

# Cerebral Cavernous Malformations

What does it mean for Me and my Family ?

Dr Jonathan Berg

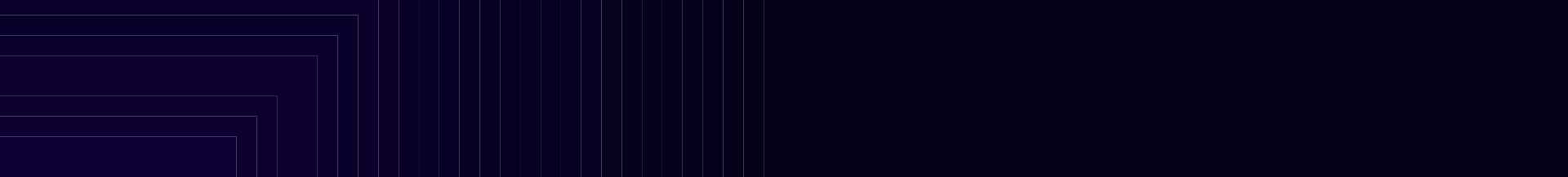
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# Clinical Genetics

Medical specialty

Diagnosis of Hereditary Conditions

Deciding if conditions are inherited

Management of rare and hereditary conditions

Everyone in the UK should have access to

- Clinical Genetics Services
- Gene Testing if Appropriate

# Frequently Asked Questions

What is the risk to my family ?

Can I have a gene test ?

What does the gene test mean ?

# Key Point

Only a small proportion of Cerebral Cavernous Malformations are inherited

When this is the case we use the term -

Familial Cerebral Cavernous Malformations (FCCM)

# How do we know if it is familial ?

## Non - Familial

Single lesion  
No family history

The majority of  
cases

## Familial CCM

Multiple lesions  
Definite Family History  
May have additional clues  
Skin marks  
At the back of the eye

1 in 10,000 to 1 in 40,000  
people in the UK

# What is a gene ?

An instruction in each cell that makes a protein

You have 2 copies of every gene

There are 30,000 different genes

The genes are written in DNA

# What is DNA

A string of letters

There are about 3 billion letters in the human genome

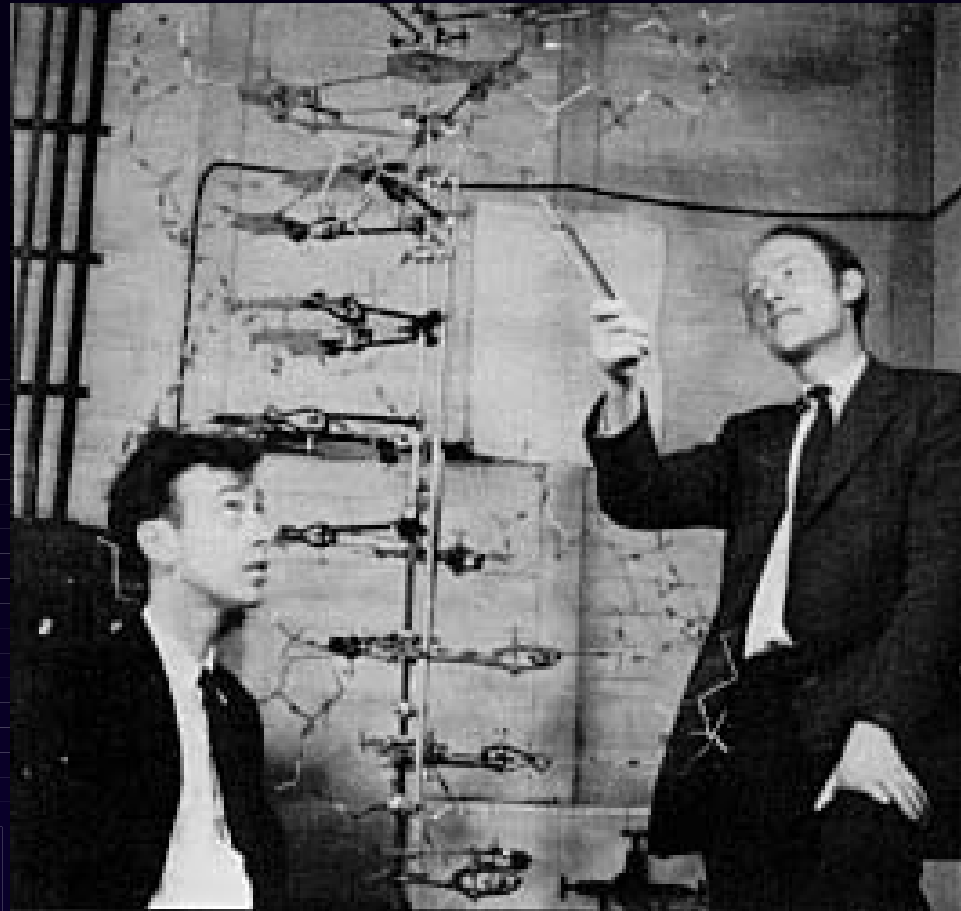
A gene might have 10,000 to 1,000,000 letters in it

