Cytogenetics

3rd Lecture

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Chromosomal Abnormalities

-- Classifications

-- Constitutional أنتقالي & Acquired مكتسب

-- Homogenousمتجانس & Mosaic مختلط

--Structural تركيبي and Numerical عددي

Constitutional Chromosomal Abnormalities

1. They exist in all individual body cells when they inherited.
2. Mostly they inherited from one parent - Chromosome Inborn Syndromes .
3. Or they occurred after first embryonic divisions - de novo.
4. Caused by non disjunction in meiosis or mitosis divisions.

How Can we distinguish between Inborn syndrome from de novo?

Normal Meiosis

Mother

Father

46 chromosomes

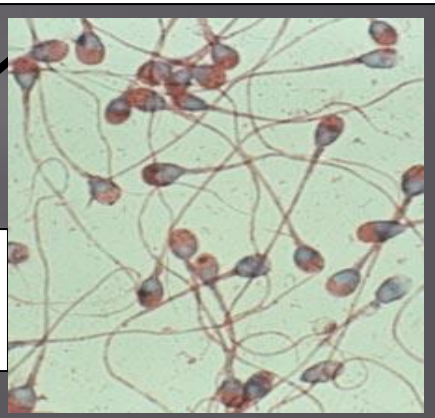
46 chromosomes

Sex cells

Meiosis

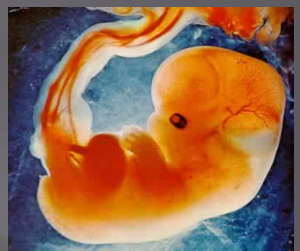
23 chromosomes

23 chromosomes

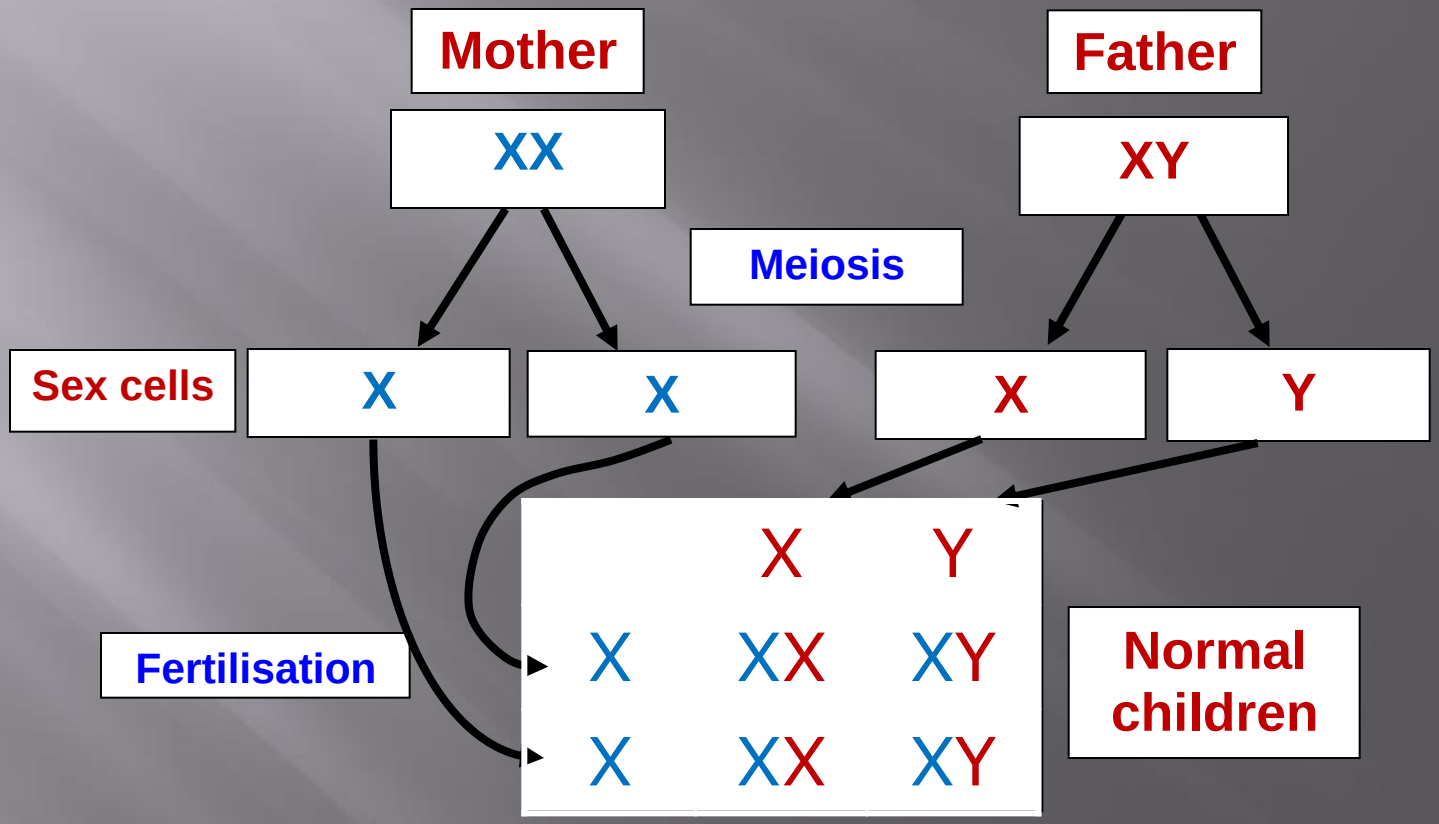


Fertilization

Embryo with 46 chromosomes



Normal Meiosis



Abnormal Meiosis-Constitutional

Mother

46 chromosomes

Sex cells

Meiosis

23 chromosomes

Father

46 chromosomes

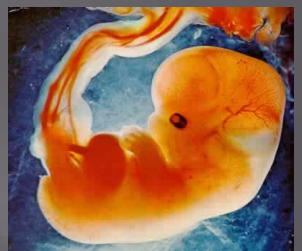
Non disjunction

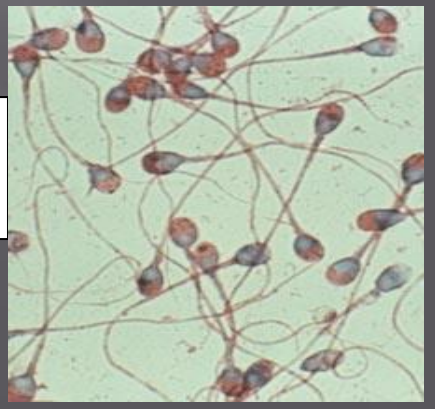
