

## Determine The Risk

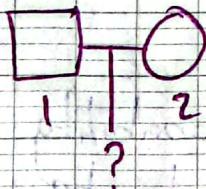
A

Autosomal recessive Disease

N for normal allele (dominant)  
d for mutant allele (recessive)

case 1] The parents have no family history

Given the probability for a person to be heterozygote in this population is  $\frac{1}{20}$ .



Risk = probability for father to be hybrid x probability for mother to be hybrid x probability to give affected child if parents are hybrids

- probability for father to be hybrid =  $\frac{1}{20}$  [since they have no family history]

- probability for mother to be hybrid =  $\frac{1}{20}$

- probability to give affected allele =  $\frac{1}{4}$

$\left( \frac{1}{2} \text{ gametes father carry d allele} \right)$

$\left( \frac{1}{2} \text{ gametes mother carry d allele} \right)$

	N	$\frac{1}{2}$	$\frac{1}{2}$	d
$\frac{1}{2}$ (gametes father carry d allele)	N	$\frac{1}{2}$	$\frac{1}{4}$	$\frac{1}{4}$
$\frac{1}{2}$ (gametes mother carry d allele)	d	$\frac{1}{2}$	$\frac{1}{4}$	$\frac{1}{4}$

$$\Rightarrow \text{Risk} = \frac{1}{20} \times \frac{1}{20} \times \frac{1}{4} = \frac{1}{1600}$$

## Case 2) Both parents have affected brother or sister

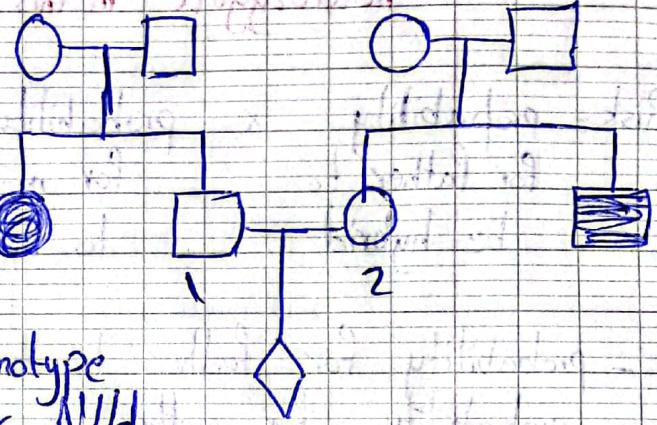
Risk = probability for father to be hybrid  $\times$  probability for mother to be hybrid  $\times$  probability to give an affected child if both parents are heterozygotes

$\Rightarrow$  probability for father to be hybrid =  $\frac{2}{3}$

since he has affected sister of genotype  $d/d$

who inherited the mutant allele from parents (Heterozygote)  $\Rightarrow$  So

the father 1 has normal phenotype and his genotype is  $N/N$  or  $N/d$ .



$\Rightarrow$  probability for mother to be hybrid =  $\frac{2}{3}$  same justification for the mother 2 as the father 1)

$\Rightarrow$  probability to give affected allele =  $\frac{1}{4}$

( $\frac{1}{2}$  gamete carry  $d$ -allele from mother)  
 $\frac{1}{2}$  gamete carry  $d$ -allele from father)

$\Rightarrow$  Risk to have affected child =  $\frac{2}{3} \times \frac{2}{3} \times \frac{1}{4} = \frac{1}{9}$

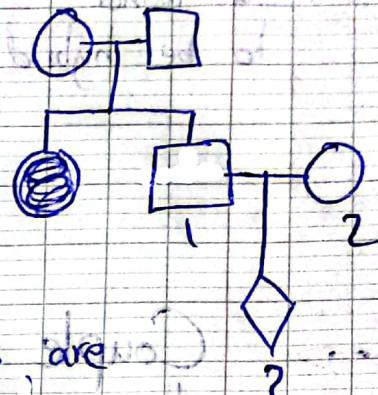
	$N \frac{1}{2}$	$d \frac{1}{2}$
$N \frac{1}{2}$	$N/N \frac{1}{4}$	$N/d \frac{1}{4}$
$d \frac{1}{2}$	$N/d \frac{1}{4}$	$d/d \frac{1}{4}$

Case 3: One parent has an affected sister or brother

The other parent has no family history

Given: the probability for a person to be heterozygote in this population is  $\frac{1}{20}$

Risk = probability for father to be hybrid  $\times$  probability for mother to be hybrid  $\times$  probability to have affected child if both parents are hybrids



$\Rightarrow$  probability for mother to be hybrid =  $\frac{1}{20}$  (since she has no family history)

$\Rightarrow$  probability for father to be hybrid =  $\frac{2}{3}$  since he has an affected sister of genotype  $d/d$  so she inherits the mutant allele from each parent who must be heterozygotes  
 $\Rightarrow$  So the genotype of father is  $N/d$  or  $N/N$ .

