PEDIGREE FULL RULES AND APPROACHES

PEDIGREE ANALYSIS

❒ Before solving any question related to pedigree analysis, it is easier to first convert the information into a pedigree diagram if one is not already provided.

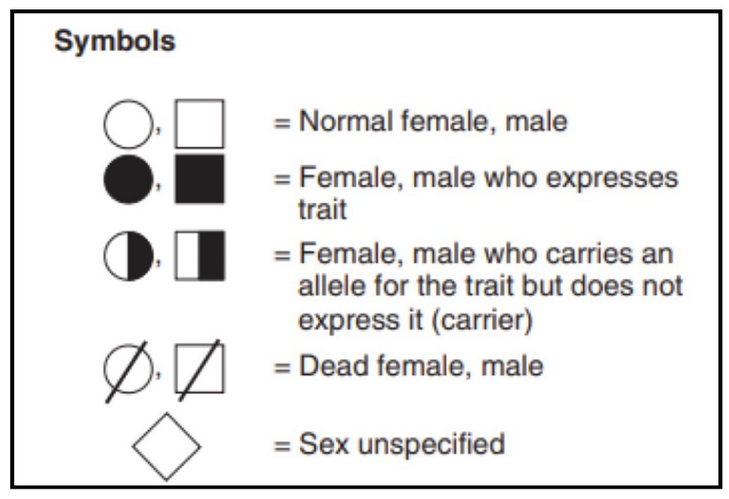
For example if you see a question like this:

Question (1): An affected male and a normal female had four children: two affected daughters and two normal sons. Each of the affected daughters (and their normal husbands) produced affected sons and affected daughters. The couple's normal sons married normal women and had all normal children. What is the most likely mode of inheritance for this trait?

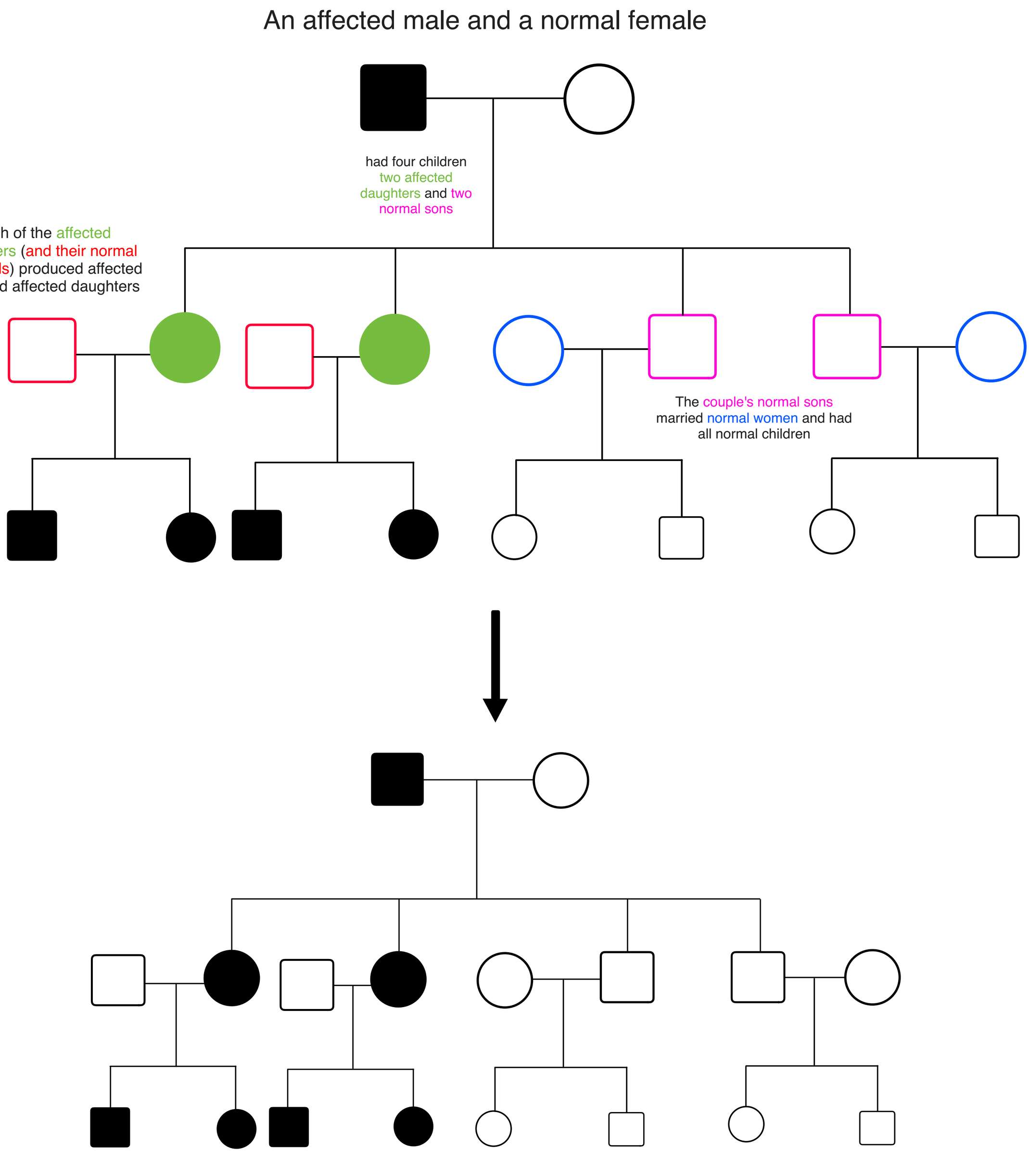
(A) Autosomal dominant
(B) Autosomal recessive
(C) X-linked dominant
(D) X-linked recessive
(E) Y-linked
(F) Mitochondrial inheritance

The answer is in **slide 9**

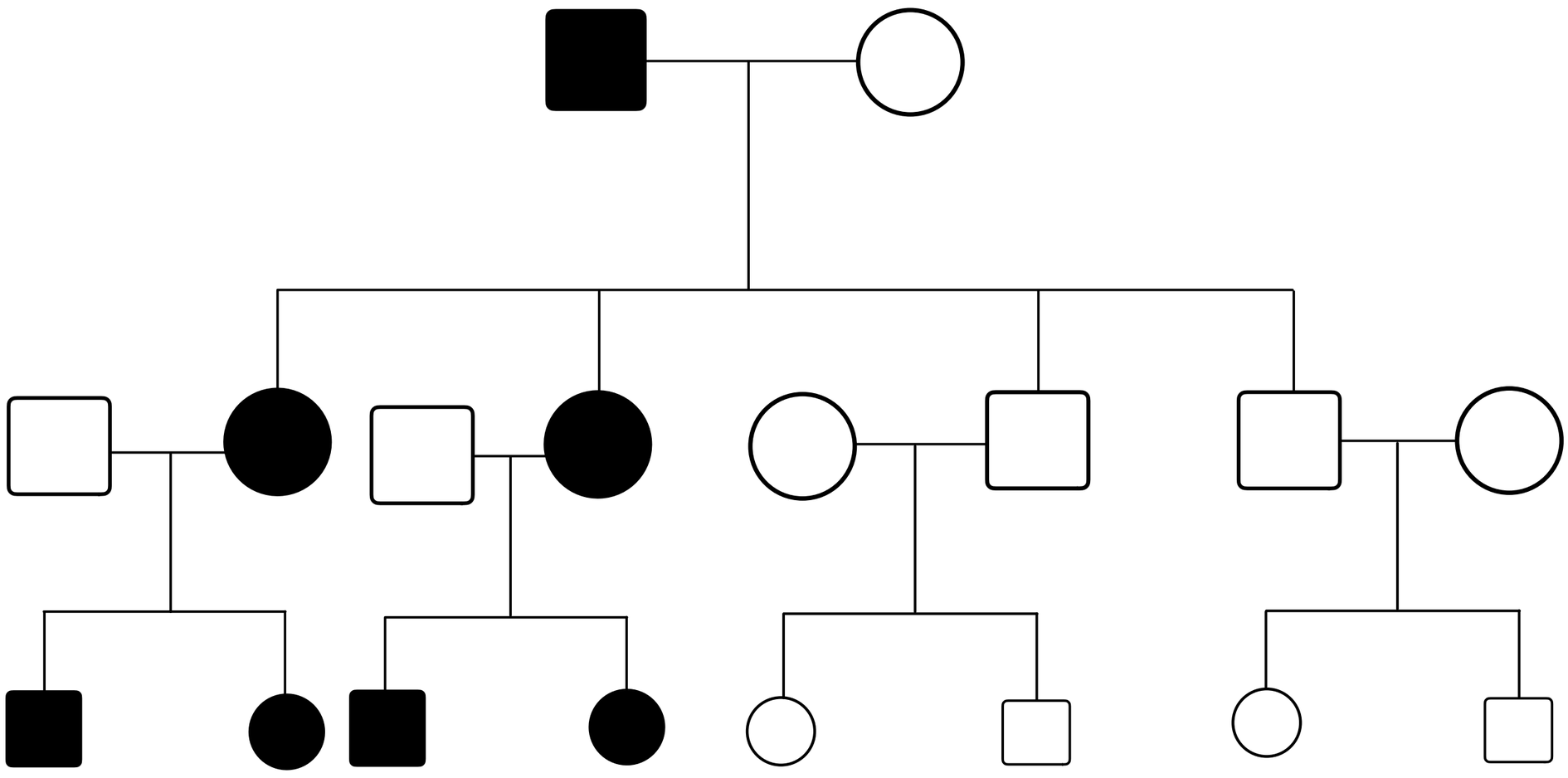
In order to do that, you have to know these symbols first:



Now, the draw the pedigree



(Pedigree question 1).



