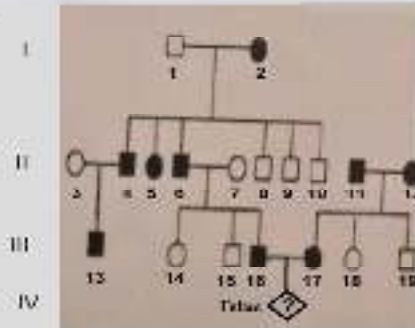


Training Exercise :

Pedigree Analysis

Below is a pedigree of a family, whose members exhibit a dominant trait (L) leading to abnormally long fingers, while the recessive trait (n) allows for a normal length.



1- Show that the responsible gene is not gonosomal but autosomal.

2- Specify the genotypes of individuals 1, 2, 4, 11, 12 and 13.

3- Determine the genetic risk of fetus (?) to be affected.

1- ⇒ If the gene is localized on the non-homologous segment of Y chromosome, then none of the females should be affected. This is not the case, since female 18 is an affected one.

Or: Father and son would be of the same genotype X/Y^L and same phenotype (long fingers), because the son must inherit his Y^L from his father, but son 19 is normal and his father 11 is affected, which is not the case.

⇒ If the gene is localized on the non-homologous segment of X chromosome, then all daughters of affected father should be affected of genotype X^L/X^L or X^L/X^n , because every daughter must inherit X^L from her father who would have as genotype X^L/Y , but daughter 18 is normal of genotype X^n/X^n and her father 11 is affected, which is not the case. (1/4).

⇒ If the gene is localized on the homologous segments of X and Y chromosomes, then the affected female would have as genotype X^L/X^L or X^L/X^n , similarly the affected male 19 would have as genotype X^L/Y^L , but female 18 must inherit X^L from her father 11 while male 19 must inherit Y^L from the same father. The father as such should have as genotype X^L/Y^L , but female 18 is normal, which is not the case.

Thus the gene is not gonosomal, therefore autosomal.

L: symbol of allele leading to abnormality of long fingers.

n: symbol of normal allele.

2- The genotype of father 1 is **n/n**, because he has a recessive normal phenotype and the recessive normal allele **n** can express itself only when present in homozygous state.

-The genotype of mother 2 is **L/n**, because she has a dominant affected phenotype then she has allele **L** and since she has normal children 8, 9 and 10, then she must carry a recessive allele **n** in the masked state.

- The genotype of son 4 is **L/n**, because he has a dominant affected phenotype then he has allele **L** and since he has a normal father 1 then, he must inherit from him a recessive allele **n**.

- The genotype of each parent 11 and 12 is **L/n**, because this couple are of dominant affected phenotype and they give birth to recessive normal children 18 and 19, then each of these children should inherit a recessive allele **n** from each parent which is present in masked state (not expressed).

- The genotype of son 13 is **L/n**, because he has a dominant affected phenotype then he has allele **L** and since he has a mother 3 of recessive normal phenotype (**n/n**) then, he must inherit from her a recessive allele **n**.

3- Father's 16 genotype : L//n.

Justification: Since he has the abnormality then he has allele L, but his mother 7 has a recessive normal phenotype, her genotype is obligatorily n//n, so, he has also allele n.

-Mother's 17 genotype: L//L or L//n.

Justification: Since she has the abnormality and she has heterozygous parents (since they have normal children 18 and 19), and the allele responsible for the abnormality is dominant where it can be expressed in both homozygous and heterozygous states.

To determine the genetic risk of the fetus (?) of this couple to be affected, we can find the probability (P) of this couple to have a normal child and subtract it from the total (1).

Conditions to have a normal child:

- The father should be carrier of the normal allele (heterozygote) of $P = 1/1$.
- The mother should be carrier of the normal allele (heterozygote) of $P = 2/3$, since she is affected and has heterozygote parents **who has affected children (18, 19)**.
- The child should inherit **allele n** from the mother, $P = 1/2$ (if the mother is heterozygote, then she produces two types of gametes one having allele L and the other having allele n each with probability $\frac{1}{2}$).
- The child should inherit **allele n** from the father, $P = 1/2$ (same justification as the mother...)

The probability that the fetus is normal = probability of the father to be heterozygote \times probability of the mother to be heterozygote \times probability of the fetus to inherit normal allele from the mother \times probability of the fetus to inherit normal allele from the father = $1 \times 2/3 \times 1/2 \times 1/2 = 2/12 = 1/6$

Therefore, the risk of the fetus (?) to be affected is: $1 - 1/6 = 5/6$.

3- Another method:

- Father's 16 genotype: L//n.

Justification: Since he has the abnormality then he has allele L, but his mother 7 has a recessive normal phenotype, her genotype is obligatorily n//n, so, he carries also allele n in the masked state.

- Mother's 17 genotype: L//L or L//n.

Justification: Since she has the abnormality, she has heterozygous parents (since they have normal children 18 and 19), and the allele responsible for the abnormality is dominant where it can be expressed in both homozygous and heterozygous states.

To determine the genetic risk of the fetus (?) to be affected of this couple, we can proceed as follows:

Conditions to have a affected child:

- The father 16 should possess the affected allele **L**, he is necessarily heterozygote (**L//n**) of $P = 1/1$.
- The mother 17 could be either homozygote (**L//L**) of $P = 1/3$ (**case 1**), or heterozygote (**L//n**) of $P = 2/3$ (**case 2**).

Case 1:

- The child should inherit **allele L** from the father and since he is heterozygote, he produces two types of gametes one having allele L and the other having allele n, each with probability $\frac{1}{2}$.
- The child can only inherit **allele L** from the mother, since the mother is homozygote, she produces only one type of gametes having **allele L** with probability 1/1.

The genetic risk of the fetus (?) to be affected = probability of the father to be heterozygote \times probability of the mother to be homozygote \times probability of the couple to give affected children.

- The couple in this case will have all their children affected of probability 1/1.

The genetic risk of the fetus (?) to be affected = $1/1 \times 1/3 \times 1/1 = 1/3$.

Case 2:

- The child can inherit **allele L** or allele n from the father, since he is heterozygote, he produces two types of gametes one having allele L and the other having allele n, each with probability $1/2$.
- The child can inherit **allele L** or allele n from the mother, since the mother is heterozygote, she produces two types of gametes one having **allele L** and the other having allele n, each with probability $1/2$.

-The couple in this case will have their children affected of probability $3/4$.

The genetic risk of the fetus (?) to be affected fetus is affected = probability of the father to be heterozygote \times probability of the mother to be heterozygote \times probability of the couple to give affected children.

The genetic risk of the fetus (?) to be affected = $1/1 \times 2/3 \times 3/4 = 6/12 = 1/2$.

Finally, add: genetic risk of case 1 + genetic risk of case 2 therefore, the genetic risk of the fetus (?) to be affected = $1/3 + 1/2 = 5/6$.