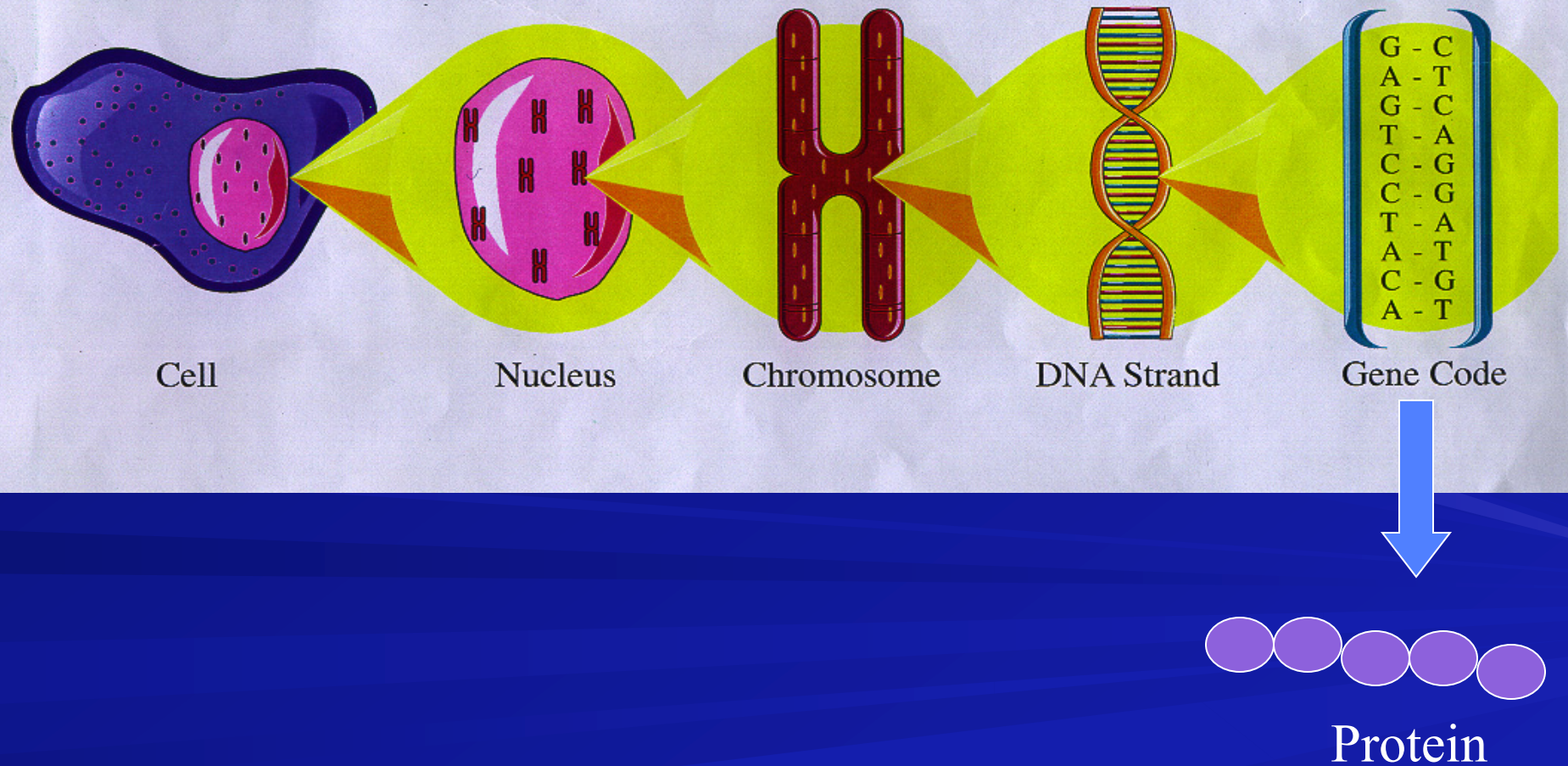


Inheritance of Dystroglycanopathies

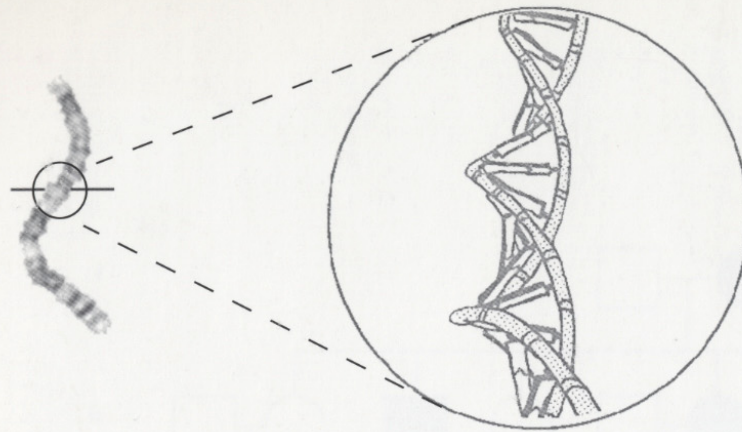
Christina Trout, RN, MSN
Iowa Neuromuscular Program
Pediatrics

From Cell to Protein



Genes & Proteins

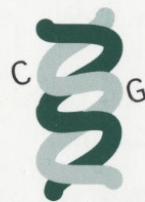
CHROMOSOME → GENE → PROTEIN PRODUCT



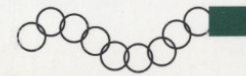
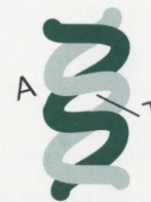
Each chromosome is composed of one large DNA molecule