❒ How to know the mode of inheritance for nearly any pedigree:

1. **RULE OUT THE Y-LINKED INHERITANCE MODE.**
How do you do that?

❒ If it is Y-linked, you would see that the only gender that is affected is the MALE gender, doesn't matter if its Y-linked recessive or dominant.

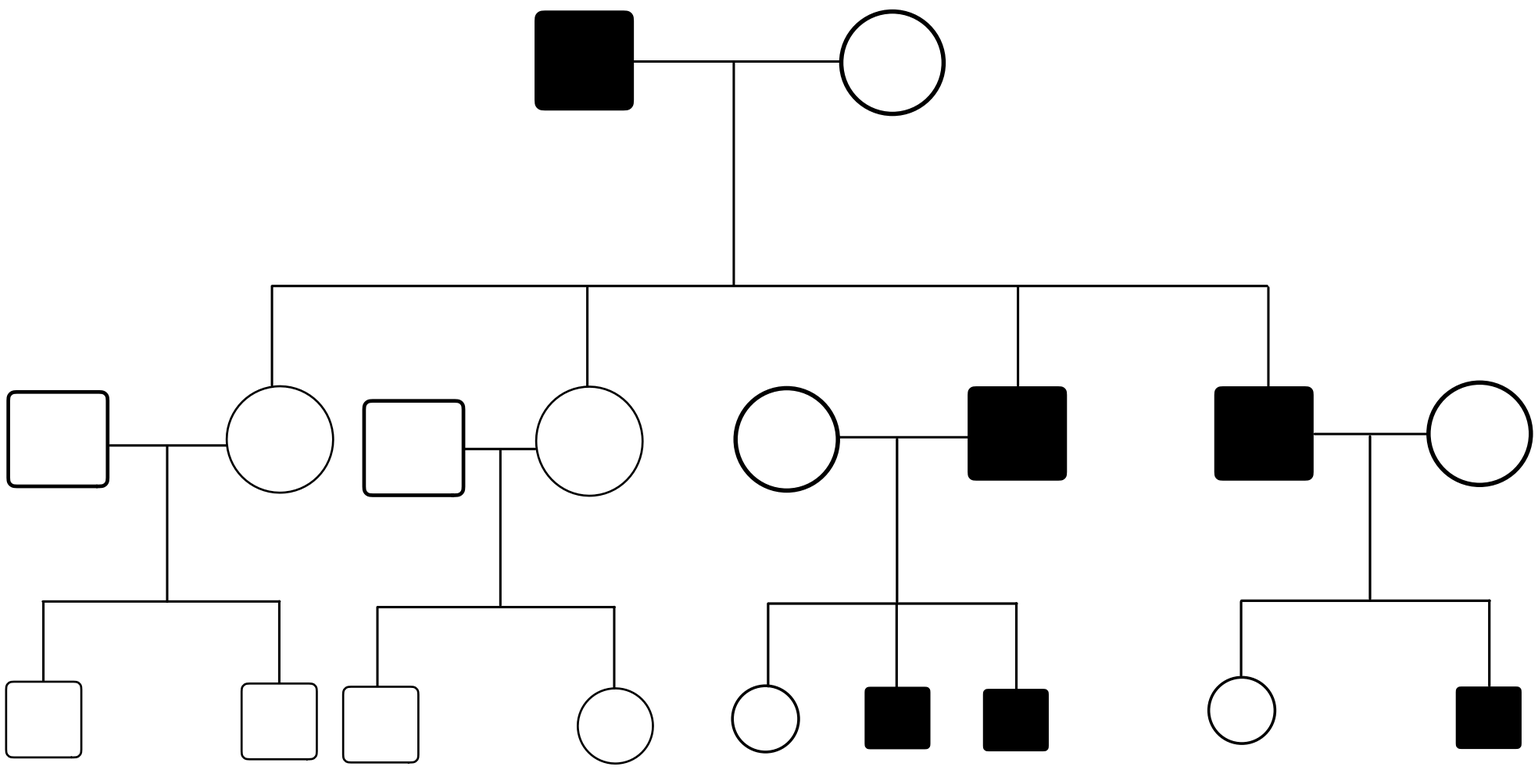
❒ If only males are affected (filled symbols) in the pedigree -> **Y-linked right away** (**unless** the question states otherwise like "its not gender limited").

❒ If both females and males are affected (filled symbols) in the pedigree -> **NOT** Y-linked.

❒ If the question states that this mode of inheritance is NOT linked to a specific gender then -> **NOT** Y-linked.

❒ Because it's Y-linked, if the father isn't affected (not filled), then none of his children will be affected either (also since daughters don't have a Y chromosome, they won't be affected regardless of whether the father is affected or not).

Take a look at pedigree (1) for reference.



Pedigree (1).
Y-linked inheritance

Back to pedigree question 1, since **both genders are affected (filled)** here, then it is NOT Y-linked.

We ruled out Y-linked mode of inheritance.

Question (1): An affected male and a normal female had four children: two affected daughters and two normal sons. Each of the affected daughters (and their normal husbands) produced affected sons and affected daughters. The couple's normal sons married normal women and had all normal children. What is the most likely mode of inheritance for this trait?

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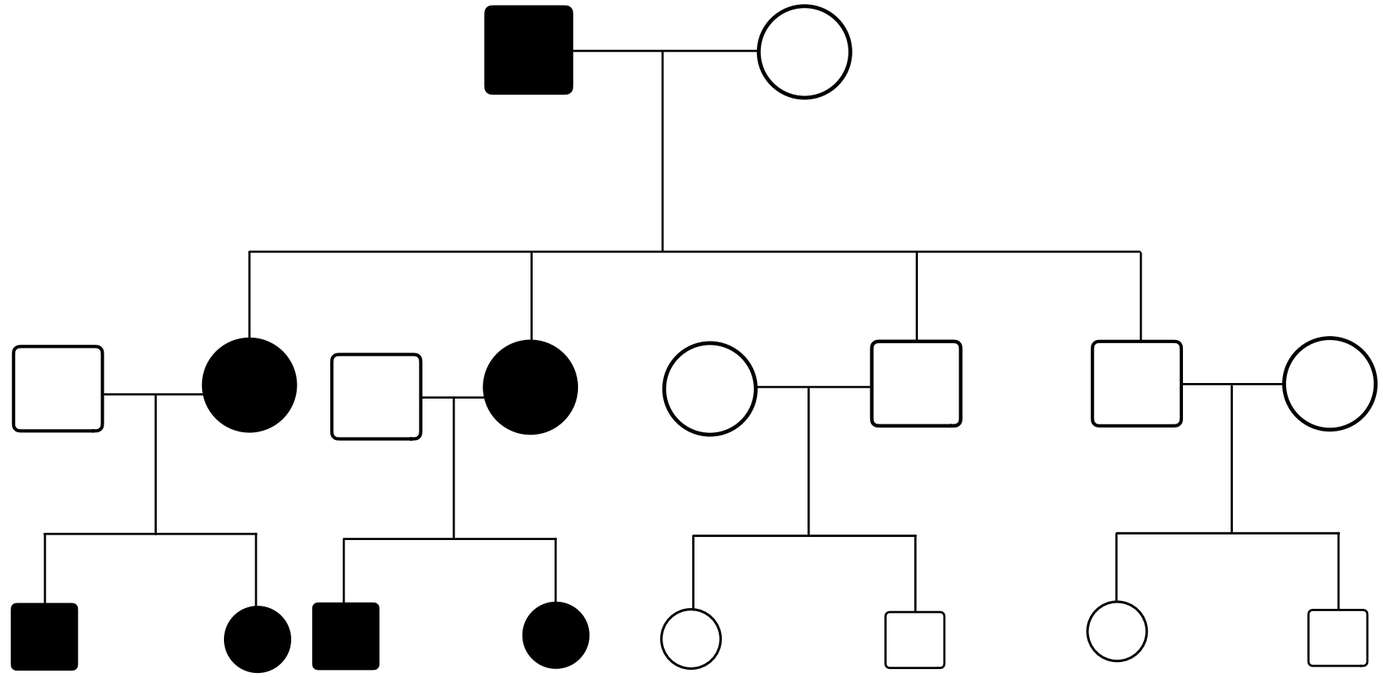
~~(E) Y-linked~~
(F) Mitochondrial inheritance



(Pedigree question 1).

❒ How to know the mode of inheritance for nearly any pedigree:

2. **RULE OUT THE MITOCHONDRIAL INHERITANCE MODE.**
How do you do that?

