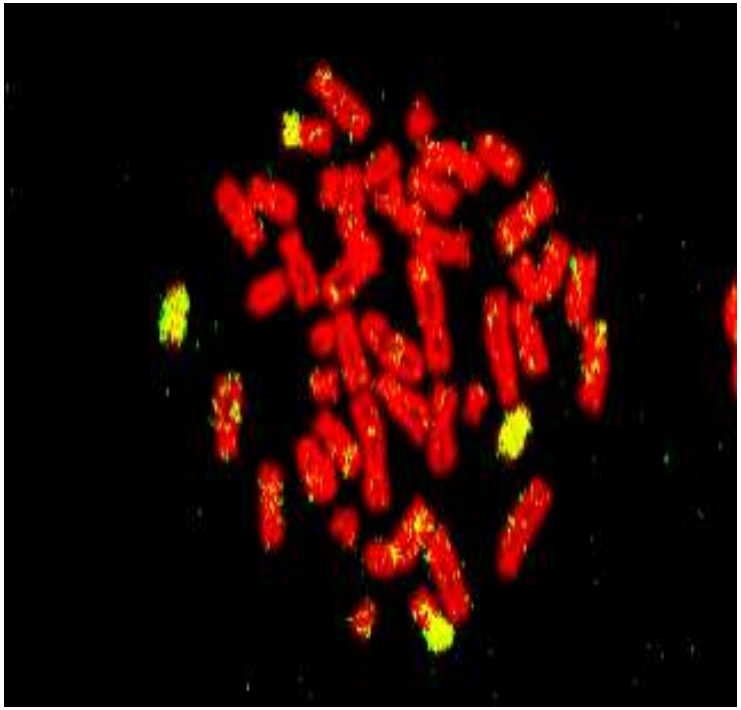
Chapter 15~ *The Chromosomal Basis of Inheritance*

The Chromosomal Theory of Inheritance

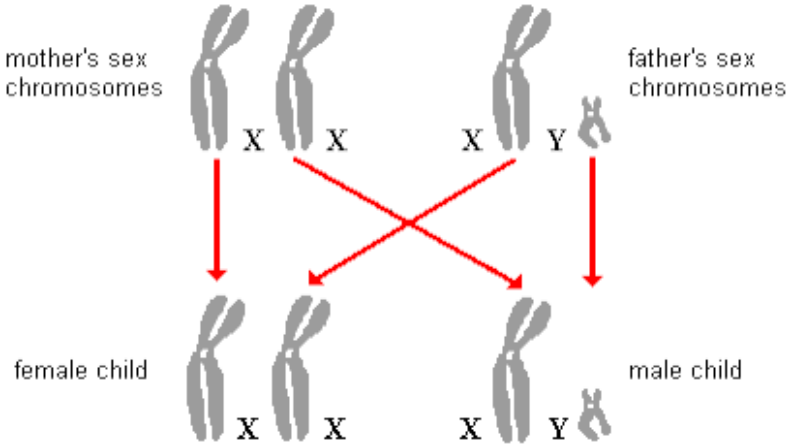
- Genes have specific loci on chromosomes and chromosomes undergo segregation and independent assortment



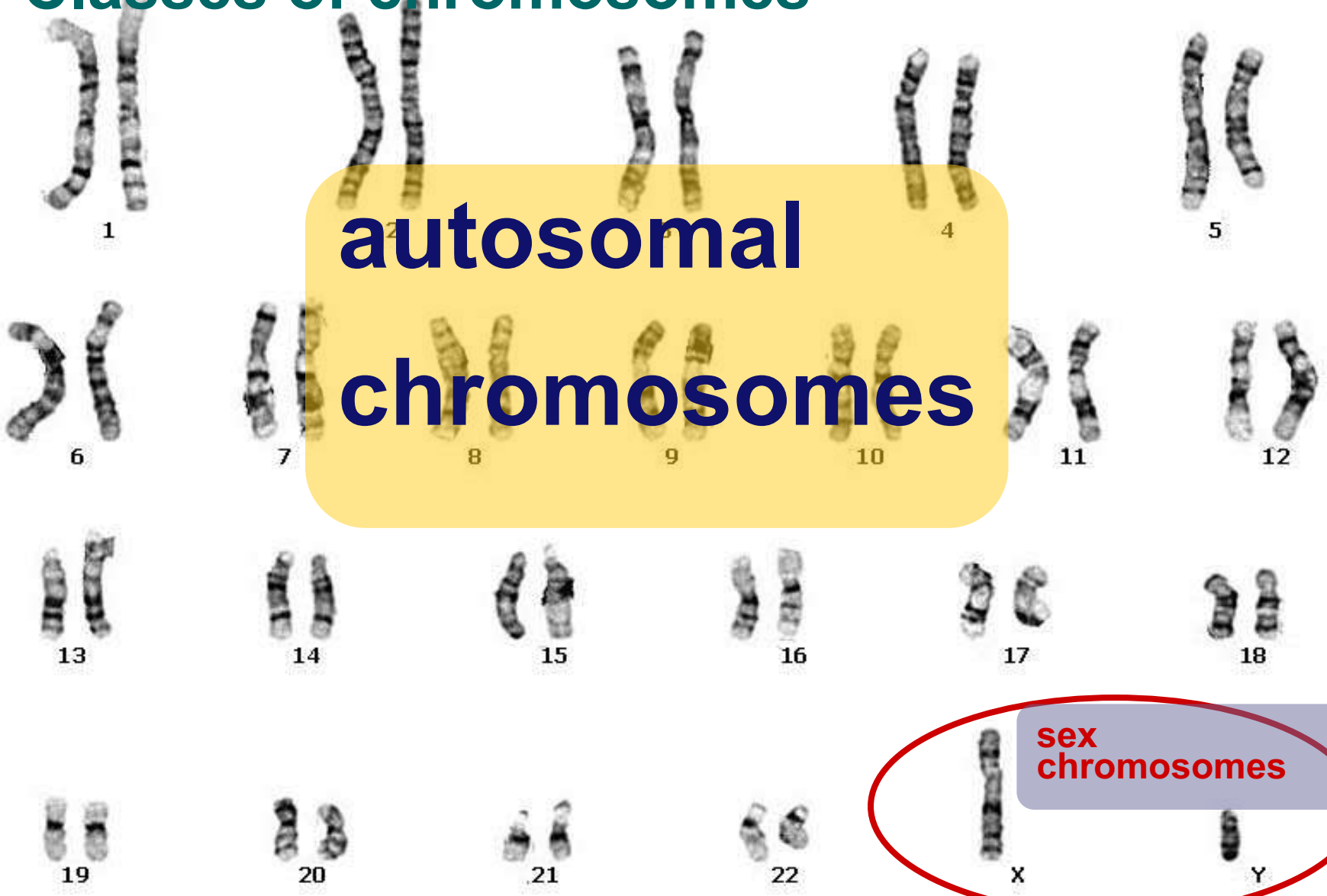
Chromosomal Linkage

- Morgan
- *Drosophilia melanogaster*

- Linked genes: genes located on the same chromosome that tend to be inherited together



Classes of chromosomes



autosomal chromosomes

sex chromosomes

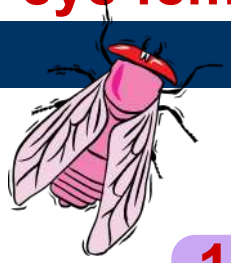
Discovery of sex linkage

P

true-breeding red-eye female

x

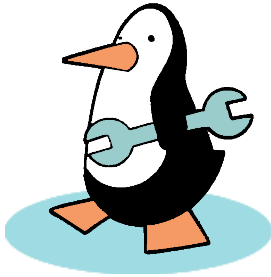
true-breeding white-eye male



Huh! Sex matters?!

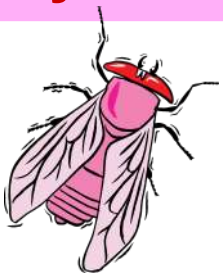
F_1 generation (hybrids)

100% red eye offspring

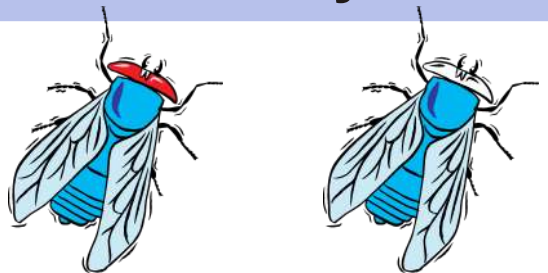


F_2 generation

100% red-eye female



50% red-eye male
50% white eye male



What's up with Morgan's flies?

	r	r
R	Rr	Rr
R	Rr	Rr

100% red eyes

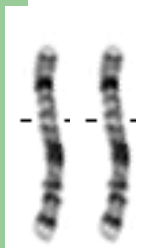
Doesn't work that way!

