University of Basrah
Al-Zahraa Medical College

Ministry of Higher education
and Scientific Research

**Block: child health**

**Lecture: chromosomal abnormalities**

**Lecturer: Dr. Miami Kadhim**

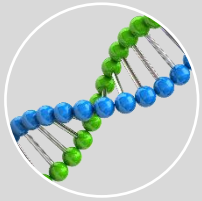
Block staff:

Dr. Jawad Ramadan (supervisor)
Dr. Miami kadhim (leader)
Dr. Rehab abdulwehab (co-leader)
Dr. Ahmad Jaafar (co-leader)

Dr. Ahmad Alsamak (coordinator)
Dr. Dhaighum Imad
Dr. Khalid Ahmad
Dr. Basim Abdulkareem

Dr. Ahmed Ibrahim
Dr. Dheyaa Jameel

Nelson Textbook of Pediatrics, 20th edition.
Nelson Essentials of Pediatrics, 7th Edition 2015
Pediatric Decision-Making Strategies
Illustrated Textbook of Pediatrics
Short Atlas in Pediatrics



# Learning outcomes

**Understand abnormalities in the number and structure of chromosomes LO1**

**Study the genetic syndromes associated with the chromosomal abnormalities:**

| | |
|---|---|
| **Down** | **LO2** |
| **Edward** | **LO3** |
| **Patau** | **LO4** |
| **Klinefelter** | **LO5** |
| **Turner** | **LO6** |
| **Cri-du-chat** | **LO7** |
| **Fragile X** | **LO8** |
| **Prader-Willi and Angelman Syndromes** | **LO9** |

# Chromosomal abnormalities LO1

## Changes in chromosomes number

A - increase in entire sets ( polyploidy), lethal

B – increase or reduction in one chromosome (aneuploidy)

-Trisomy: having extra chromosome

-Monosomy: missing a single chromosome

## Changes in chromosome structure

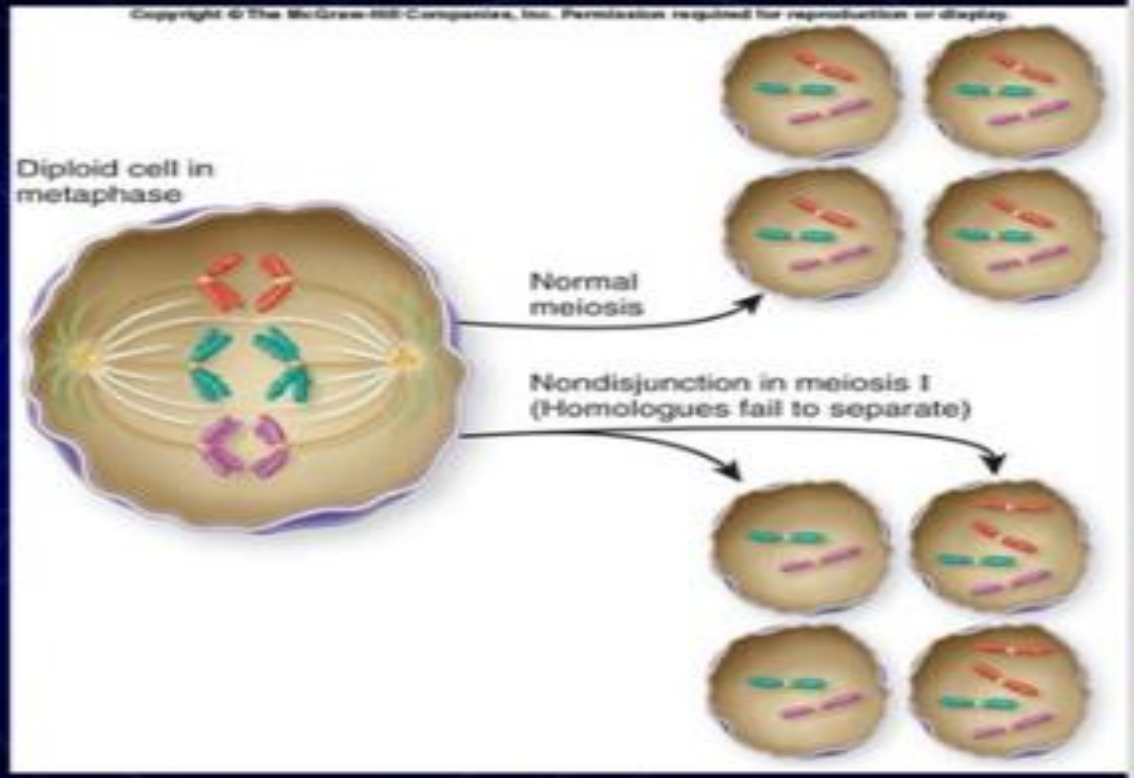
A – translocation/ chromosomal breaks

B – deletions

C – fragile sites

- **The most common cause of aneuploidy is nondisjunction, the failure of chromosomes to disjoin normally during meiosis so the resulting gamete either lacks a chromosome or has 2 copies resulting in monosomic or trisomic zygote respectively.**
- **Trisomy can be complete and present in all cells, or it may be in mosaic form.**