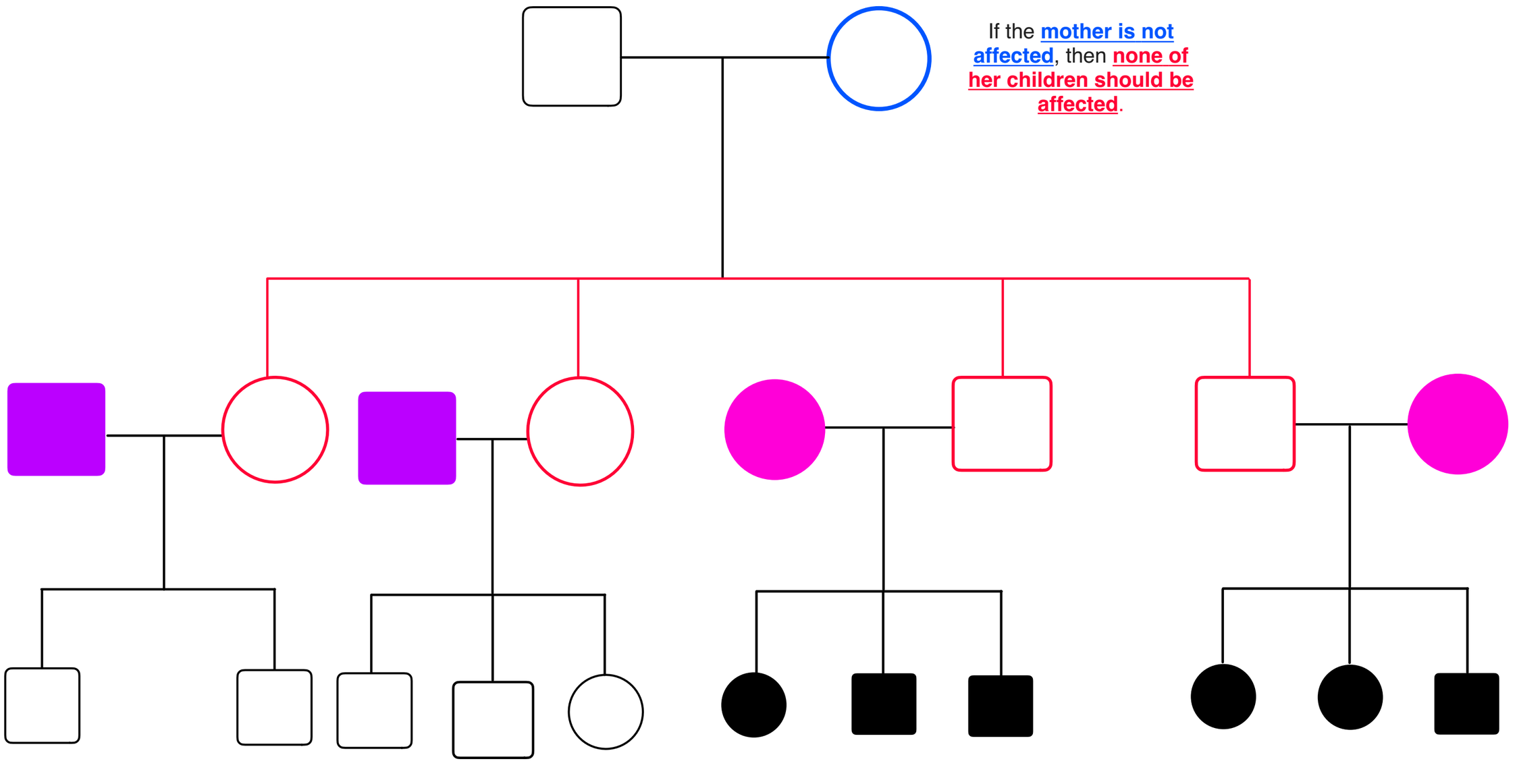
❒ In cases of mitochondrial inheritance, only females can transmit the mutation, and **ALL** their offspring will be affected **throughout the generations.**

❒ If the father is affected by mitochondrial mutations, **none** of his children will inherit the condition, as **mitochondria are inherited solely from the mother.**

❒ If the mother is affected and **not all** of her children are affected, **then mitochondrial inheritance IS be RULED OUT.**

❒ If the **mother is not affected**, then **none of her children should be affected**. If you see that the mother is not affected and her children are affected, **then mitochondrial inheritance IS be RULED OUT.**

Look at pedigree (2) for example:



Pedigree (2).
Mitochondrial inheritance

Back to pedigree question 1, since **the first mother is not affected**, then none of her children in generation 1 (F1) should be affected, but if you see, **2 of her children** are affected, then right away, this IS not mitochondrial inheritance, since in mitochondrial inheritance, the mutations are NOT transmitted by **their father**.

We ruled out Mitchondrial mode of inheritance.

Question (1): An affected male and a normal female had four children: two affected daughters and two normal sons. Each of the affected daughters (and their normal husbands) produced affected sons and affected daughters. The couple's normal sons married normal women and had all normal children. What is the most likely mode of inheritance for this trait?

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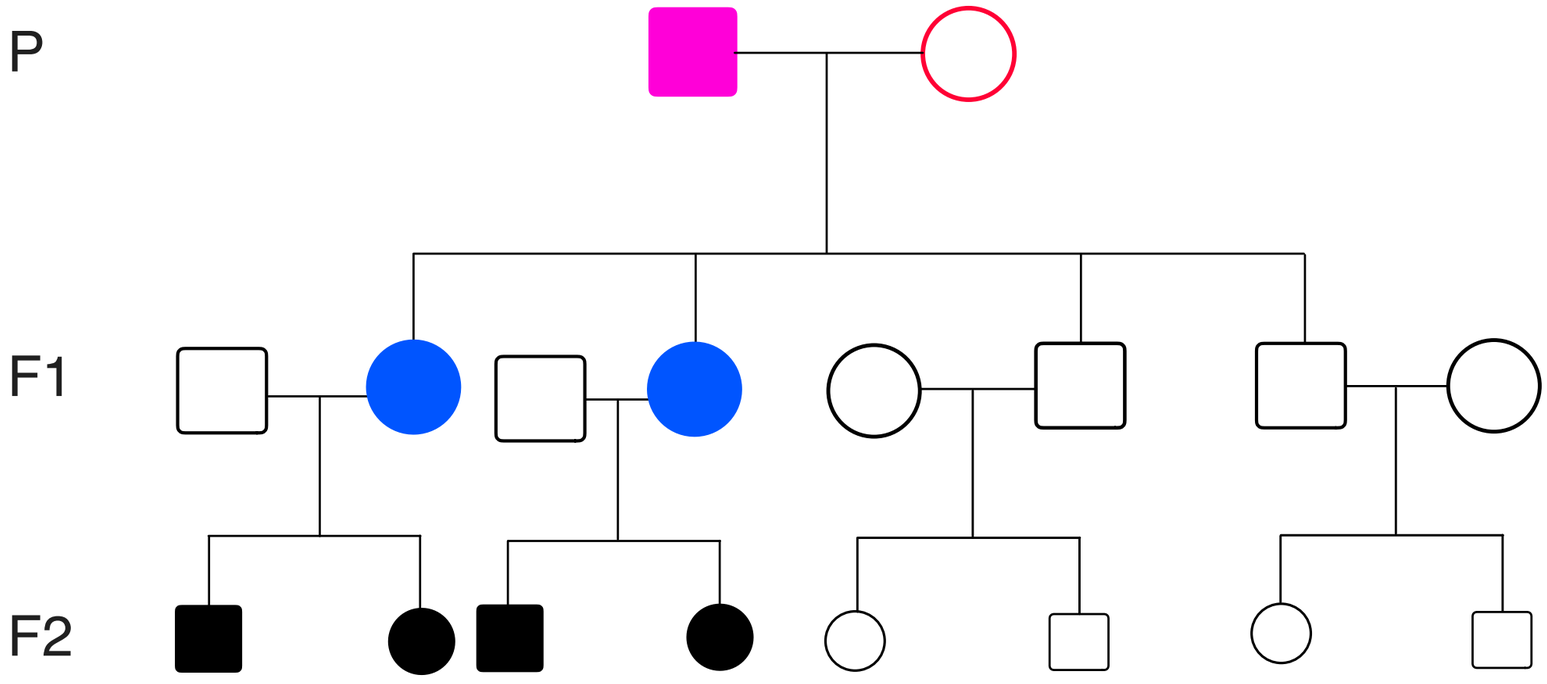


(Pedigree question 1).

❒ How to know the mode of inheritance for nearly any pedigree:

3. **RULE OUT THE X-LINKED DOMINANT INHERITANCE MODE.**
How do you do that?

❒ In cases of X-linked dominant inheritance mode, **FIND an affected** (filled, carrying the dominant allele on his X chromosome) **father married with unaffected mother**, and assume that he's (X^AY), now, since the father gives (Y) chromosome to his sons, **none of his sons should affected** (unless the mother is also affected, this is why you should look for an affected father married (X^AY) to an unaffected mother (X^aX^a)).

❒ Since the affected father passes the (X^A) chromosome to **ALL** his daughters, **every daughter SHOULD be affected.**

So..

