Chromosomal disorders

Prof Vandana Rai
Department of Biotechnology
VBS Purvanchal University
Jaunpur

- Chromosomal disorders include all conditions associated with visible changes of the chromosomes .
- About 20% of all conceptions have a chromosomal disorders ,but most of these are spontaneously aborted so that birth frequency is 0.6%.
- Amongst early spontaneous abortions the frequency of chromosomal disorders is 60%,whereas in late spontaneous abortions and still births the frequency is 5%.

Triploid fetuses may survive to term, but the majority aborts/still birth.

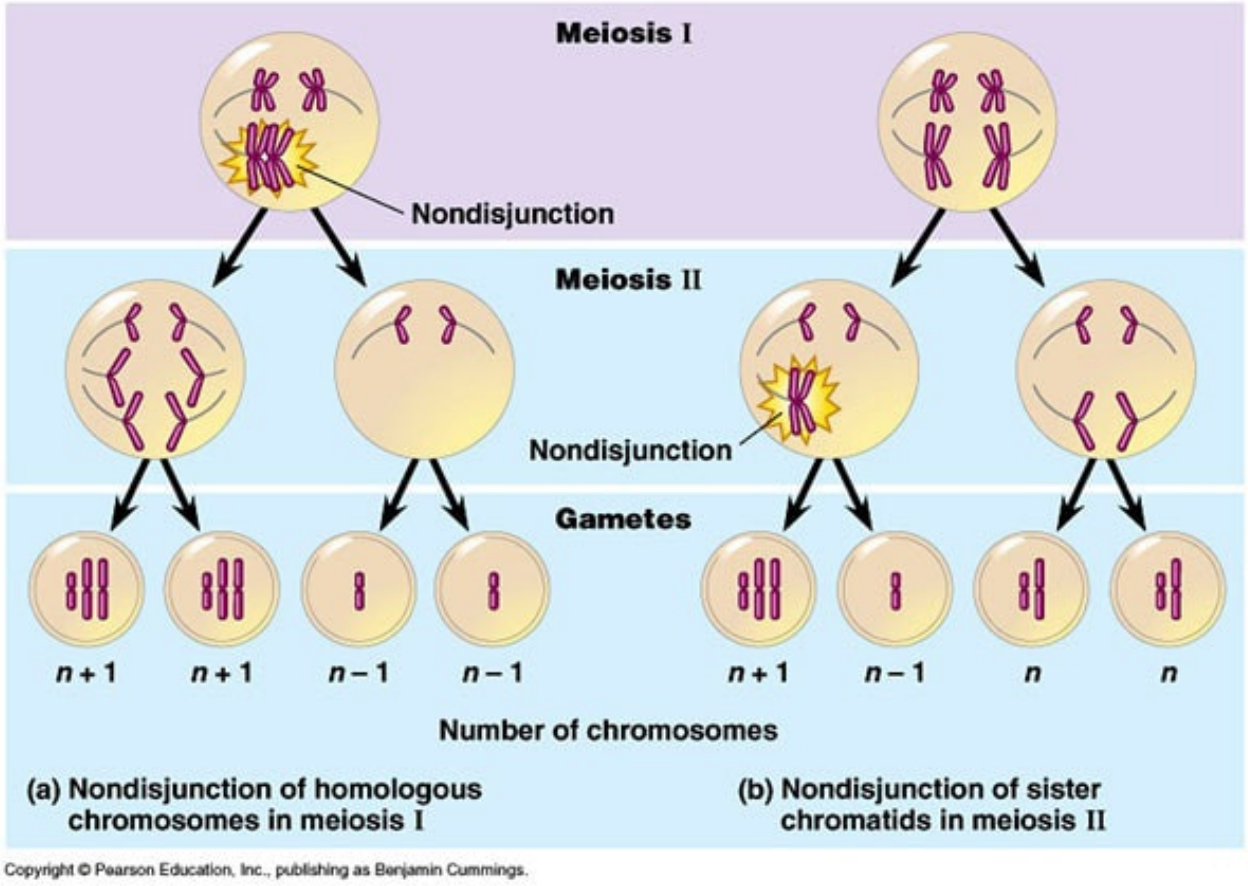
The commonest chromosomal disorders seen in newborns are balanced and unbalanced translocations, deletions, duplications, trisomies 21, 18 and 13, sex trisomies and monosomy etc.

Not all of these chromosomal changes are associated with disease ,but in general autosoaml abnormalities tend to be more severe than sex chromosomal abnormalities, and deletions tends to be more severe than duplications.

The failure of chromosome to segregate properly during meiosis I and meiosis II can result in gametes with an extra chromosome or the loss of a whole single chromosome .

Usually result from nondisjunction, chromosomes line pair up properly but fail to segregate.

