# GENETIC DISORDERS

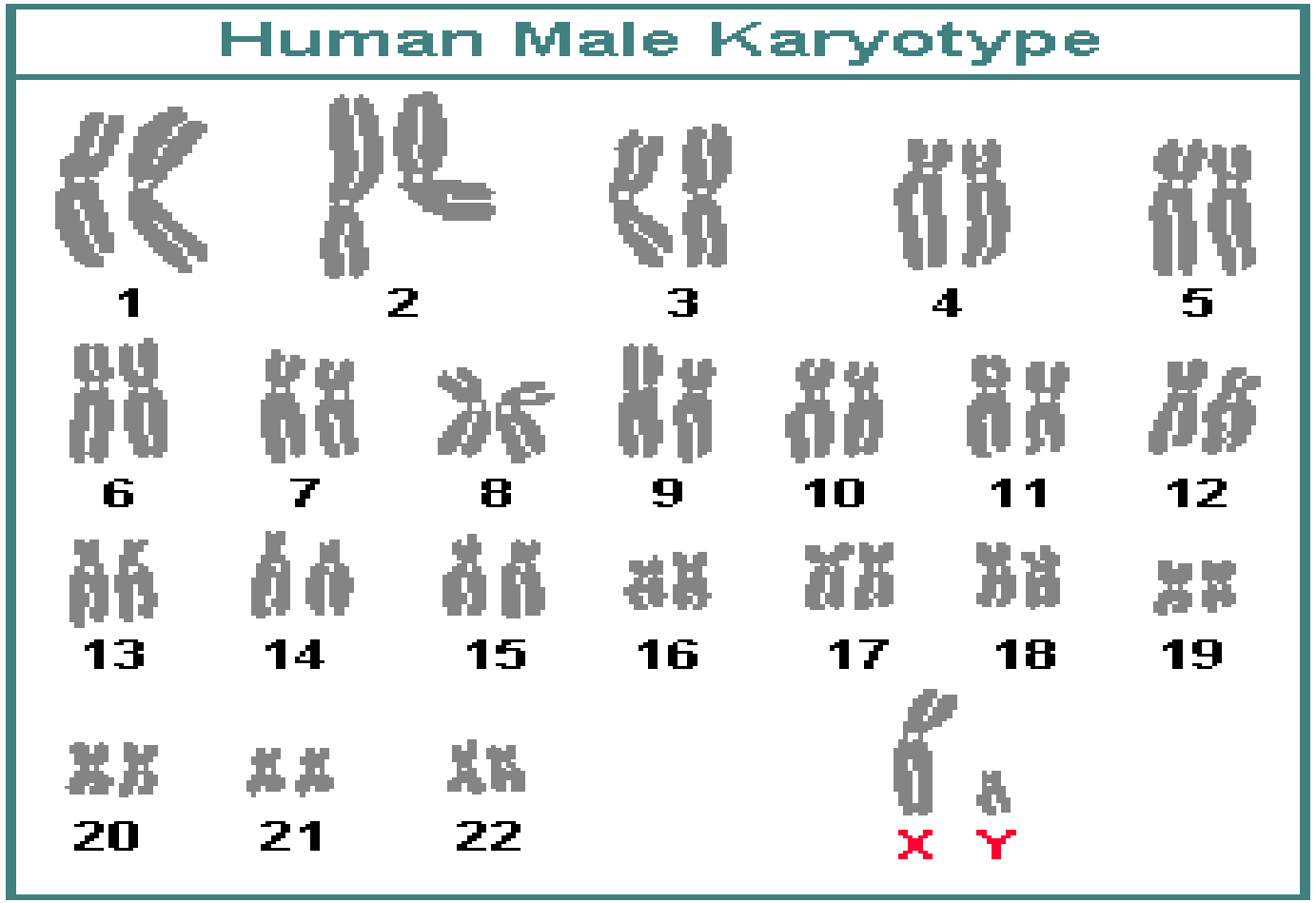
# GENETIC DISORDER

- ✓ Genetic disorder is a disease that is caused by an abnormality in an individual's DNA. Abnormalities can range from a small mutation in DNA or addition or subtraction of an entire chromosome or set of chromosomes.

- ✓ Most Genetic disorders are quite rare and affect one person in every several thousands or millions.

- ✓ Genetic disorders may results by
- Point mutation, or any insertion/deletion entirely inside one gene
- Deletion of a gene or genes
- Whole chromosome extra, missing, or both

# CHROMOSOME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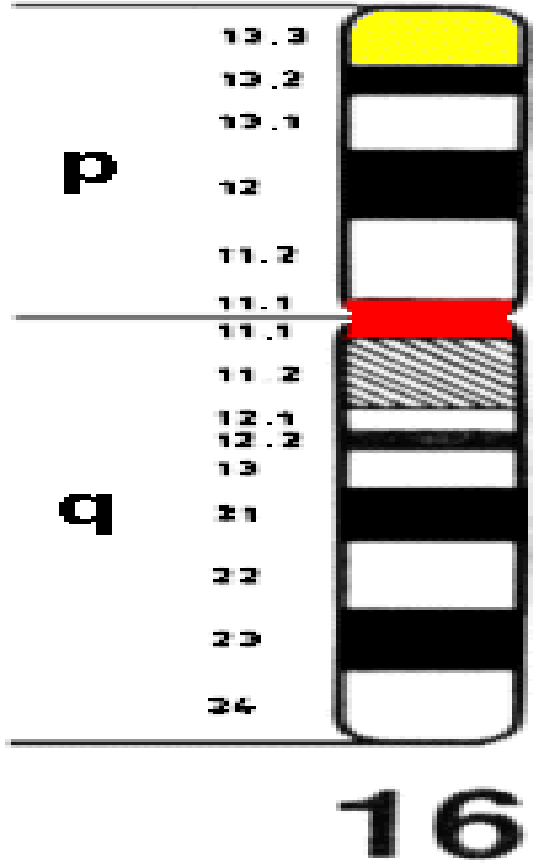
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# TYPES OF INHERITED DISEASE

1. **Autosomal Disorder**
   - Autosomal Dominant
   - Autosomal Recessive

2. **Allosomal Disorder**
   - X- linked dominant
   - X- linked recessive
   - Y- linked

3. **Mitochondrial Disorder**

# AUTOSOMAL DISORDERS

- An **autosome** or somatic chromosomes carry genes which determine the somatic characteristics and do not have any influence on determining the sex of the individual.
- Autosomes appear in pairs
- humans have a diploid genome that usually contains 22 pairs of autosomes and one allosome pair (46 chromosomes total).
- Disorders related to Autosome are autosomal disorders
- Examples of Autosomal disorder

**1. Downs syndrome**

**2. Haemophilia**

**3. Sickle cell anemia**

# TYPES OF AUTOSOMAL DISORDER

1. Autosomal Dominant

   If the disorder is Autosomal dominant only one infected gene from any one parent is enough to cause the disease in the child.

1. Autosomal Recessive

If the disorder is Autosomal recessive there should be transfer of both affected genes from both the parents to cause the disease. If gene from only one parent is transferred then the child becomes a carrier but does not get the disease.

# ALLOSOMAL DISORDERS

- Allosomes are sex chromosomes which carry genes responsible for sexual characteristics and as such have a significant role in the determination of sex.

