CYTOGENETICS '3'

Chromosomal abnormalities

Abnormal karyotypes

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Types of chromosomal abnormalities

Numerical

- Aneuploidy (monosomy, trisomoy, tetrasomy)
- Polyploidy (triploidy, tetraploidy)

Structural

- Translocation
- Inversion
- Insertion
- Deletion
- Ring
- Isochromosomes
- ESAC

Numerical

Aneuploidy

- Autosomal trisomy, 47
- Sex chromosomes, 45,47,48,49

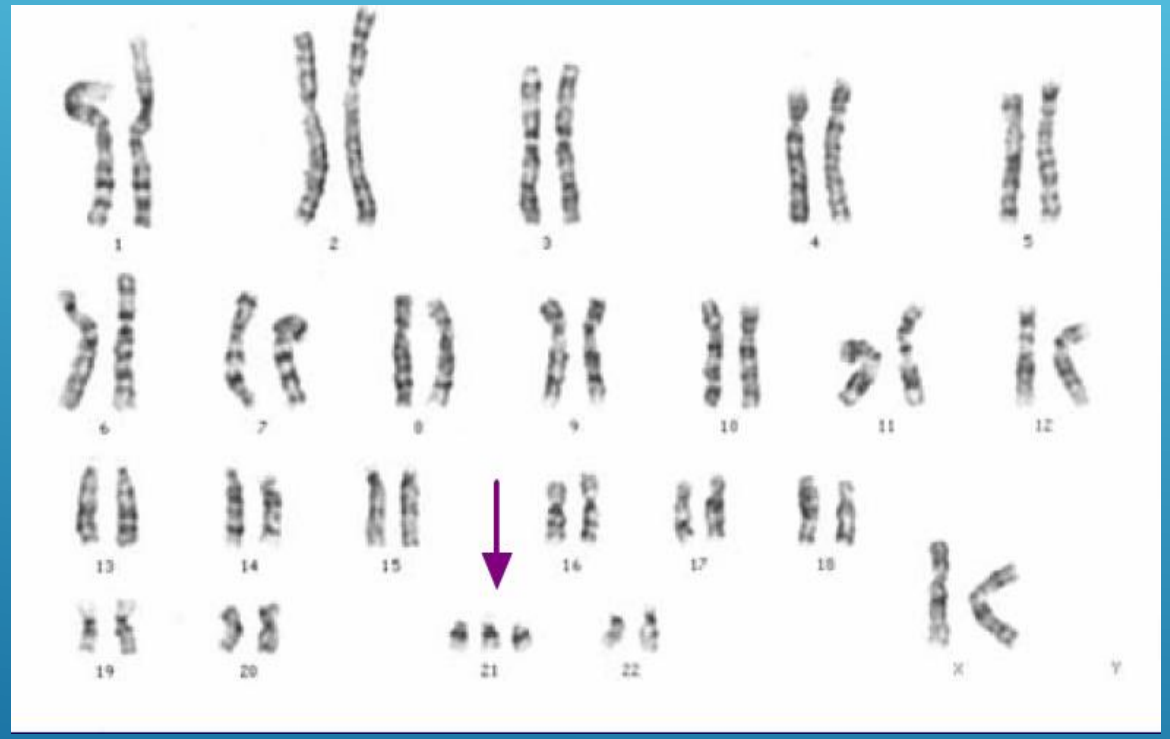
Polyploidy

- Whole chromosome set
- Triploidy, 69
- Tetraploidy, 92

Aneuploidy

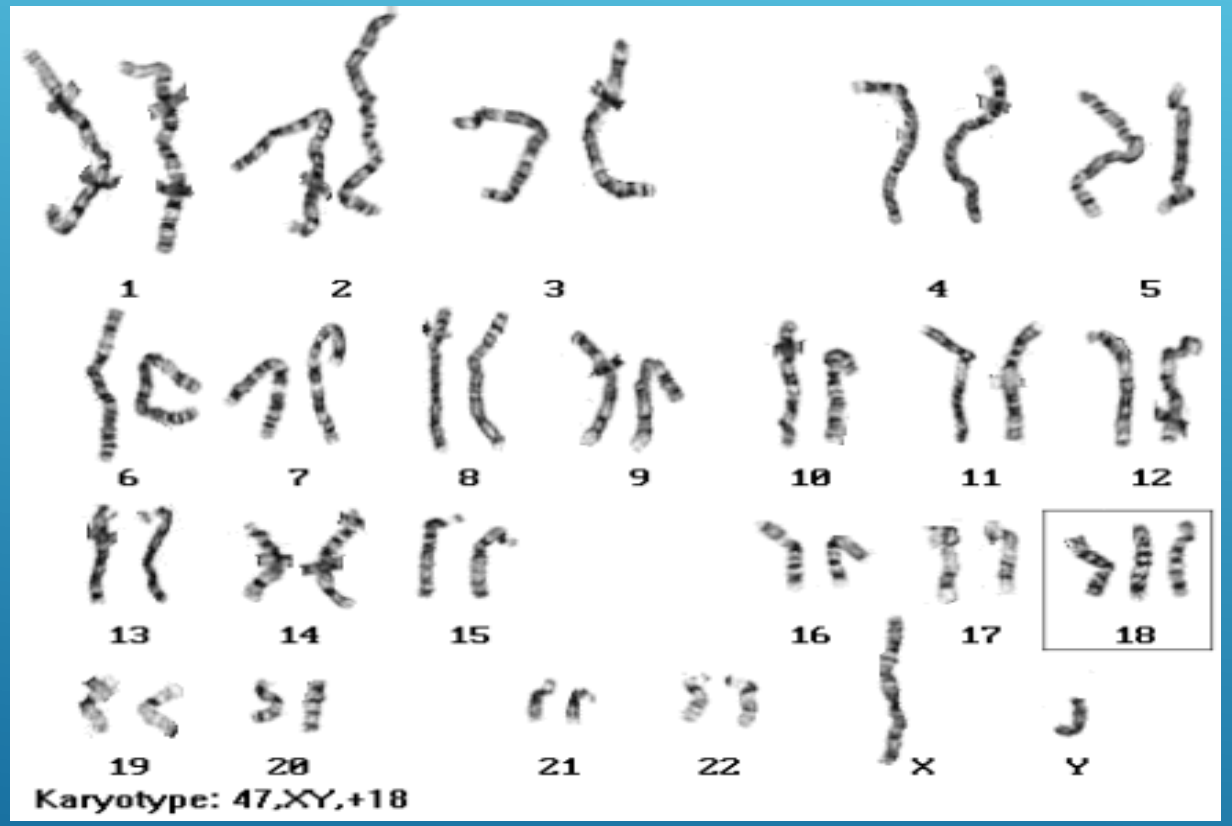
- Almost all types found in oocytes and early embryo
- Most lethal (miscarry)
- Don't see in pregnancy or live born
- Expect sex chromosomes and Down (incidence at birht1/800)
- Some is age related

