Genetics
& Cell biology

◉ Sheet ○ Slides

Number

10+11

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Introduction

• Punnet square

it is a diagram that is used to predict an outcome of a particular cross or breeding experiment. What we care about in this sheet is the prediction of outcomes for recessive and dominant disorders **if both parents are heterozygous**.

For recessive disorders (e.g. cystic fibrosis gene), if an individual is heterozygous for this gene, then he/she is a *carrier*, but not affected with {Aa} gentotype.

For dominant disorders (e.g. retinoblastoma gene), if an individual is heterozygous for this gene, then he/she is affected (has the disease and the clinical features), with {Aa} gentotype.

-recessive disorder and both parents are carriers:

Father/mother	A	a
A	AA	Aa
a	Aa	aa

Memorize the following: (condition of the child)

Possibility of having **affected child**: 1/4

Possibility of having **carrier child:** 1/2

Possibility of having **healthy child**: 3/4

Important notes for solving the questions:

1- cystic fibrosis is a recessive disorder, while retinoblastoma is dominant.

2- Never assume that an individual is affected unless the question tells that.

3- It is a game of probabilities, and we have two cases:

I) you are sure that both parents are carriers: you just multiply the probability of the father to pass the mutant allele by the probability of the mother to pass the mutant allele.

II) You are not sure that both parents are carriers:

you need to know:

A- *the probability for both parents to be carriers. (=probability of the father to be a carrier * probability of the mother to be a crrier)*

B- the probability to have the condition of the child (affected, carrier or healthy).

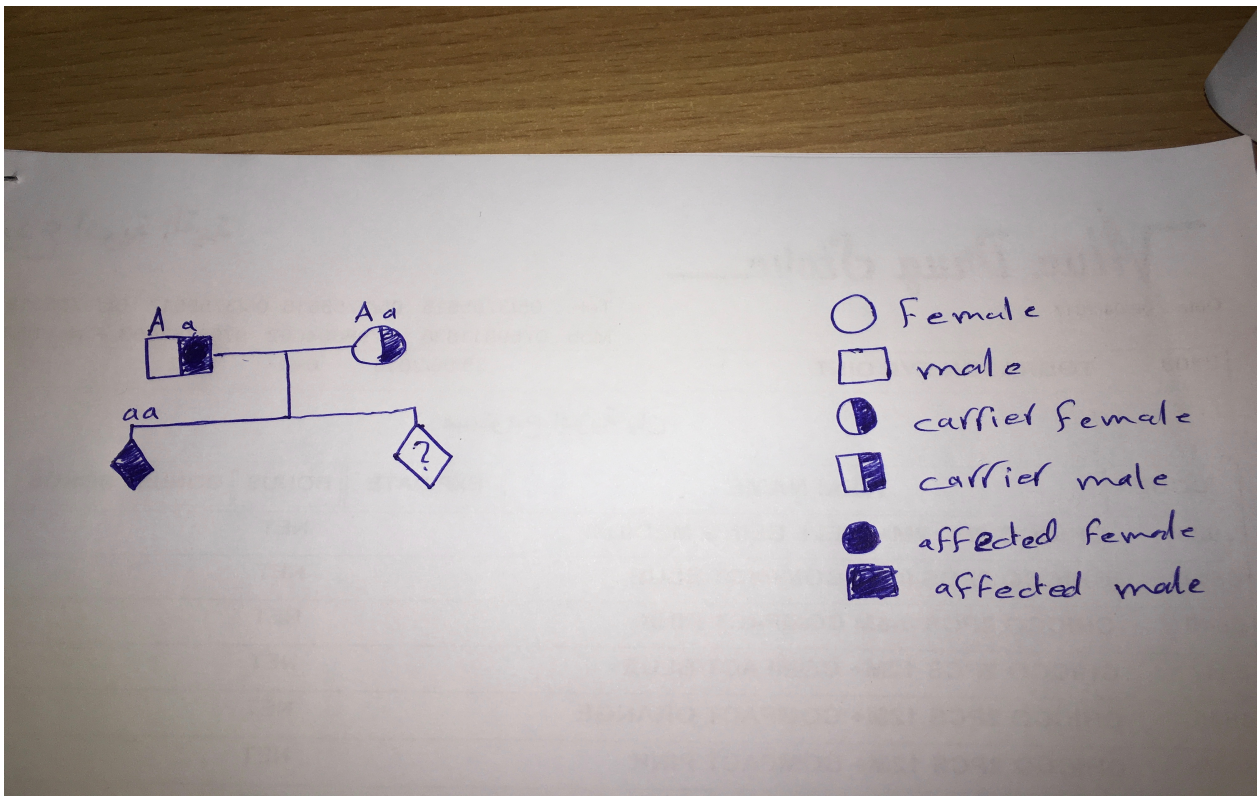
Then the answer is: A*B

4- The key step to understand the question and be able to solve it is to draw the family pedigree.