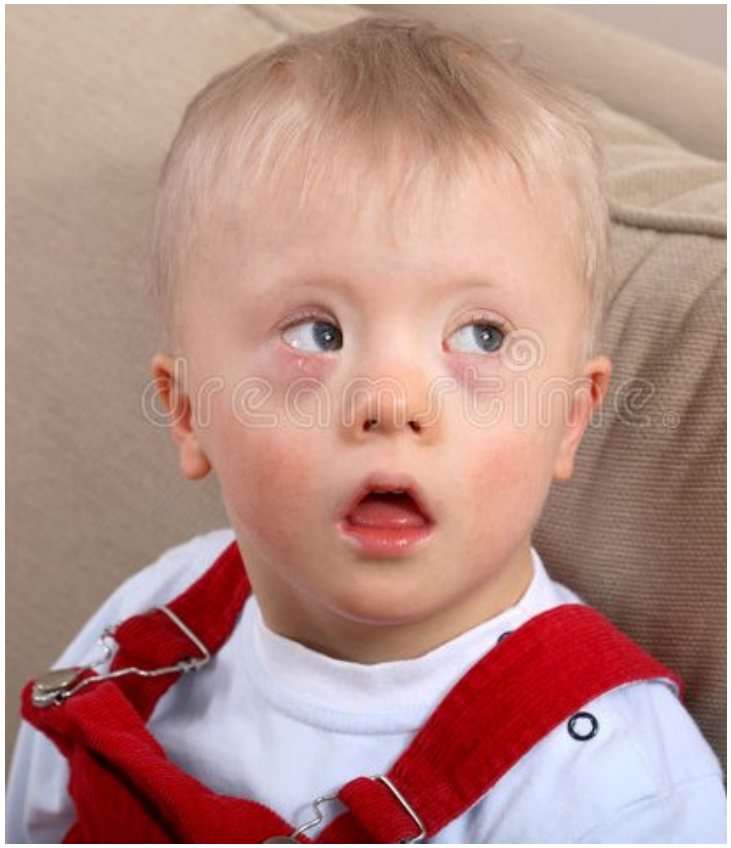
Less common causes are premature separation of paired chromosomes and normal meiotic segregation in a trisomy parent.



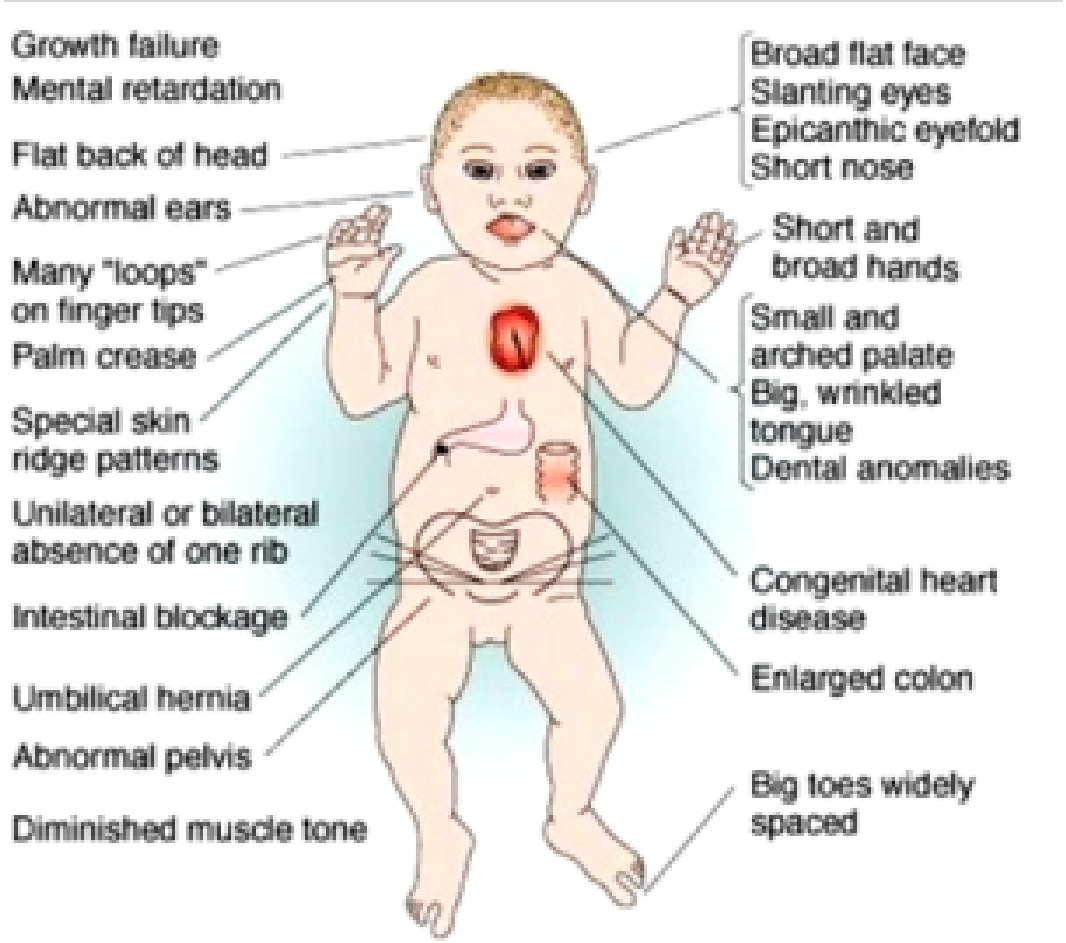
In meiosis, the parent cell is meant to split, and give one of each chromosome to each reproductive cell, when non-disjunction occurs, both copies of a chromosome end up in the same reproductive cell, which then combines with the single chromosome of the other parents cell during fertilization, leading to a trisomy.

