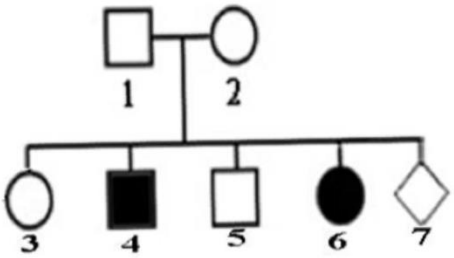
- **How to determine the risk of a fetus to be diseased(affected)**

  1st before calculation of the risk we should already know the mode of inheritance whether dominant or recessive and the location of the gene whether sex-linked or autosomal.

Determine the risk of the fetus to be affected .

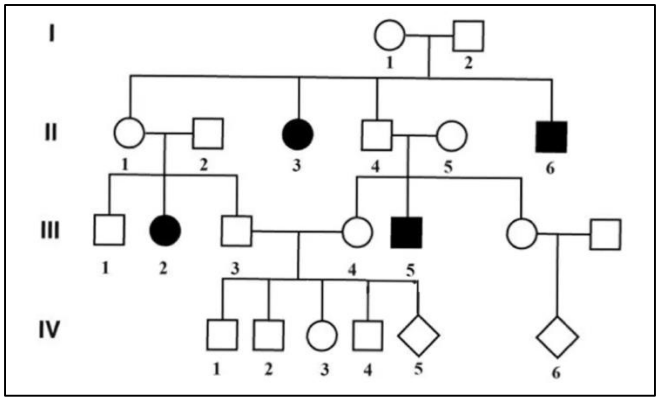
Example 1:*After analysis of the pedigree ,N>d and the gene is autosomal.* **Autosomal recessive**



- Both parents 1 and 2 have genotypes Nd since they are normal and they have affected children 4 and 6 that inherited "d" from each parent.
- The fetus will be affected only if he inherited allele"d" from each parent.
- The probability to inherit "d" from the father is ½.
- The probability to inherit "d" from the mother is ½.
- Therefore the risk to have affected child= P(to inherit "d" from the father)x P(to inherit "d" from the mother)=1/2 x1/2=1/4

Example 2: N>d, Autosomal recessive

Determine the risk of fetus 5 and fetus 6 to be affected



***Note:** to know the risk of the fetus to be affected, directly you should check for the genotypes of his parents.

Risk of fetus 5 to be affected (dd):

Here all the members of his family are normal but this doesn't mean that he might not be affected. Look for probability of the mother to be carrier since if any one of the parents is normal, there is no risk for the fetus to be affected. The only risk for the fetus to be affected is when both parents are hybrid. His mother III4 has the probability to be hybrid 2/3 since the pedigree shows that she is phenotypically normal. So she's either NN or Nd .Check for her parents who have an affected child III5 by looking at the punnet square

Probability of the mother to be carrier Nd is 2/3 since we're sure that she 's not affected from the pedigree so it remains 2/3

	N	d
N	NN	Nd
d	Nd	dd

The same analysis for father III3.

P for fetus to take d from mother is ½ and the probability for fetus to take d from father is ½ .

Risk= P(mother to be carrier)xP(father to be carrier)xP(fetus to inherit d from mother)x P (fetus to inherit d from father)= 2/3x2/3x1/2x1/2= 1/9

Risk of fetus 6 to be affected:-If one of the parents is normal homozygous(NN) or both are homozygous normal there is no risk for the fetus to be affected; but if both parents (mother and father are hybrid),there is risk for the fetus to be affected.

Probability of the mother to be carrier= 2/3 since her parents have affected child so they are hybrid

Probability of the father to be carrier=1/20 (given in the text) since he doesn't have a family history.

P of the fetus to inherit the affected allele "d" from his mother=1/2

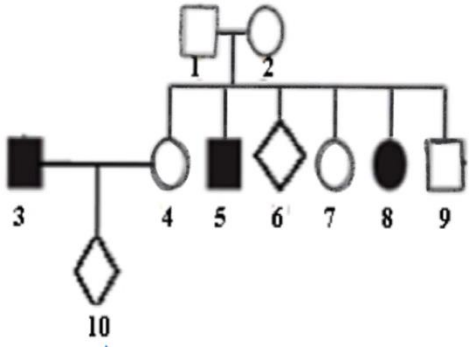
P of the fetus to inherit the affected allele "d" from his father=1/2

Thus, Risk= P(mother to be carrier)xP(father to be carrier)x P(fetus to inherit "d" from father)xP(fetus to inherit "d" from mother)= 2/3x1/20x1/2x1/2= 1/120

Example 3 of autosomal recessive

Calculate the risk of fetus 10 to be affected

Risk= P(mother 4 to be carrier)x P(fetus to inherit "d" from his mother)= 2/3 x1/2= 1/3



Example 4 :Session 2008 II

Exercise 1 (5pts)

Phenylketonuria is a recessive autosomal disease that affects 1/10,000 of newborns world wide. This disease is related to a deficiency in an enzyme called PAH. In normal conditions, this enzyme metabolizes phenylalanine into tyrosine, in the presence of a co-factor DHBP. This deficiency leads to an increase in the amount of phenylalanine in the blood accompanied with serious troubles.

