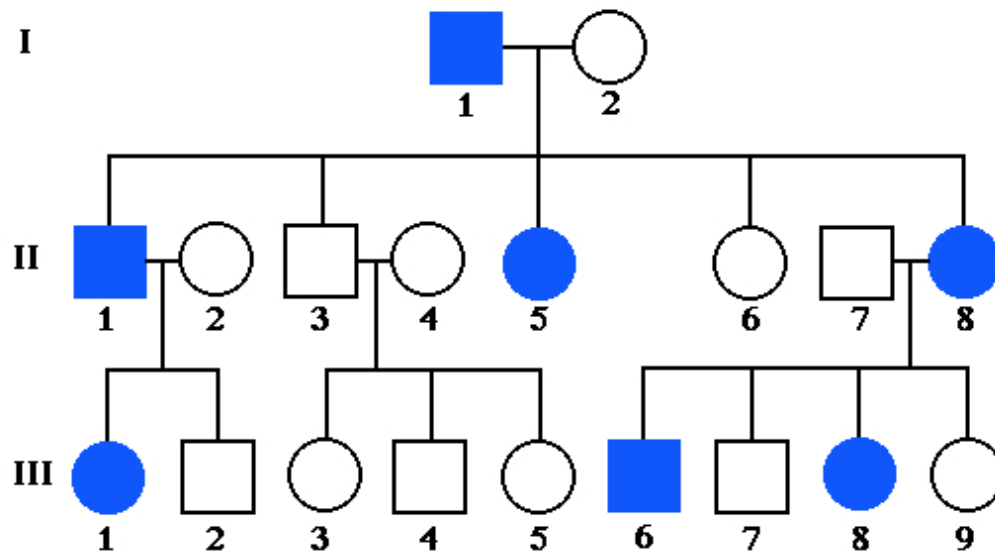
3. What kind of inheritance pattern?
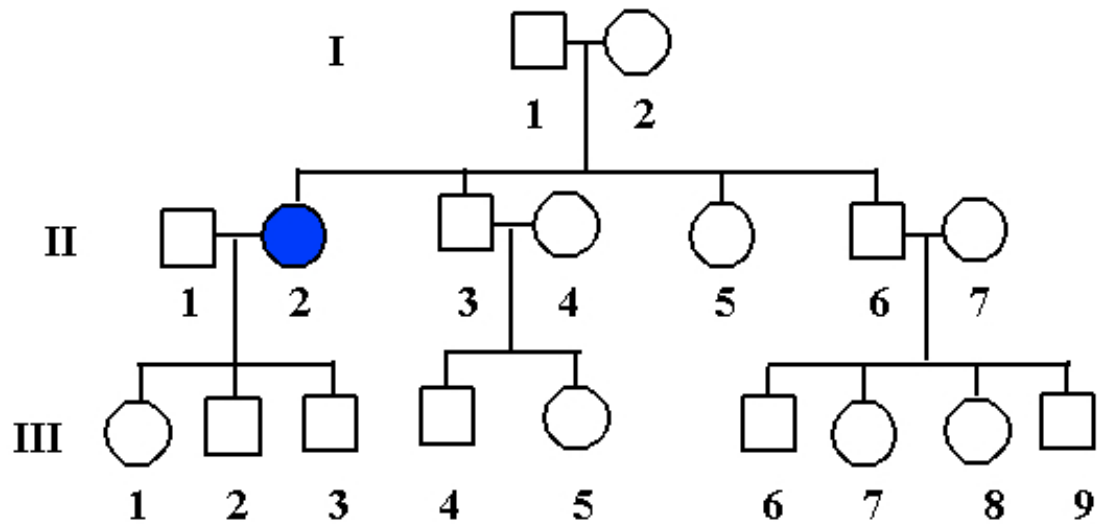
4. What is the inheritance pattern?

5. What kind of inheritance pattern?

1. What kind of inheritance pattern?   Autosomal Dominant

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.