24 chromosomes

22 chromosomes

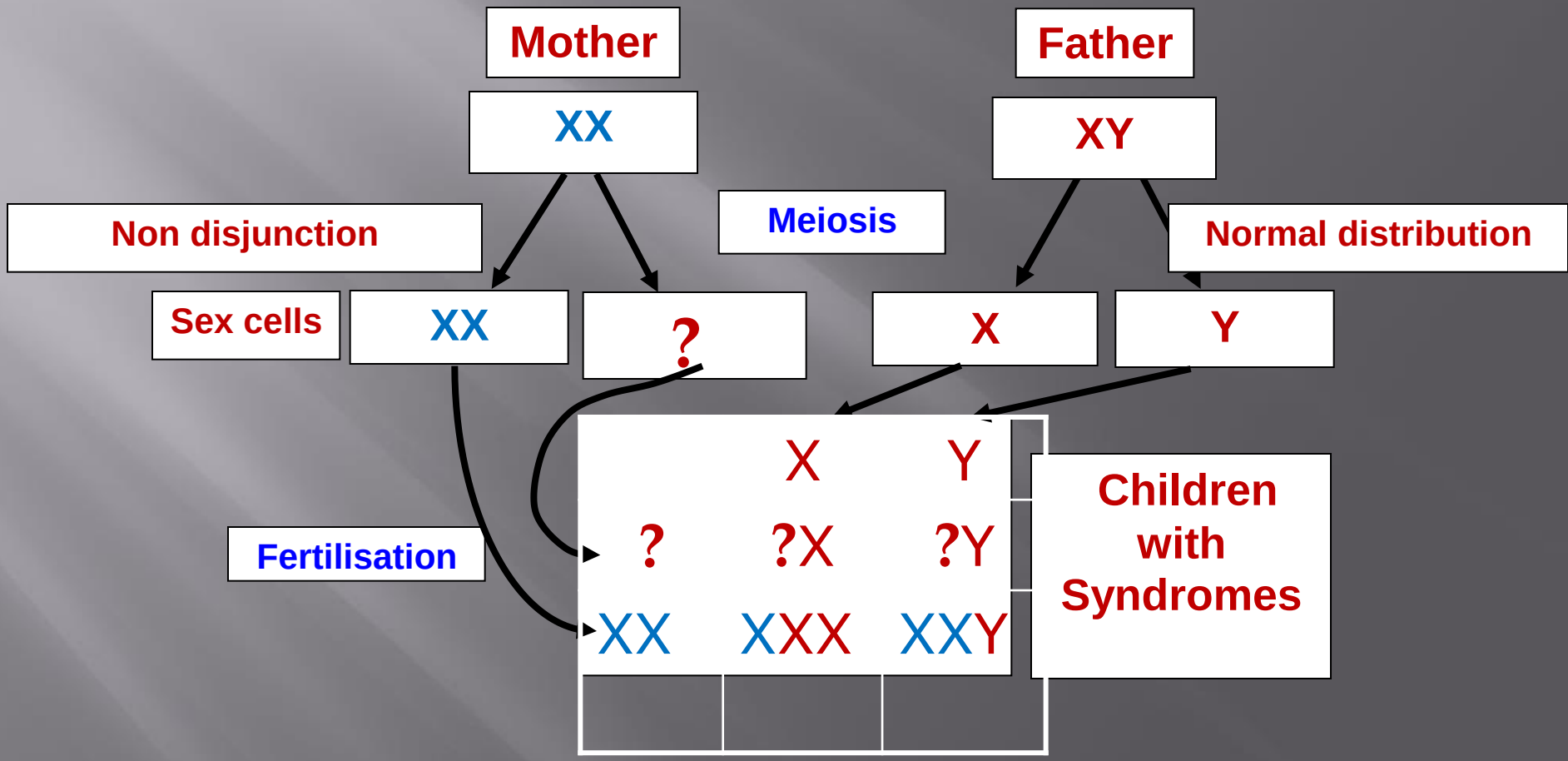
Fertilization

Embryo with 47 or 45 chromosomes





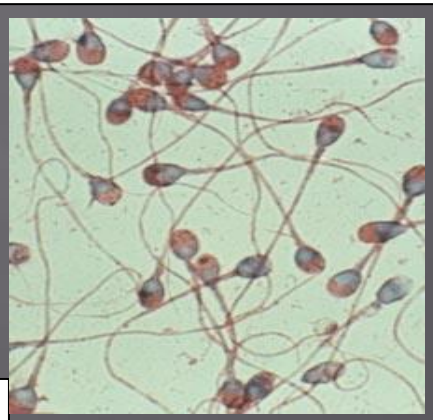
Abnormal Meiosis-Constitutional



Abnormal Mitosis- de Novo

23 chromosomes

23 chromosomes



Fertilization

Frtilizing ovum with 46 chromosomes

Mitosis

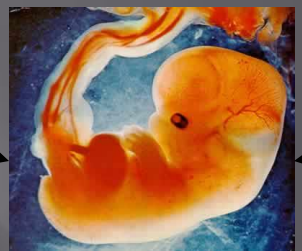
Non disjunction

Cell with 46 chromosomes

Cell with 46 chromosomes

Cell with 47 chromosomes

Cell with 45 chromosomes



Acquired Chromosomal abnormalities

1. Damages appear in the life spine of the individuals.
2. Caused by viruses ,Chemical , Rays , etc.
3. The defect reach the exposed tissue-local.
4. The genetic defect is not inherited unless reach the germ tissue.
5. Acquired abnormalities mean always cancer.

Homogenous & Mosaic Chromosomal Abnormalities

1. Homogenous

- Constitutional …. Downs Syndrome ???

- Acquired ... Chronic Myelocytic Leukemia- t(9;22)

2. Mosaic

- Constitutional …. Downs Syndrome, ??? 46,XY/47,XY,+21 or 46,XX/47,XX,+21

- Acquired ...Most cancer, Acute Lymphoblastic Leukemia- ALL- 46,XY/46,XY,t(4;11)/46,XY,t(4;11),i7q

