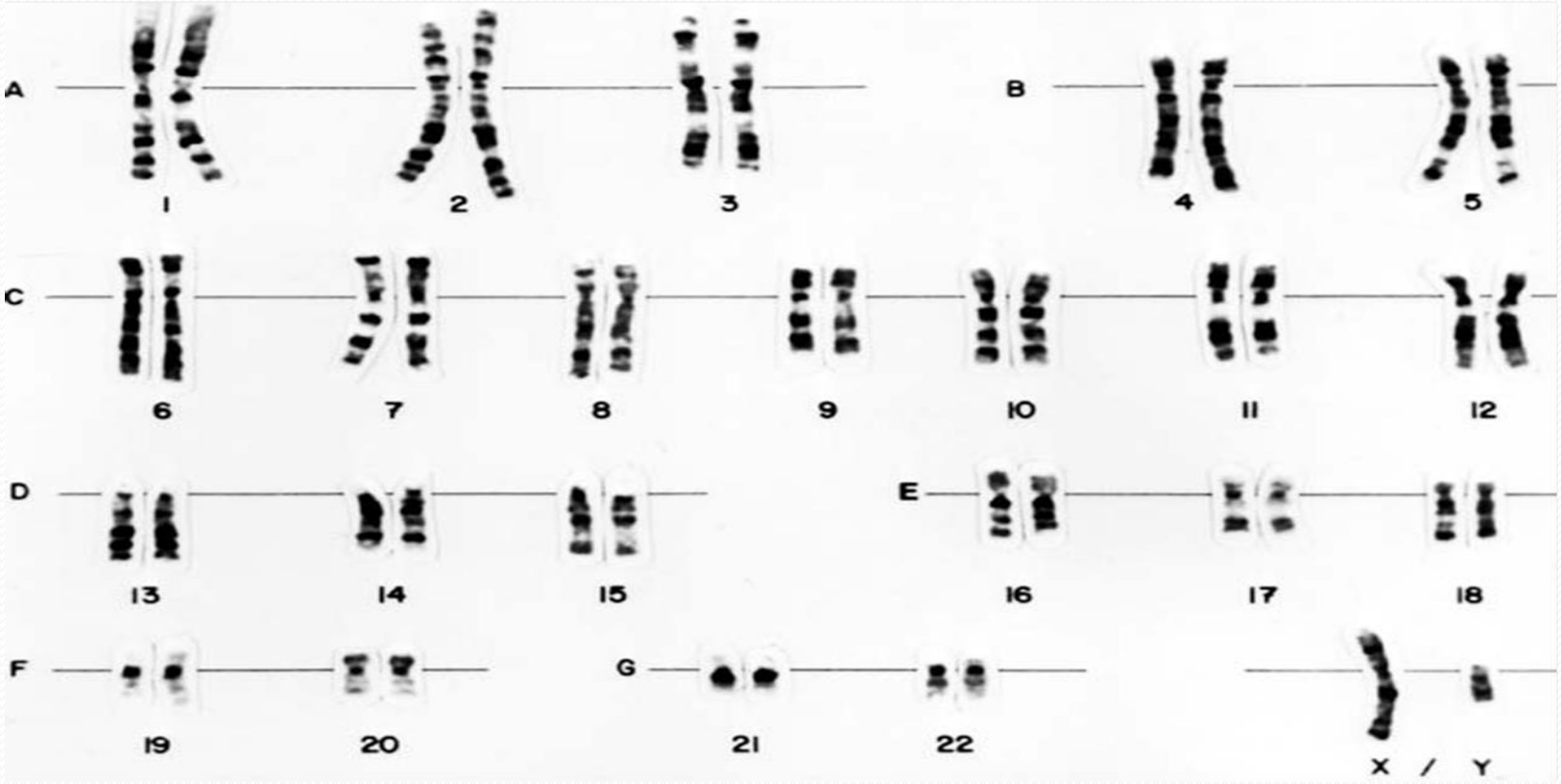
Chromosomal abnormalities

Dr. Liqaa M. Al- Sharifi

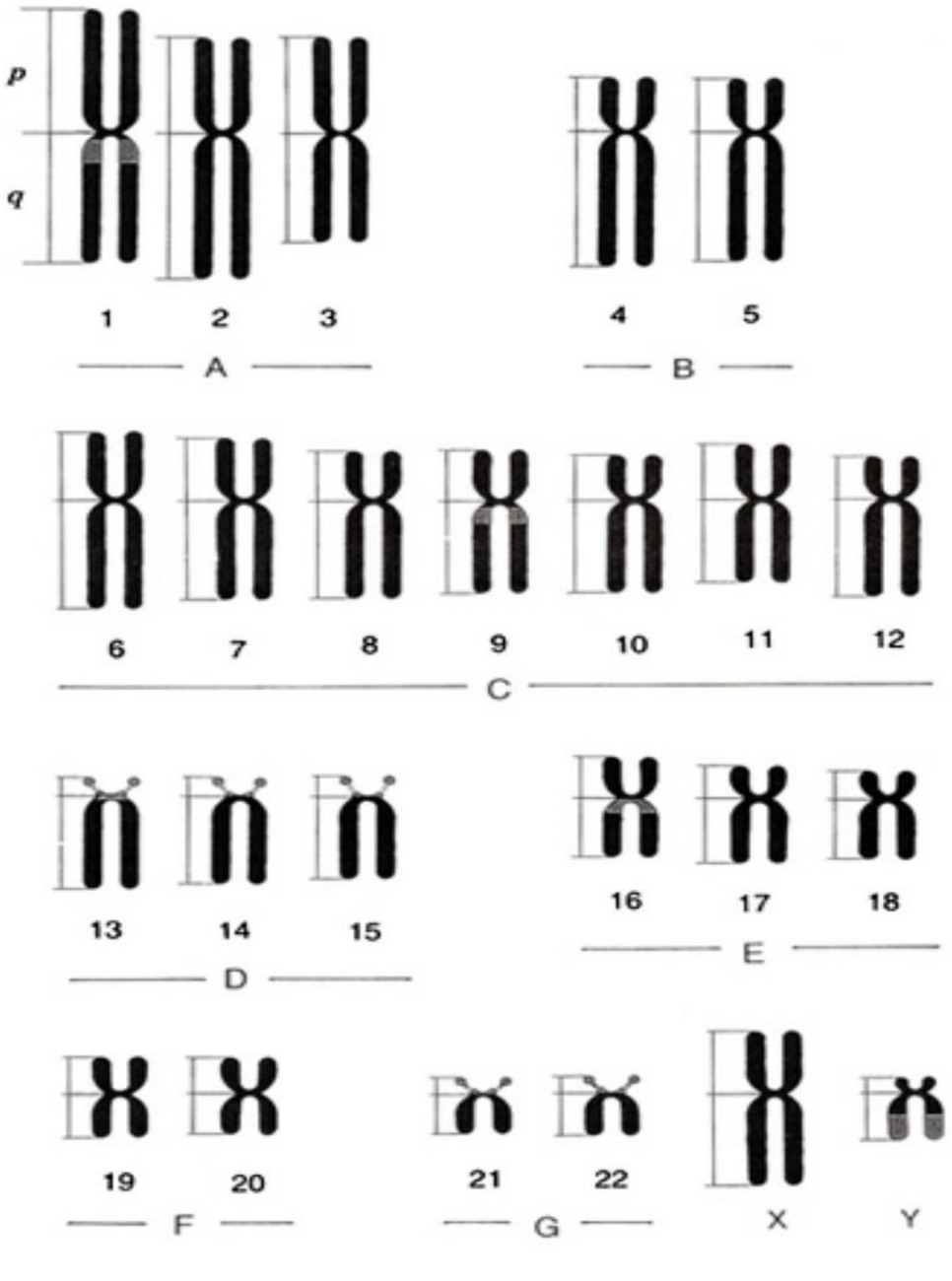
- **Karyotyping:** is the basic tool of cytogenetic**.**
- **A karyotype** is a photographic representation of a stained metaphase spread in which the chromosomes are arranged in order of decreasing length. Chromosomal studies can be obtained from any dividing nucleated cell, but usually done on lymphocyte. In prenatal diagnosis it is done on amniotic fluid or chorionic villi or fetal blood, so these cells are cultured, arrested in mitosis during metaphase in which (400-600) bands are usually visible, or during prophase where (600-1200) bands are visible, and then the cells are fixed and stained .

- The chromosomes can be distinguished from each other by:
- **(1): size:** where they rearranged in (8)groups from larger to the smaller chromosome



(2): Centromere position: where they rearranged in to:

- **A: Metacentric** (Centromere is in the middle), e.g.: group (A).
- **B: Sub metacentric** (Centromere is between the middle and the end of the chromosome), e.g.: group (B,C).
- **C: Acrocentric** (Centromere at the end of the chromosome), e.g.: group (D,E).