	R	r
R	RR	Rr
r	Rr	rr

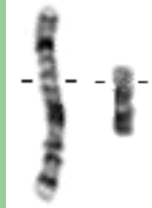
3 red : 1 white

Genetics of Sex

- In humans & other mammals, there are 2 sex chromosomes: X & Y
  - 2 X chromosomes



    - develop as a female: XX
    - gene redundancy, like autosomal chromosomes
    - an X & Y chromosome
  - develop as a male: XY



    - no redundancy

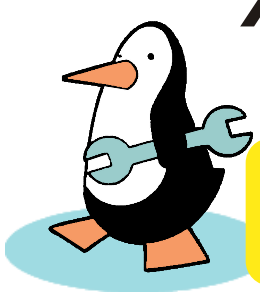
	X	Y
X	XX	XY
X	XX	XY

50% female : 50% male

Let's reconsider Morgan's flies…

	X^r	Y
X^R	X^RX^r	X^RY
X^R	X^RX^r	X^RY

100% red eyes

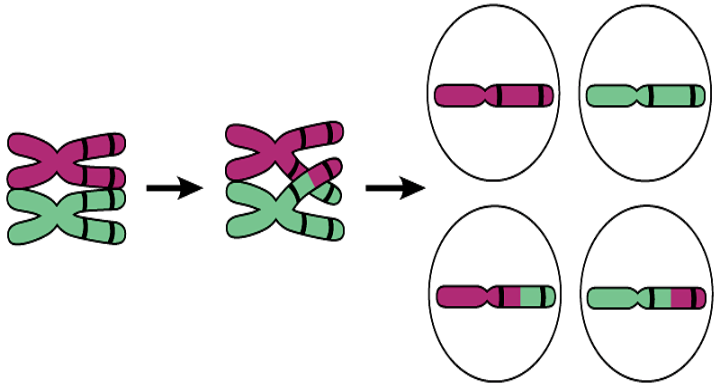


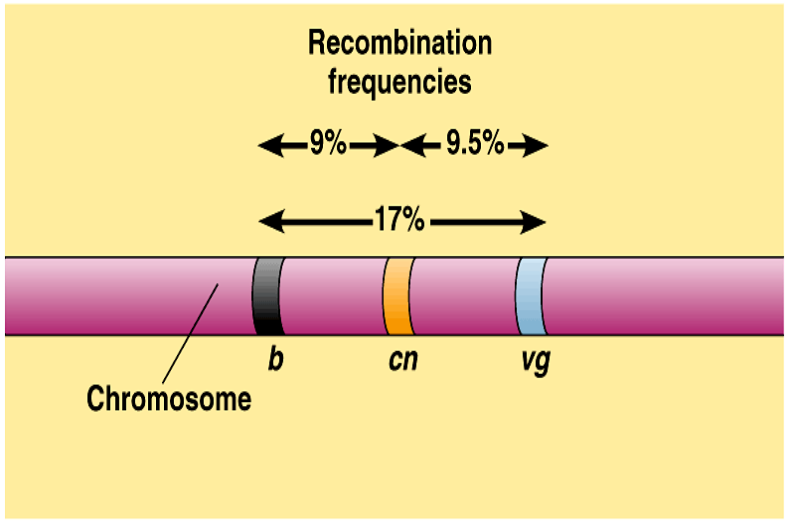
	X^R	Y
X^R	X^RX^R	X^RY
X^r	X^RX^r	X^rY

100% red females
50% red males; 50% white males

Genetic recombination

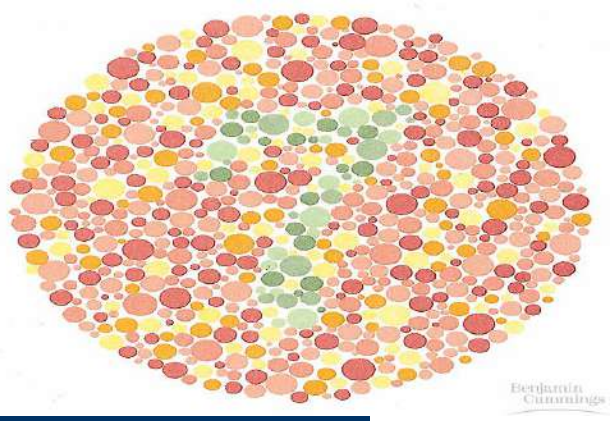
- **Crossing over** Genes that DO NOT assort independently of each other
- **Genetic maps** The further apart 2 genes are, the higher the probability that a crossover will occur between them and therefore the higher the recombination frequency
- **Linkage maps** Genetic map based on recombination frequencies





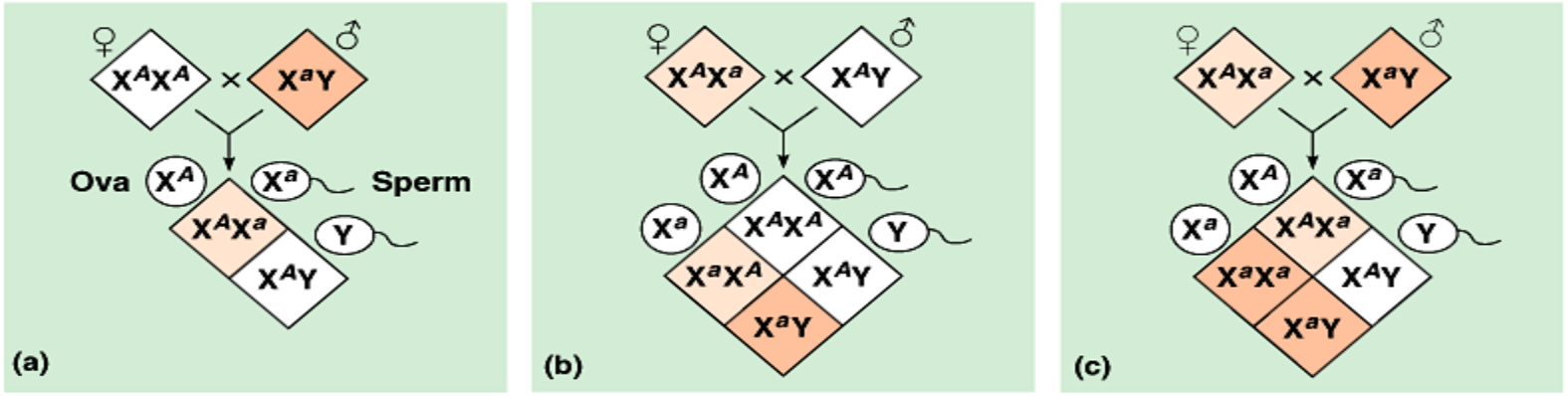
Genes on sex chromosomes

- Y chromosome
  - **SRY**
    - sex-determining region
    - master regulator for maleness
    - turns on genes for production of male hormones
      - many effects = pleiotropy*!*
- X chromosome
  - other genes/traits beyond sex determination
    - mutations:
      - hemophilia
      - Duchenne muscular dystrophy
      - color-blindness