Structural Chromosomal Anomalies

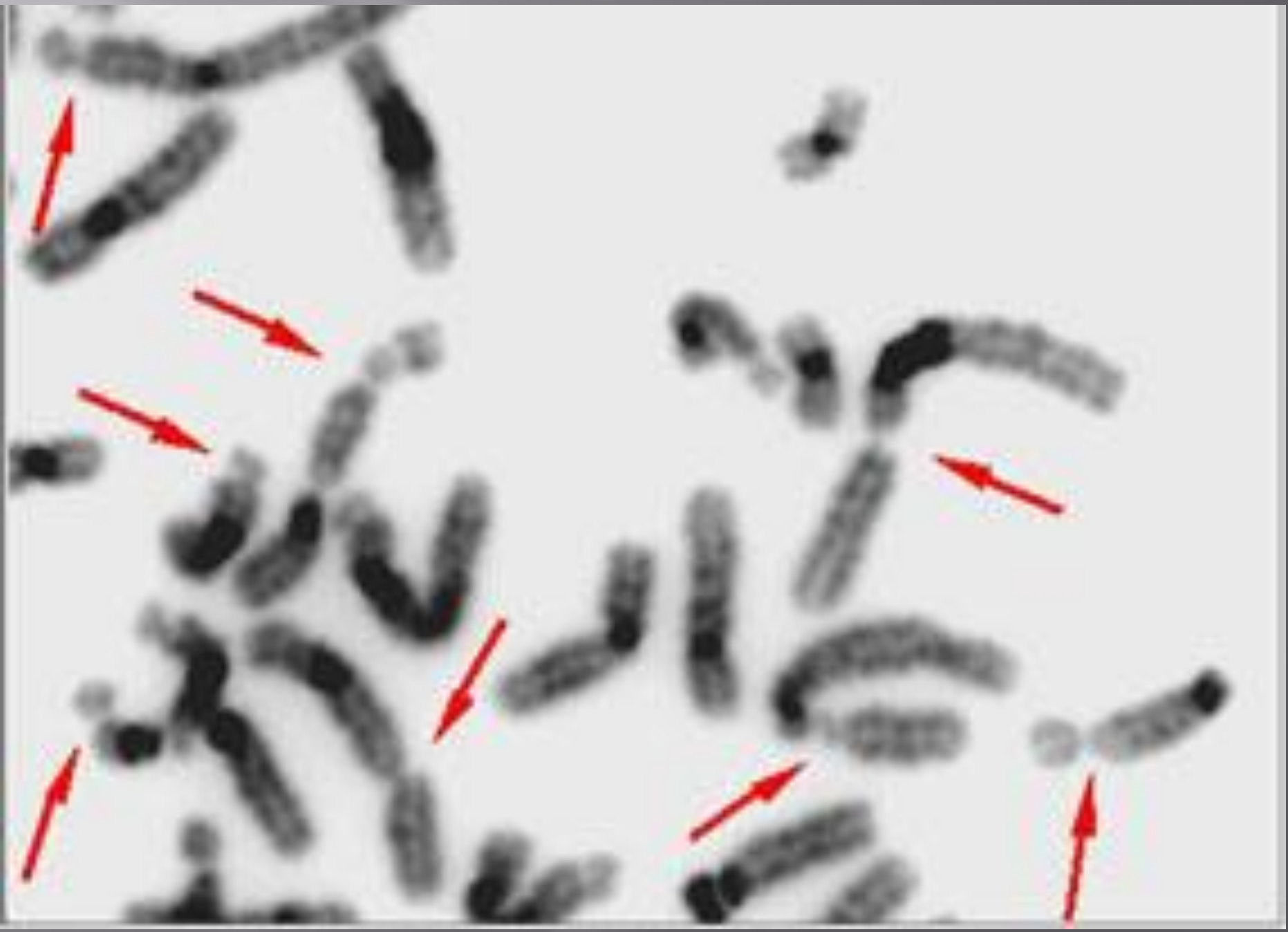
. Exogenous and Endogenous factors.

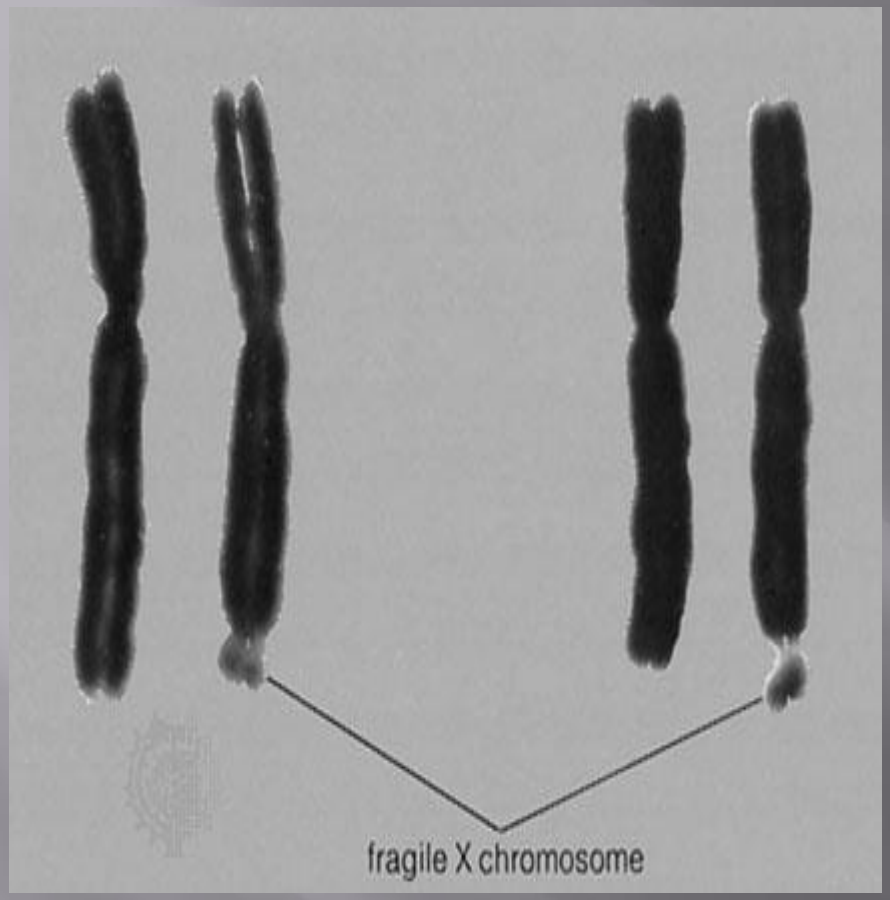
. Low Copy number Repeats- LCRs and High Copy Number Repeats- HCRs +hot spots.

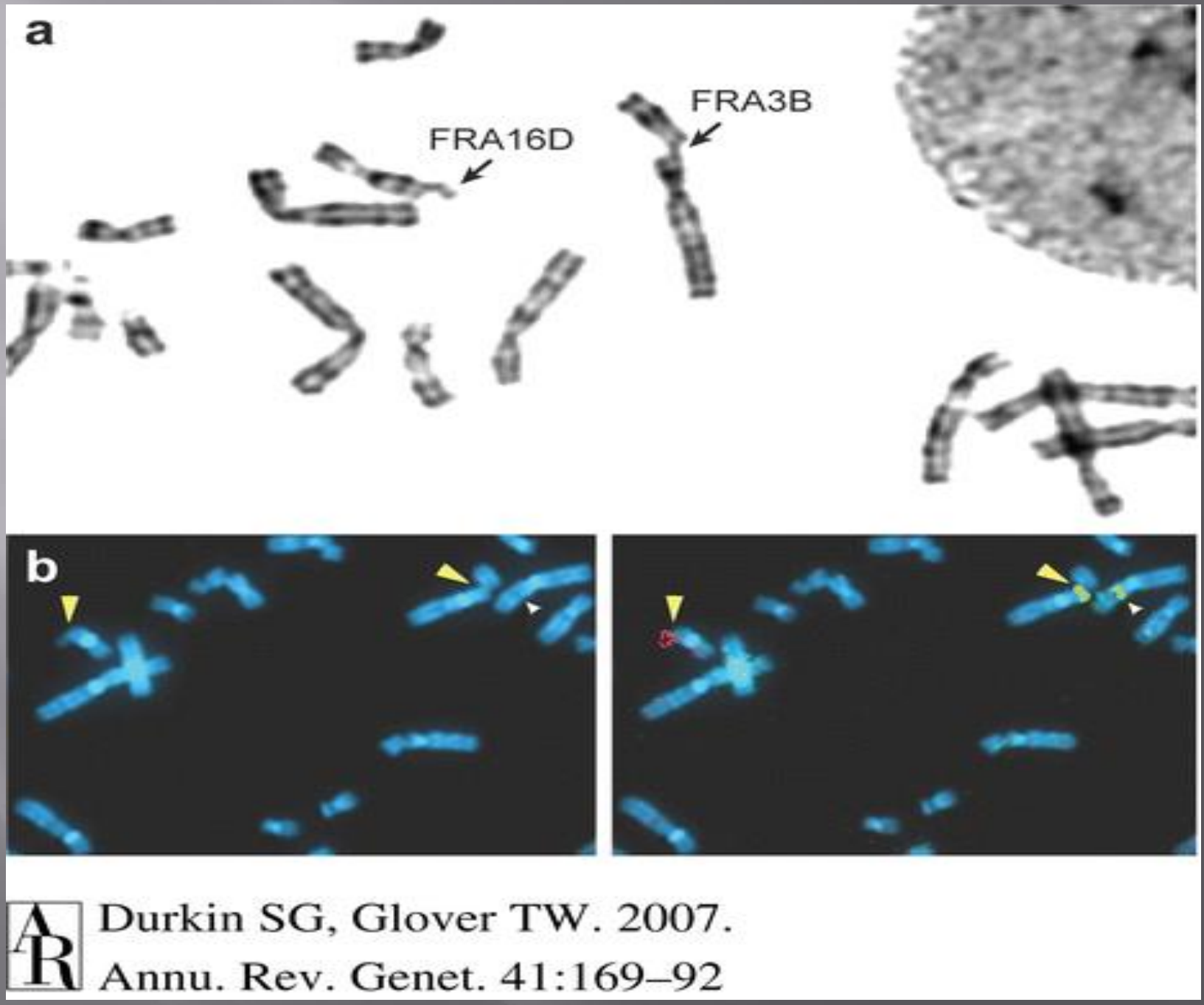
. Fragile sites in Chromosomes.