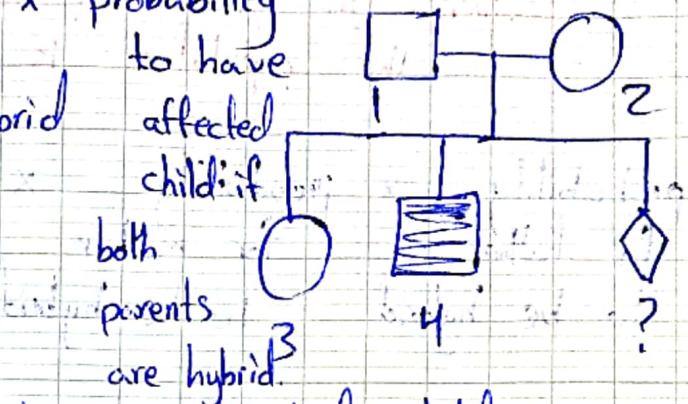
$\Rightarrow$  probability to give affected allele from both parents =  $\frac{1}{4}$

$(\frac{1}{2} \text{ gamete carry } d- \text{ allele from father})$	$\frac{1}{2}$	$\frac{N}{2}$	$\frac{d}{2}$
$(\frac{1}{2} \text{ gamete carry } d- \text{ allele from mother})$	$\frac{1}{2}$	$\frac{N}{2}$	$\frac{d}{2}$
$Risk = \frac{1}{20} \times \frac{2}{3} \times \frac{1}{4} = \frac{1}{120}$	$\frac{1}{120}$	$\frac{N}{120}$	$\frac{d}{120}$

$$Risk = \frac{1}{20} \times \frac{2}{3} \times \frac{1}{4} = \frac{1}{120}$$

## Case 4] Both parents have an Affected child

Risk = probability for father to be hybrid  $\times$  probability for mother to be hybrid  $\times$  probability to have affected child if both parents are hybrid.



⇒ Couple 1 and 2 have affected child 4, so the mutant allele must be present and masked in their genotype and they have normal phenotype.  $\Rightarrow$  So, they should be Heterozygote of genotype (N/d)

- probability for father to be hybrid = 1
- for mother " = 1
- probability to give affected allele from both parents =  $\frac{1}{4}$

$$\Rightarrow \text{Risk} = 1 \times 1 \times \frac{1}{4} = \boxed{\frac{1}{4}}$$

	$\sigma^+$	N $\frac{1}{2}$	d $\frac{1}{2}$
♀	N $\frac{1}{2}$	N/N $\frac{1}{4}$	N/d $\frac{1}{4}$
d $\frac{1}{2}$	N/d $\frac{1}{4}$	d/d $\frac{1}{4}$	d/d $\frac{1}{4}$

## Case 5] Parents have an affected child and affected siblings

⇒ Same solution as case 4.

$$\text{Risk} = 1 \times 1 \times \frac{1}{4} = \boxed{\frac{1}{4}}$$

Case 6] One parent has no family history.

The other parent is affected.

Given: the probability for a person to be heterozygote in this population is  $\frac{1}{20}$ .



$\Rightarrow$  probability of father 1 to be hybrid =  $\frac{1}{20}$   
(has no family history)

and he gives  $\geq$  types of gametes  $\frac{1}{2} N + \frac{1}{2} d$

however, the mother is affected of genotype  $d/d$   
 $\Rightarrow$  gives only one type of gamete  $d$ .

$$\text{Risk} = \frac{1}{20} \times \frac{1}{2} = \frac{1}{40}$$

$\text{♀}$	$\text{♂}$	$N$	$d$
$d$		$N/d$	$d/d$

Affected children

B

## Autosomal Dominant Disease

( D for mutant allele , dominant  
n for normal allele , recessive )

Case 7 ]

Affected

Parents

having normal children

↳ Should describe the factorial Analysis

→ Both parents 1 and 2 have affected phenotype , however they give normal children 3 and 5 which means that the normal allele (n) is masked in their genotype .

