

# The Role of Genetic Testing in Family Planning & Pregnancy

Ebony Richardson

Associate Genetic Counsellor, PhD Candidate UTS



# The pathway for genetic testing in family planning and pregnancy



Family history of genetic disease

Understanding your risk of an affected child.

Options for prevention

No known family history of genetic disease

Genetic testing before becoming pregnant:

- *Reproductive carrier screening*

Genetic testing during pregnancy:

- *First trimester screening*
- *Diagnostic tests*

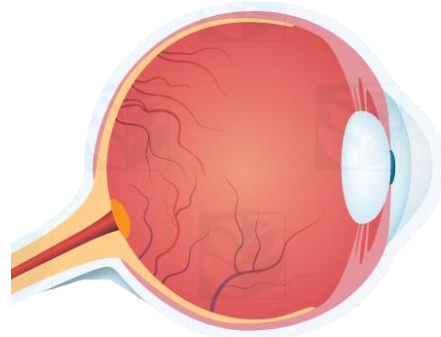
All types of genetic testing for family planning or during pregnancy are optional

## Meet Tom and Sandra

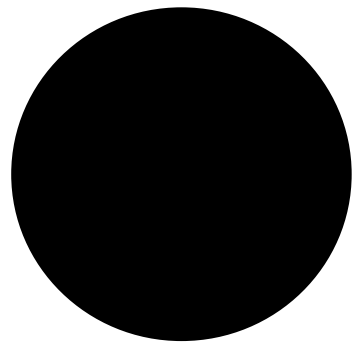
Tom and Sandra are planning to start a family, however Tom is nervous because he has recently been diagnosed with retinitis pigmentosa, a condition which is causing him to gradually lose his vision.



**NORMAL EYE**



**RETINITIS PIGMENTOSA**



Meet Tom  
and Sandra



Family history of  
genetic disease

Understanding your  
risk of an affected  
child.

Options for  
prevention

No known family history of genetic disease

Genetic testing before  
becoming pregnant:

- *Preconception carrier screening*

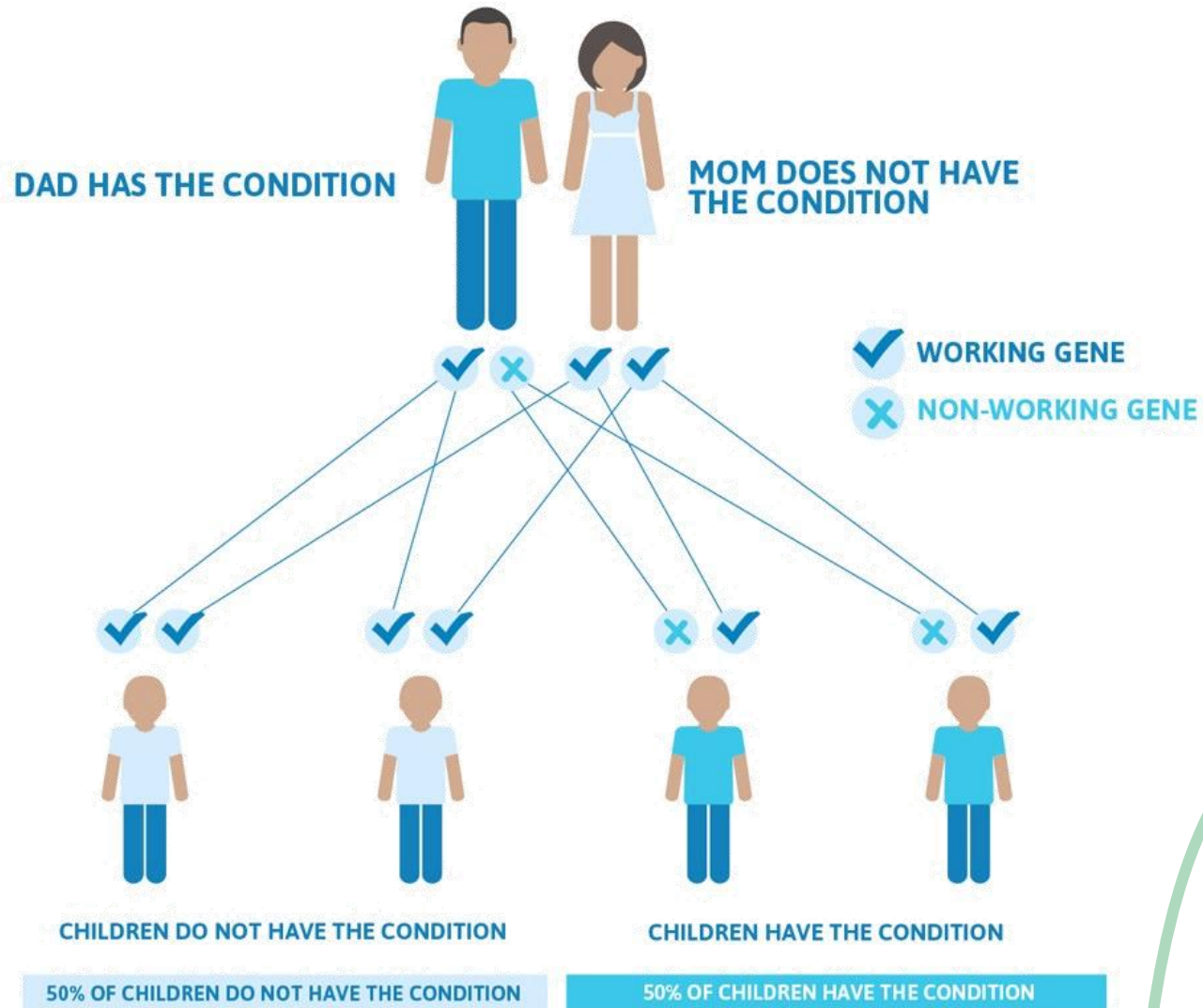
Genetic testing during  
pregnancy:

- *First trimester screening*
- *Diagnostic tests*

Retinitis pigmentosa is a  
complicated condition because  
it can also be inherited in  
different ways.



