# Patterns of inheritance

Prof. Dr. Mohammed A. Younis
Tikrit University
College of Medicine
Pediatrics Department

# Patterns of inheritance

The objectives of this presentation are to:

- Understand how genes are inherited
- Understand the differences between the inheritance patterns associated with Autosomal dominant, Autosomal recessive, X-linked recessive and chromosomal abnormalities
- Understand that the environment can impact on some common complex conditions

# Karyotypes

- To analyze chromosomes, cell biologists photograph cells in **mitosis**, when the chromosomes are fully condensed and easy to see (usually in **metaphase**).

- The chromosomes are then arranged in homologous pairs.

# Karyotypes

- The homologous pairs are then placed in order of descending size. The sex chromosomes are placed at the end.

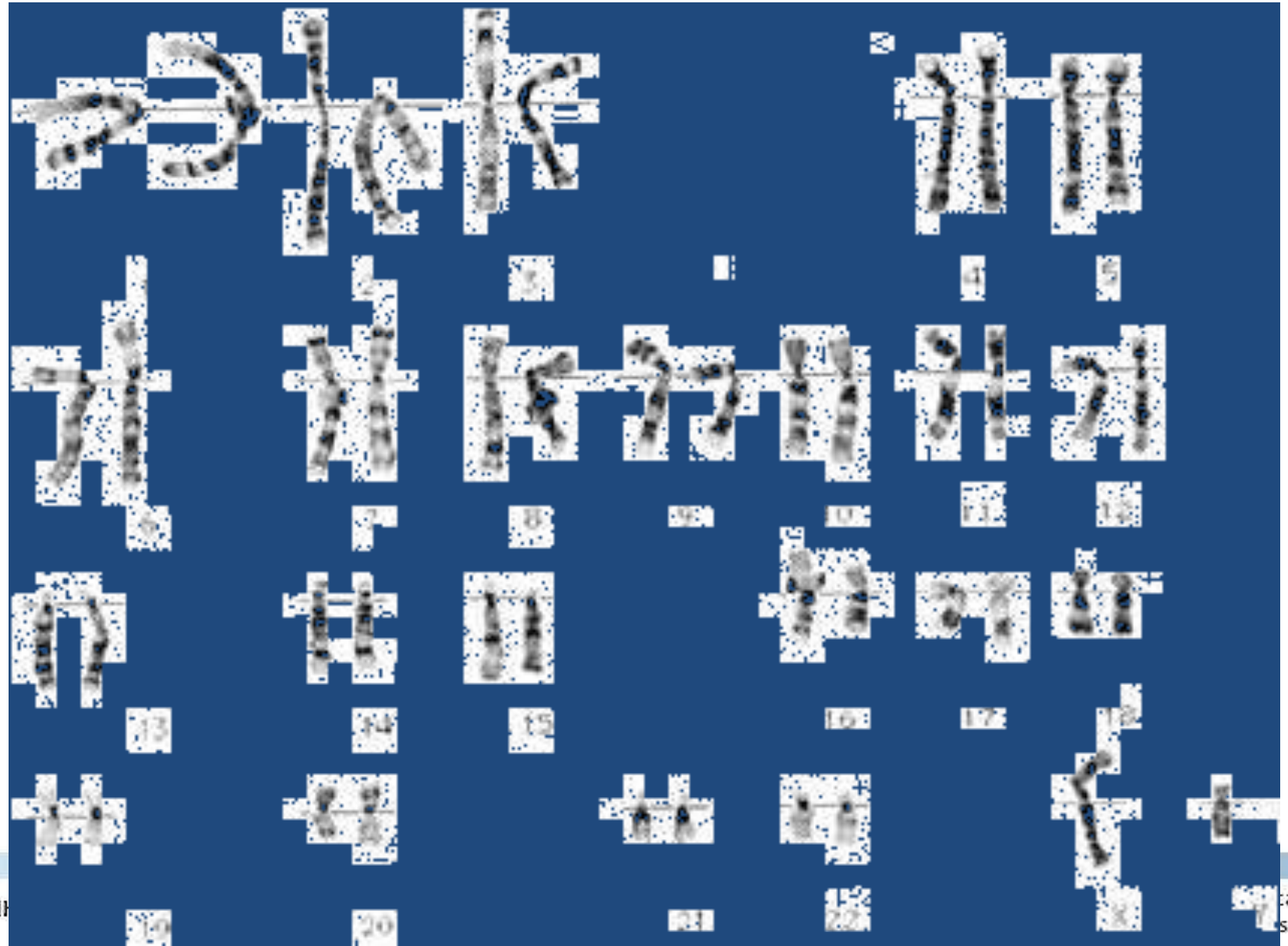
- A picture of chromosomes arranged in this way is known as a **karyotype.**

# Karyotypes

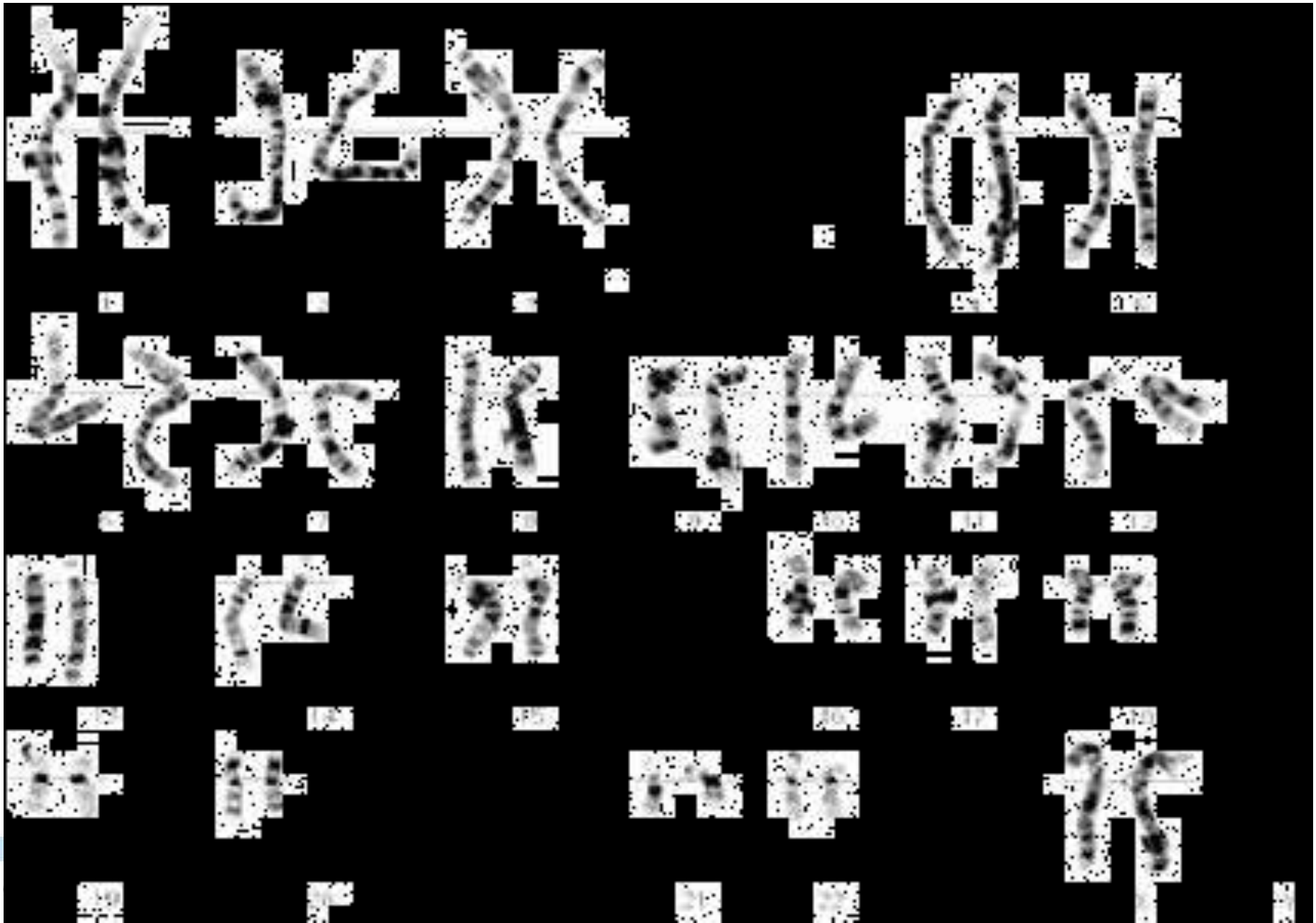
- The **karyotype** is a result of a haploid sperm (23 chromosomes) fertilizing a haploid egg (23 chromosomes).