Nomenclature:

Nomenclature: in human ,the normal chromosome count is 46.

p: Short arm of the chromosome.

q: Long arm of the chromosome.

46,XX,5p-: Deletion of short arm of the chromosome 5.

45,XX,t(13q 14q): Translocation of long arm between chromosome 13and 14.

47, XY, +21: Extra 21 chromosome (Down syndrome).

Haploid: Cell contain 23 chromosomes, e.g.(sperm and ova).

Diploid: Cell contains 46 chromosomes.

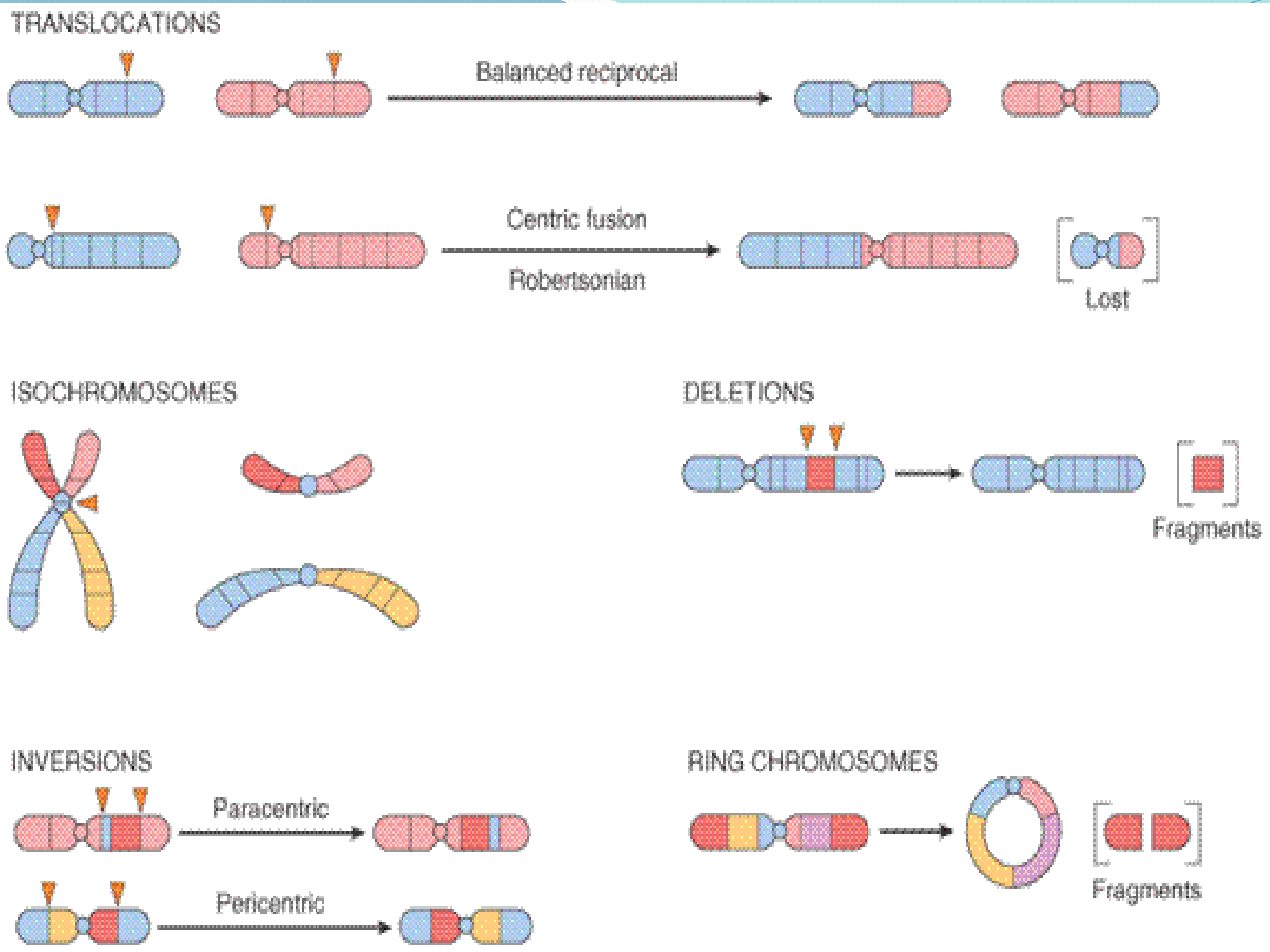
Triploid: Cell contains 69 chromosomes .

