CHROMOSOMAL ABNORMALITIES

CAUSES OF BIRTH DEFECTS & SPONTANEOUS ABORTIONS ARE

- Chromosomal abnormalities
- Genetic factors

INCIDENCE FOR MAJOR CHROMOSOMAL ABNORMALITIES

- 50% of conceptions end in spontaneous abortions and

  50% of these abortions have major chromosomal abnormalities

- Thus approx. **25% of conceptuses** have major chromosomal defects
- Chromosomal abnormalities account for 7% of major

irth defe ts; Co o est is Tur er's sy dro e

- Gene mutations account for an additional 8% cases

- A Karyotype refers to a full set of chromosomes from an individual which can be compared to a "normal" Karyotype for the species via genetic testing.
- **Ploidy** Is the number of sets of chromosomes in a biological cell.

- **Haploid** = n (in normal gametes)
- **Diploid**=2n (in Normal somatic cell)
- **Euploid** = An exact or multiple of n or of the monoploid number.

  A human with abnormal, but integral multiple of the monoploid number, (69 chromosomes) would

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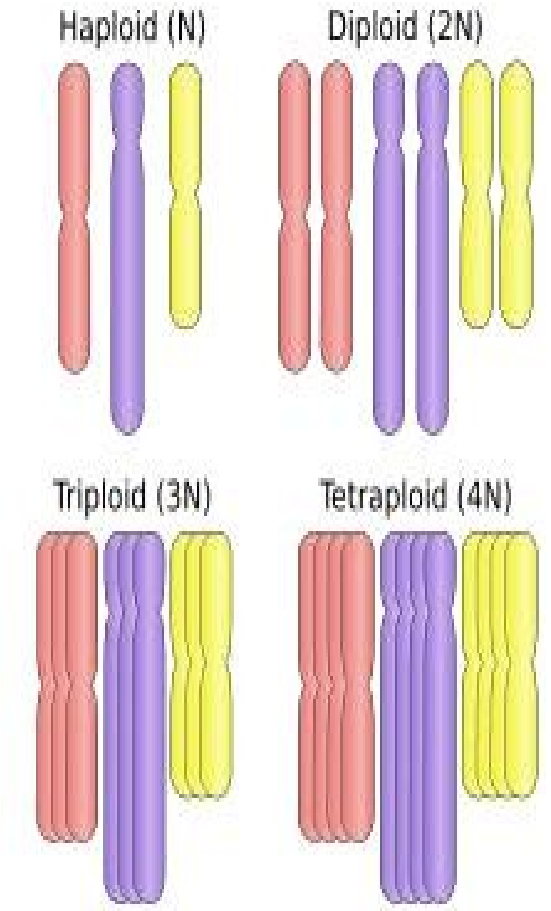
also be considered as euploid e.g. (2*n*, 3*n*,*4n* etc)



POLYPLOID

- Many organisms have more than two sets of homologous chromosomes and are called polyploid.
- A chromosome number that is a multiple of haploid number of 23 other than the diploid number eg. 69
- True polyploidy rarely occurs in humans, although it occurs in

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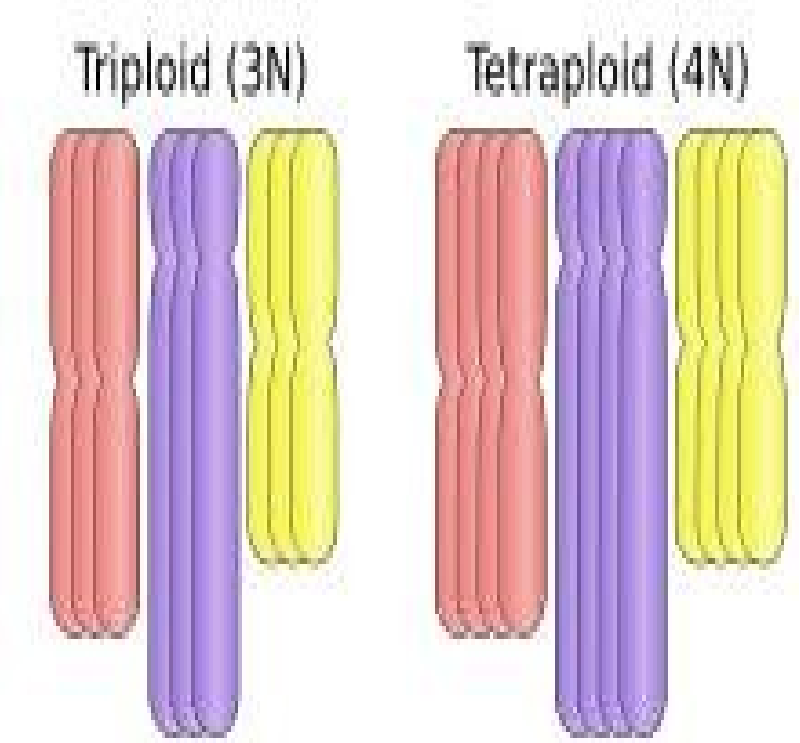
some tissues (especially in the liver).



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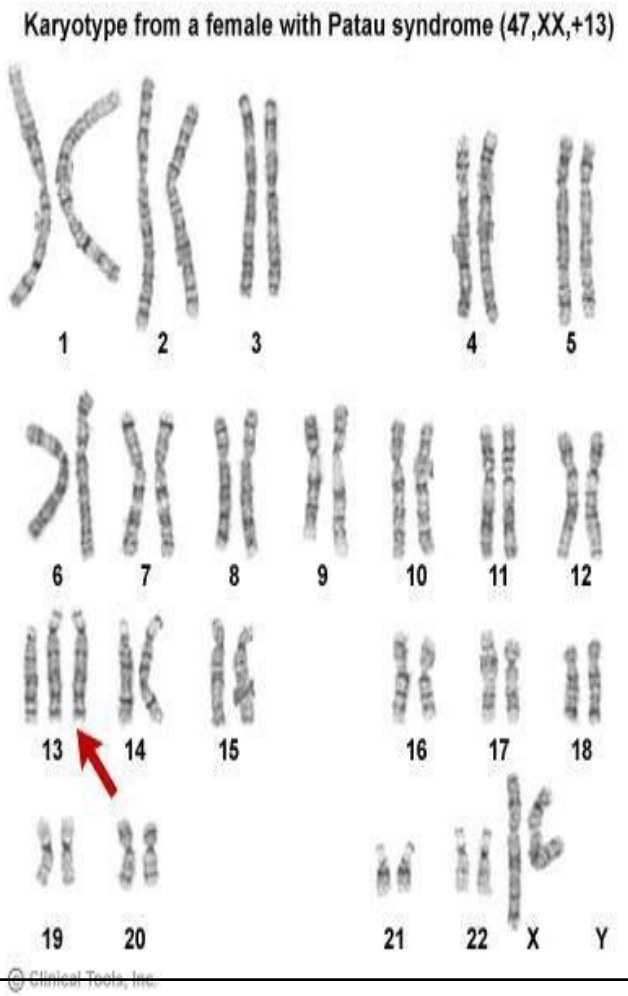
ANEUPLOID

- Is any chromosome number that is not euploid.
- **Aneuploidy** is an abnormal number of chromosomes such as having a single extra chromosome (47), or a missing chromosome (45).
- Aneuploid (not good) karyotypes are given names with the suffix -*somy* (rather than -*ploidy*, used for euploid



karyotypes), such as trisomy and monosomy.