- The **diploid** zygote (fertilized egg) contains the full 46 chromosomes. (in humans)

# Normal Human Male Karyotype: 46,XY



# Normal Human Female Karyotype: 46,XX



# So how are genes passed on from parent to child?

- Genes in the cell nucleus are physically located on 23 pairs of chromosomes
- One set of 23 chromosomes is inherited from each parent
- Therefore, of each pair of genes, one is inherited from a person's mother, and one from their father

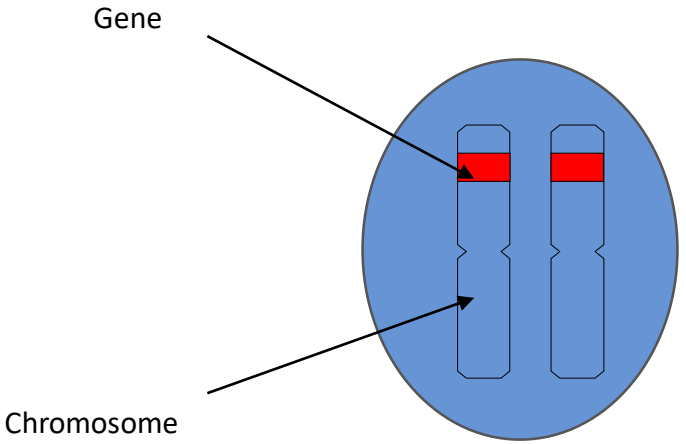


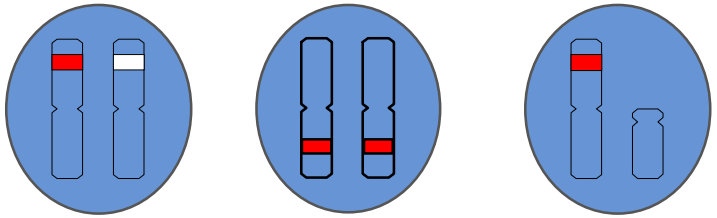

Diagram showing just one pair of the 23 pairs of chromosomes in the cell nucleus. The location of one of the genes on this chromosome is shown.

# Classification of genetic disorders



Alterations in single genes

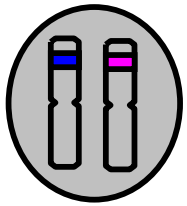
Single Gene Disorders



**Male**

Variants in genes

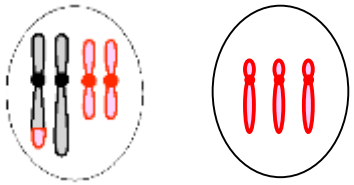
Multifactorial diseases



+ environment

Chromosomal imbalance

Chromosome disorders

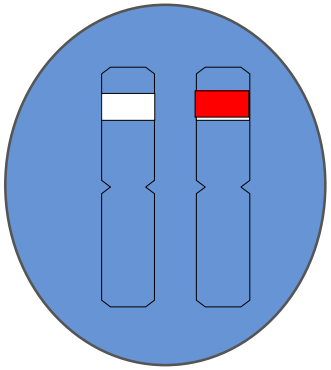


# Single gene disorders

**Some medical conditions are caused by a change in just one or both copies of a particular pair of genes. These are called "single gene disorders".**

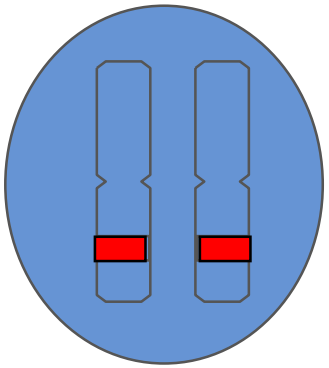
The three common types of single gene disorders are called:

- Autosomal dominant
- Autosomal recessive
- X-linked



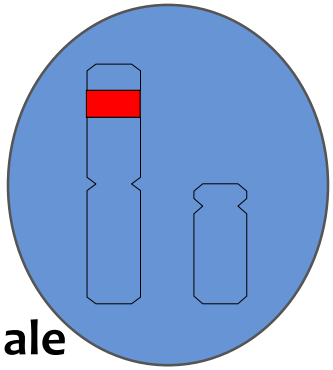
## *Dominant*

These individuals are called Heterozygotes with **one copy** of the altered gene they are affected