- Inherited disorders which are related to sex chromosomes are called as **Allosomal disorders**

- Examples of allosomal disorder are

1. **Kleinfelter's syndrome**
2. **Turners syndrome**

# TYPES OF ALLOSOMAL DISORDER

1. X- linked dominant
2. X- linked recessive
3. Y-linked

# MITOCHONDRIAL DISORDER

- It is a disorder caused by mutations (or changes) in either mitochondrial DNA or nuclear DNA.
- If there is mutation in the genes that code for mitochondrial proteins, decreased ATP production leads to energy failure of the cell and eventually, to the organ.
- These are only passed on from mother since mitochondria is absent in spermatozoa.
- Frequency: 1 in 4000.
- Example,

# DIFFERENCES

| AUTOSOMAL DISORDER | ALLOSOMAL DISORDER |
| --- | --- |
| **These arise by gene mutation in autosomal chromosomes.** | These arise by gene mutation in sex chromosomes (mainly X chromosome) |
| **They affect the both sexes i.e males and females.** | They affect more males than females. |
| **The mutated gene can be dominant or recessive.** | The mutated gene is recessive. |
| **The suffer is homozygous or heterozygous. Eg Down syndrome, sickle cell anemia.** | The suffer is hemizygous. Eg Klinefelter syndrome |

# CONDITIONS THAT LEADS TO AUTOSOMAL DISEASES

1. Trisomy
2. Autosomal Deletion
3. Microdeletion
4. Chromosomal Instability

# TRISOMY

- A trisomy is a type of polysomy in which there are three instances of a particular *chromosome*, instead of the normal two. A trisomy is a type of aneuploidy (an abnormal number of chromosomes)

- If the chromosome pairs fail to separate properly during cell division, the egg or sperm may end up with a second copy of one of the chromosomes (non-disjunction). If such a gamete results in fertilization and an embryo, the resulting embryo may also have an entire copy of the extra chromosome.

# TRISOMY

- The most common types of autosomal trisomy that survive to birth in humans are:
- Trisomy 21 (Down syndrome)
- Trisomy 18 (Edwards syndrome)
- Trisomy 13 (Patau syndrome)

# TRISOMY 13 (PATAU SYNDROME)

- **Patau Sundrome**, also known as Trisomy 13 and Trisomy D.

- Is a chromosomal abnormality, a syndrome in which a patient had an additional chromosome 13 due to non-disjunction of chromosomes during meiosis. Some are caused by **Robertsonian Translocations**. The extra chromosome 13 disrupts the normal course of development, causing heart and kidney defects, amongst other features characteristic of Patau syndrome.

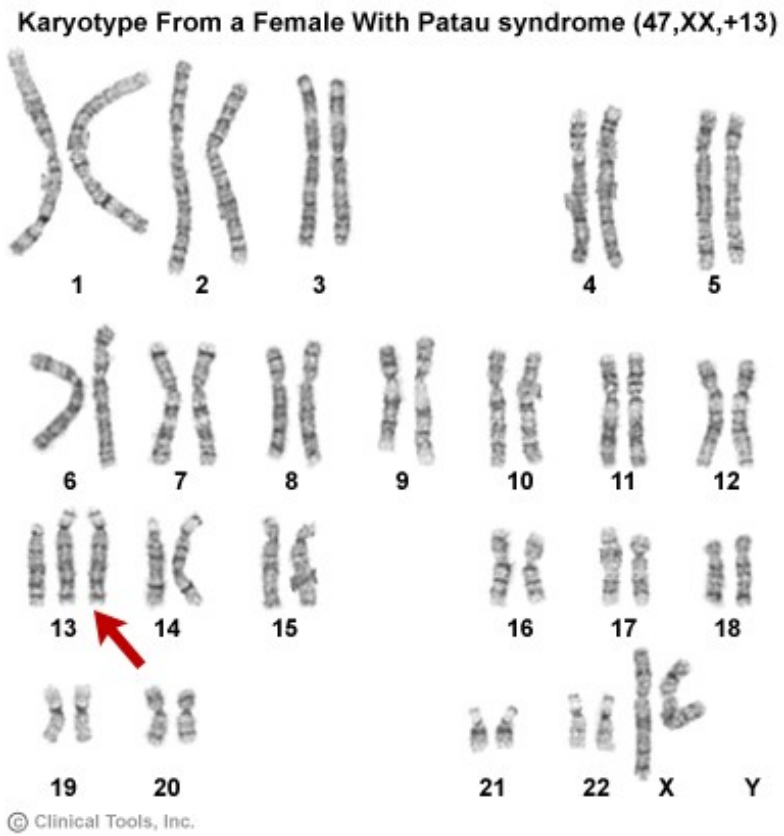
- Patau syndrome affects somewhere between 1 in 10,000 and 1 in 21,700 live births.

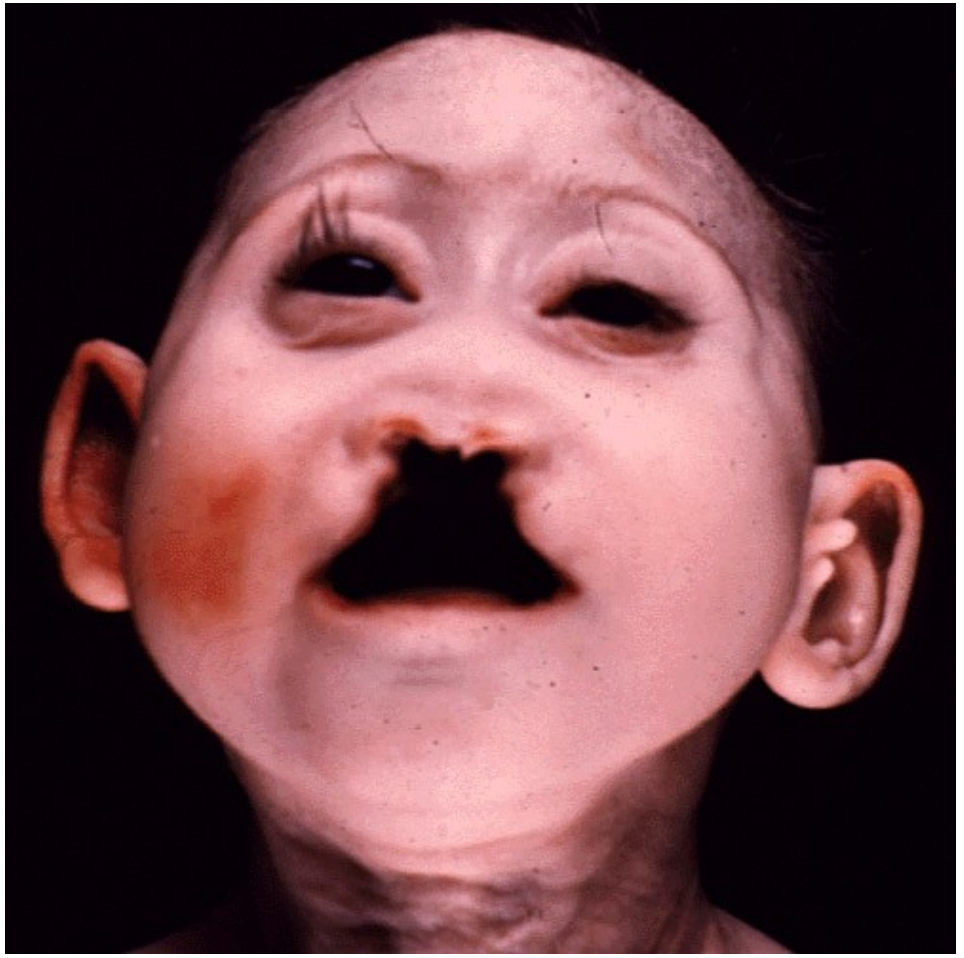
✘TRISOMIC in the chromosome 13.
✘47 chromosomes