e.g. FRA11B, Bcl2, (11q23.3), Jacobsen Syndrome.

-- Palindromic Sequences , Loops-hairpin , t(11;22) , t(7;22)




fragile X chromosome



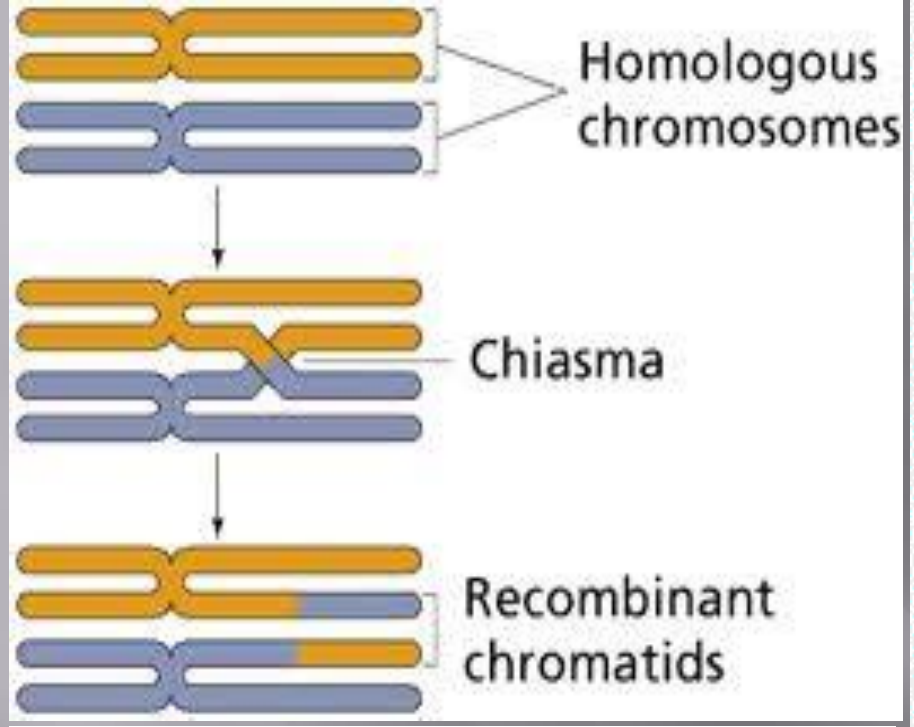
Durkin SG, Glover TW. 2007.
Annu. Rev. Genet. 41:169–92

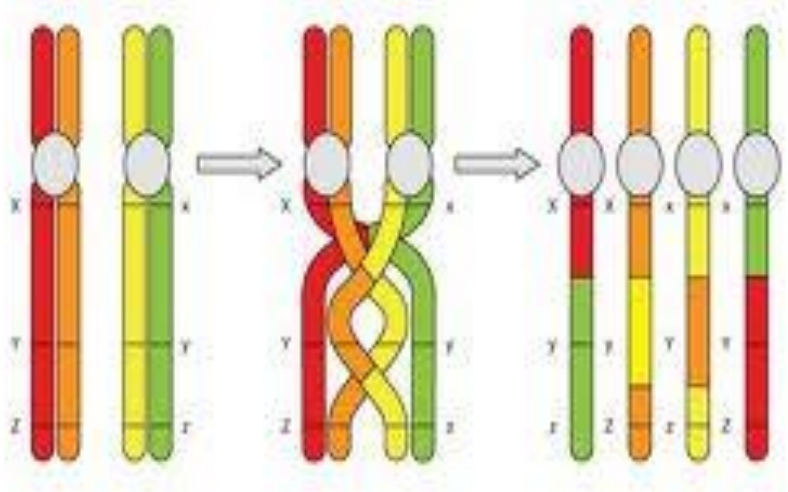
Structural Chromosomal Anomalies

- Crossing Over , Genetic Exchange & chromosomal breaks.
- Single Chromatid break & Double Chromatid breaks.
- Consequences of chromosomal breaks,

Deletions,Microdeletions, Acentric, Dicentric, etc.