A gene is a segment of DNA that makes a protein product

Normal gene



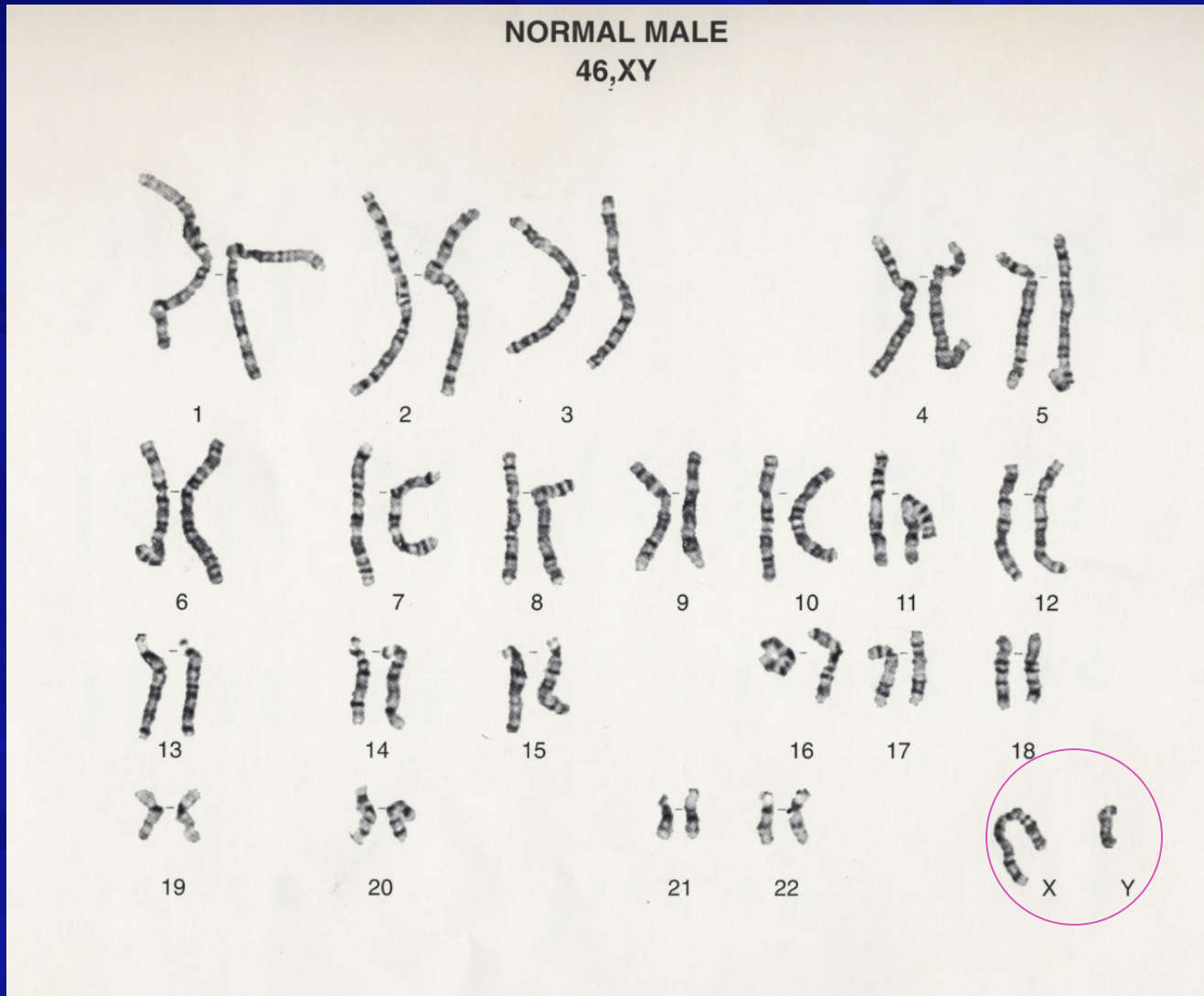
Working Protein



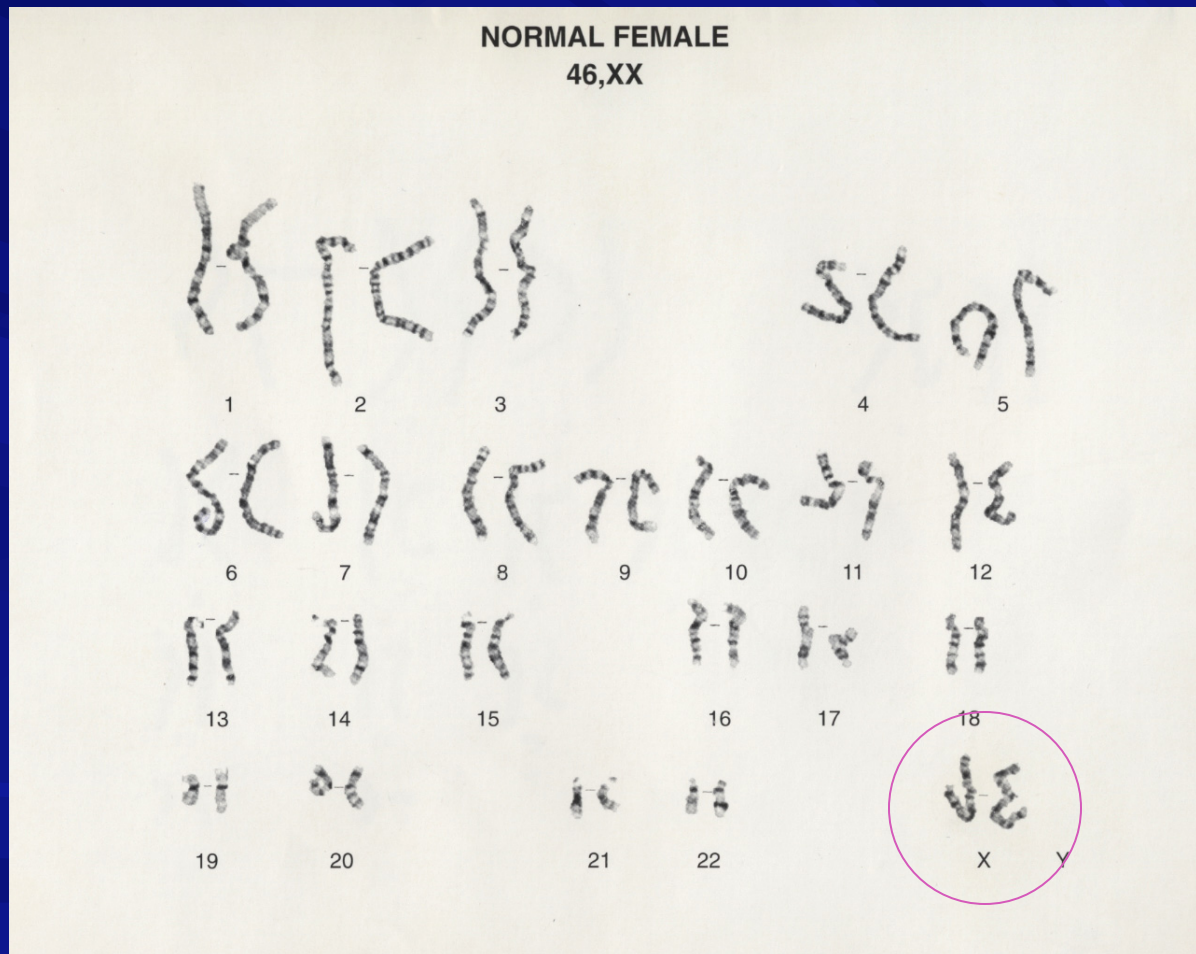
Non-working Protein