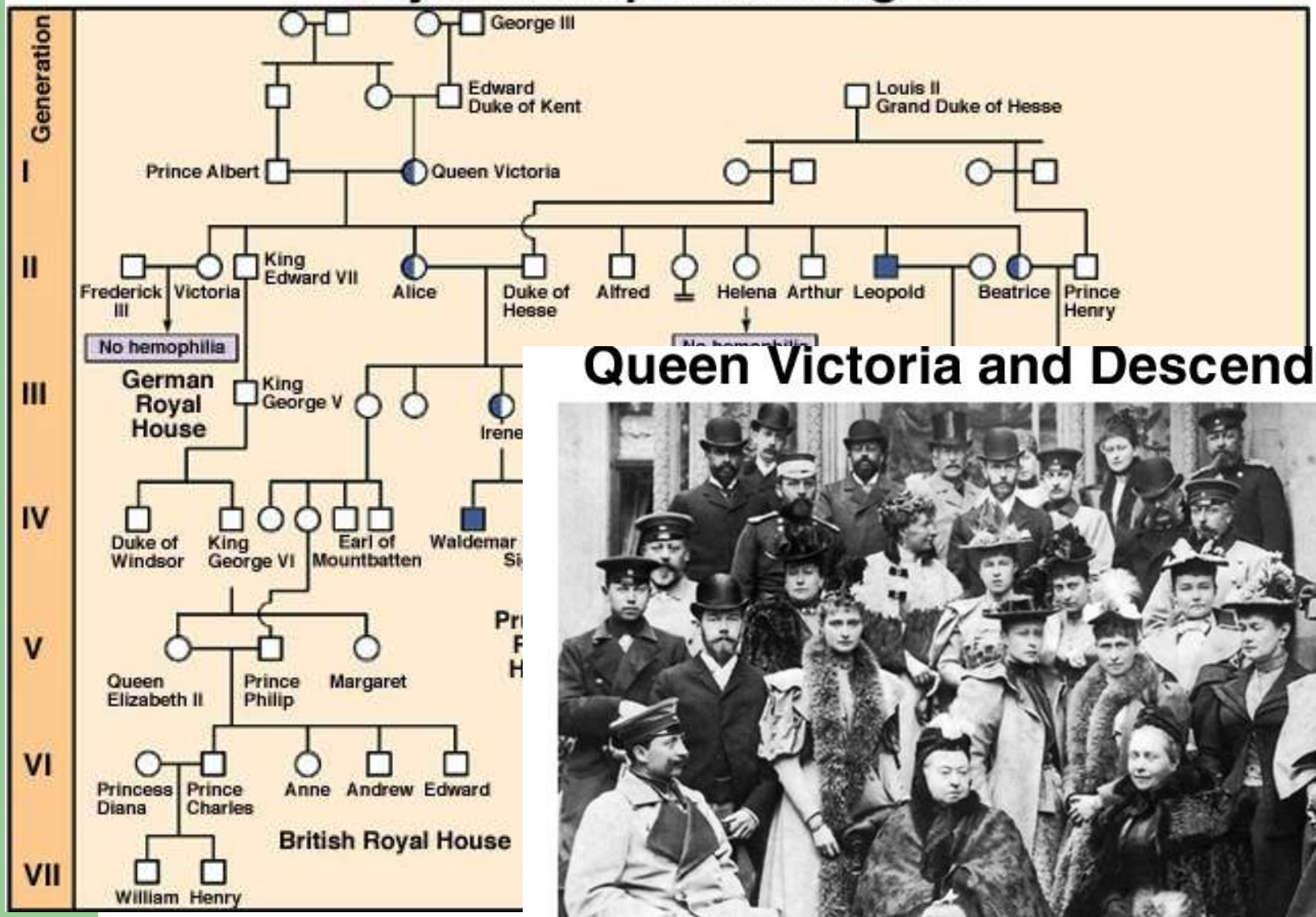


Human sex-linkage

- SRY gene: gene on Y chromosome that triggers the development of testes
- Fathers= pass X-linked alleles to all daughters only (but not to sons)
- Mothers= pass X-linked alleles to both sons & daughters
- Sex-Linked Disorders: Color-blindness; Duchenne muscular dystropy (MD); hemophilia



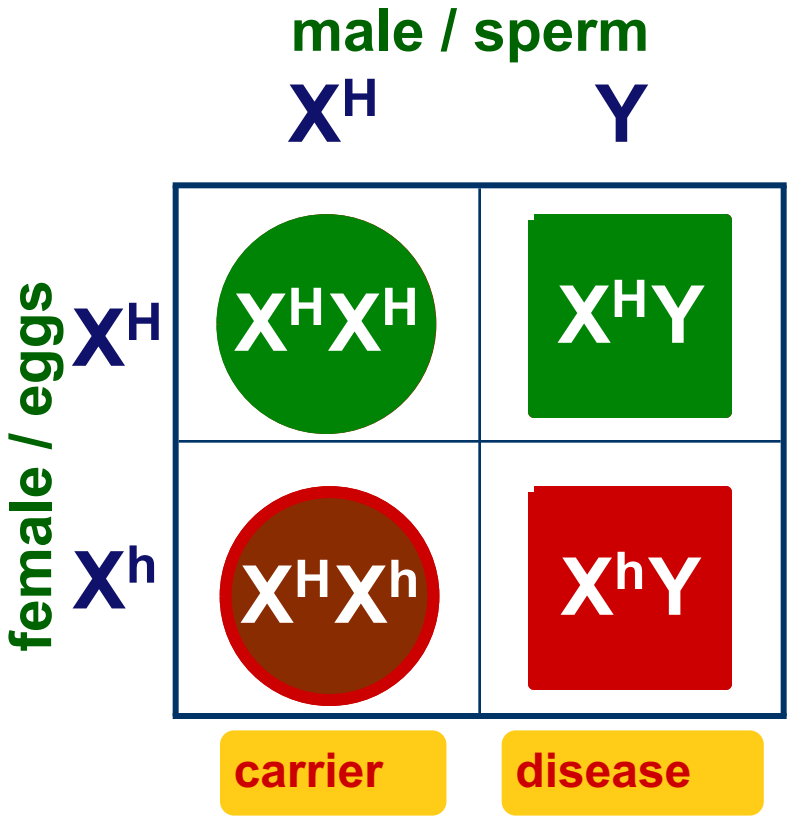
Royal Hemophilia Pedigree

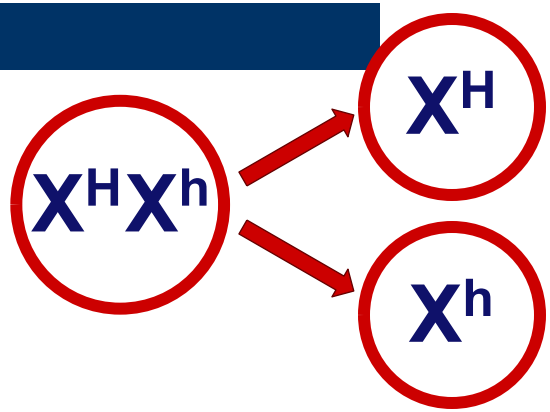


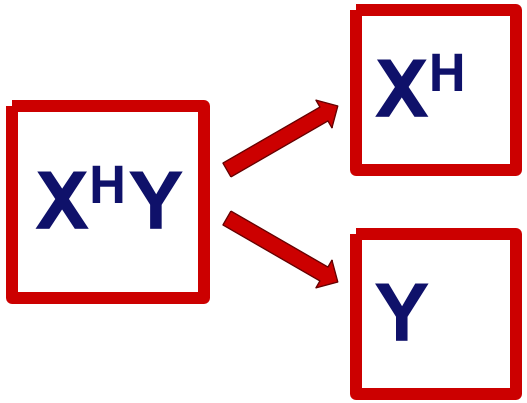
Queen Victoria and Descendants

Hemophilia

sex-linked recessive



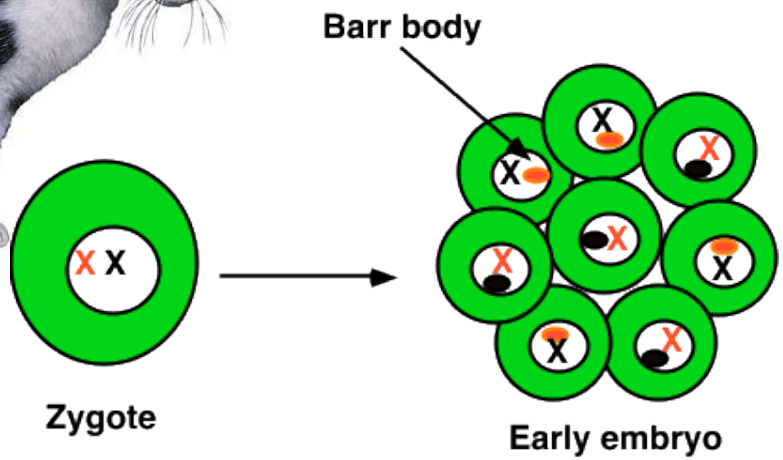


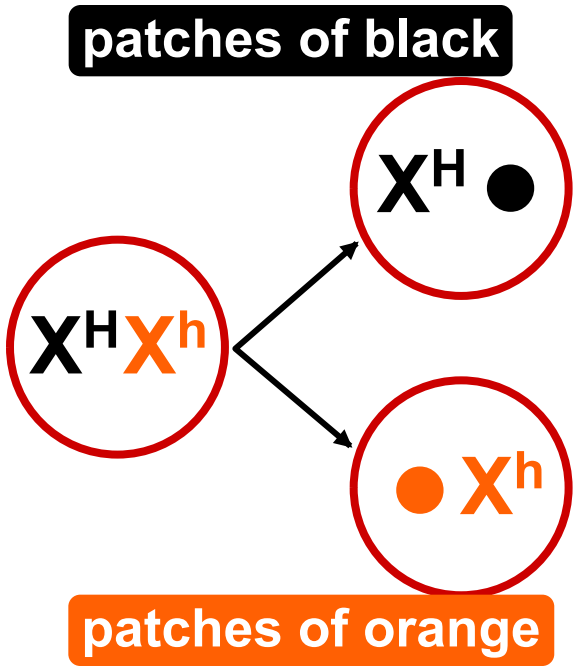


X-inactivation

- Female mammals inherit 2 X chromosomes
  - one X becomes inactivated during embryonic development
    - condenses into compact object = Barr body
    - which X becomes Barr body is random
      - patchwork trait = "mosaic"