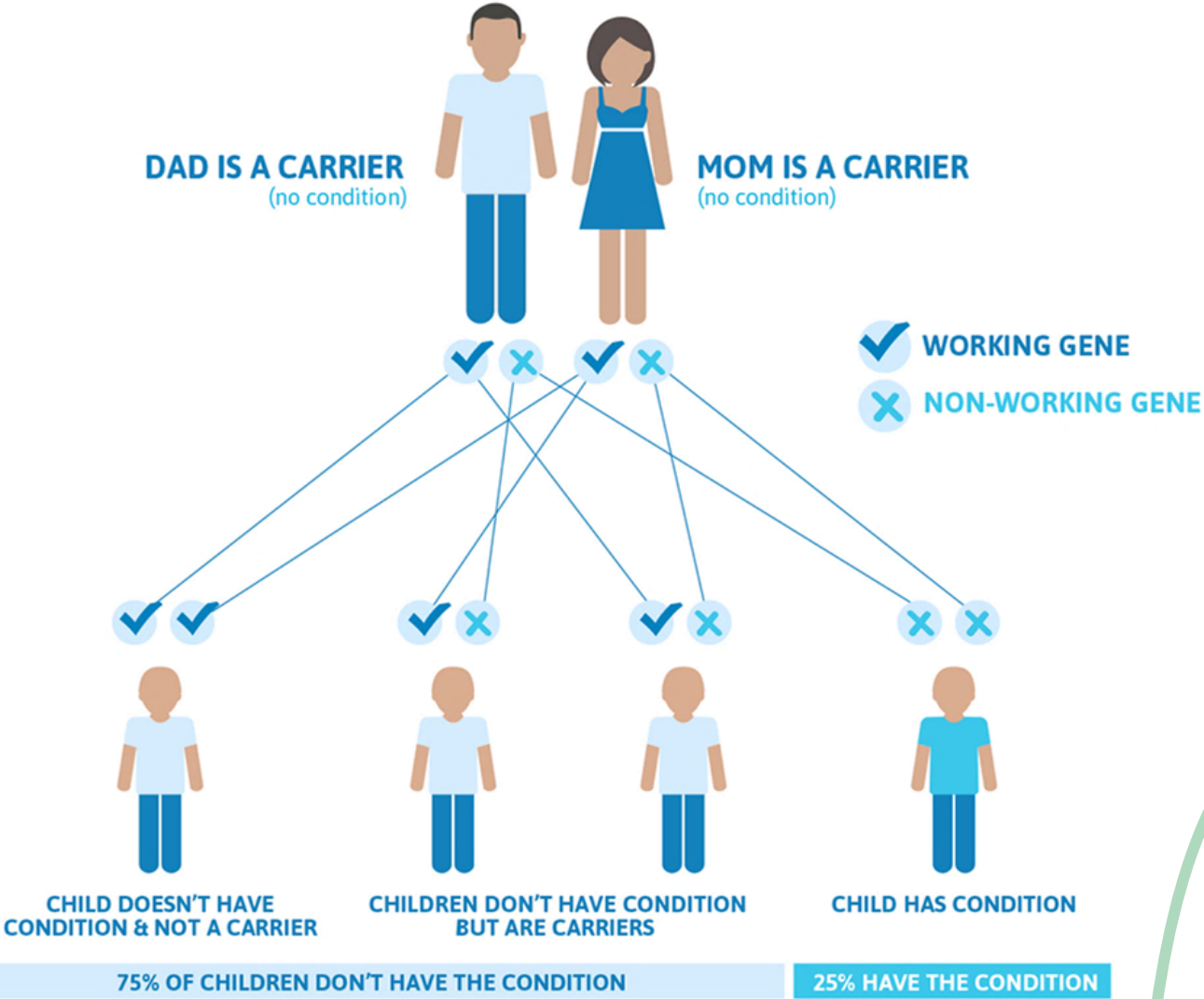
# Autosomal Dominant Inheritance Pattern