**Meiotic *nondisjunction* causes either gain or loss of single chromosomes**



## Trisomy

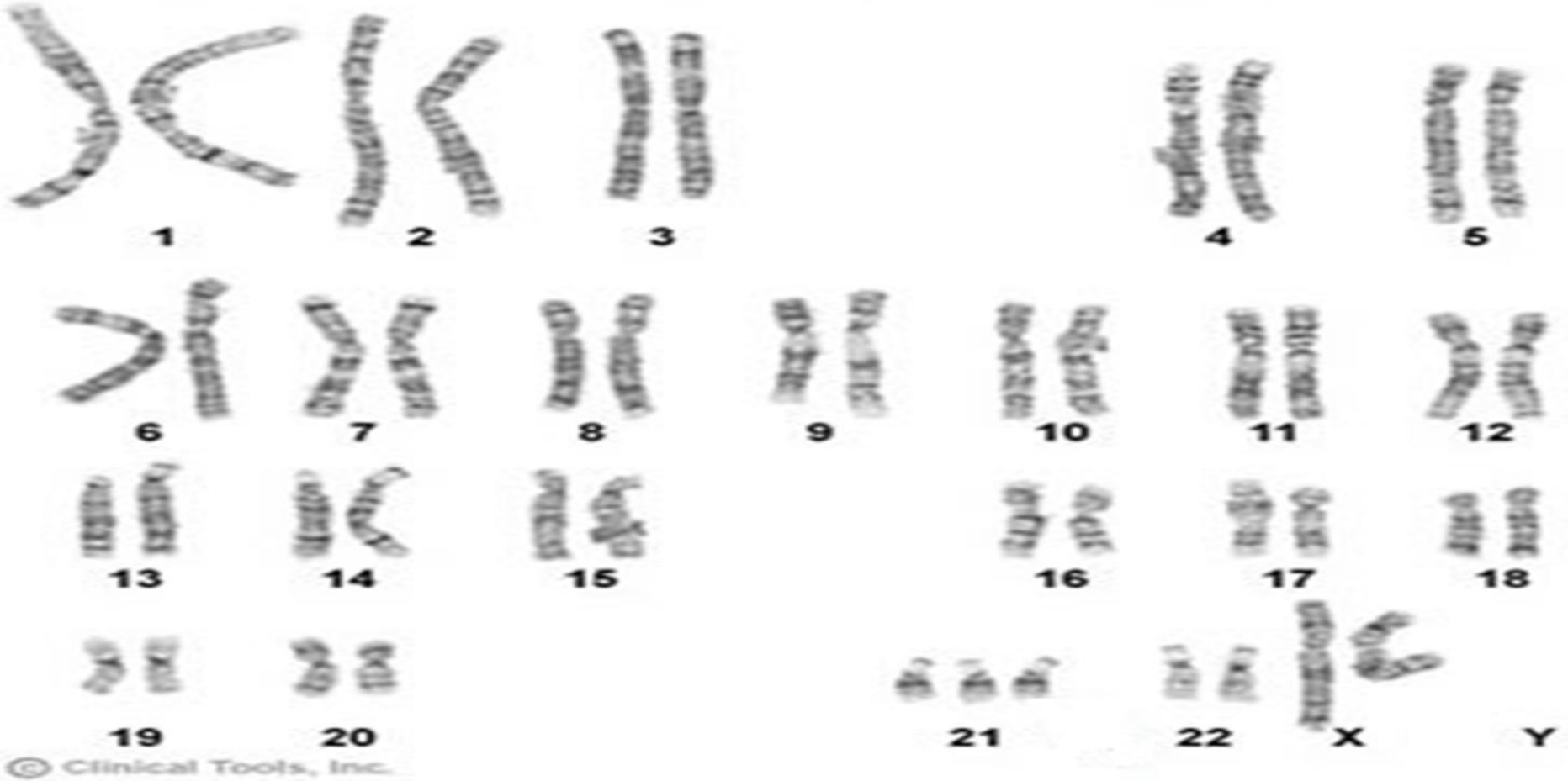
- **Autosomal trisomy ( 21, 18, 13……)**
- **Sex chromosome trisomy (47, XX)**

## Monosomy

**45, X0**

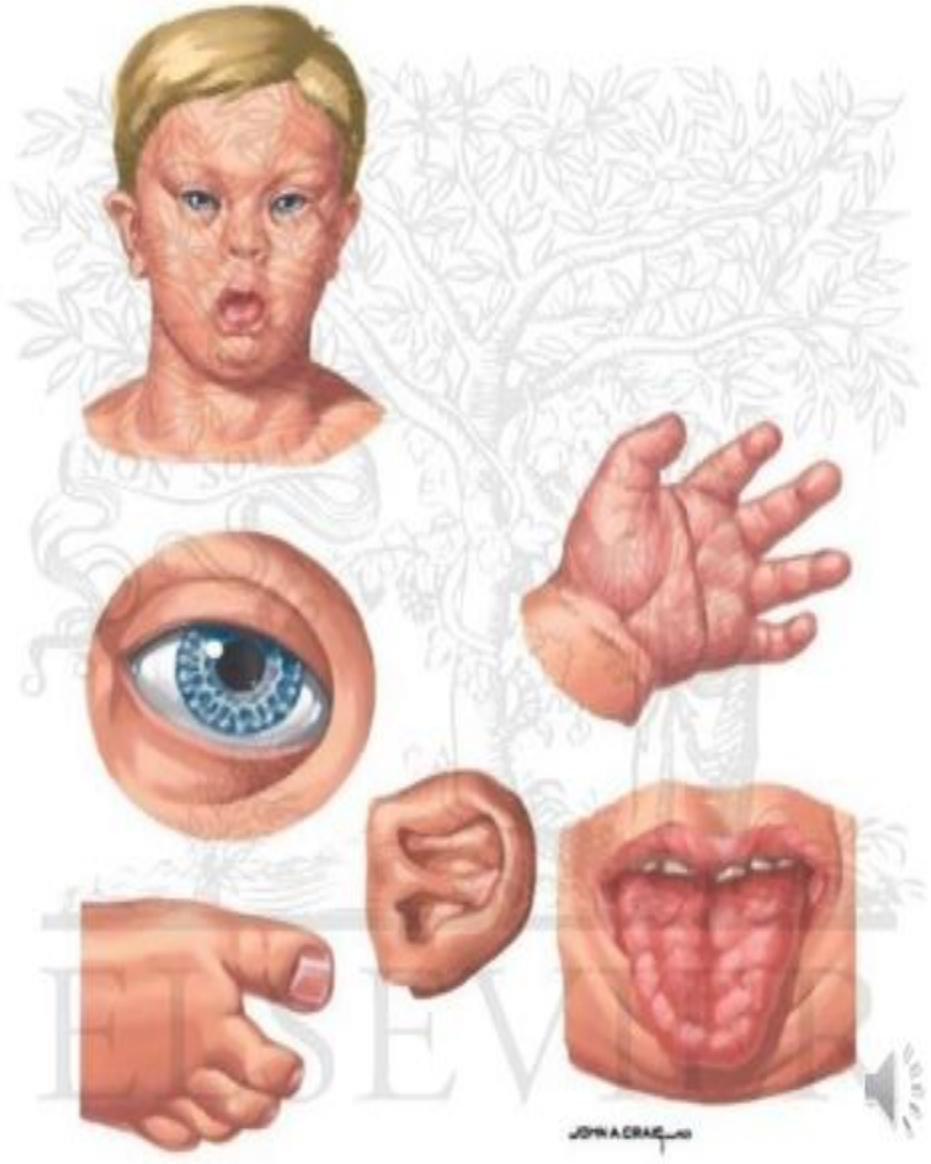
# Down syndrome LO2

- The only autosomal trisomy that allows survival until adulthood
- Karyotype: 47, xx,+21 or 47, xy,+21 extra chromosome is maternal in origin in 97% of cases