## *Recessive*

Homozygotes must have **two copies** of the altered gene to be affected



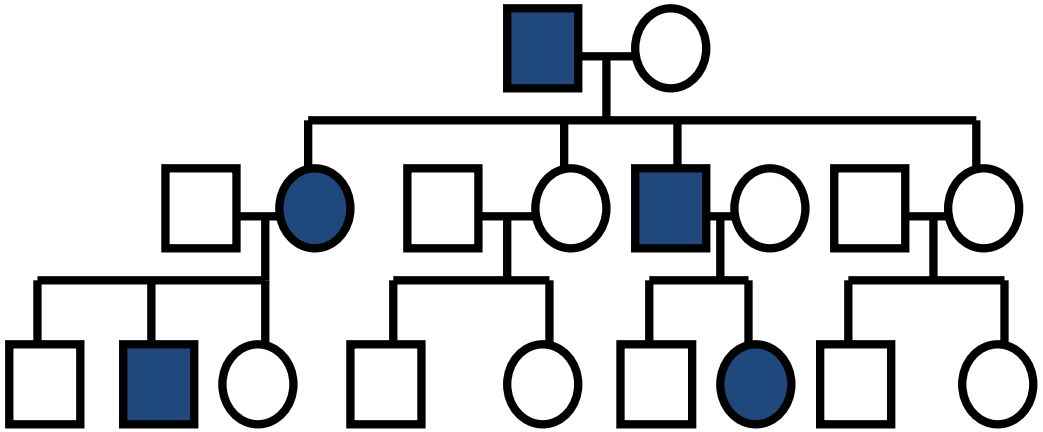
Male

## *X-linked recessive*

Males with an altered gene on the X-chromosome are always affected

- On a pedigree:
  - A circle represents a female
  - A square represents a male
  - A horizontal line connecting a male and female represents a marriage
  - A vertical line and a bracket connect the parents to their children
  - A circle/square that is shaded means the person **HAS** the trait.
  - A circle/square that is not shaded means the person does not have the trait.
  - Children are placed from oldest to youngest.
  - A key is given to explain what the trait is.

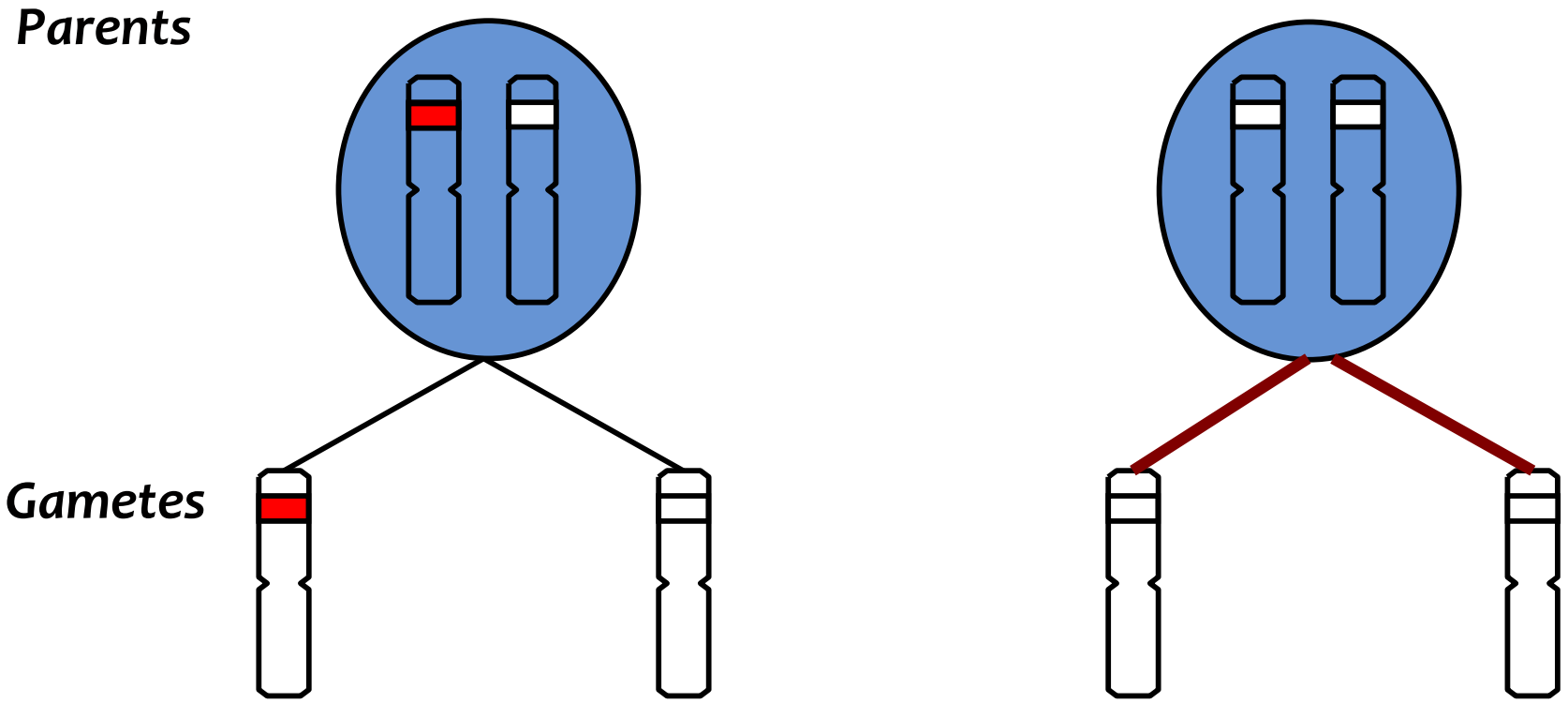
# Autosomal Dominant



- Vertical pattern: multiple generations affected
- Males and females equally likely to be affected
- See male to male transmission
- Each child of an affected individual has a 50% chance to be affected
- Unaffected individuals do pass on the gene
- Every affected child has an affected parent

