CELL BIOLOGY, GENETICS AND EVOLUTION

BOT-401 4(3-1)

Chromosomal Mutations-II

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- **Ploidy**

  is the **number** of sets of chromosomes in the nucleus of a cell

- **Hetero-ploidy**

  Changes in number of whole chromosomes is called

1. **Aneuploidy**

   loss or addition of single whole chromosomes

   A. Monosomy
   B. Trisomy
   C. Polysomy

2. **Euploidy**

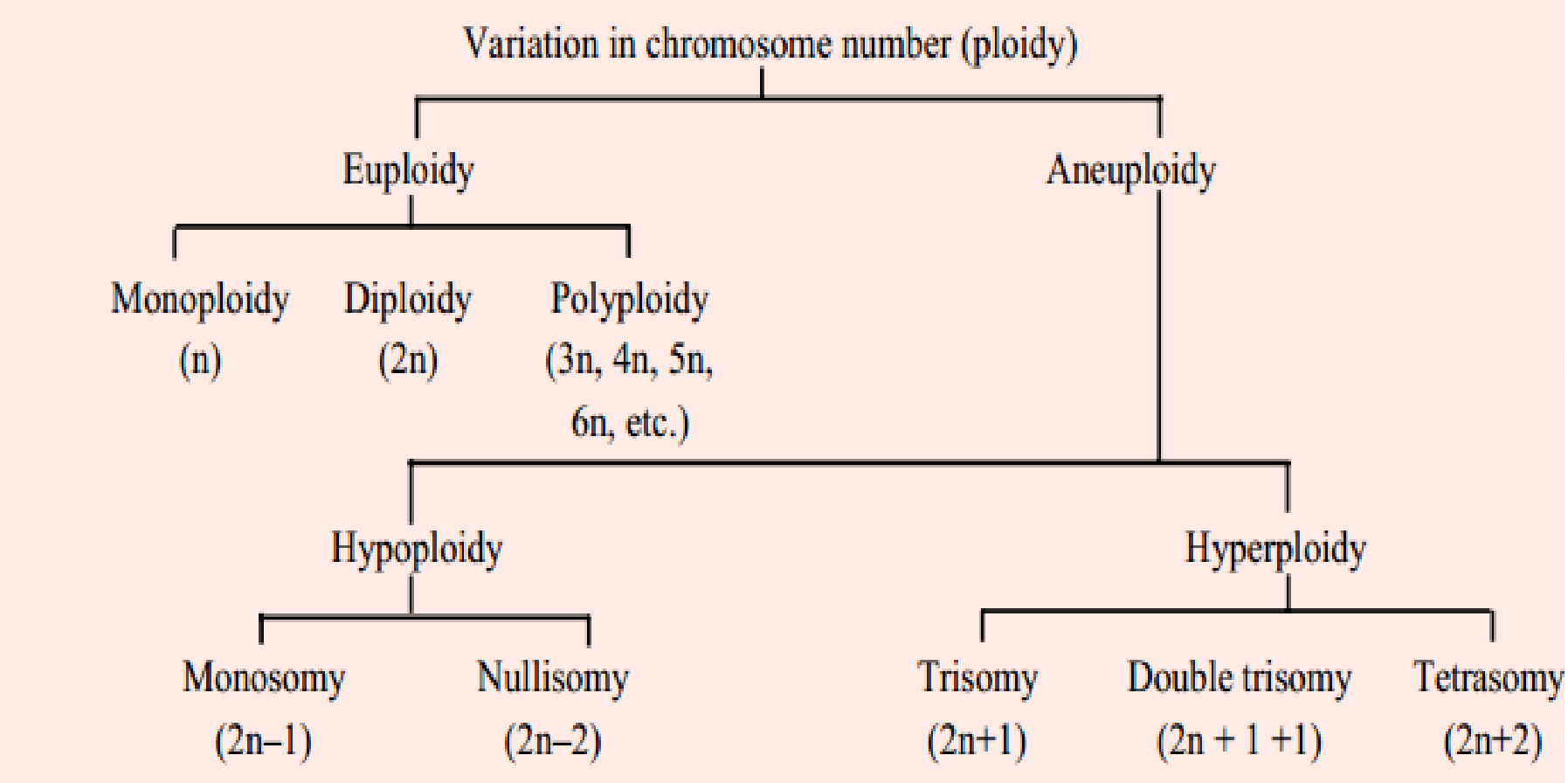
   Variations involve **entire sets** of chromosomes

   A. **Haploid**
   B. **Diploid**
   C. **Triploid**
   D. **Tetraploid, etc…**

Each may produce

- ***Phenotypic changes***
- ***Modifications of phenotypic ratio***
- ***Alteration of linkage groups***
- ***Many are of some evolutionary significance***

VARIATION IN CHROMOSOME NUMBER



Aneuploidy

Changes that involve **loss or addition of single whole chromosomes**, results in individuals, called **aneuploids** (Gr. *aneu* = uneven ; *ploid* = unit)

1. Aneuploidy can be either due to the loss of one or more chromosomes (**hypo**ploidy) and
2. Due to addition of one or more chromosomes to the complete chromosome set (**hyper**ploidy).

Hypoploidy vs Hyperploidy

- Hypoploidy is mainly due to the substraction (or loss) of a **single** chromosome, called **monosomy** (2n–1) or

- Due to the loss of **one pair** of chromosome called **nullisomy** (2n–2 ; two lost chromosomes are homologs).

- Hyperploidy may involve addition of either **a single**** chromosome, called **tri**somy (2n+ 1) or

Since the extra chromosome may belong to **any one of different chromosomes of a haploid complement