# FEATURES OF PATAU SYNDROME

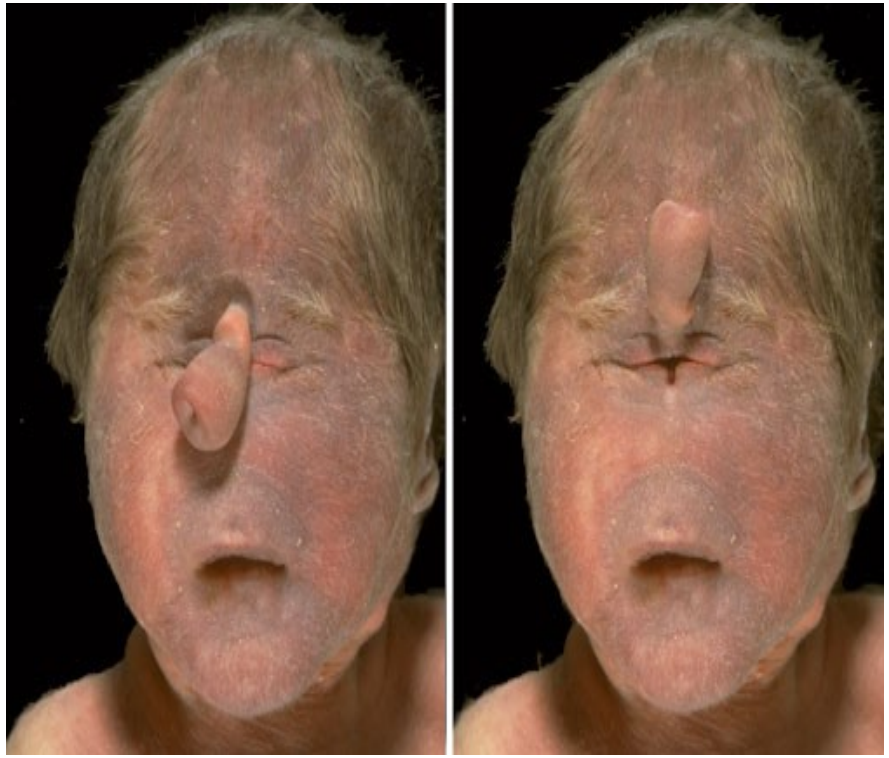
- Mental deficiency
- Low birth weight
- Abnormal development of frontal lobe
- Absence of corpus callosum
- Hypoplasia of cerebellum
- Sloping forehead
- Scalp defects
- Malformed ears
- Congenital heart defects
- Renal tract anomalies
- Microphthalmia
- Bilateral cleft lip/palate
- Polydactyly with rudimentary digits
- Rocker-bottom heel