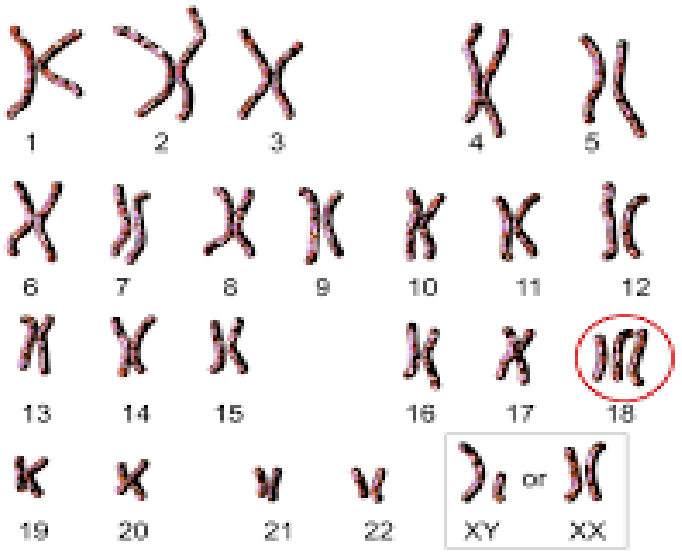
# Clinical findings

**Hypotonia,**
**Eyes: upward and slanted palpebral fissures and epicanthic folds, speckled irises( Brushfield spots)**
**Hands: short broad, simian crease, hypoplasia of middle phalanx of 5th finger**
**Flat occiput**
**cardiac malformations, duodenal atresia, high arched palate.**
**varying degrees of mental and growth retardation**