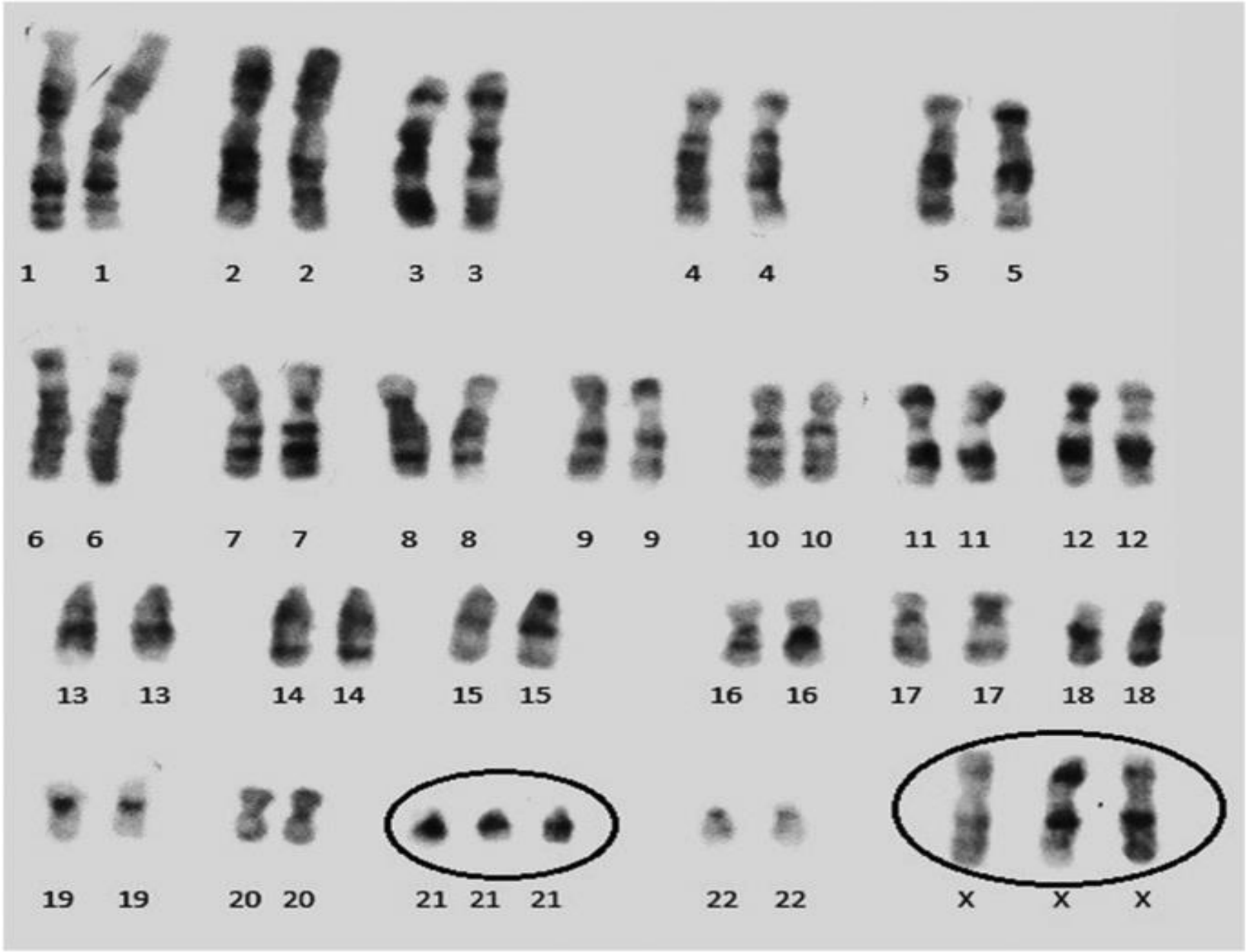
- A **pair** of chromosomes, called **tetra**somy (2n + 2).

Hypoploidy vs Hyperploidy

- **Double Trisomy**

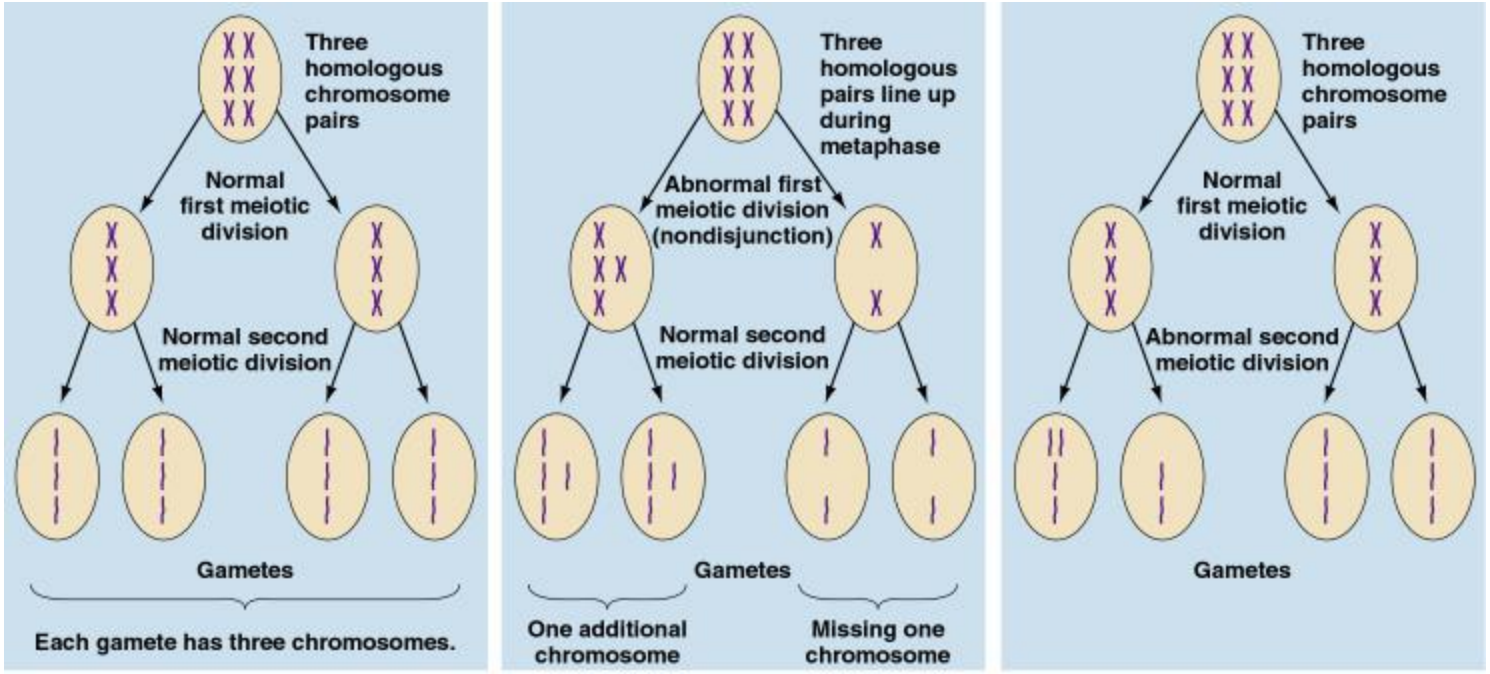
In a diploid organism when ***two*** different chromosomes are represented in triplicate, the double trisomic is resulted. The double trisomic causes great genetic imbalance and has the genomic formula 2n+1+1.

Double Trisomy



Aneuploidy

- All of these aneuploids are probably produced by **nondisjunction*** during mitosis or meiosis.
- *Non-disjunction = failure of **homologues** or ***chromatids*** to separate during meiosis