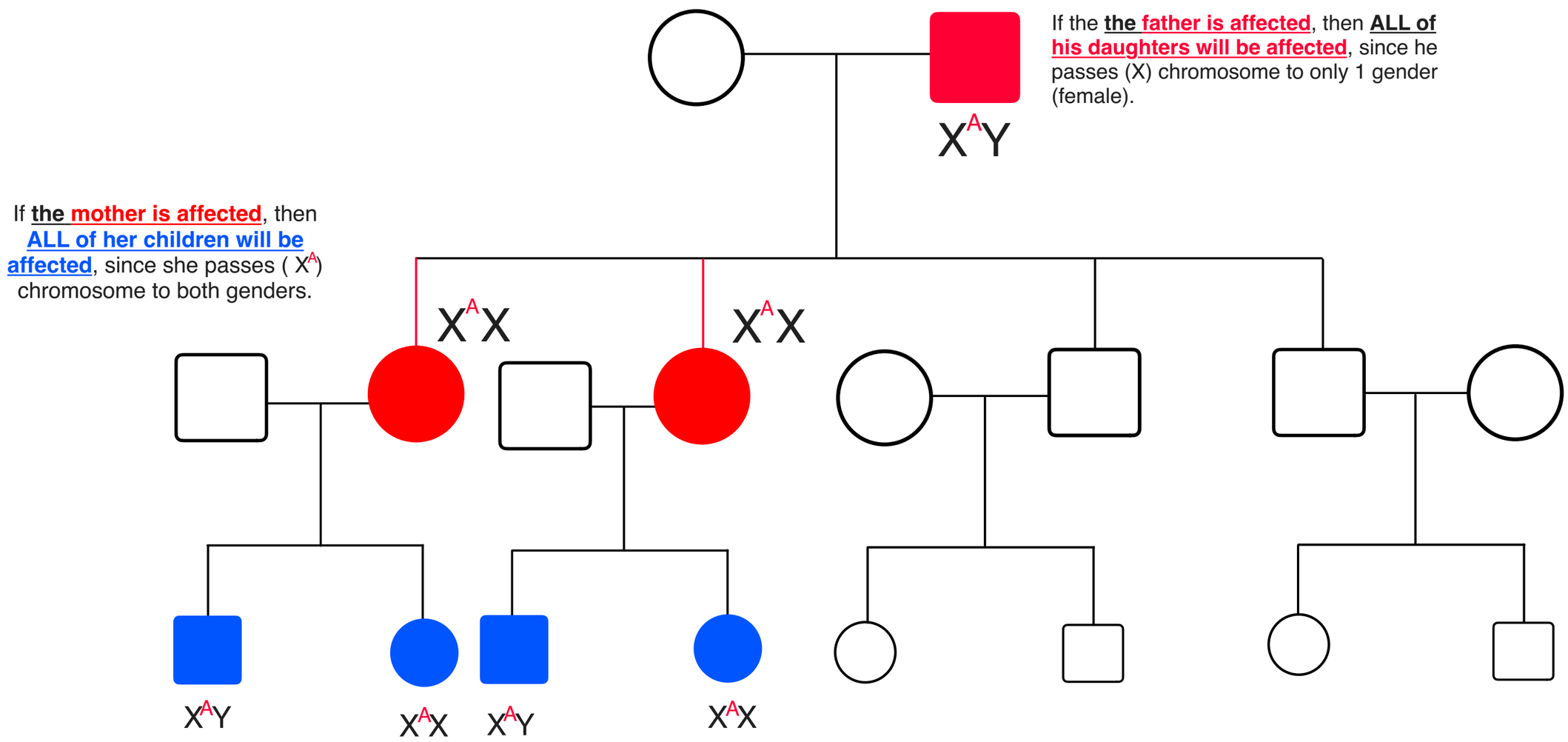
❒ If the **the father is affected**, then **ALL of his daughters will be affected**, since he passes (X^A) chromosome to only 1 gender (female).

❒ If **the mother is homozygous affected**, then **ALL of the children will be affected**, since she passes (X^A) chromosome to both genders.

❒ If the father is affected, and **NOT all** of his daughters are affected, **then X-dominant is ruled out.**

❒ If the father or the mother NOT affected, then **NONE of their children** should be affected, if you find otherwise (that the father is not affected, but one of his daughters is affected) **then X-dominant is ruled out.**

Look at pedigree (3) for example:



Pedigree (3).
X-linked dominant inheritance

❒ How to know the mode of inheritance for nearly any pedigree:

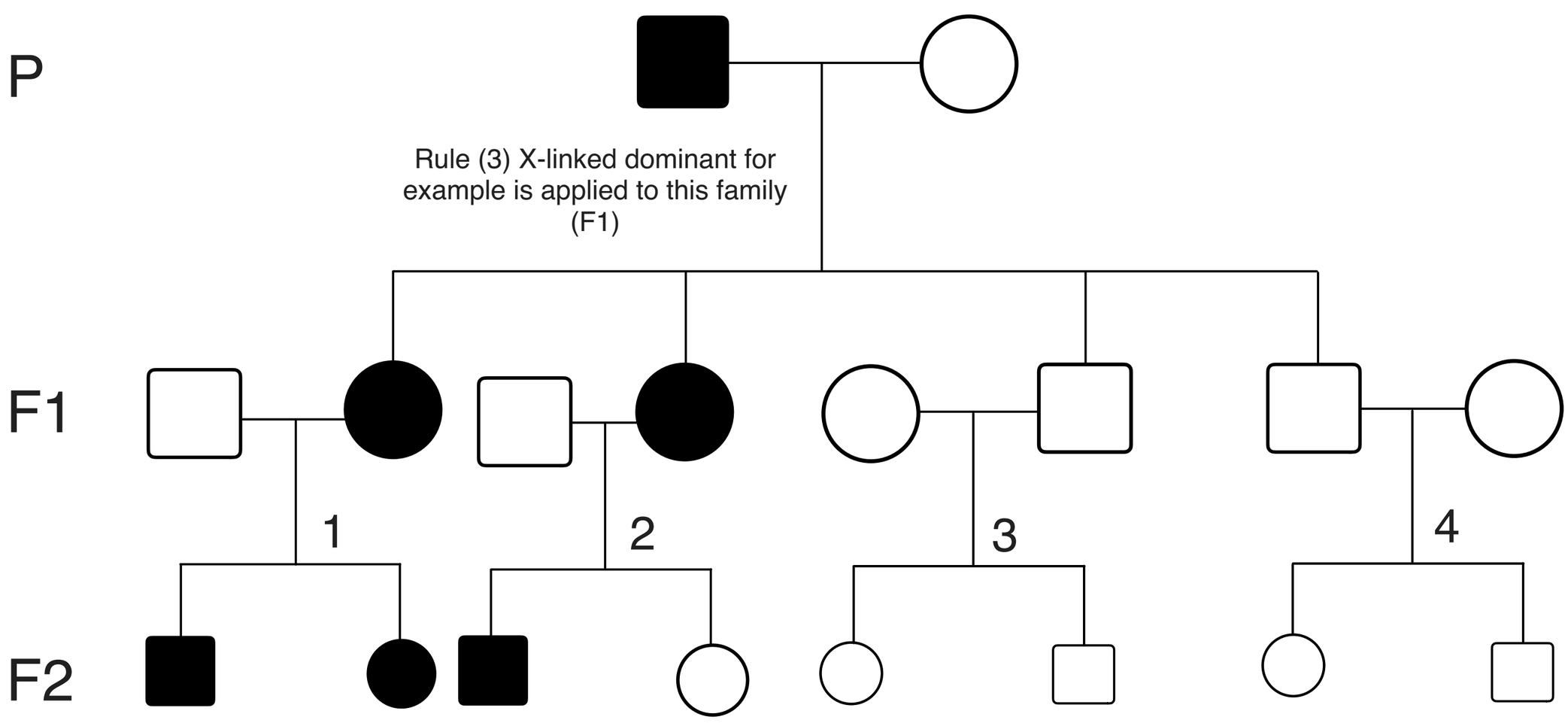
Continue..

❒ The rules that i just gave you, try to check it on more than 1 family. If the rules applied to only 1 family, and not the others, or most of the families but NOT all of them, **then X-linked dominant (rule 3) IS RULED OUT.**

(THIS ALSO APPLY TO ALL THE RULES I GAVE YOU, DO NOT STICK TO ONE FAMILY, YOU HAVE TO CHECK THE OTHER FAMILIES)

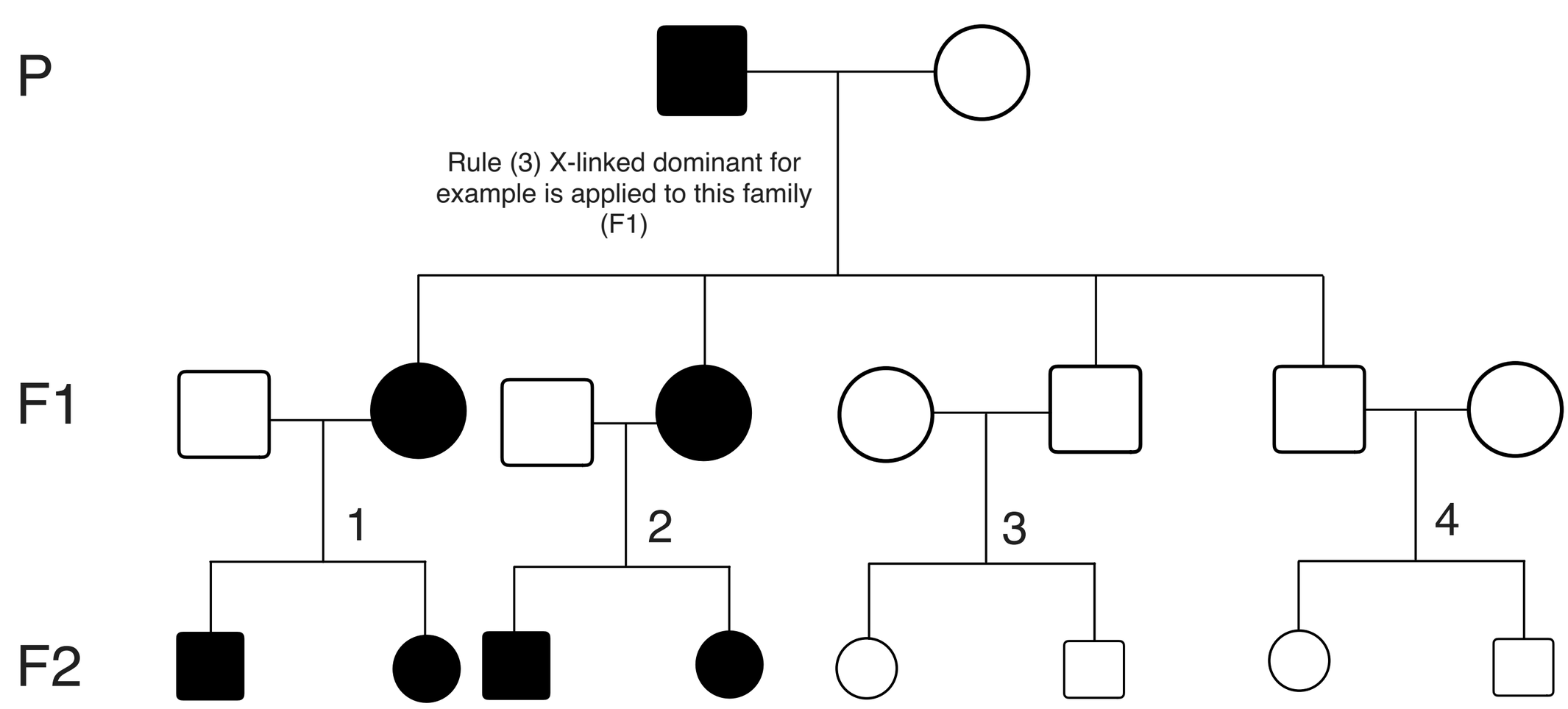
Look at pedigree (4, 5) for example:

Pedigree (4)



Rule (3) X-linked dominant for example here is applied to families (1, 3, 4) but NOT for family (2) in F2, then right away **X-linked dominant IS RULED OUT**

Pedigree (5)



Rule (3) X-linked dominant for example here is applied to all families (1, 2, 3, 4), then right away its **X-linked dominant.**

Back to pedigree question 1, since **the first father is affected**, then all of his daughters in generation 1 (F1) **should be affected**, and also the affected females in (F1) should pass that trait to every child they will have as seen in (F2).

This is X-dominant right away.

Question (1): An affected male and a normal female had four children: two affected daughters and two normal sons. Each of the affected daughters (and their normal husbands) produced affected sons and affected daughters. The couple's normal sons married normal women and had all normal children. What is the most likely mode of inheritance for this trait?

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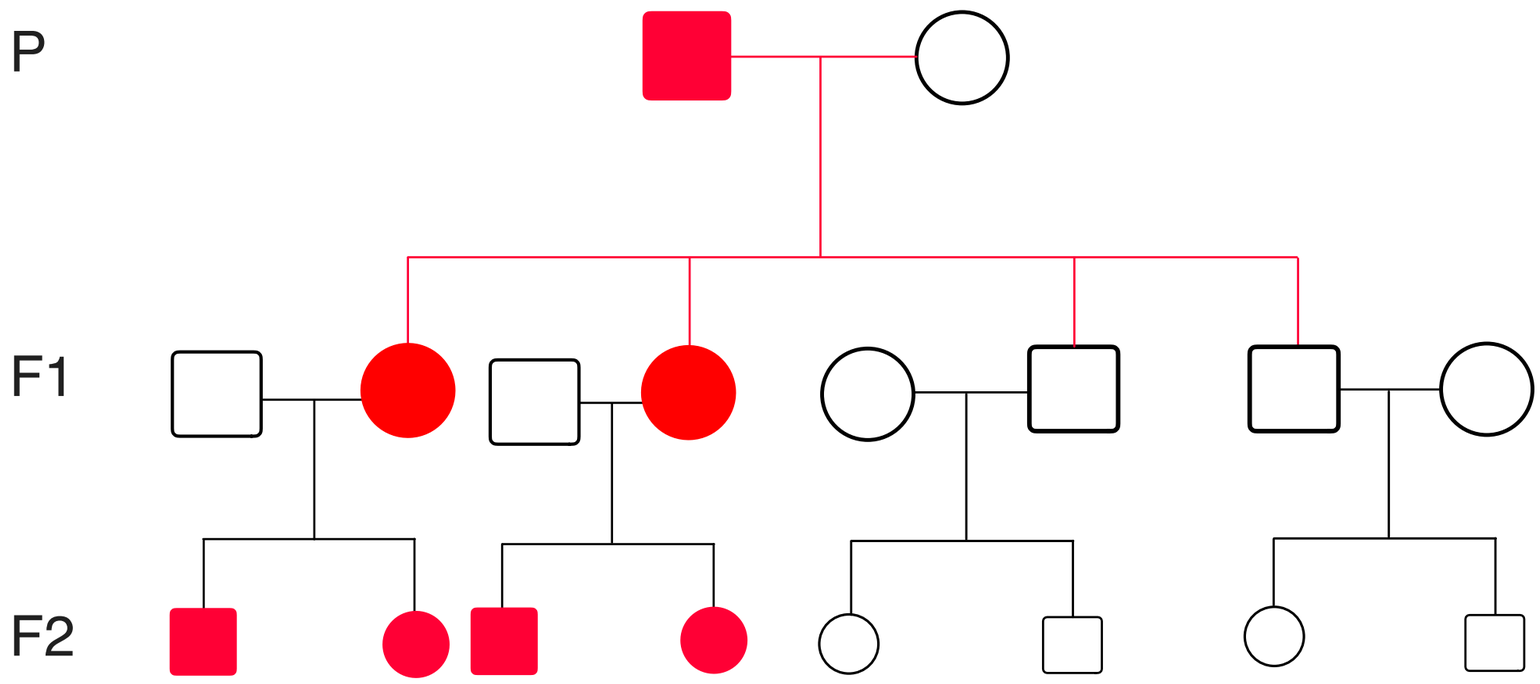


(Pedigree question 1).

❒ How to know the mode of inheritance for nearly any pedigree:

4. **RULE OUT THE X-LINKED RECESSIVE INHERITANCE MODE.**
How do you do that?

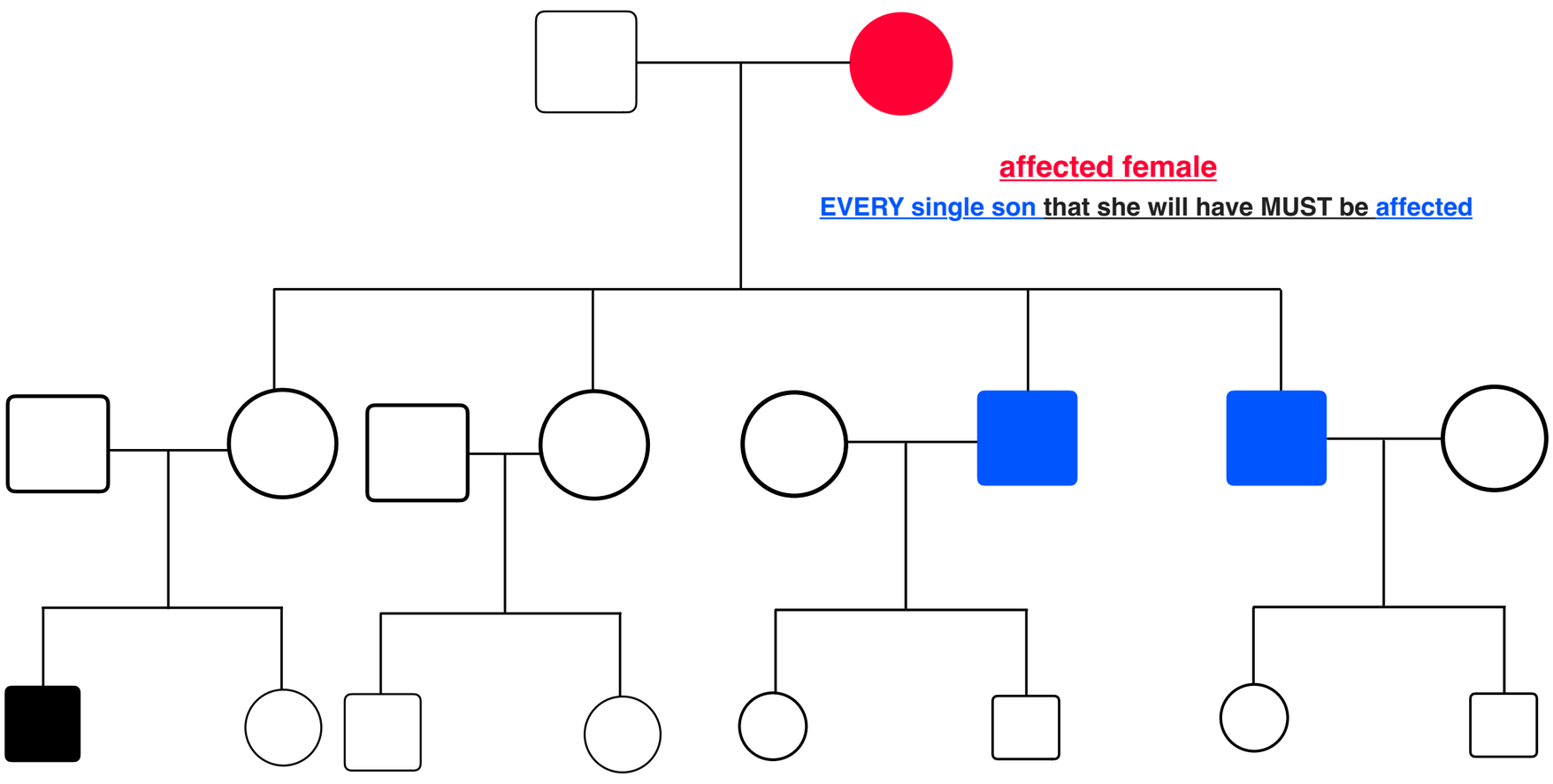
❒ Find an **affected female** (X^aX^a), since the mother passes one of her X chromosomes (X^aor X^a) to her sons, **EVERY single son that she will have MUST be affected** (X^aY).