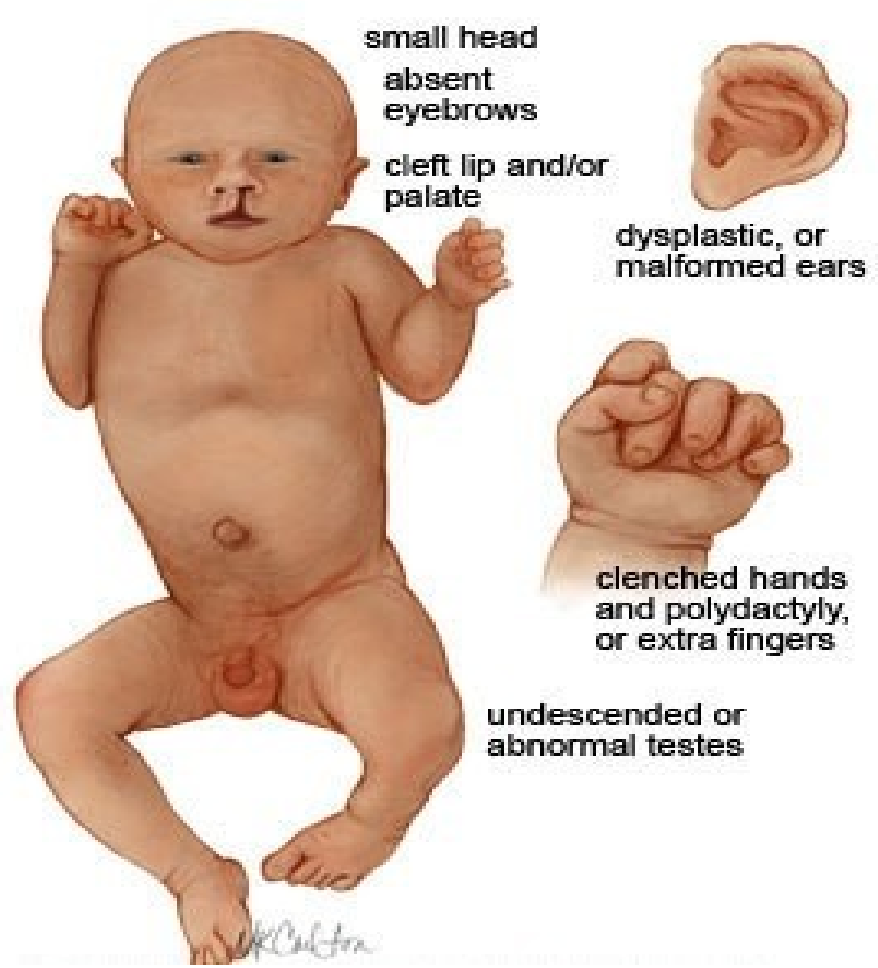
# Patau syndrome



# Patau syndrome

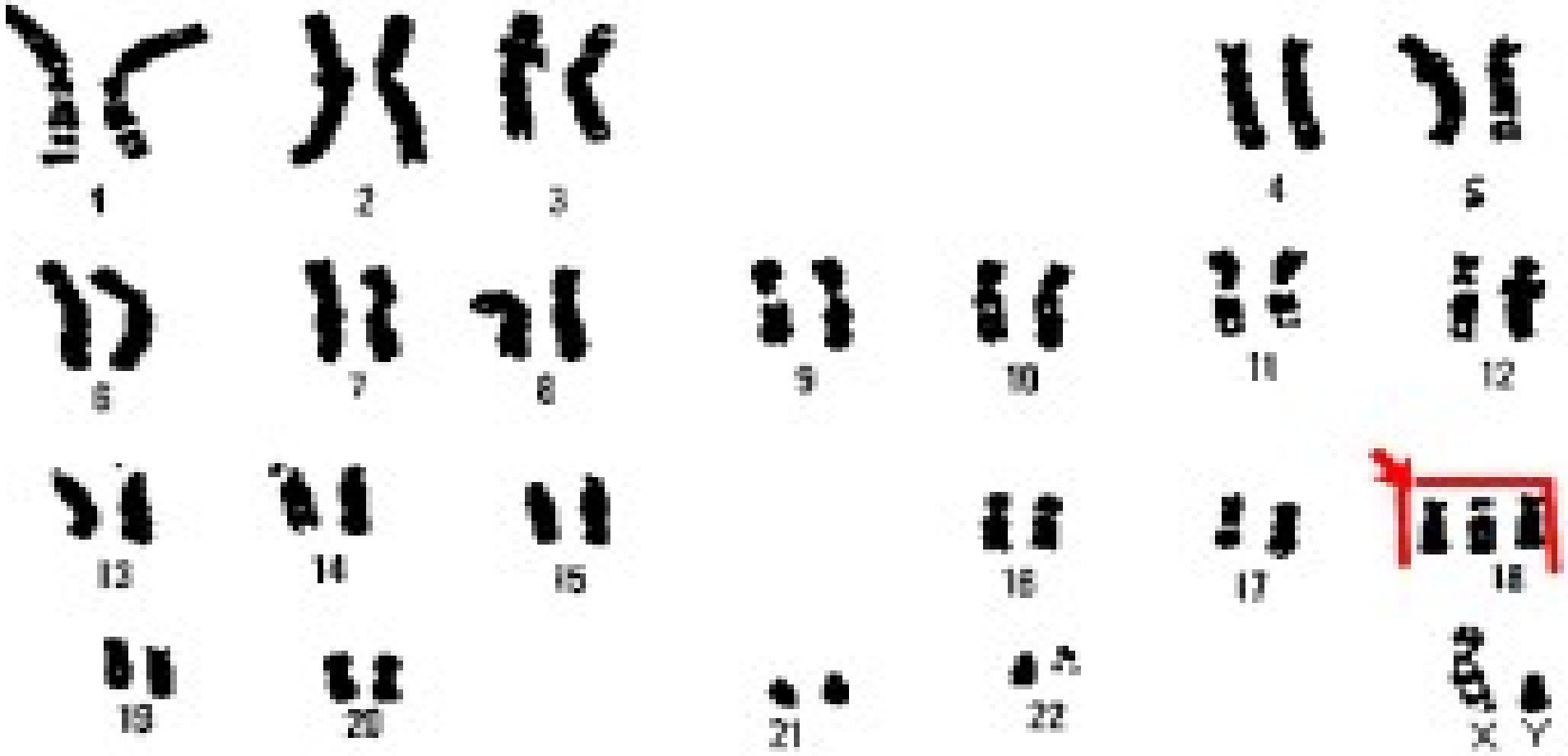




# Trisomy 18 (Edward Syndrome)

- **Edward's Syndrome** also kwnon as **Trisomy 18** (T18) or Trisome E.
- It is a genetic disorder caused by the presence of all of an extra 18$^{th}$ chromosome (Trisomy 18) due to meiotic nondisjunction.
- It is named after **John H. Edwards**, who first described the syndrome in 1960. It is the second most common autosomal trisomy, after Down Syndrome, that carries to term.
- Edward's Syndrome occurs in around 1 in 6,000 live births and around 80 % of those affected are female.

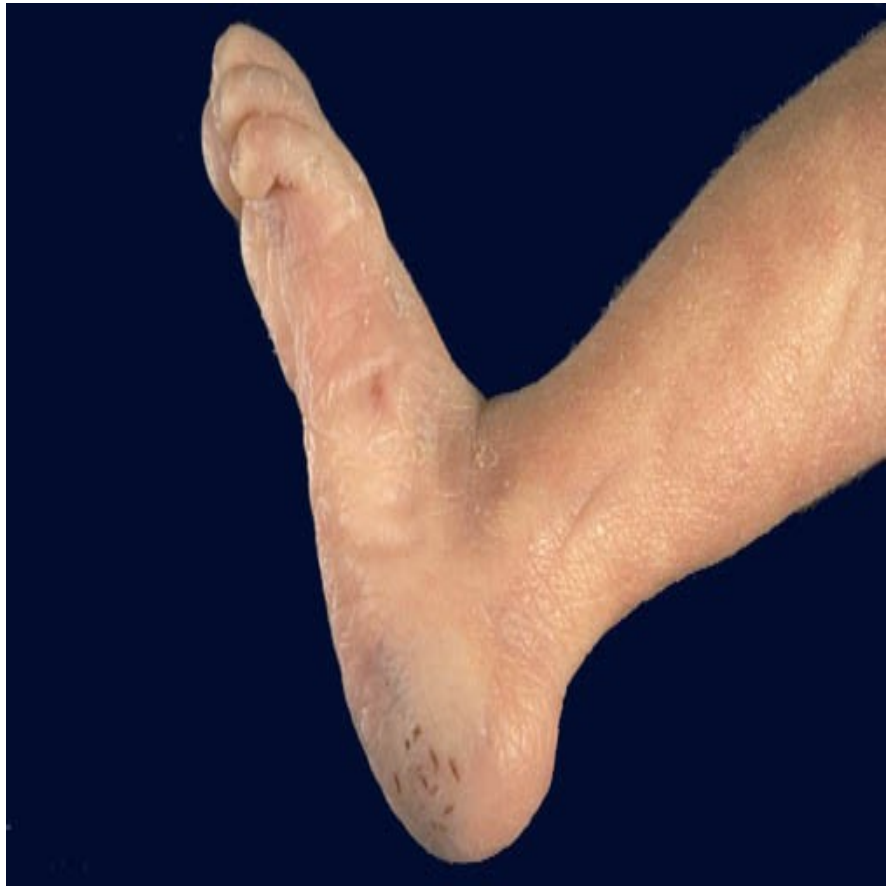
# EDWARD SYNDROME

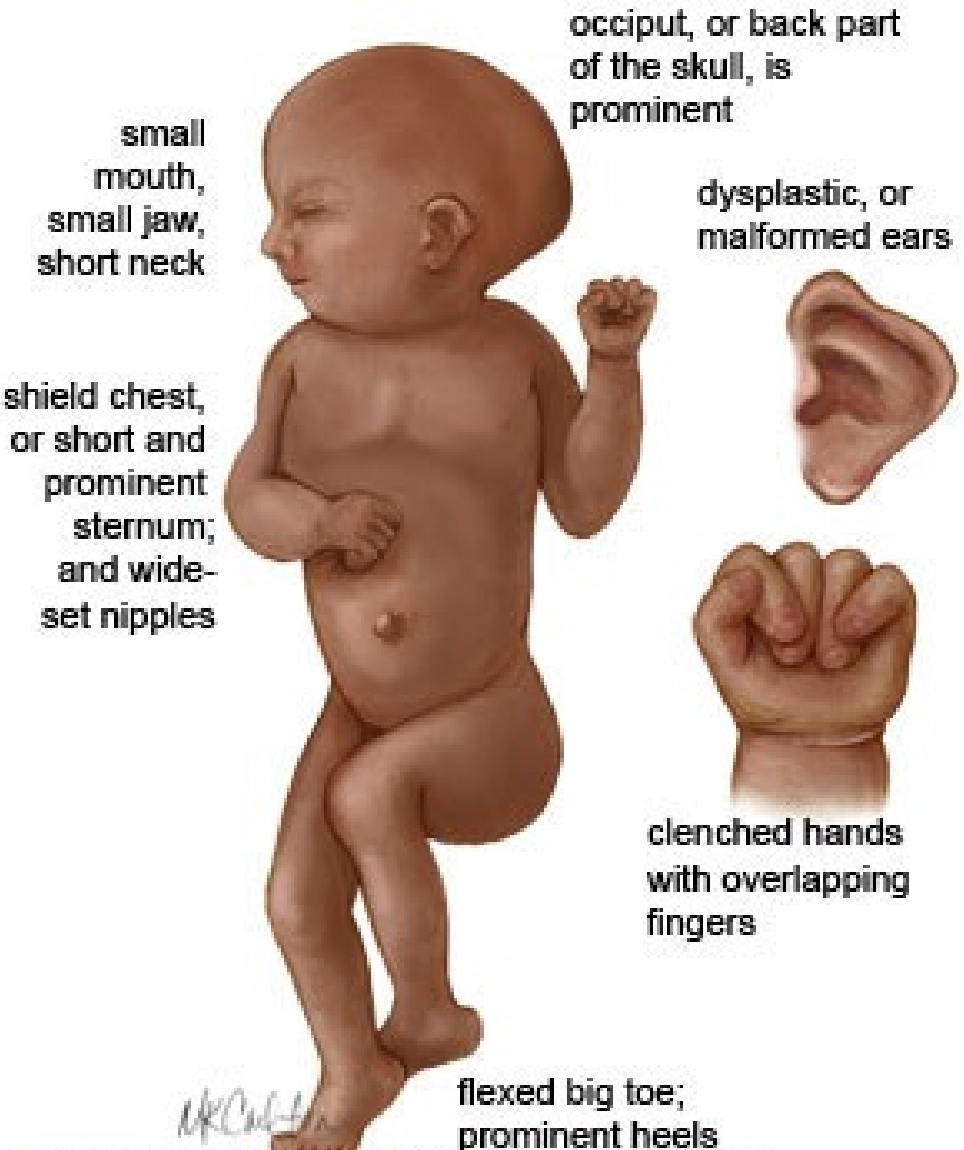


# Features of Edward Syndrome

- Mental deficiency
- Growth retardation
- Prominent occiput with elongated head
- Webbing of the neck
- Short sternum
- Micrognathia
- Low-set malformed ears
- Ventricular septal defects
- Renal anomalies
- Clenched fists with overlapping of fingers
- Hypoplastic nails

