A *Two Houses* consultation guide

A request for genetic testing

The House of Discovery: work out what matters

To the patient

Who is the test for? Themselves, a partner or a child?

What do they want to find out? Is it future risk for their own health, or for their current or future children?

What do they know of the condition they are concerned about? Have they done their own research? What is the family history? Why have they come now rather than at another time in their life?

What is their understanding of genetic testing? Do they already have a good understanding of patterns of inheritance, or is one of their key objectives to gain a better understanding of how the condition is inherited?

What advice have they already received? This might be from doctors, family members or a website, but people have often done helpful groundwork before coming for an appointment like this.

To the doctor

Does the condition in question have a known pattern of inheritance, such as autosomal dominant, recessive or x-linked inheritance, or is inheritance multifactorial, such as ischaemic heart disease, diabetes, coeliac disease?

Think about which pieces of the jigsaw are already in place (known cases or carriers in the family) and which pieces need to be filled to answer the patient's questions.

Are there ethical problems with testing? (eg testing a child for a condition like Huntington's Disease – see Locked Rooms).

What would be the implications of a positive test? Has the patient considered this?

Do the required genetic tests exist and are they available?

What to look out for in the *House of Discovery*

Finding Dry Rot

Genetic tests are sometimes requested for reassurance, but the implications of some genetic tests are considerable. This is especially the case with an untreatable condition like Huntington's or discovering that you carry a gene that could harm your children.

Is the patient ready for bad news? It may be important to prepare them for this possibility before arranging a test. What will they do with the result? How might it impact other people in the family?

Tools for the toolbox

Consider drawing a family tree with the patient so that you can share an understanding of the inheritance.

"What would you like to ask?"

"If the test comes back positive, where will that leave you?"

"While there is no specific treatment for this, if we can keep your blood pressure under control then that will really help."

Tending the Garden

Some genetic conditions may have significant implications for lifestyle decisions. eg alpha-1-antitrypsin deficiency will cause premature COPD in smokers; or the impact of a strong family history of heart disease might be lessened by good attention to lifestyle measures. This might be a helpful motivator for lifestyle changes.

Some conditions require close monitoring, eg Adult Polycystic Kidney Disease should be managed with close attention to blood pressure and renal function.

Foundations

Autosomal Dominant Only a single copy of the defective gene is required. Apart from spontaneous mutations, this can only be inherited from a parent who is affected by the condition, or will be if it starts later in life, with a 50% chance of inheritance. This means only parents need to be tested, and if they are unaffected then their children cannot be affected.

Autosomal Recessive Inherited by receiving 2 copies of the defective gene, one from each parent. People with a single copy are carriers and usually have no, or mild symptoms, but a 50% chance of passing on the gene to children. Children of parents who are both carriers will have a 25% chance of being affected by the condition, 50% chance of being a carrier and 25% chance unaffected . If one parent is a carrier then the other will need to be tested to see if children might be affected.

Classic examples of AD inheritance: Huntington's Disease; Adult Polycystic Kidney Disease; Marfan's Syndrome; BRCA 1 and 2.
Other less common examples include spherocytosis, neurofibromatosis, tuberous sclerosis and Von Hippel-Lindau Syndrome.

Classic examples of AR inheritance: Cystic fibrosis; Thalassaemias; Sickle Cell; Homocystinuria; Phenylketonuria; Albinism.

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The House of Decision: decide together what to do

Rooms to look out for

Empty Rooms

There may an expectation for an easy genetic test that does not exist – for instance cancer risk that is not typical of BRCA 1/2 pattern, or a genetic test for autism. Paternity testing is sometimes requested, but not available on NHS.

Hidden Rooms

Some inherited conditions, including carrier status, can be tested for without testing DNA, eg haemoglobinopathies (test Hb electrophoresis) and familial hypercholesterolaemia (diagnosed on cholesterol level and Simon Broome criteria).

Locked Rooms

Ethical considerations limit genetic testing in children. Tests should not be done for conditions where there is no treatment in childhood (eg Huntington's, carrier status for CF) since the decision to test should be delayed until the child is able to choose for themselves. International guidelines are quite clear about this, but it can be difficult for parents to accept, since they may believe they have the right to choose for their children and have the right to know. Testing estranged partners can also be an issue if they do not wish to co-operate.

Key decisions in the *House of Decision*

Are any tests needed at all?
It may be that all the required information is already known – eg the son of a man with Haemophilia will not be affected, so no need to test them.

Which piece(s) of the jigsaw are missing?
Help the patient to work out which are the key pieces of the jigsaw that would need to be in place in order to answer their questions. Often testing a parent or grandparent first will help to see who else needs to be tested, if anyone. Try to work out who is the 'index' case at the heart of the inheritance.

Is a genetic referral required?
DNA tests will always require a secondary care referral; family history of cancer may require referral – there are good NICE guidelines on this for breast/ovarian/bowel cancer. For cancer, genetic units usually ask for patients to complete a family history questionnaire before deciding if they should be seen.

Should other people in the family consider testing?
For instance, if you recommend that your patient is tested, should their siblings be tested also?

The High Tech Room

It is easy to get in a tangle when explaining genetics! Find out prior understanding, since the patient may have limited biological understanding, or a degree in genetics!

Will it help to use technical terms like dominant and recessive, or would it be more helpful to explain the significance of inheriting genes from one or both parents? If technical terms are used then find an effective way to explain them.

Tools for the toolbox

"How much do you know about how cystic fibrosis is inherited?" (remember not to ask "what do you know?" as it is too much like a quiz).

"Let's work out who is the best person to test in order to answer your questions."

Drawing the patient's family tree can be very helpful, since it can help both doctor and patient to visualise the problem and see where the gaps are. There is less need for the patient to hold a complex inheritance pattern in their head as they will be able to see it on paper.

Every genetic condition is likely to have its own support group and website to signpost the patient to after the consultation.

Foundations

X-Linked Recessive The defective gene is on the X Chromosome and a single healthy copy is required to prevent the condition. This means that boys can NEVER be carriers and can ONLY inherit it from their mother, who must be a carrier.

X-Linked Recessive (cont)
Girls will only ever be affected if their father is affected and their mother also a carrier (very rare), but will ALWAYS carry the gene if their father is affected. This often gives certainty to the genes of some family members without needing to test them.

Classic examples of X-linked recessive
Haemophilia A and B; Glucose-6-phosphate dehydrogenase (G6PD) Deficiency; Red-Green colour-blindness.

Some conditions have subtypes that can be dominantly or recessively inherited (eg Von Willebrand Disease), while Ehler's Danlos can be either and also X-linked, depending on type.