## Trisomy 18, Edward's syndrome

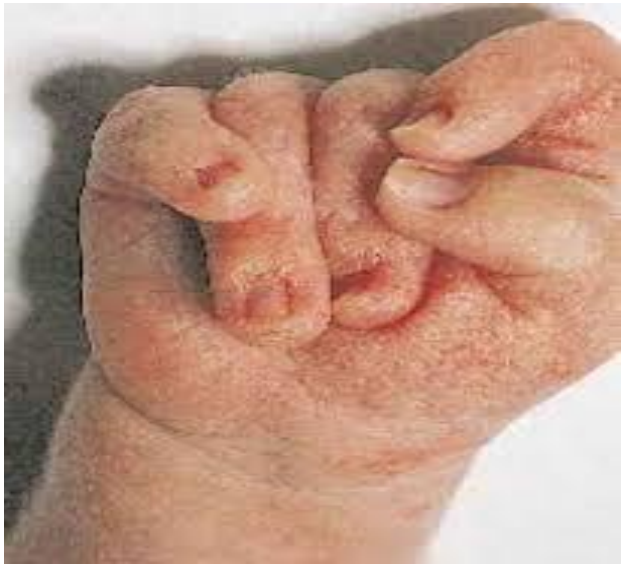
## LO3




**clinical findings:**

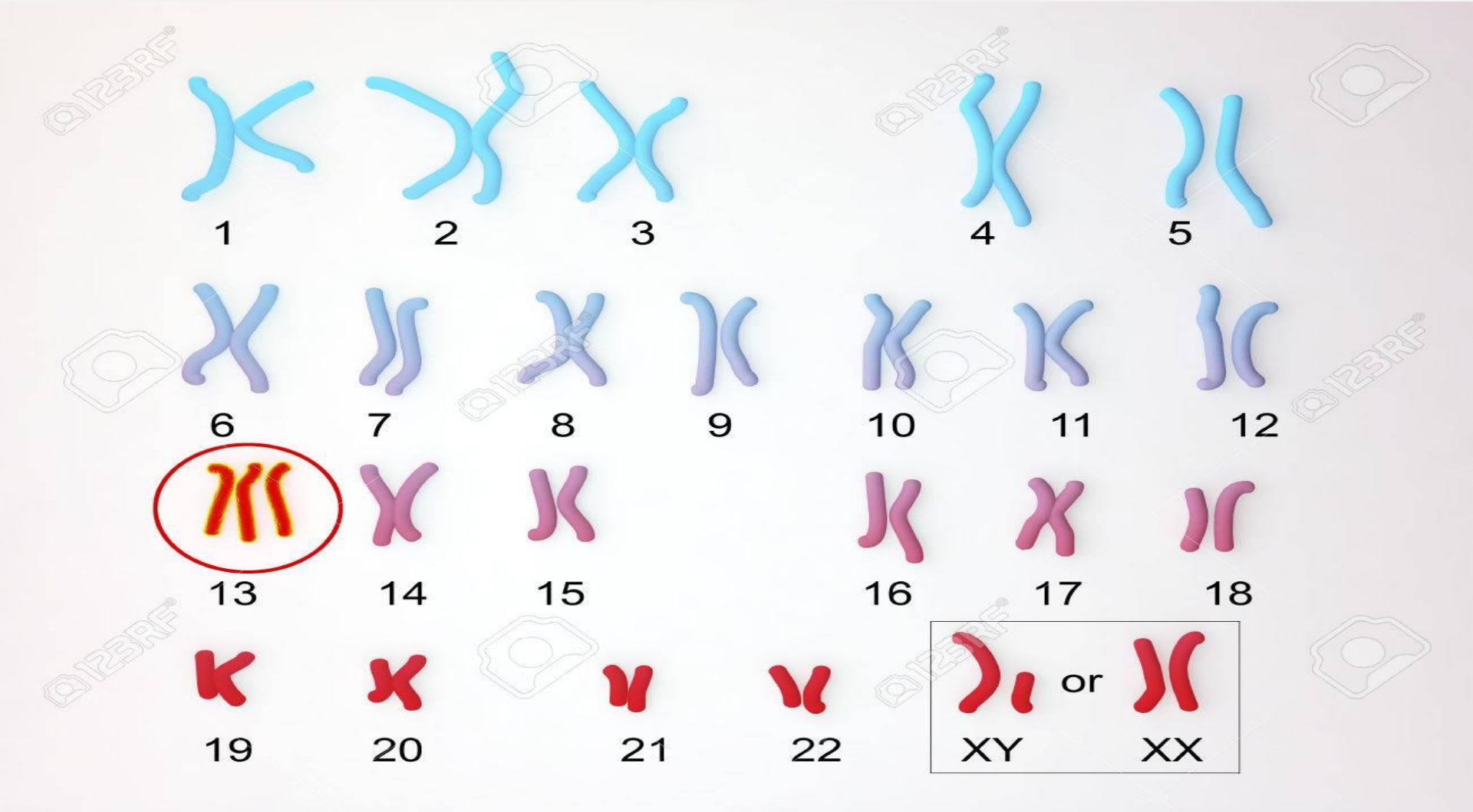
**Low birth weight**

**closed fists with index finger overlapping the 3rd digit and the 5th digit overlapping the 4th**

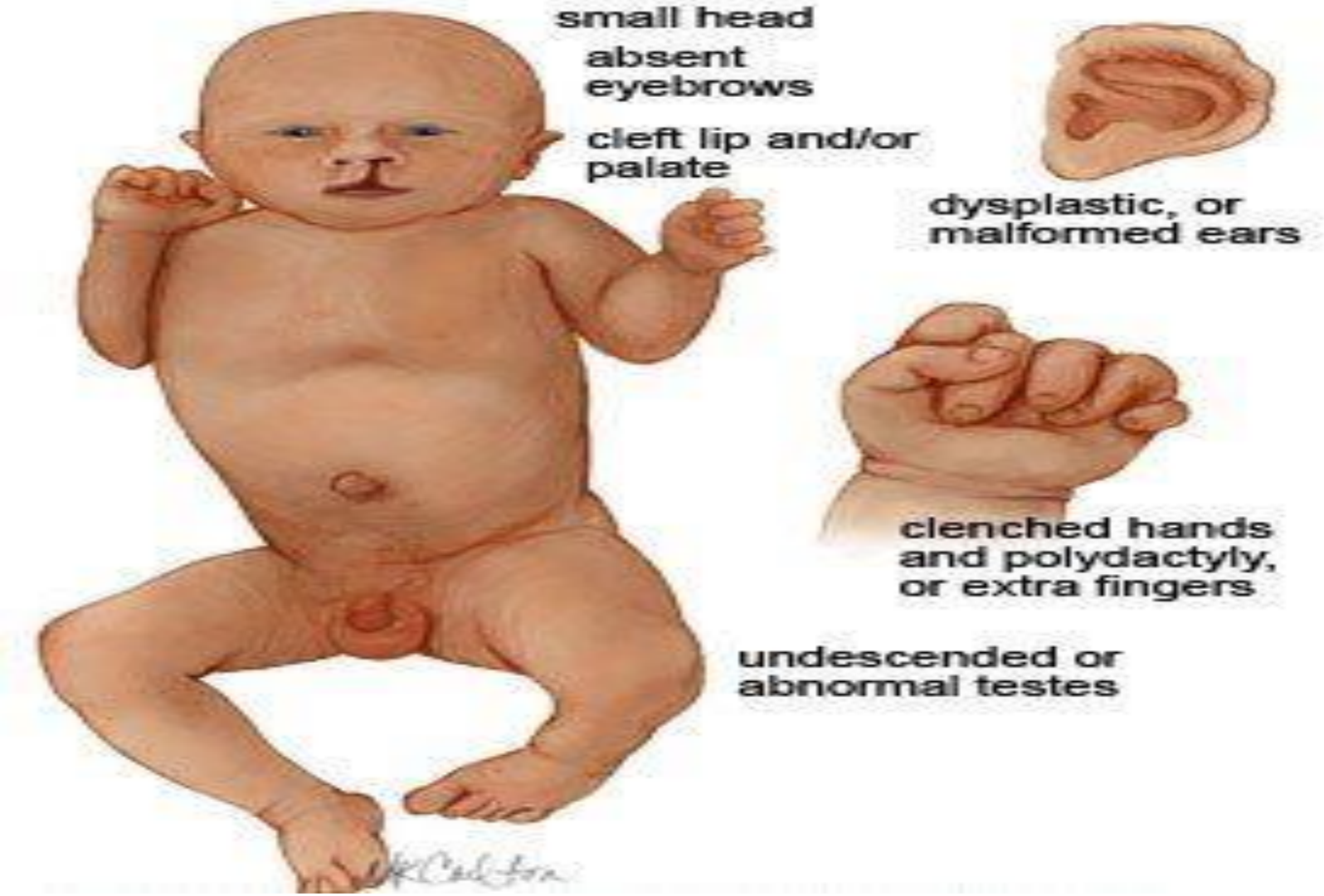


**narrow hips with limited abduction, short sternum, rocker-bottom feet, microcephaly, prominent occiput, micrognathia, cardiac and renal malformations, mental retardation and lethal in 95% of cases in the 1st year**