# Edward syndrome





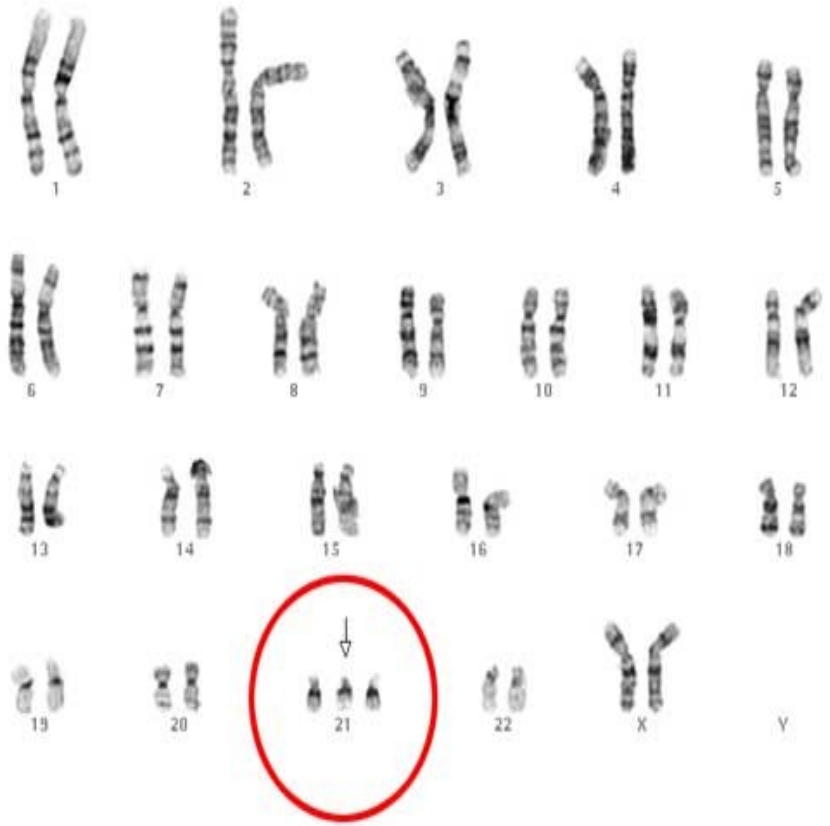
# Trisomy 21 (Down Syndrome)

- **Down Syndrome** also known as **Trisomy 21**, is a chromosomal condition caused by the presence of all or part of an extra 21$^{st}$ chromosome.
- It is named after **John Langdon Down**, the British physician who described the syndrome in 1866. The condition was clinically described earlier in the 19th century by **Jean Etienne Dominique Esquirol** in 1838 and **Edouard Seguin** in 1844.
- Down syndrome was identified as a chromosome 21Trisomy by **Dr. Jerome Lejeune** in 1959.
- The average IQ of children with Down syndrome is around 50, compared to normal children with an IQ of 100.
    - ✘With extra genetic material in chromosome 15.
    - ✘47 chromosomes

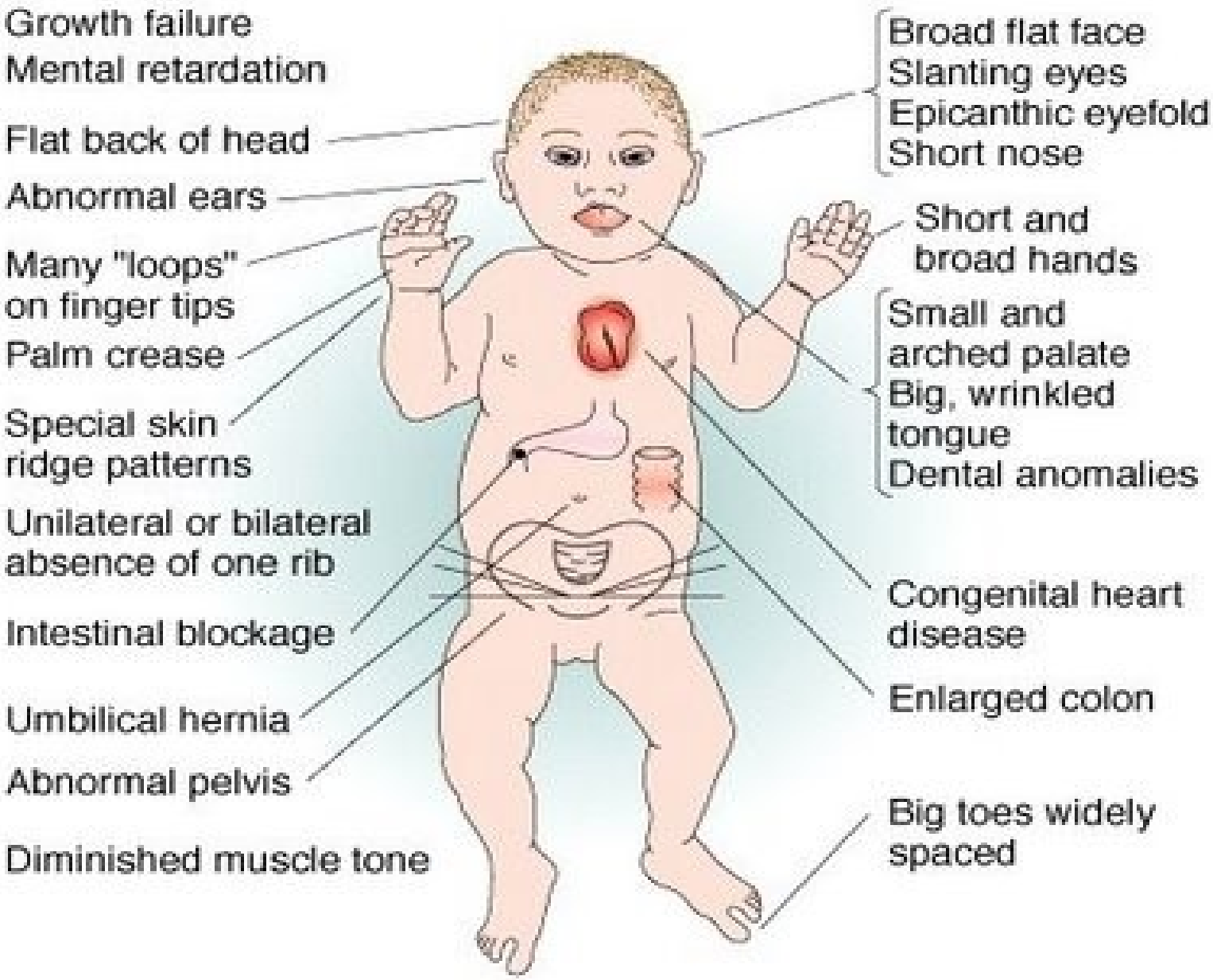
# Features of Down Syndrome

- Short height
- Severe mental deficiency with decline in the IQ with age
- Brachycephaly with flat face and occiput
- Flat and low nasal bridge
- Upward slant to palpebral fissures
- Malformed large ears
- Epicanthal folds of the eyes
- Brushfield spots in iris
- Renal anomalies
- Prominent and protruding tongue (scrotal tongue)
- Simian crease
- Clinodactyly of $5^{th}$ digit