2. What kind of inheritance pattern?   Autosomal Recessive

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.
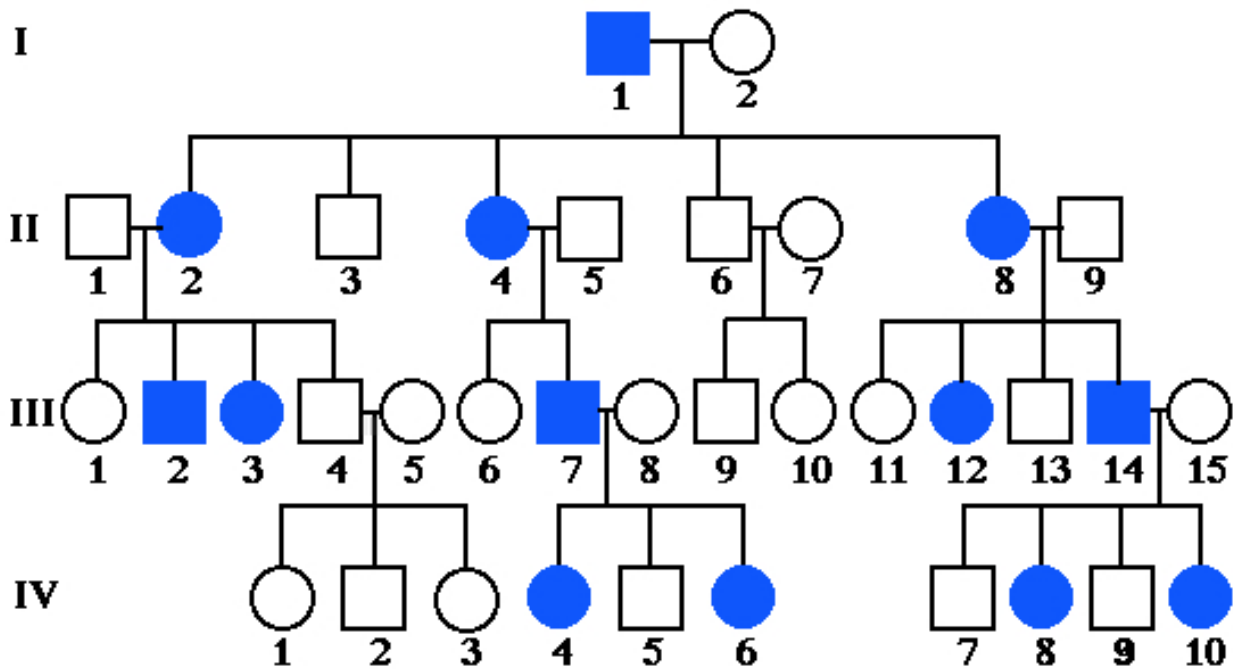
3. What kind of inheritance pattern?   X-linked Dominant

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.
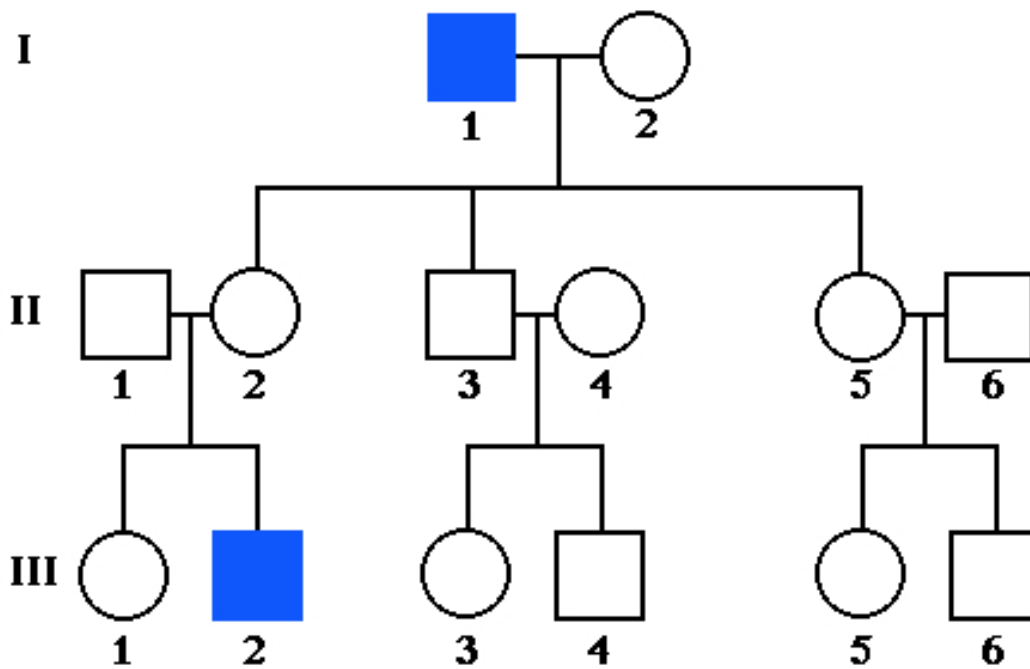
4. What is the inheritance pattern?   X-linked recessive

In Pedigree above, which of the following females is least likely to be a heterozygote for the rare X-linked recessive gene, III-1, III-3, or III-5? The answer of course is III-3. III-1 and III-5 each have a 1/2 chance of being a carrier but III-3 has almost a 0 chance of being a carrier. Why? Let's look at the Punnett Squares for X-linked recessive inheritance.