Down syndrome

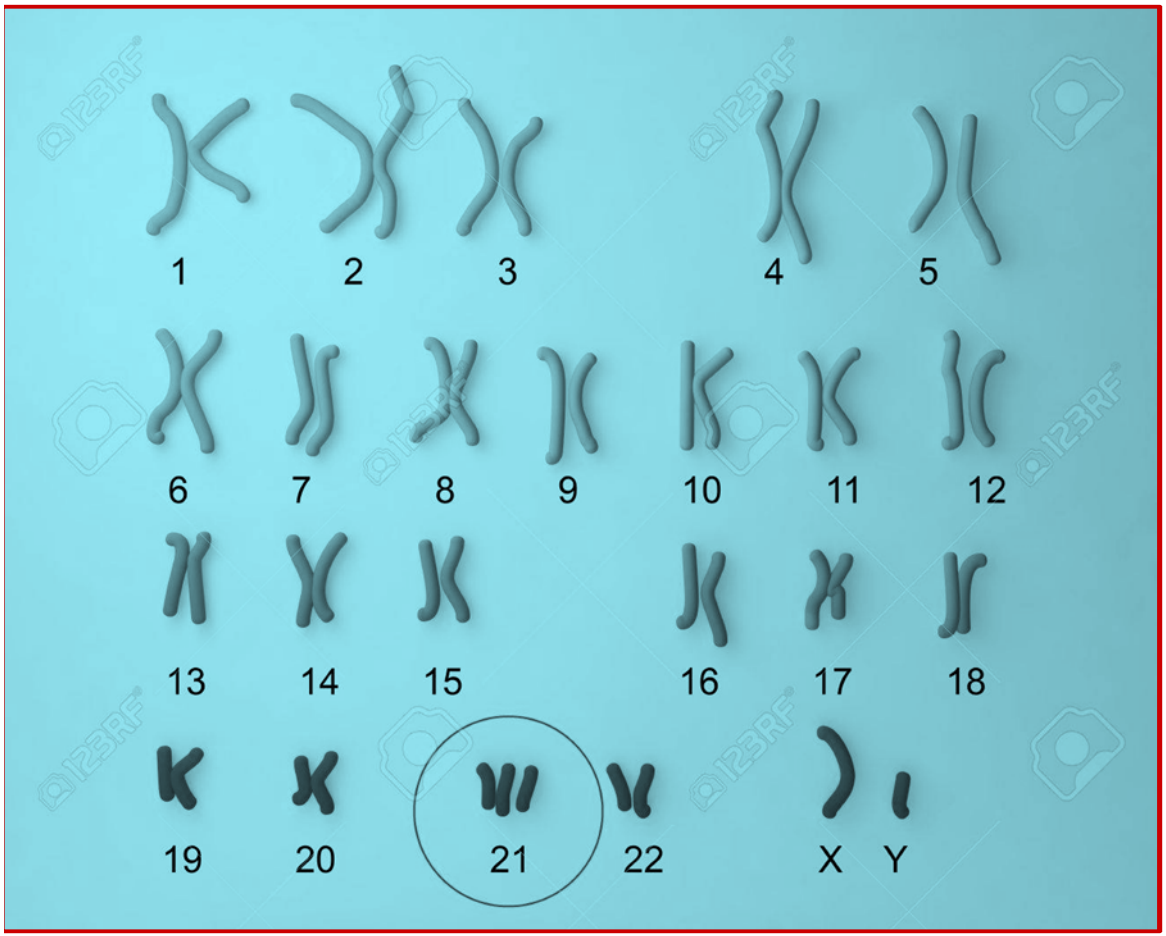
- Trisomy 21, have 3 copies of chromosome 21
- Can be male or female
- Physically and intellectually challenged
- Incidence is 1 in 800-1000 births
- Most common non-lethal trisomy
- 95% due to maternal nondisjunction
- Remaining 5% result from mosaicism or translocation
- In the majority of cases, the egg passes on the extra chromosome. But there are some cases where the sperm passes on the extra chromosome.
- Affected children have marked hypotonia, tongue protrusion, small head, flattened occiput, flat nasal bridge, epicanthal folds with up-slanting, palpebral fissures, loose skin around neck, short, stubby fingers, single