Normal Meiosis

Non-disjunction in Meiosis I

Non-disjunction in Meiosis II

Human Chromosomal Aneuploids

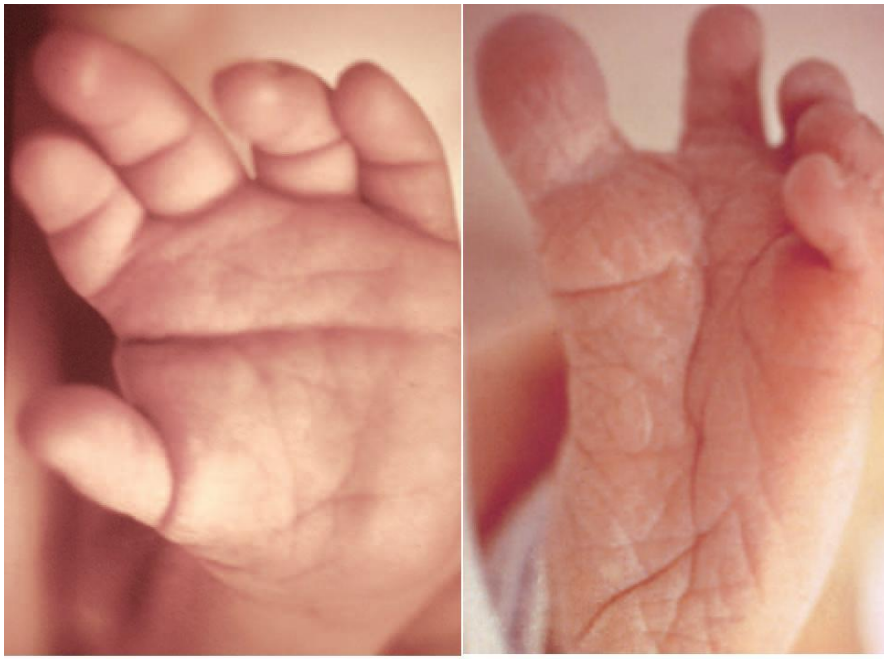
Autosomal Aneuploids

Down Syndrome	Trisomy 21
Edward Syndrome	Trisomy 18
Patau Syndrome	Trisomy 13

Trisomy: three copies of one chromosome

Down syndrome (DS) or Down's Syndrome

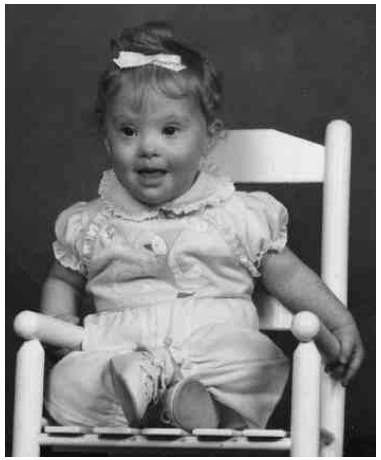
- Down's syndrome is named after the physician **J.Langdon Down** who first described this genetic defect in 1866 and it was formally called **mongolism** or **mongolian idiocy (**extremely stupid behaviour**)**
- It is usually associated with a trisomic condition for one of the smallest human autosomes (*i.e.,* chromosome 21)
- It is the most common chromosomal abnormality in live births (1/650 births)
- There are about 50 physical characteristics shown by DS infants soon after birth
- These include
  1. Mild or moderate mental retardation;
  2. Eyes that slant up and out
  3. A tongue that is large, swollen and protruding
  4. Small and under developed ears;
  5. A single palmar crease (a line or ridge);
  6. Short stature;
  7. Stubby fingers;
  8. An enlarged liver and spleen.



Down syndrome (DS) or Down's Syndrome

- Women over 45 years of age are about twenty times more likely to give birth to a child with DS than women aged 20.
- Nondisjunction of chromosome pair 21 during **oogenesis** is the main cause of occurrence of trisomy-21.
- This event is found to be affected either by senescence (the condition or process of loss of division/growth with age) of oocytes, virus infection, radiation damage, etc. (*e.g.,* mothers who have had infectious hepatitis prior to pregnancy may have three times more chances to give birth to DS infants).
- **Nondisjunction** of chromosome pair 21 during **spermatogenesis** can also produce child with DS, but **paternal age does not** seem to be associated with its incidence.
- Lastly, in about 2 to 5 per cent cases, the normal chromosome number is present (2n = 46), but the extra chromosome 21 ***is attached*** (translocated) to one of the larger autosomes (usually chromosome 14).

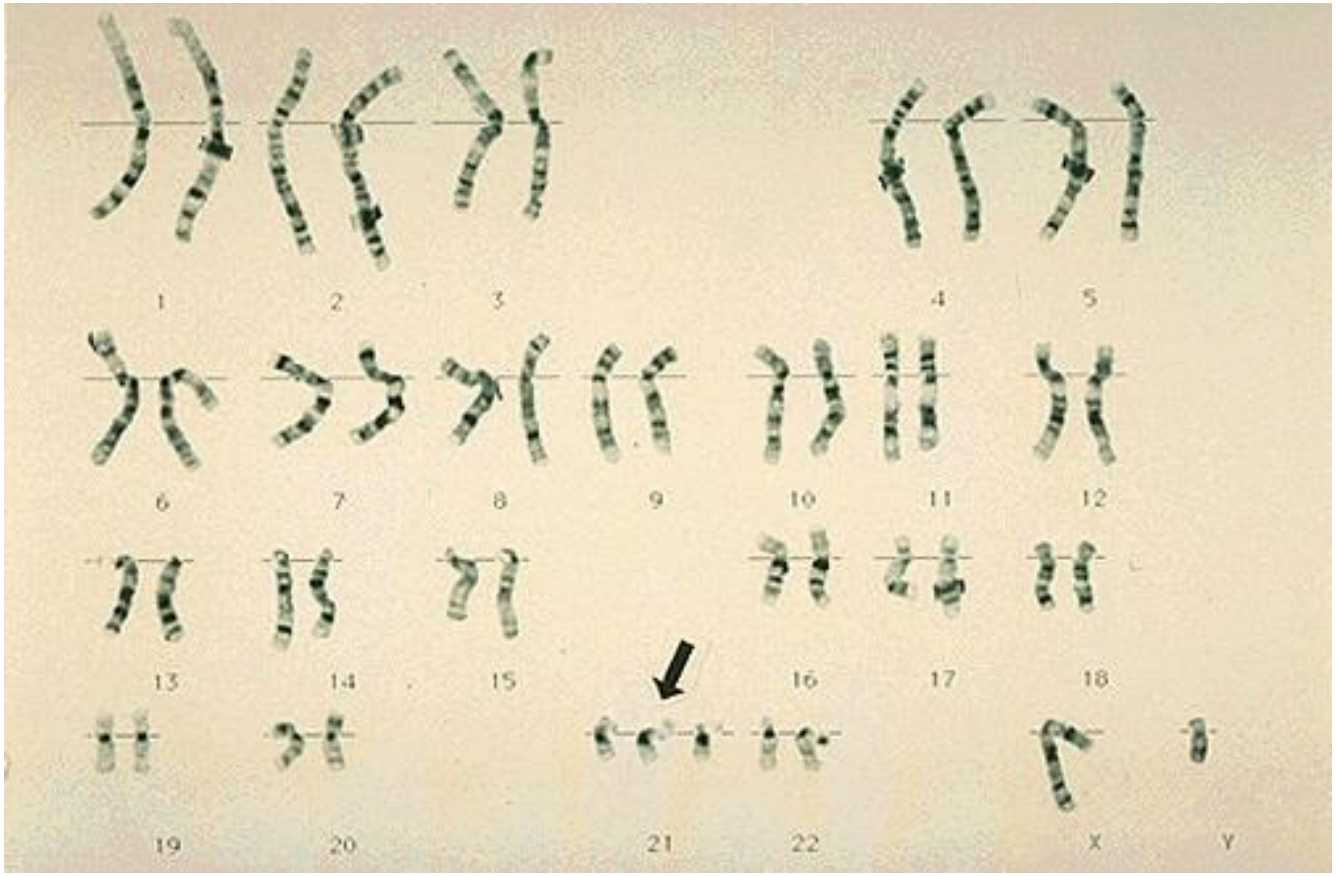
Human Autosomal Abnormality

Down Syndrome	Trisomy 21
	Three copies of chromosome 21

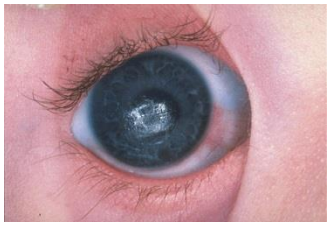
How can Down Syndrome occur?

