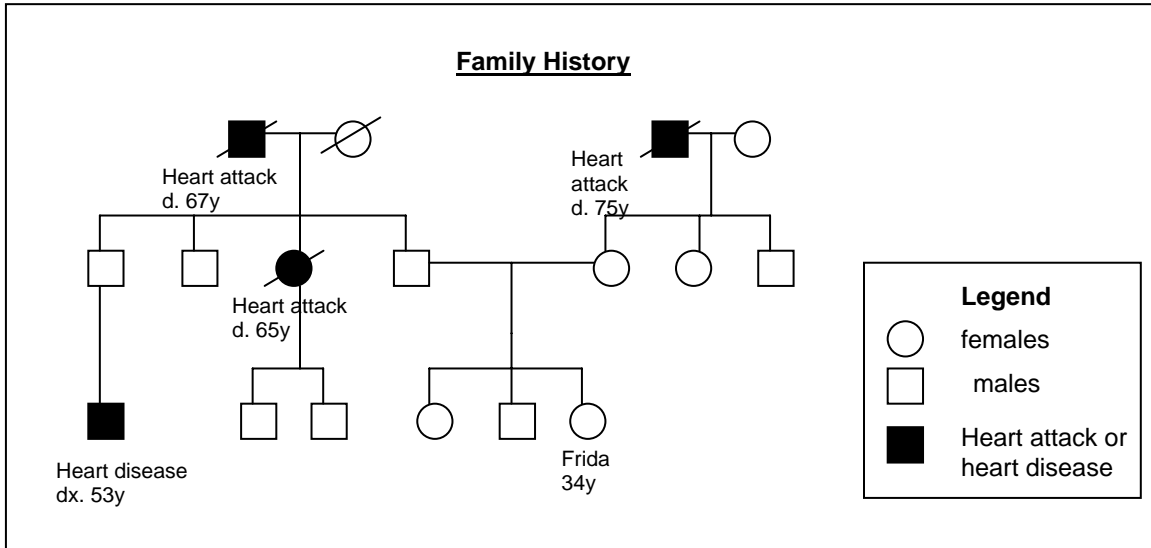


Case I

Frida, 34 years old, has always led a healthy lifestyle by playing soccer and eating healthy foods. Frida noticed that many family members have coronary heart disease and have suffered heart attacks (diagrammed below). She always thought this must be because her family has traditionally eaten a diet full of fried foods and aren't very athletically inclined. A news program recently claimed "It may not be the lifestyle you lead but the genes that you're born with that determine if you'll get heart disease". This worried Frida – is she destined for heart disease because of her genetics, or will her healthy lifestyle offer some protection?



Multifactorial Inheritance

Many common, long-term (chronic) diseases that show up later in life are thought to be inherited in a multifactorial way. This includes conditions such as diabetes, high blood pressure (hypertension), Alzheimer's and heart disease. A person's height and weight are other examples of traits that are inherited in a multifactorial pattern.

Unlike dominant, recessive and x-linked conditions that are caused by a mutation in a single gene, multifactorial conditions are thought to result from a combination of many genes and many environmental factors that must reach a threshold level for the condition to occur.

Take a bucket of water for example. If some people start off with their bucket almost full of water, then they will only need to add a small amount of water for the bucket to overflow. This would be like a person born with many genetic alterations that on their own do not cause disease but if exposed to just enough negative environmental factors would cause the condition to develop (the bucket would overflow). Similarly, if a person starts off with a small amount of water in their bucket (i.e. few negative genetic factors), they would have to fill the bucket up with a lot of water (many environmental exposures) for the bucket to overflow.



- 1) Why are each of the following inheritance patterns NOT a good fit for the heart disease in this family? Dominant, Recessive and X-linked.
- 2) Why are so many people affected with heart disease in Frida's family?
- 3) Will Frida definitely develop heart disease?

Frida's friend Wilma is also concerned about her risk of developing heart disease. Wilma leads a healthy lifestyle and does not have a family history of heart disease.

- 4) Who most likely has the greater chance of developing heart disease – Frida or Wilma? Why?
- 5) Is it possible for Wilma to develop heart disease?

Consider the four sibling types below when answering questions 6&7. Assume each pair of siblings are being raised in the same house together.

- Identical twins (who share 100% of their DNA)
 - Fraternal twins (who share 50% of their DNA)
 - Regular full siblings (who share 50% of their DNA)
 - Step siblings (who do not share DNA)
- 6) Which type of siblings are most likely to both be affected with the same multifactorial condition? Why?
 - 7) Which type of siblings would you least expect to both be affected with the same multifactorial condition?

Case I Answers

Question 1

ANSWER:

- Dominant inheritance is not a good fit because not all affected individuals have affected parents (the heart disease looks like it 'skips' generations)
- Recessive inheritance is not a good fit because there are many affected people across many generations
- X-linked inheritance is not a good fit because both men and women are affected

Question 2

ANSWER: Because of the shared genes among the family members and/or because of shared negative lifestyle factors (no exercise and eating fried foods) and/or by chance.

EXPLANATION:

- Because relatives share a greater proportion of their genes with each other than with unrelated individuals, multifactorial traits can cluster in families.
- BUT, having many affected people in a family doesn't always mean there's a genetic component to the condition. Family members share more than their genes – they often share similar lifestyle and environmental exposures.
- Many family members may also have developed the same condition by chance (especially possible if the condition is common in the population like heart disease is).

Key points about Multifactorial Conditions:

- Conditions do not follow a simple mendelian pattern of inheritance (i.e. do not follow dominant, recessive or x linked patterns)
- Clusters of family members may be affected. This is because relatives are more likely to have the same predisposing genes in common.
- Relatives who share the same 'at risk' genetic factors as the affected member may not develop the condition (because of the role of environmental factors in developing disease)
- Disease is more common among close relatives (parents, full siblings) and becomes less common in more distant relatives (eg. cousins)
- For most conditions, the number (and identity) of genes involved, as well as environmental factors are unknown.

Question 3

ANSWER: NO

EXPLANATION:

Even if Frida and her family members all share a genotype that predisposes them to developing heart disease, Frida may never develop the condition. This is because she would still need to accumulate enough environmental 'hits' to reach a threshold level for heart disease to develop. Eating a healthy diet low in fat and getting regular exercise, will help Frida to lower her chance of developing heart disease.

Question 4

ANSWER: Frida

EXPLANATION:

- We have no way of knowing if the heart disease in Frida's family was caused mostly by genetic predisposition (and a little by environment) or mostly by an unhealthy lifestyle with a small genetic contribution.

- Regardless, it is reasonable to assume that Frida's family history puts her at increased risk for heart disease over Wilma who does not have a history of heart disease in her family.

Question 5

ANSWER: Yes

EXPLANATION:

- While Wilma's healthy family history suggests that she is not very genetically loaded towards heart disease and her healthy lifestyle puts her on the right track to avoiding heart disease, she could still accumulate enough other environmental factors, (especially if she becomes less diligent in the future about maintaining a healthy lifestyle) that could push her over the threshold and cause her to develop heart disease.

Question 6

ANSWER: The identical twins

EXPLANATION:

Identical twins have exactly the same DNA. If a genetic predisposition to a condition is present in one twin, it will be present in the other as well.

Question 7

ANSWER: The step siblings

EXPLANATION:

Step siblings have as much DNA in common as any other unrelated individuals. Therefore if one sibling is genetically predisposed to and develops a multifactorial condition, the step-sibling would not share the same predisposition. (However the step-sibling could still develop the multifactorial condition if exposed to unfavourable environmental factors)