❒ Again, this rule applies to all families. Make sure not to focus on just one family; look at the others and ensure it applies to them as well.

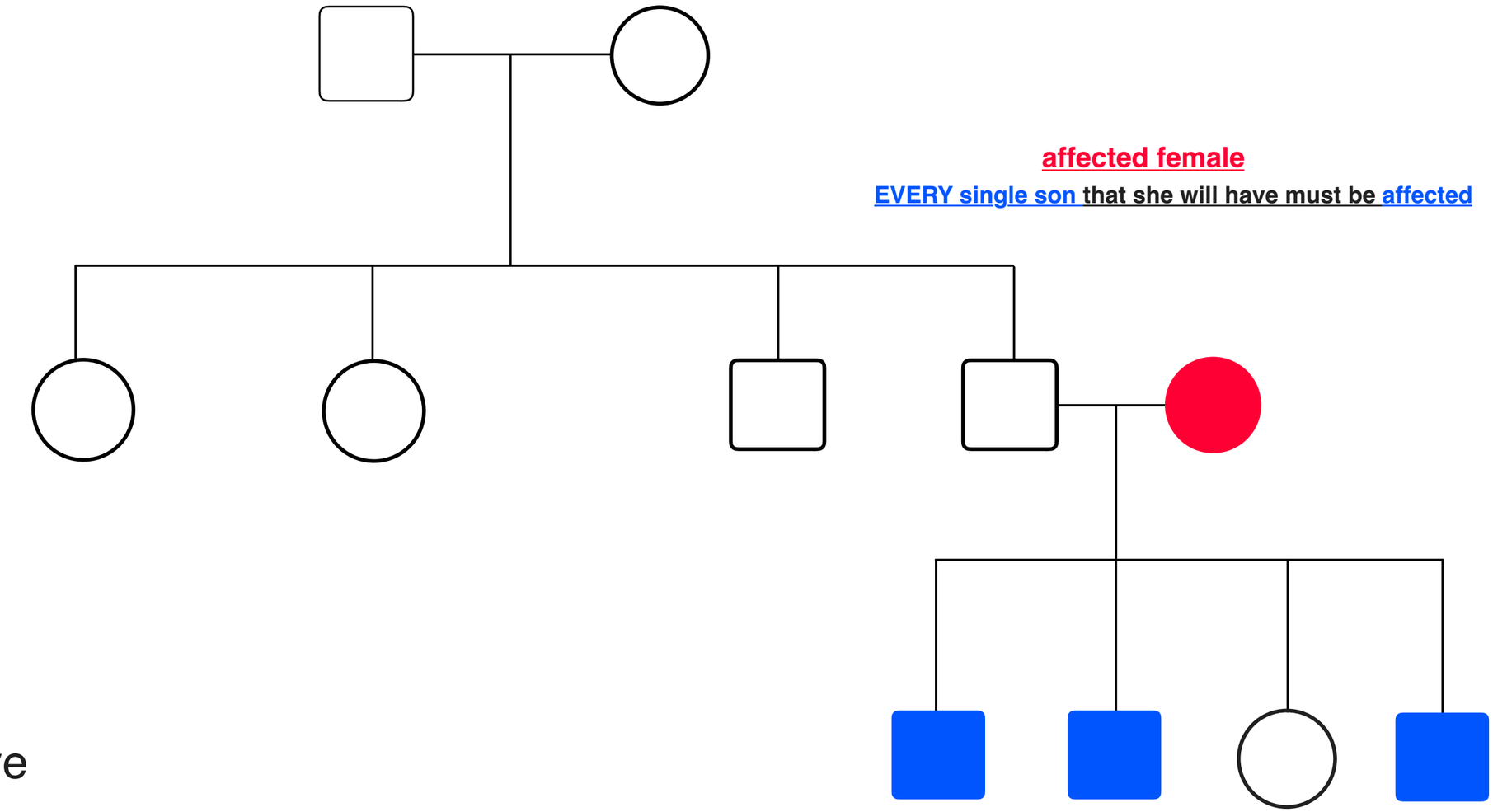
❒ If you find **affected female (X^aX^a)**, and **NOT ALL of her sons are affected**, then X-linked recessive is **RULED OUT**.

❒ If this rule **apply** OR ANY OTHER RULE we talked about **to all families except one of them**, **then the rule (mode of inheritance) is RULED OUT.**

Look at pedigree (6, 7) for example:



Pedigree (6).
X-linked recessive



Pedigree (7).
X-linked recessive

❒ How to know the mode of inheritance for nearly any pedigree:

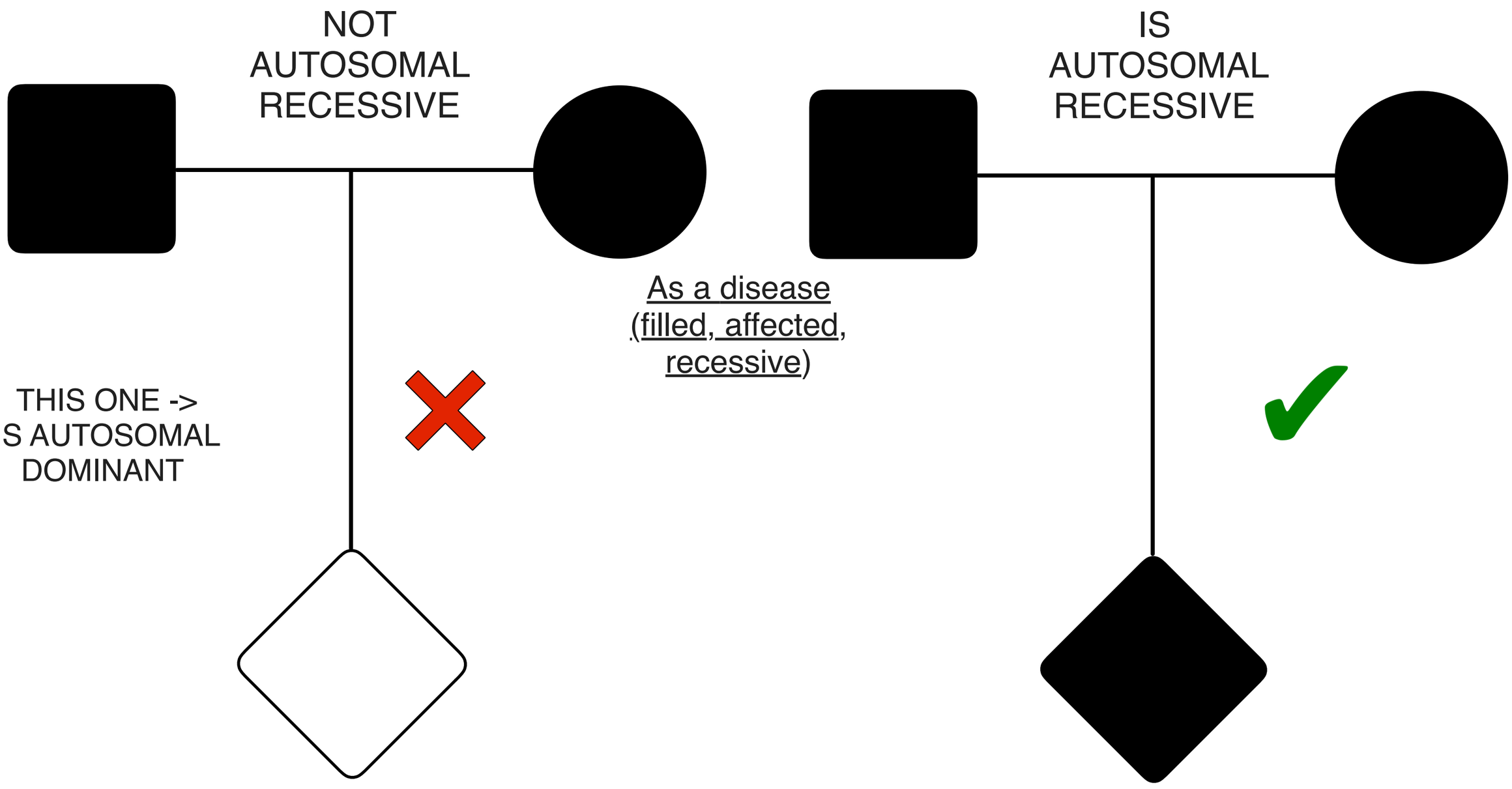
5. **AFTER YOU RULED OUT Y-LINKED, MITOCHONDRIAL, X-LINKED DOMINANT, AND X-LINKED RECESSIVE.**

YOU WILL BE LEFT OUT WITH BOTH AUTOSOMAL RECESSIVE AND AUTOSOMAL DOMINANT.

HOW TO DIFFERENTIATE BETWEEN THEM?

❒ Look at the following pedigrees, and read the notes for each, every single note should make sense depending on your understanding of autosomal inheritance mode.

