Inheritance patterns, recurrence risks and reproductive choices in centronuclear myopathies

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Inheritance patterns in Centronuclear Myopathies

- X-linked recessive
  - MTM1
- Autosomal Dominant
  - DNM2
- Autosomal Recessive
  - BIN1
  - RYR1

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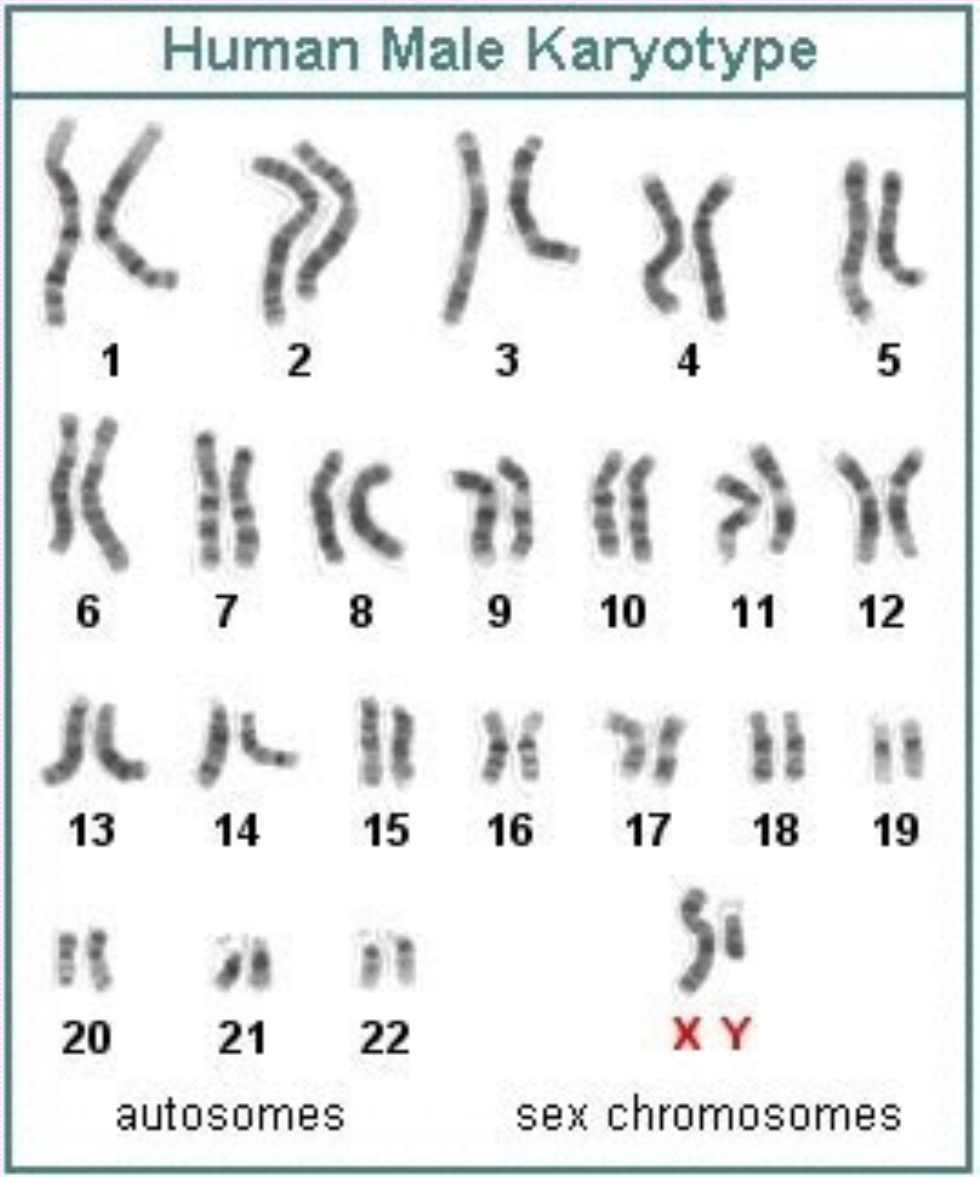