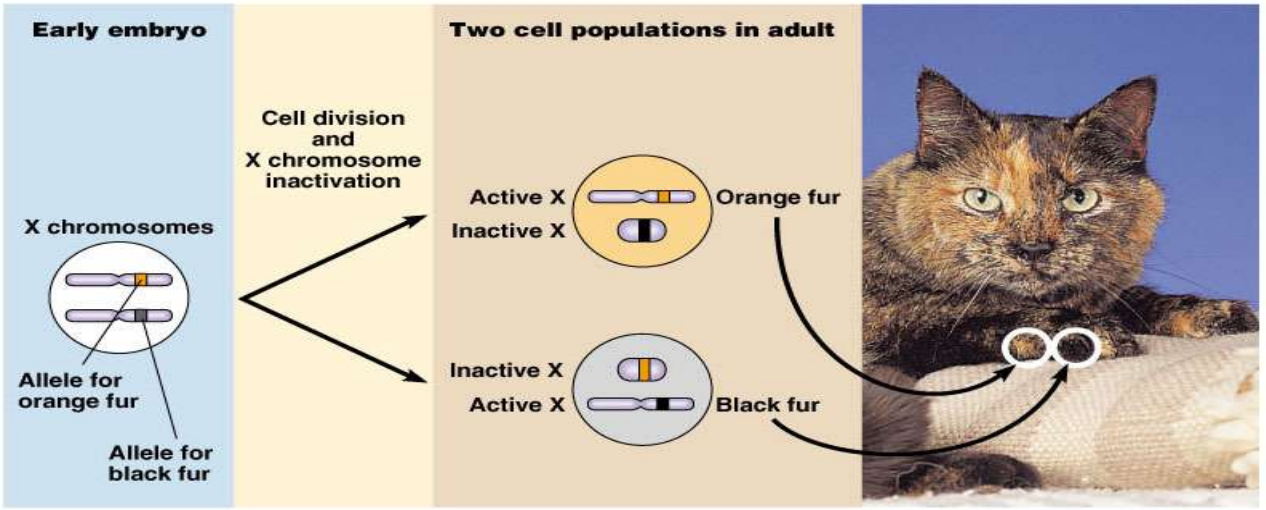
tricolor cats can only be female

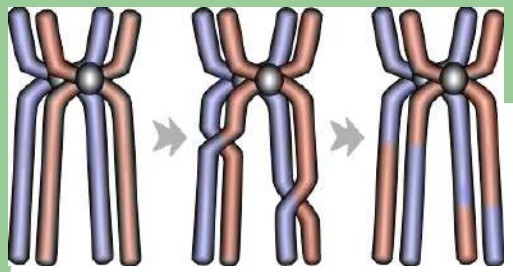




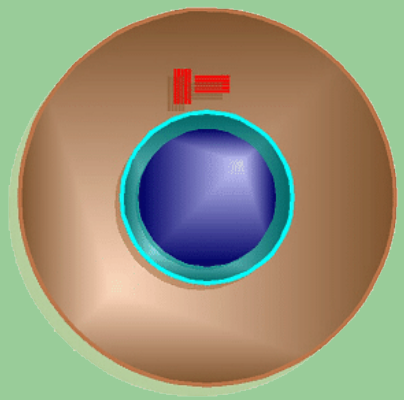
Human sex-linkage

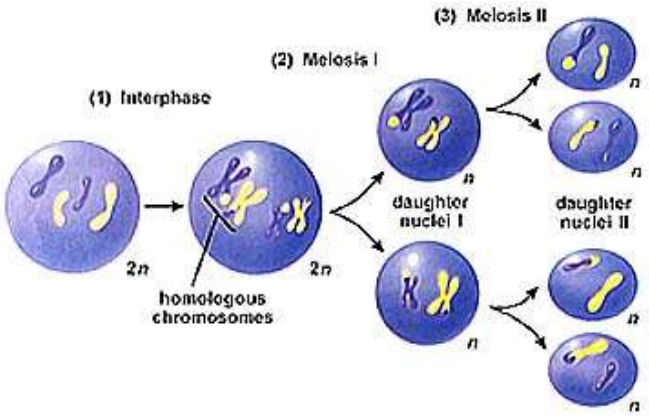
- X-inactivation: 2nd X chromosome in females condenses into a Barr body (e.g., tortoiseshell gene gene in cats)





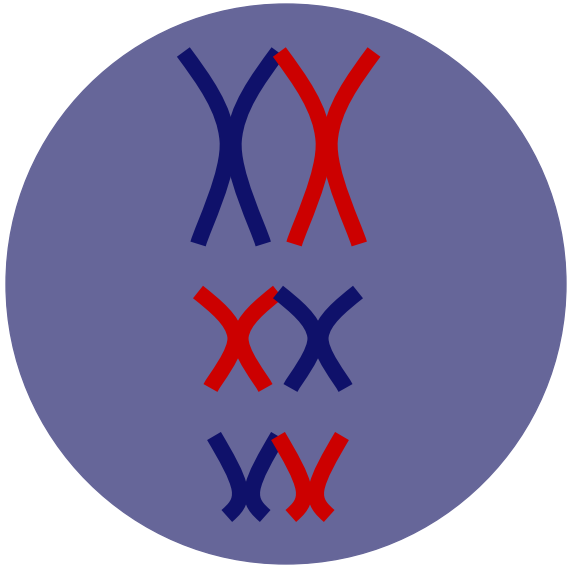
Errors of Meiosis
Chromosomal Abnormalities





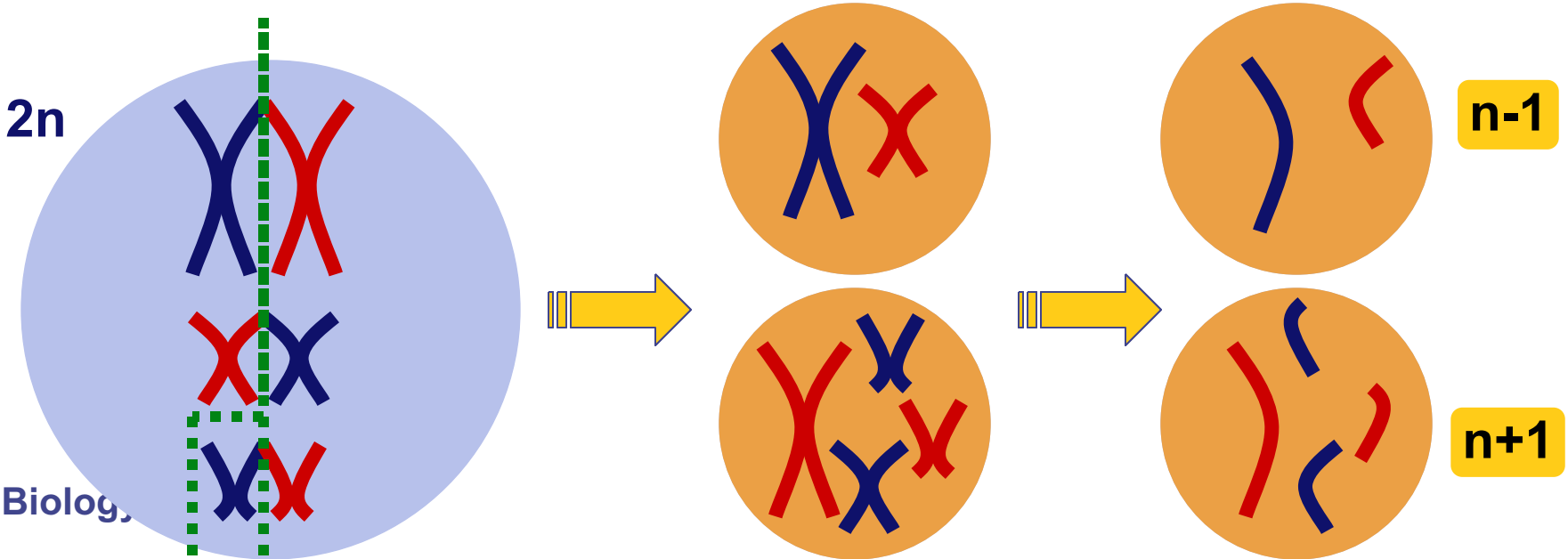
Chromosomal abnormalities

- Incorrect number of chromosomes
  - nondisjunction
    - chromosomes don't separate properly during meiosis
  - breakage of chromosomes
    - deletion
    - duplication
    - inversion
    - translocation

