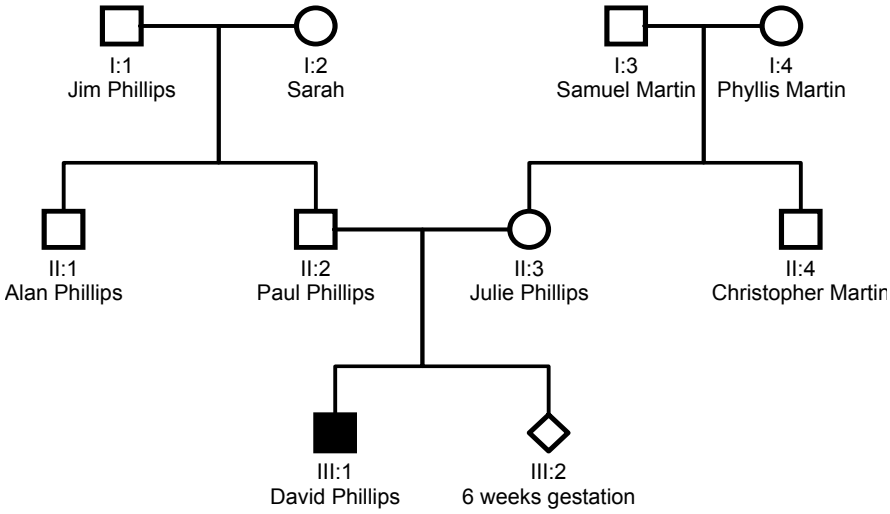
2 Will it be possible to have a test in pregnancy?

David Phillips (III-1) is undergoing investigations for symptoms suggestive of cystic fibrosis. His mother Julie (II-2) is six weeks pregnant.



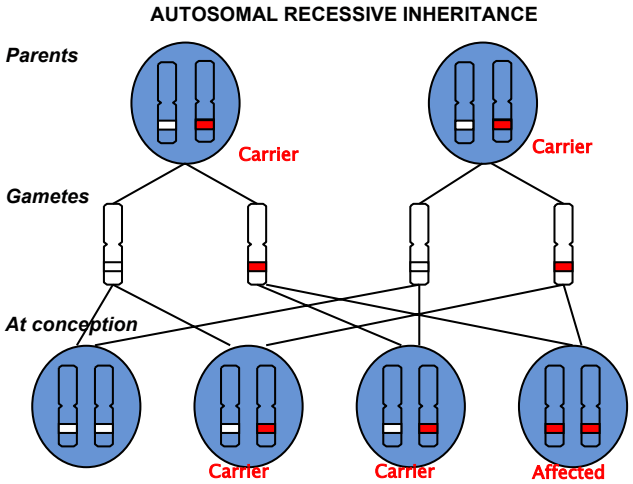
Q1 How can genetic testing help confirm the diagnosis of cystic fibrosis in David?

As the DNA code for the CFTR gene (cystic fibrosis transmembrane regulator) is known a DNA test can be offered to identify the mutations causing the CF in David. In about 75% of carriers for cystic fibrosis in the West Midlands, the mutation is the Delta F508 mutation. Three bases are deleted resulting in the deletion of a phenylalanine residue at position 508 in the amino acid chain. There are several other less common mutations, and then several hundred extremely rare mutations. If both mutations can be identified prenatal diagnosis can be offered.

Q2 If the diagnosis of cystic fibrosis is confirmed in David, what is the probability that his brother or sister (III-2) will also have cystic fibrosis?

1 in 4; 25%
Cystic fibrosis is an autosomal recessive condition.
As David has the condition, both Mr and Mrs Phillips must be carriers (heterozygotes - ie each has one normal and one altered CF gene). Each can pass on either the normal or the altered gene, and so there are 4 possible combinations. This is explained in more detail in the animated tutorial on autosomal recessive inheritance on this website.

When the baby has been born, and is known not to have cystic fibrosis, he or she has a 2/3 chance of being a carrier.
(See the animated tutorial)



Q3 What further genetic information is needed before offering a genetic test in this pregnancy?

As highlighted above identifying the mutations in the CFTR gene in David, and confirming that each of his parents has one of these mutations.

Q4 Alan Phillips (II-1) wants to know if there is a high likelihood of his being a carrier for cystic fibrosis. Would you test him for carrier status?

This depends on the probability that Alan is a carrier. As Paul must be a carrier, then Paul must have inherited the altered CFTR allele from one of his parents (We cannot tell which without DNA testing). We usually assume that only one of Paul's parents is a carrier as it would be unlikely that both were carriers. Therefore Alan could inherit either the normal or altered CFTR allele from his parent who is a carrier and he has a ½ (50%) probability of being a carrier and carrier testing is warranted.