Common  
Inheritance  
Patterns

Autosomal Dominant

# Autosomal Recessive Inheritance Pattern

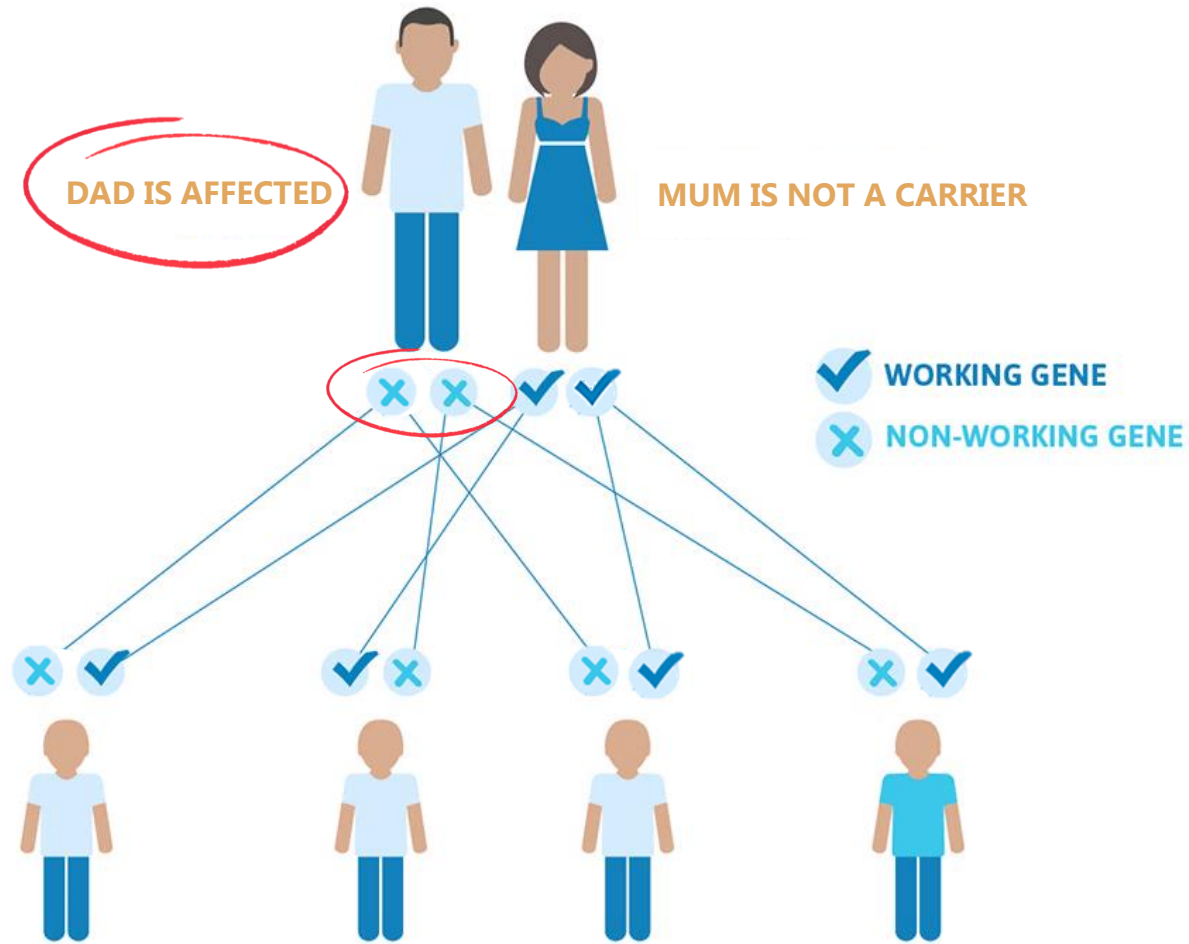


## Common Inheritance Patterns

Autosomal Dominant

Autosomal Recessive

# Autosomal Recessive Inheritance Pattern



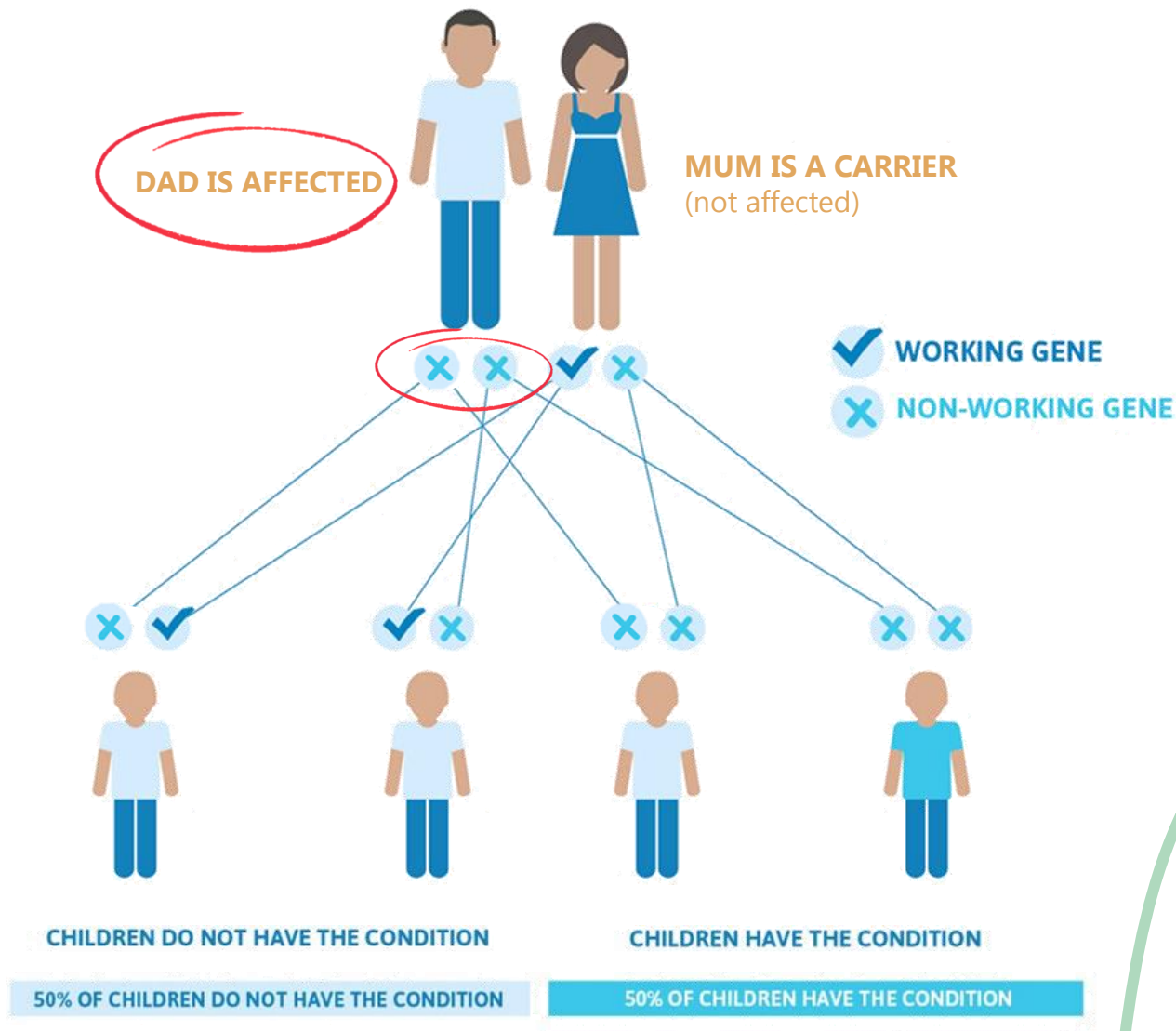
ALL CHILDREN WILL BE UNAFFECTED, BUT CARRIERS OF THE CONDITION

## Common Inheritance Patterns

Autosomal Dominant

Autosomal Recessive

# Autosomal Recessive Inheritance Pattern



## Common Inheritance Patterns

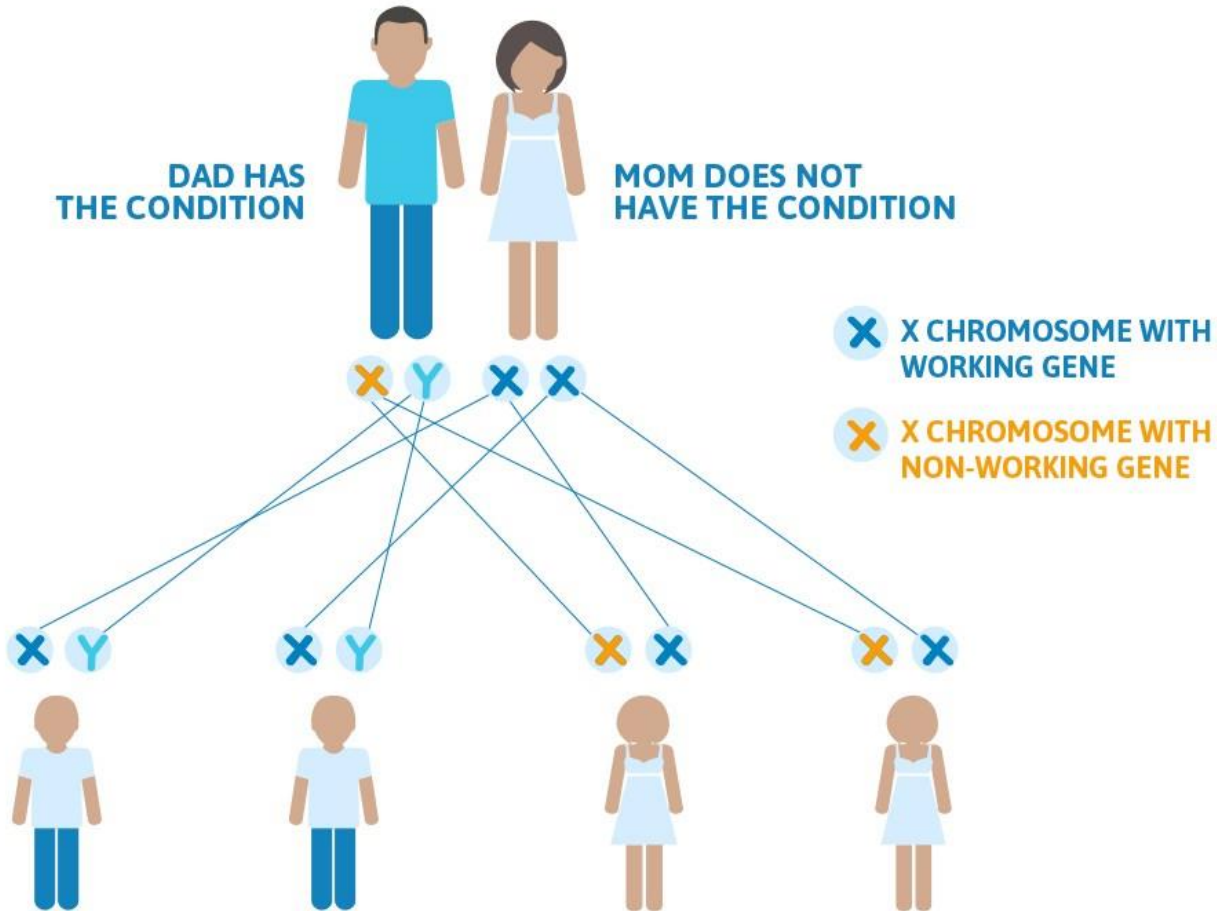
Autosomal Dominant

Autosomal Recessive



# X-Linked Recessive Inheritance

Father has the Condition



ALL SONS DO NOT HAVE THE CONDITION

ALL DAUGHTERS ARE CARRIERS BUT DO NOT HAVE THE CONDITION\*

\*THERE ARE EXCEPTIONS TO THIS. SOME FEMALE CARRIERS OF X-LINKED RECESSIVE CONDITIONS MAY HAVE SYMPTOMS. ONE EXAMPLE OF THIS IS FRAGILE X SYNDROME