- About the size of War and Peace

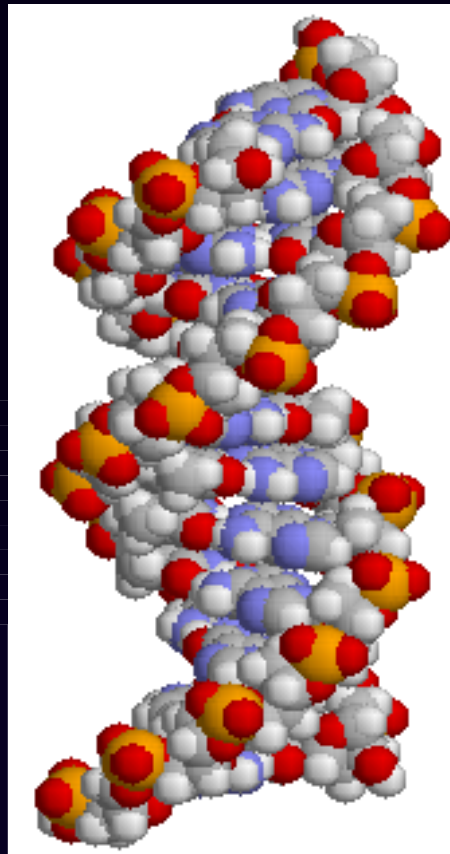
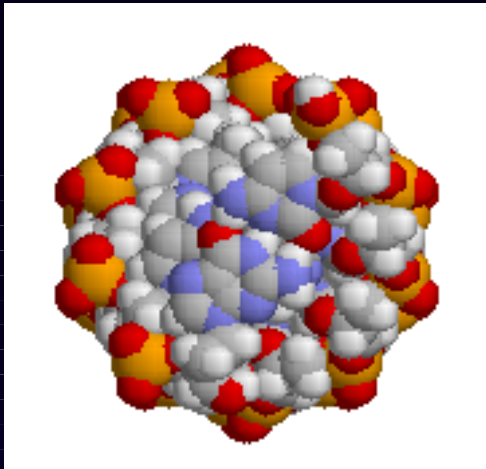
# A gene fault