Down syndrome



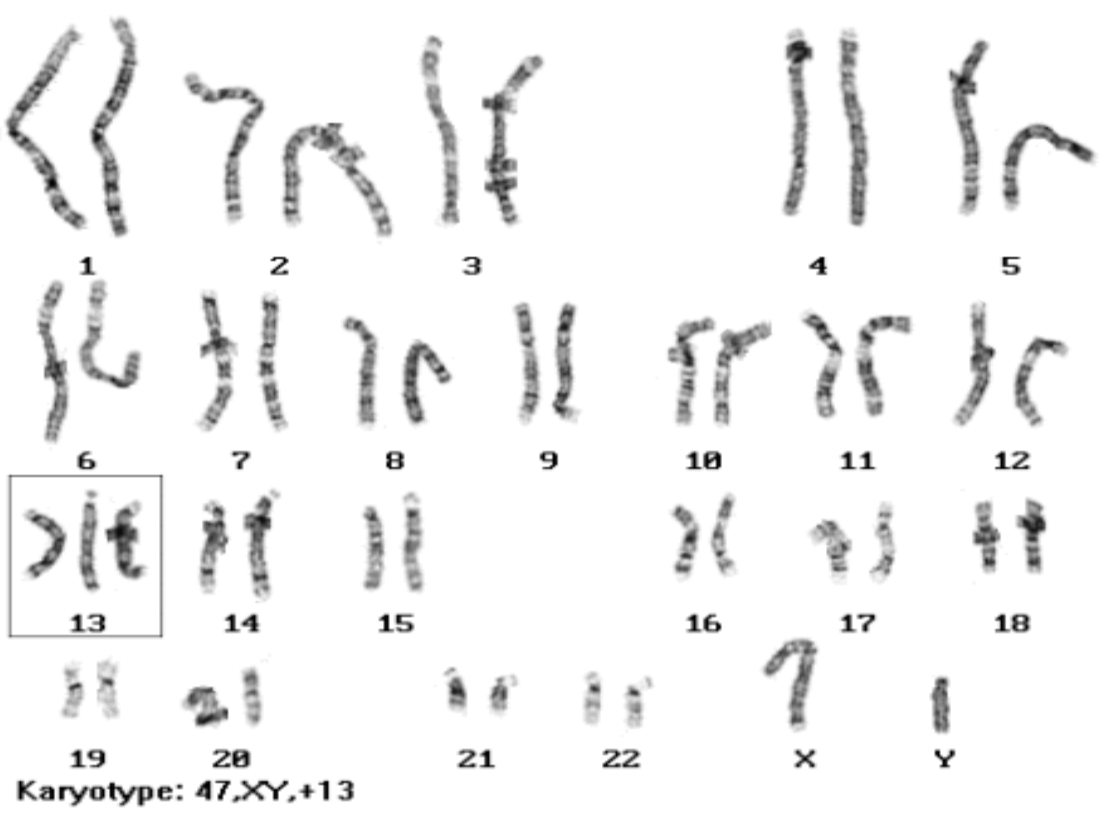
47,XX,+21

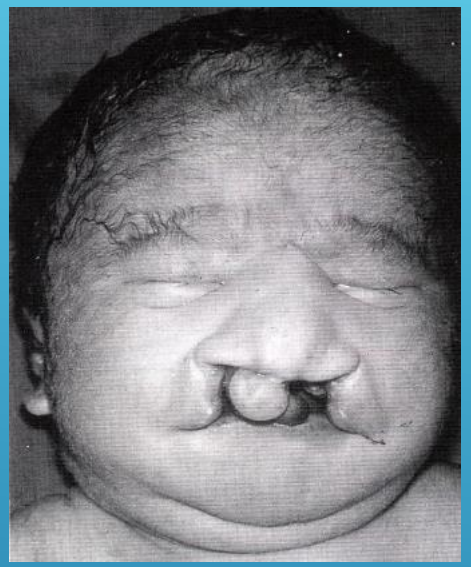
Edward syndrome (trisomy 18)



Incidence at birth 1/6000

Patau syndrome (trisomy 13)





Incidence at birth 1/12,000

Sex chromosomes

- More tolerated abnormalities

- If extra Y … few genes mainly for sex determination
- If extra X … excess X is inactivated

Sex chromosomes

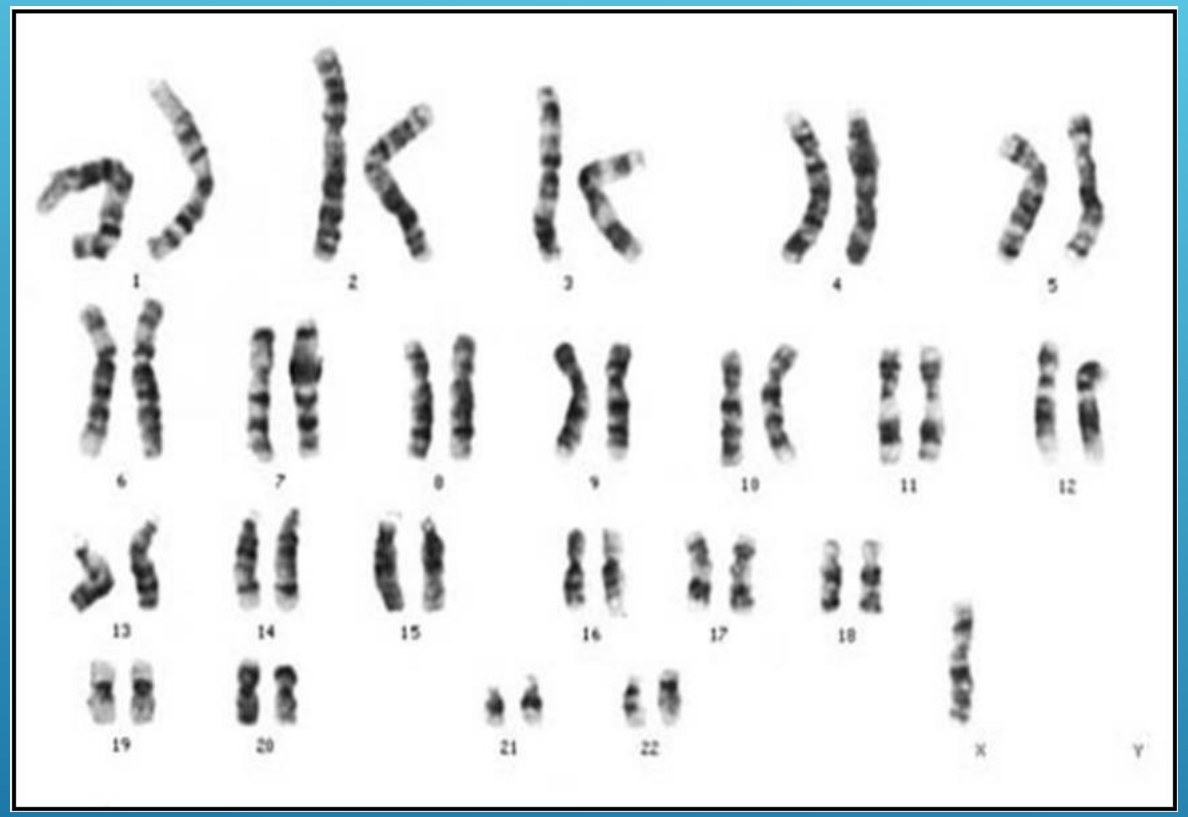
Turner syndrome:

- Majority die during development
- Only few survive to birth
- Short and infertile