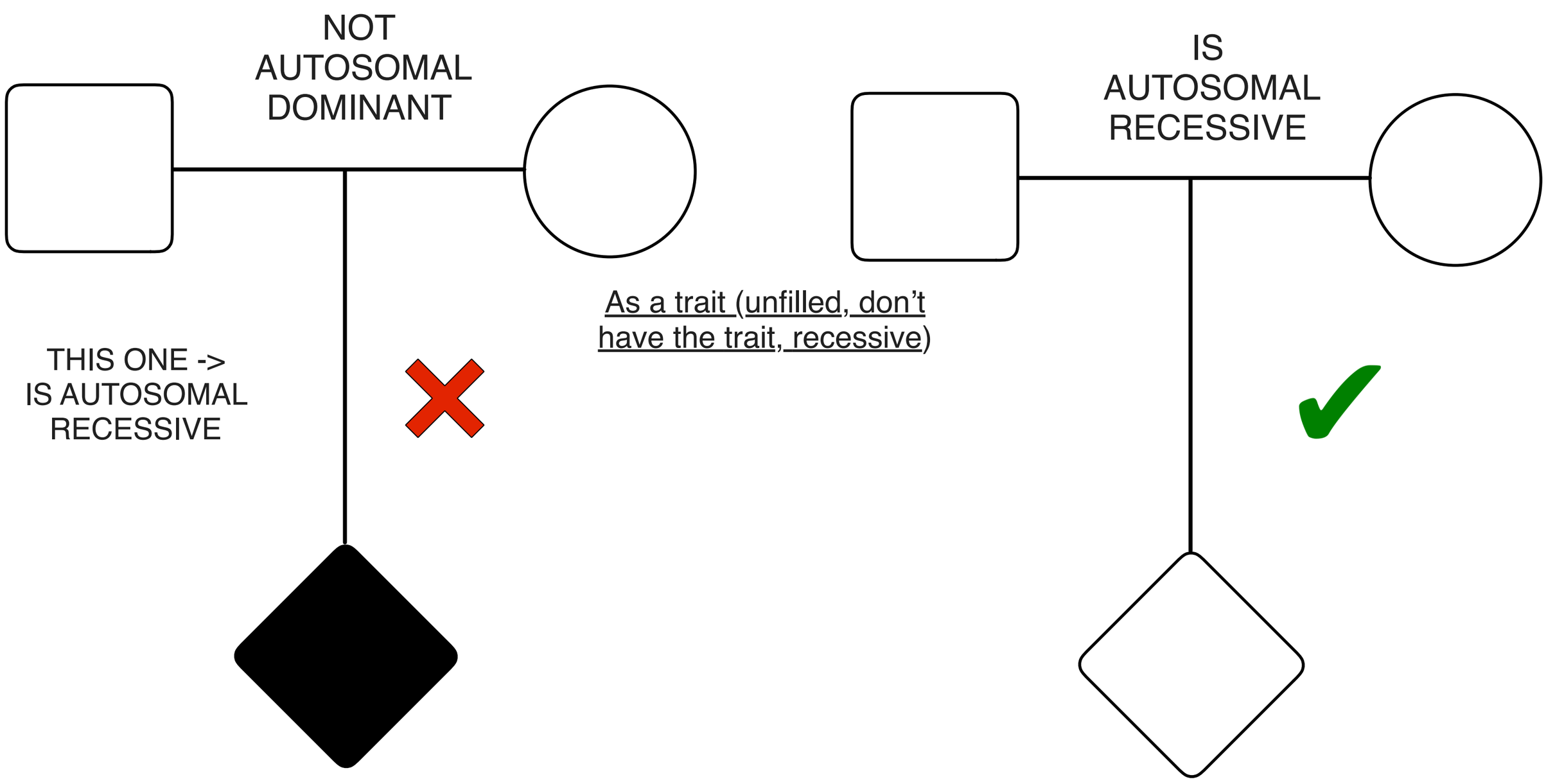
❒ Note that autosomal inheritance is not specific to a single gender; it affects both males and females. If you encounter a pedigree where only females or males are affected, the question should state that it is not sex-limited in order to think of autosomal mode. This clarification will prevent any confusion about Y-linked inheritance. In such cases, the inheritance could still be either X-linked or autosomal. Please refer to the following examples for further clarification.



Supposing both parents are affected (filled) with recessive alleles (**aa**), then there is **NO WAY** ✗ that their son will NOT be affected (unfilled, has dominant allele), since both parents have to be homozygous with recessive alleles (**aa**) to be affected (filled), they will give their child both alleles, so the child will be affected (filled). ✓

(You can not have 2 parents that are recessive (filled) having a dominant (unfilled) child). ✗

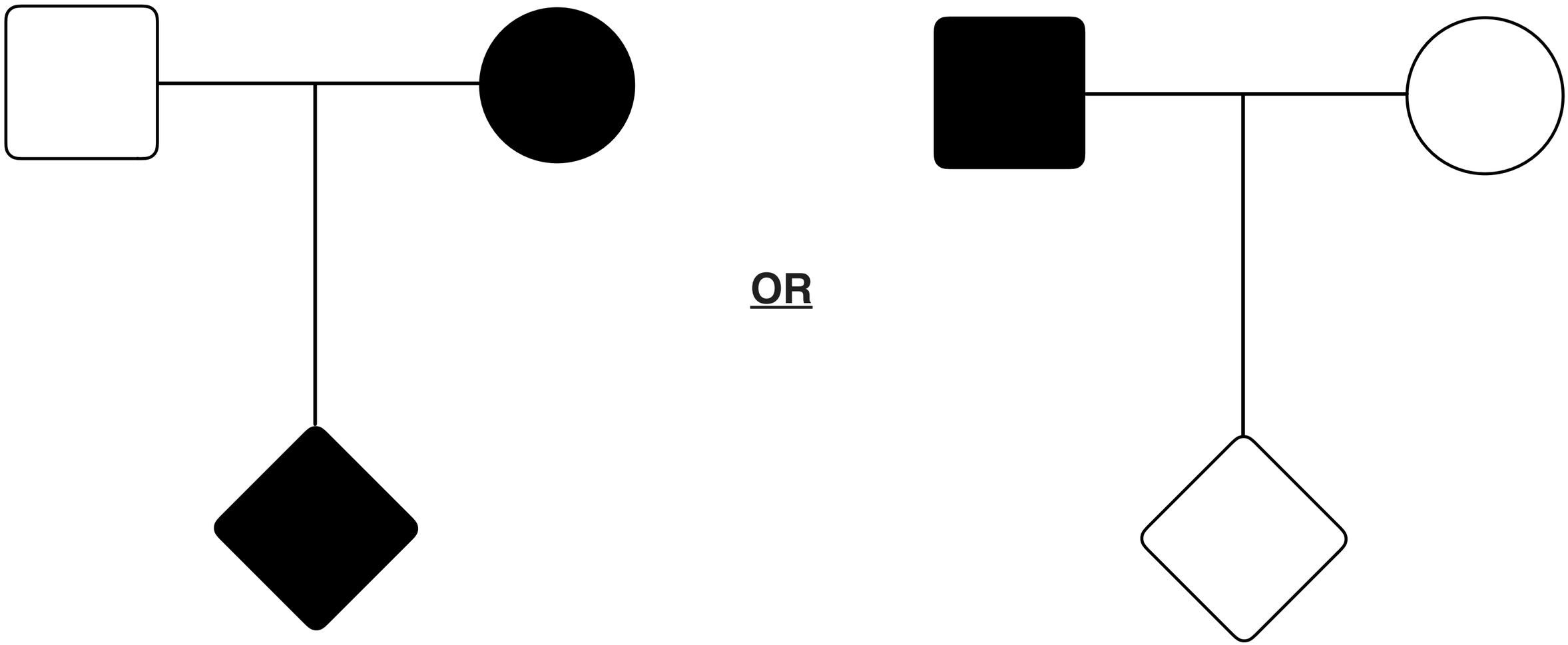
OR



Supposing that both parents here don't have the dominant trait (**aa**, unfilled), then there is **NO WAY** ✗ that their child will have the dominant trait (filled, has dominant allele), since their child requires at least one of the dominant allele to have the trait (**Aa** or **AA**).

(You can not have 2 parents that are recessive (unfilled) having a dominant (filled) child). ✗

Now, what if its like this:
(Most cases حيجي هيك)
Random



OR

See, after you **ruled out** nearly every single possible mode of inheritance (**Y-LINKED, MITOCHONDRIAL, X-LINKED DOMINANT, AND X-LINKED RECESSIVE**), you will be left out with both modes the AD and the AR.
how do i know?

In autosomal dominant

1. a trait can appear in **either sex** because an autosome carries the gene.