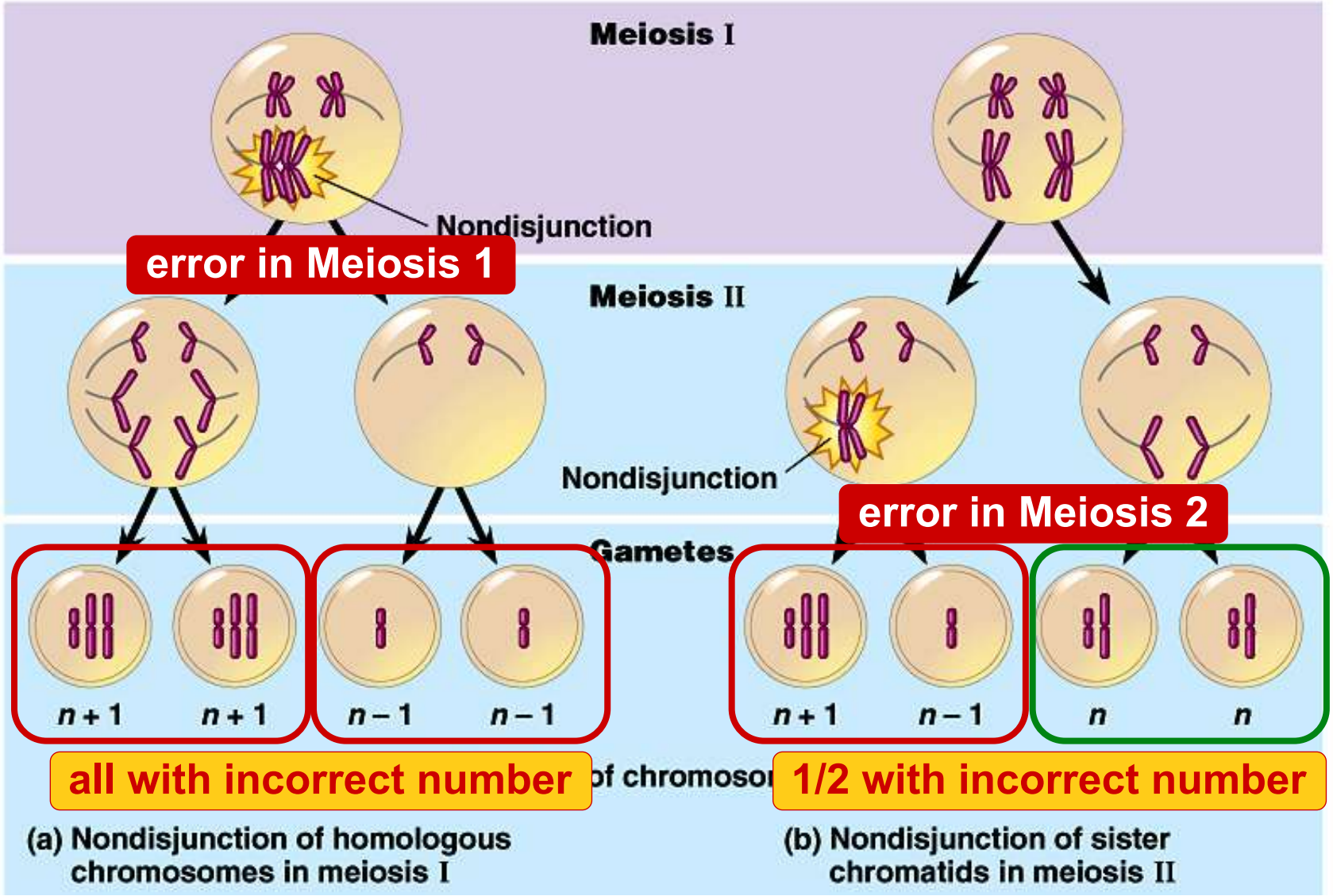


Nondisjunction

- Problems with meiotic spindle cause errors in daughter cells
  - homologous chromosomes do not separate properly during Meiosis 1
  - sister chromatids fail to separate during Meiosis 2
  - too many or too few chromosomes

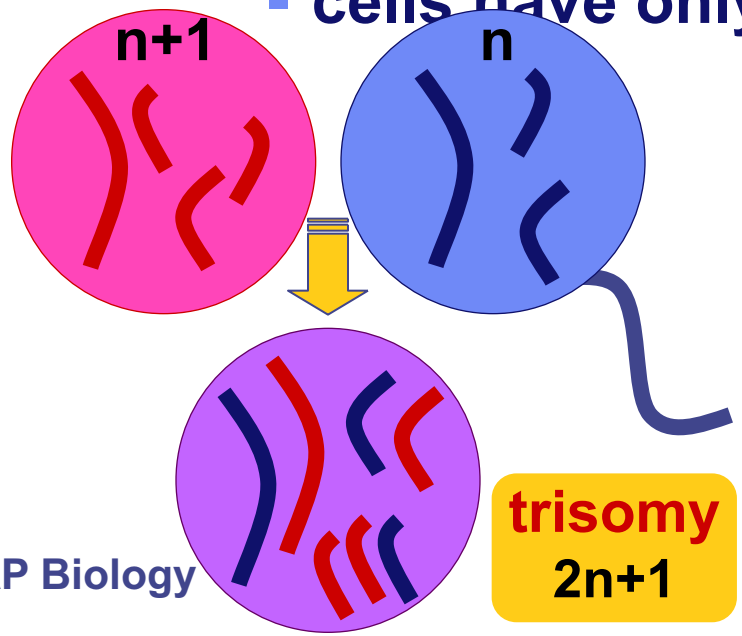


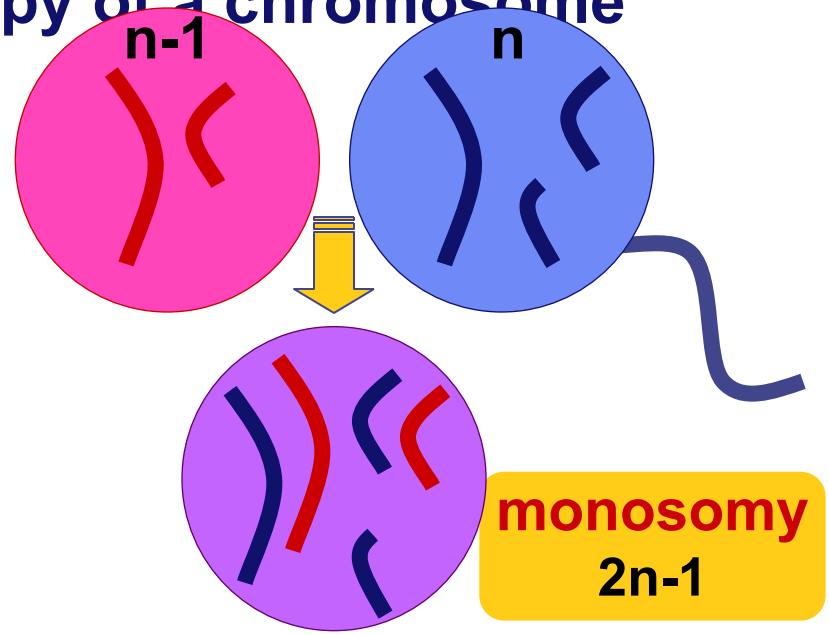
Alteration of chromosome number



Nondisjunction

- ⑩Baby has wrong chromosome number~ aneuploidy
  - **trisomy**
    - cells have 3 copies of a chromosome
  - **monosomy**
    - cells have only 1 copy of a chromosome