Sex chromosomes

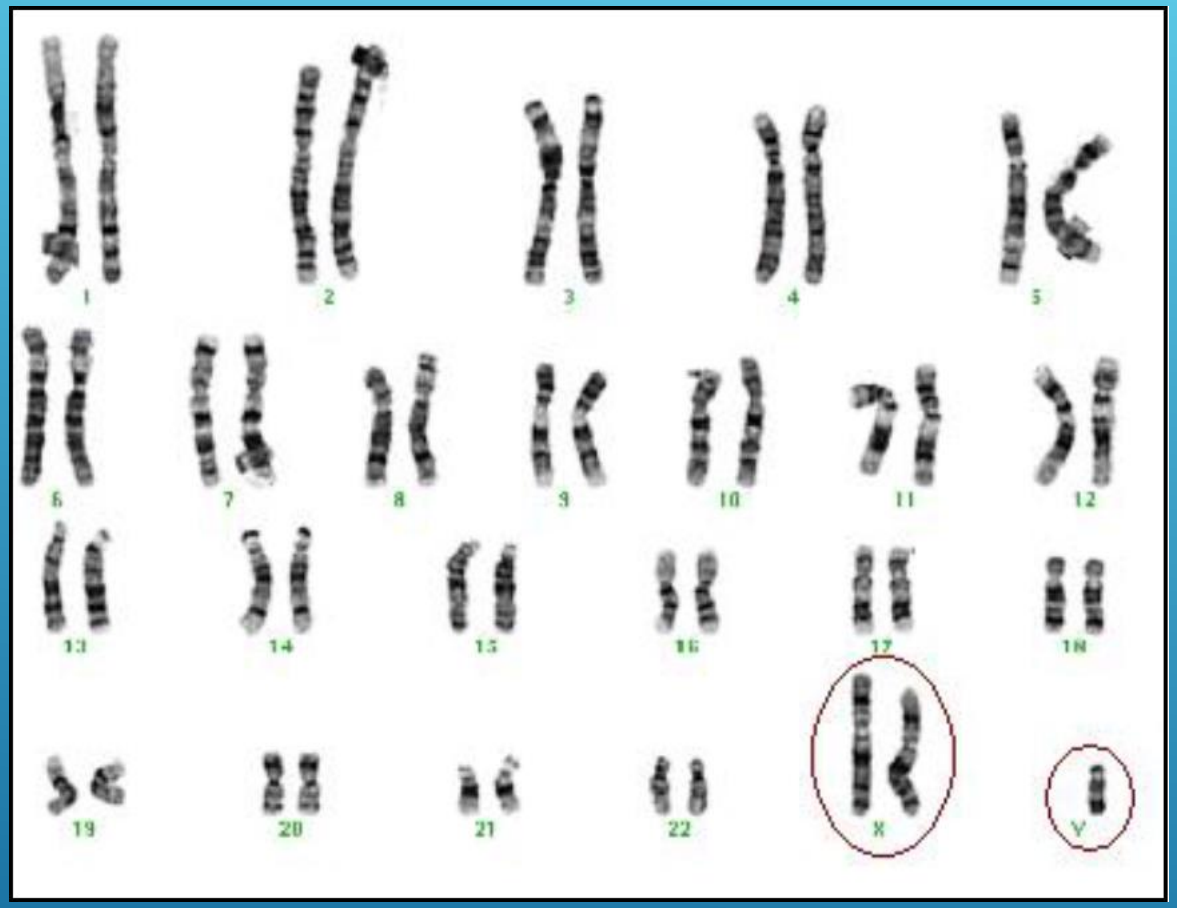
- Turner (monosomy) 45, X0 (female)
- Trisomy X 47,XXX (female)
- Klinefelter syndrome 47,XXY (male)
- Extra Y chromosome 47,XYY (male)

Turner Syndrome



45, X

Klinefelter Syndrome



47, XXY

Structural abnormality

Breaks in at least 1 chromosome

Translocations:
2 different chromosomes breaks and re-join incorrectly
Inversion:
2 breaks in same chromosome
Insertion:
Piece of chromosome inserted
Deletion:
Piece of chromosome missing

Translocations

A portion of chromosome moves to another chromosomes

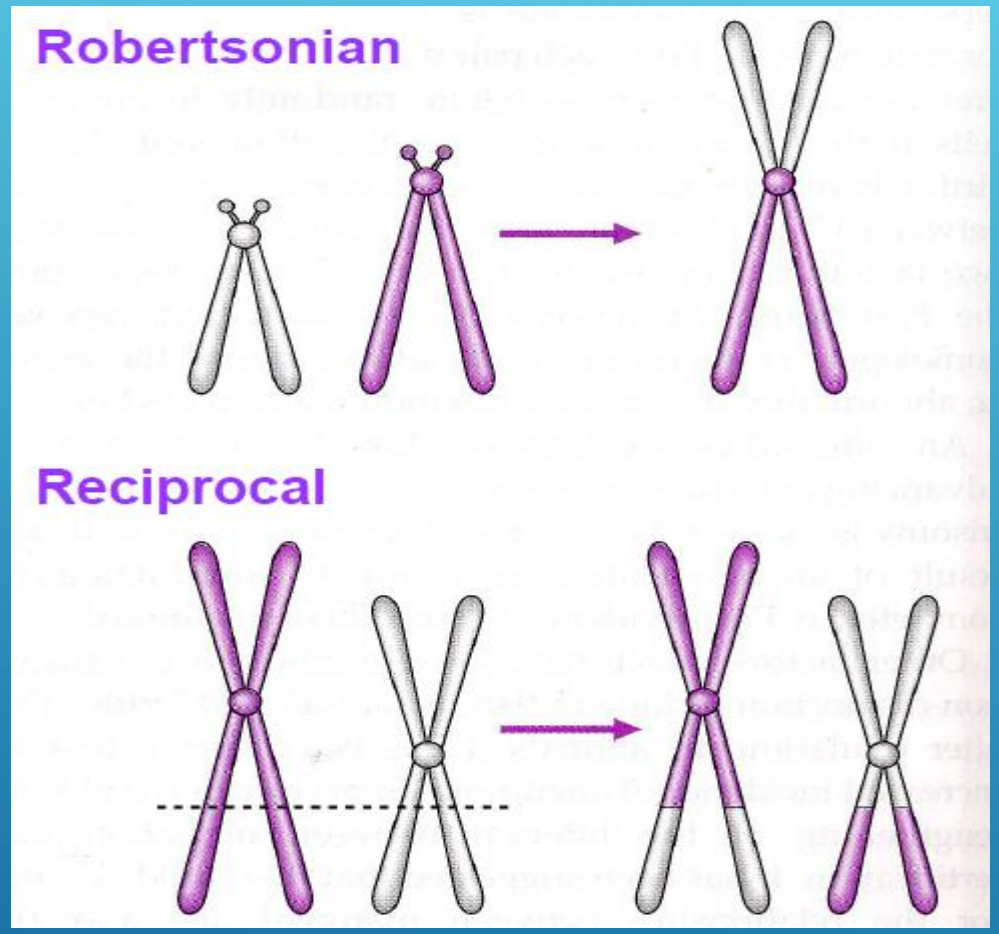
Robertsonian:

- An entire chromosome attach to another at the centromere.
- Acrocentric
- D and G group (13,14,15, 21, 22)

Reciprocal:

- Segment of 2 different chromosomes has been exchanged
- Any chromosomes

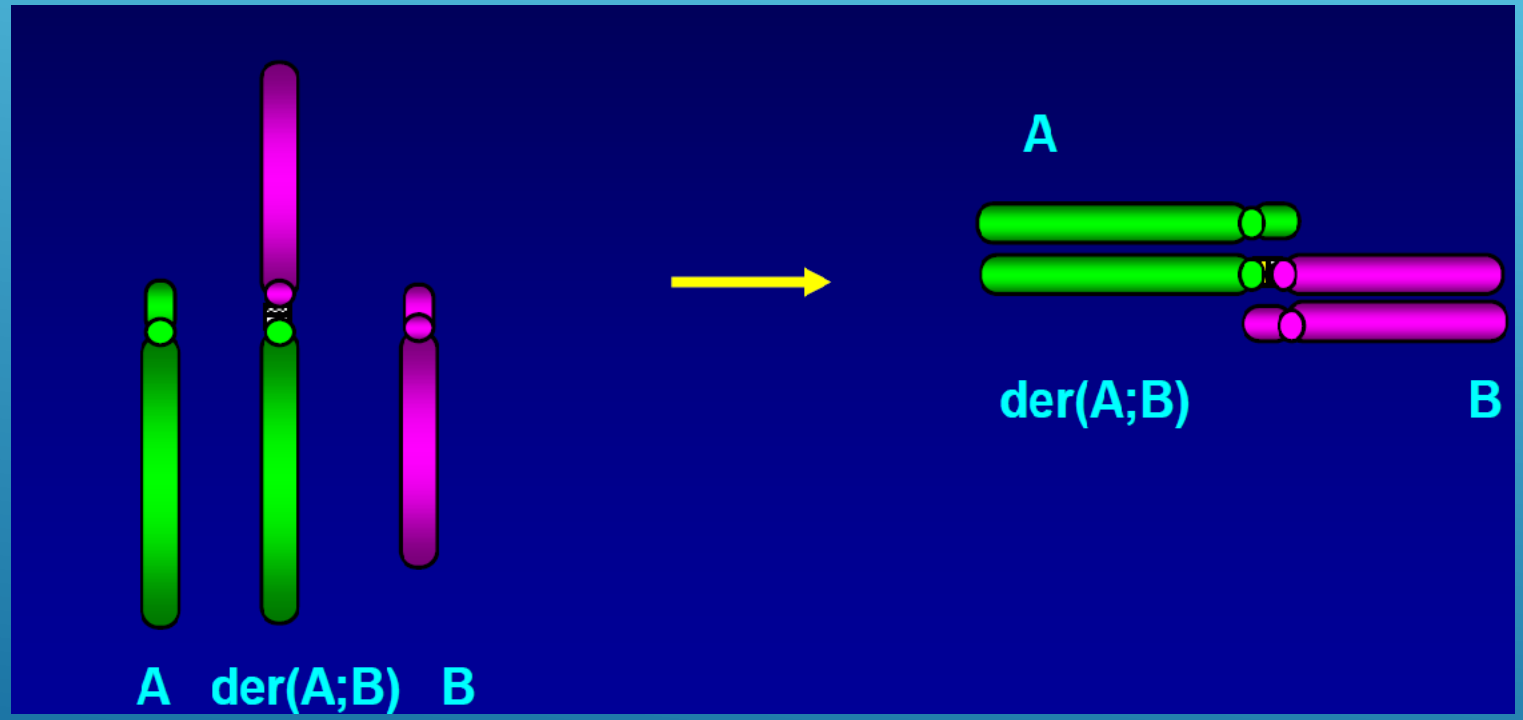
Translocations



Robertsonian translocation

- Loss satellite and short arms
- Repeated on other acrocentric chromosome
- Reduce chromosome number by one 45
- No loss from long arm
- Phenotypically normal (problem at meiosis)
- Involved in evolution

Robertsonian translocation



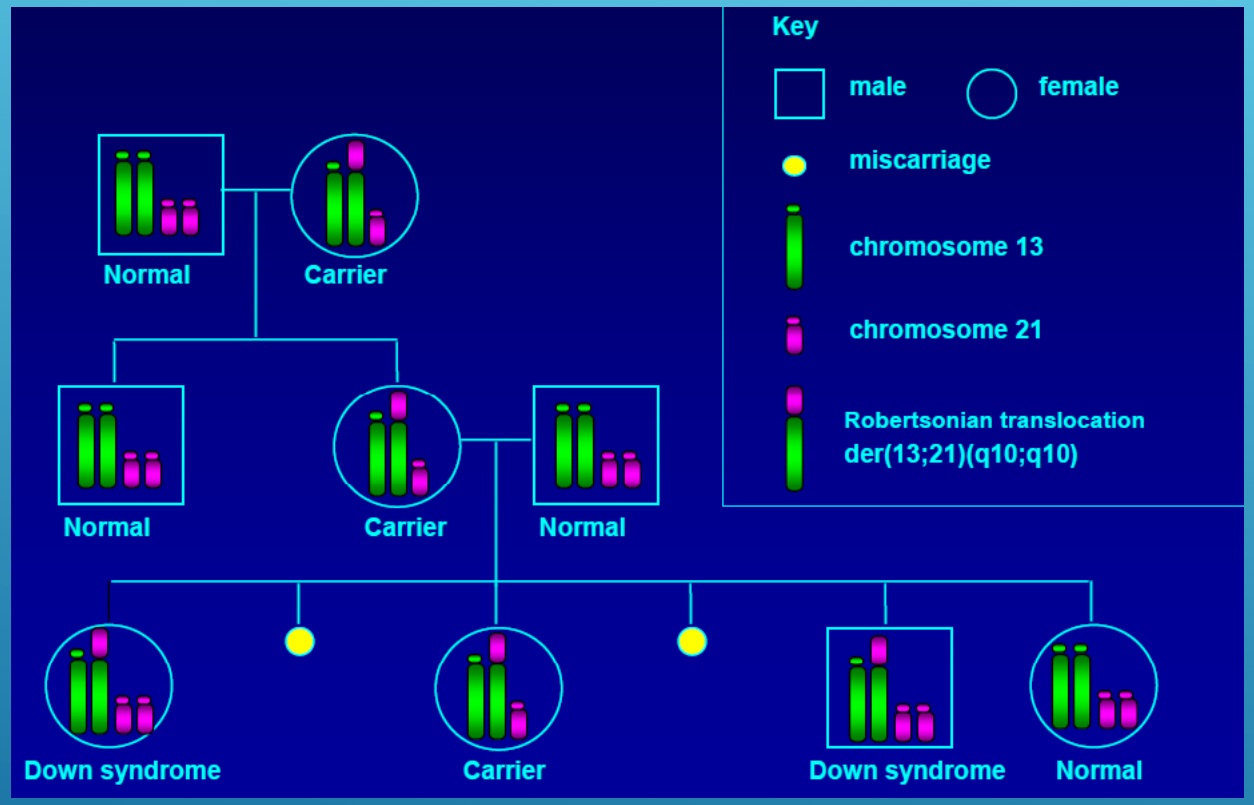
Robertsonian translocation

Occur in 1/500

D:G translocation	14:21 joined	
D:D translocation	13:14 joined	
G:G translocation	21:22 joined	21:21 joined