# Trisomy 13 – Patau syndrome LO4



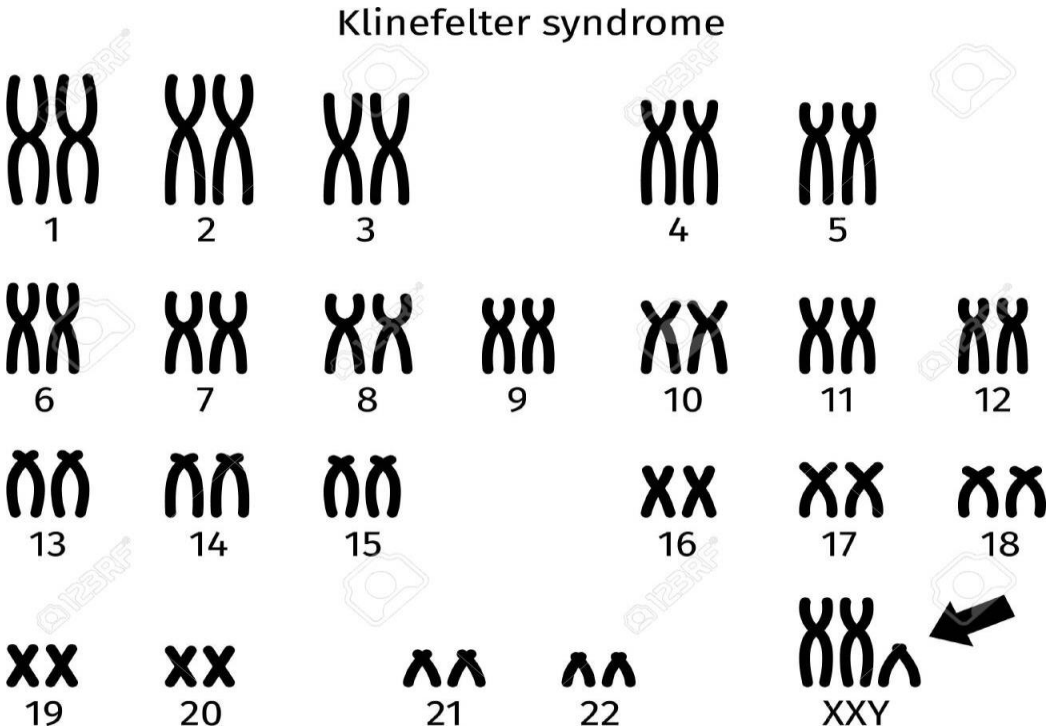
# Clinical features



# Sex chromosomes aneuploidy

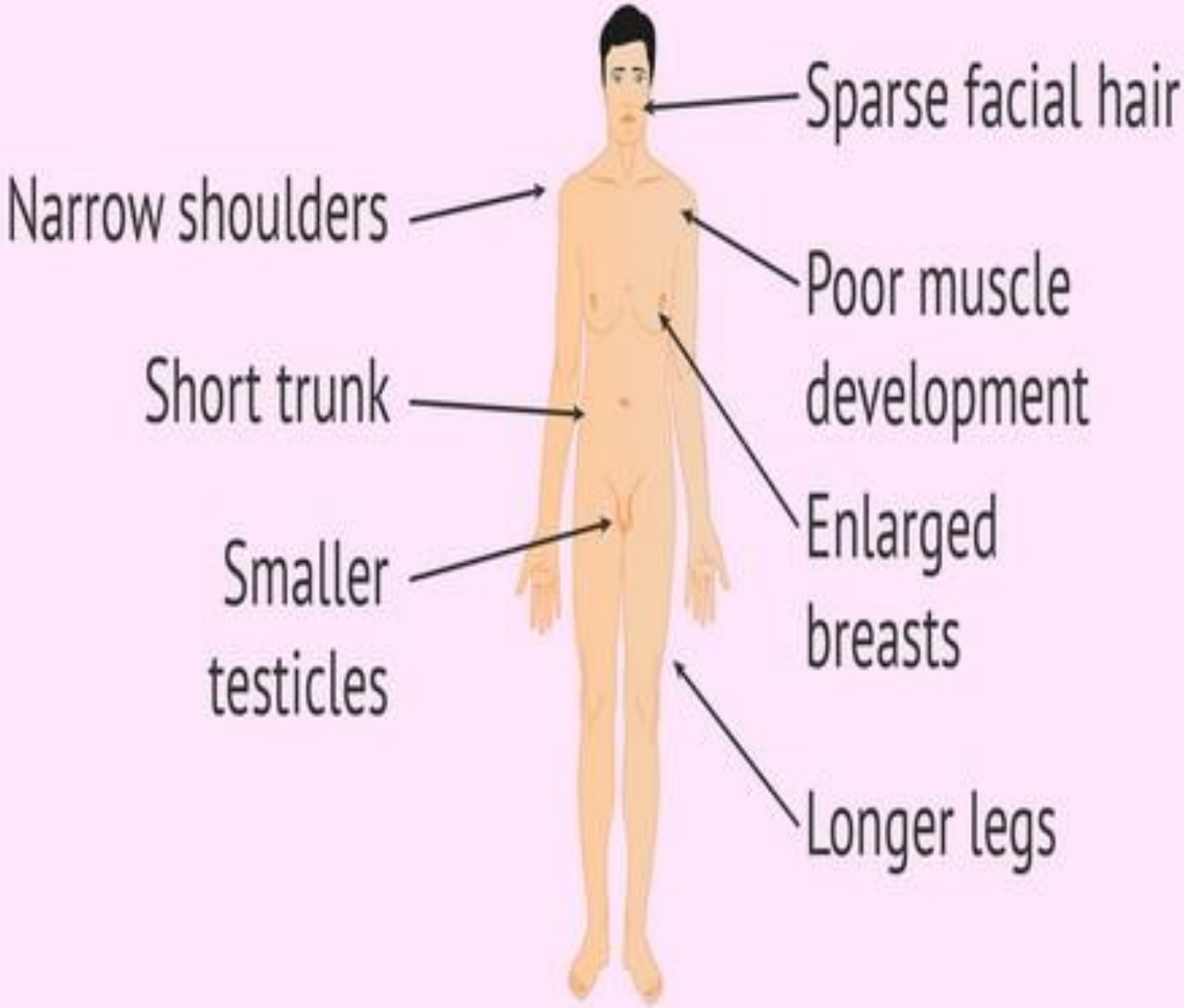
**Klinefelter syndrome** **LO5**

- **80% have a male karyotype with 47,xxy**
- **20% with 48,xxxy; 48,xxyy; 49,xxxxy or Mosaicism 46,xy/47,xxy**
- **The greater the aneuploidy, the more sever the sexual and mental impairment.**



# Clinical features

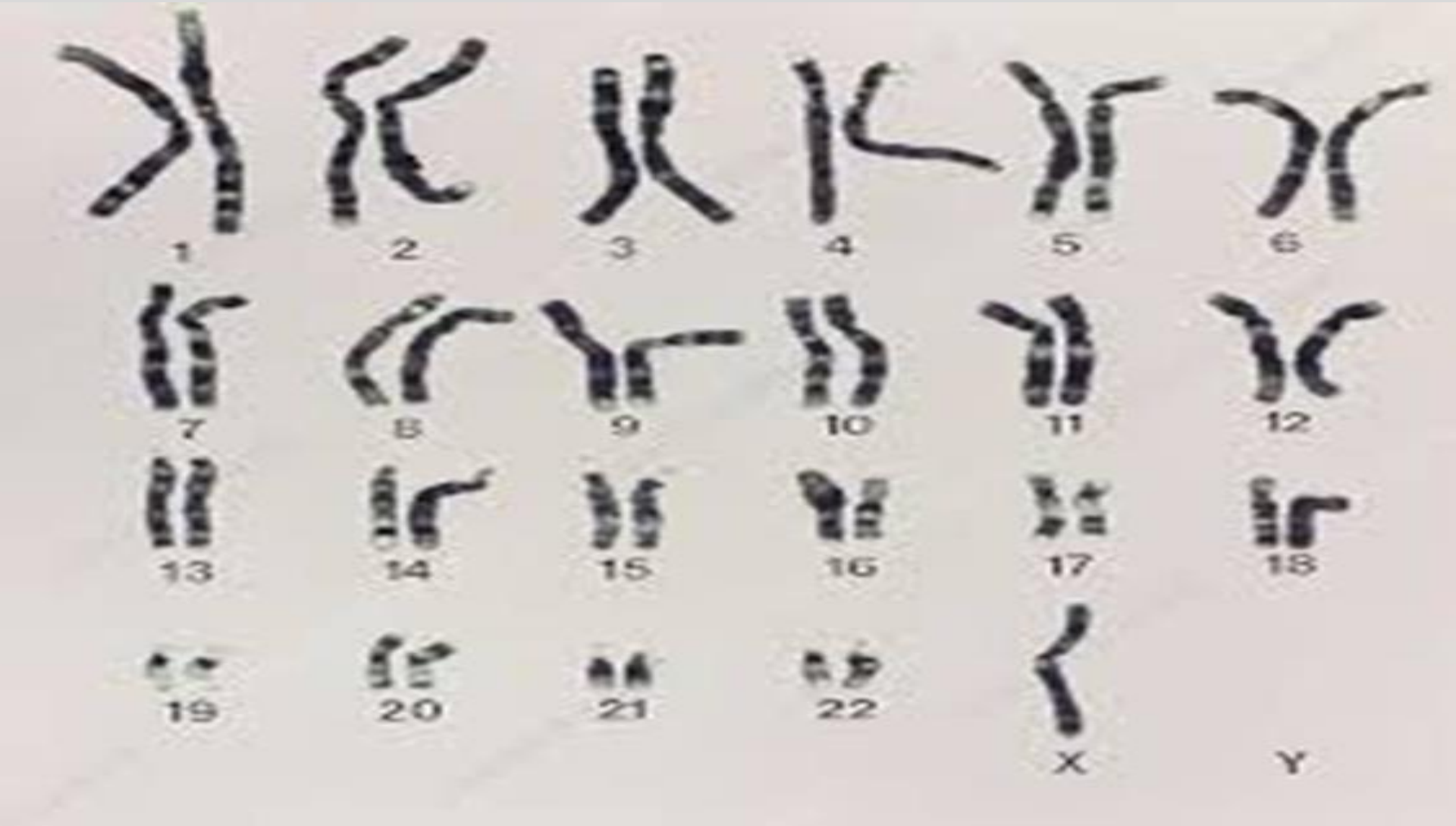
**It is the most common cause of hypogonadism and infertility in males. Patients are phenotypically normal until puberty, puberty occurs at normal age but the testes remain small. Patients develop secondary sexual characteristics later, 50% develop gynecomastia, they usually do not have reduced intellect but may show deficits in language and executive functions.**