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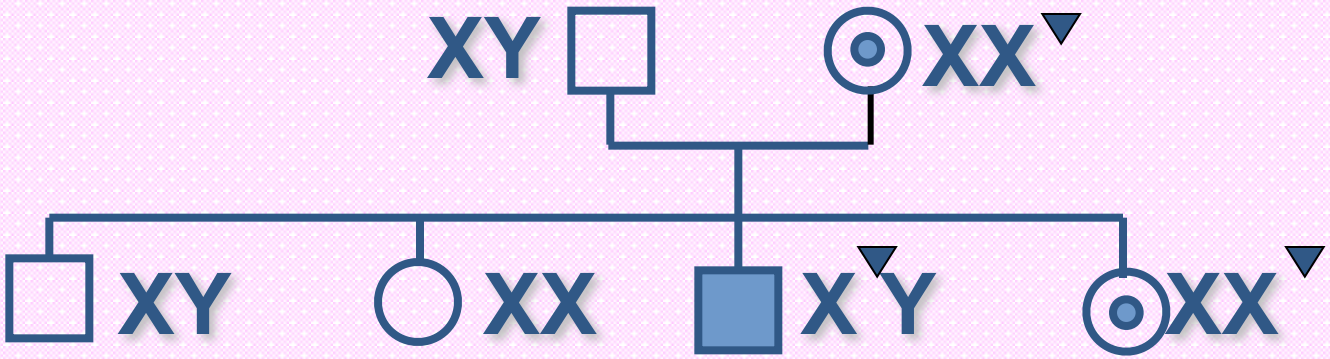
X linked recessive inheritance



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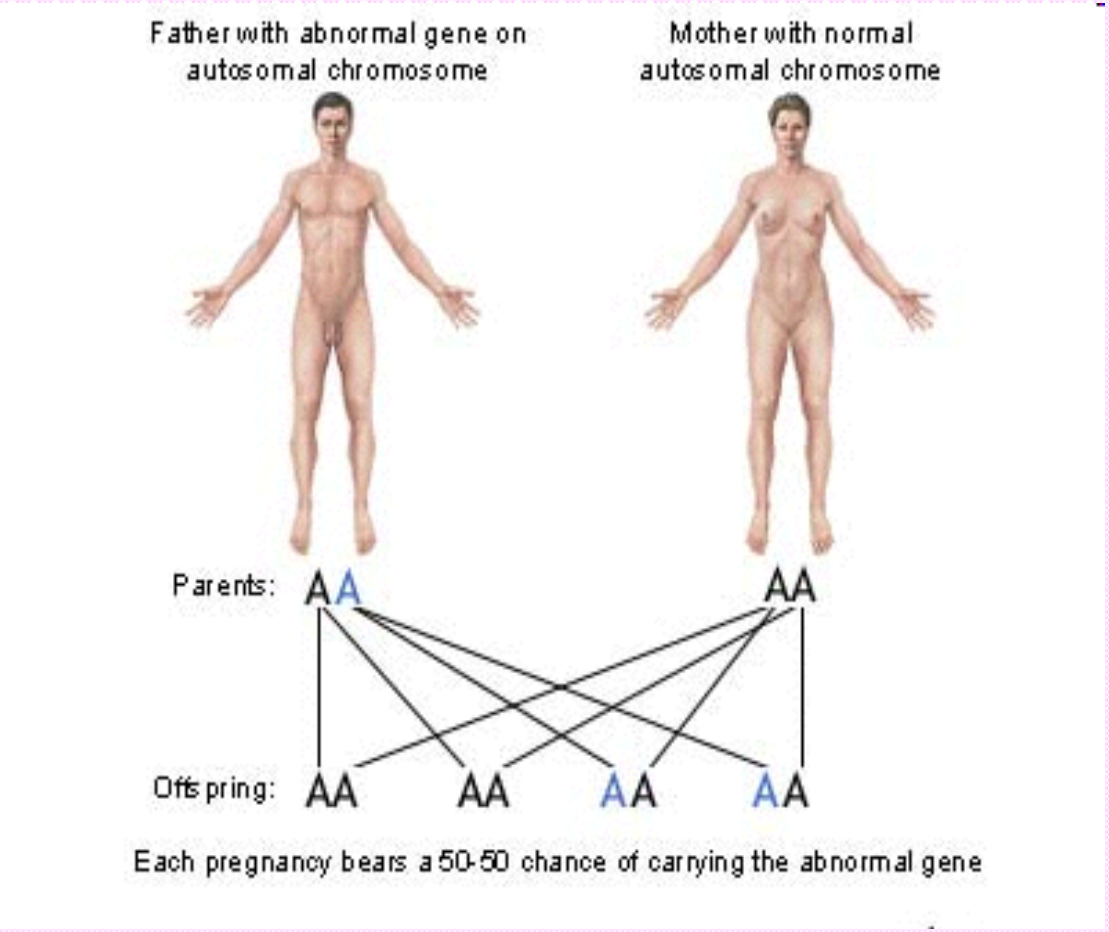
X-MTM Recurrence risks in future children