Eg. Egg with 2 copies of #21 (24 chromosomes)
+ Sperm with 1 copy of #21 (23 chromosomes)
= Embryo with 3 copies of #21 (47 chromosomes)

Karyotype for Down Syndrome

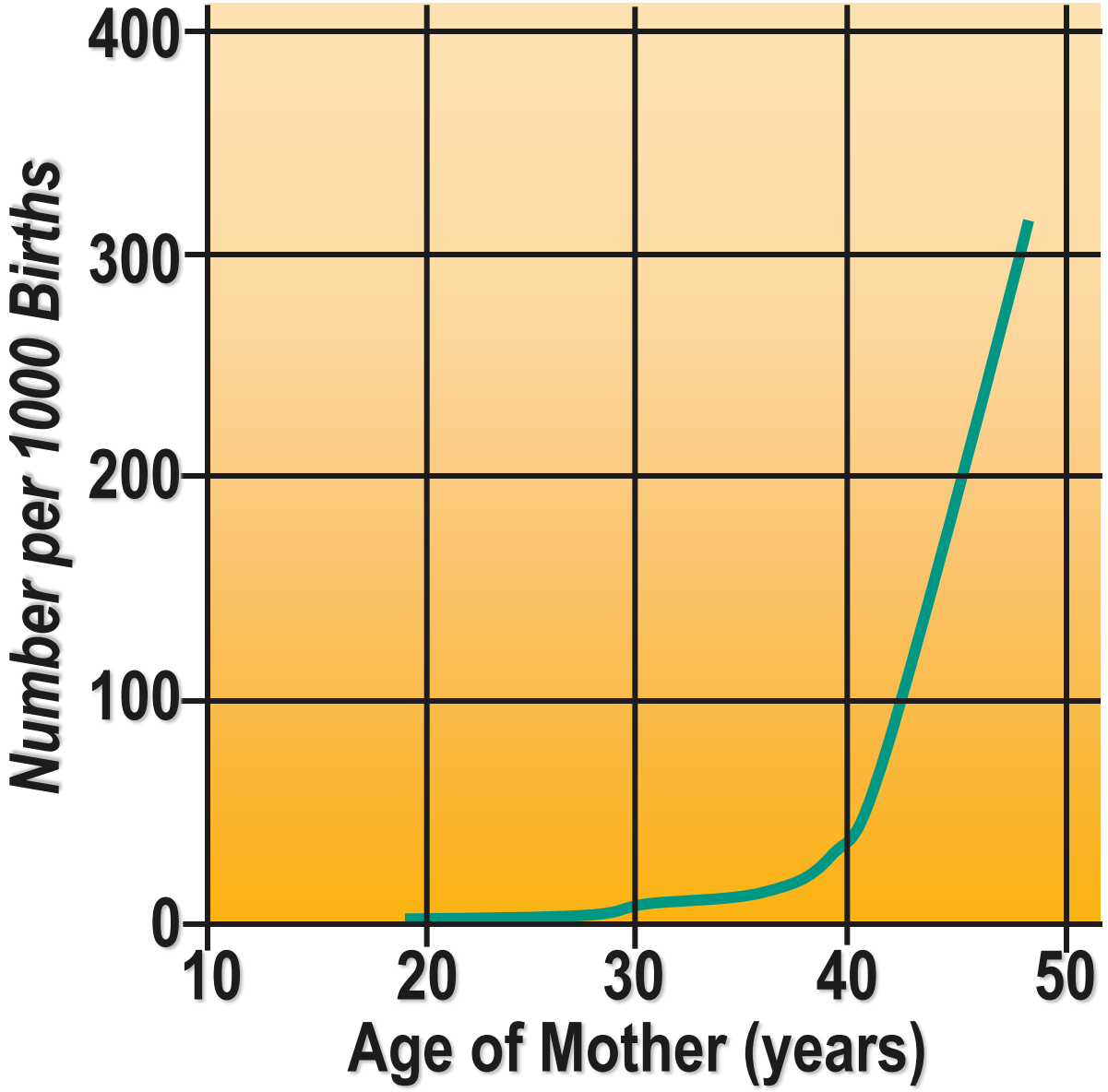


Physical Features



Eye fold

Incidence of Down Syndrome Increases with Maternal Age

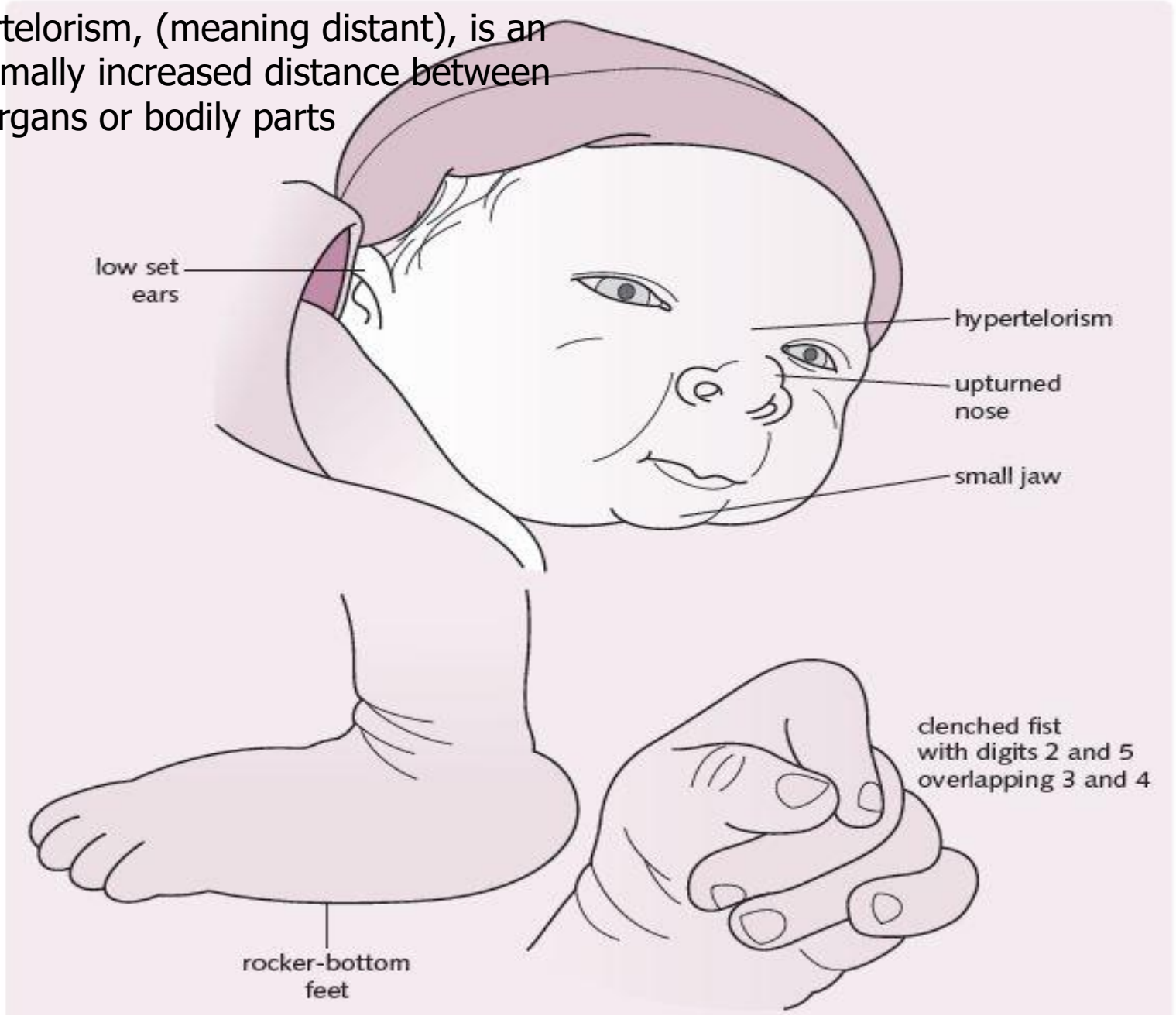


Edwards syndrome

- **Edwards syndrome** (also known as **Trisomy 18**) is a genetic disorder caused by the presence of all or part of an extra 18th chromosome.
- This genetic condition almost always results from nondisjunction during meiosis.
- It is named after John Hilton Edwards, who first described the syndrome in 1960.
- It is the **second** most common autosomal trisomy, after Down syndrome that carries to term.
- It is characterized by multiple malformations,

1. **Primarily low-set ears;**
2. **small receding lower jaw;**
3. **flexed and clenched fingers;**
4. **Cardiac malformations;**
5. **various deformaties of skull, face and feet.**

Hypertelorism, (meaning distant), is an abnormally increased distance between two organs or bodily parts