Gene with a (G to T) mutation
(message has changed)

Males have 1 X chromosome



Females have 2 X chromosomes

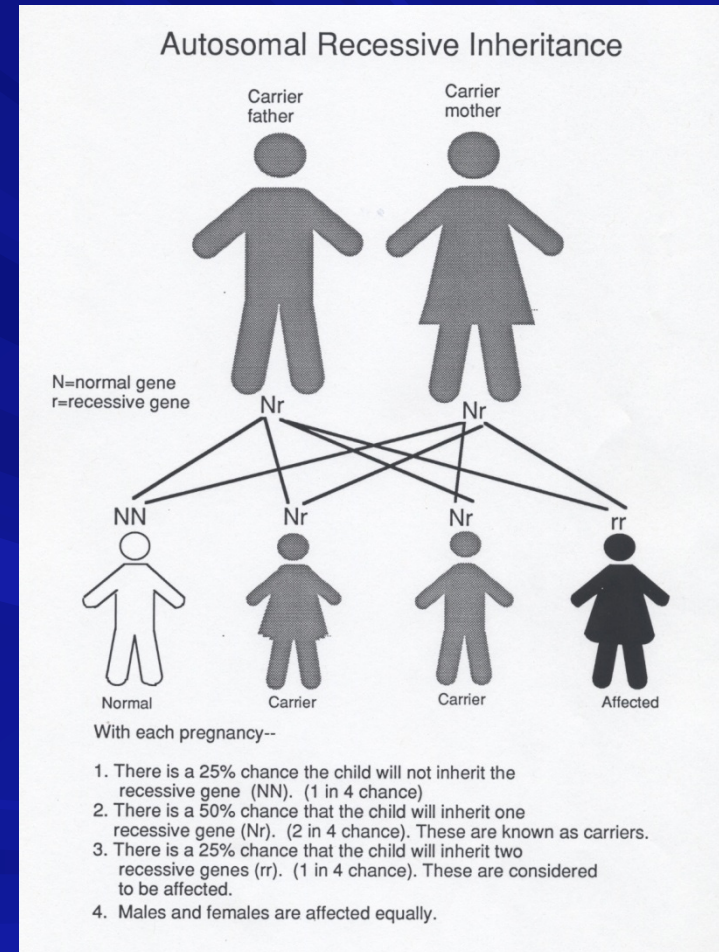


Autosomal Recessive Inheritance

- Most Limb-girdle muscular dystrophies
- Most congenital muscular dystrophies
- **Genes associated with dystroglycanopathy**
 - LARGE
 - FKRP
 - FKTN
 - POMGnT1
 - POMT1
 - POMT2
 - ISPD