Euploid: Cell contains extra multiples of haploid (69,92…).

An Euploid: Cell deviating from multiples of haploid number, e.g.(Trisomy, Monosomy).

Abnormalities of chromosomal Structure

- **1-Deletion:** A piece of chromosome is missing. This deletion may be located at the end of the chromosome or in the interstitial segment. They are usually associated with mental retardation and malformation. E.g.(***Cri due Chat syndrome*** 46,XX,5p^{-}):
- **2-Translocation:** Transference of chromosomal material from one chromosome to the another. It occurs in a frequency of 1/500 live born human infants. It may be inherited from a parent or appear de novo. The carriers of translocation are usually phenotypically normal, but there is increased risk of miscarriage and abnormal off springs.
- **3-Inversion:** Occurs in 1/100 live born. The chromosome breaks at two points and this broken piece is then inverted and joined in the same chromosome.


TRANSLOCATIONS
Balanced reciprocal
Centric fusion
Robertsonian
Lost
ISOCHROMOSOMES
DELETIONS
Fragments
INVERSIONS
Paracentric
Pericentric
RING CHROMOSOMES
Fragments

- **4-Ring chromosome:** Very rare, deletion at each end of chromosome and then the sticky ends joined to form the ring. Phenotypically ranging from mental retardation and multiple congenital anomalies to normal or near-normal depending on the amount of chromosomal material that is lost.
- **5-Duplication:** Presence of extra genetic material from the same chromosome
- **6-Insertion:** A piece of chromosome breaks at two points and incorporated into a break in the another part of chromosome (i.e.): it requires three break points and it may occurs between two chromosomes or within one chromosome.
- 7-Isochromosome: break at the centromere result in pp ,qq

Cell division

Mitosis: Somatic cell division, which occurs in four, stages (Prophase, Metaphase, Anaphase and Telophase).

Meiosis: Germ cell division. The main error in this stage is **(Non-disjunction),** in which two chromosomes fail to separate and migrate together in to one of new cell, producing one cell with two copies of chromosomes and one cell with no copy.

Abnormalities of chromosomal number

- The most common is Trisomy, which are usually results from meiotic non-disjunction and the most frequent examples are **Trisomy 21** (Down syndrome), **Trisomy 18** (Edward syndrome), **Trisomy 13** (Patau syndrome).

Down syndrome:

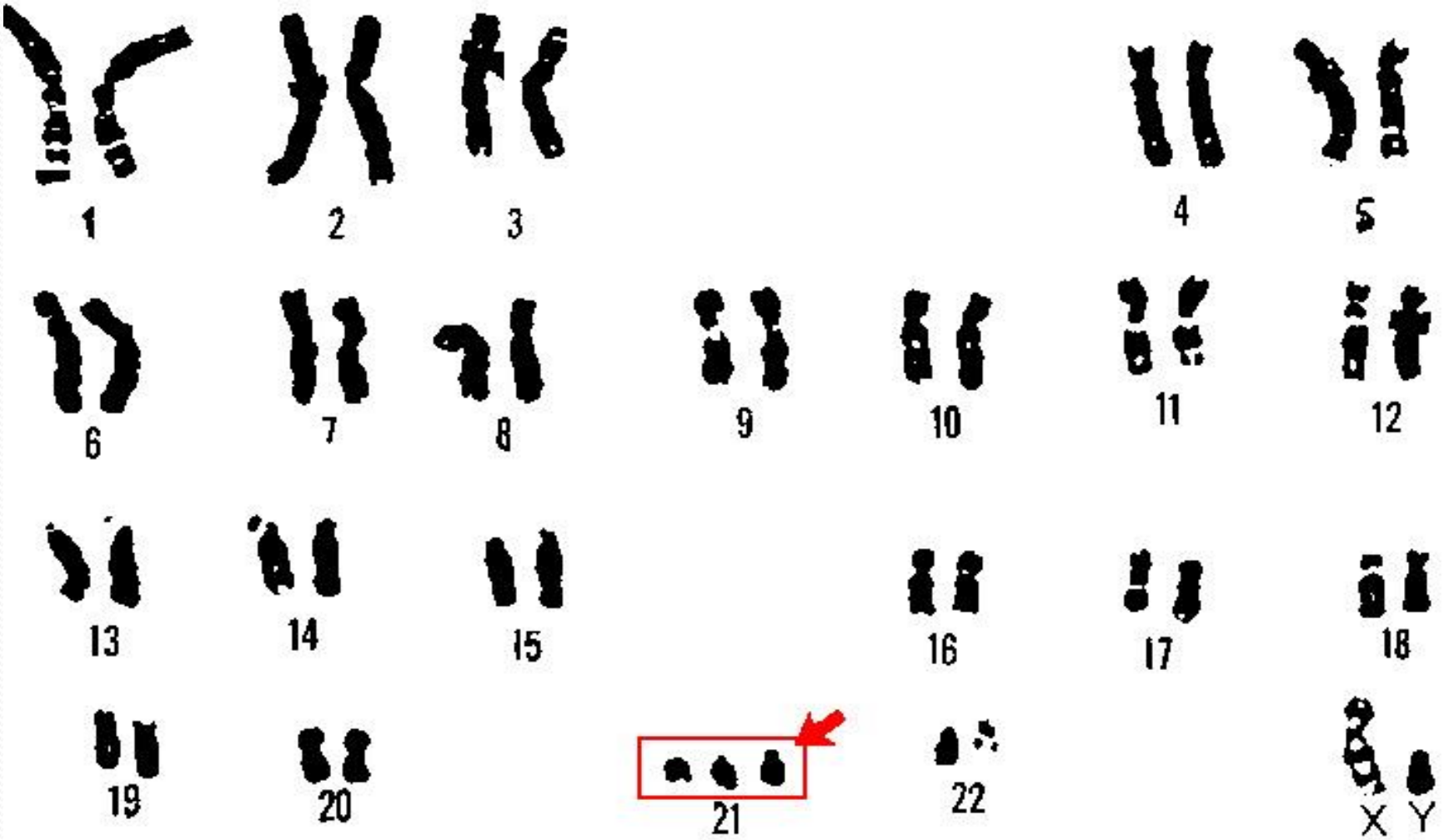
- is the most common of the chromosomal disorders. The incidence of this syndrome increased with maternal age. Even younger women have a lower risk, they represent half of all mothers with babies with Down syndrome because of their higher overall birth rate. All women should be offered screening for Down syndrome in their second trimester by means of (free B-hCG, unconjugated estriol, and α-fetoprotein)

Genetics/etiology of Down's Syndrome

- Trisomy 21, 94% of cases. Occurs following nondysjunction during meiosis in one of the parents. Though this can occur with either parents' advancing age, there is a stronger correlation with the maternal age.
- Chromosomal translocation, 3.3%. When genetic material from chromosome 21 attaches to another chromosome (14, 21 or 22). Could be de novo (75%) or transmitted from the parents (25%).
- Mosacism, 2.4%. Mostly from a trisomy zygote (after fertilization) that loses one chromosome leading to a mixture of trisomy 21 and normal karyotype autosomal cells. This results in a variety of phenotypes from near normal to classical trisomy 21 phenotype.