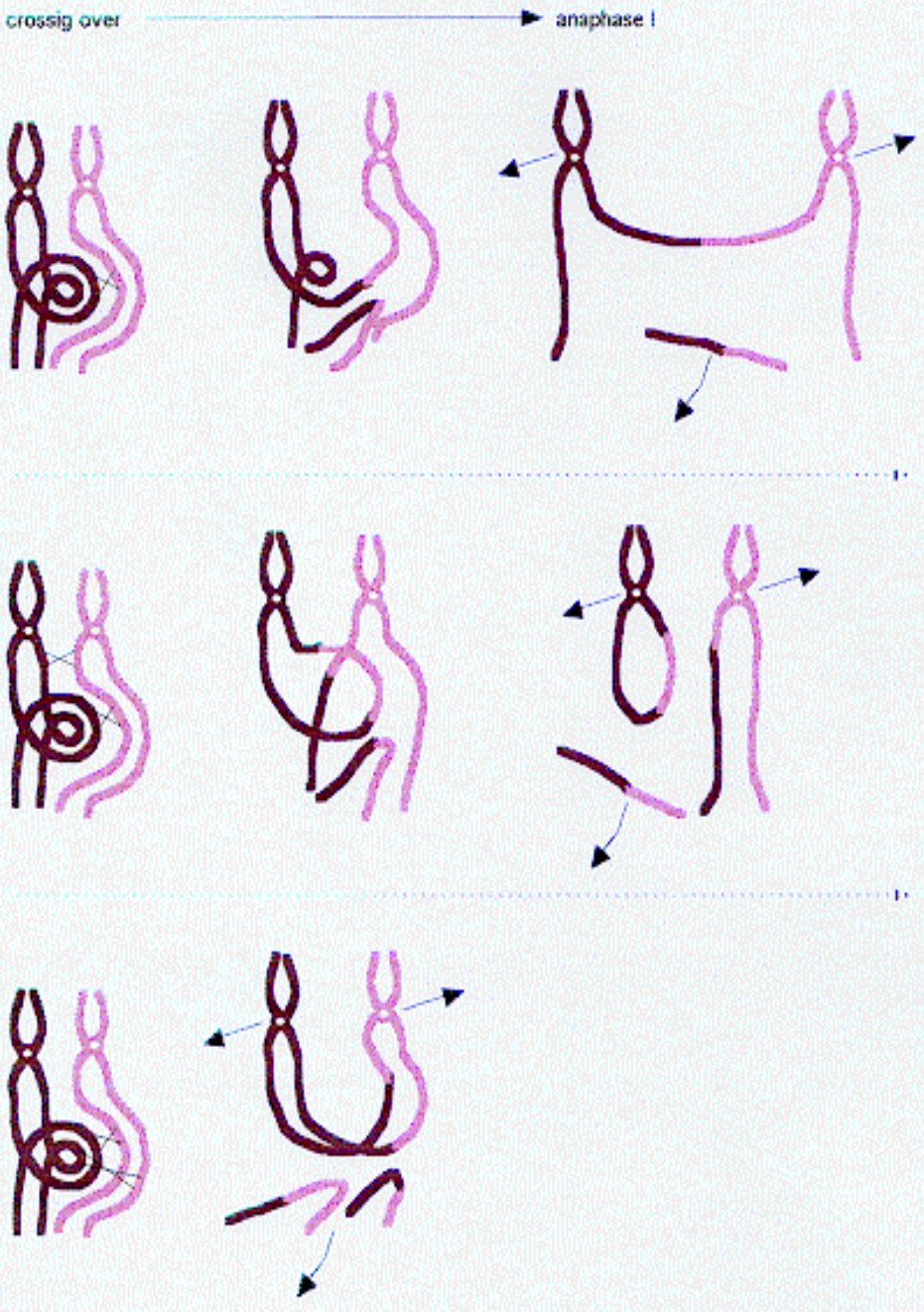
- Source of anomalies , Dad or Mom.



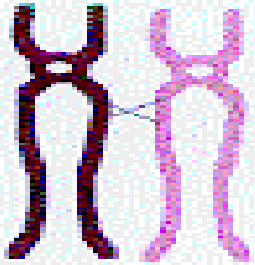


PARACENTRIC INVERSION: CONSEQUENCES

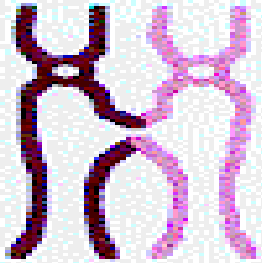
-Meiosis 1st division-

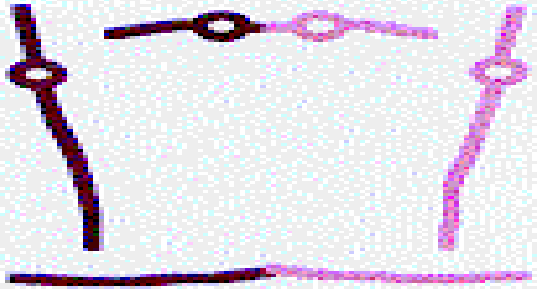


ISOCHROMOSOME: MECHANISMS OF FORMATION

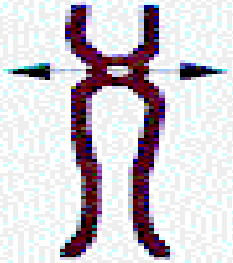


crossing over
during meiosis

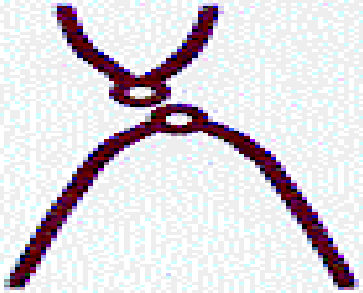




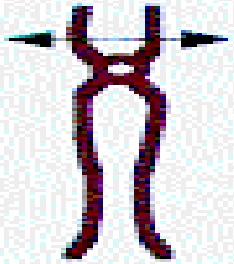
--> dicentric and heterozygote
isochromosome