# Down Syndrome




# Down syndrome

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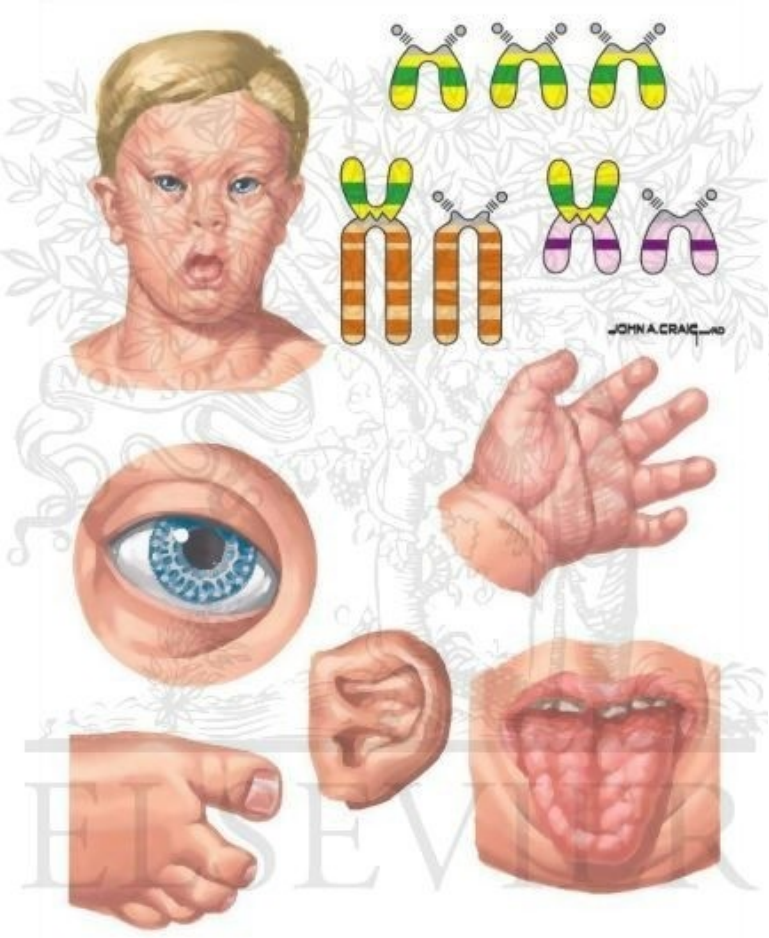
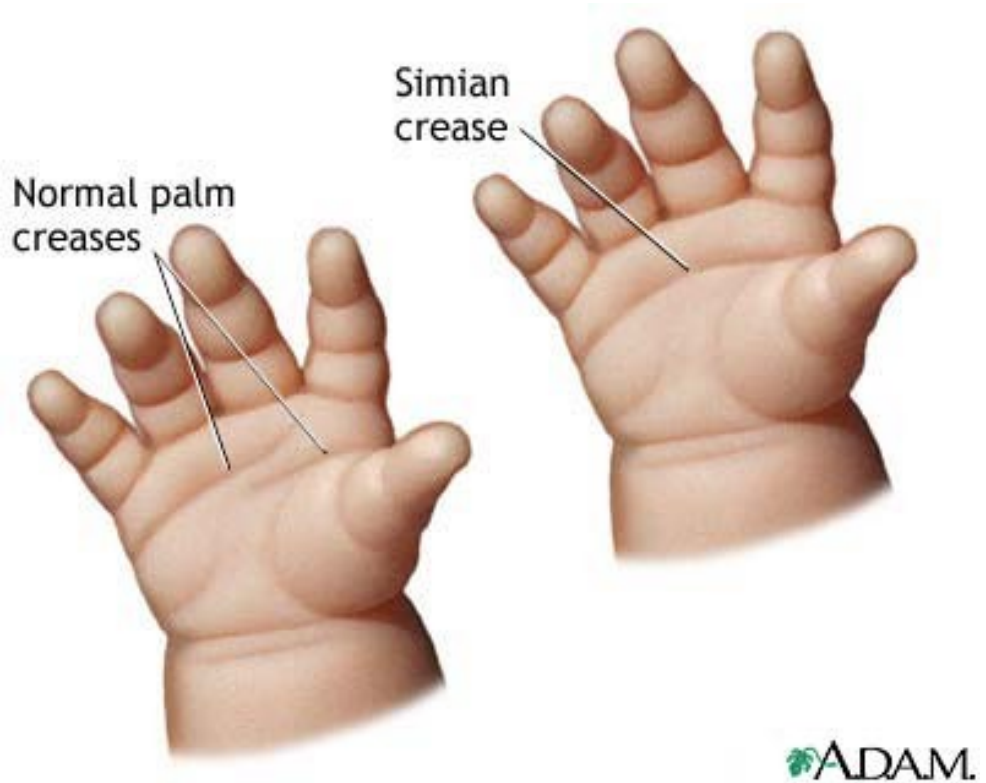
# Down syndrome



# AUTOSOMAL DELETION

- Autosomal: involves one of the numbered (ie, non-sex chromosomes)

- Deletion: an abnormality of DNA that involves missing material. These can range from very small (as little as 1 base pair) to very large (involving millions of base pairs of DNA)

# AUTOSOMAL DELETION

- The most common types of autosomal deletion syndromes are:

1. Wolf-Hirschhorn Syndrome
2. Cri Du Chat
3. Langer Giedion Syndrome

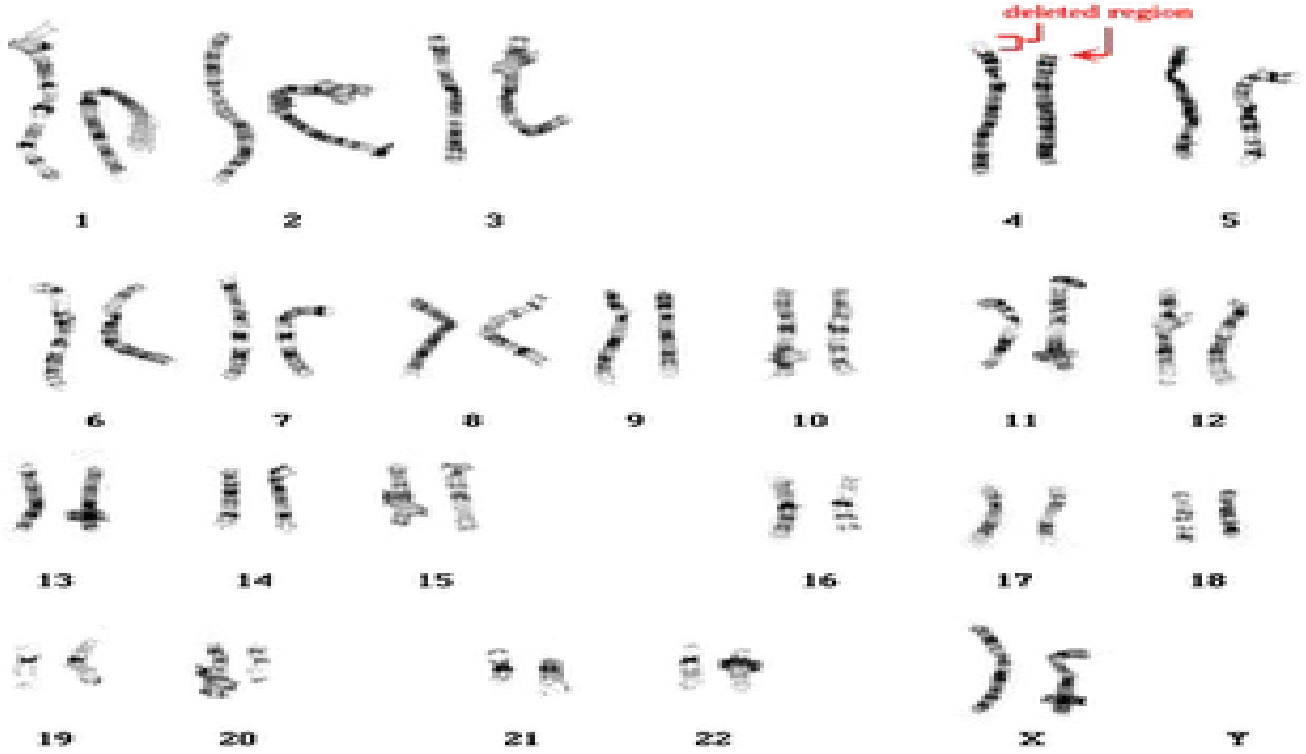
# Wolf-Hirschhorn Syndrome

# WOLF-HIRSCHHORN SYNDROME

- **Wolf-Hirschhorn Syndrome** (WHS) , also known as Pitt-Rogers-Danks Syndrome or Pitt Syndrome ----- was first described in 1961 by Americans **Herbert L. Cooper** and Kurt Hirschhorn and thereafter, gained worldwide attetion by publications by the German Ulrich Wolf and Hirschhorn, *Humangenetik* a German scientific magazine.