Sparse facial hair
Narrow shoulders
Poor muscle development
Short trunk
Enlarged breasts
Smaller testicles
Longer legs

# Turner syndrome

LO6

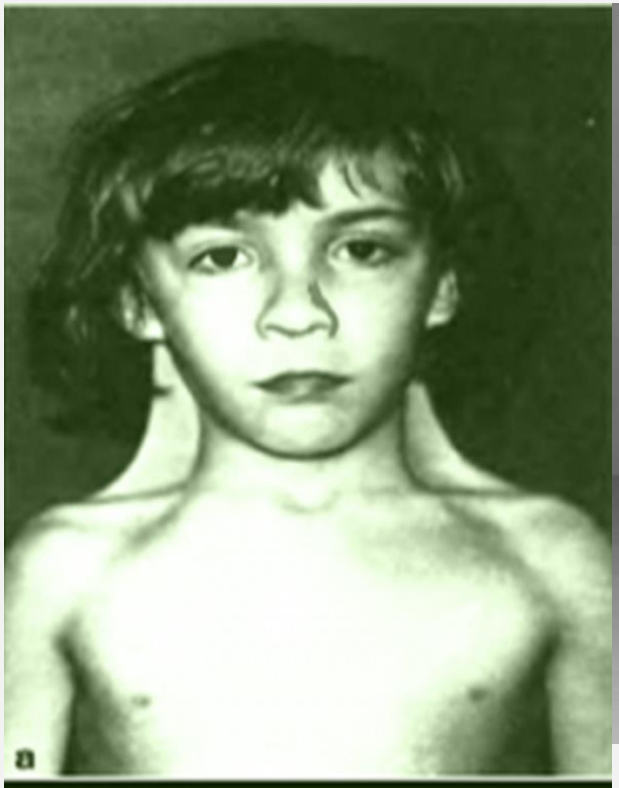
Complete or partial absence of the 2nd sex chromosome (45, XO)



# Turner syndrome

Common symptoms of Turner syndrome include:

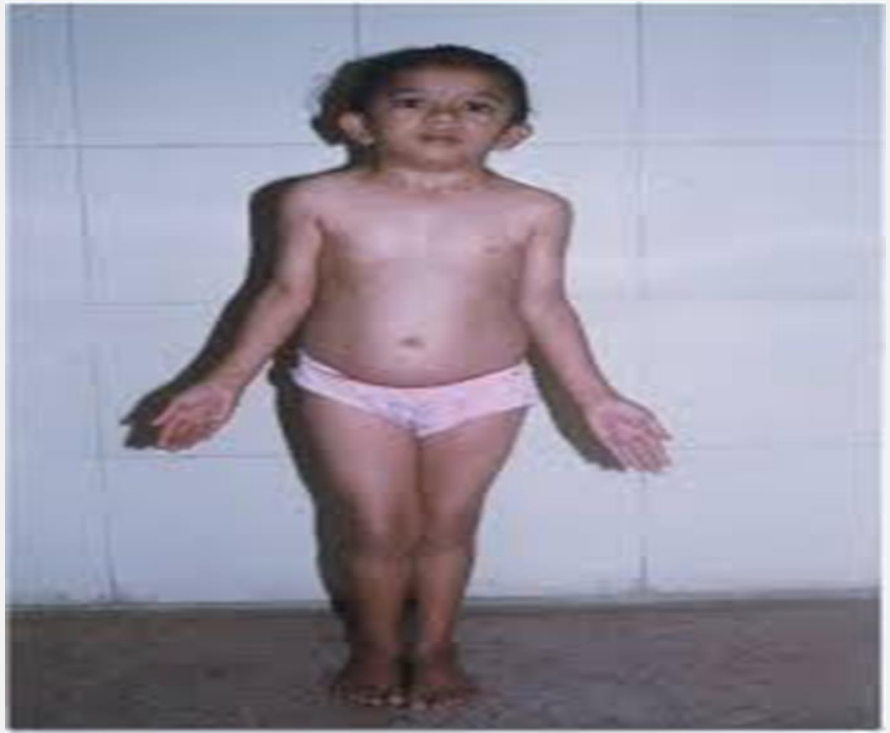
- Short stature
- Lymphedema (swelling) of the hands and feet
- Broad chest (*shield chest*) and widely spaced nipples
- Low hairline
- Low-set ears
- Reproductive sterility
- Rudimentary ovaries
- Amenorrhoea
- Increased weight, obesity
- Normal intelligence
- Increased carrying angle of elbow
- Webbed neck
- Bicuspid aortic valve