⇒ Genotype of both parents is Dl/n

→ each parent gives 2 types of gametes

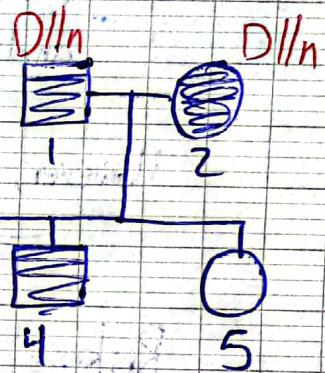
$\frac{1}{2} D$  and  $\frac{1}{2} n$

This couple has 4 combinations

Risk =

$$\frac{1}{4} D/D + \frac{1}{4} D/l/n + \frac{1}{4} D/l/n$$

=  $\frac{3}{4}$  affected children



g	$\delta'$	D	n
D	$\frac{1}{2}$	Dl/n	Dl/n
n	$\frac{1}{2}$	Dl/n	n/n

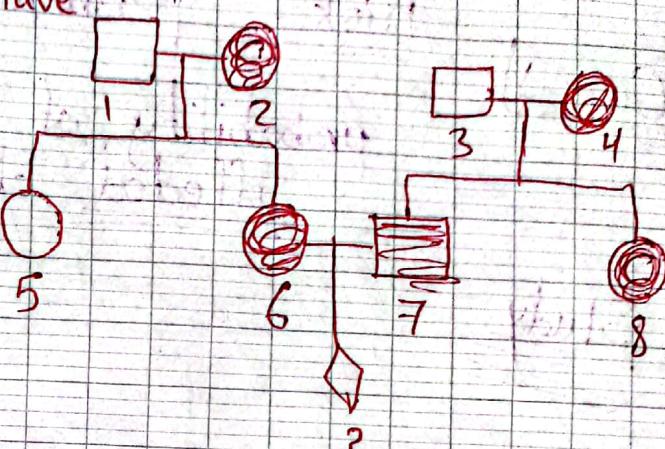
## Case 8) Parent with normal children

Risk for couple (6) & (7) to have affected child.

Mother 6 is affected but her father 1 is normal of genotype n/n (recessive allele expressed only in homozygote state)

Then, mother 6 should be heterozygote of genotype D/n  $\Rightarrow$  will give 2 types of gamete  $\frac{1}{2} D \quad \frac{1}{2} n$

Father 7 has affected phenotype so must have D allele but he has normal father 3 with normal phenotype of genotype (n/n)  $\Rightarrow$  So father 7 inherits n allele from his father 3 to be heterozygote of genotype (D/n)  $\Rightarrow$  Gives 2 types of gametes  $\frac{1}{2} D \quad \frac{1}{2} n$



This couple gives 4 combination

$$\frac{1}{2} D \times \frac{1}{2} D = \frac{1}{4} D/D$$

$$\frac{1}{2} D \times \frac{1}{2} n = \frac{1}{4} D/n$$

$$\frac{1}{2} D \times \frac{1}{2} n = \frac{1}{4} D/n$$

$$\frac{1}{2} n \times \frac{1}{2} n = \frac{1}{4} n/n$$

<del>♀</del>	<del>♂</del>	D $\frac{1}{2}$	n $\frac{1}{2}$
	D $\frac{1}{2}$	D/D $\frac{1}{4}$	D/n $\frac{1}{4}$
	n $\frac{1}{2}$	D/n $\frac{1}{4}$	n/n $\frac{1}{4}$

Risk =  $\frac{3}{4}$  affected

C

## Gonosomal Recessive Disease

Risk = Probability of mother to be hybrid  $\times$   
probability of the couple to have an  
affected child.

Study

probability for mother to be hybrid

=  $\frac{1}{2}$  if she has an affected brother.

= 1 if her father, sister, or son is affected

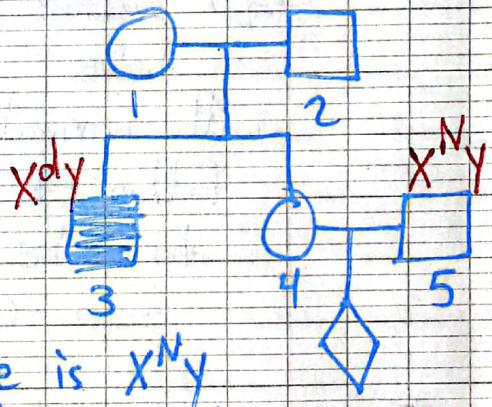
Example

Determine the risk for this fetus  
to be affected.

Fetus

If the ↑ is a girl:

Father 5 is normal, his genotype is  $X^N Y$   
she will inherit  $X^N$  from his father.



Her mother 4 has normal phenotype, her genotype  
is either  $X^N X^N$  or  $X^N X^d \Rightarrow$  So the  
girl will inherit  $X^N$  or  $X^d$  from her mother.  
 $\Rightarrow$  But the girl will have normal phenotype  
since the normal allele is dominant can be  
expressed in heterozygote or homozygote state.

$\Rightarrow$  The risk to have affected girl is null.  
(no need to use formula)

Important  
should be  
written

case 9

→ If the fetus is a boy → formula

Risk = probability to be heterozygote  $\times \{$  probability of both couple to have affected child if mother is hybrid  
 $\frac{1}{2}$  since she has affected brother ?



