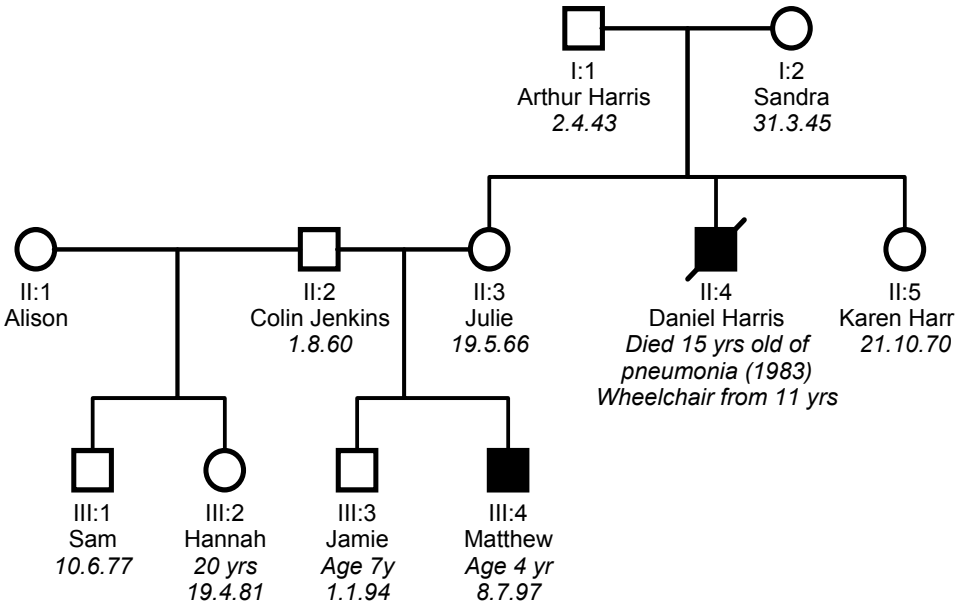
4 Please - tell me my son does not have the same condition as my brother had

A 4 year old boy, Matthew Jenkins started to show difficulty in getting up from sitting on the floor, and also going up and down steps. His mother noticed that his calves appeared very prominent. He started walking much later than his 7 year old brother who had no difficulties.



Q1 Are there any clues in the pedigree that might indicate an inherited condition in the family, and if so what is the likely mode of inheritance?

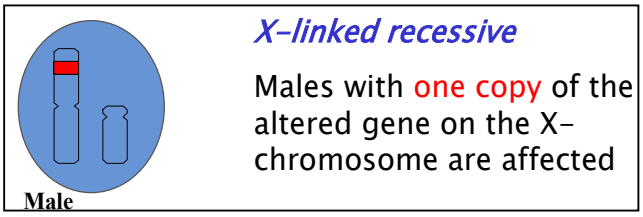
X-linked recessive inheritance is suggested because

1 Two males are affected (in successive generations)
2 No affected females
3 Affected males are linked through unaffected females in a"knight's move" pattern

This is highly suggestive of X-linked inheritance, but to prove X-linked inheritance (which would have implications for females in the family) both boys would need to be confirmed as having an X-linked condition.

In practice, the medical records of Matthew's uncle Daniel Harris would be consulted. We are also likely to have the results of muscle and DNA tests in Matthew.

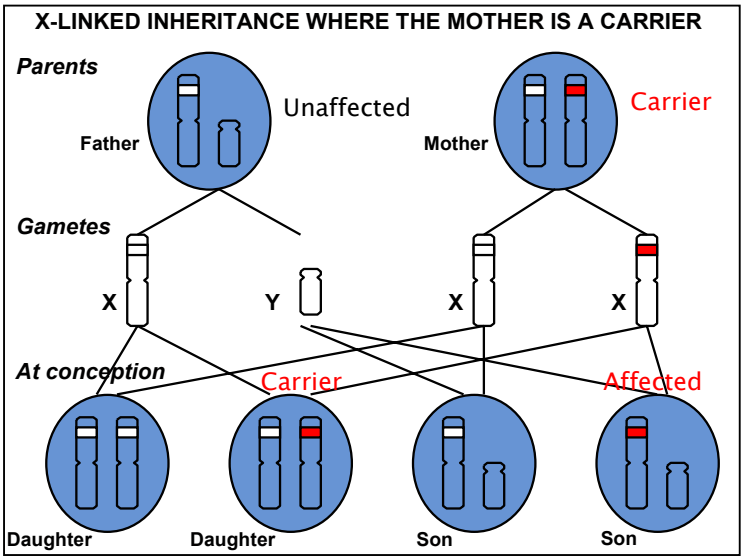
Duchenne muscular dystrophy is an X-linked recessive condition – a trait caused by a gene on the X chromosome expressed in hemizygous males and which is carried by females.