- **Clinical features:**

- It is the most common chromosome disorder and the single most common genetic cause of moderate mental retardation, hypotonia, microcephaly, flat occipit and face,
- **Eyes** (up slanting palpebral fissure, epicanthal fold)
- **Ears** (small, low set, and over folded upper helix),
- **Face** (protruded tongue, large cheeks, and low flat nasal bridge),
- **Skeletal** (short broad hands, gap between big toe and second toe, short stature, and simian crease),
- **Cardiac** 50% (most characteristic defect is VSD, while the most common defects are VSD, PDA, and TOF).
- I.Q is ranging between (35-65) with the mean of 54.
- **GIT** Cleft palate, Intestinal atresia, hirschsprung disease, Imperforated anus,
- **Hematological** (increased incidence of leukemia, neonatal polycythemia, increased MCV, decreased HbF and Eosinophiles
- **Others** Liability for immune dysfunction, hypothyrodism, diabetes mellitus, problems with hearing and vision, and Alzheimer disease,
- Most males are sterile; some females have been able to reproduce.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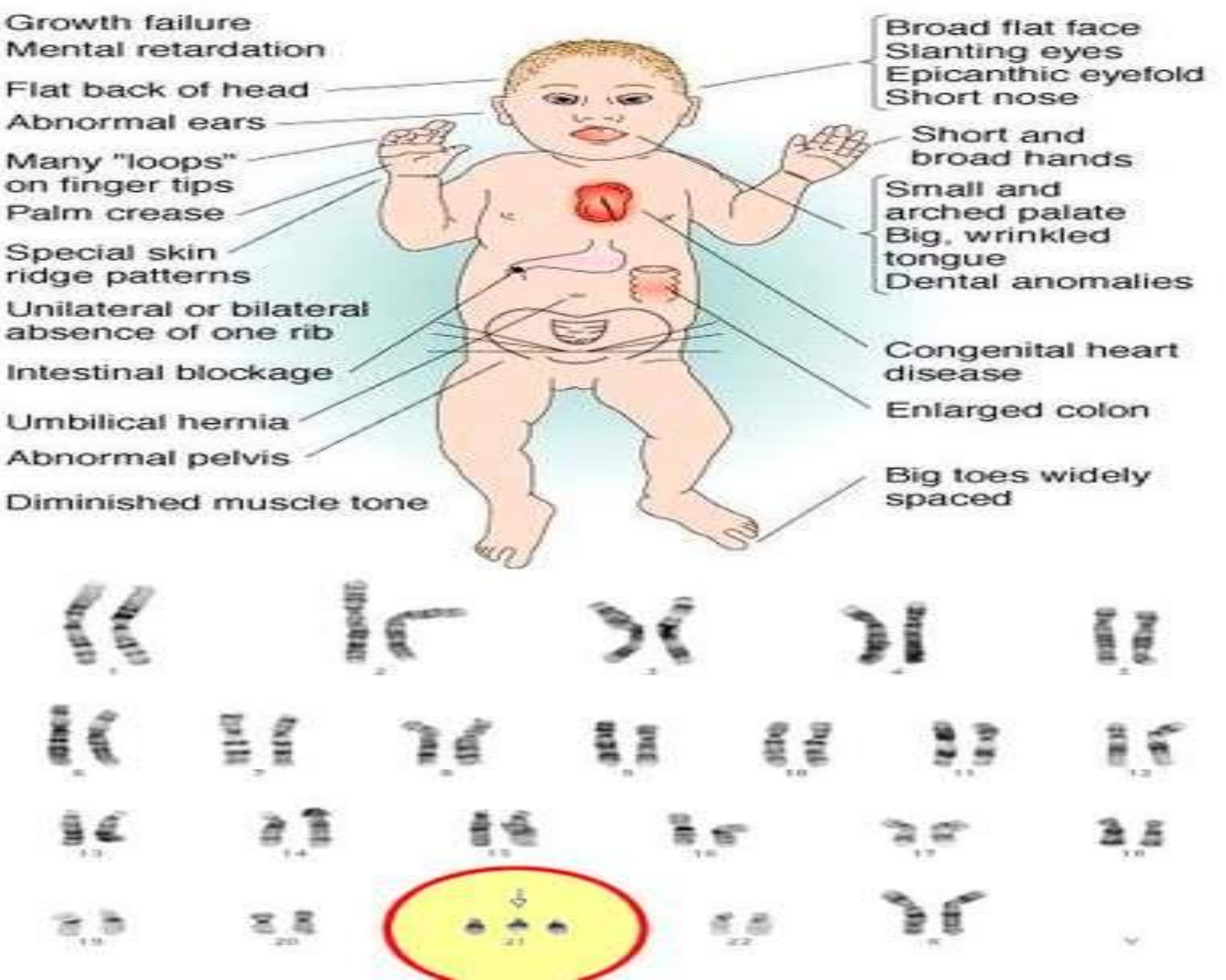
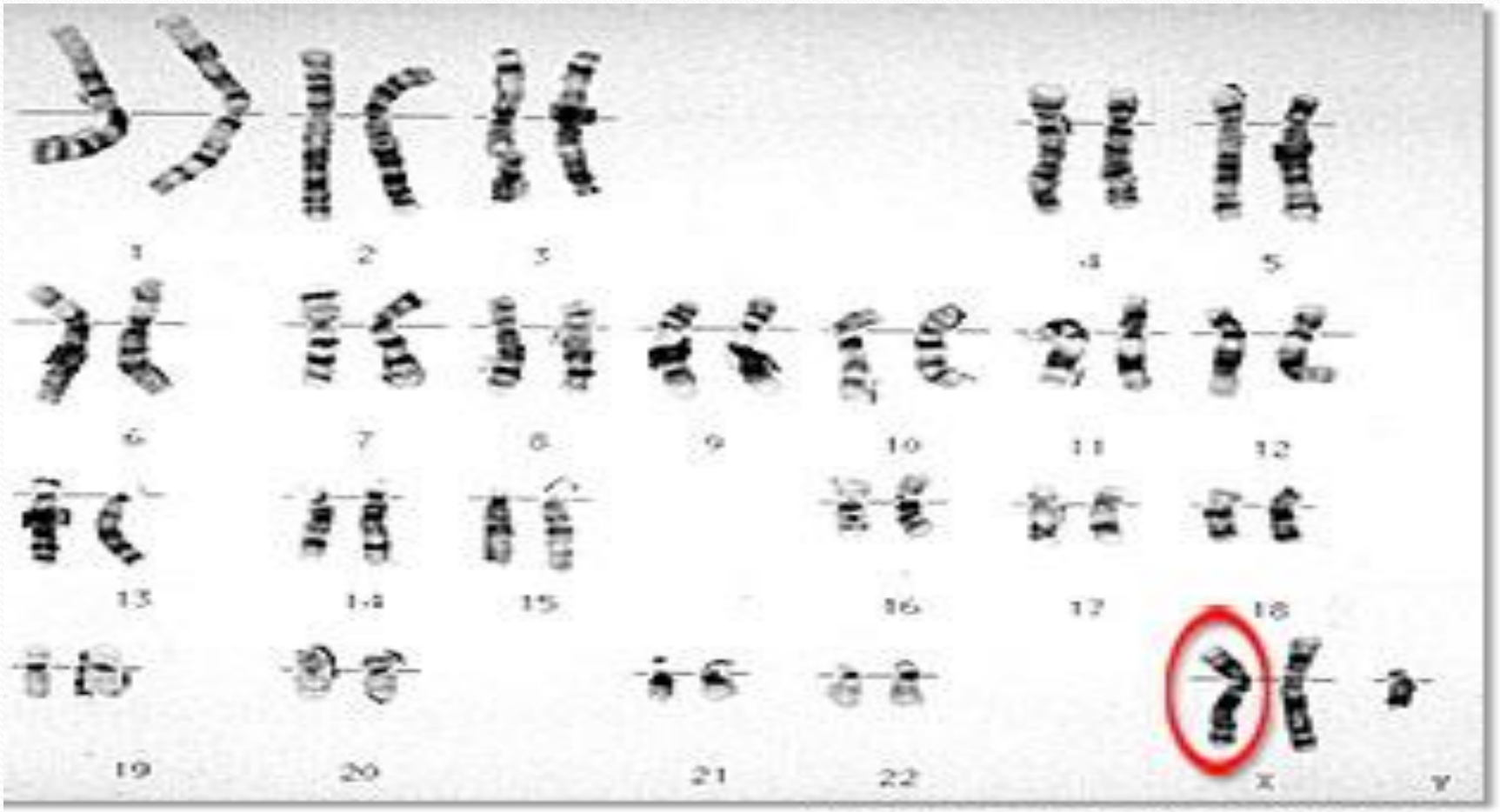