A study performed on 1,200 children selected from an isolated community, showed that 30 children were heterozygous for PAH.

1. Calculate the proportion of heterozygous children in this community; and then determine the genetic risk for a child to be affected with phenylketonuria.

1 . The proportion of heterozygous children in this community= 30/1200 = 1/40

The genetic risk for a child to be affected with phenylketonuria:

If the parents are pure normal or if one of them is pure normal, there is no risk to have an affected child.

Based on the mode of transmission, the parent should be carrier and the child should inherit allele "d" from each one of them.

The probability for each parent to be Nd is 1/40 since they live in this community and they are without family history.

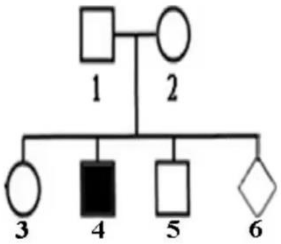
The probability for the child to inherit allele"d" from each parent is ½ .

So, Risk=Prob.(father to be carrier)xProb.(mother to be carrier)xProb.(fetus to inherit "d" from father)x Prob.(fetus to inherit "d" from the mother)=1/40x1/40x1/2x1/2= 1/6400

Example 5 Risk in case of X-linked /recessive (N/d)

Genotype of father 1: X^NY

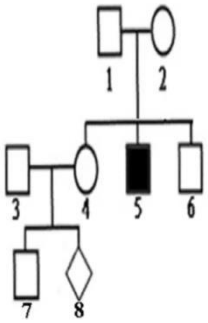
Genotype of mother: X^NX^d ,since she's normal and has affected son 4 whose genotype X^dY and must inherit X^d from his mother



So, Risk of the fetus to be affected: Prob.(to inherit X^d from his mother)= 1/2

Example 6 Risk in case of X-linked /recessive(N>d)

Genotype of father 3: X^NY (Note: here you can't say that the father doesn't have a family history since we're sure of his genotype X^NY unlike in case of autosomal disease)



Genotype of mother 4: X^NX^N or X^NX^d,since she has affected brother 5 that must inherit d from each one of his parents who must be hybrid(carrier Nd)

Risk (girl) =0 since she will take X^N from her father and whether she takes X^N or X^d from her mother, she is phenotypically normal

Risk (boy)=P(mother to be carrier) x P (boy to inherit X^d from his mother)=1/2 x1/2=1/4

1 \ 2	X^N	X^d
X^N	X^NX^N	X^NX^d
Y	X^NY	X^dY

Example 7 : Risk of fetus to be affected in case of X-linked dominant(D>n)

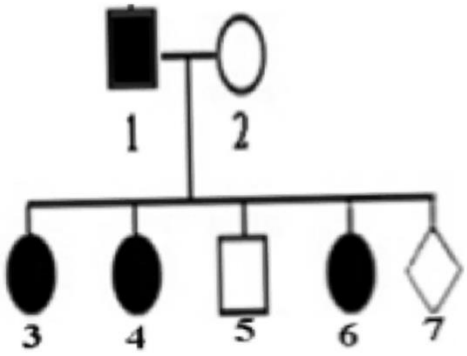
Genotype of father : X^DY

Genotype of mother: X^nX^n

Risk (girl)=1 since she must inherit "X^D" from her father 1and will be affected

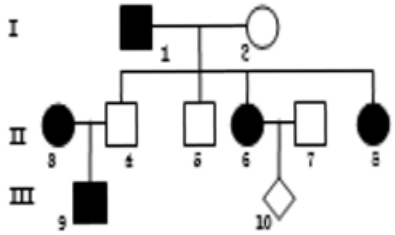
Risk(boy)= 0 since he will inherit X^n from his mother 2 and Y from his father 1;so he's normal.