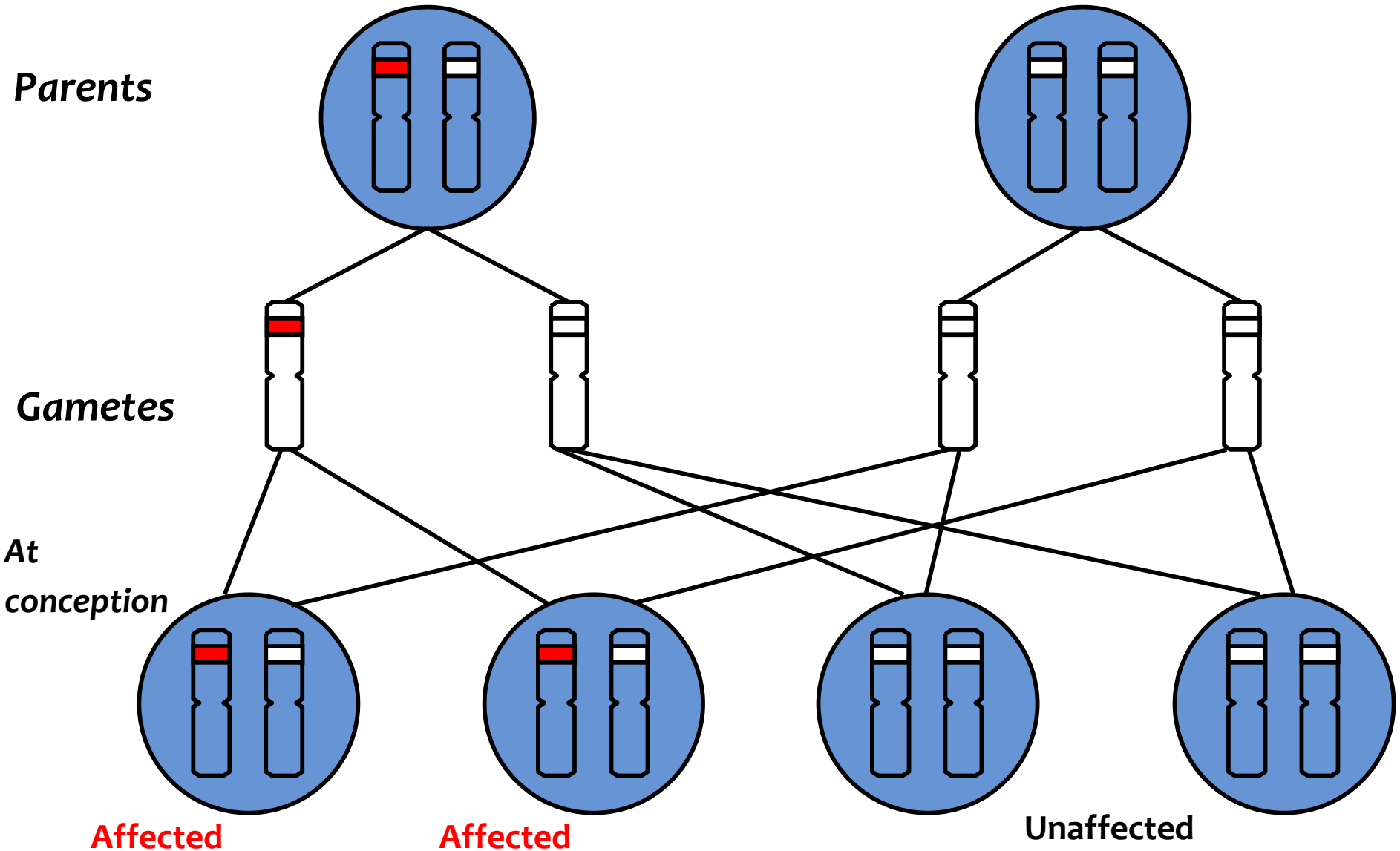
Adapted from The Pedigree: A Basic Guide, by Jorgenson, Yoder & Shapiro

# Autosomal dominant inheritance



# Autosomal dominant inheritance

NHS
National Genetics Education and Development Centre

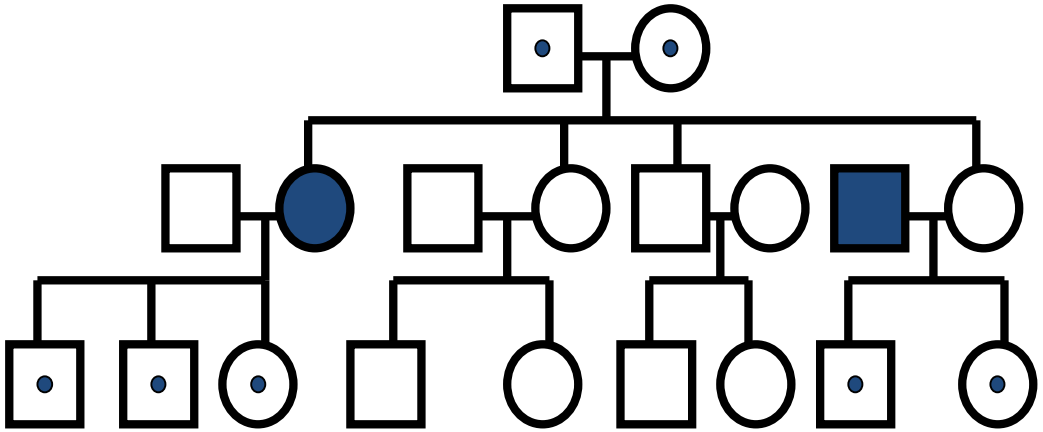


# Autosomal dominant inheritance

## Examples of Autosomal Dominant Conditions

- Huntington disease
- Neurofibromatosis type 1
- Marfan syndrome
- Familial hypercholesterolemia
- Familial Adenomatous Polyposis (FAP)
- Prader-willi

# Autosomal Recessive

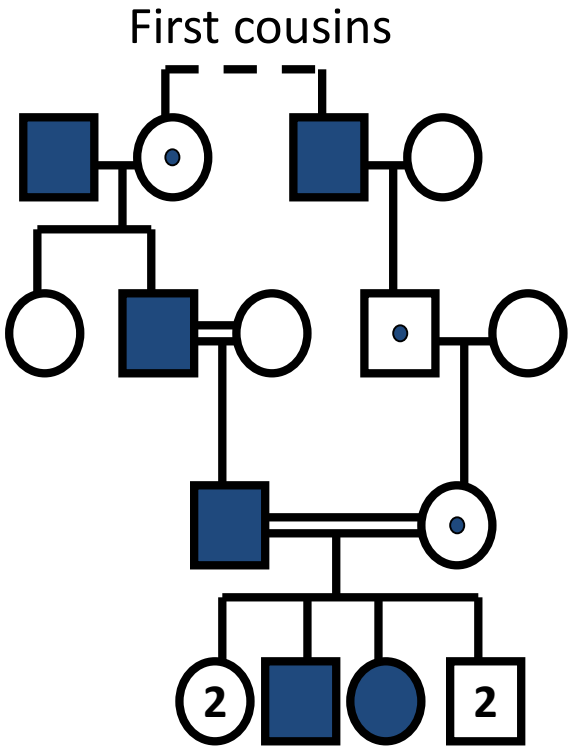


- Horizontal pattern:  single generation affected.
- Males and females equally likely to be affected
- Parents of affected child are unaffected gene carriers and have a 1 in 4 or 25% recurrence risk
- Unaffected siblings have a 2/3 or 67% chance to be carriers.
- Children of affected individuals are obligate carriers.