## Common Inheritance Patterns

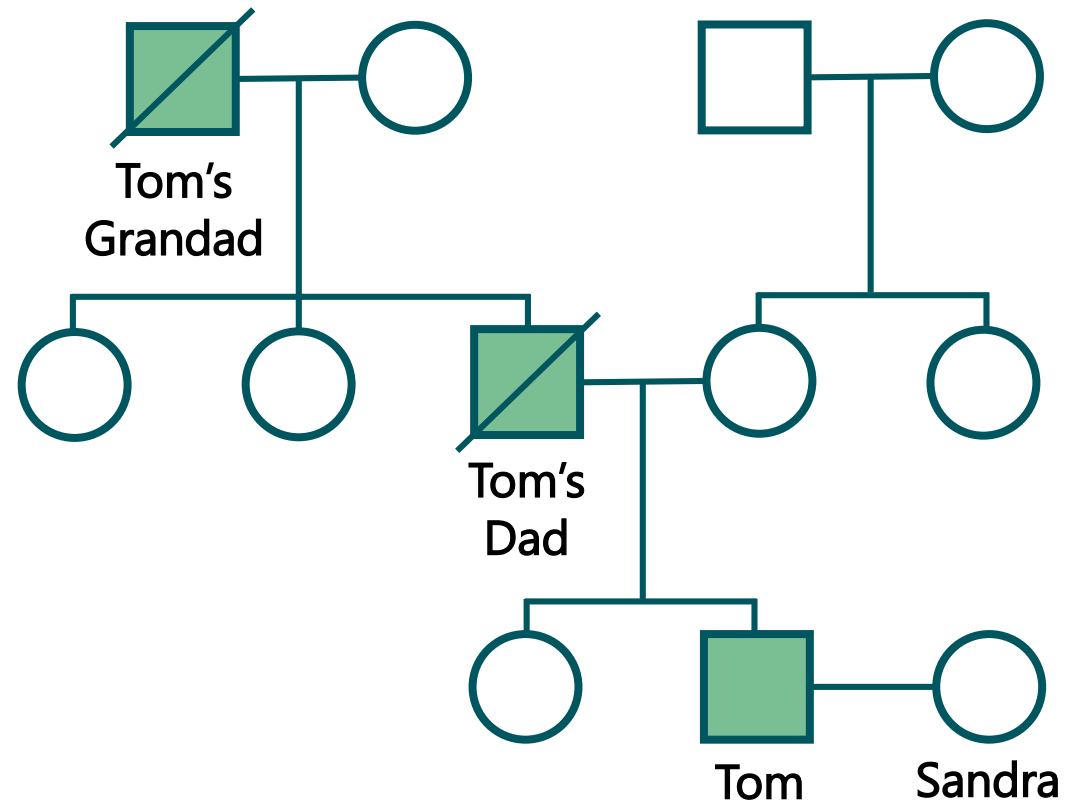
Autosomal Dominant

Autosomal Recessive

X-Linked Recessive

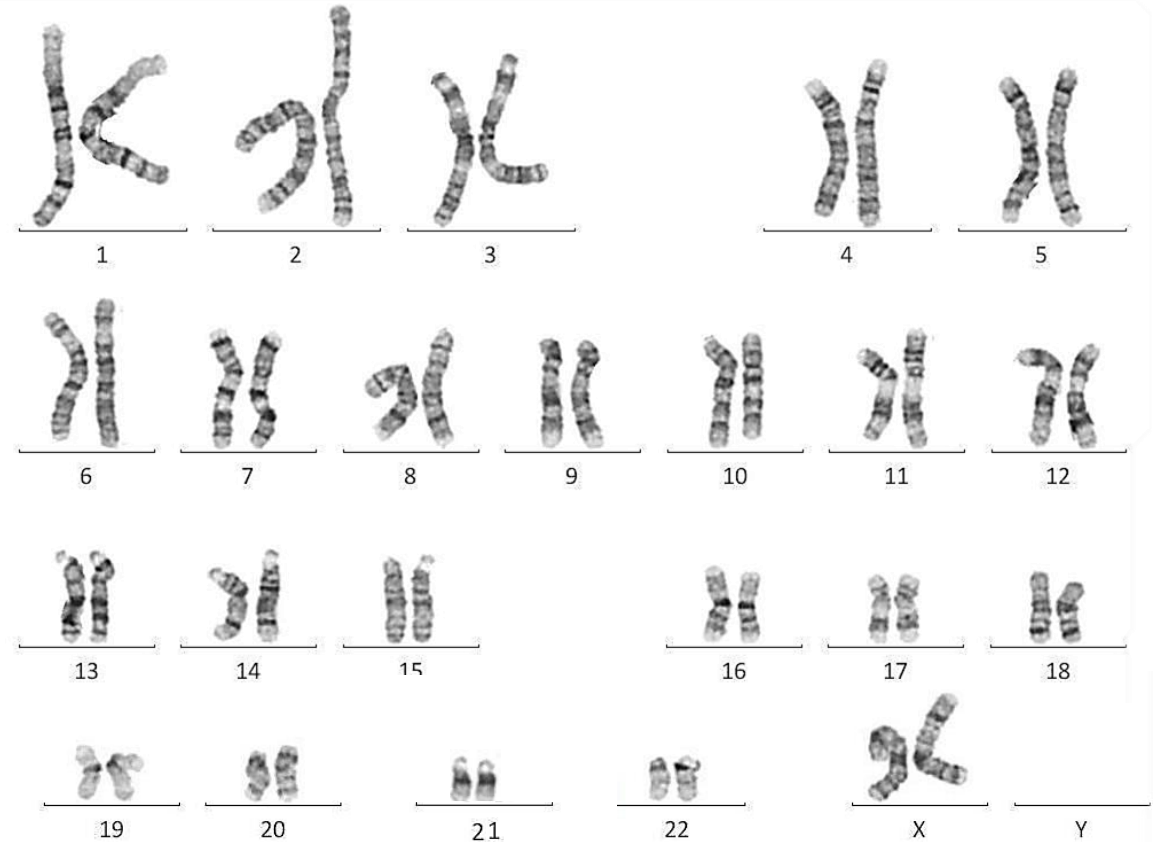
# The Genetics Consultation

Tom books in to see a genetics team, meeting with a genetic counsellor and clinical geneticist to discuss his options for genetic testing and family planning. They first ask about his family history:



# Genetic Testing Options

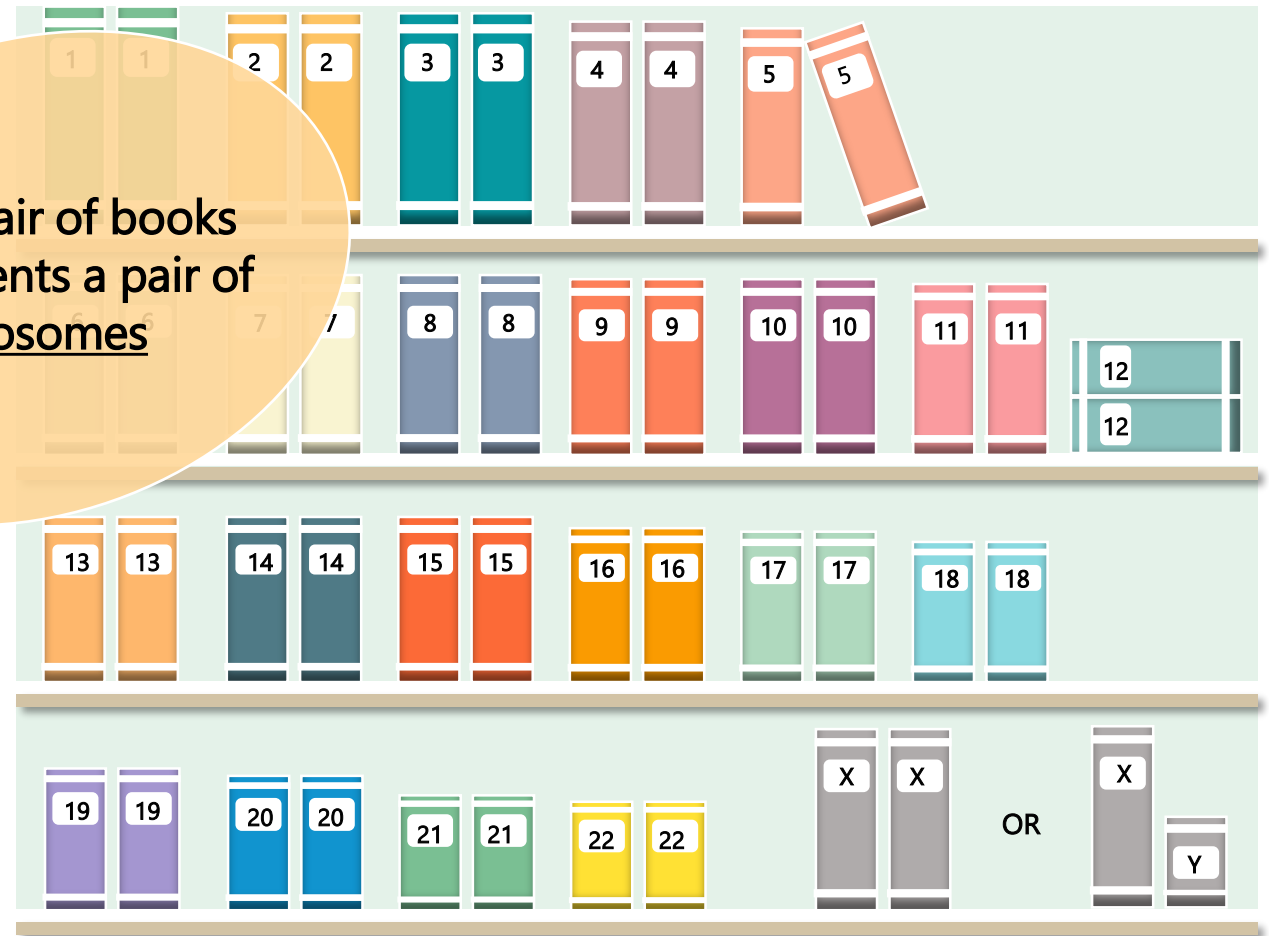
Next the genetics team discusses what options are available for Tom to try to identify the genetic variant that has caused his Retinitis Pigmentosa.