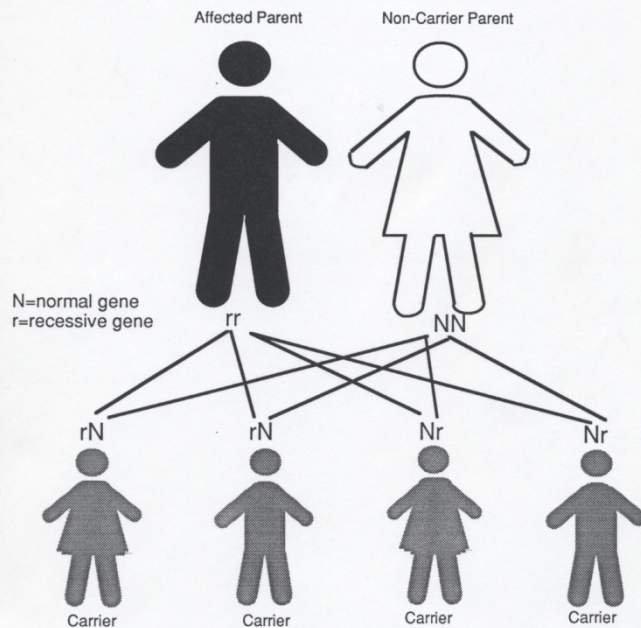
Autosomal Recessive Inheritance

- Males and females are affected equally
- Both parents are carriers
- $\frac{1}{4}$ chance that carrier parents will have an affected child
- If not affected, the offspring have a $\frac{2}{3}$ chance to be carriers



Autosomal Recessive Inheritance: One parent is affected

Autosomal Recessive Inheritance:
One parent affected



With each pregnancy---

1. Either parent can be affected--male or female.
2. All children will be carriers (Nr or rN)
3. Carriers can be male or female.

■ All the offspring will be carriers

– Unless the other parent is affected or a carrier (unlikely)

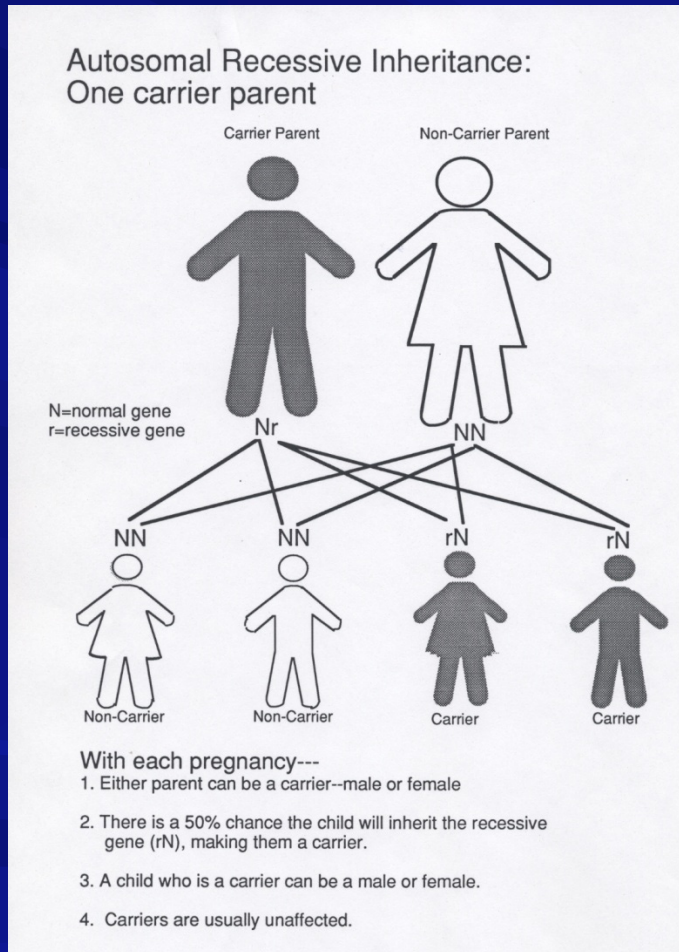
– Carrier testing of the other parent is recommended for common conditions!!

■ 1:40 are SMA carriers

■ 1:110 are F-ataxia carriers

■ 1:400?? Are carriers for more rare forms of MD

Autosomal Recessive Inheritance: One parent is a carrier



- Unlikely to have affected children, unless the other parent is a carrier
- We all are carriers of 4-6 recessive genetic conditions

Prenatal Genetic Diagnosis

■ Preconception

- Genetic counseling—know the chances!