Adapted from The Pedigree: A Basic Guide, by Jorgenson, Yoder & Shapiro

# Autosomal Recessive

**Consanguinity**



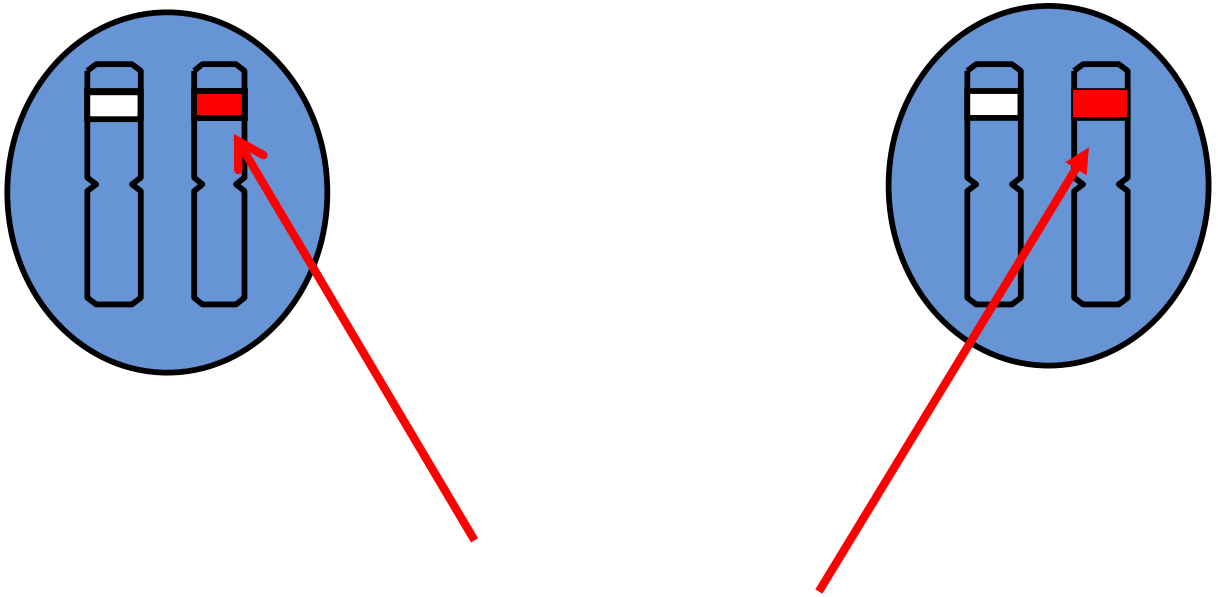

- Increased consanguinity (over general population) is often found between parents of a child with a rare autosomal recessive disorder
- Condition may appear to be dominant in a consanguineous family

Adapted from The Pedigree: A Basic Guide, by Jorgenson, Yoder & Shapiro

# AUTOSOMAL RECESSIVE INHERITANCE



## *Parents*



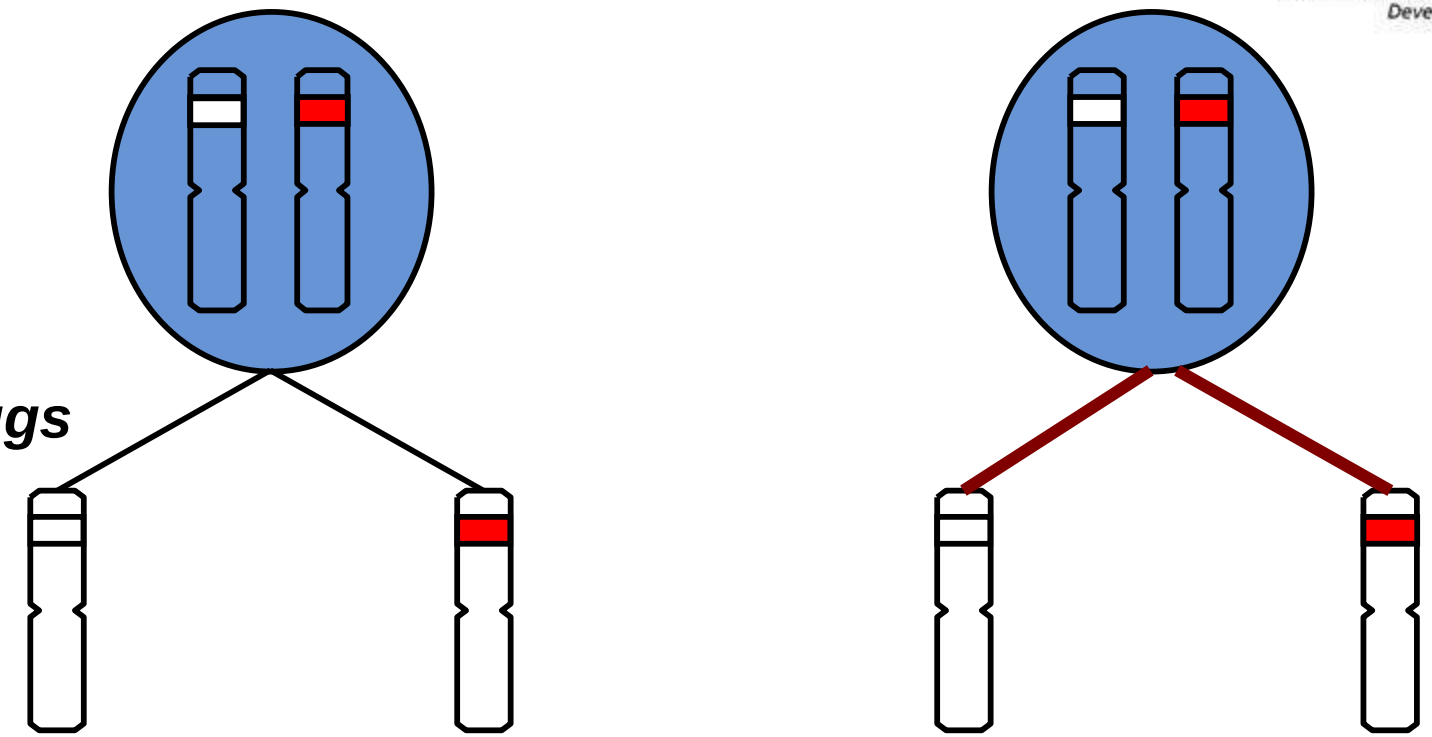
Parent who are carriers for the same autosomal recessive condition have one copy of the usual form of the gene and one copy of an altered gene of the particular pair