# Genetic Testing Options

Next the genetics team discusses what options are available for Tom to try to identify the genetic variant that has caused his Retinitis Pigmentosa.

Each pair of books represents a pair of chromosomes



## Genetic Testing Options

Next the genetics team discusses what options are available for Tom to try to identify the genetic variant that has caused his Retinitis Pigmentosa.

Each chapter represents one gene.  
A gene is a set of instructions for one thing that our body needs.



### Chapter 1: RHO Rhodopsin

Forms part of the light sensing cells at the back of the eye

# Single Gene Test



## Genetic Testing Options

Next the genetics team discusses what options are available for Tom to try to identify the genetic variant that has caused his Retinitis Pigmentosa.

Many chapters often work together to ensure that our body is functioning correctly



### Chapter 1: RHO Rhodopsin

Forms part of the light sensing cells at the back of the eye



### Chapter 2: USH2A Usherin

Helps support and maintain the light sensing cells

# Multi-Gene (Panel) Test

## Genetic Testing Options

Next the genetics team discusses what options are available for Tom to try to identify the genetic variant that has caused his Retinitis Pigmentosa.

Sometimes when a condition is not well understood or very rare, we might need to look at all the chapters to find an answer



*Whole Exome/Genome Sequencing*

# Genetic Testing Options

There are different types of results that Tom can expect from his testing:

How likely is it that we'll find out what's causing my condition?

We find the genetic variant that is causing Tom's condition. This result can be used to help estimate risk for a future pregnancy

We find a variant of uncertain significance. We have enough information to know if this is Tom's condition and therefore can provide information to help us understand risk for a future pregnancy

50-80%  
chance

We find the genetic variant that is causing Tom's condition. This result does not provide information to help us understand risk for a future pregnancy



# Reproductive Carrier Screening

While at the clinic, Tom and Sandra talk about wanting to start a family and the team explain that they might want to also think about reproductive carrier screening.



## Autosomal Recessive

Both parents need to be carriers

25% chance of an affected child

## X-Linked

Only the mother needs to be a carrier

Sons have a 50% chance of being affected

## Reproductive Carrier Screening

While at the clinic, Tom and Sandra talk about wanting to start a family and the team explain that they might want to also think about reproductive carrier screening.



A recent guideline from the Royal Australian & New Zealand College of Obstetricians and Gynaceologists (RANZCOG) recommends that reproductive carrier screening be offered to all women planning a pregnancy or in their first trimester.



- Because X-linked conditions are carried by the female partner, testing is usually started in her to look for both X-linked and recessive conditions.
- If she is found to be a carrier of a recessive condition, her male partner will be tested to see if he is a carrier of the same condition.
- Alternatively, couples can be tested at the same time





## Reproductive Carrier Screening

While at the clinic, Tom and Sandra talk about wanting to start a family and the team explain that they might want to also think about reproductive carrier screening.



### *Target Screening:*

Only looks at conditions that are common in those of particular ethnic backgrounds:

- For those of a Caucasian background, often three conditions (cystic fibrosis, spinal muscular atrophy, and fragile X) are tested
- For those of an Ashkenazi Jewish background more than 200 conditions that have an increased prevalence in their community may be tested.



## Reproductive Carrier Screening

While at the clinic, Tom and Sandra talk about wanting to start a family and the team explain that they might want to also think about reproductive carrier screening.



### *Expanded Screening:*

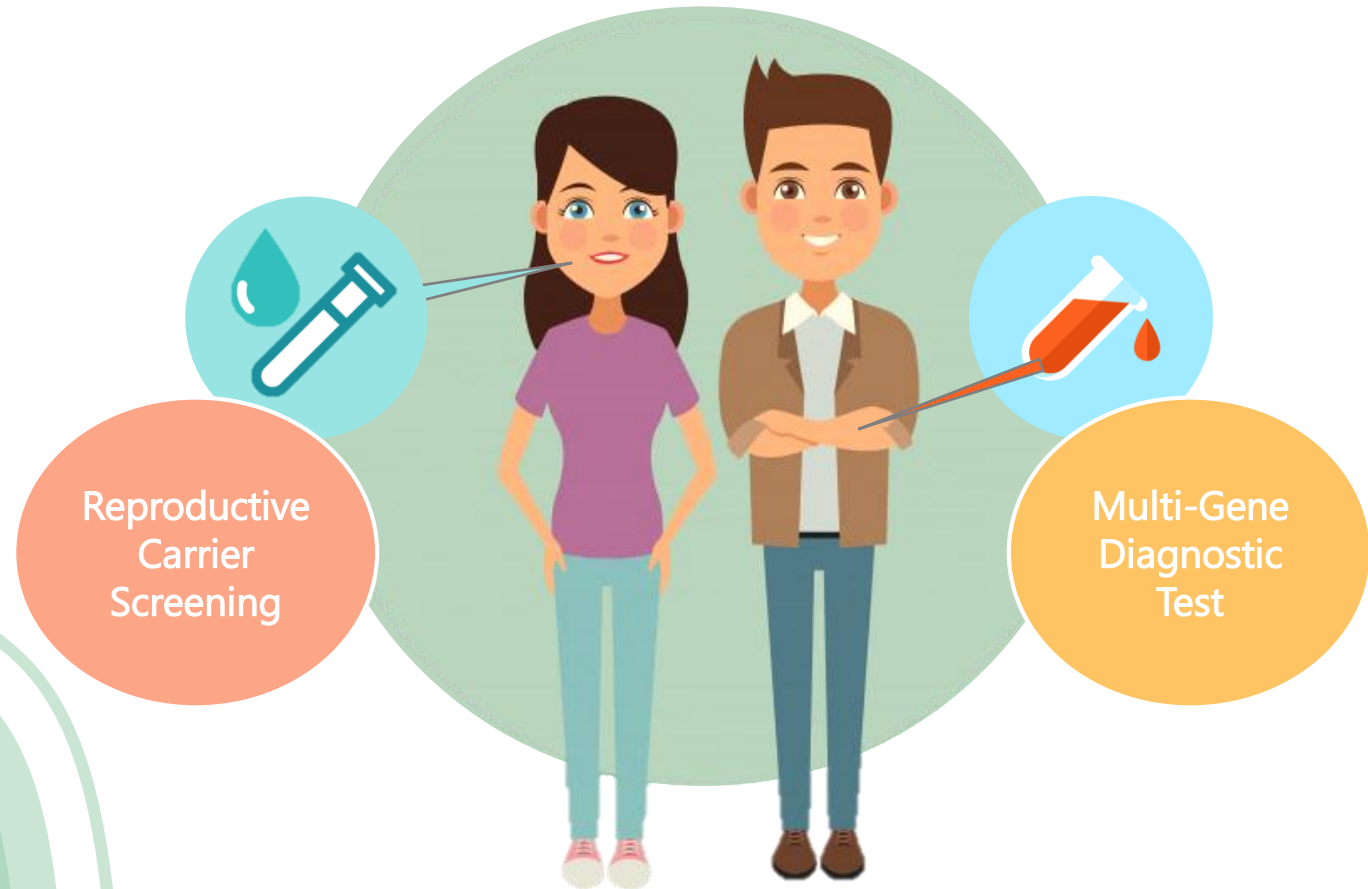
Takes a much broader approach and looks at many hundreds of conditions in a single test:

- Applicable for an increasing pan-ethnic (diverse) population
- Covers many severe or life-limiting conditions
- Also includes some more variable conditions, where the outcome for a child may be difficult to predict.
- Some conditions may have implications for carriers



# Making a Decision

Tom and Sandra discuss all their options and decide what testing they want to have.