X linked Dominant



Example 8 : Risk of fetus in case of X-linked dominant (D>n)

Genotype of father 7: X^nY, since he's normal and the recessive allele n is expressed in males



Genotype of mother 6: X^DX^n, since she 's affected and must inherit X^D from her father1 and X^n from her mother 2 who's normal and has genotype X^nX^n

Risk (boy)=Prob.(to inherit X^D from his mother)=1/2

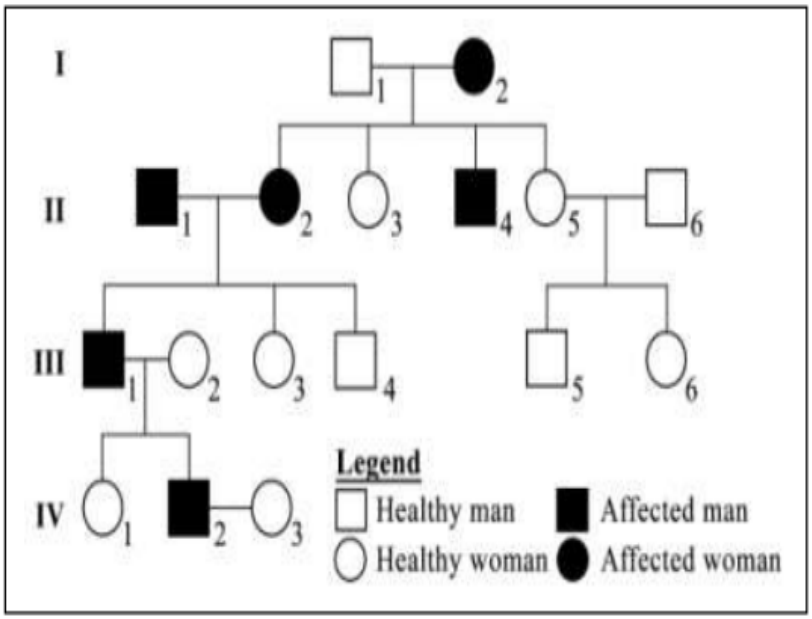
Risk (girl)= Prob.(to inherit X^D from her mother) =1/2

Exercise 3 (5 points) Huntington Chorea

Huntington Chorea is a serious neurodegenerative hereditary disease. Its first symptoms appear in adults starting fromthe age of 25 years.
We seek to determine the mode of transmission of this disease as well as its origin.

Document 1 shows the pedigree of a family whose certain members are affected by this disease.

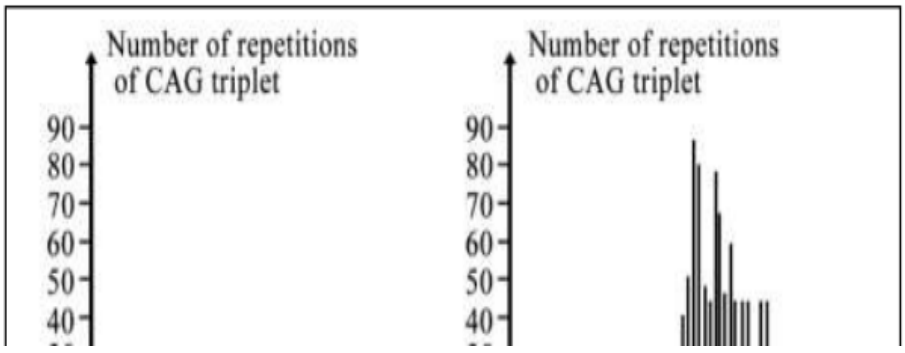
1- Indicate whether the allele determining this disease is dominant or recessive. Justify the answer.
2- Determine the localizationof the gene responsible for this disease.



Document 1

All the members of this family are over 25 years oldexcept individuals III3 and III5. The latter are willing to get married but are afraid of being affected by this disease.

3- Determine the risk for each of individuals III3 and III5 to be affected by this disease.



3	The mother II2 is affected by the disease and is heterozygous since she inherited the allele H from her mother and the allele n from her homozygous healthy father who produces only one type of gametes having the allele n. Thus she produces two types of gametes of equal probabilities: ½ H and ½ n. The affected father II1is heterozygous since he already has a healthy homozygous son III4 to whom he must have transmitted the recessive allele n. Thus he produces two types of gametes equal probabilities: ½ H and ½ n. Since the affected allele of the disease is dominant; it is sufficient for III3 to have at least one allele of the disease in order to be affected . The genotype of III3 can be either H//H ¼ or H//n ½ . Thus the risk for III3 to be affected is 3/4 of the children. Couple II5- II6 is healthy and recessivity is a criterion of purity. These parents produce only one type of gametes carrying the normal allele n. Thus all their children will be healthy. Therefore the risk for III5vto be affected is null.	½ ½