Therefore the distinction between aneuploidy and polyploidy is:

Aneuploidy refers to a numerical change in part of the chromosome set, whereas **polyploidy** refers to a numerical change in the whole set of chromosomes.

CHROMOSOMAL ABNORMALITIES

CHROMOSOMAL ABNORMALITIES

Can occur during meiotic or mitotic divisions

Two types:

- Numerical
- Structural

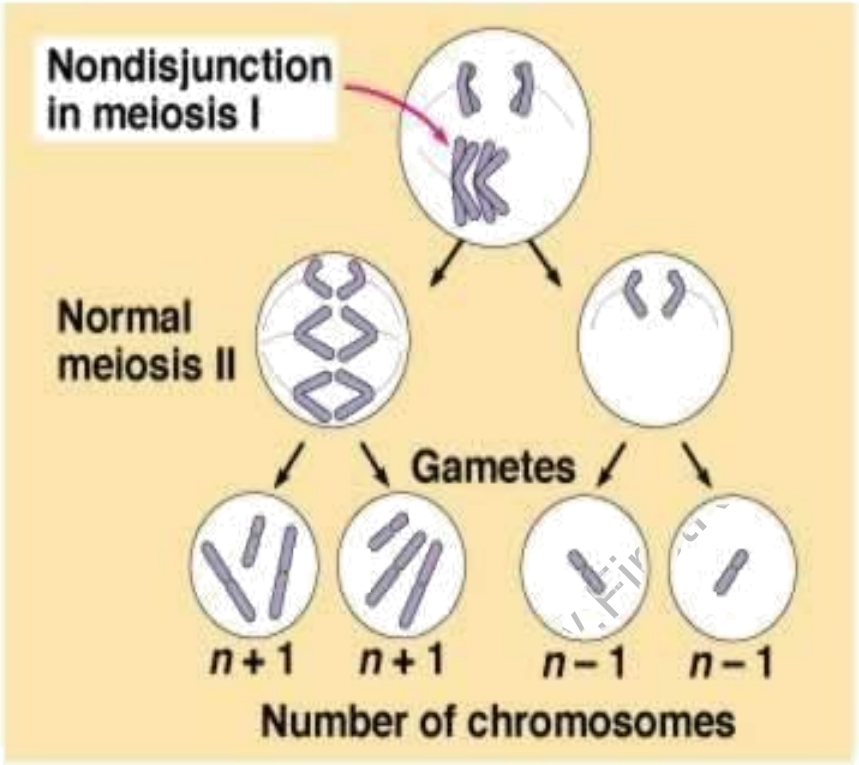
NUMERICAL CHROMOSOMAL ABNORMALITIES

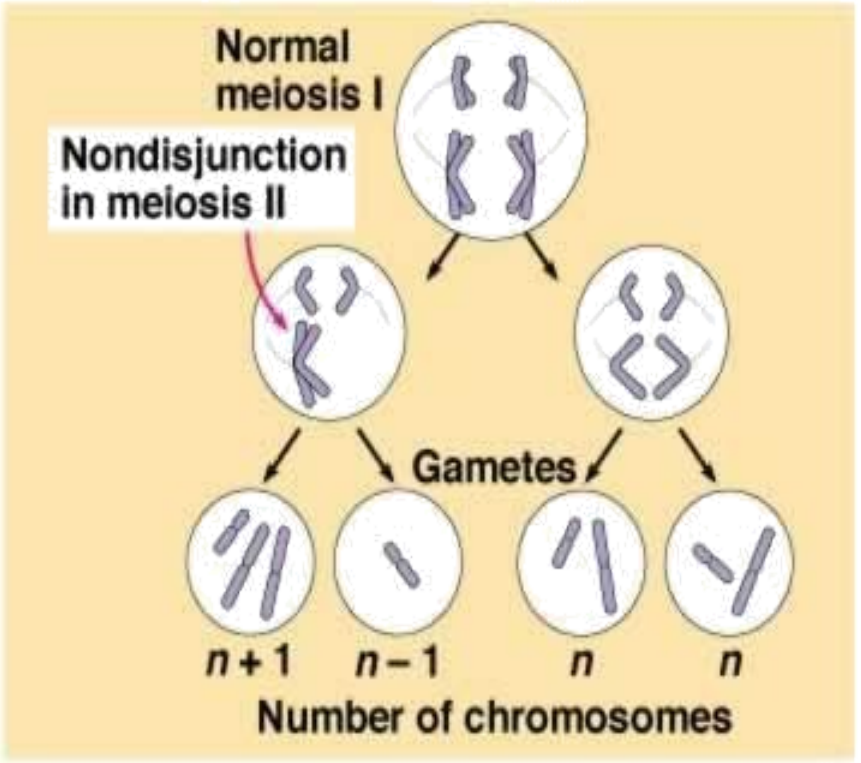
- Meiotic Non disjunction
- Mitotic Non disjunction
- Chromosomal translocations

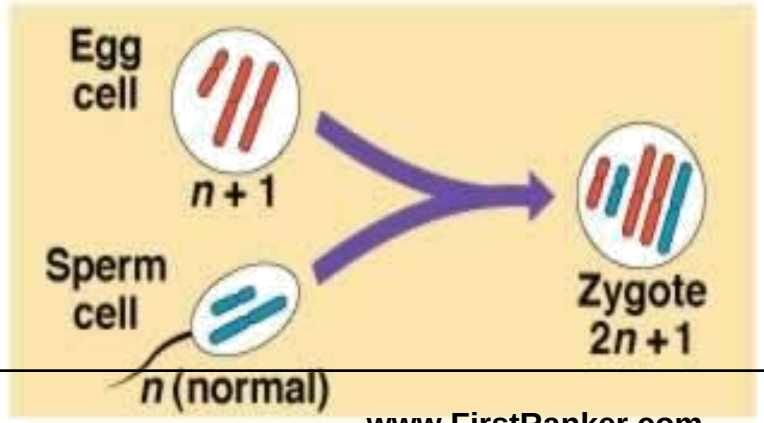
MEIOTIC NON DISJUNCTION

MEIOTIC NON DISJUNCTION

- **May involve autosomes or sex chromosomes**
- In females incidence increases with age 35yrs or more.
- **Meiosis I:** Two members of homologous chromosomes fails to separate and both members of a pair move into one cell.
- **Meiosis II:** When sister chromatids fail to separate.