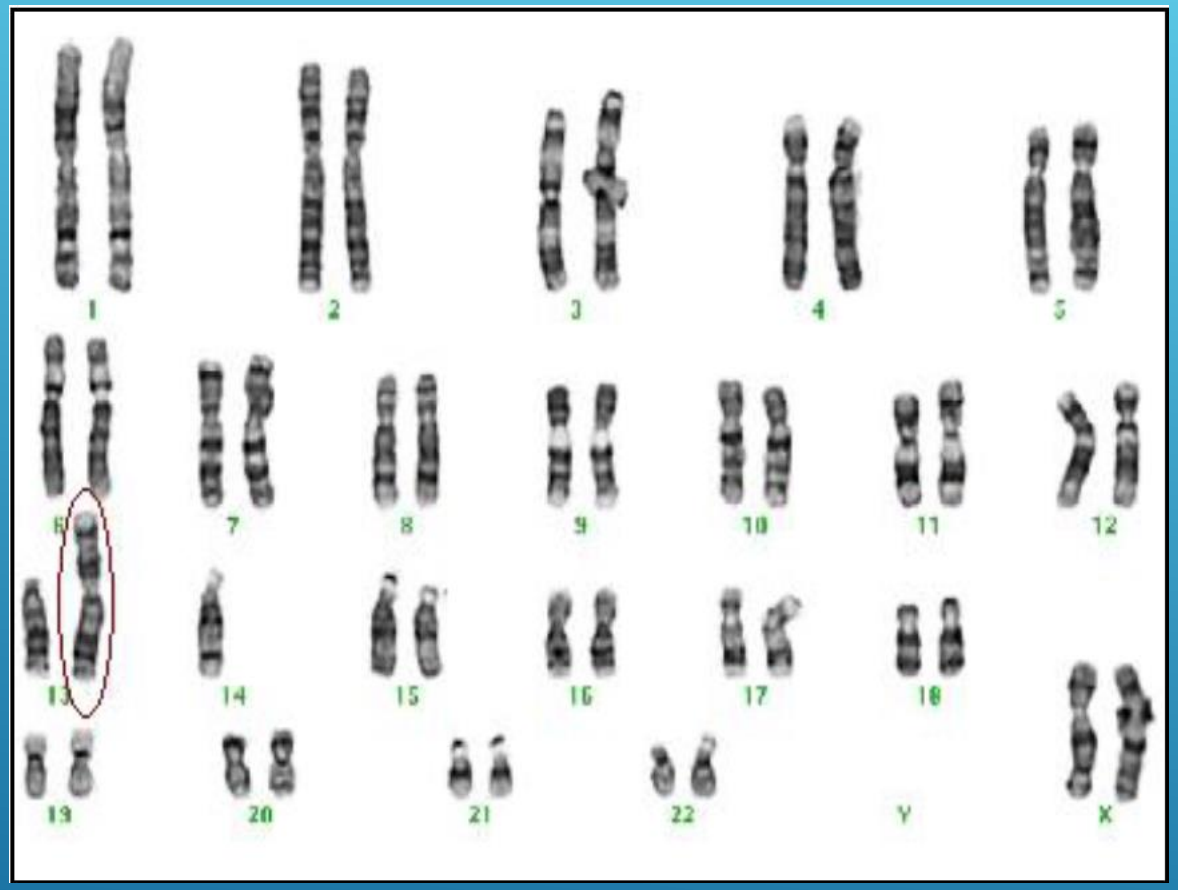
45, XY, der(13q:14q)(q10:q10)
45, XX, der(13q:21q)(q10:q10)

Robertsonian translocation



Family pedigree of robertsonian translocation

Robertsonian translocation

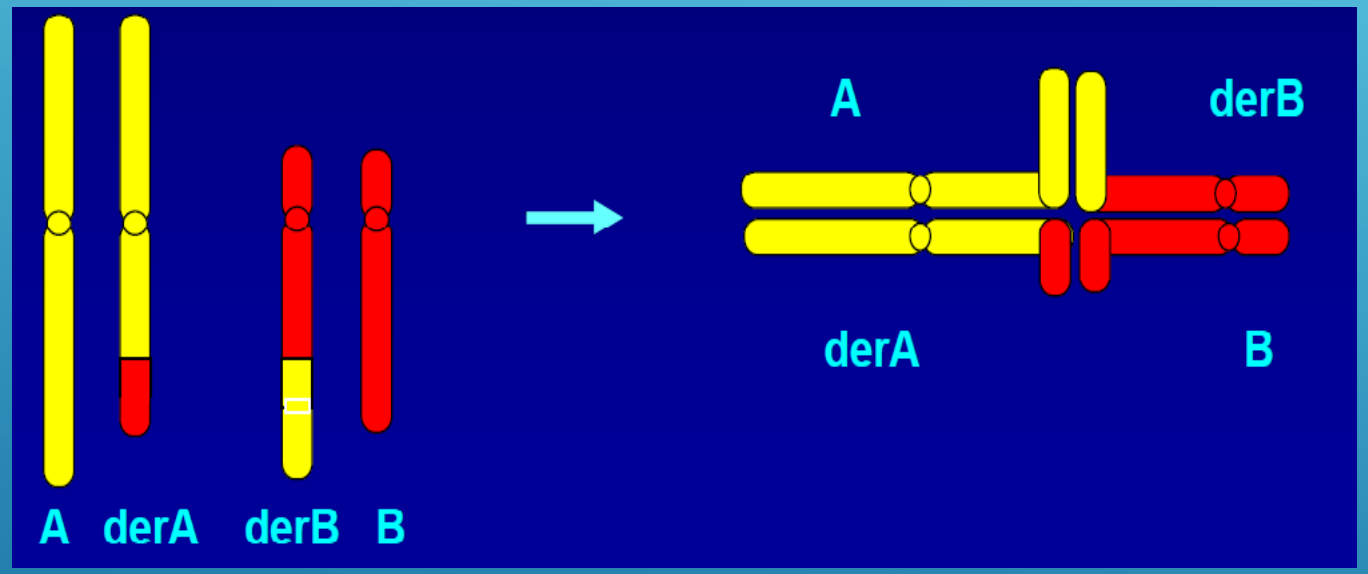


45, XX, der(13q:14q)(q10:q10)

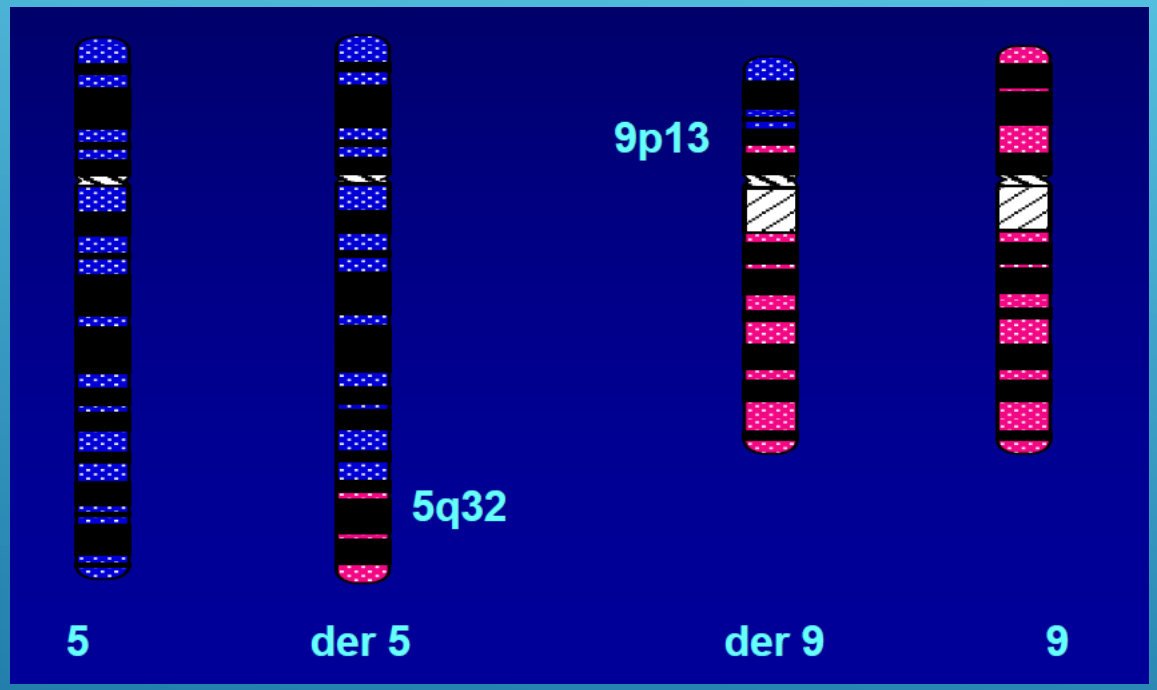
Reciprocal translocation

- More common than Robertsonian translocation
- Break in any chromosome at any point
- Phenotypically normal (problem at meiosis)