Recessive disorders and Risk assessment.

Q1/ couple with affected child with CF(cystic fibrosis).what it is the risk of having another affected child.

Answer/ draw the pedigree



from the pedigree: since the parents have an affected child, so they are either carriers or affected, but what to assume? As I told you, never assume that someone is affected unless the question tells that. By this rule, we are sure they are carries.

a- So as I said, we are sure that both parents are carriers, so the fraction for each parent to pass the mutant allele is 1/2 (they have two alleles and one of them is mutant, so its passing fraction is 1/2) . Now, we just need to multiply the probability for the father to pass the mutant allele, which is ½ , by the probability for the mother to pass the mutant allele, which is also ½.

½ * ½ = ¼

Another method: Punnet square

Mother/father	A	a
A	AA	Aa
a	Aa	aa

Note: in this question we were sure that the parents are carries, so our calculations were just at the level of the offspring,, in the coming questions we will have different scenarios.(case 2)

Important term: carrier frequency (CF).
It is the fraction of the population that carry the disease, i.g. , assume we have a population of 100 person,, and you were given that the carrier frequency for cystic fibrosis in this population is 1/25,, it means that one person out of 25 is a carrier of cystic fibrosis and 24 are not.

Q2/ a Caucasian couple with no family history, what is the risk of having affected child with beta thalassemia ?
Info ; carrier frequency for beta thalassemia in Caucasian populations is 1/25.

Answer/ Okay, what it is different in this question from the previous one is that we are **not sure that the parents are carriers, thus, we need calculate the fraction of both parents to be a carrier then multiply it by the fraction of having an affected child if both parents are carriers.**
The probability for the father to be a carrier is 1/25 and so the mother.
The father is carrier AND the mother is carrier = 1/25 * 1/25 = 1/625 , by now we finished calculating at the level of parents , now we **calculate the final answer by multiplying by the fraction of having affected child when both parents are carriers** (which is always ¼ when its recessive disorder)
=1/625 * 1/4 = 1/2500

other scenarios;

1-one parent is carrier and nothing known about the other parent.

Fraction of the first parent to be a carrier * fraction of the other parent to be a carrier * fraction of having affected child if both are carriers = 1* 1/25 * ¼

2- one parent is affected the other unknown.

Fraction of the first parent to pass the mutant allele * fraction of the other parent to be a carrier * fraction of having affected child when one parent is affected and the other is carrier
If both are carriers = 1*1/25*1/2

3-if the previous question was asking about having **healthy child.**

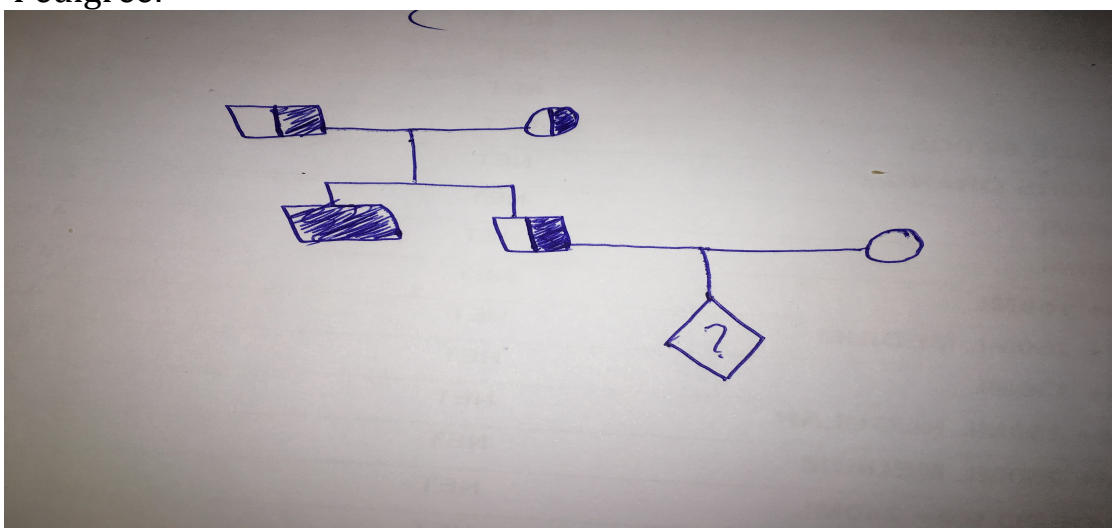
Simply, we just adjust the final step,, we multiply by the fraction of having healthy child (which is always ¾ when it is recessive disorder) instead of multiplying by the fraction of having affected child.