# AUTOSOMAL RECESSIVE INHERITANCE

NHS
National Genetics Education and Development Centre

***Parents***

***Sperm/Eggs***



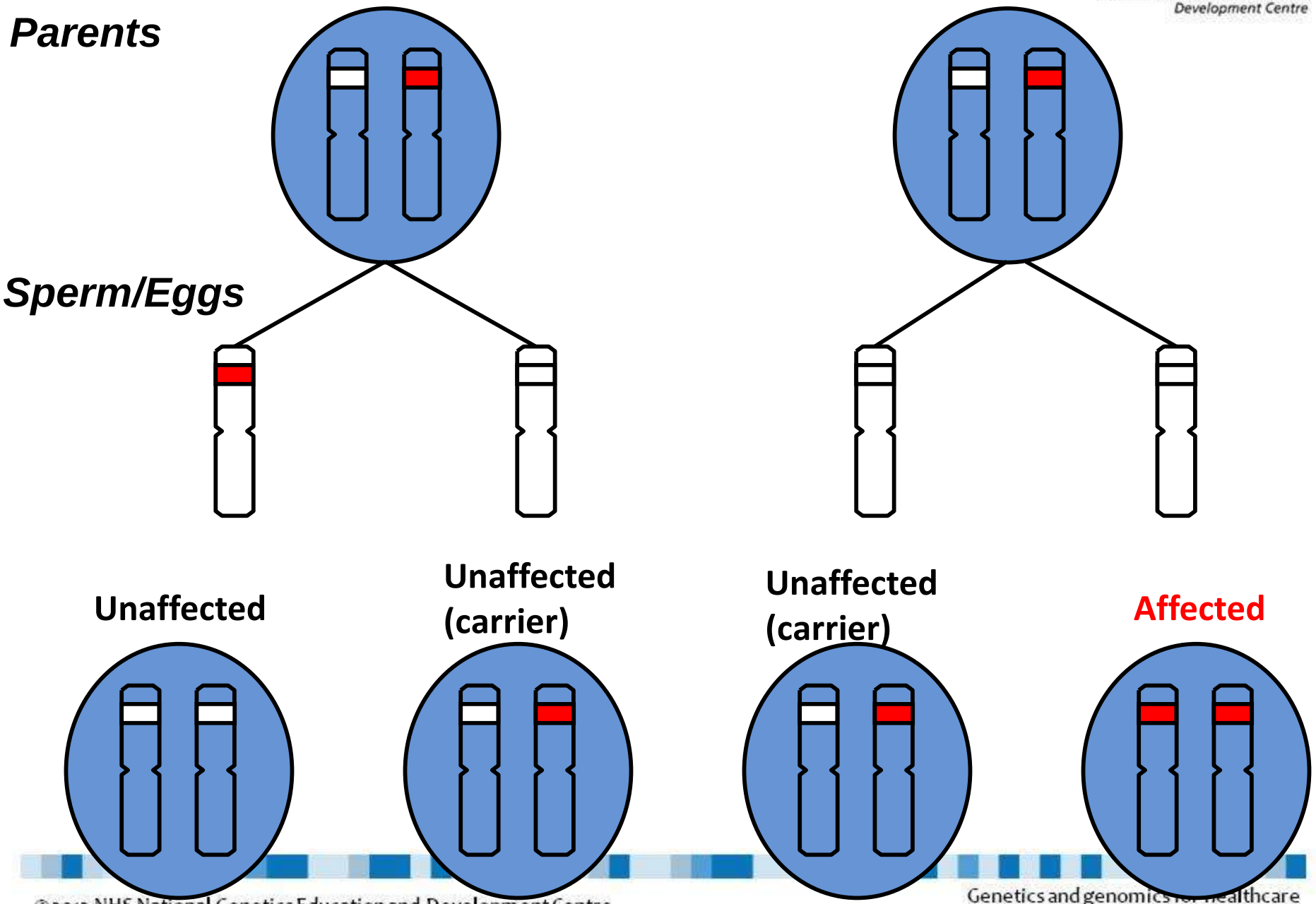
A parent who is a carrier passes on either the usual gene

or the altered gene into the eggs or sperm

The other parent who is also a carrier for the same condition passes on either the usual gene or the altered gene into his/her eggs or sperm

# AUTOSOMAL RECESSIVE INHERITANCE

NHS
National Genetics Education and Development Centre

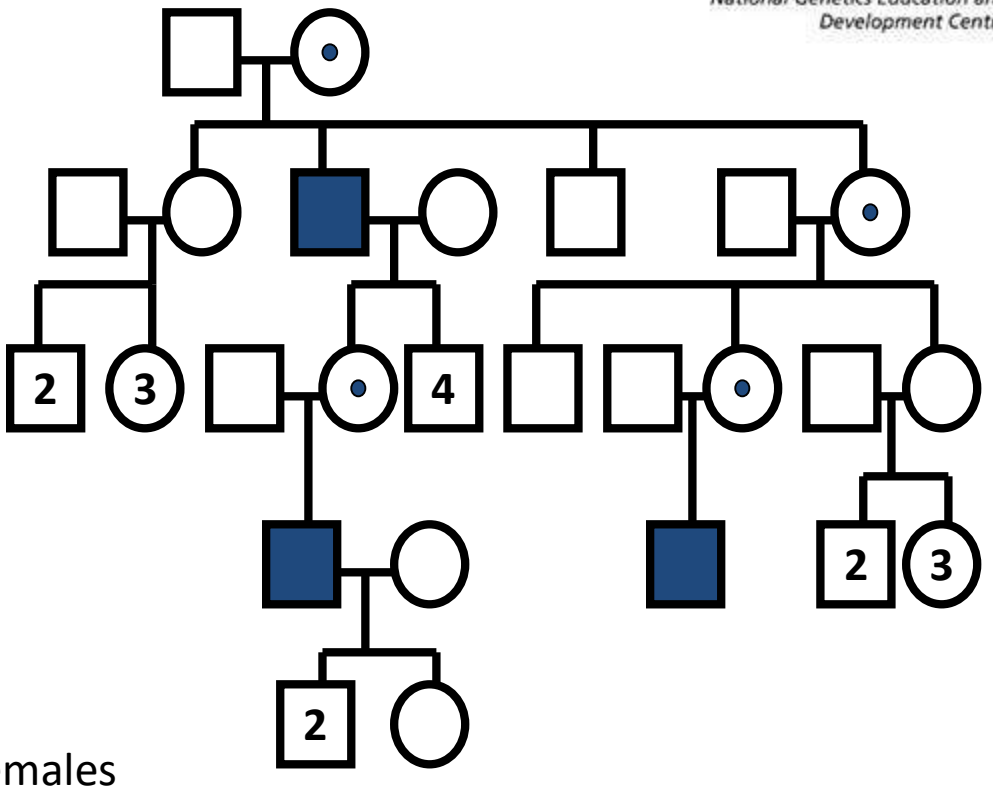


# Autosomal recessive inheritance

## Examples of Autosomal recessive conditions

- Sickle Cell disease
- Cystic fibrosis
- Batten Disease
- Congenital deafness
- Phenylketonuria (PKU)
- Spinal muscular atrophy
- Recessive blindness
- Maple syrup urine disease

