Inheritance patterns, recurrence risks and reproductive choices in centronuclear myopathies

Dr Meriel McEntagart
Consultant in Clinical Genetics, St George’s Hospital
meriel.mcentagart@stgeorges.nhs.uk
Inheritance patterns in Centronuclear Myopathies

- X-linked recessive
  - MTM1
- Autosomal Dominant
  - DNM2
- Autosomal Recessive
  - BIN1
  - RYR1
X linked recessive inheritance
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% (1 in 2)
- Variable expression (severity)
- Can only test if mutation known
Autosomal Recessive

2/3

25%

50%

25%

2/3
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
Amniocentesis

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