- For carrier mothers
  - 25% affected son
  - 25% carrier daughter
  - 25% unaffected son
  - 25% non-carrier daughter
- For non-carrier mothers
  - Germline mosaicism risk ~1%

Autosomal dominant inheritance

- Can be passed from parent to child
- Affects males and females equally
- Risk to offspring is 50% (I in 2)
- Variable expression (severity)
- Can only test if mutation known



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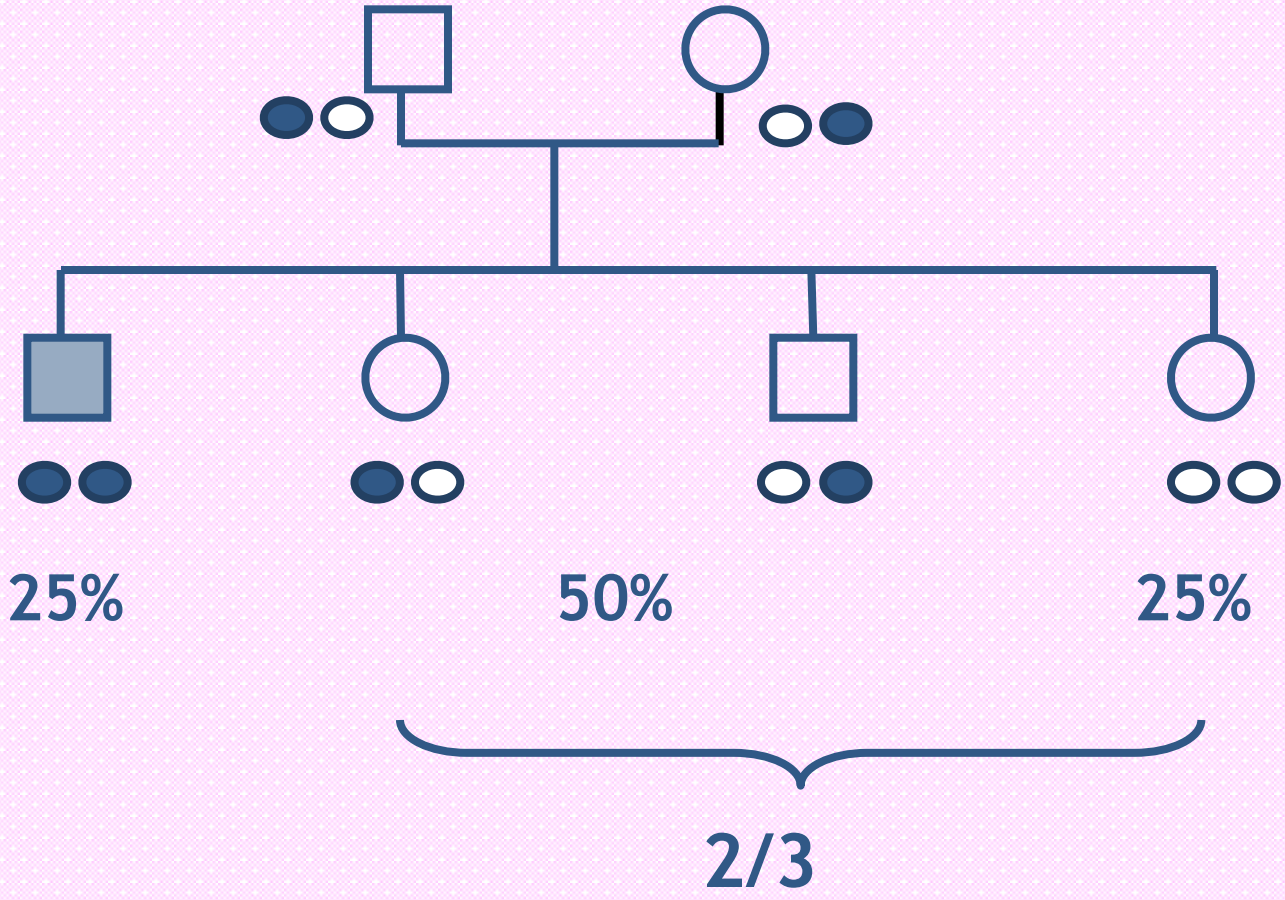
Autosomal Recessive