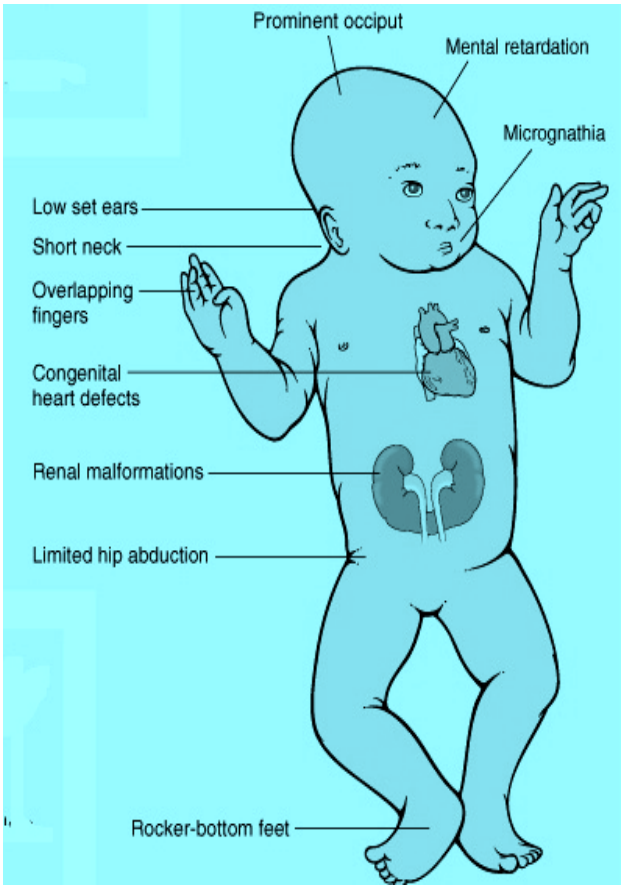
https://www.dreamstime.com/stock-images-boy-down-syndrome-image4277234



https://www.studyblue.com/notes/note/n/4b-clinical-cytogenetics-chromosomal-abnormalities/deck/16732552
https://qsota.com/wp-content/uploads/2015/06/Down-syndrome-in-a-child.jpg



https://www.123rf.com/photo_71338408_stock-illustration-down-syndrome-karyotype-male-labeled-trisomy-21-3d-illustration.html



https://i.pinimg.com/600x315/8b/bd/af/8bbdafff4323803116510 96b944525c1.jpg

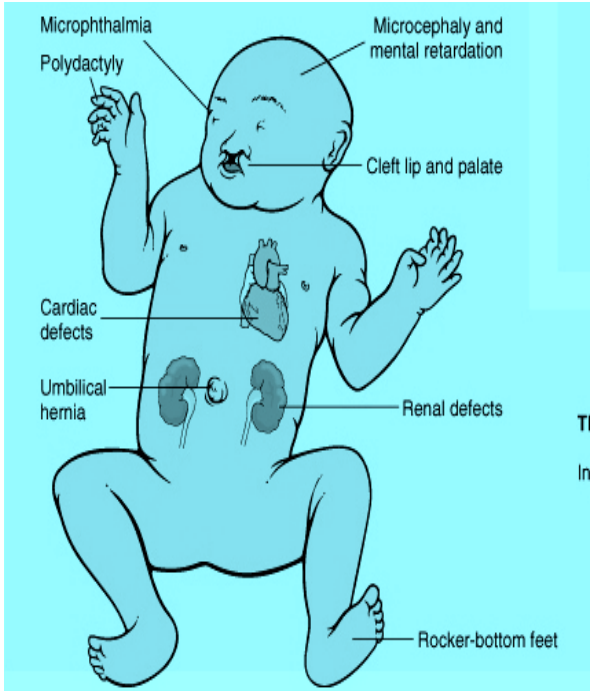
Down syndrome

- Narrow eye openings
- Up-slanting eyes
- Arched eyebrows
- Arched palate (cleft)
- Flat nose bridge
- Bow shaped mouth
- Small, low set ears
- Short neck
- Sloping shoulders
- Associated defects include heart defects (endocardial cushion), GI atresias, leukemia and thyroid disease

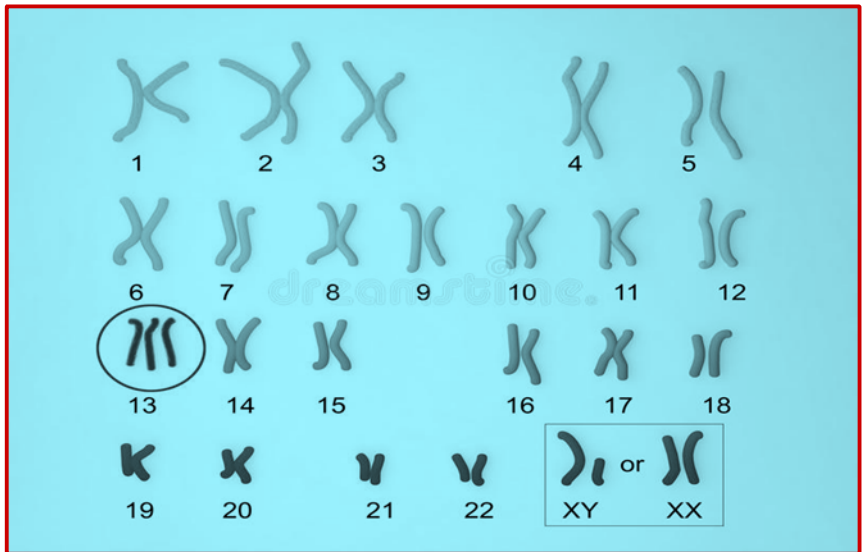
https://www.dreamstime.com/stock-photo-portrait-cute-baby-boy-down-syndrome-bed-home-bedroom-image88850471