Reciprocal translocation



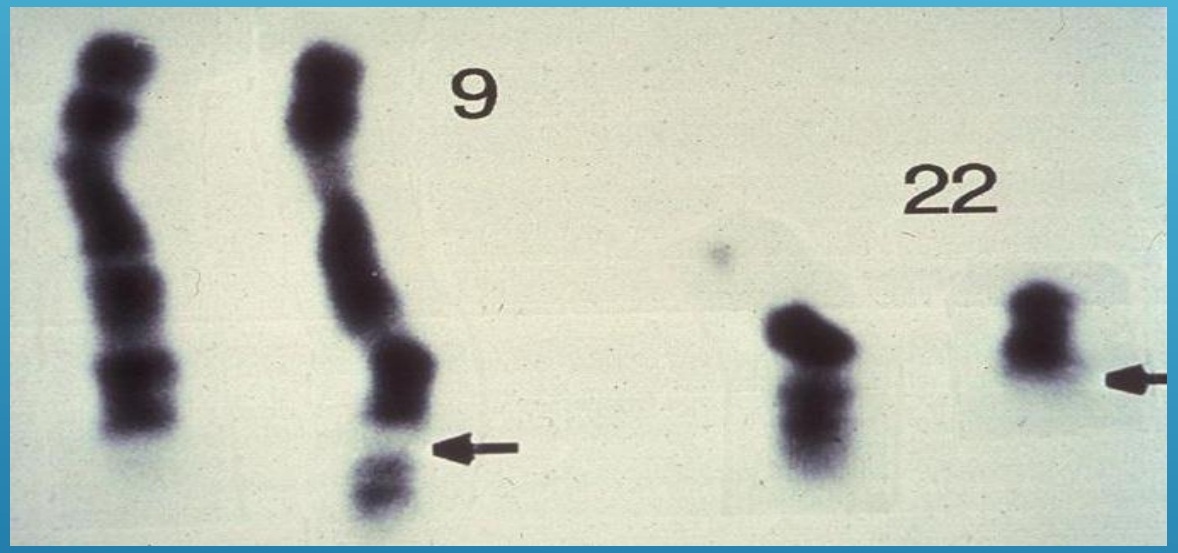
Reciprocal translocation



46,XX,t(5;9)(q32;p13)

Reciprocal translocation

Philadelphia chromosome

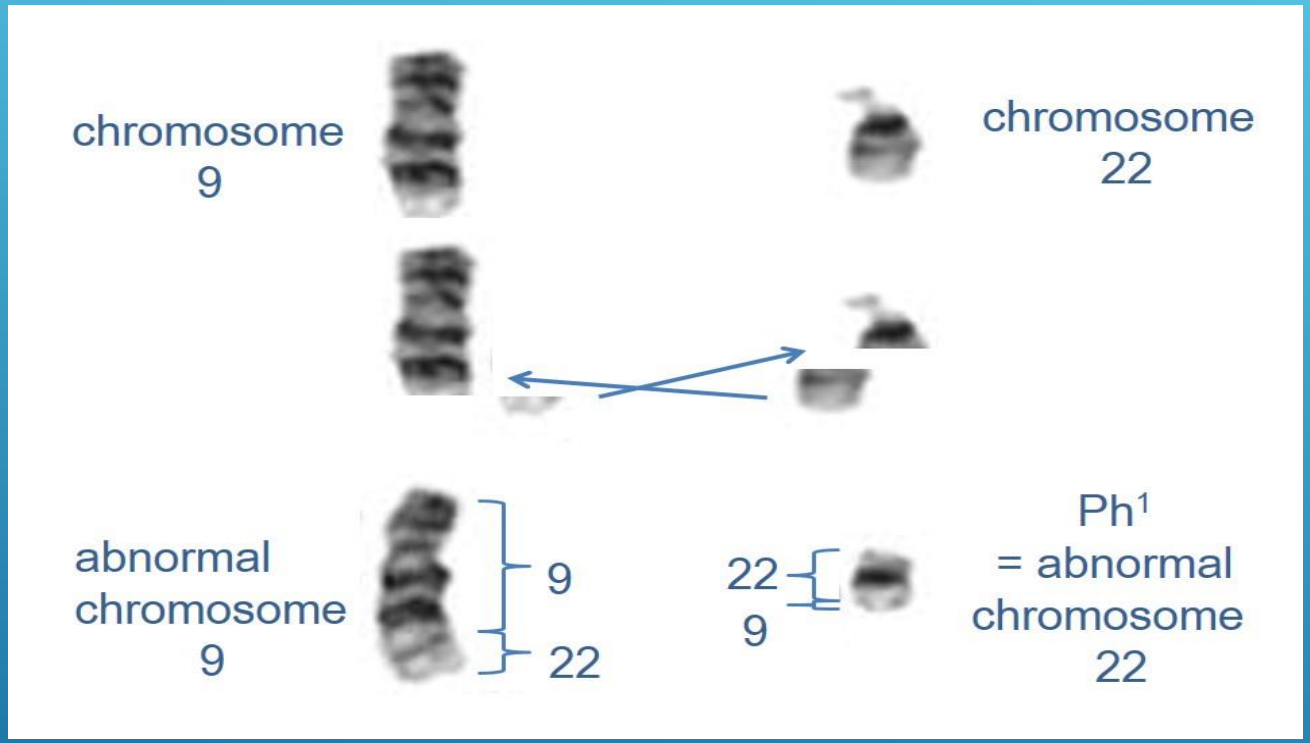


Peter C. Nowell, MD, Department of Pathology and Clinical Laboratory of the University of Pennsylvania School of Medicine, 1960

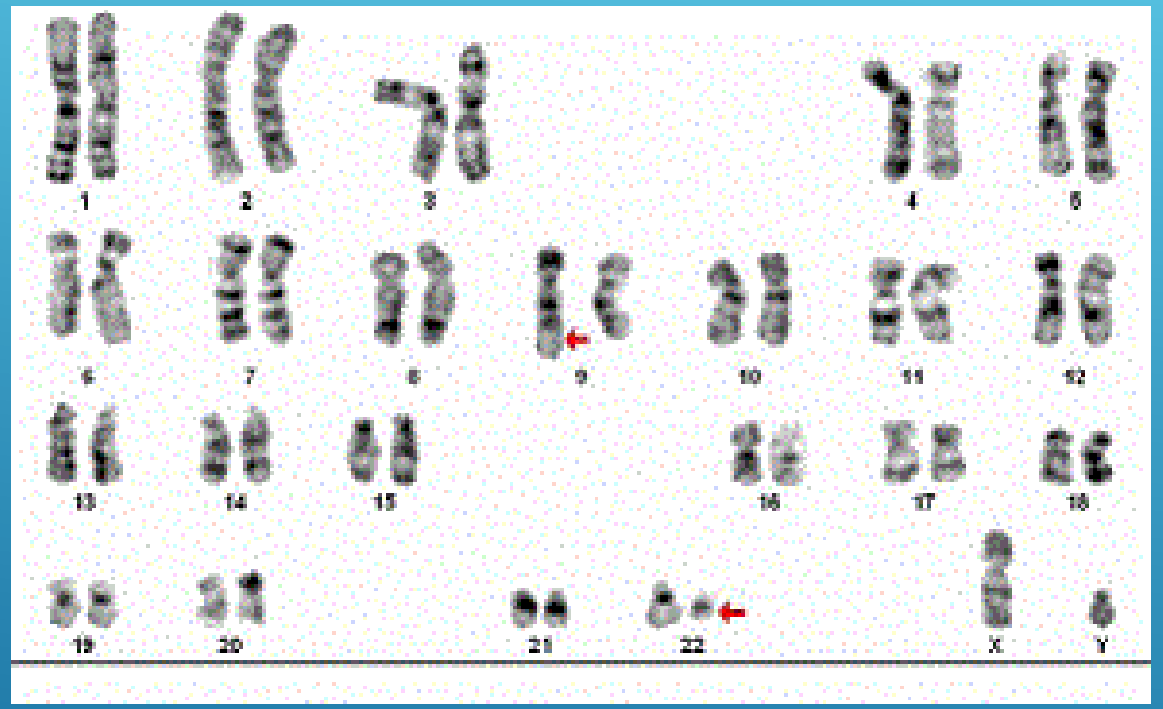
Philadelphia Chromosome

- 1960, in Philadelphia
- reciprocal translocation of 22q to the lower arm of 9 and 9q
- Associated with CML but not sufficiently specific
- Seen also in AML