May only be a single letter that is changed

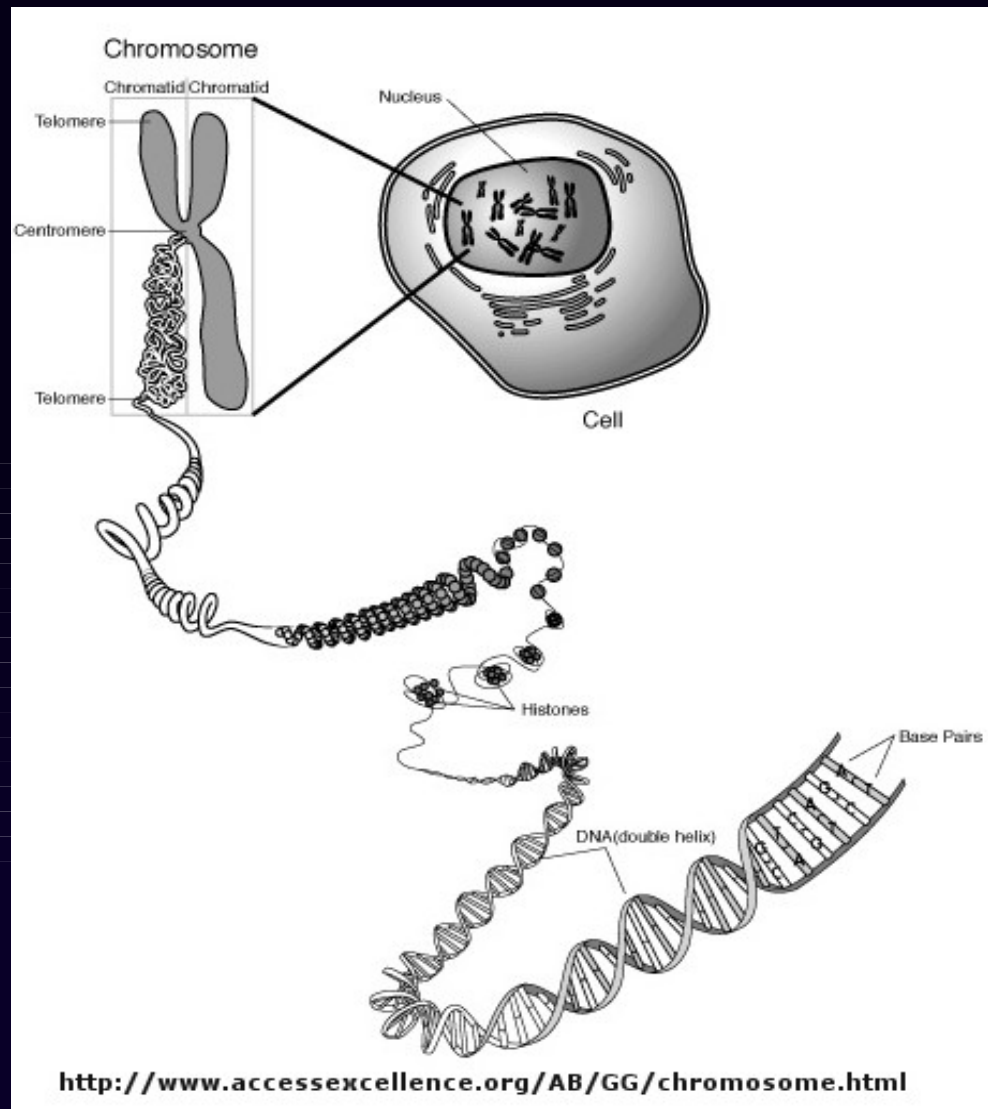
Could be anywhere in the gene

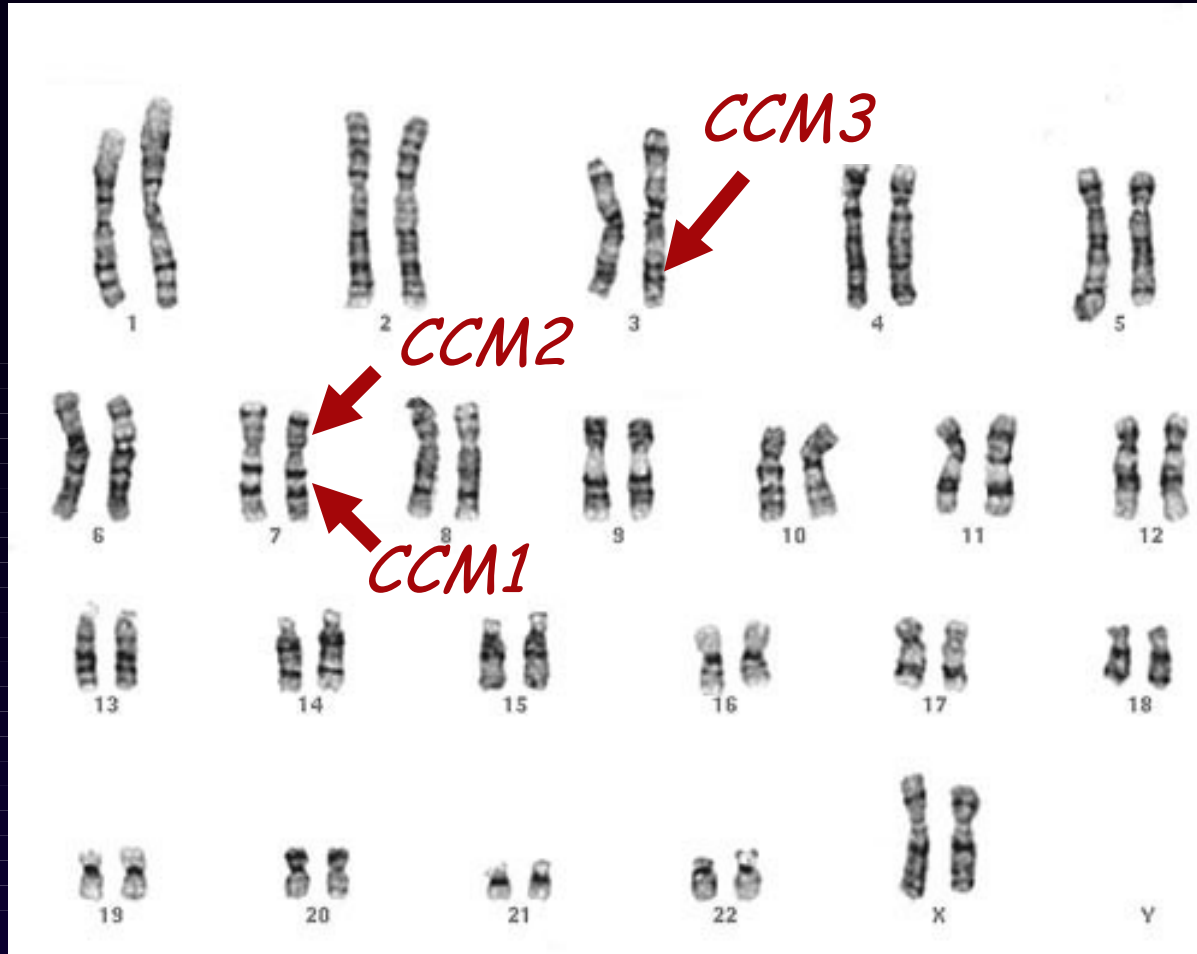


# Views of DNA Structure



-  nitrogen
-  carbon
-  hydrogen
-  oxygen
-  phosphorus





# What's in a name

Krev Interaction Trapped 1 (KRIT1):	CCM1
Malcavernin:	CCM2
PCDC10	CCM3

There may be other genes, that we don't know about, but the genes we know account for most gene changes

# Key Points

If you have FCCM

You will only have a fault in one of the genes

Most faults are unique to one family

# How likely are we to find a gene change:

You have at least one CCM and you have a relative who has also had at least one definite CCM

70-90% likelihood

If we don't find a gene change, there is still likely to be a gene fault that we don't know how to find

# How likely are we to find a gene change:

You have multiple CCMs on a scan but there is no affected relative you know about

Approximately 50% likelihood

If we don't find a gene change, there may still be a gene fault that we don't know how to find

# A child with at least one symptomatic CCM

Likelihood of a gene change not quantified



Paper

TAB  
2005



Document with text and a table, partially visible on the right wall.