Patau Syndrome
Trisomy 13

- Cleft lip and palate
- Extra fingers & toes
  - polydactylism
- Defects
  - Heart
  - Brain
  - Kidneys
- Most abort
- Live span < 1 month

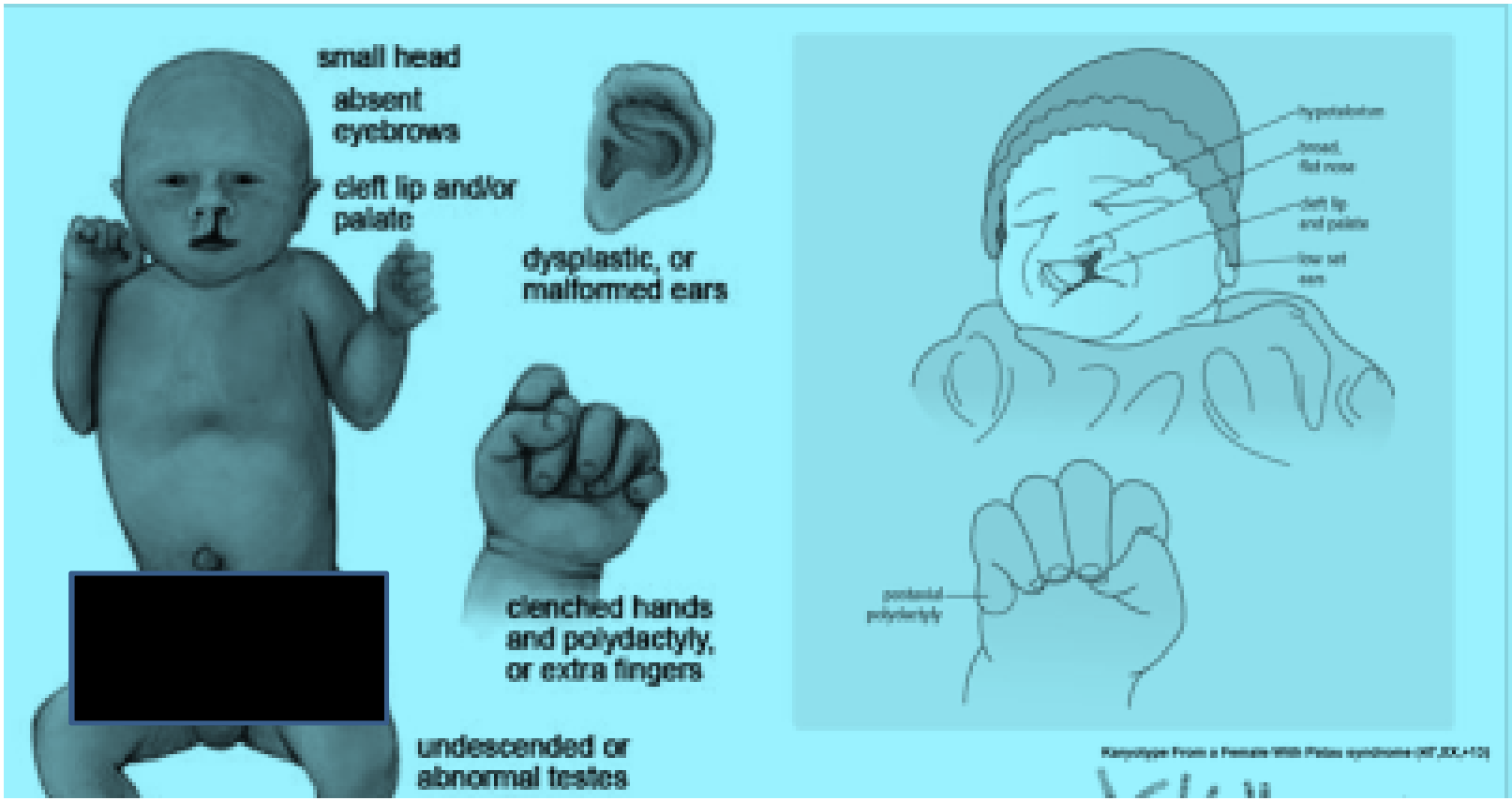


https://i.pinimg.com/600x315/8b/bd/af/8bbdafff432380311651096b944525c1.jpg



https://www.123rf.com/photo_71338446_stock-illustration-patau-syndrome-karyotype-labeled-trisomy-13-3d-illustration.html