## Receiving Results

Sandra's results are available first, let's see what they are

Reproductive  
Carrier  
Screening



Sandra's result comes back with a **negative** result

A negative result means there is only a small residual risk that Sandra is a carrier

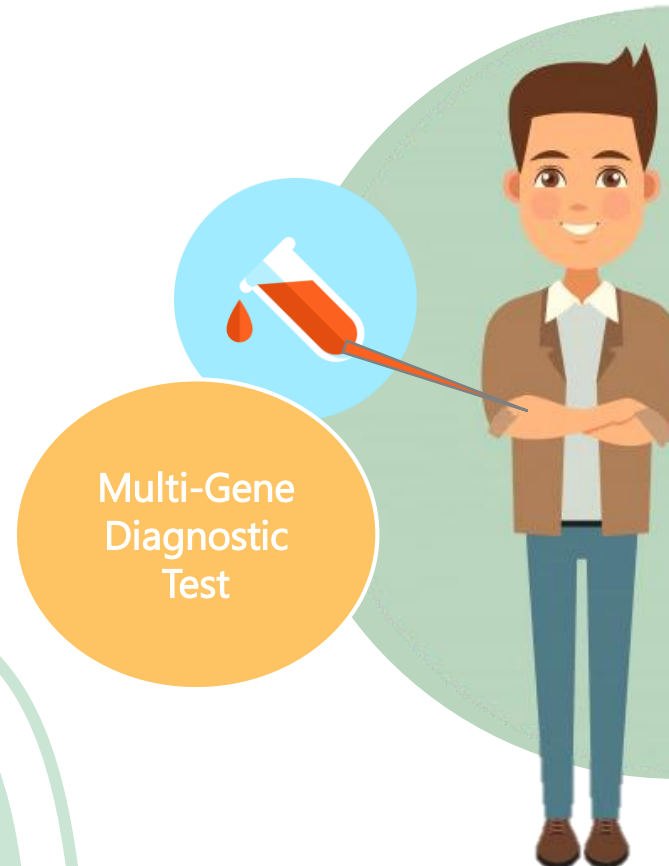
About 75% of patients are expected to receive a normal results like Sandra.

About 25% are expected to be identified as carriers of one condition. Some people will be identified as carriers of multiple conditions

Of those identified as carriers, <1% of those are expected to have a partner that is a carrier of the same condition.

## Receiving Results

Tom's results are now available first, let's see what they are



Tom is found to have a pathogenic variant in RHO


RHO is the most common cause of autosomal dominant RP

The chance that Tom will pass this onto his children is **50%**



# Family Planning Options

Tom has a 50% of passing Retinitis Pigmentosa onto his children. Let's think about what Tom and Sandra need to know next...




What are our options?

- Natural conception without further testing
- Natural conception with testing during pregnancy
- IVF with preimplantation genetic diagnosis
- Sperm donor
- Adoption

# Family Planning Options

Tom has a 50% of passing Retinitis Pigmentosa onto his children. Let's think about what Tom and Sandra need to know next...



What are our options?

## ● Natural conception without further testing

Retinitis pigmentosa is a condition that varies in severity, even within family members that have the same causative variant.

Therefore if a child does inherit Tom's variant, there is no way to know how severely they may be affected.

Tom and Sandra need to make a personal decision about whether they think the condition is severe enough to consider their options for prevention.

Let's explore what these options are...

# Family Planning Options

Tom has a 50% of passing Retinitis Pigmentosa onto his children. Let's think about what Tom and Sandra need to know next...

Can we support a child with special needs?

Are there treatment options available?



Is it life-limiting?

What is the impact on quality of life?

## ● Natural conception with testing during pregnancy

Testing during pregnancy serves two purposes.

1. Early diagnosis
  - Early intervention
  - Preparation for the birth of a child with special needs
2. Option for terminated an affected pregnancy

Differences in perspective may exist amongst medical professionals and within families regarding the termination of a pregnancy based on the diagnosis of retinitis pigmentosa.

# Family Planning Options

If they decided to test during pregnancy they have two options to consider:

## Chorionic Villus Sampling (CVS)

- Between 11-13 weeks

## Amniocentesis

- From 15 weeks



RHO  
Genetic  
Variant

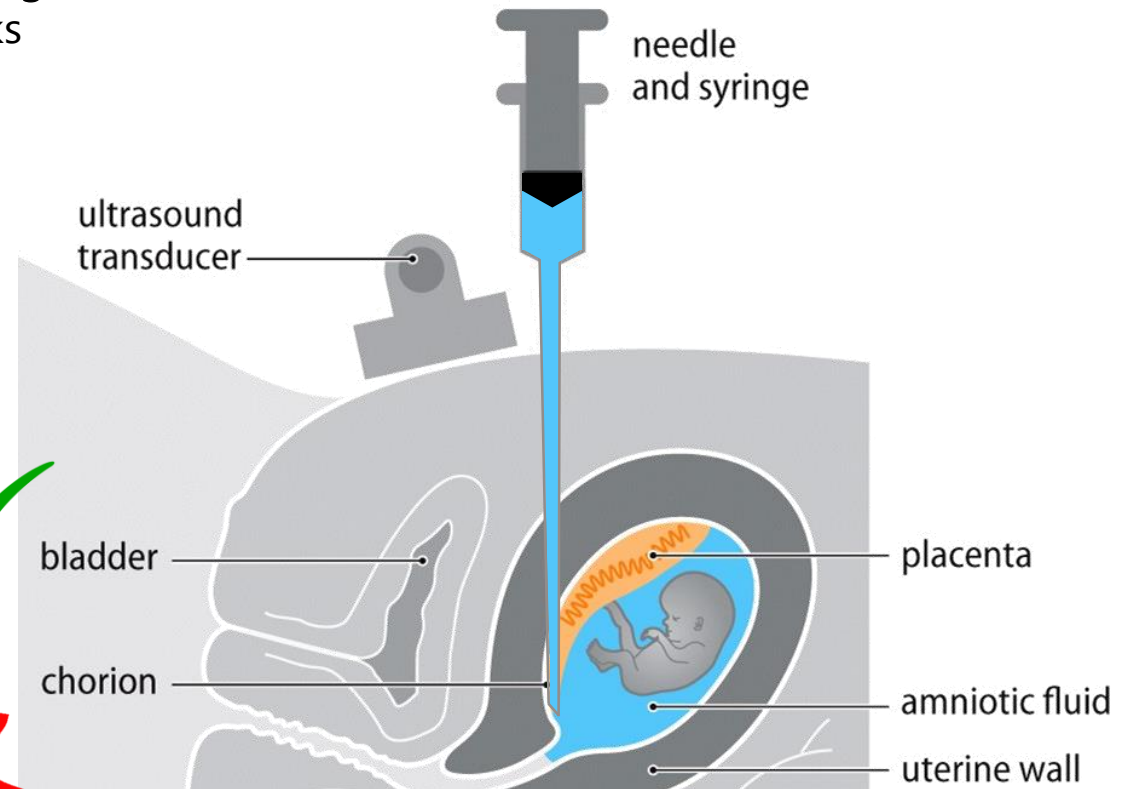


Figure 11.17a Genetics and Genomics in Medicine (© Garland Science 2015)