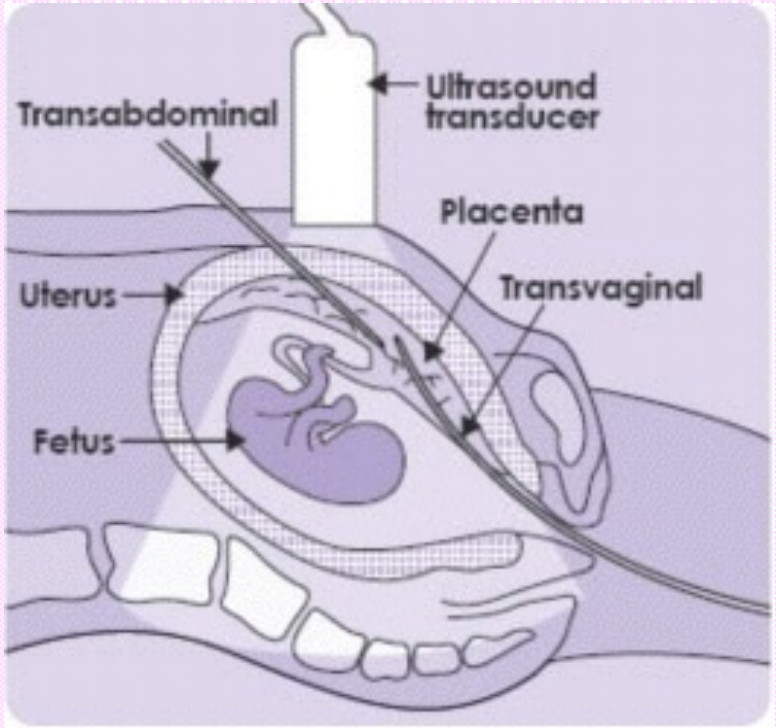
Reproductive options

- Testing a pregnancy (CVS, amnio)
- Pre-implantation genetic diagnosis
- Important factors
  - Personal Views
  - Religion
  - Cultural