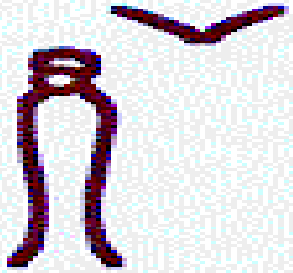


during a mitosis:
abnormal split of centromere

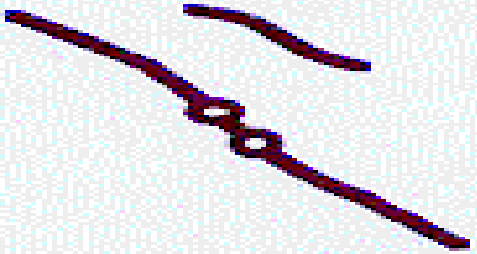


--> monocentric and homozygote
isochromosomes





during a mitosis:
break in p arm and U type joining



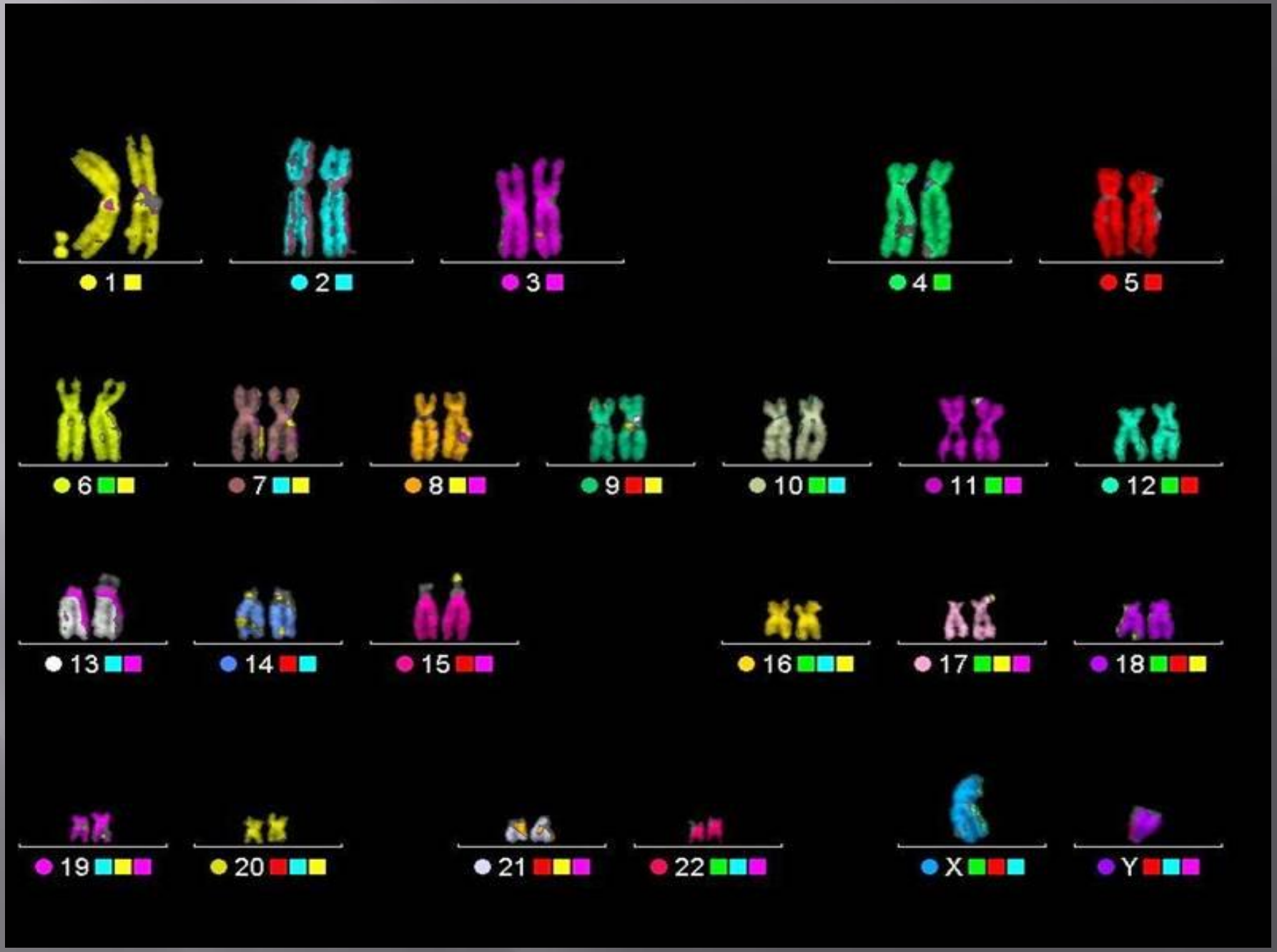
--> dicentric and homozygote
isochromosome

Identification of Structural Anomalies

. G- banding assay.

. Fluorescence In situ Hybridization-FISH

. Primed in situ Labeling- PRINs.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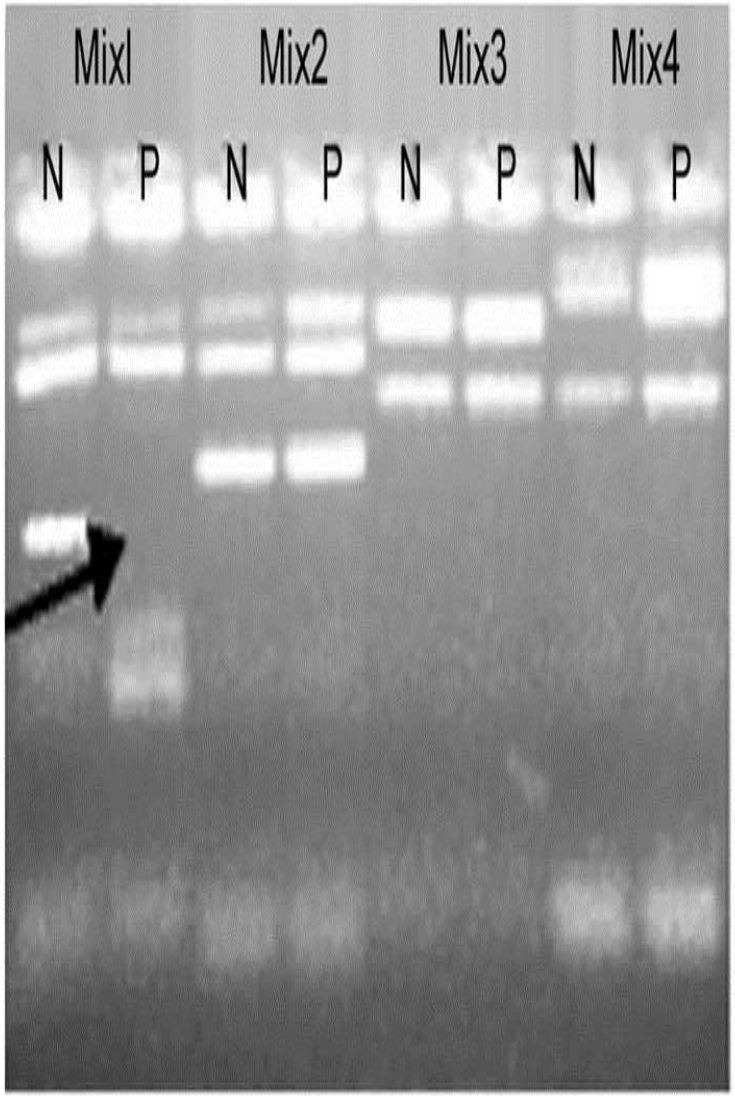
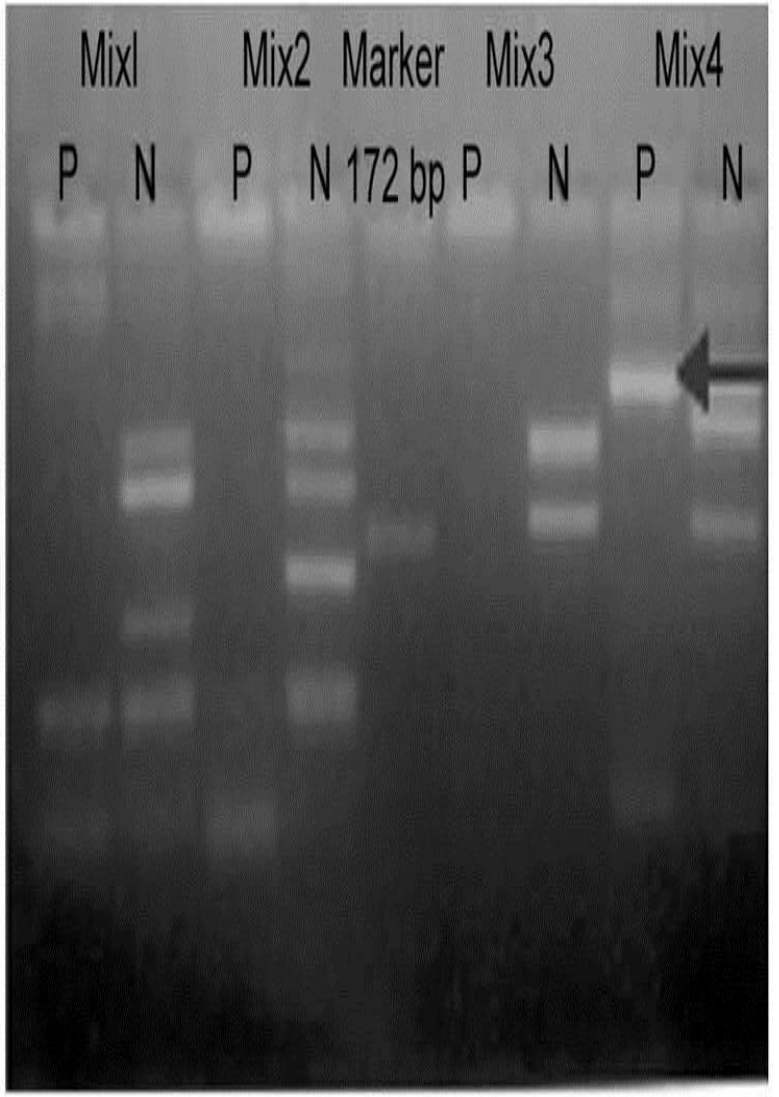
X
Y