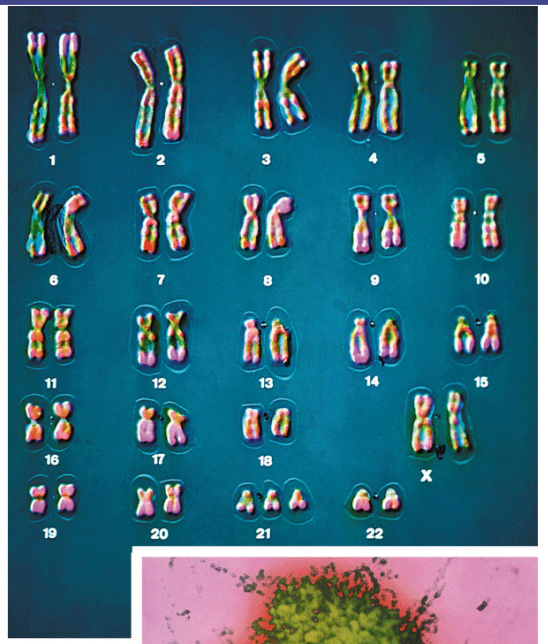


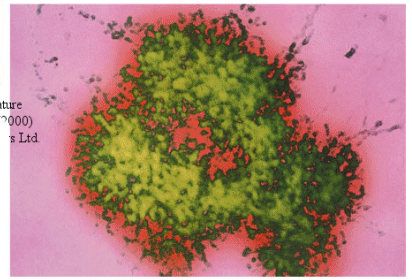
Human chromosome disorders

- High frequency in humans
  - most embryos are spontaneously aborted
  - alterations are too disastrous
  - developmental problems result from biochemical imbalance
    - imbalance in regulatory molecules?
      - hormones?
      - transcription factors?
- Certain conditions are tolerated
  - upset the balance less = survivable
  - but characteristic set of symptoms = syndrome

Down syndrome

- Trisomy 21
  - 3 copies of chromosome 21
    - 1 in 700 children born in U.S.
- Chromosome 21 is the smallest human chromosome
- but still severe effects
  - Frequency of Down syndrome correlates with the age of the mother

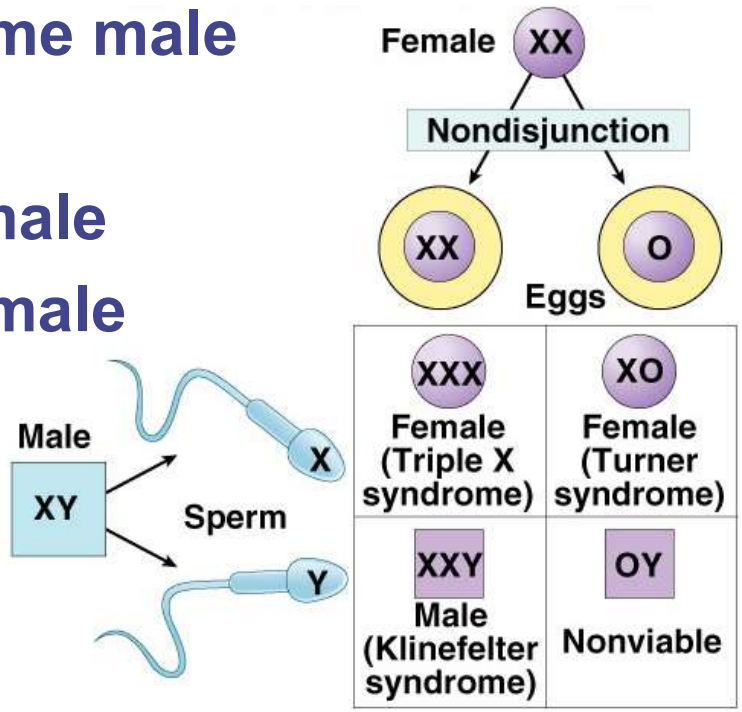




nted by permission from Nature
s Ltd

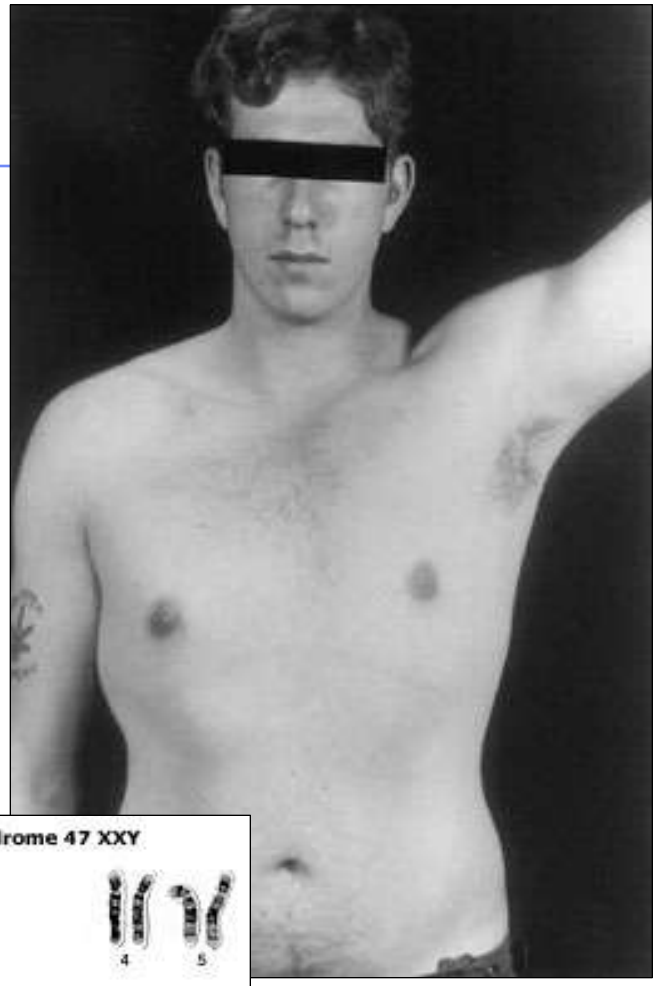
Sex chromosomes abnormalities

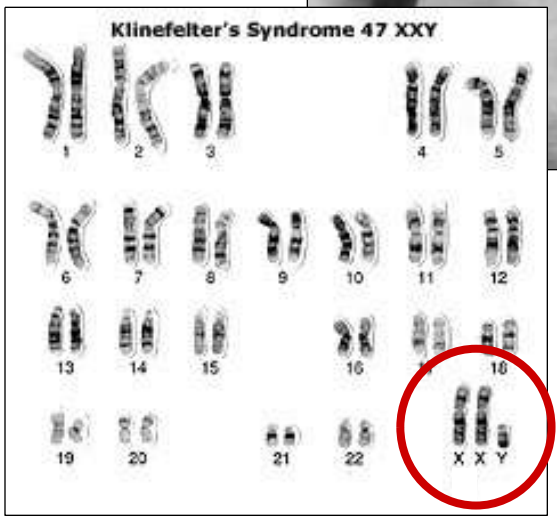
- Human development more tolerant of wrong numbers in sex chromosome
- But produces a variety of distinct syndromes in humans
  - XXY = Klinefelter's syndrome male
  - XXX = Trisomy X female
  - XYY = Jacob's syndrome male
  - XO = Turner syndrome female