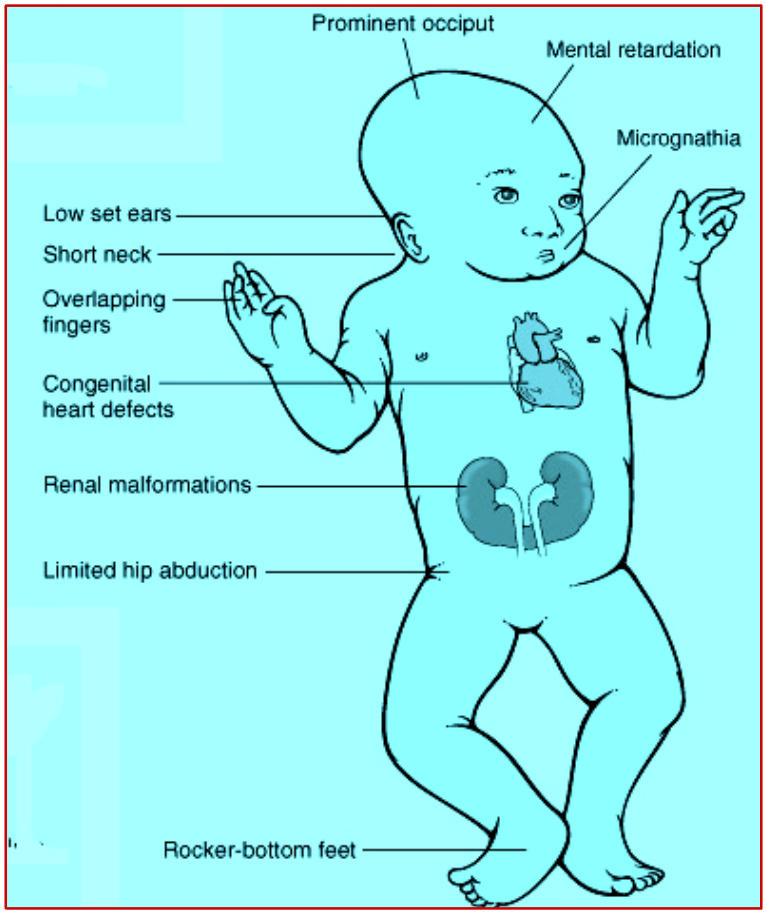
Patau Syndrome



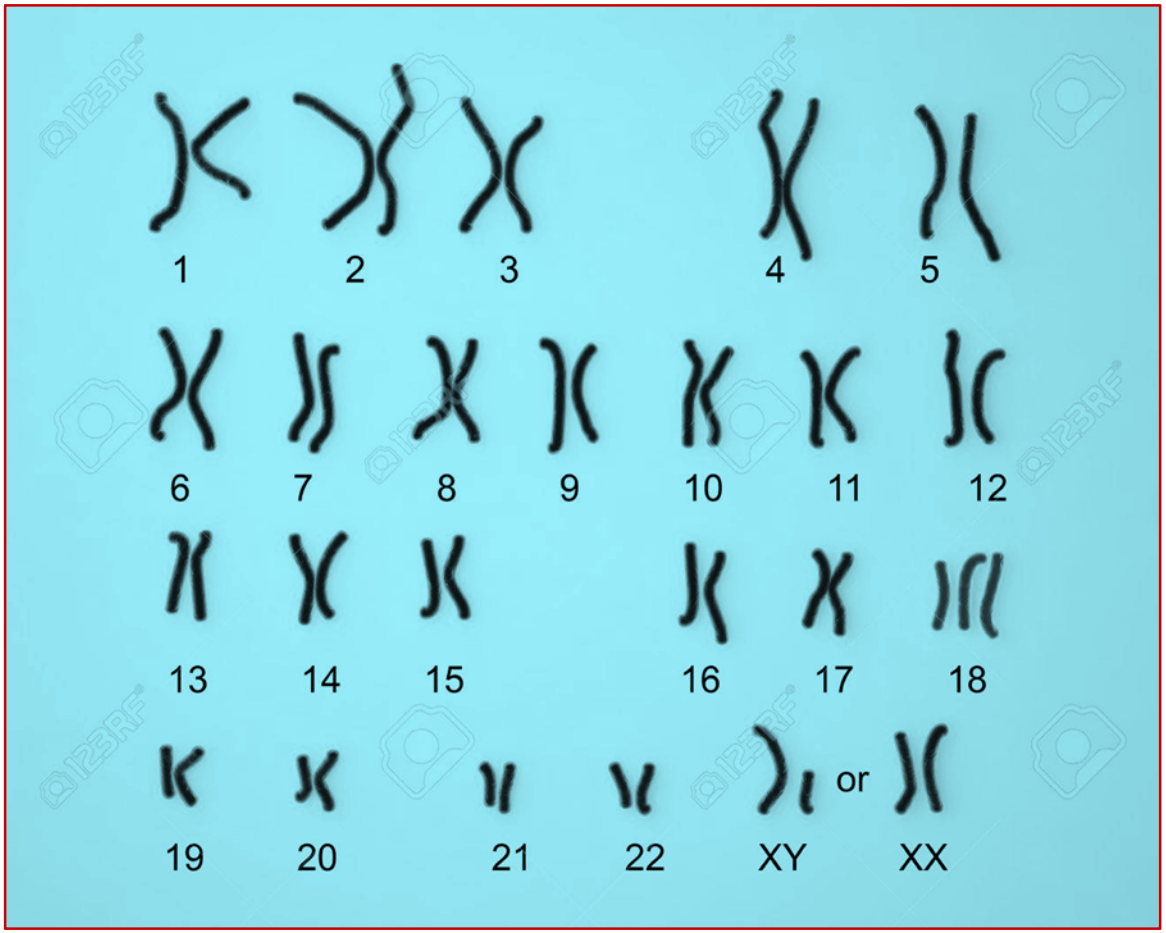
https://www.studyblue.com/notes/note/n/4b-clinical-cytogenetics-chromosomal-abnormalities/deck/16732552