If it is asking about risk of CARRIER child ,, we multiply by 1/2 instead of 1/4 in the last step.

4-if the question was gender-specific, we add another step, which is multiplying by ½ .

5-if it is asking about having TWO affected/ healthy/carrier children, we calculate normally for one child then we square it.

Q3/ couple with cystic fibrosis in father's brother, what is the risk of the fetus?
Info: cf= 1/25
Pedigree:

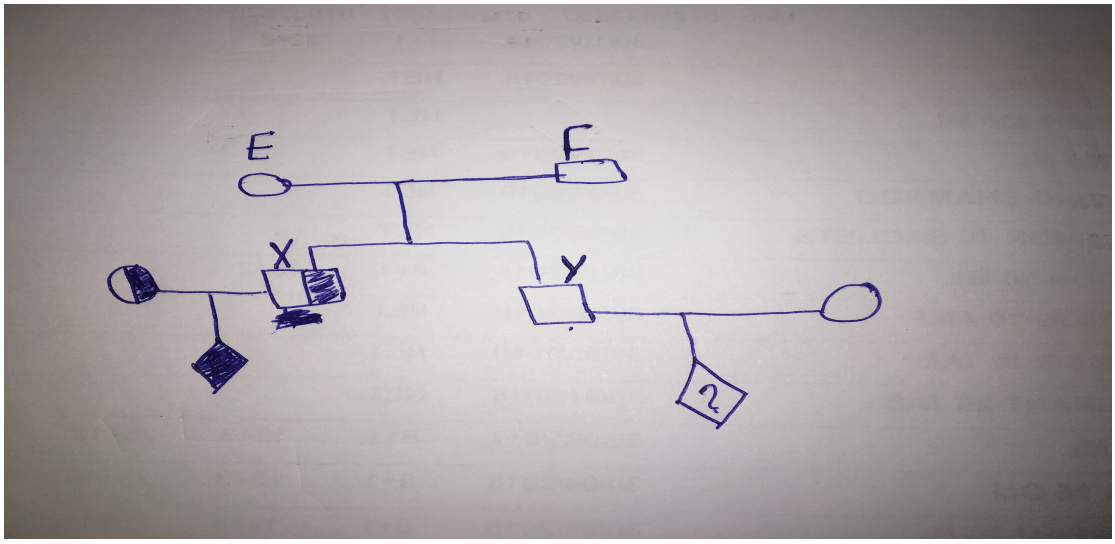


so again, since we are not sure that the parents are carriers, thus, we need figure the fraction of both parents to be a carrier then multiply it by the fraction of having an affected child if both parents are carriers.

for the mother to be a carrier --→ 1/25
for the father ^_^ --→ because he has an affected brother, his parents must be carriers,, what is the fraction for carrier parents to have a LIVING carrier child? The genotype of their children could be one of the following; AA,Aa,Aa or aa,, so having a carrier child is ½ ,, BUT the child we are talking about is alive and we know he is not affected because the question didn't tell so,, that means we must delete the "aa" from the possibilities, this leaves us with three possibilities and a fraction of 2/3 to have a carrier child. This is its explanation,, you understand it or you memorize this rule:
if a brother or a sister of one of the parents is affected, then the fraction of this parent to be a carrier is 2/3.