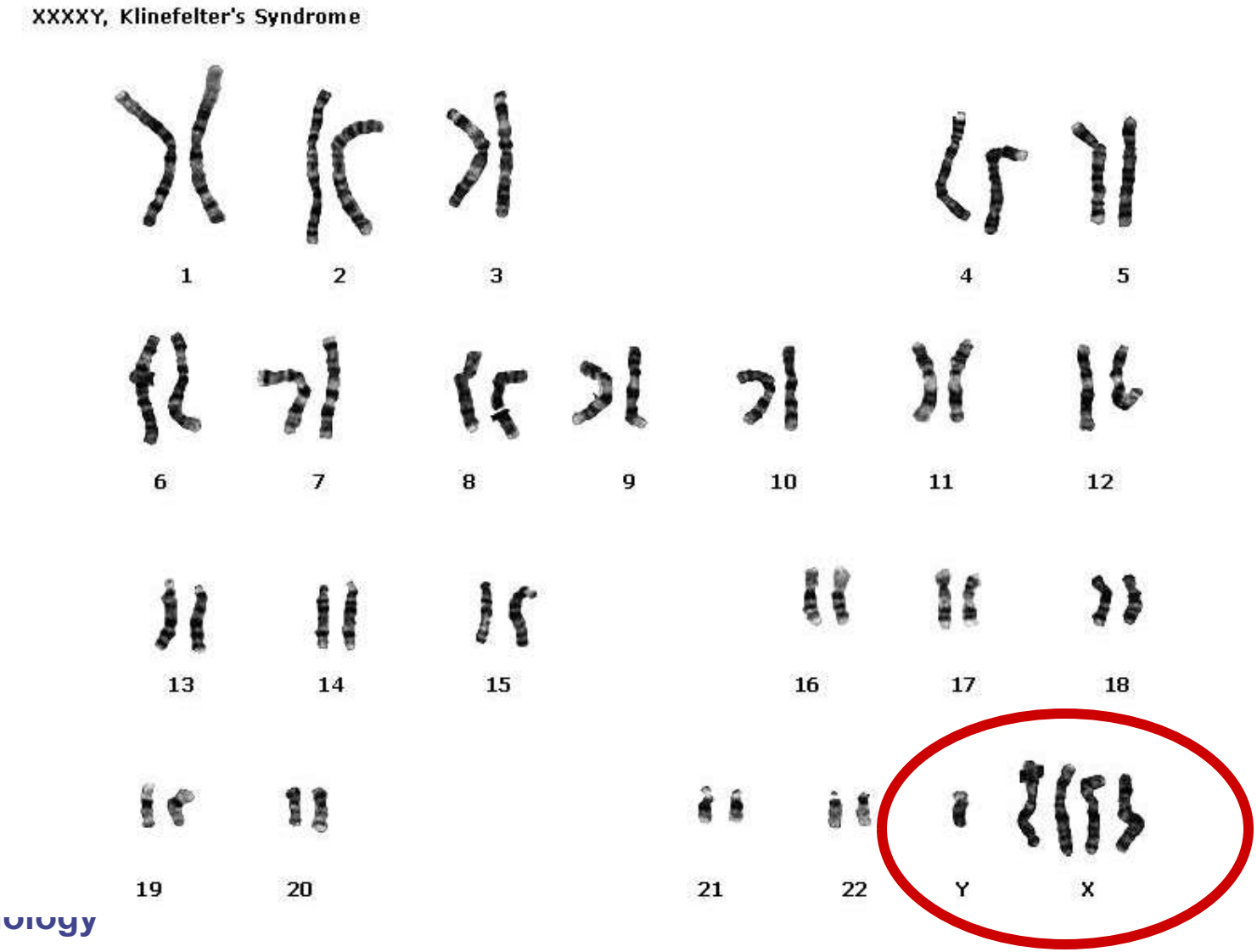
Klinefelter's syndrome

- XXY male
  - one in every 2000 live births
  - have male sex organs, but are sterile
  - feminine characteristics
    - some breast development
    - lack of facial hair
  - tall
  - normal intelligence



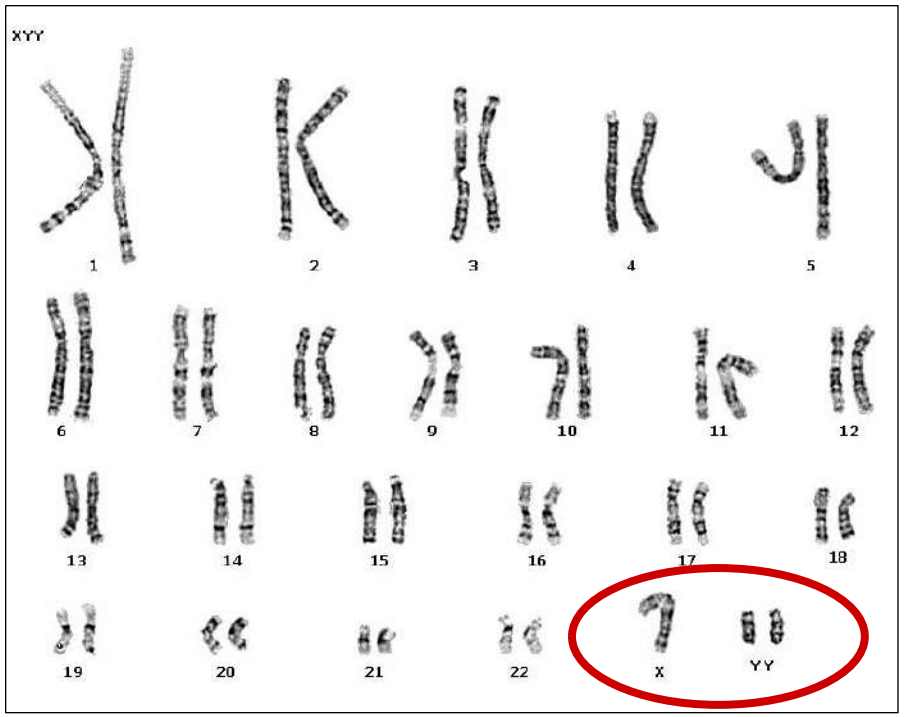


Klinefelter's syndrome



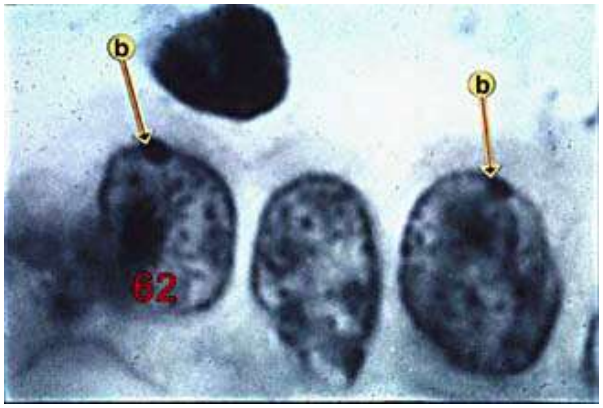
Jacob's syndrome male

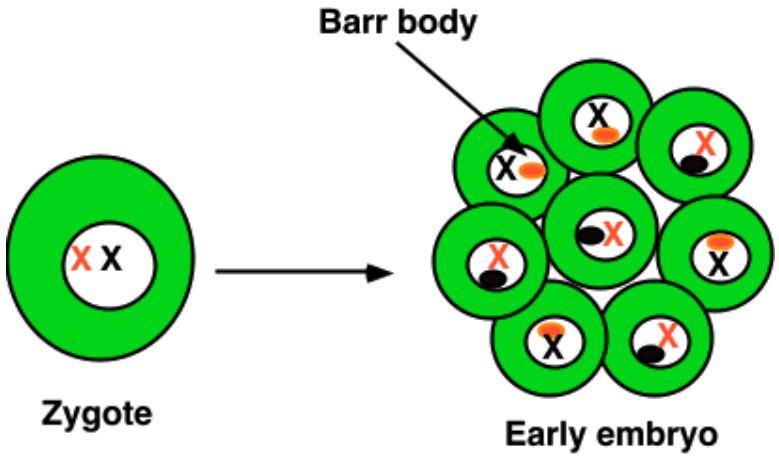
- **XYY Males**
  - 1 in 1000 live male births
  - extra Y chromosome
  - slightly taller than average
  - more active
  - normal intelligence, slight learning disabilities
  - delayed emotional maturity
  - normal sexual development