Edward Syndrome
Trisomy 18

- Heart defects
- Displaced liver
- Low-set ears
- Abnormal hands
- Severe retardation
- 98% abort
- Lifespan < 1 year



https://i.pinimg.com/600x315/8b/bd/af/8bbdafff432380311651096b944525c1.jpg



https://www.123rf.com/photo_71338409_stock-illustration-edwards-syndrome-karyotype-labeled-trisomy-18-3d-illustration.html

Turner syndrome

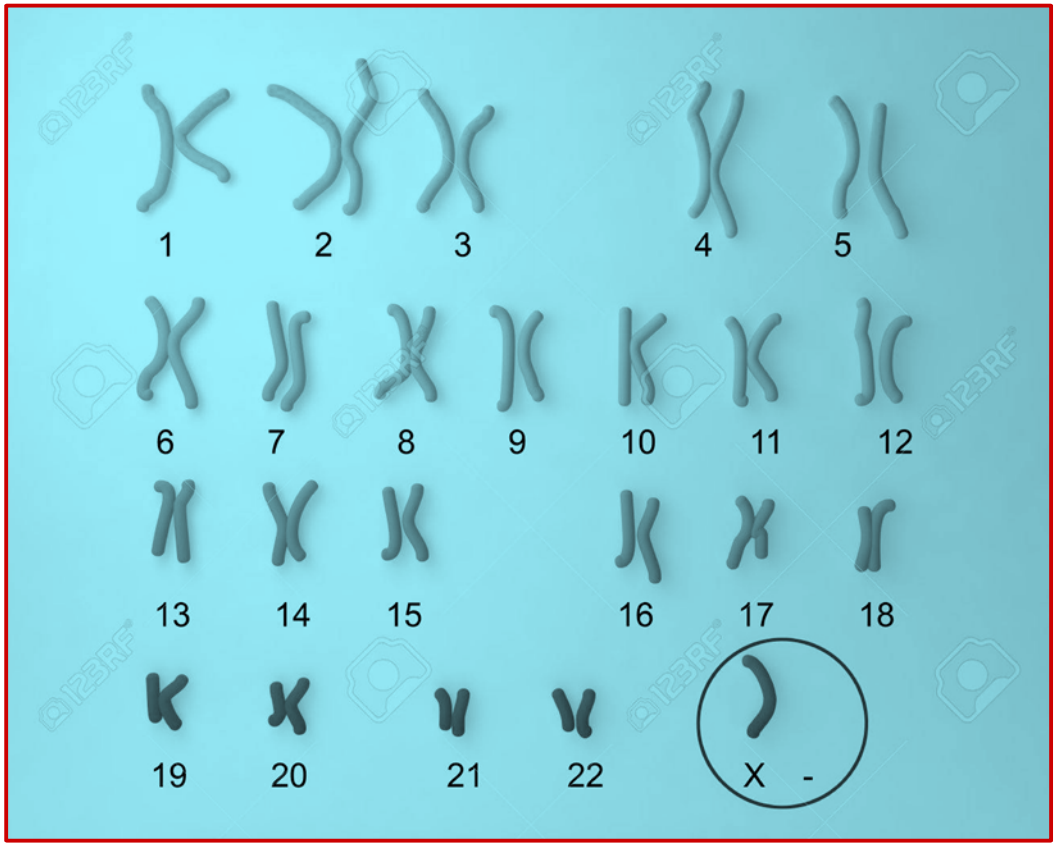
Also called XO, because people with Turner's have only 1 X chromosome: 45, X.

No Y means Turner's people are female. However, no ovaries develop, so they don't undergo the body changes of puberty and they are sterile.

Hormone treatment cures all but the sterility.

Other symptoms: short stature, webbed skin and low hairline at the neck, some oddities of spatial perception. Not retarded.

Hypogonandism with female phenotype, short body, webbing of neck, heart anomalies, infertility, amenorrhea, pigmented nevi, peripheral lymphedema at birth.



https://www.123rf.com/photo_71338417_stock-illustration-turner-s-syndrome-karyotype-labeled-x0-karyotype-3d-illustration.html

Klinefelter Syndrome

Non-disjunction can also result in a person with 2 X's and a Y: 47,XXY. This is called Klinefelter Syndrome.