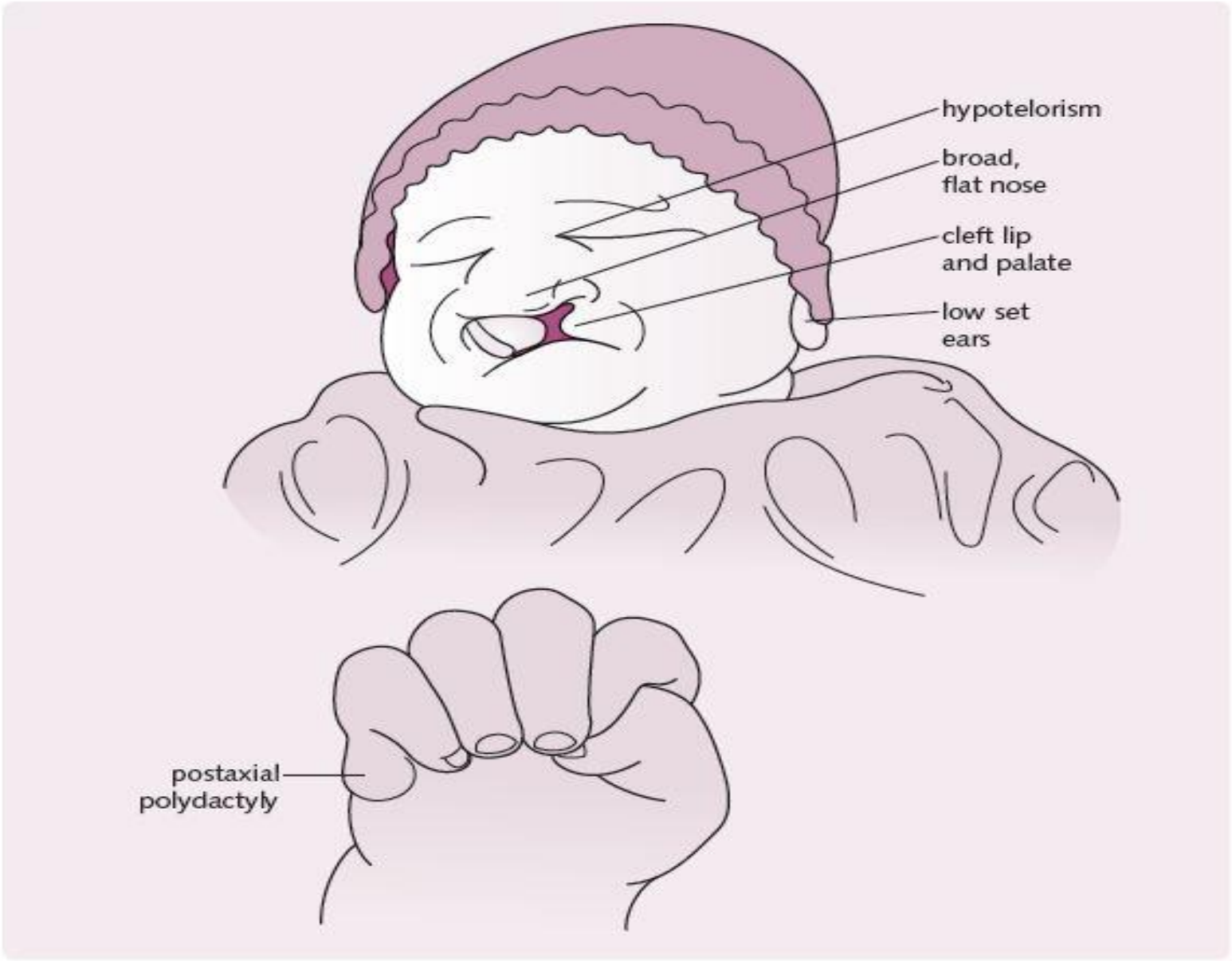
Edwards syndrome

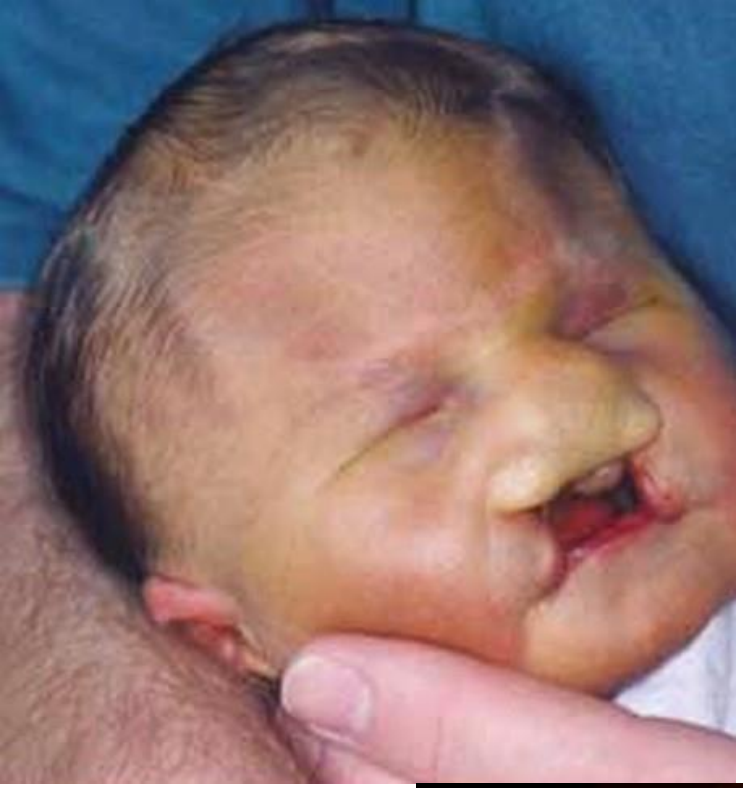
- Death takes place around 3 to 4 months of age.
- Trisomy-18 children show evidence of severe mental retardation, which is more pronounced in females (the reason is still not clear).
- Like the Down's syndrome, occurrence of Edward's syndrome is too related with maternal age (*i.e.,* 35 to 45 year old mothers have more chance of giving birth to trisomy-18 infant).

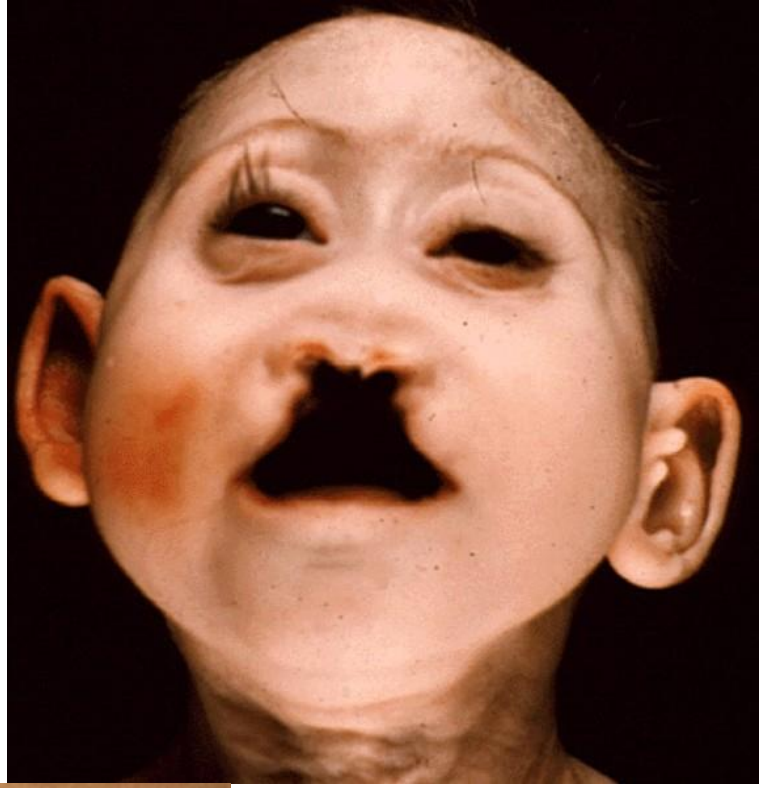
Patau syndrome or Trisomy-13