Deletion in sY272(93 bp)

A:sY272 deletion



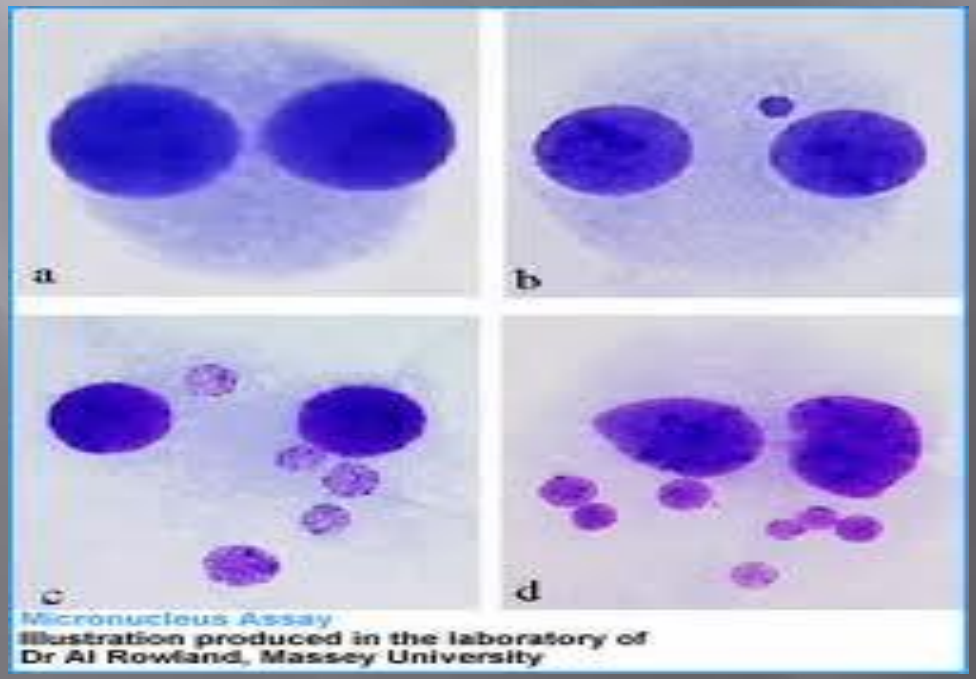
SRY (472 bp)