The Y chromosome makes a person withKlinefelter's male: possessing testes.

Often not diagnosed, or diagnosed only accidentally.

Most symptoms are helped by testosterone treatment.

Symptoms: female body hair pattern, breast development, sterile, can be some developmental delay or retardation, especially for verbal skills.

Breast development

Other Sex Chromosome Number Variations

Triplo-X, having 3 X chromosomes. No Y chromosome means female. Many with this syndrome are undiagnosed because they have no symptoms. Some have slight social and developmental problems, especially language-related. Occasional fertility problems, but many have normal fertility. Not well studied.

Typically, females have two XX chromosomes that define sex. in trisomy X, the additional X chromosome brings the total number of chromosomes to 47. This chromosomal abnormality is rare, occurring in approximately 1 in every 1,000 female births.

Other concurring minor conditions displayed by females with trisomy X include congenital heart disease, clinodactyly, and epicanthal folds. Facial

Disorders from changes in chromosomal structure

(i)Deletion

(ii)Duplication

(iii)Translocation

(iv)Inversion

Even though there is no gain or loss of genetic material in translocation and inversion, the change in location of a segment may alter the regulation of a gene in the segment.

Deletion

Deletion was the first structural aberration detected by Bridges in 1917 from his genetic studies on X chromosome of Drosophila.

An event in which a piece of chromosome is missed or deleted.

Can remove one or more genes from chromosome.

Mostly occur during meiosis due to misalignment or mismatching during paring of homologous chromosomes

Deletions can occur in autosomes or sex chromosomes

Deletion may occurs due to

Types of deletion-

Terminal Deletion In this case loss of a terminal segment occurs, with a single break in the chromosomes

Intercalary Deletion In this case, internal part of a chromosome is missing.

In human genome deletion mutation cause:

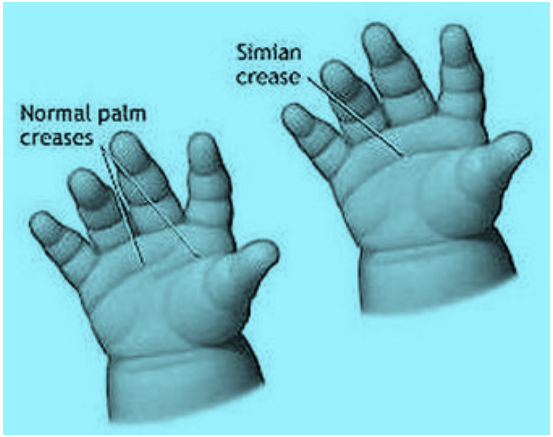
Granulocytic leukemia

Cri-du-chat syndrome

Cri du chat syndrome

Cri du chat syndrome is the deletion of 5p (short arm).

Features include high pitched cat like cry, sever mental retardation, hypotonia, and growth restriction



Duplication

- Duplication is the doubling or repetition of chromosome segment during chromosome duplication.
- As a result of it, a set of genes gets doubled or repeated.
- The extra set of genes is generally called “repeat”.
- Duplication was first detected by Bridges in 1919 from his genetic studies on X chromosome of Drosophila.

Translocation

Two pieces of different chromosomes are interchanged.

A portion of one chromosome is transferred to another chromosome

Types of Translocation

(i) Intrachromosomal translocation

Change in position of a segment within a chromosome, either from one arm to the other or from one location to another in the same arm.

a. Intraradial

Translocation from one location to another in the same arm

b. **Extraradial**

Translocation from one arm to the other

(ii) Interchromosomal Translocation

Translocation Transfer of a segment from one chromosome to other

Effects of translocation

Cause diseases in human such as cancer and infertility.

It may causes changes in chromosomes & also in gene combinations, promoting variation, speciation, & evolution.

A good example is the translocation between chromosomes 9 and 22, creating the“Philadelphia chromosome”.

This causes about 90% of the cases of chronic myelogenous leukemia.

Burkitt’s lymphoma is another example of a cancer which is usually (90%) caused by a translocation (8 and 14)

Inversion

Occurs when two breaks happen in the same chromosome.

No genetic material is lost but the rearrangement may alter gene function.

Paracentric inversions occur when the break is in one arm and the centromere is not included.

The carrier can either have a normal gamete or gametes that are extremely abnormal and fertilization can not occur.

Paracentric inversion carriers have a high risk of infertility but a low risk of abnormal off spring

Segment is turned 180 degrees

Leads to altered gene activity

Effects of inversion

- Helps to retain the original gene combination by reducing the crossing over frequency.
- Inversion enhances the position effect & there by produces phenotypic changes.
- Inversion causes chromosome polymorphism with in a population leading to karyotype evolution.
- Inversion produces balanced gene complexes(super genes) through reduction of crossing over, which in turn confers greater biological fitness and adaptability & increases the evolutionary potentiality