MITOTIC NONDISJUNCTION

Mosaicism:

- Some cells have abnormal chromosomal number and others have normal
- Occurs in the earliest cell divisions
- Affected individuals exhibit characteristics of a particular syndrome for e.g. down syndrome in1% cases

CHROMOSOMAL TRANSLOCATIONS

CHROMOSOMAL TRANSLOCATIONS

- **When a portion of one chromosome is transferred to another non homologous chromosome and a fusion gene is created.**

  There are two main types of translocations:

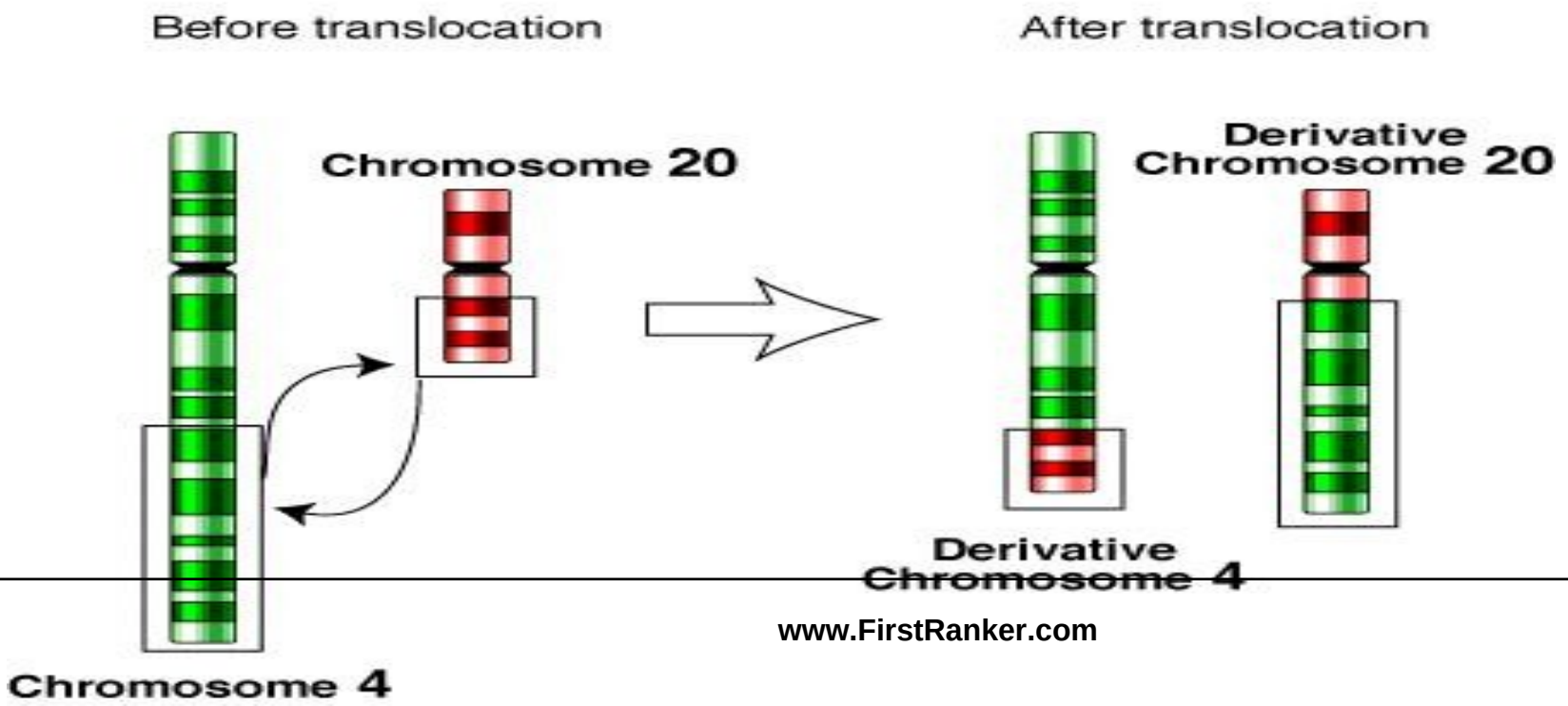
- **Balanced**: An even exchange of material with no genetic information is extra or missing, and individual is normal.

- **Unbalanced:** Where the exchange of genetic material is unequal and part of one chromosome is lost & altered
  phe otype is produ ed (Dow ’s sy dro e – 4% cases)

BALANCED TRANSLOCATION

BALANCED TRANSLOCATION

If no genetic material is lost during the exchange, the translocation is considered to be a **BALANCED TRANSLOCATION.**

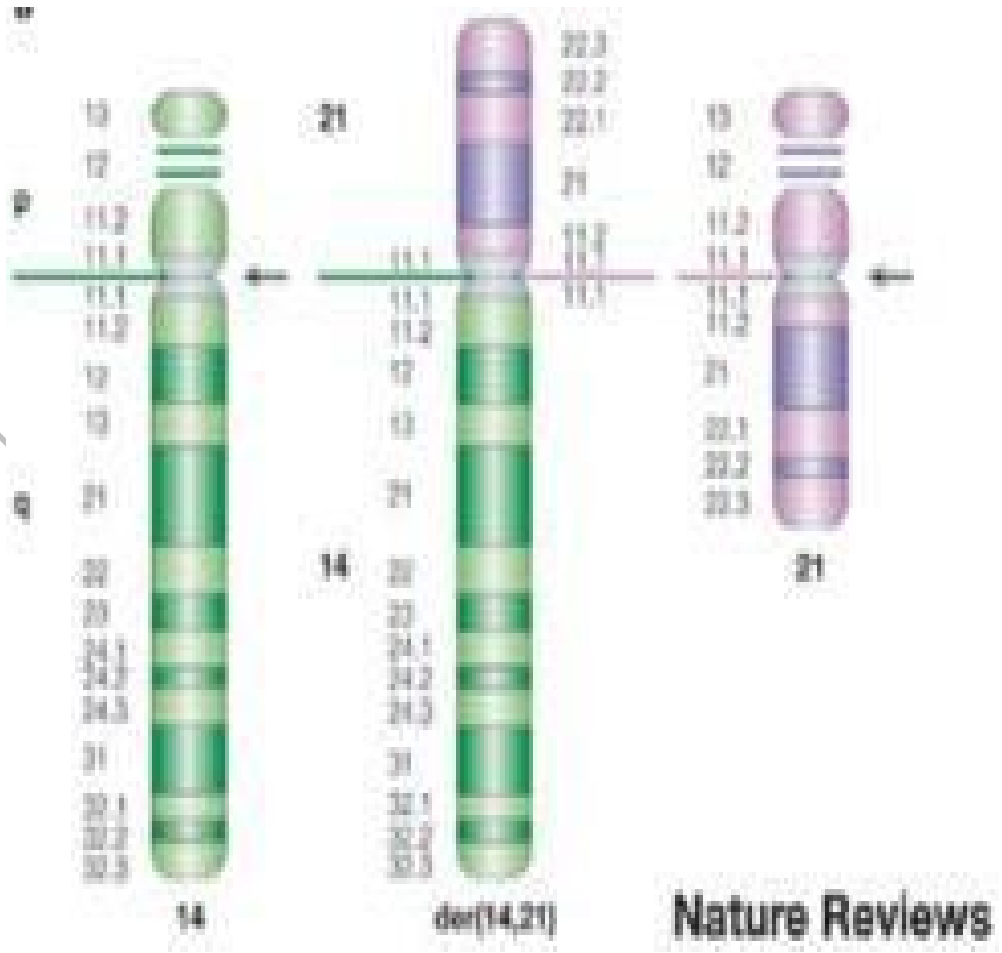


UNBALANCED TRANSLOCATIONS

UNBALANCED TRANSLOCATIONS

- An entire chromosome has attached to another at the Centromere
- long q arms of two chromosomes (14 & 21) become joined at a single centromere.
- 4% cases of down syndrome, unbalanced translocation can

