

Constructing and using a Pedigree

Duchenne's muscular dystrophy (DMD) is a well known, lethal condition. severe recessive X-linked form of muscular dystrophy characterized by rapid progression of muscle degeneration, eventually leading to loss of ambulation and death. This affliction affects one in 3500 males, making it the most prevalent of muscular dystrophies. In general, only males are afflicted, though females can be carriers. Females may be afflicted if the father is afflicted and the mother is also a carrier or affected. Symptoms usually appear in male children before age 5 and may be visible in early infancy. Muscle weakness of the legs and pelvis spreads to the arms, neck, and other areas. By age 10, braces may be required to aid in walking but most patients are wheelchair dependent by age 12. Due to progressive deterioration of muscle, loss of movement occurs eventually leading to paralysis. The average life expectancy for patients afflicted with DMD varies from late teens to early to mid 20s. Knowing how this disease is inherited through family members suspected of carrying the allele will be helpful in genetic counseling and decision making.

Procedure

1. Consider the following information gathered from four generations of a family:
 - ▶ two people marry and have four children (F_1) in the following order: daughter, son, daughter, daughter
 - ▶ the first daughter (F_1) marries and has three children (F_2): a son, a daughter, and another daughter. Her first daughter does not marry. The second daughter marries and produces a son, who develops DMD, and two daughters.
 - ▶ the son (F_1) develops DMD and dies.
 - ▶ the second daughter (F_1) marries, but produces no children.
 - ▶ the third daughter (F_1) marries and has two children: a son who develops DMD and dies, and a second son. Her second son marries and has a daughter and then a son.
2. Construct a pedigree chart to represent the family history given.

Questions

- a) If the original parents did not exhibit DMD, how could it have appeared in one of their children? (It is a recessive, X-linked disorder so the mother could be a carrier and pass it to her son.)
- b) Is there any indication from the pedigree chart that DMD is sex-linked? Explain. (In this pedigree the trait appears more frequently in males as no females are affected.)
- c) Are any of the females in F_2 definitely carriers of DMD? Explain. (The second daughter has an affected son so she is a carrier.)
- d) In the family line of the first daughter from F_1 , could the husband of the married daughter have been responsible for passing the DMD gene to his son? Explain. (No, fathers pass the y chromosome to their sons.)
- e) Is it possible for a sex-linked disease to pass from one generation to the next without appearing in any offspring? Explain. (Yes, female children could be carriers and pas it to their sons (or daughters if the female marries an affected male).)
- f) In the family line of the third daughter from F_1 , what is the probability of her grandson (F_3) developing DMD? Show your work. (The third daughter's son does not have DMD so he cannot pass it to his children. We cannot know his son's probability without knowing the family history of his wife.)
- g) In F_1 , concerned by the appearance of DMD in her brother, the second daughter and her husband decide to visit a genetic counselor before having any children. Their decision was to adopt. Suggest the reasoning they might have used to make this decision. (The mother must be a carrier because she passed it to her son, so the second daughter has a 1/2 chance of being a carrier; probability of her sons having

DMD is $1/2 \times 1/2$ and $1/2 \times 1/2$ her daughters will be carriers.)