Chorionic Villus Sampling

- 11+ weeks early result
- miscarriage rate 1-2%

- Definitive test but:
  - can fail
  - maternal contamination



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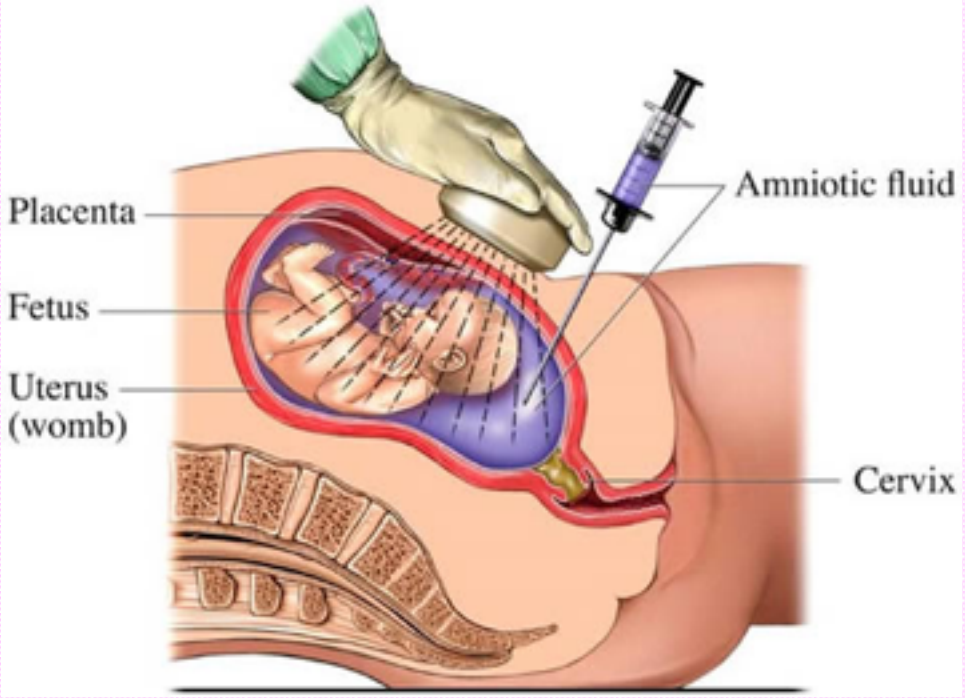
Amniocentesis

- 15-20 weeks
- Later result
- Lower miscarriage risk (0.5-1%)



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Modifying risk of invasive testing XMTM

- Free fetal DNA to sex the pregnancy
- Test done on a blood sample from the pregnant woman
- Only carry out CVS/Amnio on male pregnancy