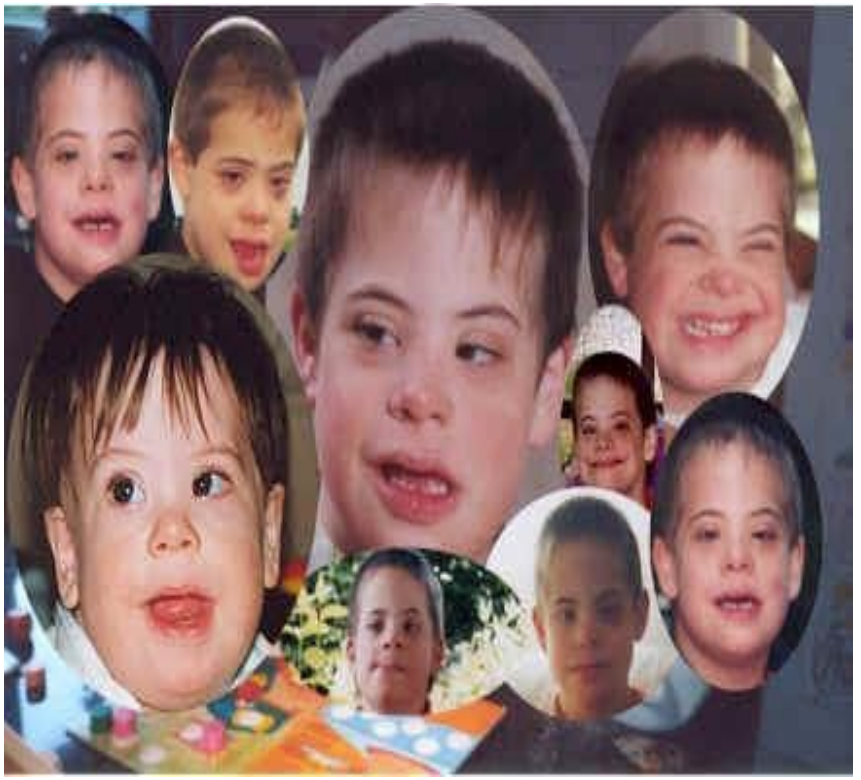
occur during meiosis I or meiosis II.



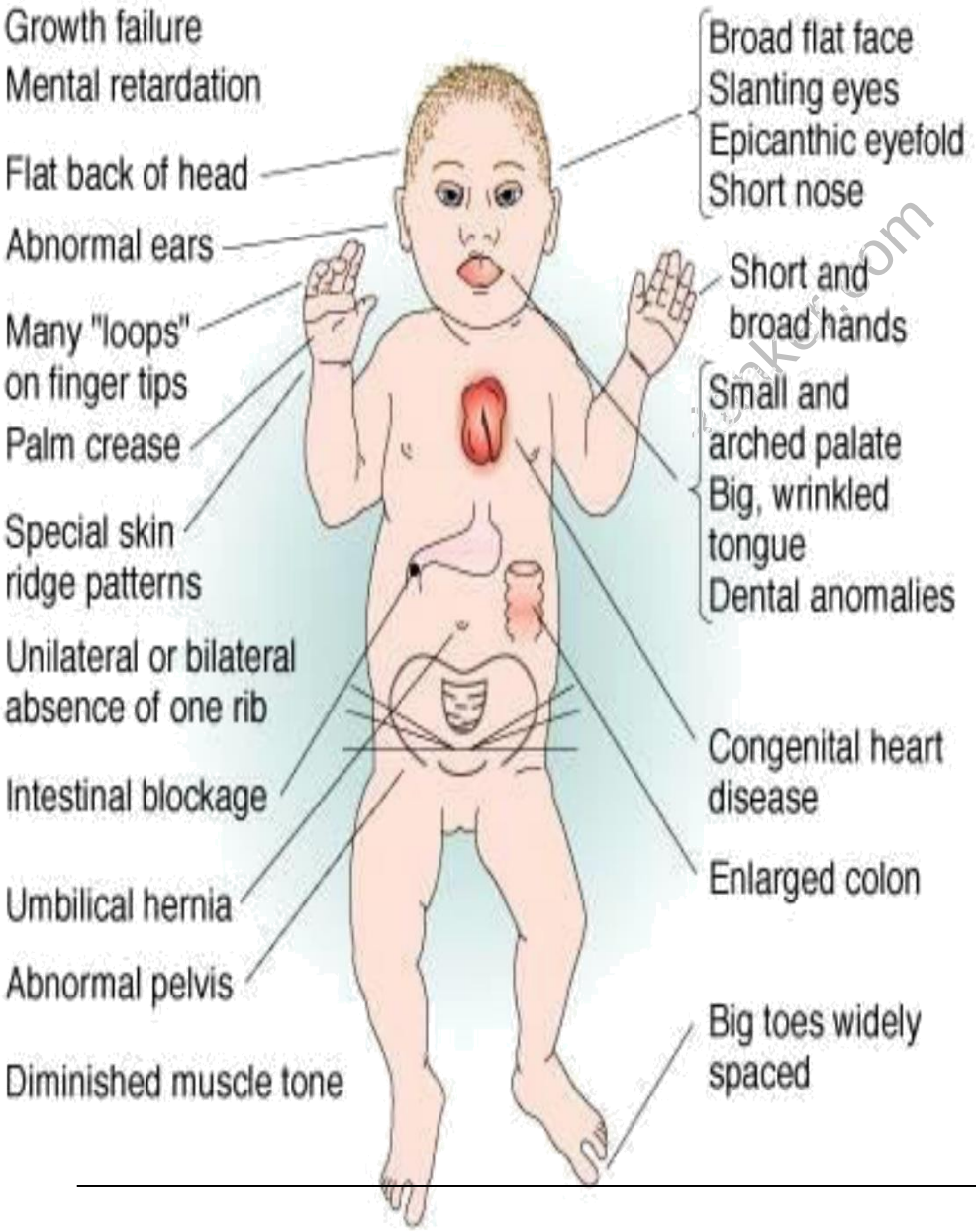
DOWN'S SYNDROME

DOWN'S SYNDROME

- **Causes:**
  - Meiotic nondisjunction - 95% (trisomy 21)
- Unbalanced translocation- 4% b/w 21 and 13,14,15
  - Mosaicism due to mitotic non dysjunction-1%
  - **Incidence:**