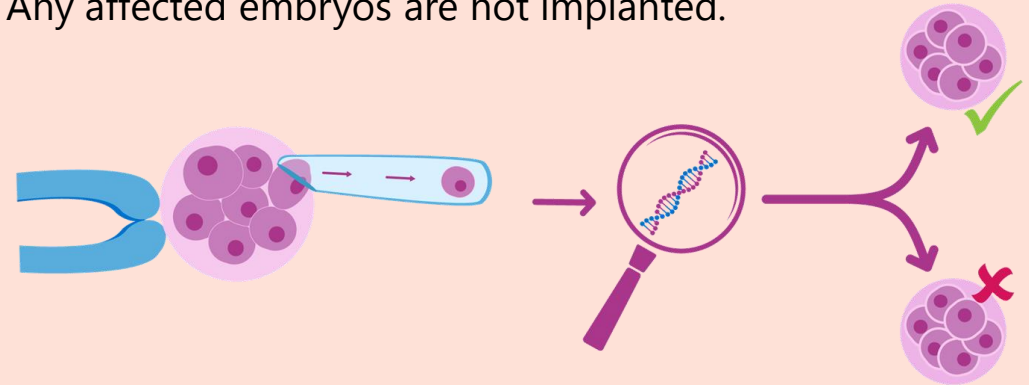
# Family Planning Options

Tom has a 50% of passing Retinitis Pigmentosa onto his children. Let's think about what Tom and Sandra need to know next...

What are our options?

## ● IVF with preimplantation genetic diagnosis

Pre-implantation genetic diagnosis involves testing a small number of cells from an embryo during the IVF process. Any affected embryos are not implanted.



IVF, even if there are no existing fertility problems is still not guaranteed to succeed.


Likely to be expensive

Image adapted from: <https://www.reproduccionasistida.org/la-reproduccion-asistida-permite-prevenir-enfermedades-geneticas/dgp-diagnostico-genetico-preimplantacional/>



# Family Planning Options

Tom has a 50% of passing Retinitis Pigmentosa onto his children. Let's think about what Tom and Sandra need to know next...



What are our options?

## ● Use a donor sperm

For many genetic conditions using a donor egg or sperm is an option.

In particular, if the causative genetic variant isn't known, would be the alternative to PGD.

## ● Adoption

Couples that are at risk can consider alternative ways of forming a family, such as adoption.

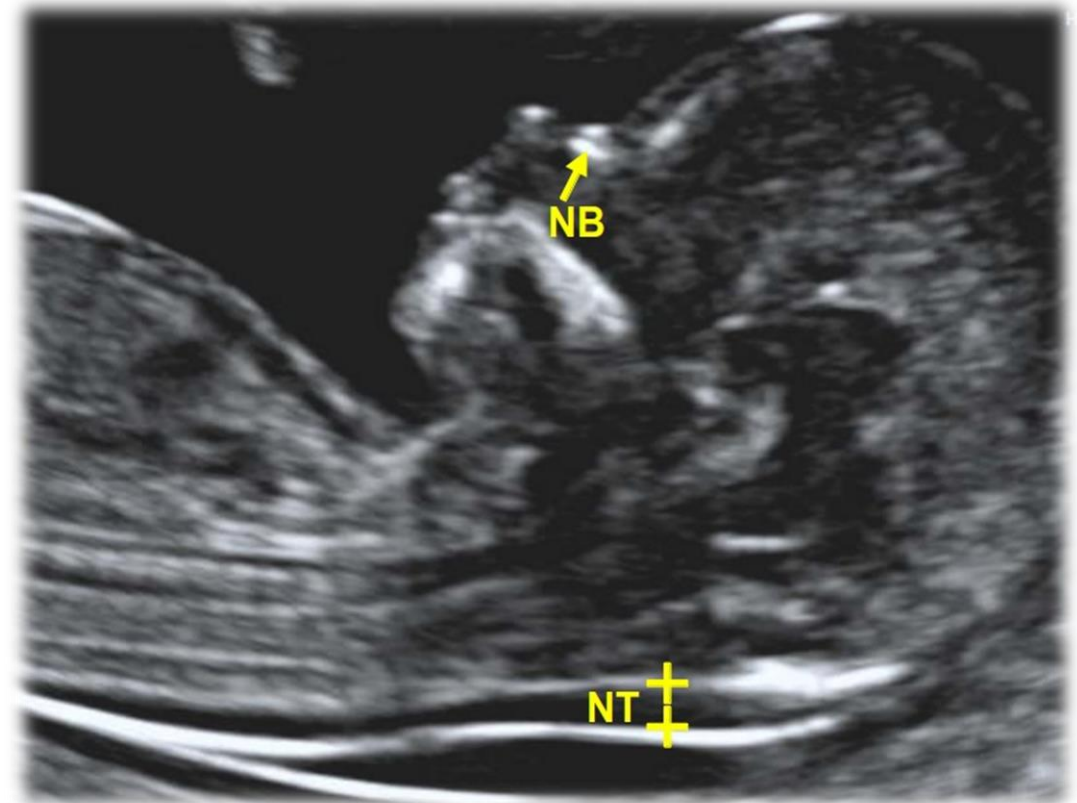
# First Trimester Screening

Sandra is pregnant!



From 12-14 weeks it is recommended to have a first trimester ultrasound to check early development