Trisomy X

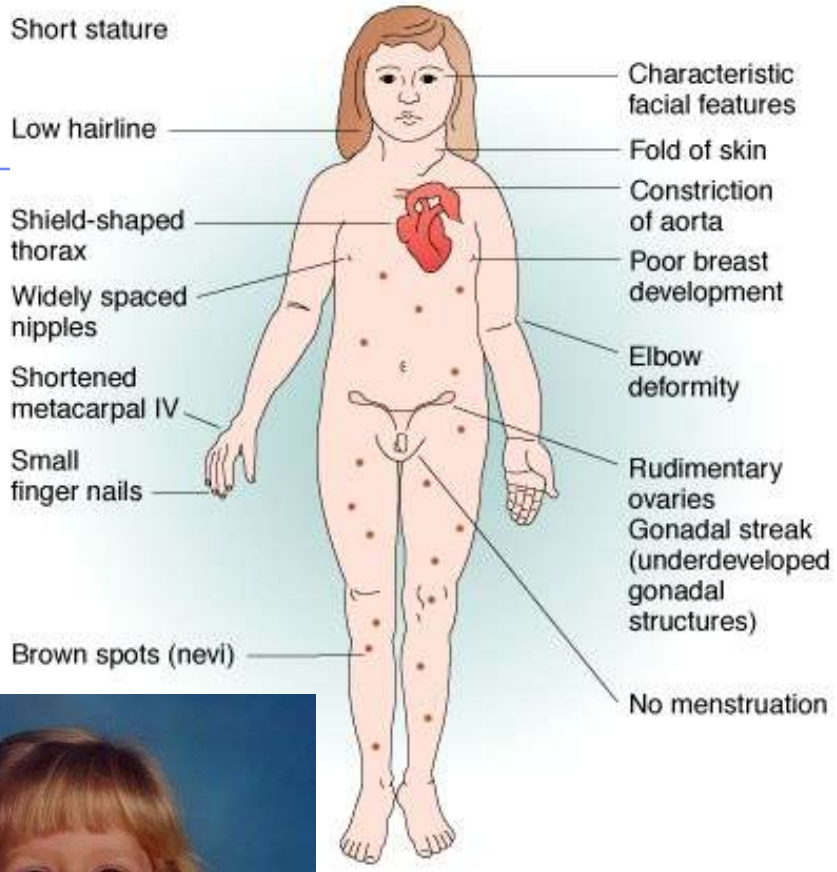
- **XXX**
  - 1 in every 2000 live births
  - produces healthy females
    - Why?
    - Barr bodies
      - all but one X chromosome is inactivated





Turner syndrome

- **Monosomy X or X0**
  - 1 in every 5000 births
  - varied degree of effects
  - webbed neck
  - short stature
  - sterile



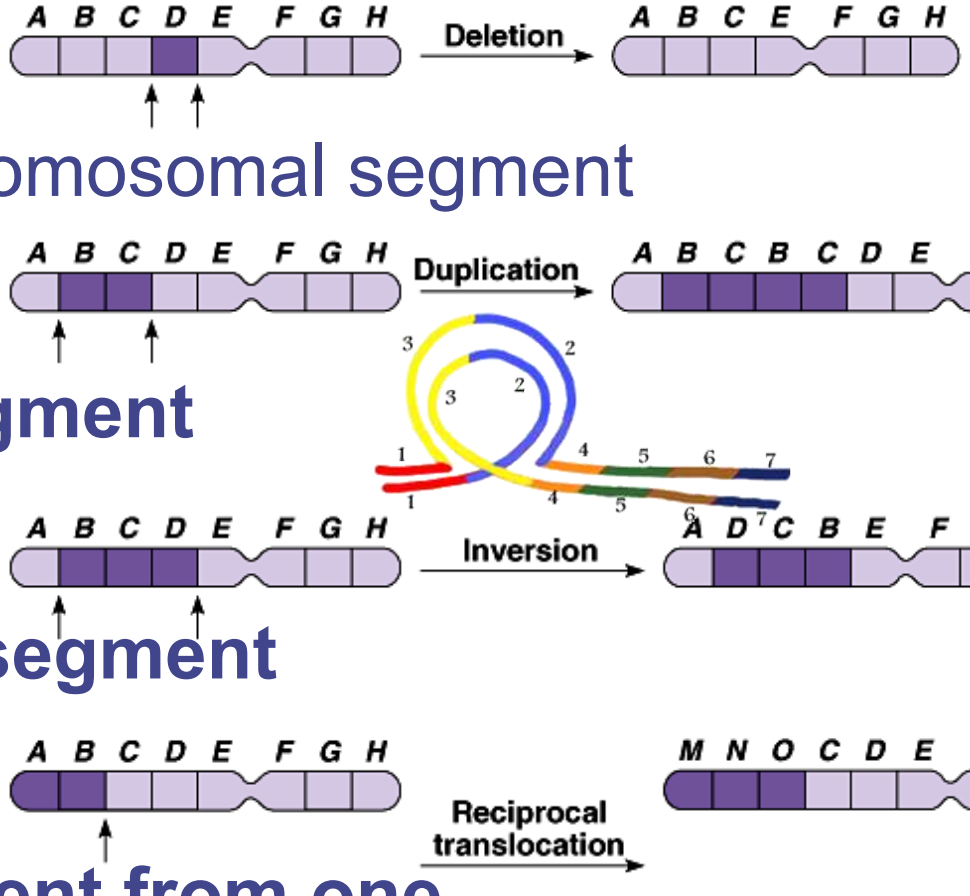
Changes in chromosome structure

error of replication

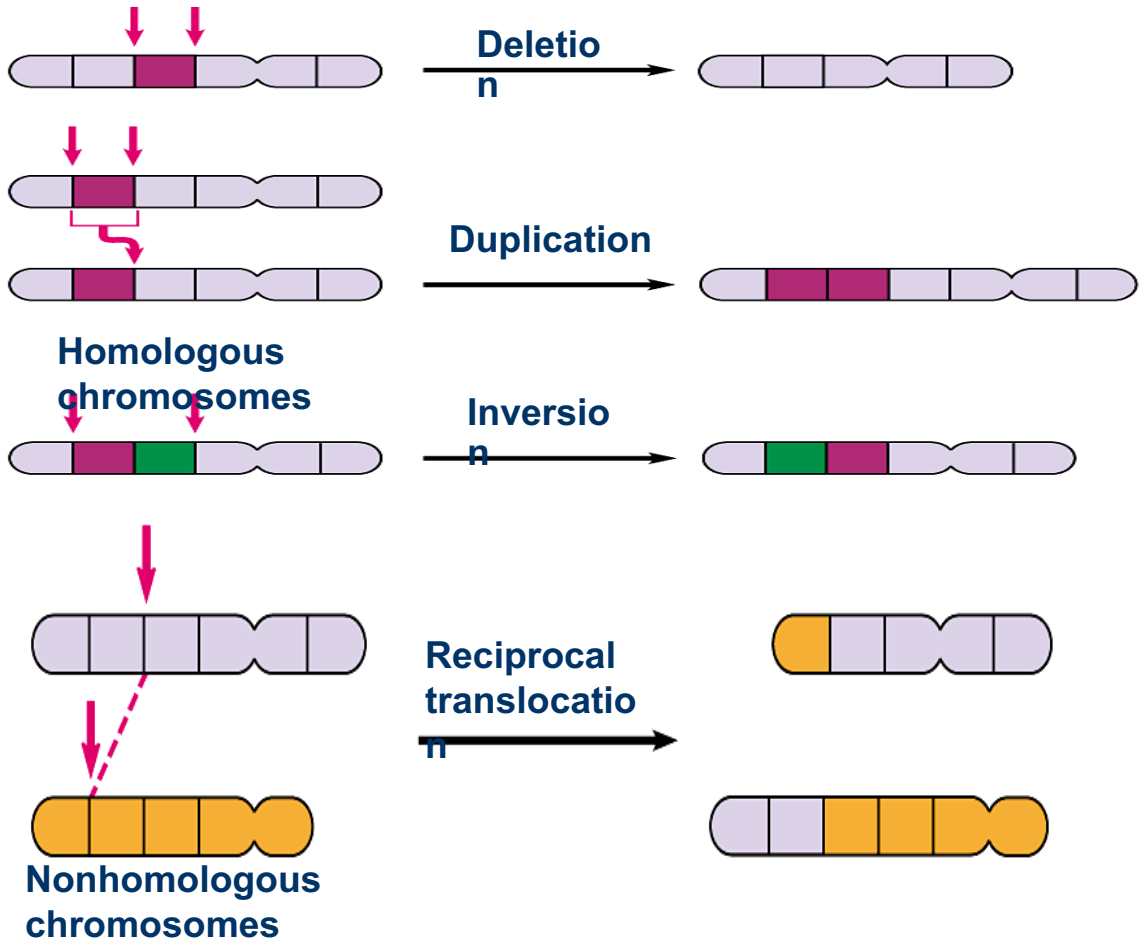
- **deletion**
  - loss of a chromosomal segment
- **duplication**
  - repeat a segment

error of crossing over

- **inversion**
  - reverses a segment
- **translocation**
  - move segment from one chromosome to another



Chromosomal errors VI



Genomic imprinting

- Def: a parental effect on gene expression
- Identical alleles may have different effects on offspring, depending on whether they arrive in the zygote via the ovum or via the sperm.
- Fragile X syndrome: higher prevalence of disorder and retardation in males