- Female under 25--- 1: 2000
- At 35 --- 1: 300
- At 40 --- 1:40



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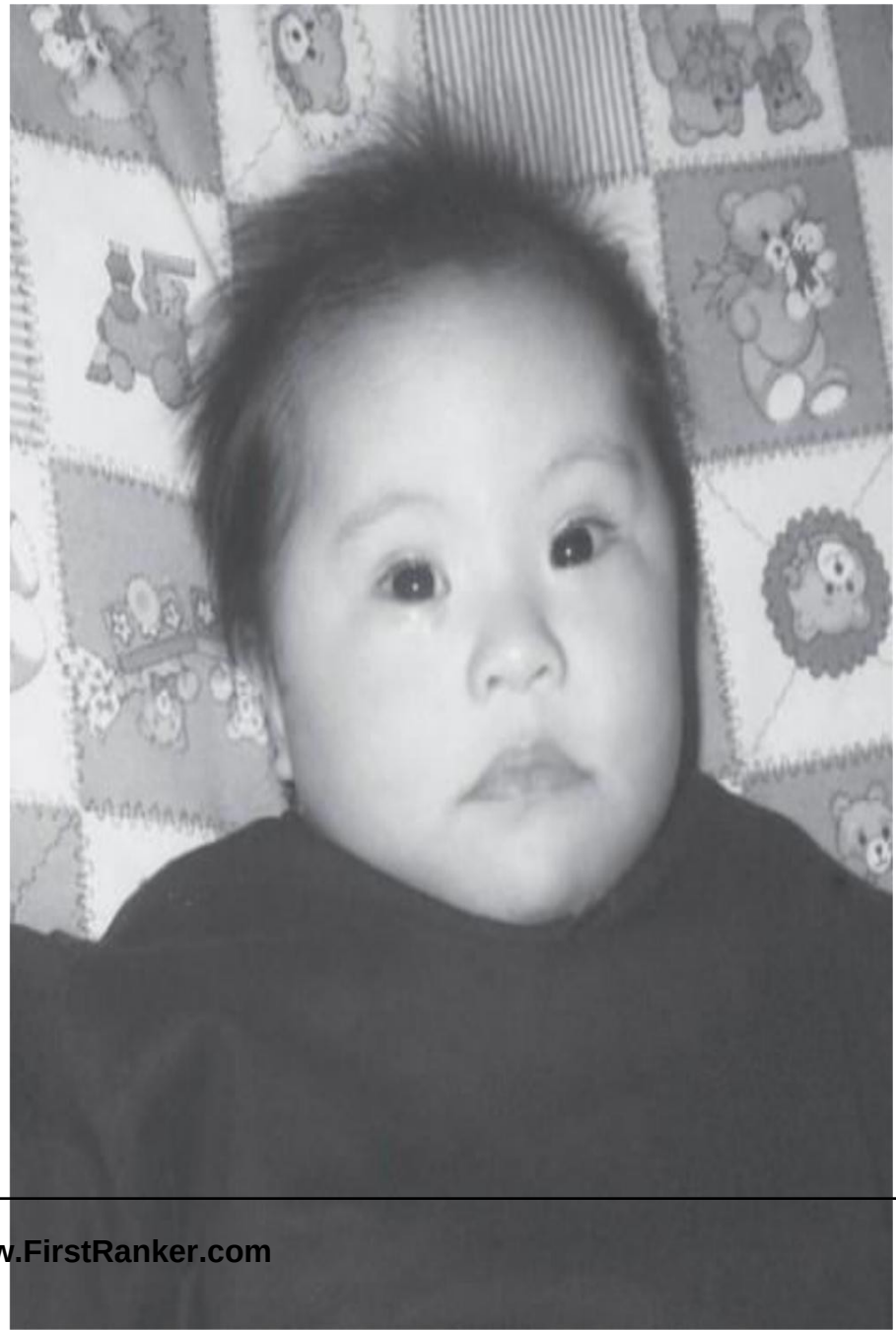
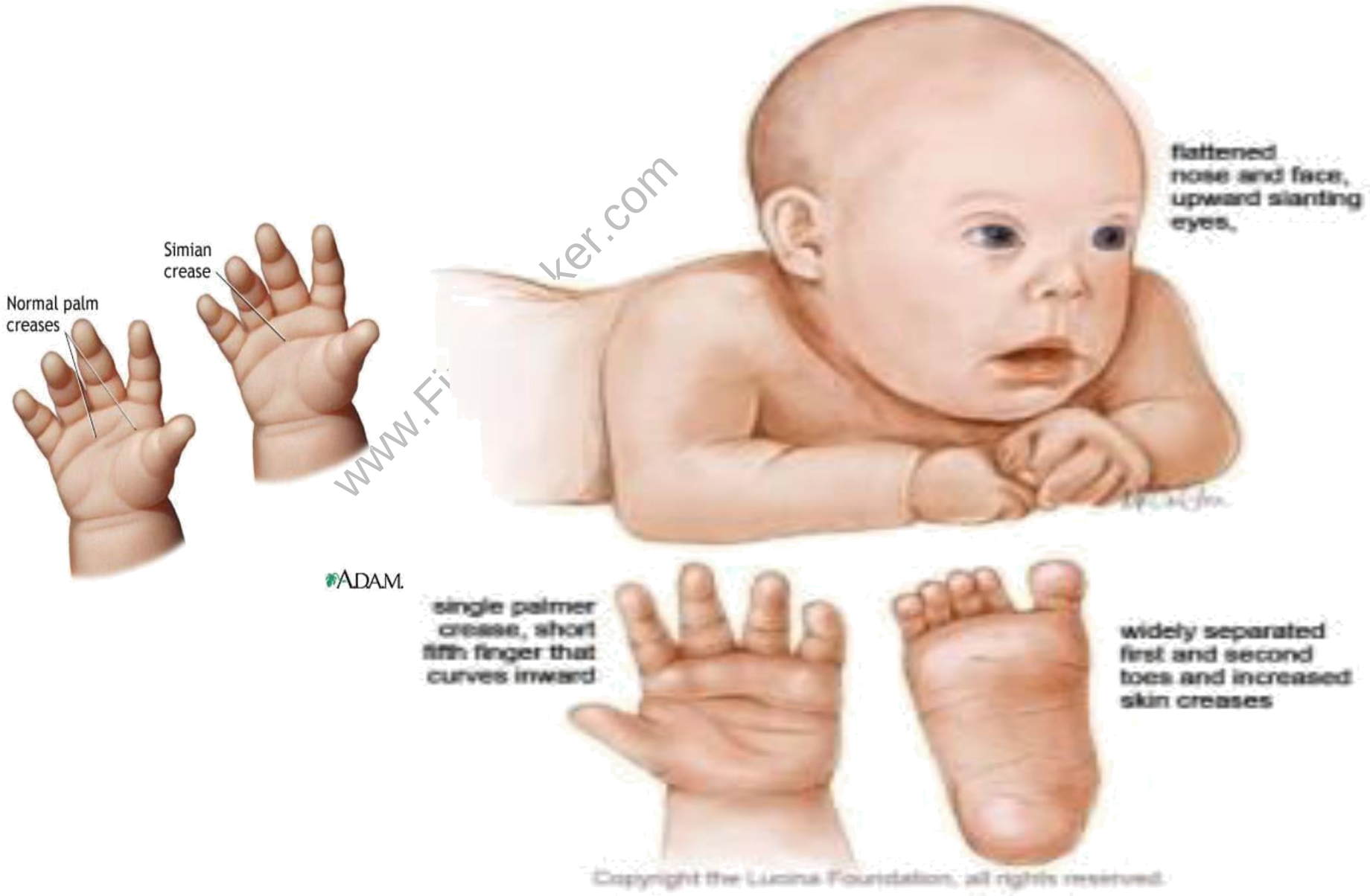