Philadelphia Chromosome



Philadelphia Chromosome



46,XY,t(9;22)(q34;q11)

Inversion

Reversal of segments of chromosome

- If too small, cant detected by karyotype
- Very rare in humans

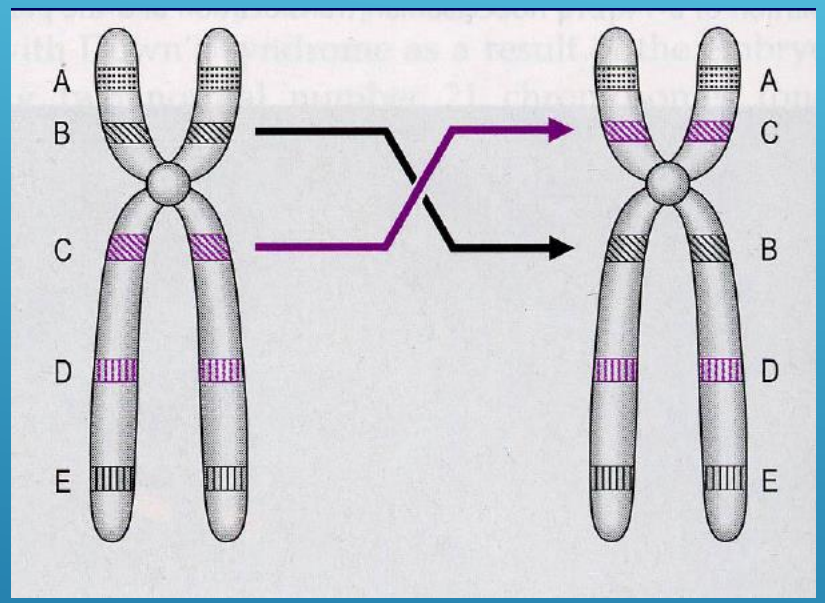
Pericentric:

Includes centromere

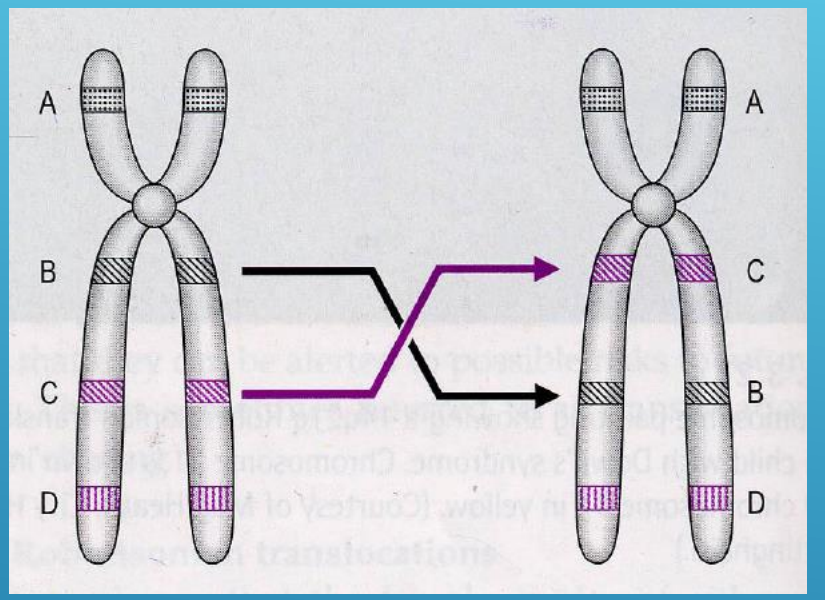
Paracentric:

Within one arm

Inversion



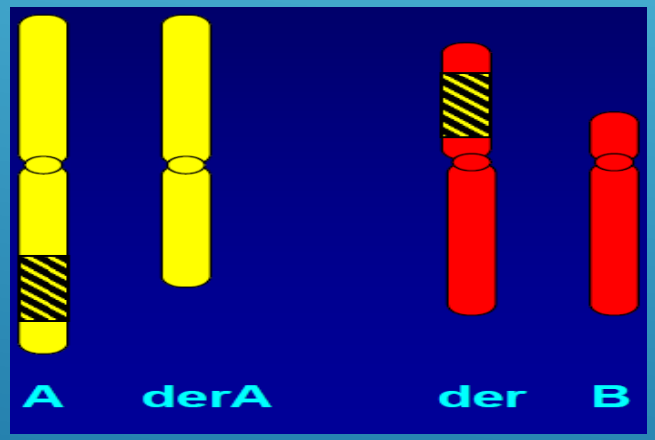
Pericentric



Paracentric

Insertion

Segment of 1 chromosome inserted into another



Deletion

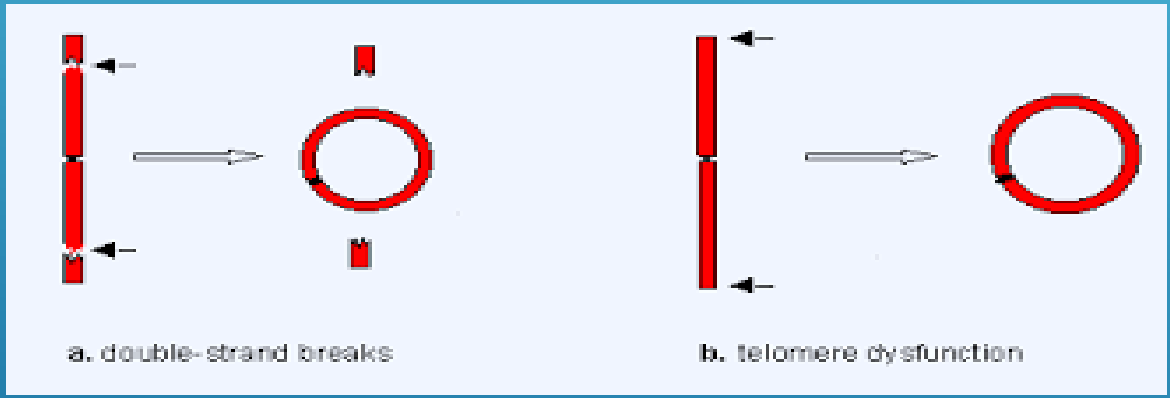
- A portion of chromosome is missing or deleted
- Unbalance karyotype
- Serious clinical effect