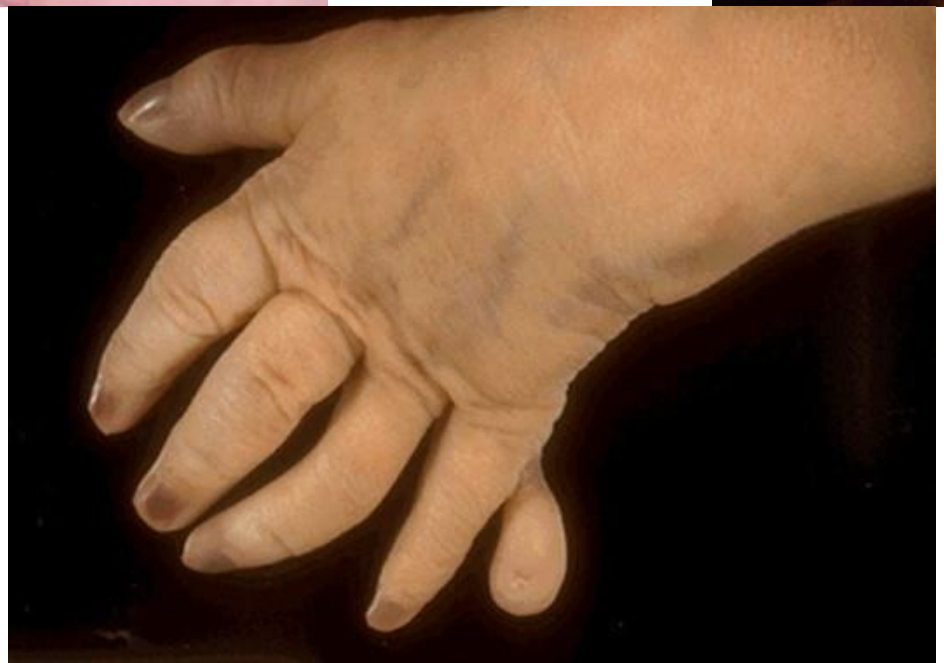
- This syndrome was described in 1960 by **Klaus Patau** and coworkers.
- Its incidence is about 0.2 per 1000 births.
- Individuals with Patau syndrome appear to be

1. Markedly mentally retarded;
2. Sloping forehead,
3. Harelip and cleft palate
4. Polydactyly (both hands and feet) is almost always present;
5. Hands and feet are deformed.
6. Cardiac and various internal defects (of kidney, colon, small intestine) are common.
7. Death usually occurs within hours or days, but the foetus may abort spontaneously.