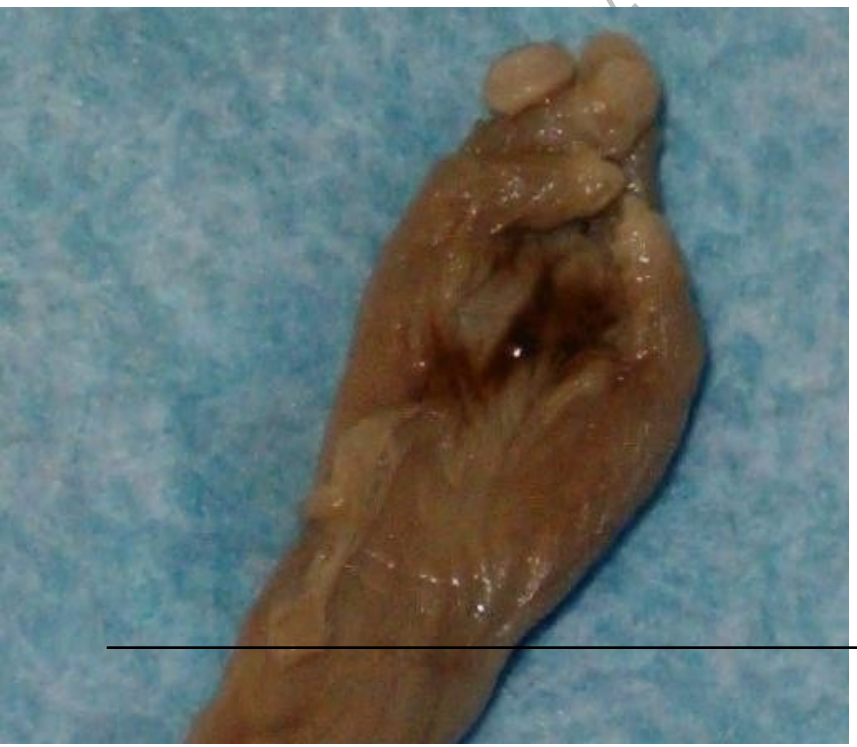


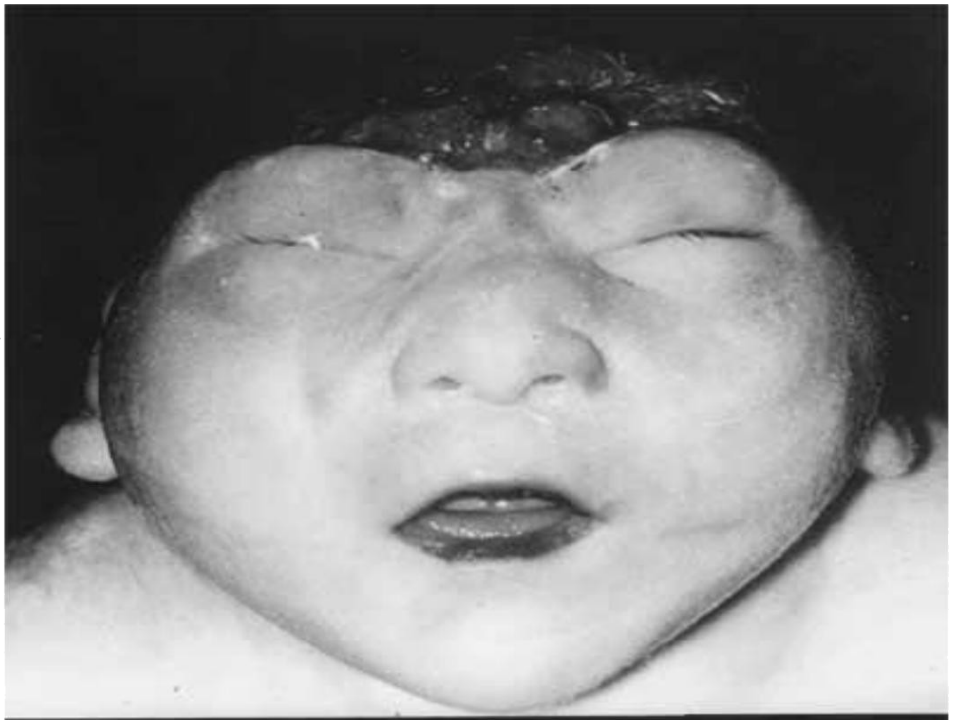
TRISOMY 18

TRISOMY 18

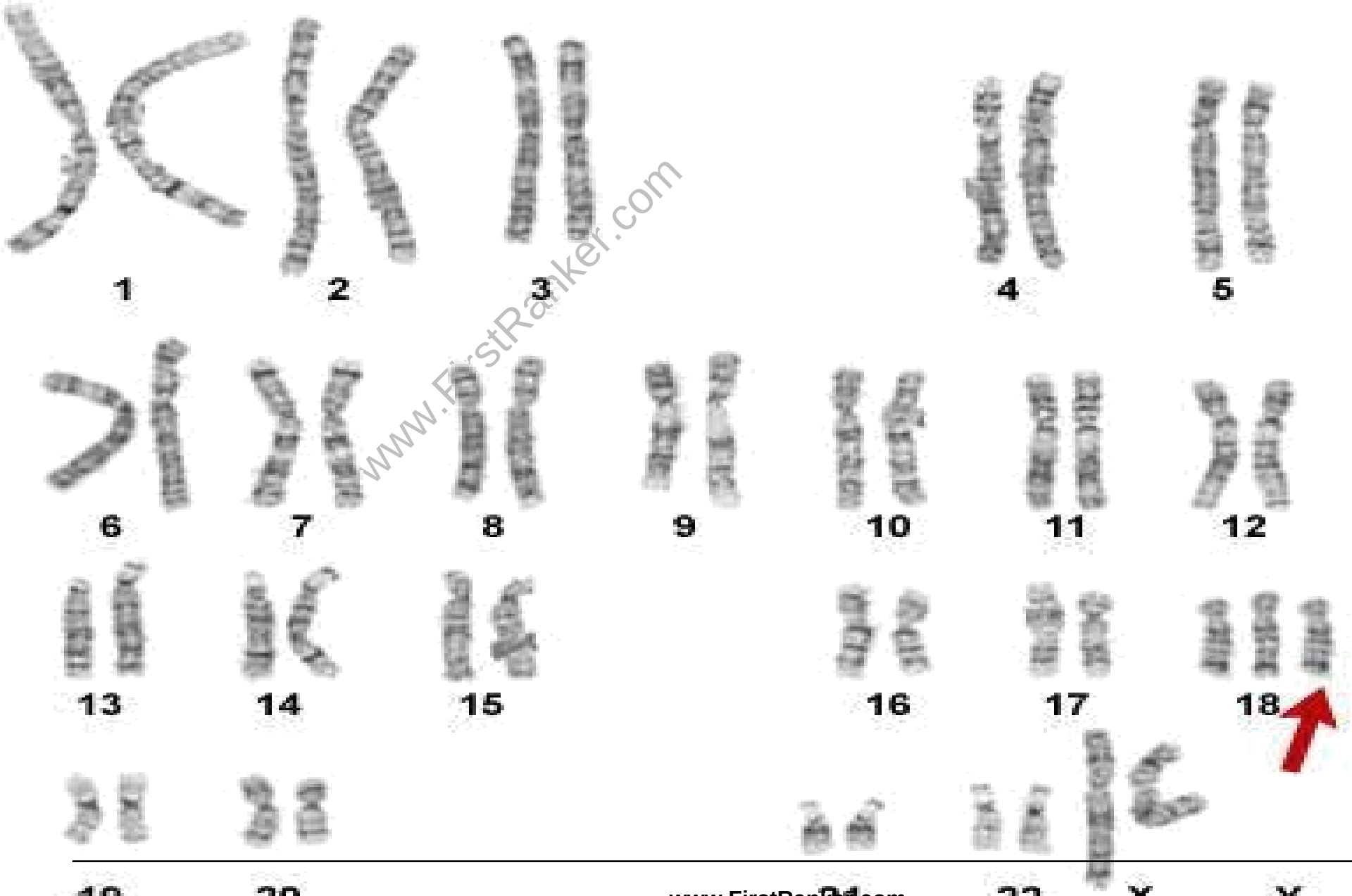
1:5000, infants usually die by age of 2months