Answer/ Fraction of the father to be a carrier * fraction of the mother to be a carrier * fraction of having an affected child = 2/3 * 1/25 * 1/4

Q4/ couple with cystic fibrosis in father's nephew, what is the risk of the fetus?
Info: cf= 1/25



mother → 1/25
father → as we mentioned in the previous question, if the parent's sibling is AFFECTED , then this parent's fraction to be a carrier is 2/3 (previous question) „ so logically speaking, if the parent's sibling is a CARRIER then the parent's fraction to be a carrier must be less, and it is 1/2.

Explanation: since the nephew is affected so his father-X- (Y's brother) is a carrier, this means he has a mutant allele and he got this mutant allele from his father **or** his mother(F and E).
The fraction of X to get the mutant allele (to be a carrier) from his parents (F & E) = the fraction of his father to have the mutant allele (carrier) (1/2) * the fraction of passing this allele (1/2) OR the fraction of his mother to have the mutant allele (carrier) (1/2) * the fraction of passing this allele (1/2)
= (1/2 * 1/2) + (1/2 * 1/2) = 1/2 (1/2 is the fraction for X to be a carrier)

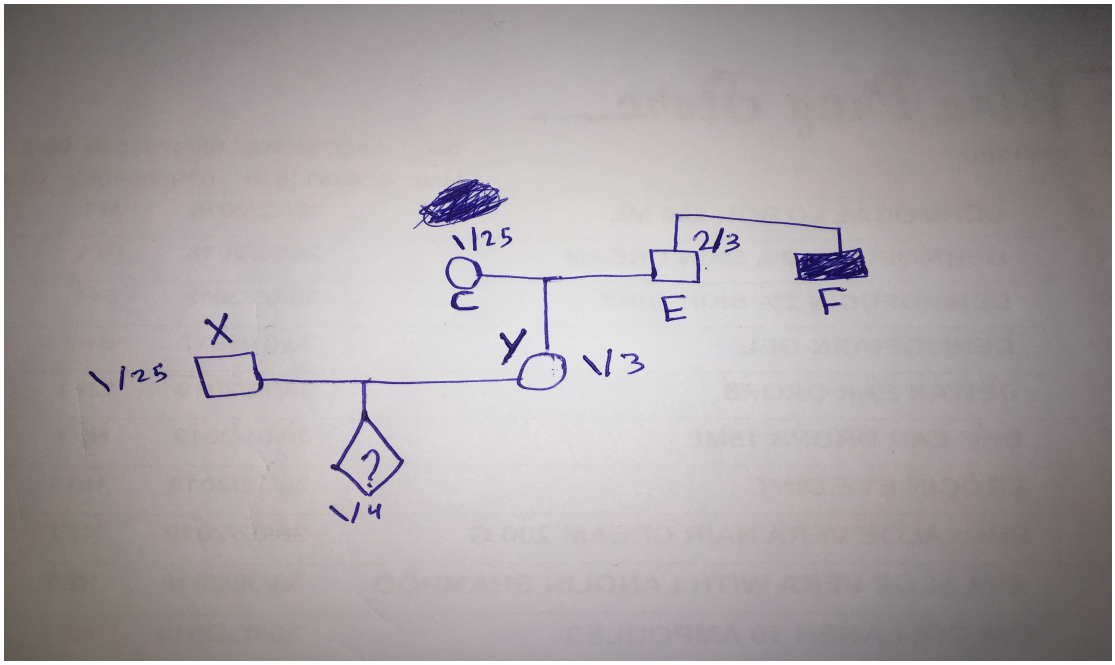
And since X and Y are brothers, they will have the same fraction of being carriers.
note; OR means + .

answer/ fraction of y to be a carrier * fraction of the mother to be a carrier * fraction of having affected child if both are carriers. 1/2*1/25*1/4

I know its hard to understand, so I recommend memorizing these two rules;

1- if the parent's sibling is affected , then this parent's fraction to be a carrier is 2/3. (question 3)
2- if the parent's sibling is a carrier , then this parent's fraction to be a carrier is 1/2.(question 4)

Q5/ couple with diagnosis of cystic fibrosis affected maternal uncle , risk of fetus? info:cf=1/25