		Affected Father's Genotype					**Normal Father's Genotype**	
		X^A	Y				X	Y
Normal	X	XX^A	XY	**Carrier**		X^A	X^AY	X^AY
Mother's Genotype	X	XX^A	XY	**Mother's Genotype**	X	XX	XY
All daughters carriers, all sons normal.				Half of sons affected, half of daughters carriers.				

In Pedigree above, II-2 and II-5 are both carriers, their father was affected and passed on his only X chromosome to his daughters. II-3 cannot be a carrier for two reasons. First, males are either affected or normal, never carriers. Second, he didn't inherit his father's X chromosome. He inherited his father's Y chromosome. III-3 couldn't have been a carrier since neither her father nor her mother had the mutant gene.
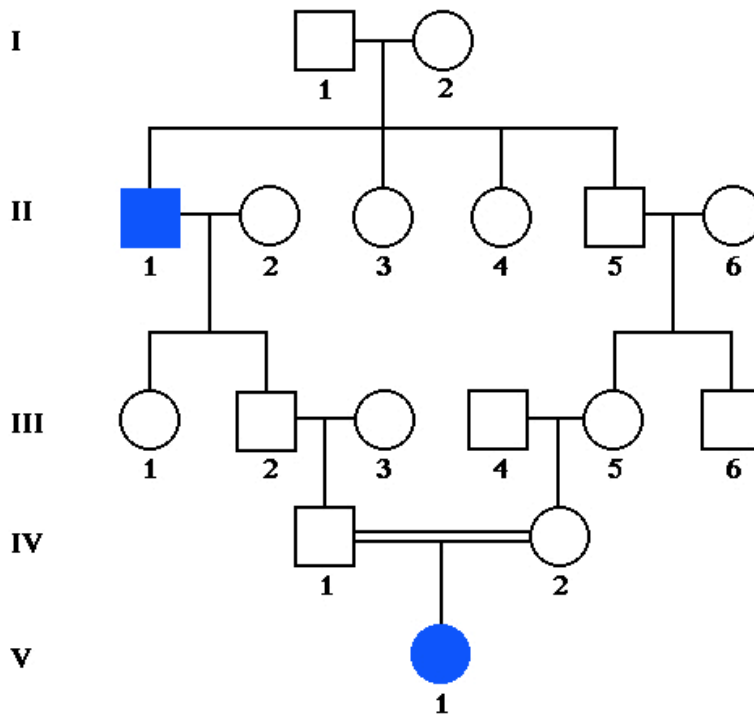
5. What kind of inheritance pattern? Autosomal Recessive - with inbreeding, consanguinity

Normally one never considers the possibility of two unrelated individuals both being carriers unless there is evidence to the contrary. Here I-1 and I-2 are the exception to the rule. There is evidence that both must be carriers.

Before he had any children, II-5 had a 2/3 chance of being a carrier and a 1/3 chance of being homozygous normal (The normal siblings of affected rule explained above). But III-5 had to get her recessive allele from someone, and her other parent, II-6 had at most a 1/50 chance before her children were born. One can compare the two probabilities and calculate that in at least 100 out of 103 times II-5 will be the carrier. This is so close to 1 that for practical purposes one can say he is the carrier. **In rare autosomal recessive diseases, when consanguinity is involved, those individuals in the direct line of descent within the family are considered to be carriers and those individuals from outside the family are considered homozygous normal unless there is evidence to the contrary.**

What can we say about the carrier probabilities of the individuals within the family that are not in the direct line of descent to the affected child? In the above pedigree, III-1 must be a carrier. She is not affected, but she must have received a recessive allele from her father (II-1) who is homozygous recessive. II-3 and II-4 each have a 2/3 chance of being a carrier since they are phenotypically normal and come from a heterozygote x heterozygote mating. III-6 has a one in two chance of being a carrier. His father is a carrier (see above calculations) and his mother is from outside the family.