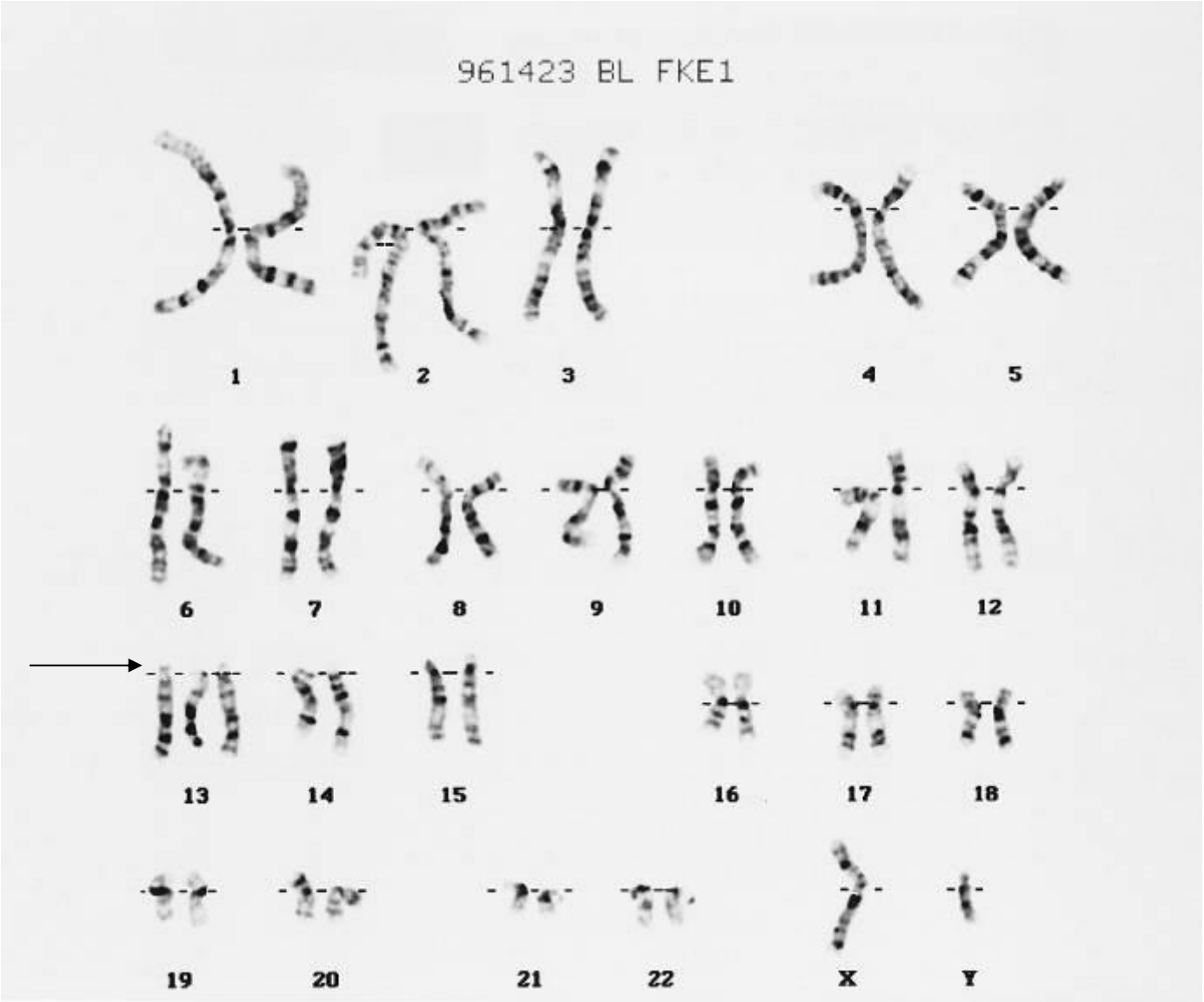

hypotelorism
broad,
flat nose
cleft lip
and palate
low set
ears
postaxial
polydactyly







Trisomy 13 Karyotype: 47, 13+

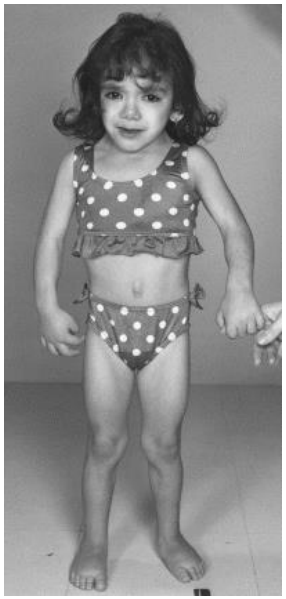


Human Chromosomal Aneuploids

Sex Chromosome Aneuploids

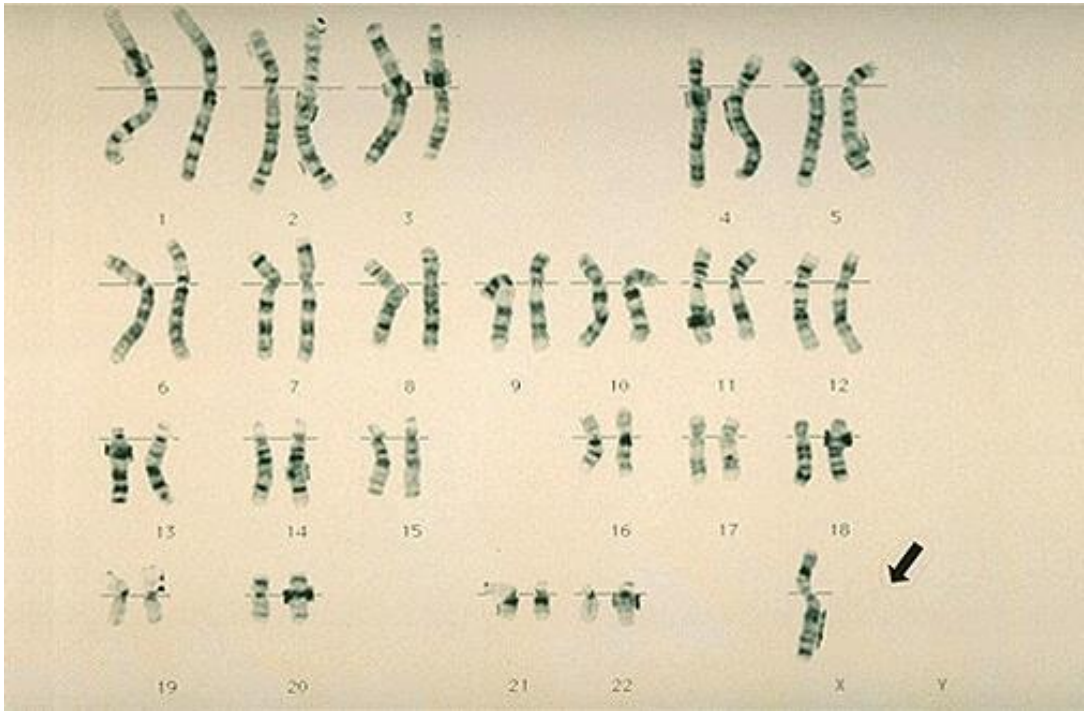
Turner Syndrome	45, XO	Sterile female
Triplo-X	47, XXX	Fertile female
Klinefelter Syndrome	47, XXY	Sterile male
XYY Syndrome	47, XYY	Fertile male

Human Sex Chromosome Abnormality

Turner Syndrome	XO
	One copy of X No second sex chromosome

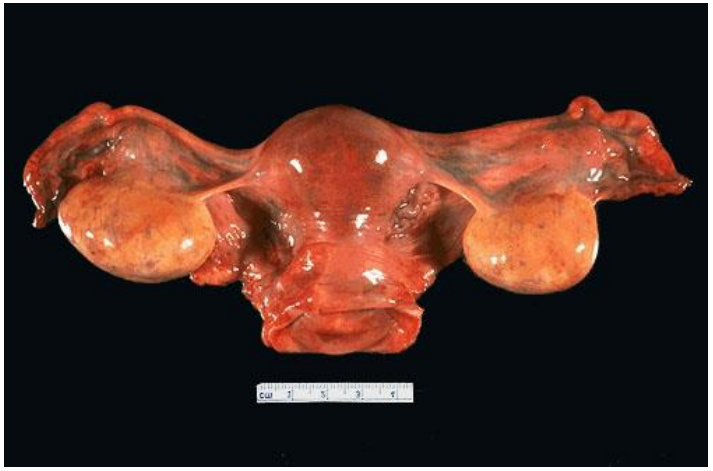
How can Turner Syndrome occur?