Growth failure
Mental retardation
Flat back of head
Abnormal ears
Many "loops" on finger tips
Palm crease
Special skin ridge patterns
Unilateral or bilateral absence of one rib
Intestinal blockage
Umbilical hernia
Abnormal pelvis
Diminished muscle tone
Broad flat face
Slanting eyes
Epicanthic eyefold
Short nose
Short and broad hands
Small and arched palate
Big, wrinkled tongue
Dental anomalies
Congenital heart disease
Enlarged colon
Big toes widely spaced

Sex- chromosomes Anomalies

- ***Klinefelter syndrome (47 XXY)***: Occurs in 1/575 live born males.
- **C.F:** Phenotypically is male with tall stature usually and has gynecomastia in 50%, Slow to develop secondary sex development, Usually had azospermia, small testes and infertile, behavioral or psychiatric disorders. Increased incidence of pulmonary diseases, varicose veins and carcinoma of breast.



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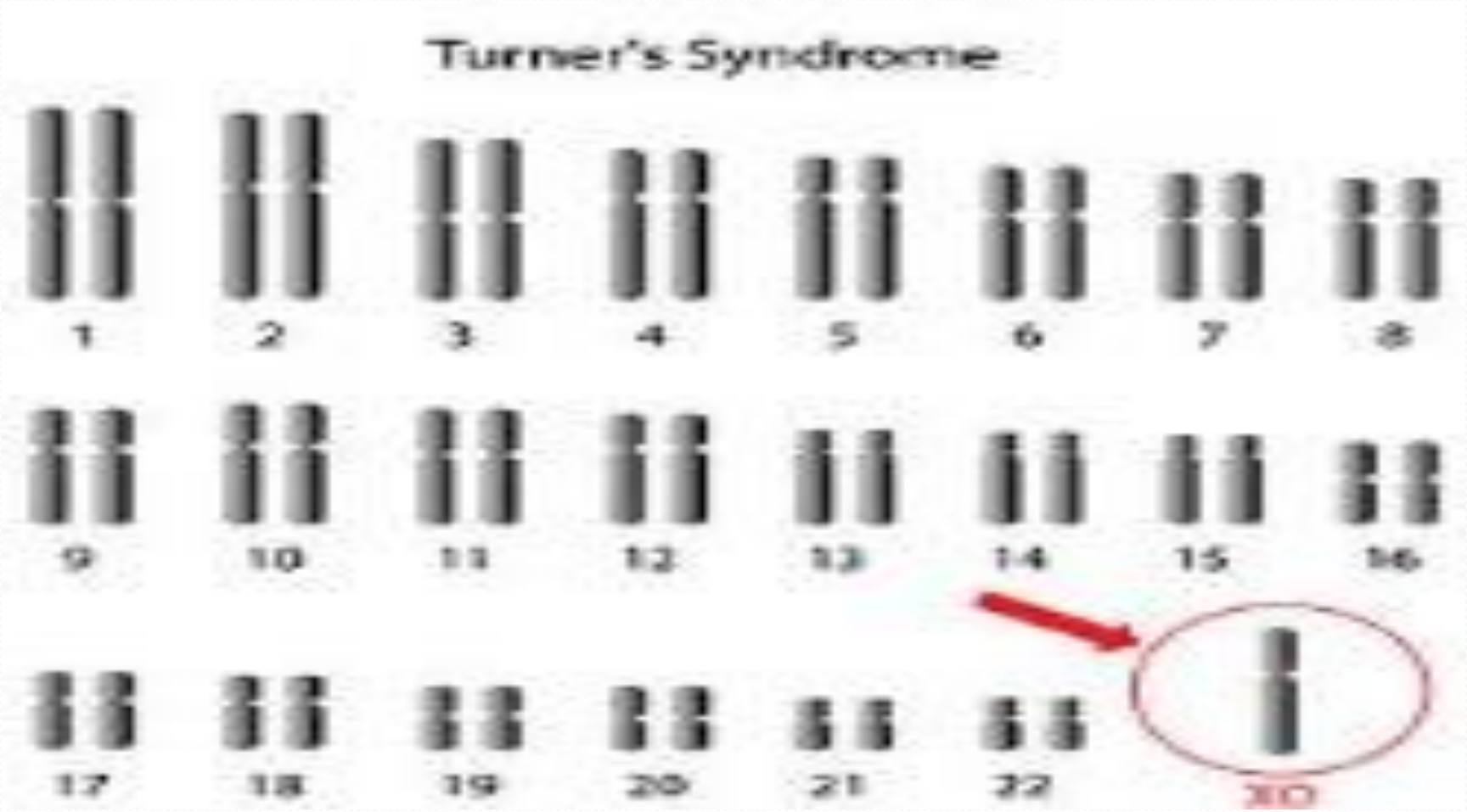
- ***Turner syndrome (45 Xo):*** It is due to loss of part or all of one of sex chromosome, so 50% of patients have ***(45 Xo)*** and others are mosiasicim the frequency is 1/5000 of live born females.
- **C.F:** The phenotype is female. Low births weight and decrease length. 50% of them have neonatal peripheral edema of dorsum of feet and hands, low posterior hairline, prominent ears, high arched palate, broad chest with widely spaced nipples (shield chest), short stature with mean adult height of 143 cm., bilateral recurrent otits media in 75% of patients, sensoneural hearing deficit is common.
- failure of development of puberty because of under development of gonads and the secondary sex characters don't appear in 90% of patients, so most cases are infertile.
- Congenital heart defects in 40%. Renal malformation in 60% (Pelvic kidney Hoarse shoe kidney). IQ is normal, but may be there is some learning disability.


Turner's Syndrome
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X0


low posterior hairline
webbed neck and extra skin
wide-set nipples
discolored spots on skin
swollen hands
swollen feet