Background information:

Duchenne muscular dystrophy (Pseudohypertrophic muscular dystrophy)
Incidence 1 in 3500 males. Usually presents between ages of 3 and 5 years, with slowly progressive muscle weakness giving awkward gait, inability to run quickly and difficulty in rising from the floor. Many affected boys have to use wheelchairs in early teenage years because of severe proximal muscle weakness in the lower limbs. Lumbar lordosis, joint contractures and cardiorespiratory failure usually lead to death in late teenage years. The calf muscles appear larger (pseudohypertrophy) due to replacement of muscle fibres by fat and connective tissue. Approximatey 1/3 boys with DMD show mild to moderate intellectual impairment.

Duchenne/Becker muscular dystrophies are allelic, caused by mutations in the dystrophin gene. Sixty per cent of boys have a deletion of part of the gene.



Carrier detection tests include measuring serum creatine kinase (CK) levels but this is not wholly reliable, as the normal and carrier distributions overlap. CK levels are not reliable as a carrier test in pregnancy. Risks of being a carrier may be amended with information from DNA probes and gene tracking. Genetic units offer to follow up families so that carrier testing can be offered to girls at risk in late teenage years.

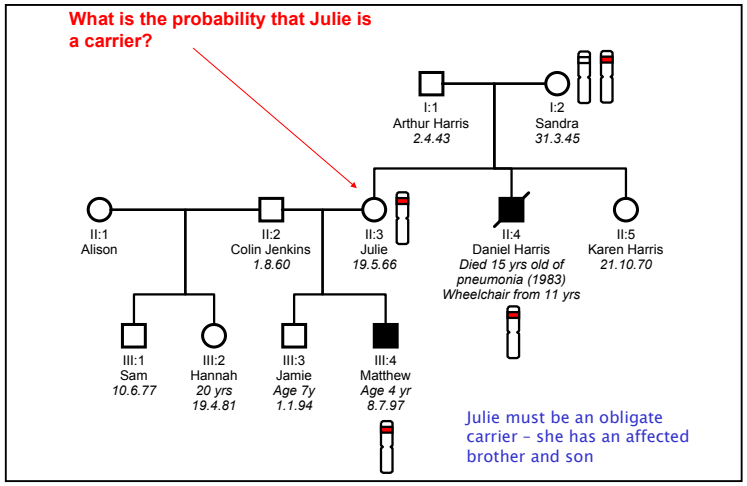
One-third of boys who are the only case in their family have their disorder as a result of a **new mutation** (the mother is a carrier in the other 2/3 of families). Prenatal diagnosis may be possible by gene tracking or by direct detection of the mutation, depending on the family.

(There is an animated tutorial on X-linked inheritance on the homepage of the genetics website)

Q2 What is the probability that Julie (II-3) is a carrier?

To work out the probabilities of other family members inheriting the altered gene, first decide who must definitely be carriers of the altered gene by their position in the pedigree.

As Matthew's mother (Julie Jenkins II-3) has an affected brother and an affected son she must be a carrier for the altered gene (an obligate heterozygote).



Q3 What is the probability that Karen (II-5) is a carrier?

Karen's mother, Sandra Harris (I-2), must also be a carrier because she has an affected son, and a daughter who is definitely a carrier. Sandra Harris's other daughter (Karen) must have inherited either the X chromosome with the altered gene or the X chromosome with the normal dystrophin gene from Sandra. Karen therefore has a 1 in 2 probability of being a carrier. If the familial mutation in the dystrophin gene were to be identified, Karen could be given a definitive answer if she wished to be tested.

Q4 What is the probability that Matthew's elder brother (Jamie, III-3) is a carrier for the condition?

As Matthew's brother (Jamie III-3) is unaffected, he must have inherited the normal dystrophin gene from his mother and therefore he cannot be a "carrier" for the condition.
His own children will of course not be at risk.
Note that unaffected males in an X-linked family are often concerned that they or their children could be at risk of inheriting the condition, so it is important to explain the genetics to them, too, at an appropriate age.

Q5 What is the probability that Matthew's sister (Hannah, III-2) is a carrier for the condition?

As Matthew's half sister (Hannah) is related to him through his father Colin Jenkins (II-2), Hannah is not at risk of inheriting the X-chromosome containing Matthew's altered gene. However the probability of Hannah being a carrier is not zero – it is that of any female in the general population - very low indeed.