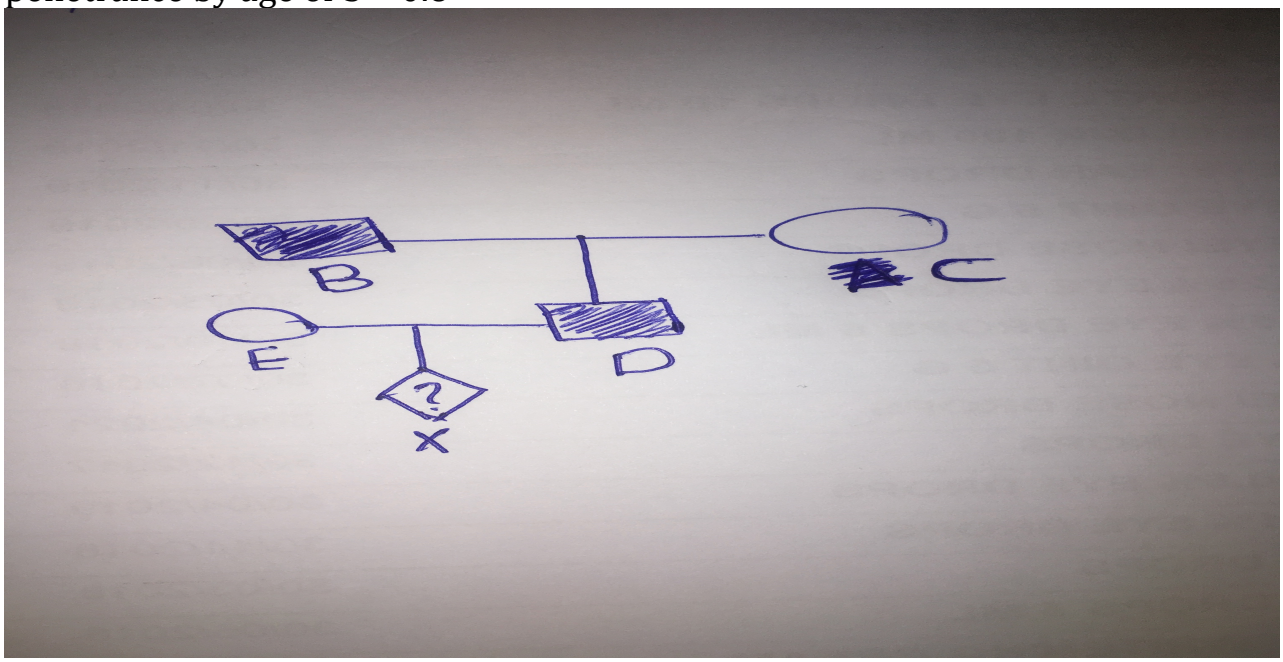


Father (X) → 1/25
Mother (Y) → to be a carrier, she must have a mutant allele, and this mutant allele is from her mother OR her father. Her uncle(F) is affected , so for sure her dad(E) is 2/3 a carrier (recall rule number one), and her mother(C) is 1/25.
So the mutant allele source is either the dad OR the mum (in other words; Y is a carrier) = the fraction of her father to have the mutant allele (carrier) (2/3) * the fraction of passing this allele (1/2) OR the fraction of her mother to have the mutant allele (carrier) (1/25) * the fraction of passing this allele (1/2)
= 2/3 * 1/2 + 1/25 * 1/2 ~ 1/3
or simply, rule #3 ; when the parent's uncle is affected , then this parent's fraction is 1/3.

answer/ 1/3 * 1/25 * 1/4

Dominant disorders

Q/ given this pedigree, what is the risk of child x: 1-carrying the mutant allele 2-to have retinoblastoma(affected=present clinical features) by the age of 5? Info RB penetrance by age of 5 = 0.8



Notes:

1- There are no carriers in dominant disorders; they are either affected or healthy.

2- If you were given in the question that an individual is affected and you don't have the enough information to know whether it is Aa or AA ,, you always assume it as Aa.

We need to know the genotype for child's father: since mother (C) is healthy and we are talking about dominant disease, then her genotype is aa, and according to note number 2 the father (B) is Aa. The child's father (D) is affected and the mutant allele came from his father so his other allele will be from his mother and there is one option which is a , so father (D) is Aa, mother (E) is aa because she is healthy

Answer/

Mother/ father	A	a
a	Aa	aa
a	Aa	aa

1- {Aa} = 1/2

2- having the mutant allele * penetrance at age of 5= 1/2 *0.8= 0.4

Sorry for any mistakes ^_^