S/S: Mental retardation, congenital heart defects, low set ears, flexion of fingers





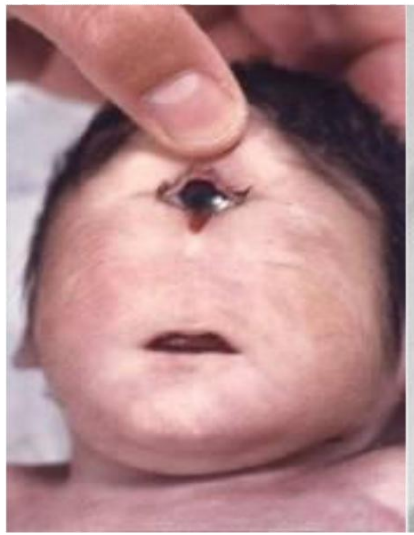
Karyotype from a female with Edwards syndrome (47,XX,+18)

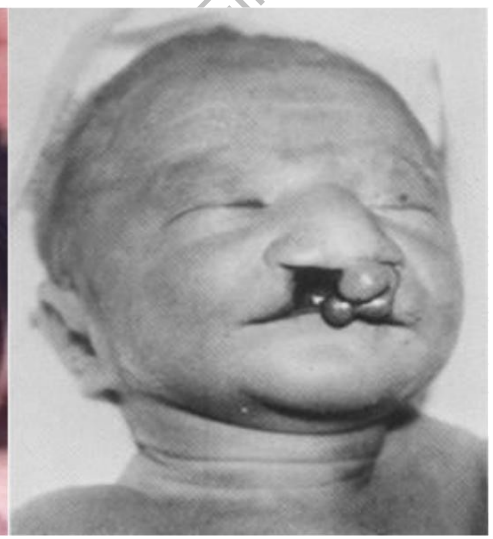


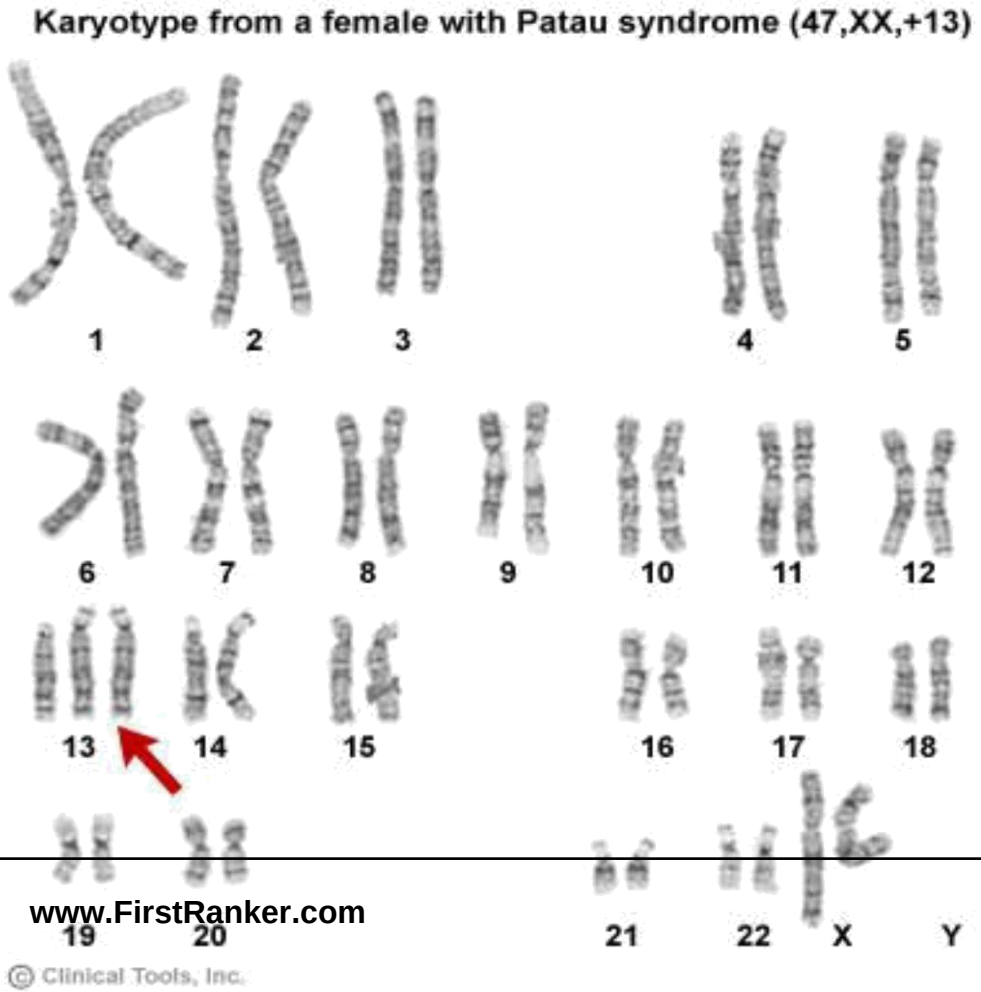
TRISOMY 13

1:5000 ; most of the infants die by age 3months

S/S: mental retardation, holoprosencephly, congenital heart defects



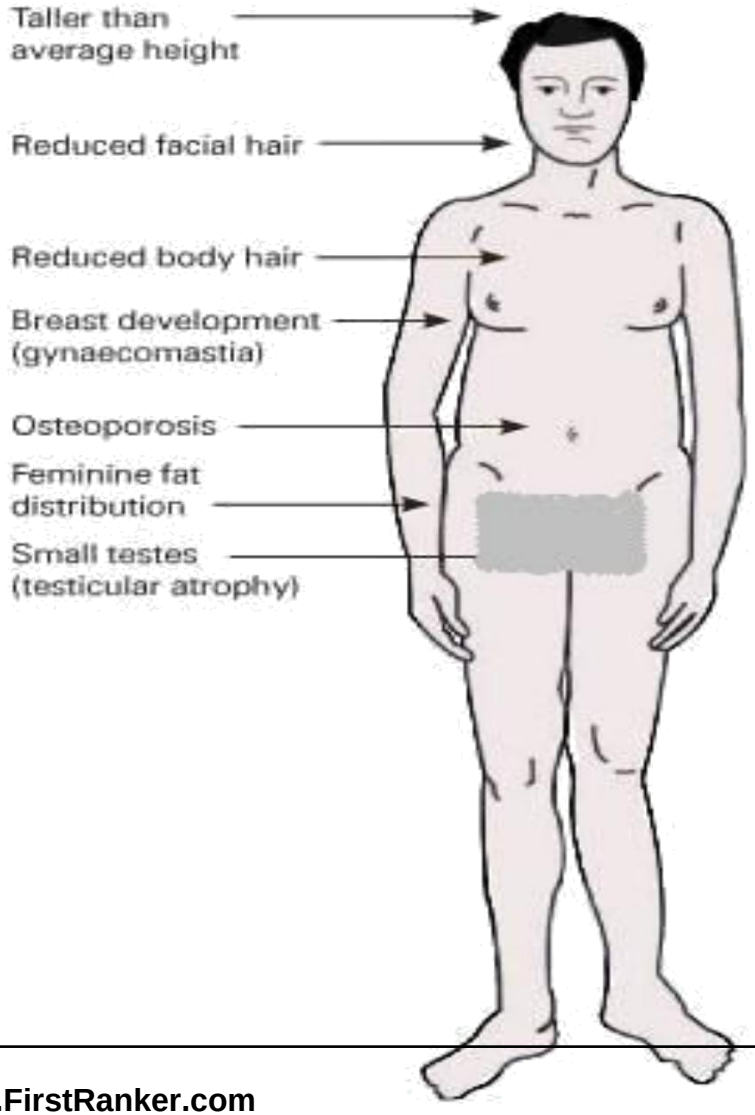




KLINEFELTER'S SYNDROME

KLINEFELTER'S SYNDROME

- Have 47 chromosomes (XXY) & a sex chromatin Barr body or 48(XXXY); more the number of X more the chances of mental impairment
- Cause:
  - **Nondisjunction of XX homologue**
- Found only in males, detected at puberty
- Incidence ---1 in 500 males



S/S

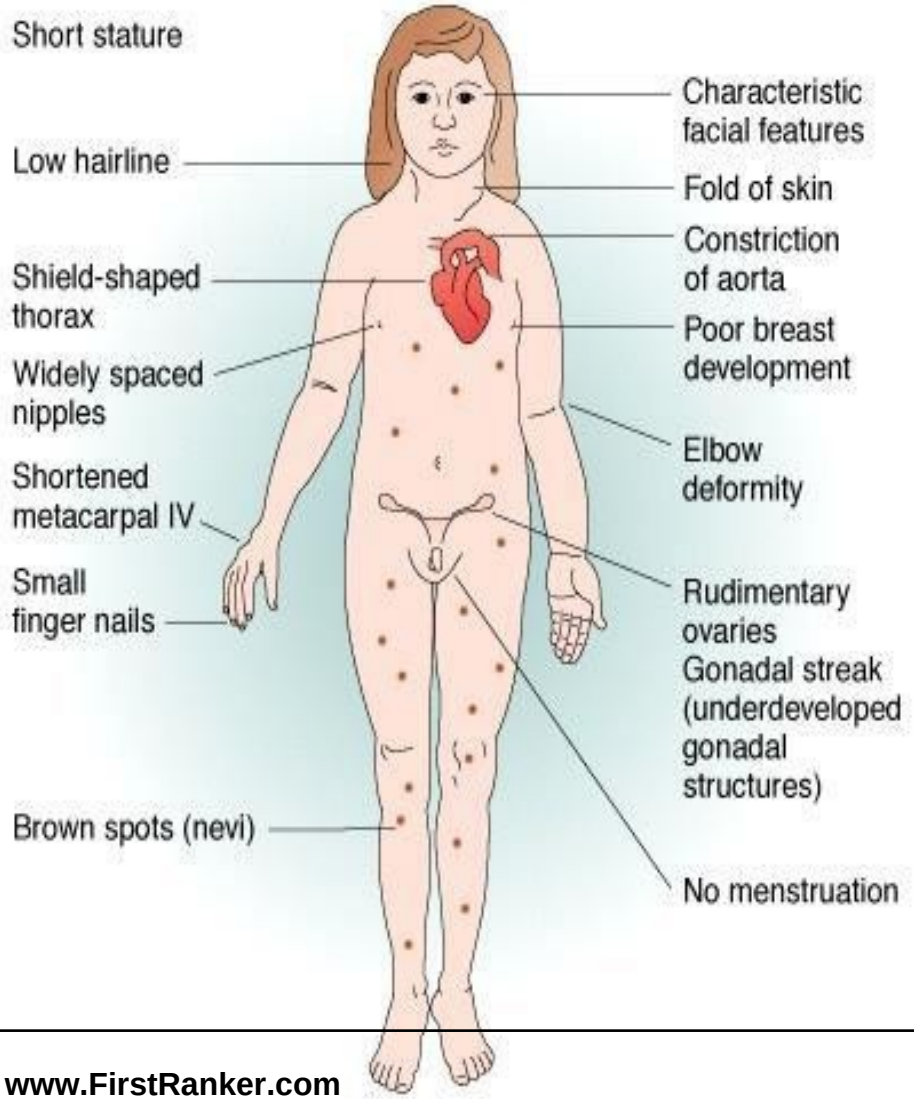
Sterility, testicular atrophy,

hyalinization of seminiferous tubules, gynecomastia.

TURNER SYNDROME

TURNER SYNDROME

- 45 X karyotype
- **Only monosomy compatible with life**