■ Prenatal testing

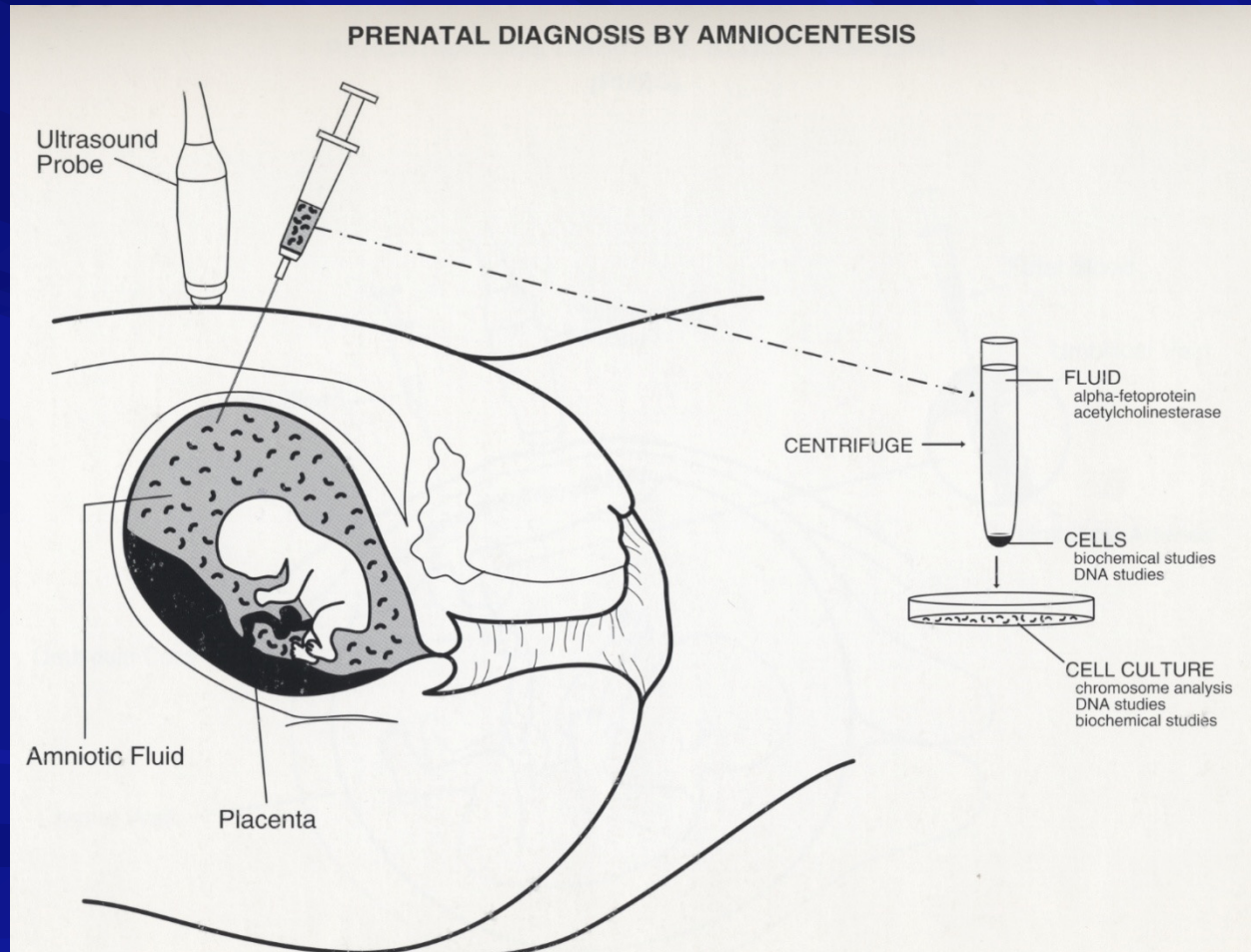
- Amniocentesis around 15 weeks
- Chorionic villus sampling (CVS), 12 weeks

■ Pre-implantation Genetic Diagnosis (PGD)