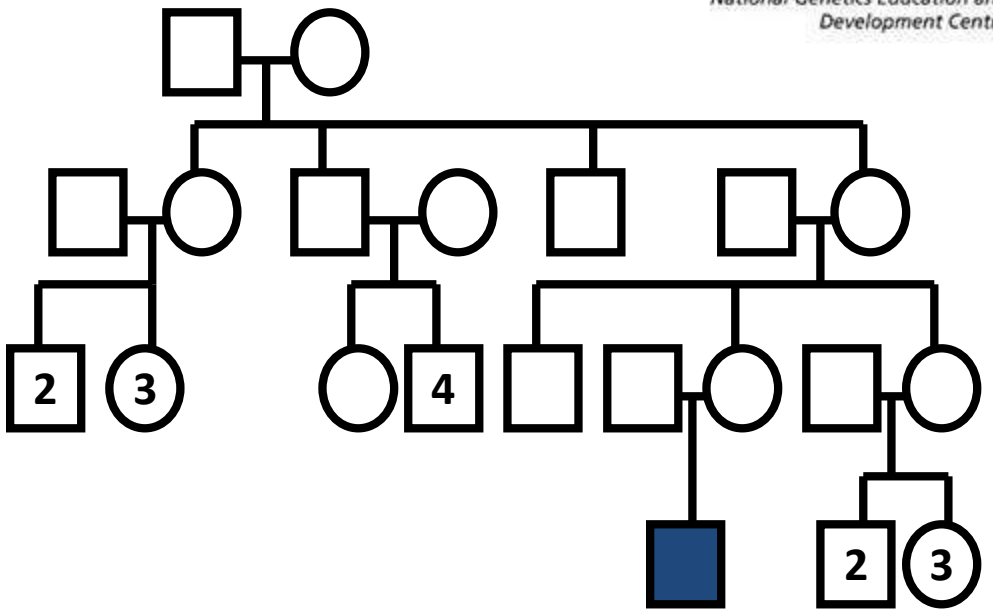
# X-linked Recessive




- Males are more often affected than females
- Affected males pass the gene to all of their daughters and none of their sons (NO male-to-male transmission)
- Daughters of carrier females have a 50% chance to be unaffected carriers. Sons of carrier females have 50% chance to be affected.
- Affected males in the family are related to each other through carrier females ("Knight's move")

# X-linked Recessive

**Other characteristics**

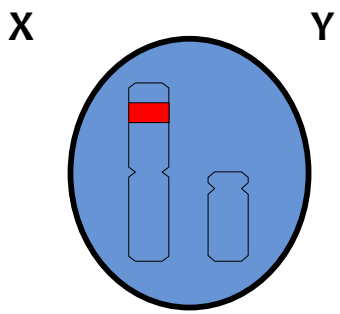



- For genetically lethal X-linked conditions, 1/3 of isolated cases (i.e. no family history) are new mutations.
- In 2/3 of cases, the mother is an unaffected carrier
- Female gene carriers are usually not affected

*Exceptions*: Turner syndrome, skewed X-inactivation, X;autosome translocation carriers

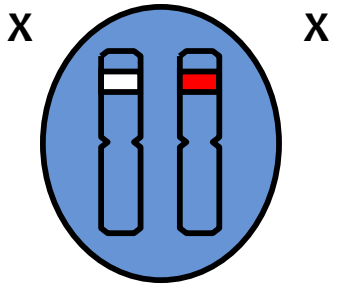
# X-linked recessive inheritance

**Male**




One copy of an altered gene on the X chromosome causes the disease in a male.

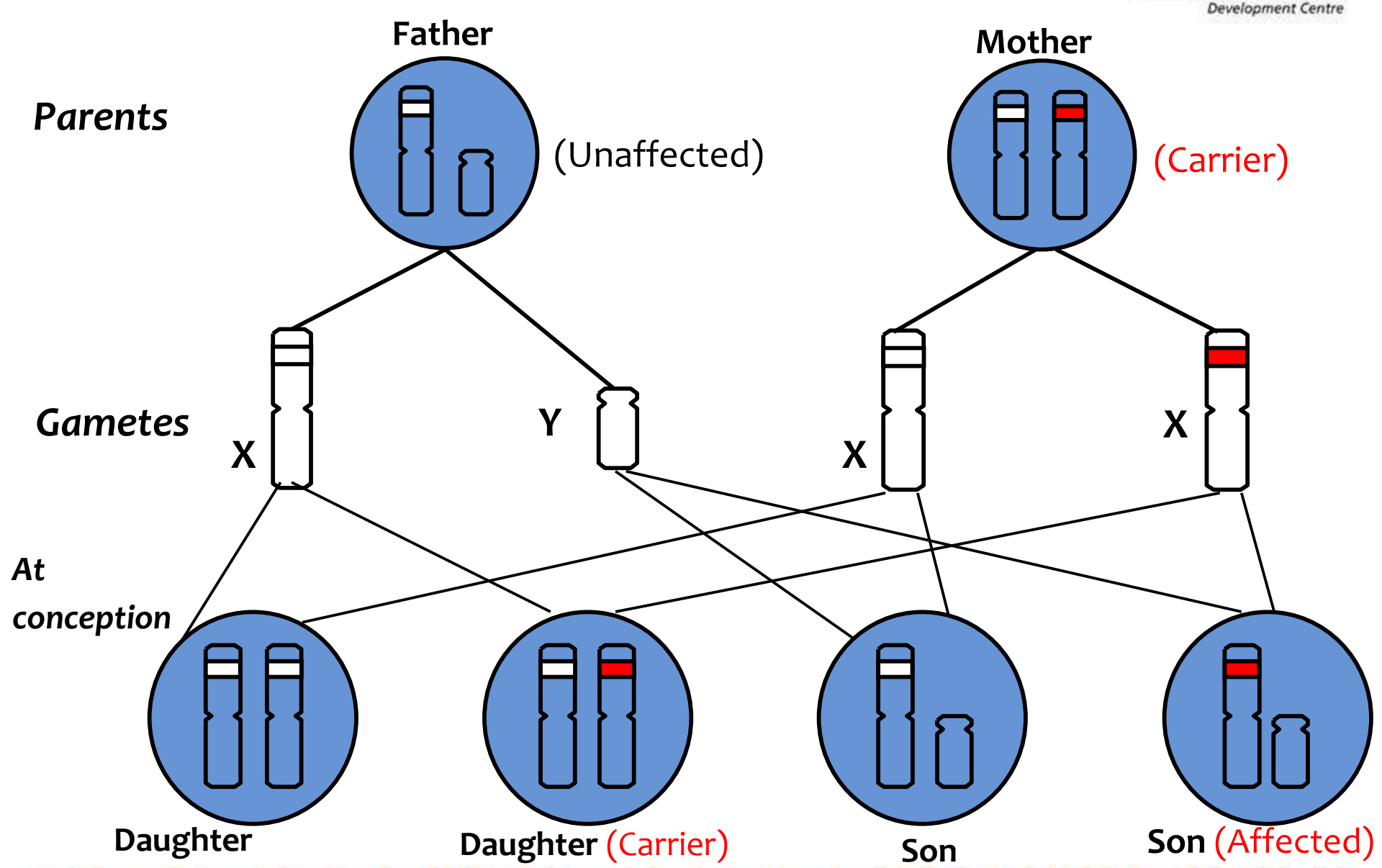
**Female**




An altered copy on one of the X chromosome pair causes carrier status in a female.