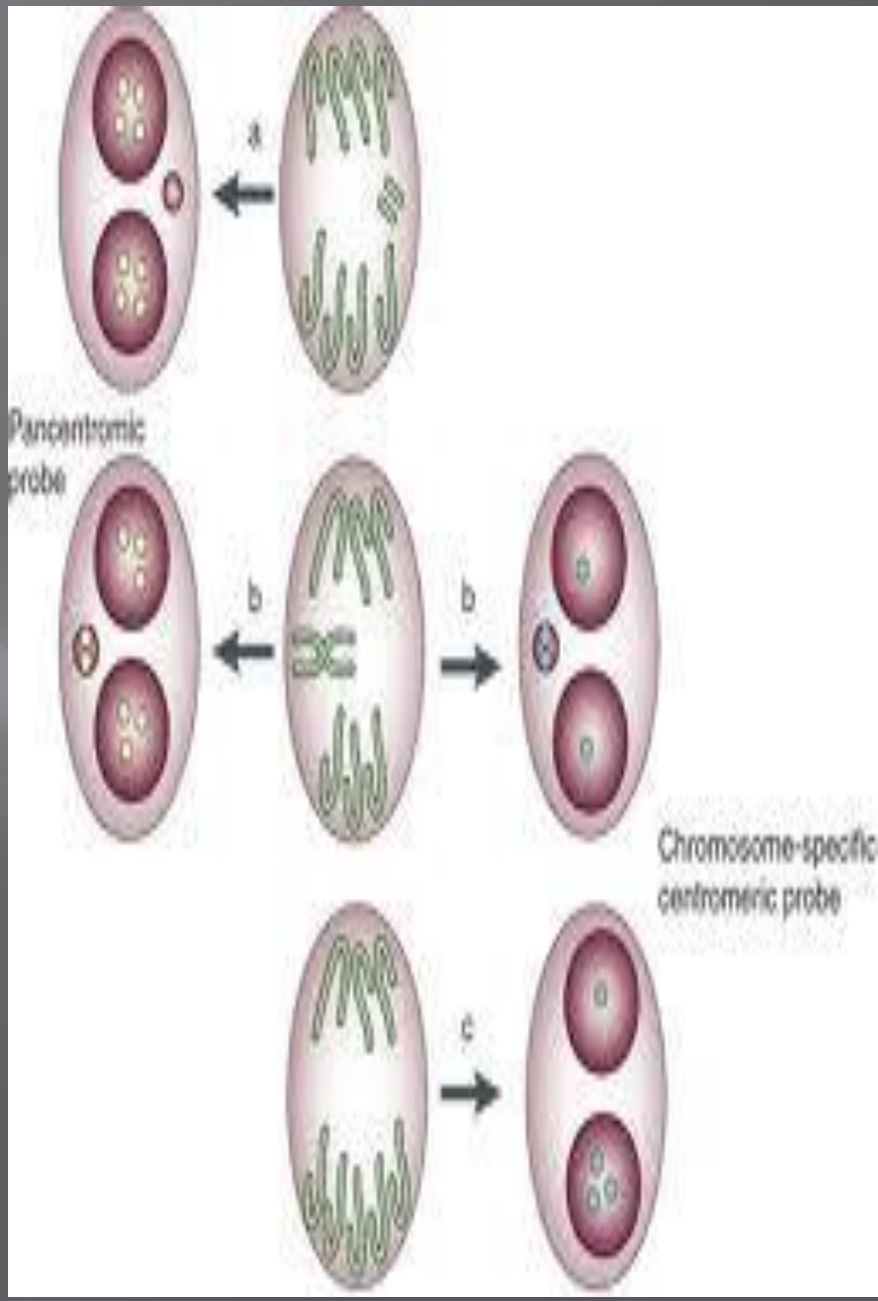
B:AZF a-deletion

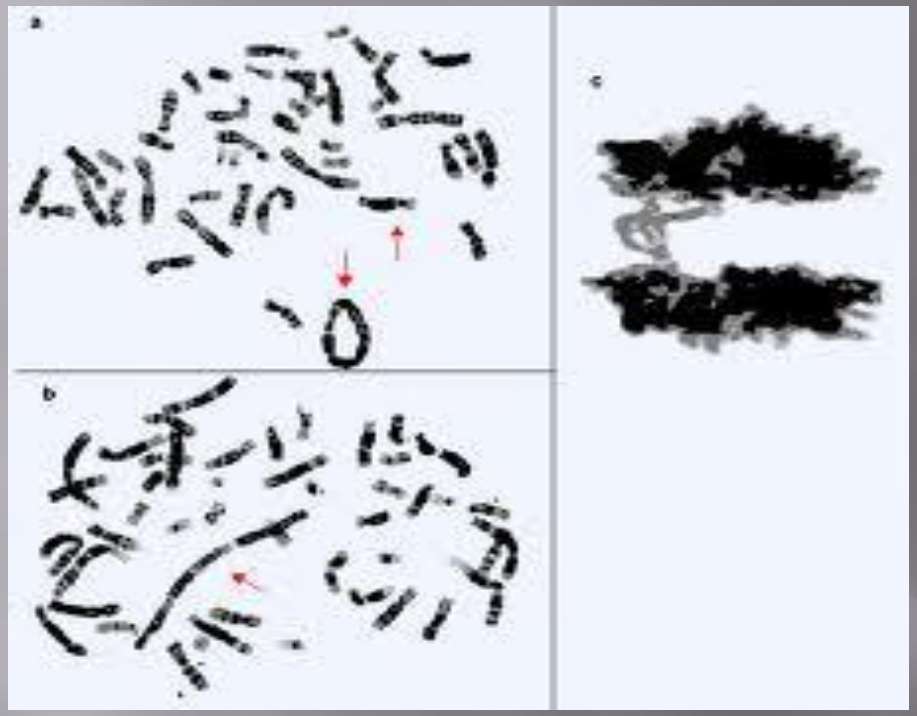
The end of chromosomal breaks and parts

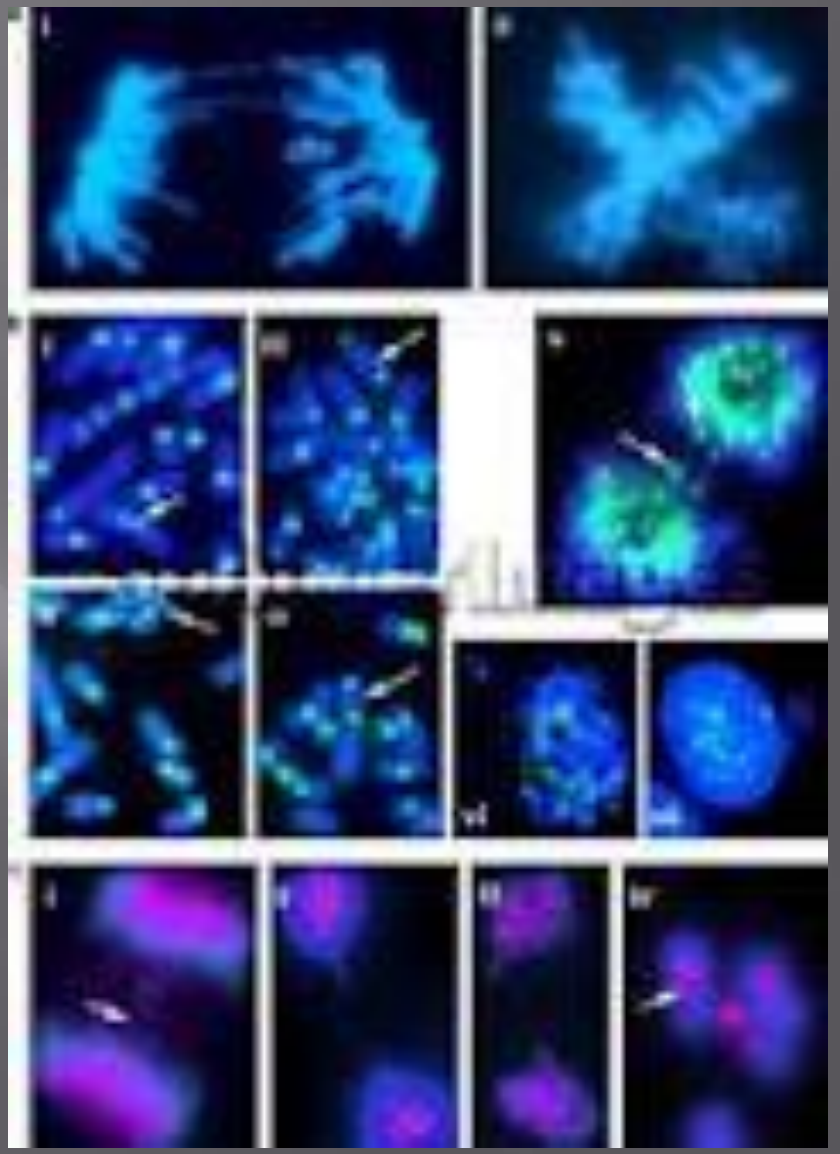
- Repaired and re-association – Sticky ends.
- Micronucleus.
- Chromosomal Bridge


micronucleus


a
b
c
d
Micronucleus Assay
Illustration produced in the laboratory of
Dr Al Rowland, Massey University


a
Pancentromic probe
b
b
Chromosome-specific centromeric probe
c





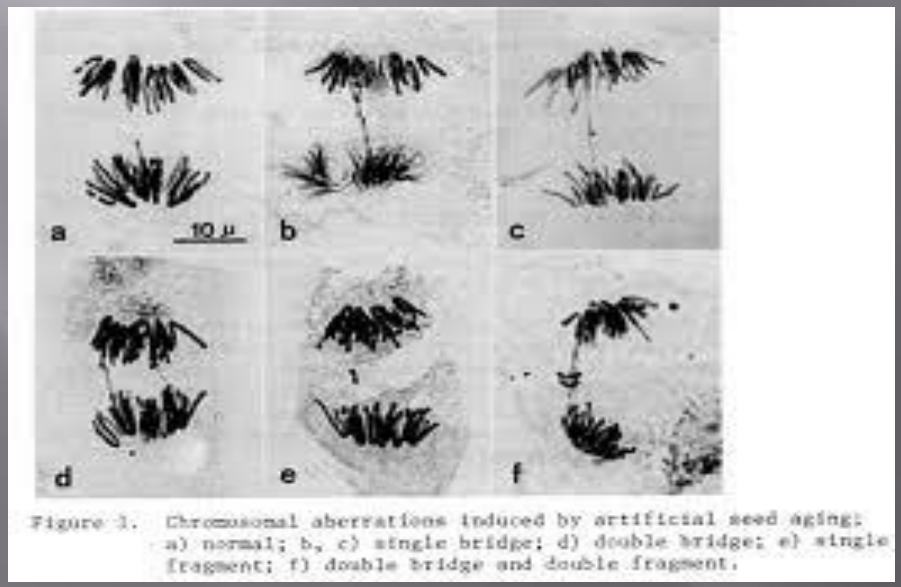


Figure 1. Chromosomal aberrations induced by artificial seed aging: a) normal; b, c) single bridge; d) double bridge; e) single fragment; f) double bridge and double fragment.

Thank you so much