The probability of both couple to have affected boy =  $\frac{1}{2}$

♀	$X^d$	$\frac{1}{2}$	$X^N$	$\frac{1}{2}$
$X^N$	$X^N X^d$	$\frac{1}{4}$	$X^N X^N$	$\frac{1}{4}$
$Y$	$X^d Y$	$\frac{1}{4}$	$X^N Y$	$\frac{1}{4}$

$$\rightarrow \text{Risk} = \frac{1}{2} \times \frac{1}{2} = \boxed{\frac{1}{4}}$$

Boys  
 $\frac{1}{2}$  normal →  $\frac{1}{2}$  affected

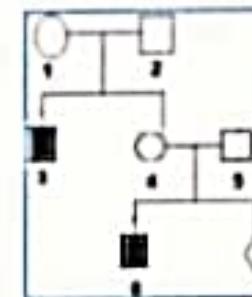
**Case 10: the mother has an affected boy**

The mother 4 is heterozygous, of genotype  $X^N X^d$  since she has an affected boy 6 (who must have inherited  $X^d$  from his mother 4 and  $Y$  from his father).

The genotype of the father is  $X^N Y$ . He transmits  $X^N$  to his daughters and  $Y$  to his sons.

If the fetus is a girl:

Since all daughters inherit  $X^N$  from their father and since allele  $N$  is dominant over allele  $d$ , then all the girls will have normal phenotype. Hence, the risk for this couple to obtain an affected girl is null.



If the fetus is a boy:

For this couple to obtain a color blind son having a genotype  $X^d Y$ , this son should inherit  $X^d$  from his mother and  $Y$  from his father.

Since the mother 4 is heterozygous of genotype  $X^N X^d$ , thus she might transmit either  $X^N$  or  $X^d$  to her sons.

The risk for the mother to transmit  $X^d$  to her son is  $\frac{1}{2}$ .

Therefore, the risk to have an affected boy is  $\frac{1}{2}$ .

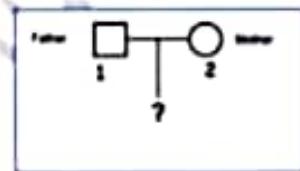
Mother gametes	$X^d \pm$	$X^N \pm$
Father gametes		
$X^d \pm$	$X^N X^d$ 	$X^N X^N$ 
$Y \pm$	$X^d Y$ 	$X^N Y$ 

### Case 11: the mother has no family history

**Given:** the probability to be heterozygous is 1/100

The probability of the mother 1 to be heterozygous, of genotype  $X^N X^d$  is 1/100 since she has no family history.

The genotype of the father is  $X^N Y$  (he is normal and has one X and then his phenotype reveals his genotype). He transmits  $X^N$  to his daughters and Y to his sons.



If the fetus is a girl:

Since all daughters inherit  $X^N$  from their father and since allele N is dominant over allele d, then all the girls will have normal phenotype. Hence, the risk for this couple to obtain an affected girl is null.

If the fetus is a boy:

For this couple to obtain an affected son having a genotype  $X^d Y$ , this son should inherit  $X^d$  from his mother and Y from his father.

Since the mother 1 is heterozygous of genotype  $X^N X^d$ , thus she might transmit either  $X^N$  or  $X^d$  to her sons.

Mother gametes Father gametes	$X^d \frac{1}{2}$	$X^N \frac{1}{2}$
$X^N \frac{1}{2}$	$X^N X^d \frac{1}{2}$	$X^N X^N \frac{1}{2}$
$Y \frac{1}{2}$	$X^d Y \frac{1}{2}$	$X^N Y \frac{1}{2}$

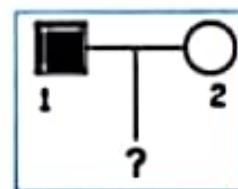
The risk for the mother to transmit  $X^d$  to her son is  $\frac{1}{2}$ .

Therefore, the risk to have an affected boy is  $1/100 \times \frac{1}{2} = 1/200$ .

### Case 12: the mother has no family history and the father is affected

**Given:** the probability to be heterozygous is 1/100

The probability of the mother 1 to be heterozygous, of genotype  $X^N X^d$  is 1/100 since she has no family history.



The genotype of the father is  $X^d Y$  (he is affected and has one X and then his phenotype reveals his genotype). He transmits  $X^d$  to his daughters and Y to his sons.

The probability for this couple to have affected children is:

$$(\frac{1}{2} X^d \times \frac{1}{2} X^d) + (\frac{1}{2} X^d \times \frac{1}{2} Y) = \frac{1}{2} + \frac{1}{2} = 1$$

THEN the risk is

$$1/100 \times 1 = 1/100$$

Mother gametes Father gametes	$X^d \frac{1}{2}$	$X^N \frac{1}{2}$
$X^d \frac{1}{2}$	$X^d X^d \frac{1}{2}$	$X^N X^d \frac{1}{2}$
$Y \frac{1}{2}$	$X^d Y \frac{1}{2}$	$X^N Y \frac{1}{2}$