Document with text, pinned to the wall on the left.

Document with a bicycle diagram, pinned to the wall.

Document with text, pinned to the wall.

Document with text, pinned to the wall.

Document with text, pinned to the wall.

Yellow sticky notes on the wall.

berg

# Dundee testing

CCM1, 2 and 3 genes

Point mutations and large genomic deletions

UK diagnostic accredited lab

Different profile of mutation to USA

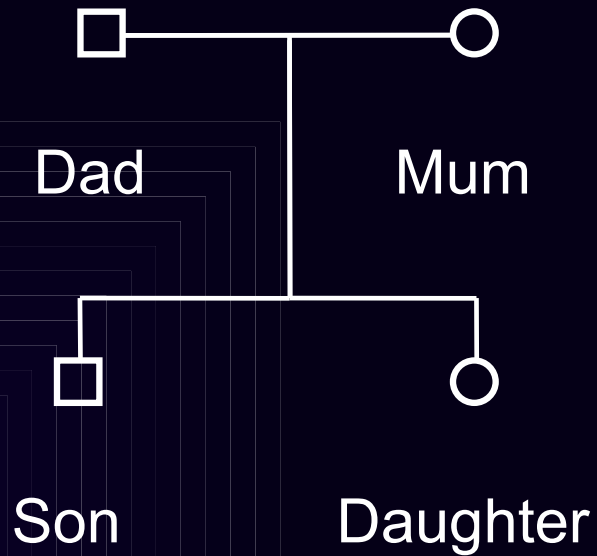
Approx 85% detection rate

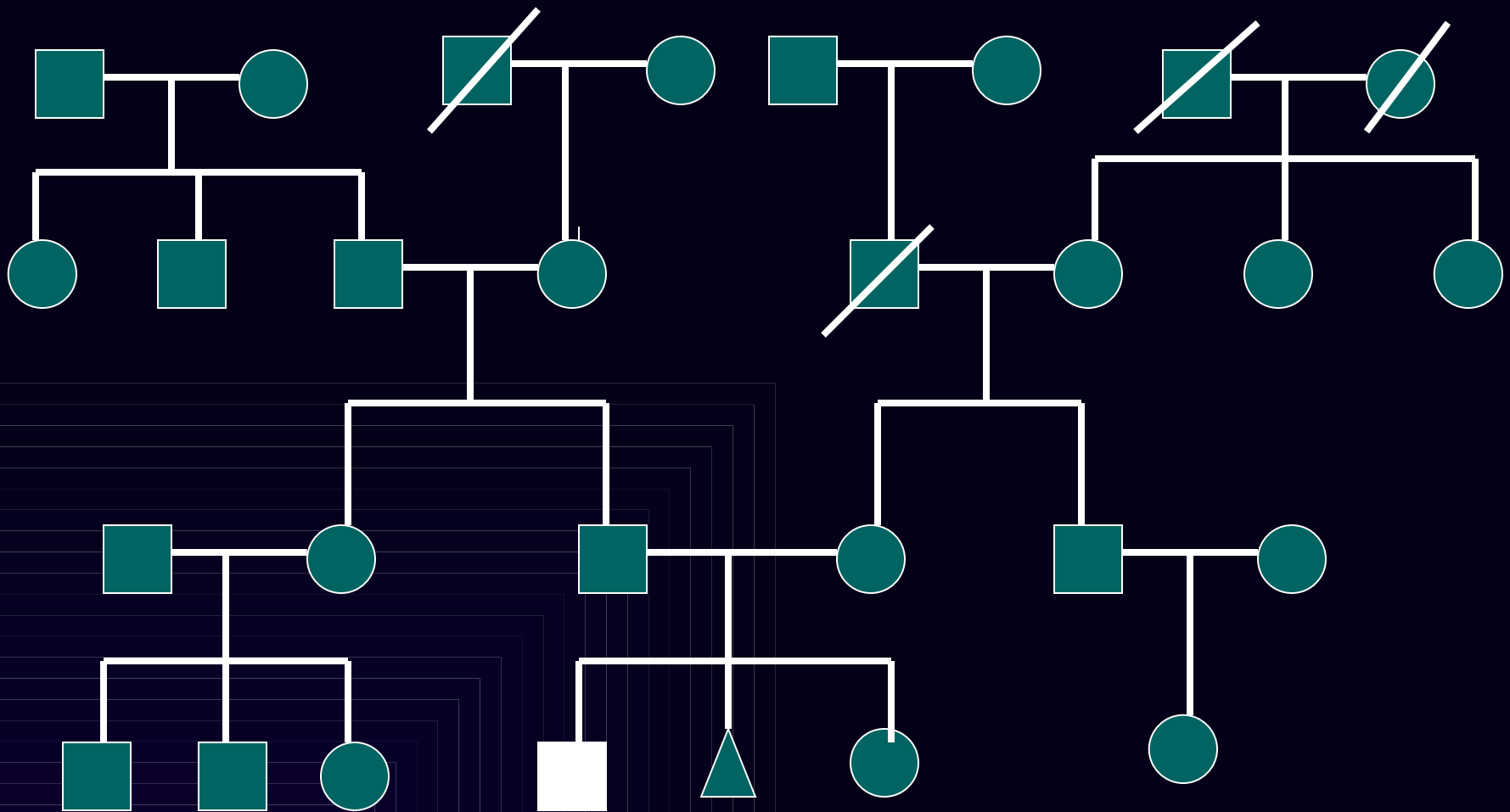
# Other tests that may help

MRI scanning

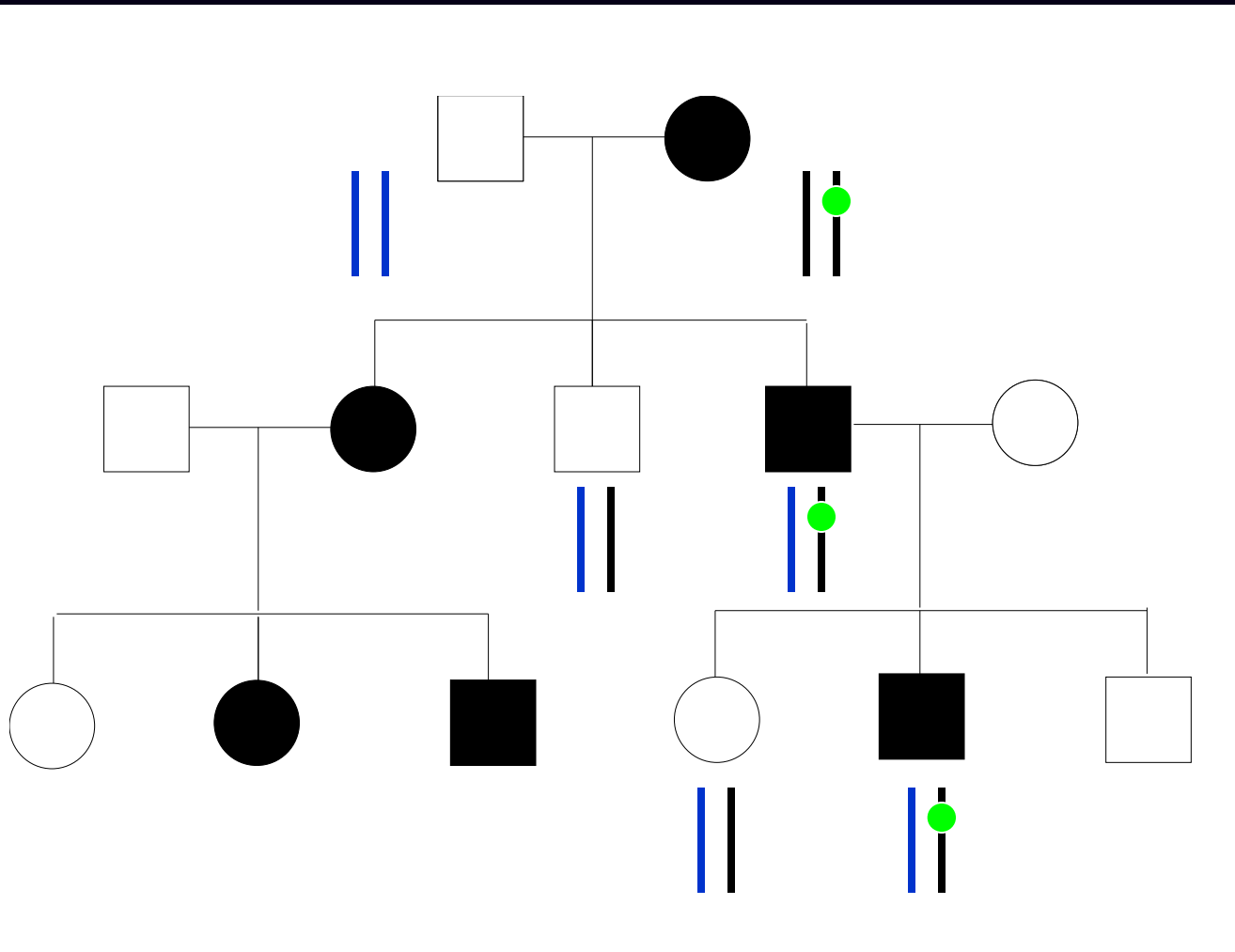
Referral to ophthalmologist

# Pedigree Drawing





# Inheritance of an FCCM gene change



# When drawing a family history

Relatives may be affected but not know about it

There are other causes of brain haemorrhage that are more common, and not a part of FCCM

# Types of testing

In a person who is affected

**Diagnostic testing**

In a person with an affected relative