2. If a child has the trait, at least one parent also has it.

3. Autosomal dominant traits **do not** skip generations.

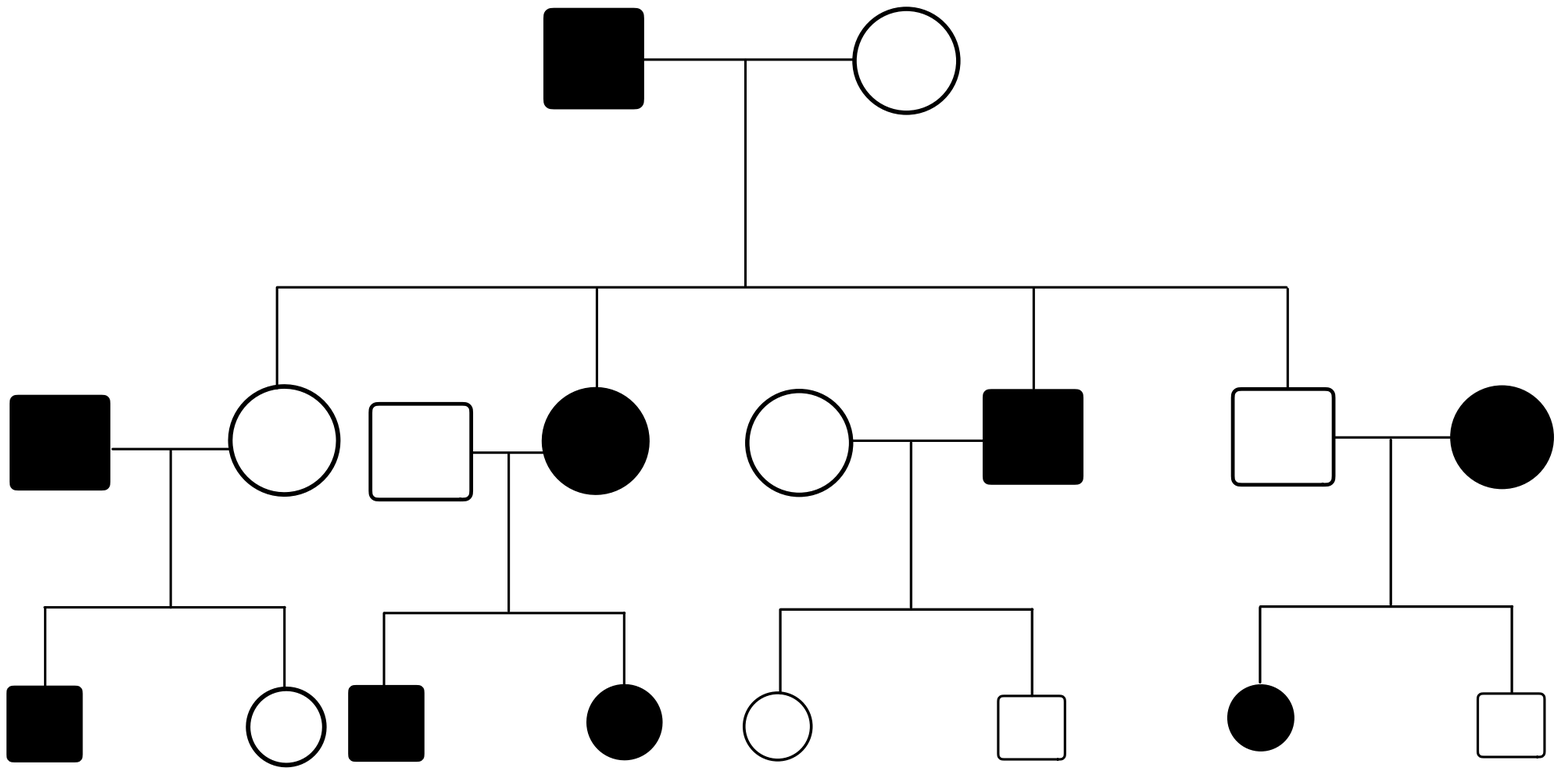
4. If no offspring inherit the trait in one generation, its transmission stops because the offspring can pass on only the recessive form of the gene

In autosomal recessive

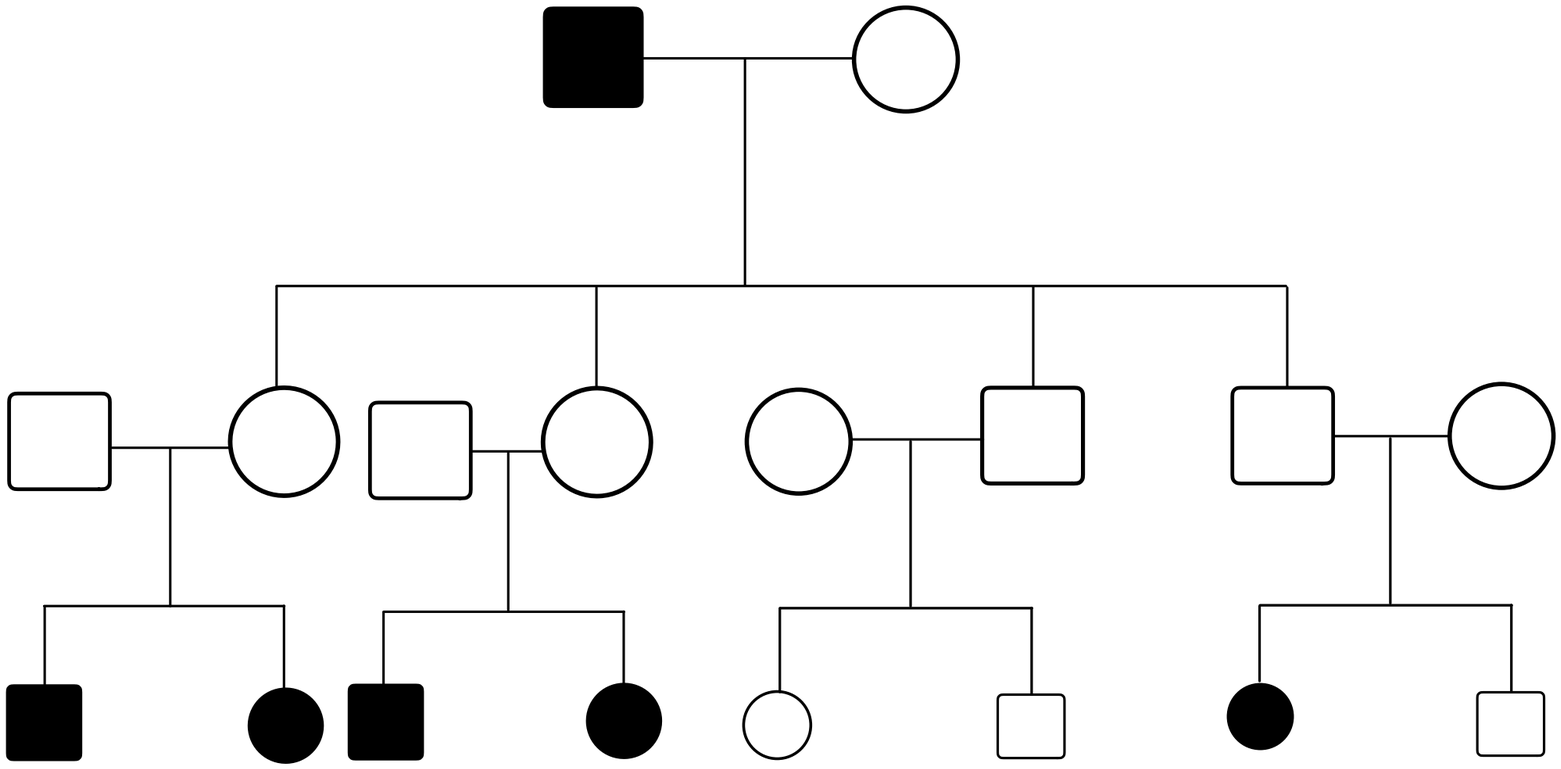
1. can appear **in either sex.**

2. Affected individuals have a homozygous recessive genotype, whereas in heterozygotes (carriers) the wild type allele masks expression of the mutant allele.

3. It **skips** generations.



Autosomal **dominant** traits **do not** skip generations.



Autosomal **recessive** traits **do** skip generations.

❒ IF **THE QUESTION ASKS WHAT IS THE GENOTYPE** PROBABILITY **IN AUTOSOMAL DOMINANT FATHER OR MOTHER** AND **THEY WERE AFFECTED** WITH THE DISORDER, ITS **MOST LIKELY HETEROZYGOUS**, since in AD (autosomal dominant), heterozygous genotype is the most common, since if the individual is homozygous (AA) for an autosomal dominant disorder or a disease they most likely wouldn't be alive till this age (adult) (lethal) or very rare.

This note just incase **you had to choose between** AA or Aa **for an adult individual** in an autosomal dominant pedigree

Other than that, and you couldn’t find a solution, check if you missed something, or keep trying but watchout for the timer in the exam.

PLEASE **DO NOT FORGET** THAT EVERY RULE OF THE FOLLOWING:

❒ Y-LINKED
❒ MITOCHONDRIAL INHERITANCE
❒ X-LINKED DOMINANT
❒ X-LINKED RECESSIVE

HAS TO FOLLOW EVERY FAMILY,
يعني لما تيجي تتطبق القوانين مو اول ما تشوف انو زبط معك من اول المخطط يعني زبط، كمل المخطط كامل وشوف اذا بتبع العائلات الثانية نفس الإشي.

اذا ما تبع عائلة معينة، خلص القانون خرب معناها بتلغي هاد الmode of inheritance.

Check slide 8 to see what i mean.

Written by Momen Allala

Please note مش شرط يزبط معك فكل سؤال لكن على الأغلب حيزبط

I wrote this file just to help others in the exam and for whoever will read this in the future.

I've shared numerous pedigrees here for you to practice solving here: [https://t.me/coronarymcq], check the media of this channel and click on the pictures.

For sheets, questions and last updated file will be uploaded here: [https://drive.google.com/drive/folders/1sYVfDEwuzg5NLNtZ-Y8okwT-hD8HGjBc].