- DELETION of the short arm of chromosome 4.

# Wolf-Hirschhorn Syndrome



# FEATURES OF WOLF-HIRSCHHORN SYNDROME

*Short Philtrum

*Immunodeficient

*Microcephaly (Small Head Size)

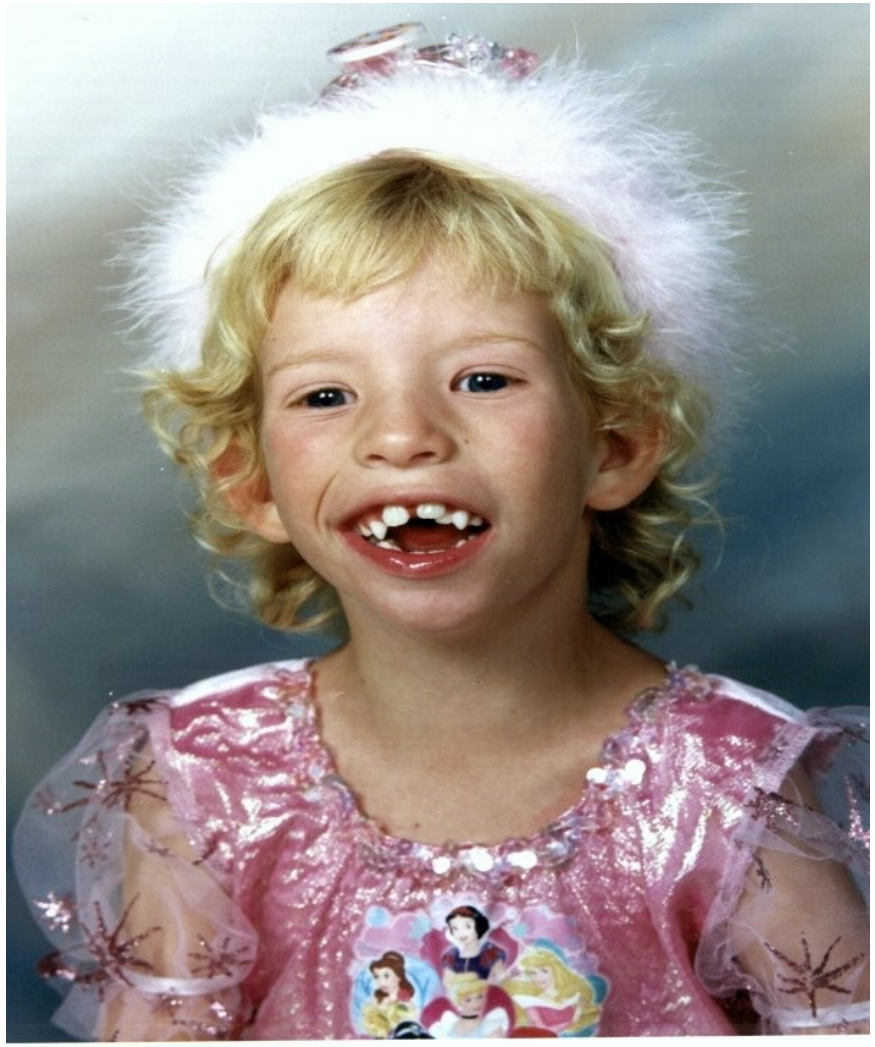
*Seizures

*Muscle Hypotonia

*Renal Anomalies

*Deafness

# Cri Du Chat



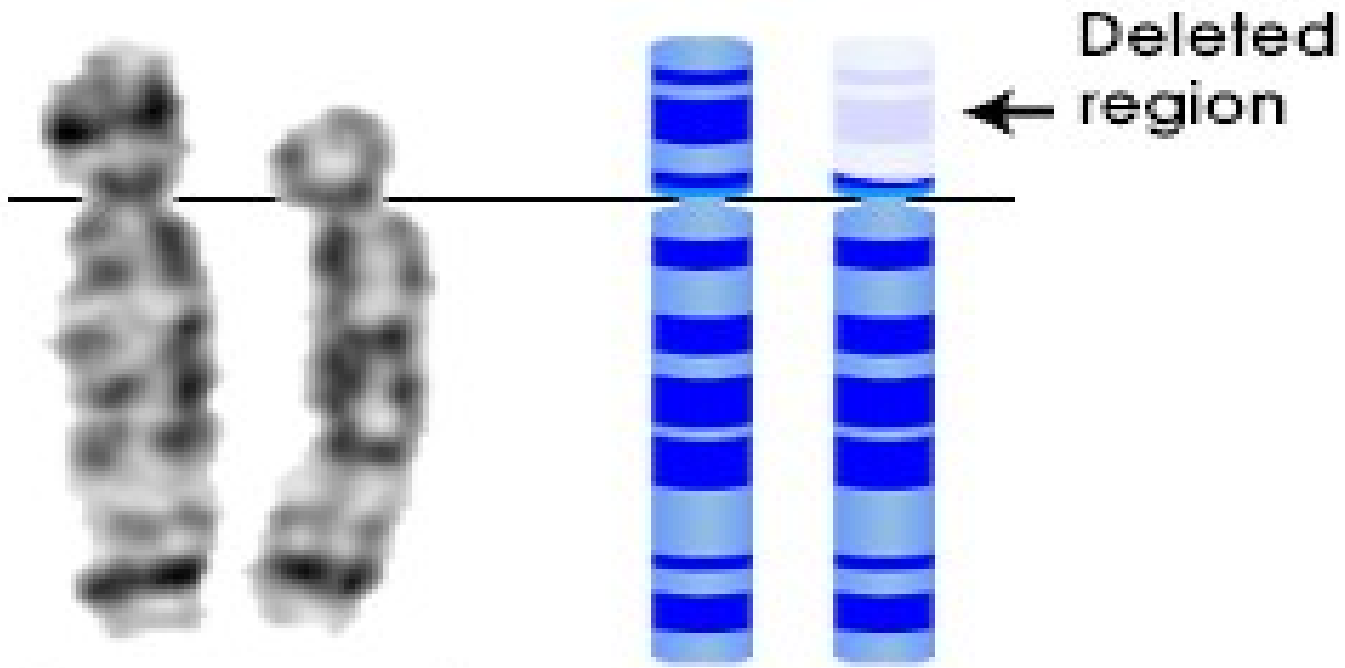
# CRI DU CHAT

- **CRI DU CHAT** also known as chromosome 5p deletion syndrome, 5p minus syndrome or Lejeune's syndrome.
- Is a rare genetic disorder due to a missing part of chromosome 5. Its name is a French term (cat-cry or call of the cat) referring to the characteristic cat-like cry of affected children.
- It was first described by **Jerome Lejeune** in 1963. The condition affects an 1 in 50,000 live births, strikes all ethnicities, and is more common in females by a 4:3 ratio.

✘ **DELETION** on the short arm of chromosome 5.