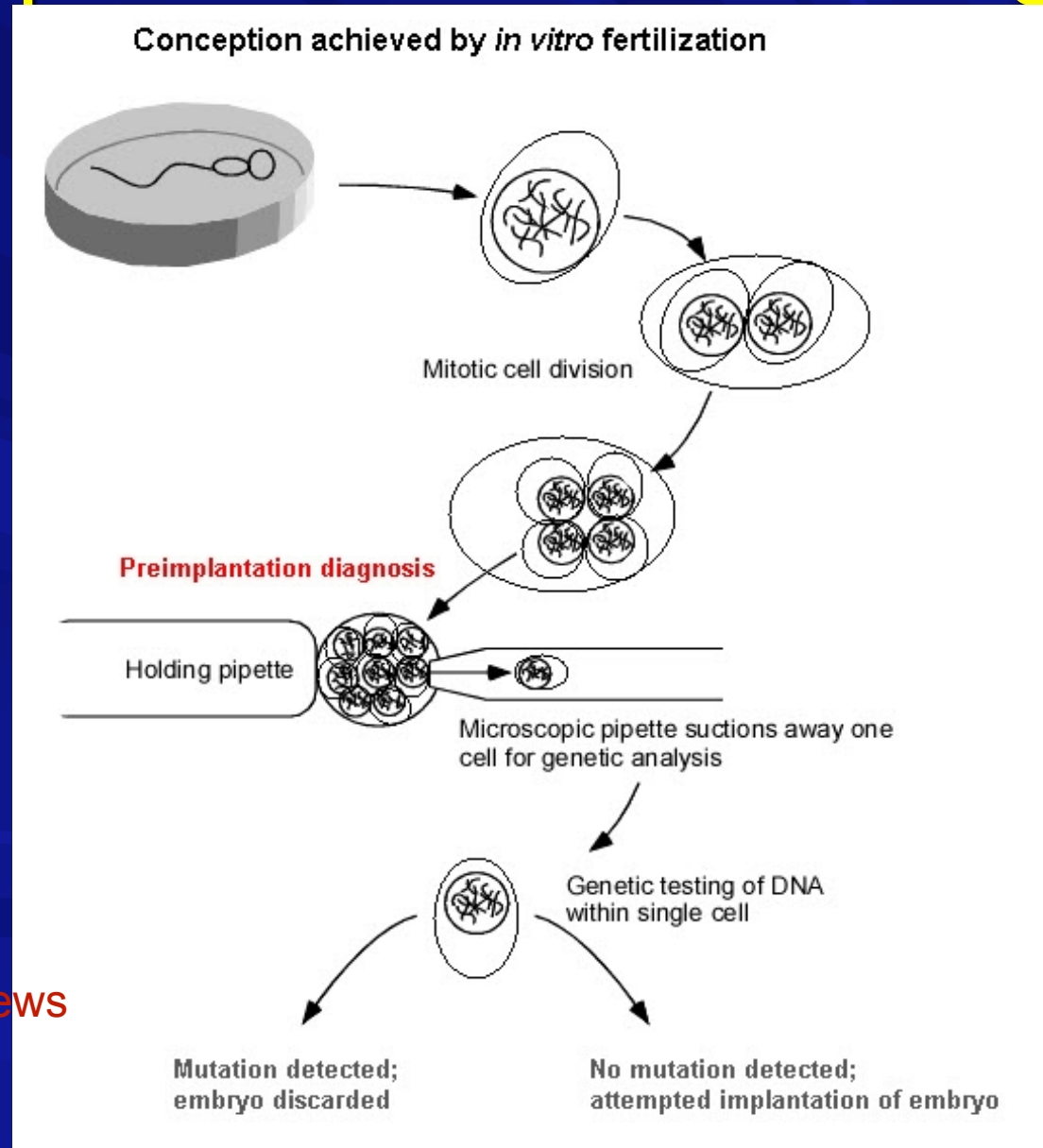
■ Donor eggs/sperm/embryos

■ Newborn screening??

Prenatal Testing



Preimplantation Genetic Diagnosis



From GeneReviews
glossary

Genetic Resources

■ Genetics Home Reference - Handbook

– <http://ghr.nlm.nih.gov/handbook/howgeneswork>

- Cells and DNA
- How genes work
- Mutations and health
- Inheritance

■ Gene Reviews – reviews LGMD & CMD

– <http://www.ncbi.nlm.nih.gov/sites/GeneTests/review?db=GeneTests>

- Characteristics, diagnostic testing, management, inheritance