Terminal:
Loss of end of chromosome

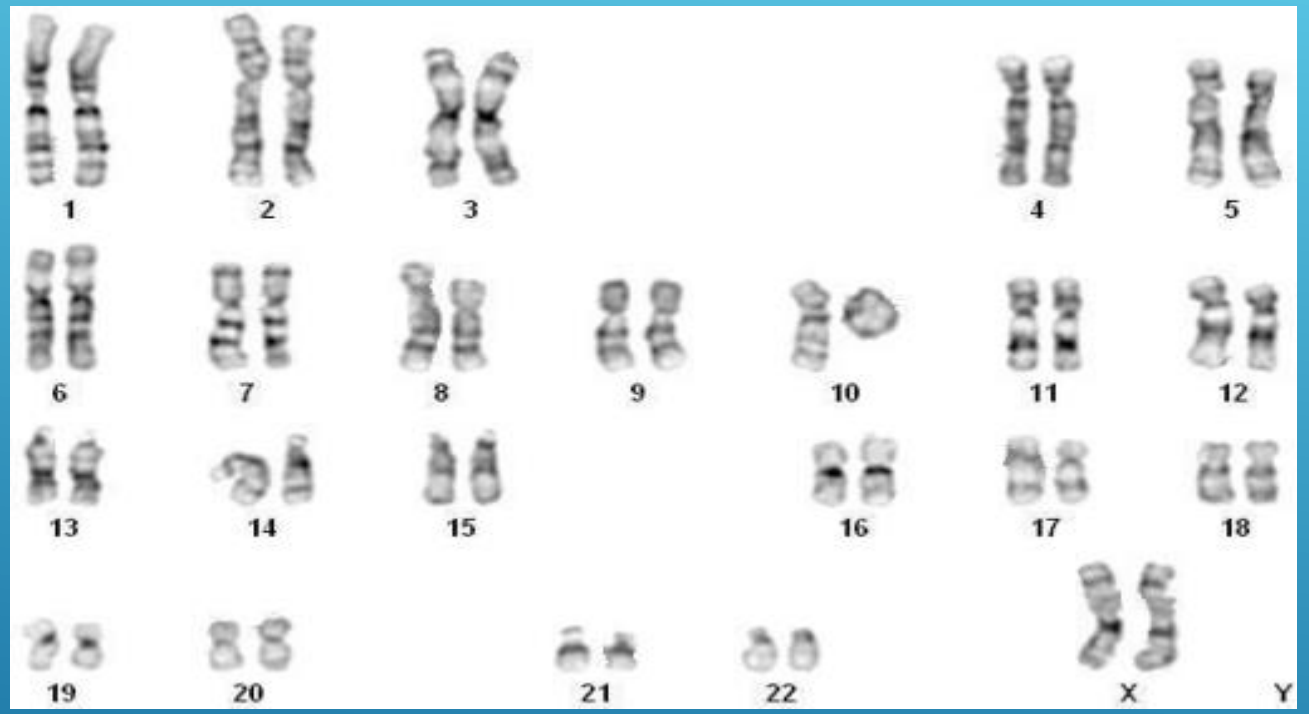
Interstitial:
Loss of segment from within chromosome

Ring chromosome

- A portion of chromosome has break off and formed a circle
- Can happen with or without loss of genetic material



Ring chromosome

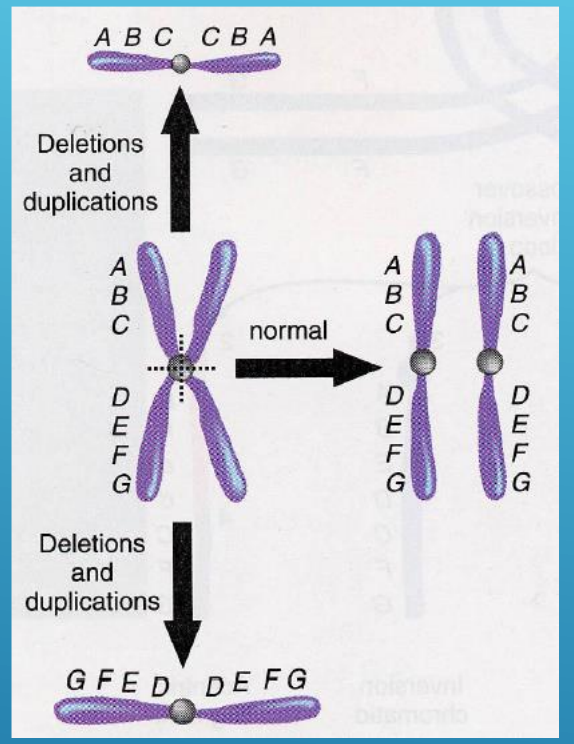


46,XX,r(10)

Isochromosmome

Mirror image around the centromere
2 copies of the same arm

Monosomy for 1 arm
Trisomy for the other arm



Karyotyping activity

You will evaluate 3 patients' case histories, complete their karyotypes, and diagnose any missing or extra chromosomes:

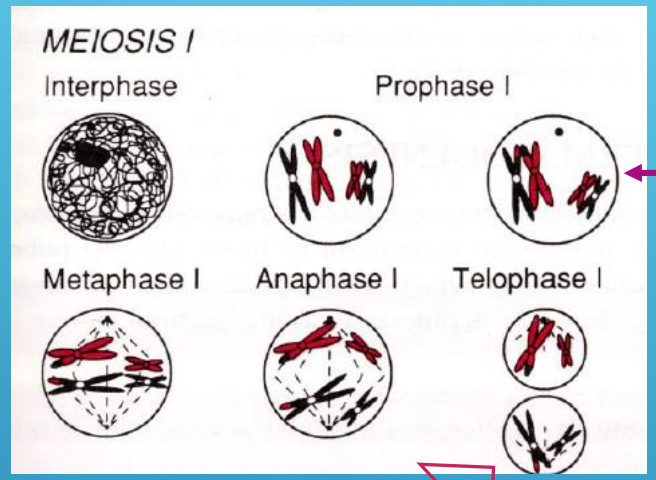
http://www.biology.arizona.edu/human_bio/activities/karyotyping/karyotyping2.html

Genetic diversity

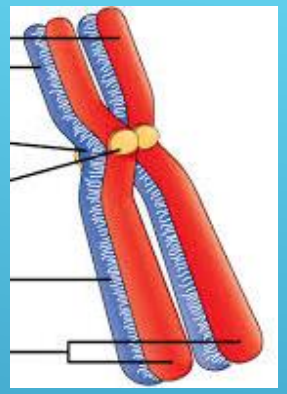
1. Crossing over in M1:

- Prophase 1
- Swap pieces of DNA bet. Maternal and paternal homologous chromosomes

2. Random assortment at the end of M1

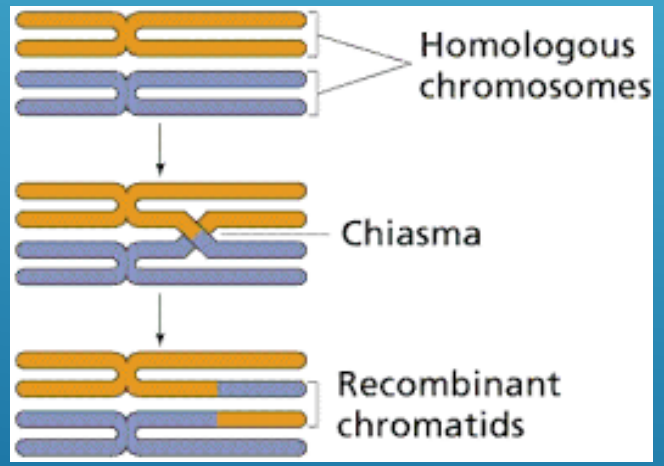


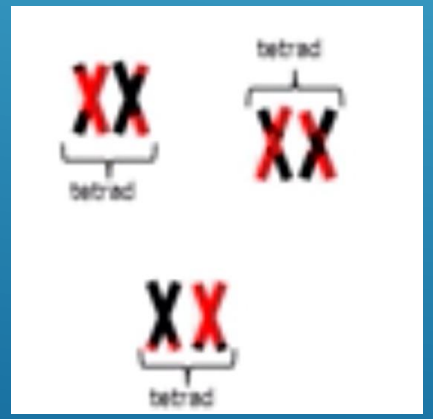
Tetrad (synapsis)



Crossing over

1st diversity





2nd diversity

Thanks for listening