✘Cries like a CAT

# CRI DU CHAT




Cri-du-chat Chromosome 5 pair

# FEATURES OF CRI DU CHAT

***Excessive Drooling**

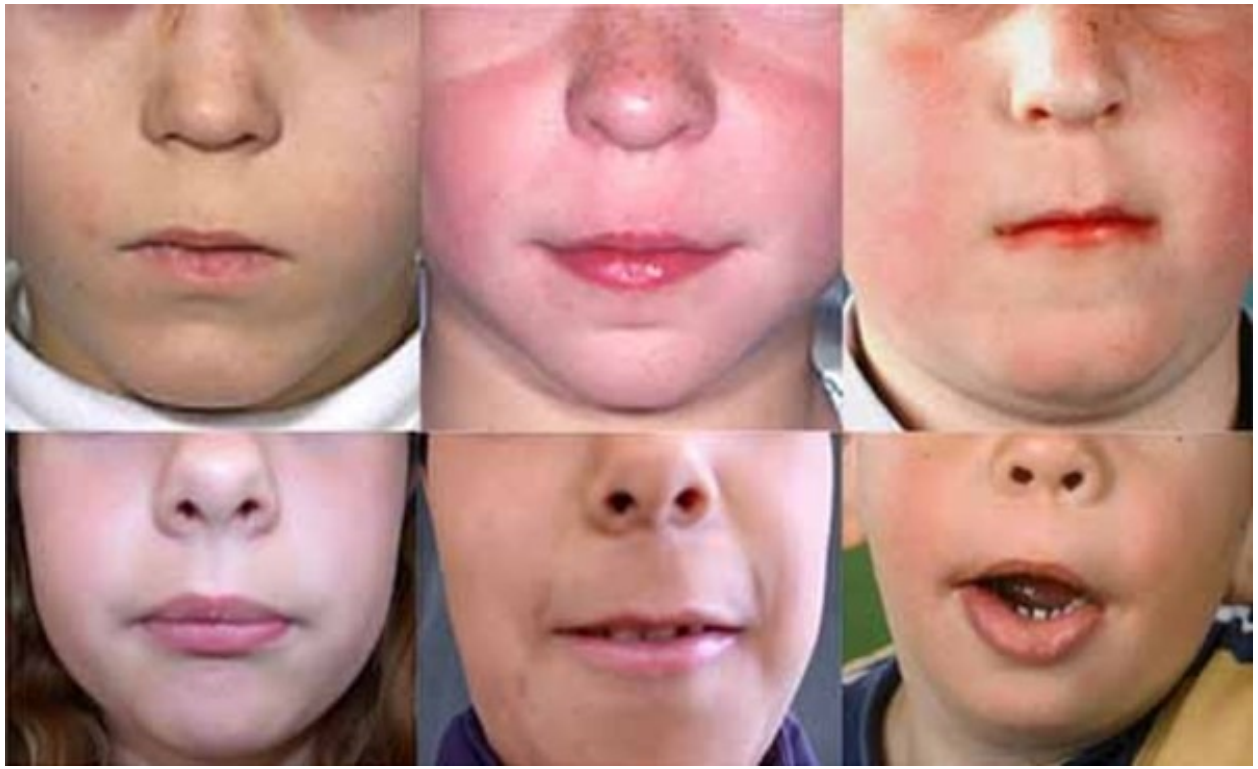
***Behavioral Problems**

***Often Mental Retarded**

***Exhibits Gastorintestinal and Cardiac Complications**

***Abnormal Development of Larynx and Glottis**

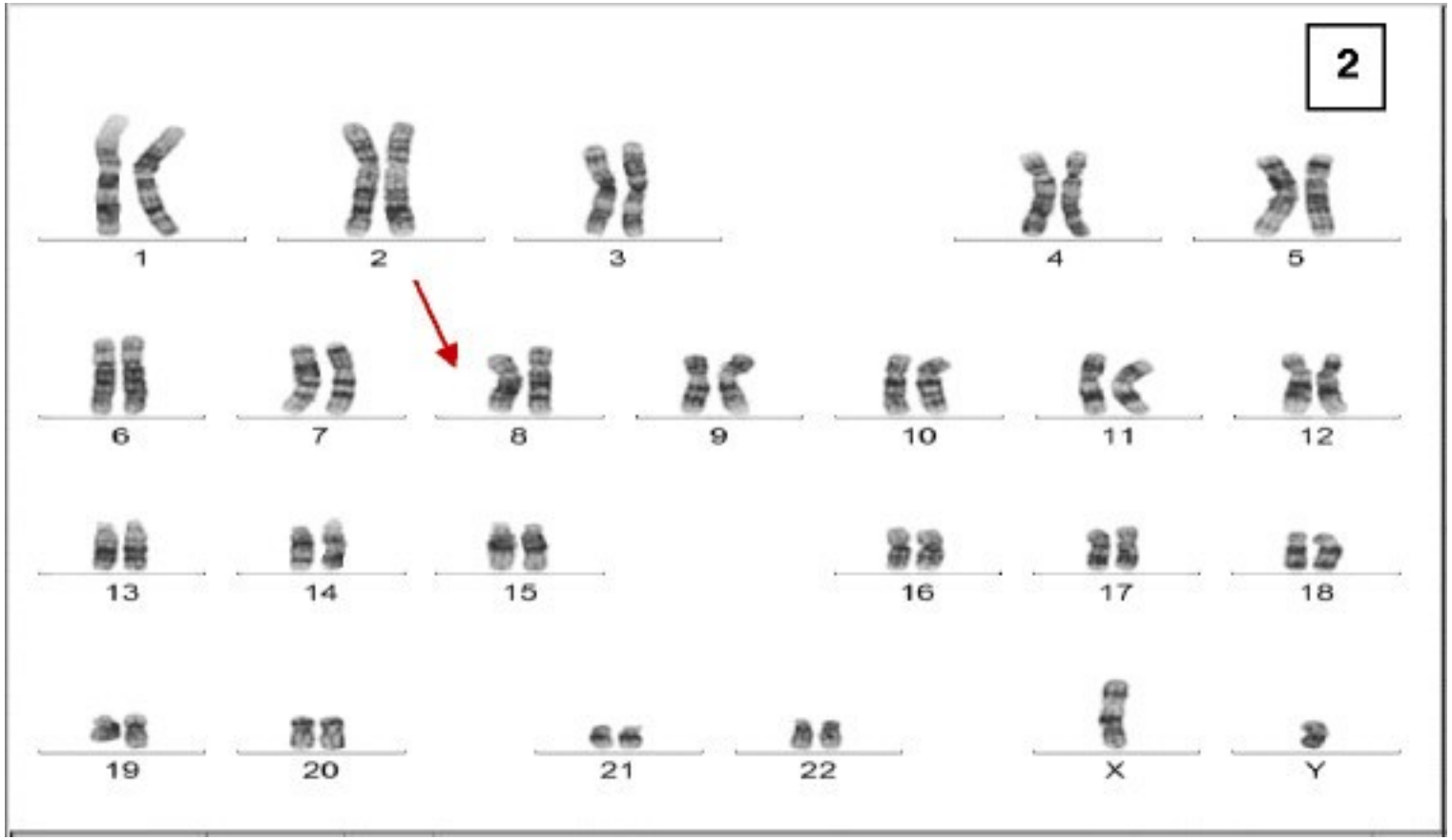
# LANGER-GIEDION



# LANGER-GIEDION

- Langer-Giedion syndrome is a condition that causes bone abnormalities and distinctive facial features.
- People with this condition have multiple noncancerous (benign) bone tumors called osteochondromas.
- Langer-Giedion syndrome is caused by the deletion or mutation of at least two genes on chromosome 8.
- The *EXT1* gene and the *TRPS1* gene are always missing or mutated in affected individuals
- *EXT1* gene is responsible for the multiple osteochondromas . Loss of a functional *TRPS1* gene may cause the other bone and facial abnormalities
- These cases occur in people with no history of the disorder in their family.
- Langer-Giedion syndrome is a rare condition; its incidence is unknown.

# Langer-Giedion



# FEATURES OF LANGER-GIEDION

- sparse scalp hair
- rounded nose
- a long flat area between the nose and the upper lip (philtrum)
- thin upper lip
- loose skin in childhood

*Thank you*

*for your Patience.*