B-hcg  
PAPP-A



Accuracy 80-90%

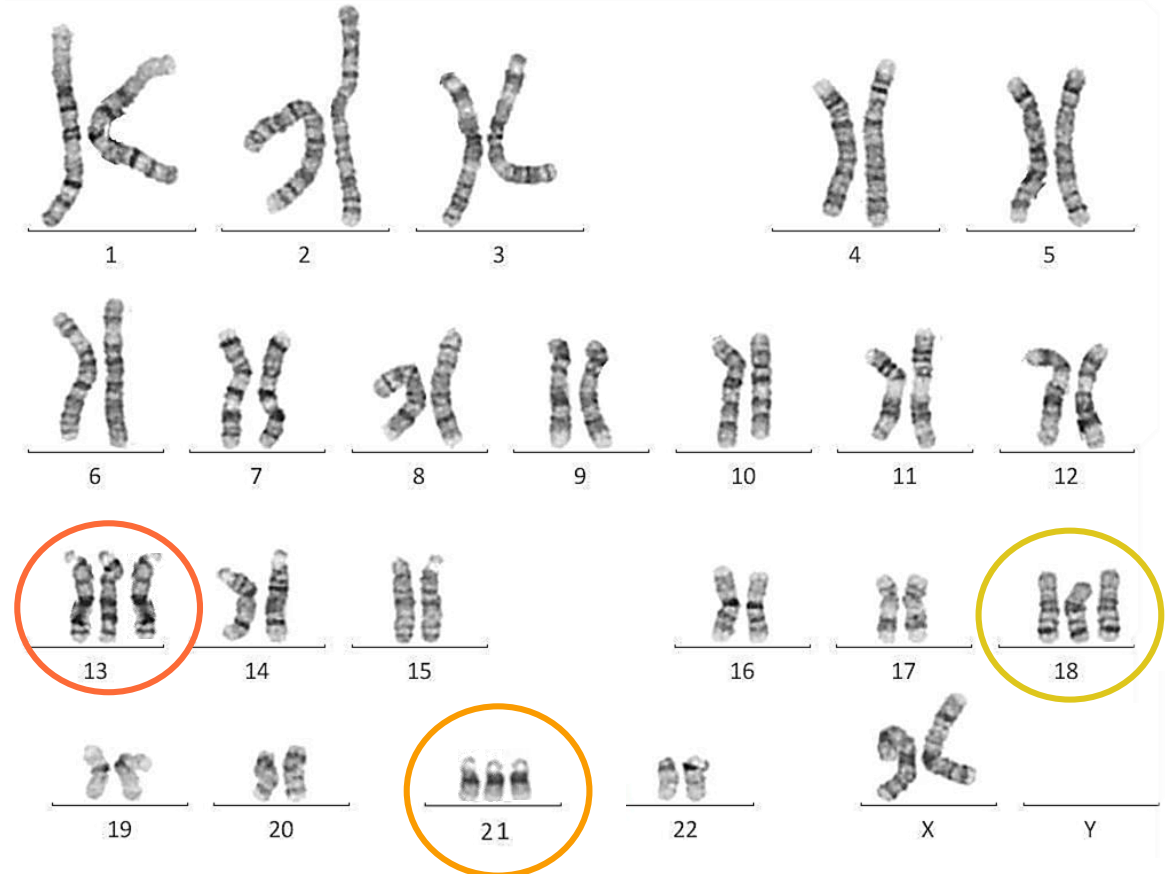
# First Trimester Screening

Sandra is pregnant!

Trisomy 21  
Down  
Syndrome

Trisomy 18  
Edward  
Syndrome

Trisomy 13  
Patau  
Syndrome



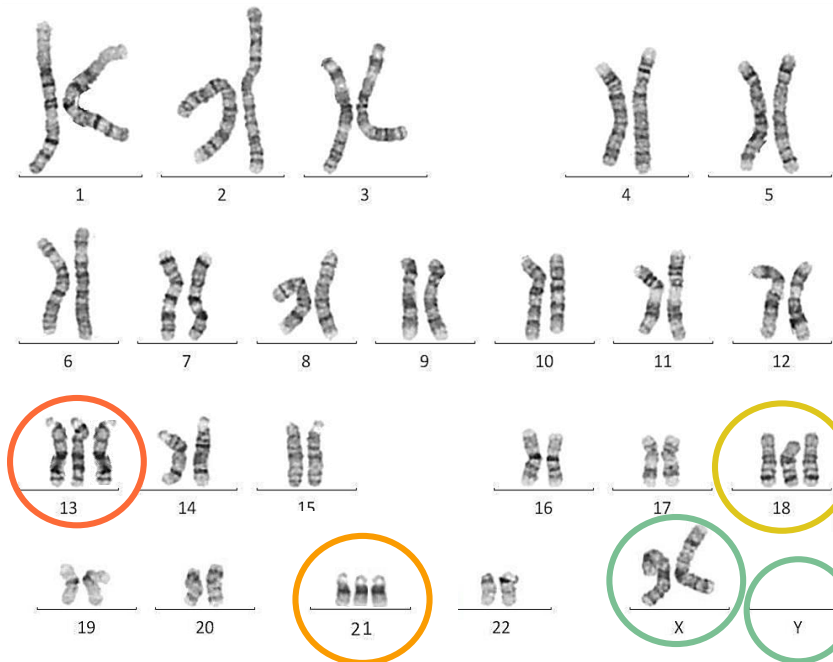
Accuracy 99%

# Non-Invasive Prenatal Screening (NIPS)

Sandra is pregnant!



T21 T18 T13



XX OR XY

Sex chromosome variations include XXY, XXX, and XYY



# Diagnostic Testing

If there were any high risk results or concerns as the pregnancy progresses, invasive testing may be used as a diagnostic test

## Chorionic Villus Sampling (CVS)

- Between 11-13 weeks

## Amniocentesis

- From 15 weeks



Microarray  
Panel Test  
WGS

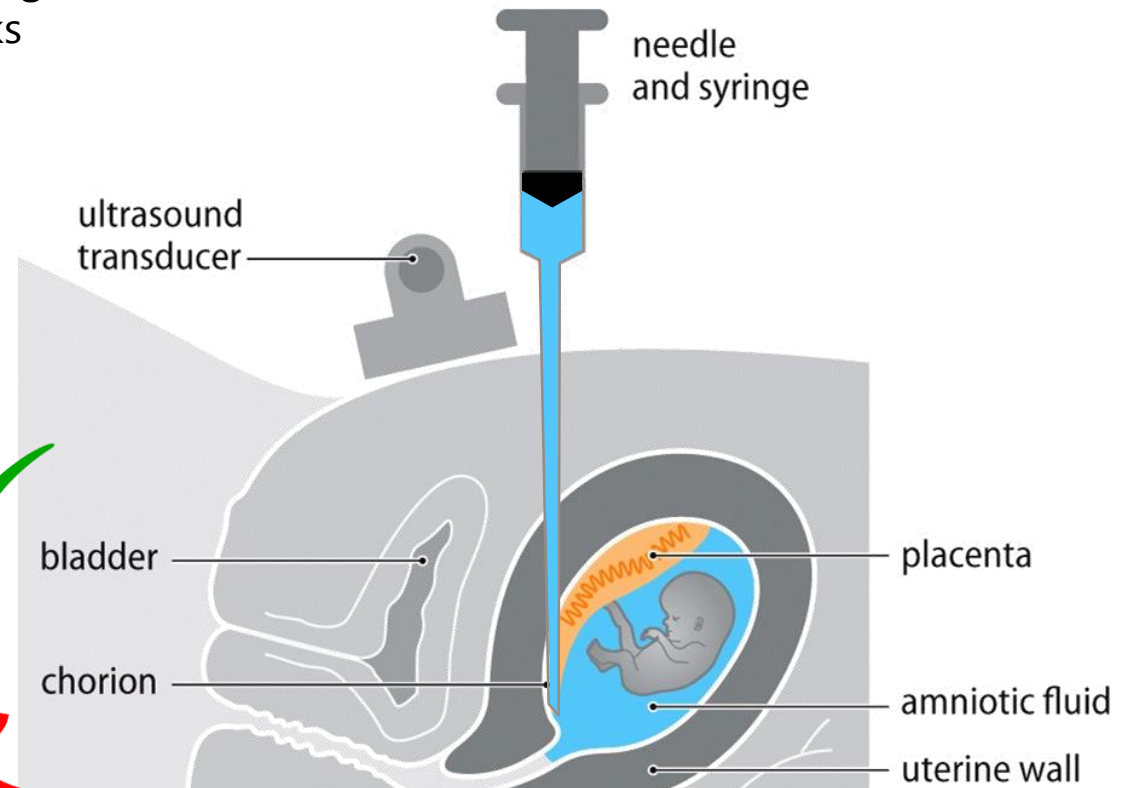
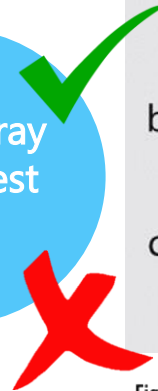


Figure 11.17a Genetics and Genomics in Medicine (© Garland Science 2015)

# Summary

## Family history of genetic disease

Single gene test	●	Understanding your risk of an affected child.
Multi-gene panel	●	
Whole genome sequencing	●	
IVF with PGD	●	Options for prevention
Prenatal diagnosis	●	

No known family history of genetic disease

Genetic testing before becoming pregnant:

● Reproductive carrier screening

Genetic testing during pregnancy:

● Nuchal translucency screening  
● NIPS  
● CVS  
● Amniocentesis

*There is no test that gives a 100% guarantee of a healthy baby*



Resources are available on [www.genetics.edu.au](http://www.genetics.edu.au) or by contacting:

The Centre for Genetics Education NSW Health  
Royal North Shore Hospital  
PO Box 317  
St Leonards NSW  
T: 02 9462 9599  
F: 02 9906 7529



Where to find more  
information



*Thank you !*