**Pre-symptomatic testing**

# Diagnostic Testing

Testing confirms the diagnosis that is already suspected by the doctor

The test itself has fewer implications

Would be carried out on a child if appropriate

# Predictive Testing

A relative has FCCM

Do you really want to know if you have  
the gene fault too ?

# Do you really want a test ?

## Advantages

Great if you don't have FCCM  
Be aware if you suddenly  
develop a problem  
Know the risks to you  
Assess risk to children

## Disadvantages

Anxiety  
Guilt  
Difficulty with insurance  
Issues with other family  
members

*Currently Gene testing Does Not Alter Treatment*

# Predictive testing in children

There should be a clear therapeutic benefit

Important to consider the child's future autonomy

At the moment there is no evidence for early intervention

Having a gene change

is not the same

As having an illness

# What if I have a gene change ?

About 60% of people develop some symptoms over their lifetime.

40% do not

Symptoms can start at any age, but commonly in early to mid-adulthood

Some people carry the gene change but do not even develop CCMs on a scan

If you have FCCM  
You only have a fault in one gene  
Does it Matter Which ?

Answer:

We don't know  
but we really need to find out

# Where gene testing may be successful

Where you have a CCM and other affected family members

Where you have multiple CCMs

? Where a child is affected with a CCM

Always test an affected person first



# Future Directions

Understanding FCCM better clinically

To be able to give you better information

This can be done fairly quickly

Understanding FCCM better at the cell and protein level

To be able to find better treatments

This will take a long time

*Laboratory  
Scientists*

*GPs*

*Radiologists*

*People affected  
Or at risk*

*Neurosurgeons*

*Geneticists*

*Pathologists*

*Neurologists*

# Acknowledgments

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