# X-linked inheritance where the mother is a carrier

NHS
National Genetics Education and Development Centre

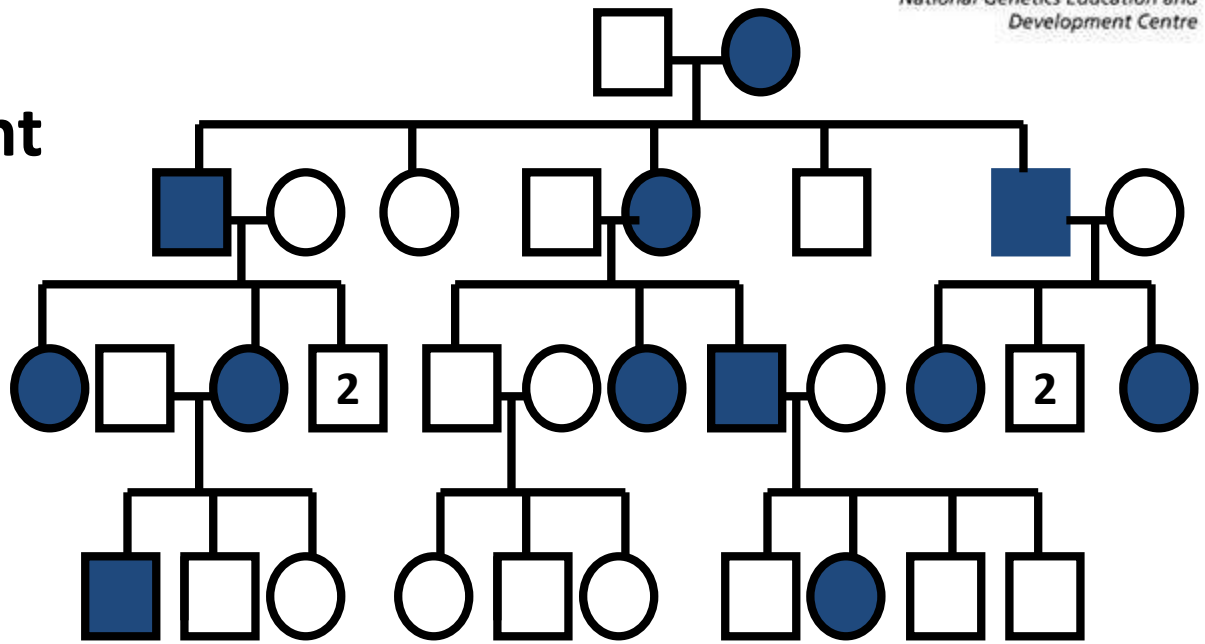


# X-Linked recessive inheritance

## Examples of X-Linked Recessive Conditions

- Fragile X syndrome
- Haemophilia
- Duchenne muscular dystrophy (DMD) (Becker BMD)
- Fabry disease
- Retinitis pigmentosa
- Hunter syndrome
- Ocular albinism
- Adrenoleucodystrophy.

# X-linked Dominant




- For rare conditions, females are about 2x as likely to be affected than males. May be lethal in males and usually milder, but variable, in females.
- Affected males pass the gene to all of their daughters, who will be affected, and to none of their sons (NO male-to-male transmission)
- Sons and daughters of affected females have 50% chance of being affected (similar to autosomal dominant)

# Polygeneic Inheritance

- Single gene disorders are quite rare
- Single gene disorders either give risk to a condition or they don't

- Most traits are Polygenic' i.e. 1 trait coded by a number of altered and unaltered genes working together

# Common Polygenic Disorders

- Alzheimer's
- Diabetes
- Cancer
- Eczema

# Multifactorial inheritance

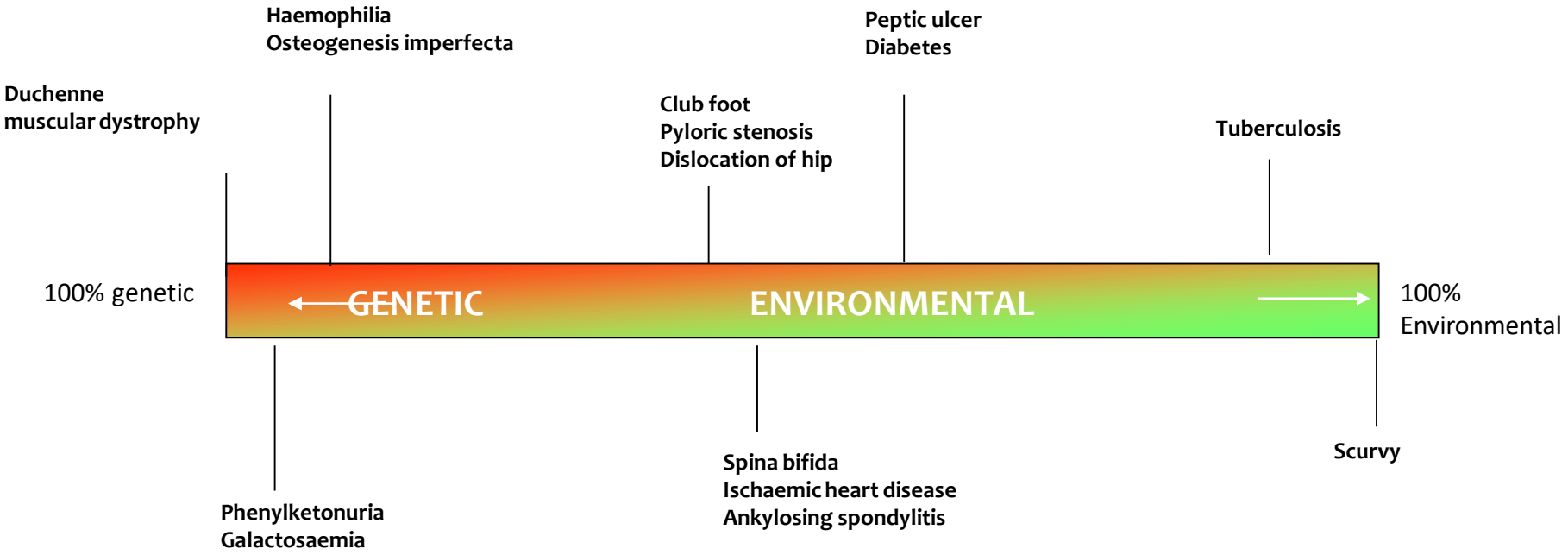
- Inheritance controlled by many genes plus the effects of the environment

- **Congenital malformations**
  Cleft lip/palate
  Congenital hip dislocation
  Congenital heart defects
  Neural tube defects
  Pyloric stenosis
  Talipes

- **Adult onset disorders**

  Diabetes mellitus
  Epilepsy
  Glaucoma
  Hypertension
  Ischaemic heart disease
  Manic depression
  Schizophrenia

# The contributions of genetic and environmental factors to human diseases




*Rare*
*Genetics simple*
*Unifactorial*
*High recurrence rate*

*Common*
*Genetics complex*
*Multifactorial*
*Low recurrence rate*