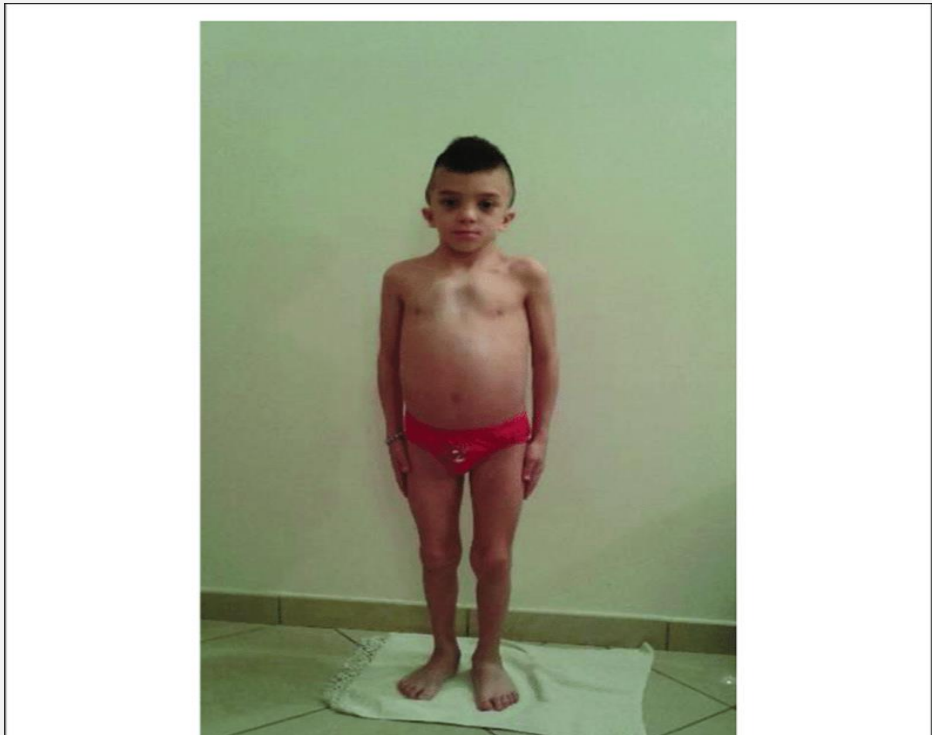


# Noonan syndrome

**Autosomal Dominant disorder affects both sexes similar to Turner in their phenotype but mentally retarded.**

**Some times called male Turner**



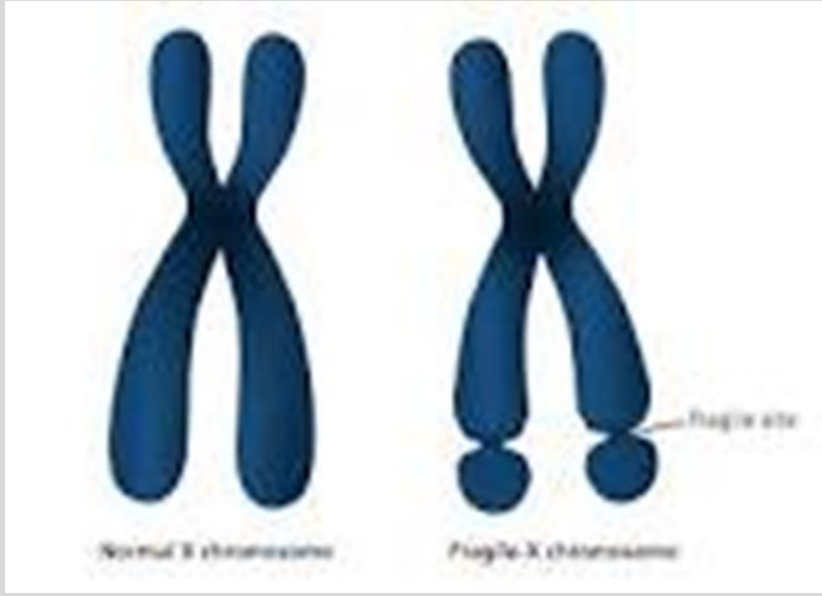


# Cri-du-chat syndrome 5P- LO7

**Low birth weight, poor growth, feeding problem, hyperactivity, aggression, unusual facial features.**

# Fragile X syndrome LO8

**Fragile sites are regions of chromosomes that show tendency for separation, breakage or attenuation under particular growth conditions. They appear as a gap in the staining, significant site is the distal long arm of chromosome X and this result in Fragile X syndrome, accounts for 3% of male with mental retardation. Other features include: autistic behavior, characteristic facial features, long face, prominent jaw, macroorchidism.**



# Prader-Willi and Angelman Syndromes LO9

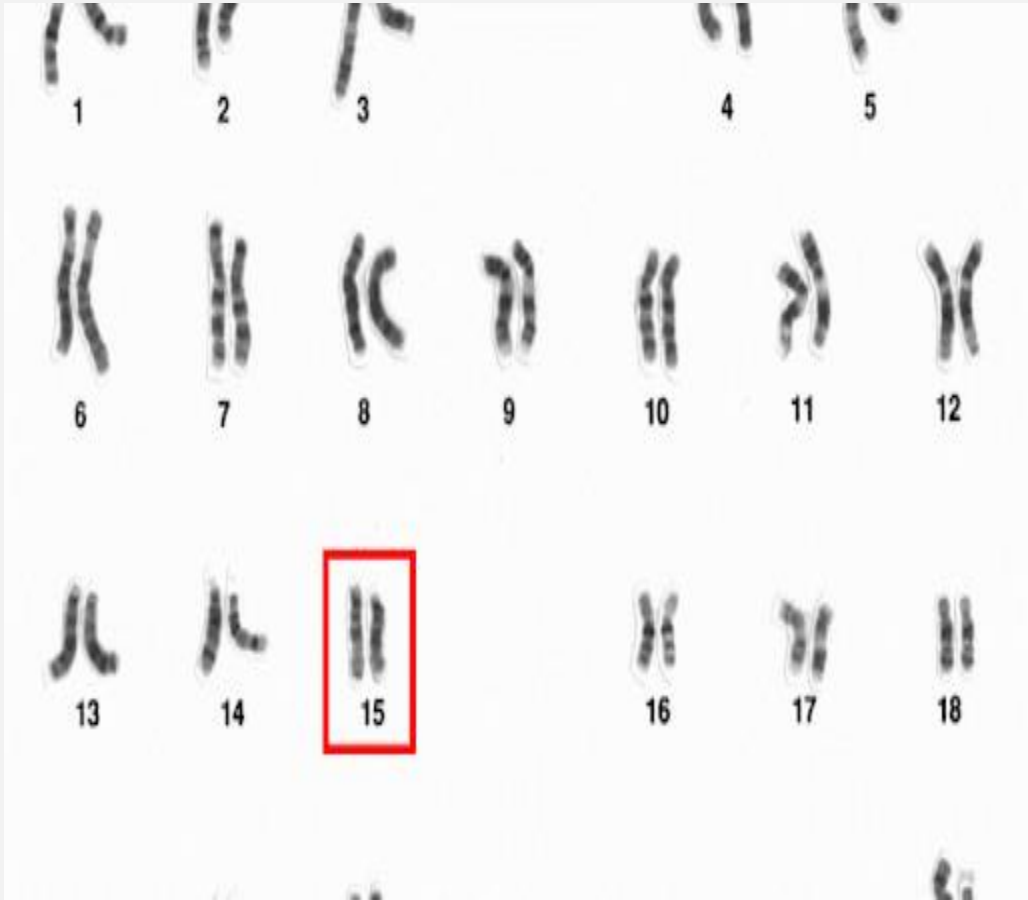
**Deletion and uniparental disomy of chromosome 15**