Eg. Egg with 0 copies of X (22 chromosomes)
+Sperm with 1 copy of X (23 chromosomes)
= Embryo with 1 copy of X (45 chromosomes)



Karyotype for
Turner's Syndrome

Normal uterus, tubes
and ovaries



Non-functional Ovaries From Adult
Female with Turner's Syndrome

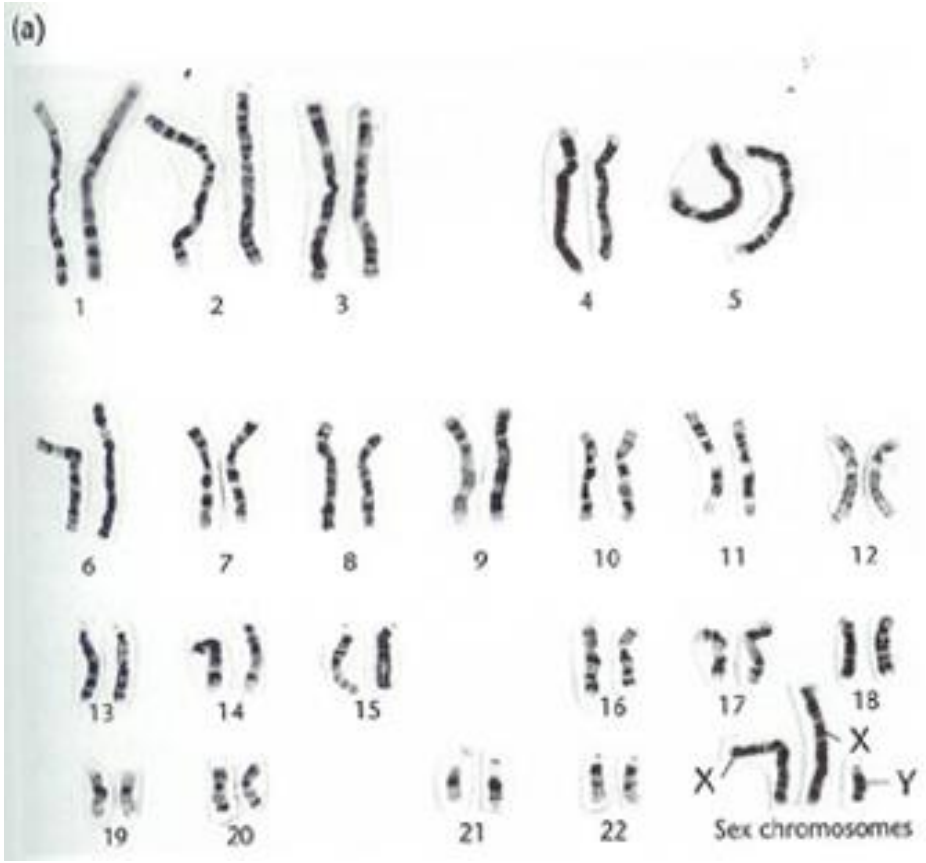
Human Chromosomal Aneuploids

How can XYY Syndrome occur?

One Copy of the X chromosome
Two Copies of the Y chromosome

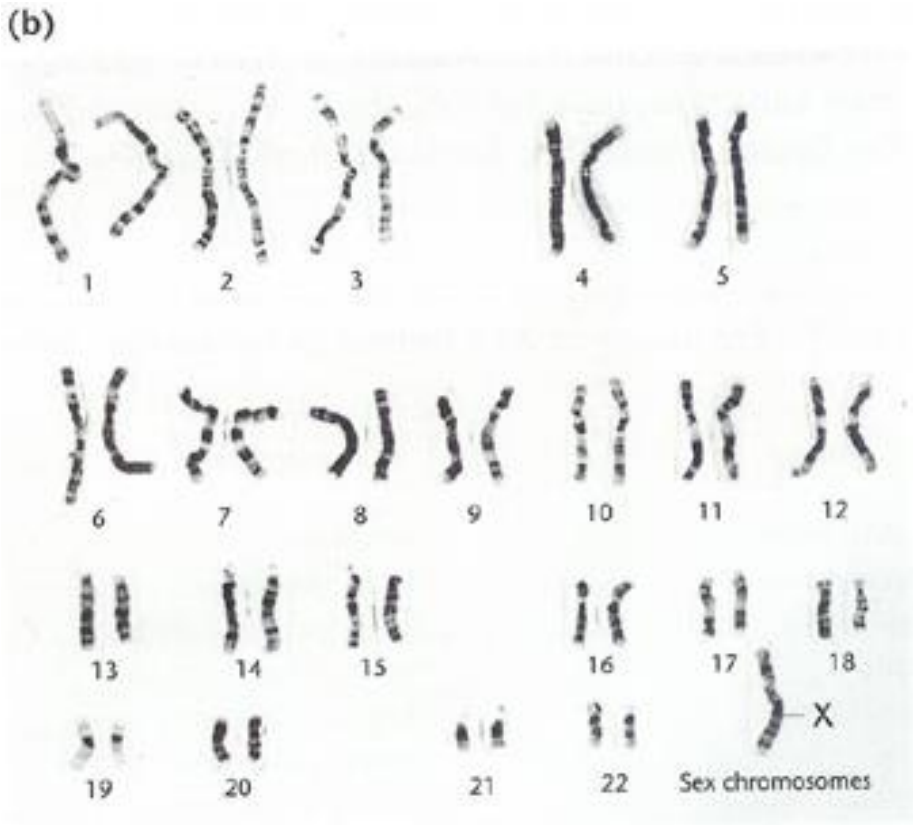
Eg. Egg with 1 copy of X (23 chromosomes)
+ Sperm with 2 copies of Y (24 chromosomes)
= Embryo with XYY (47 chromosomes)

Aneuploidies of the Sex Chromosomes



47, XXY

Klinefelter syndrome



45, X

Turner syndrome

TABLE 8.1
Aneuploid Conditions in Humans

Condition	Frequency	Syndrome	Characteristics
Autosomal			
Trisomy 21	1/800	Down	Mental retardation, abnormal pattern of palm creases, slanted eyes, flattened face, short stature
Trisomy 18	1/6,000	Edward	Mental and physical retardation, facial abnormalities, extreme muscle tone, early death
Trisomy 13	1/15,000	Patau	Mental and physical retardation, wide variety of defects in organs, large triangular nose, early death
Sex Chromosomal			
XXY	1/1,000 (males)	Klinefelter	Sexual immaturity (no sperm), breast swelling
XYY	1/1,000 (males)	Jacobs	Tall
XXX	1/1,500 (females)	Triple X	Tall and thin, menstrual irregularity
X0	1/5,000 (females)	Turner	Short stature, webbed neck, sexually undeveloped