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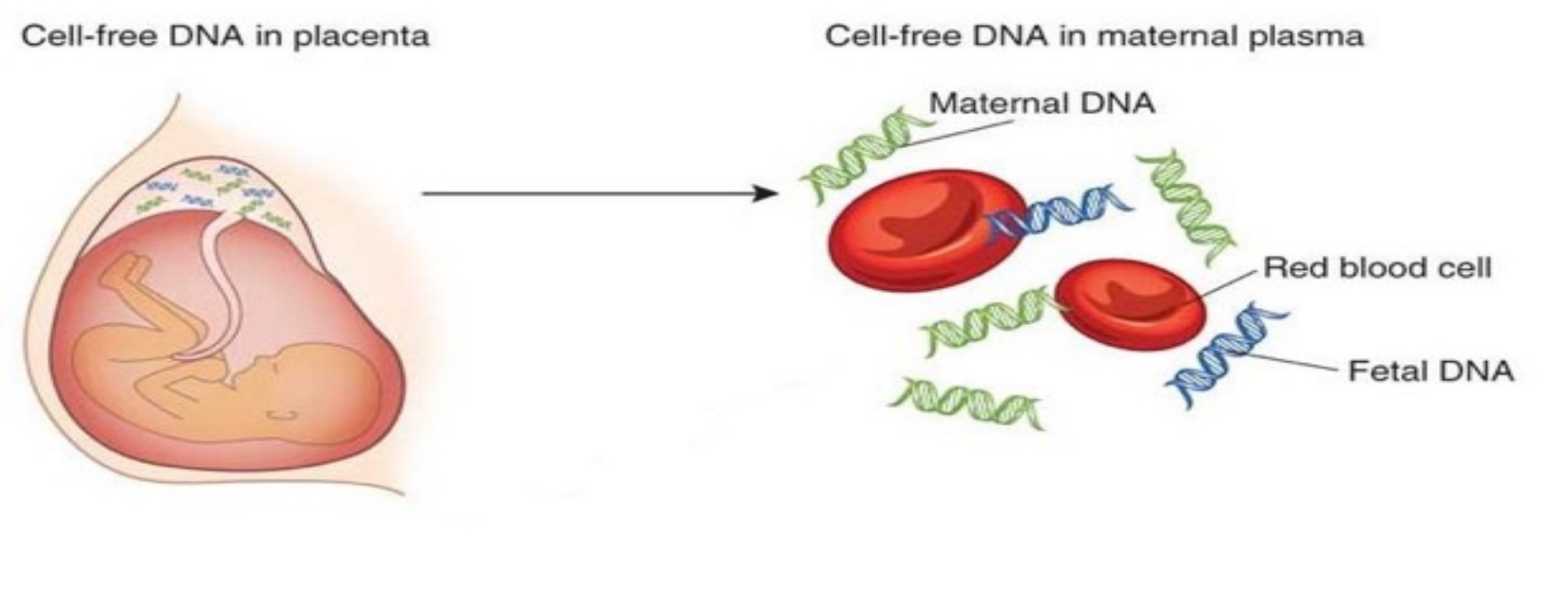
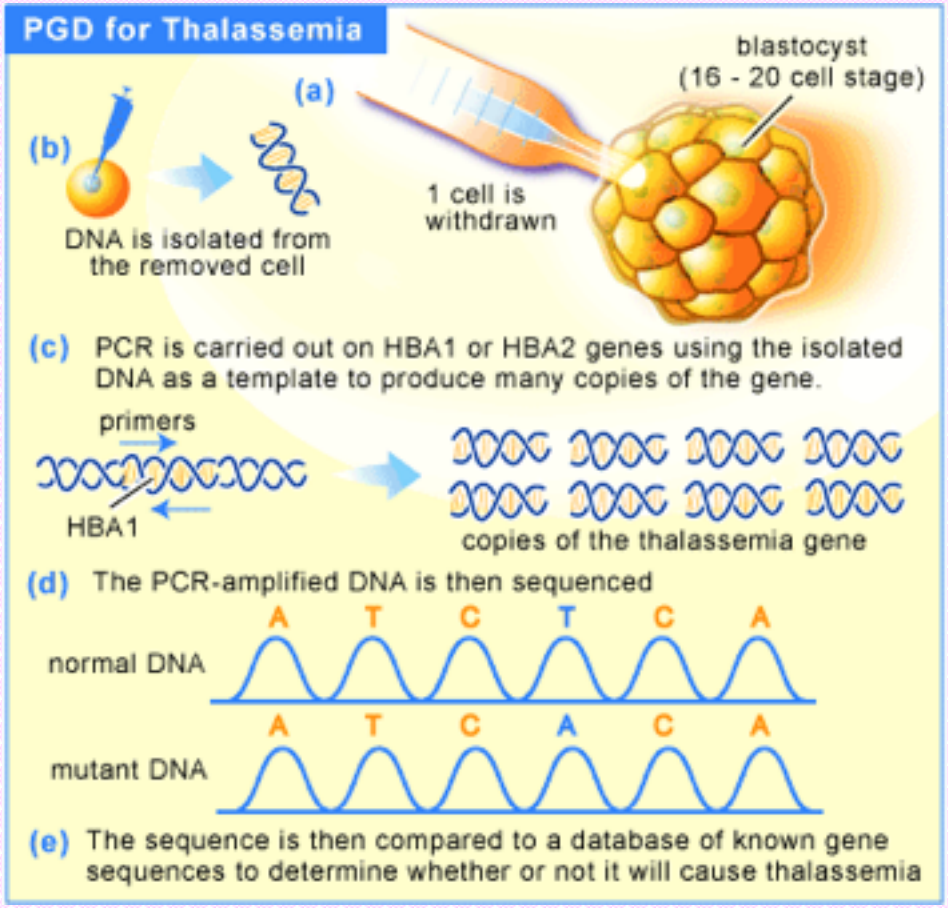
Prenatal Diagnosis – Free fetal DNA for sexing



Pre-implantation genetic diagnosis

- Avoids termination of pregnancy
- BUT
- 1 in 3 “take home baby rate”
- Expensive ~ £12-15,000
- Takes time to work up - ~12 months depending on license



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Questions