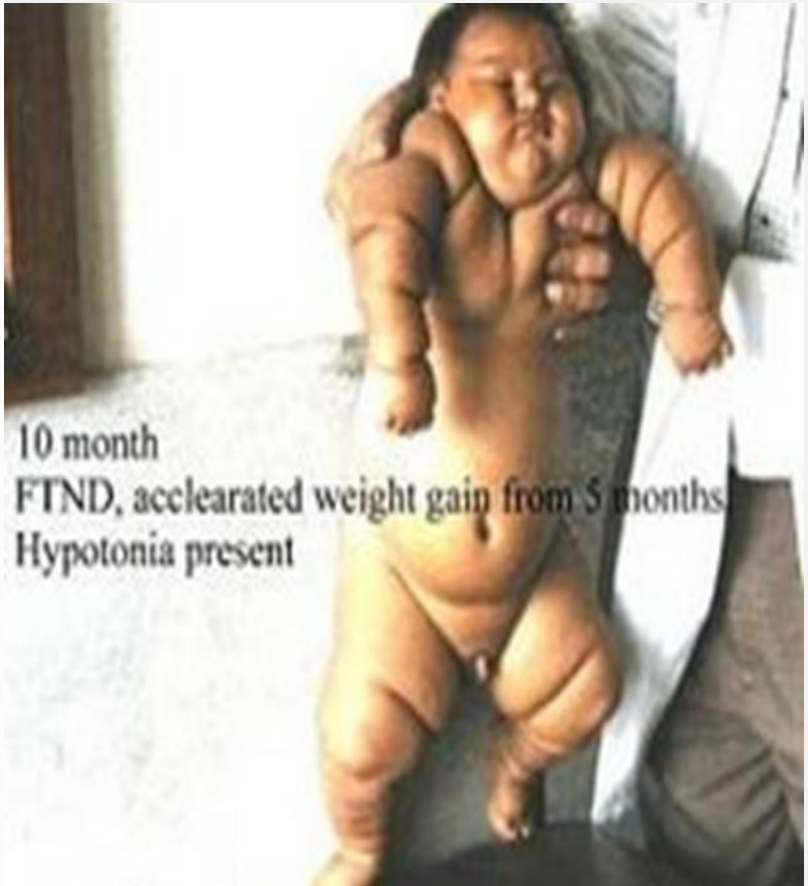
**Lack of paternal segment of chromosome 15 result in Prader-Willi syndrome.**

**Lack of maternal segment (same segment) of chromosome 15 result in Angelman syndrome.**

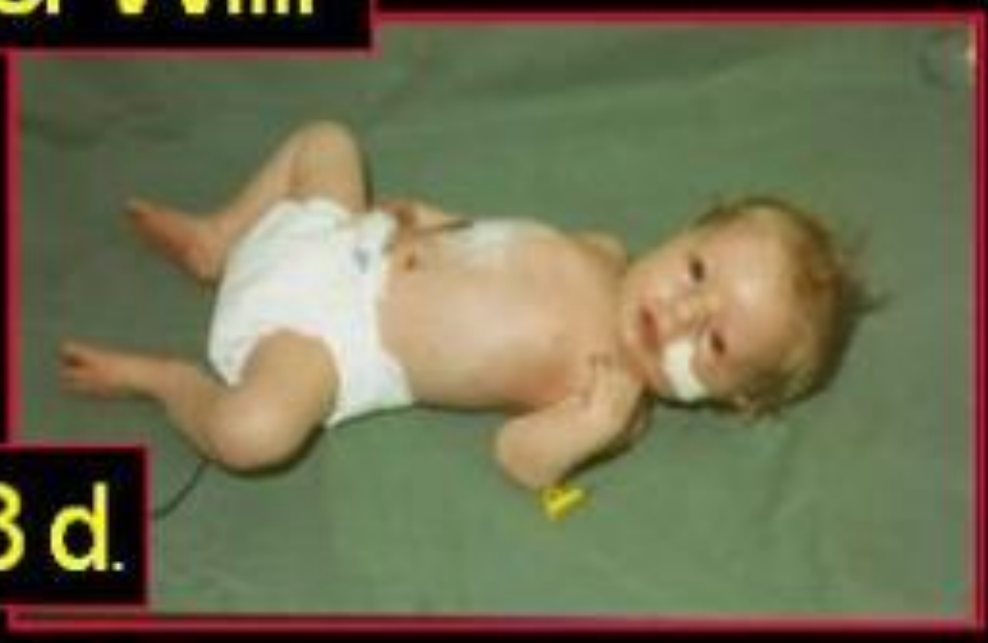
# Clinical features

**Prader-Willi**: short stature, hypotonia, hypogonadism, behavior changes



# Prader Willi



18 d.

2 m.

# Clinical features

**Angelman**:

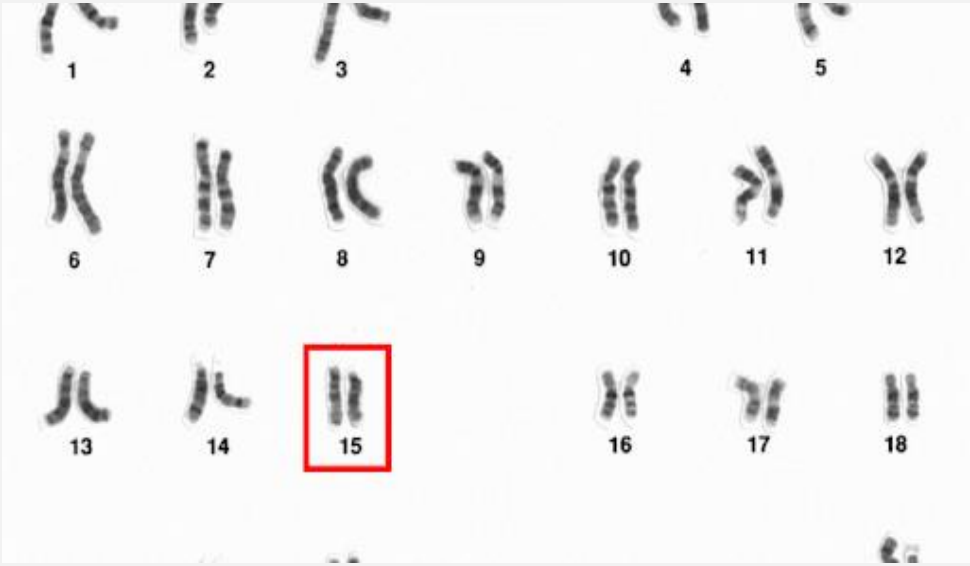
Developmental delays, Intellectual disability.

No speech or minimal speech.

Frequent smiling and laughter.

Happy, excitable personality.

Trouble going to sleep and staying asleep. unusually fair skin with light-colored hair




# Assignment

1- what is meant by imprinting and uniparental disomy

2- write the karyotype of Noonan syndrome and the karyotype of a male with trisomy 18