- Cause
  - Nondisjunction in male gamete
  - Structural abnormalities of X chromosome



- One X chromosome is missing
- Mitotic nondisjunction

STRUCTURAL ABNORMALITIES

STRUCTURAL ABNORMALITIES

- Occur when the chromosome's structure is altered, this can take several forms: Translocation, deletion or duplication of chromosomes
- Chromosome breaks occur either as a result of damage to DNA (by radiation or chemicals) or as part of the mechanism of recombination.

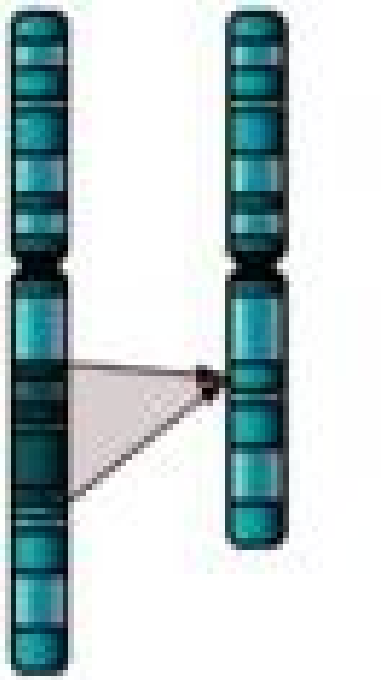
- However, the total number of chromosomes is usually normal.

CHROMOSOMAL DELETION

CHROMOSOMAL DELETION

- A part of a chromosome is missing or "deleted."
- Breaks are caused by environmental factors
- A very small piece of a chromosome can contain many different genes.
- When genes are missing, "instructions" are missing

resulting in errors in the development of a fetus.



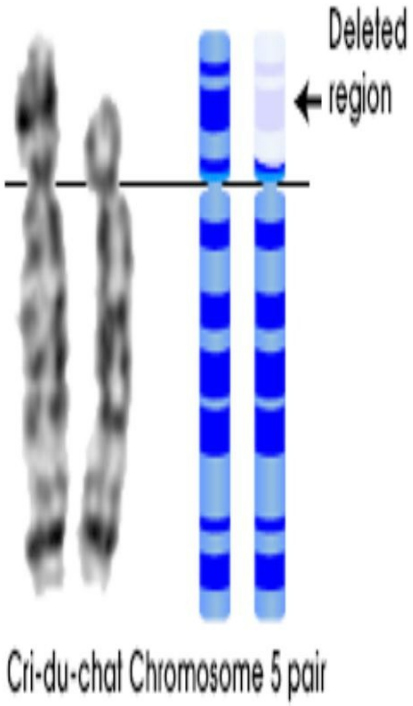
CRI-DU-CHAT SYNDROME

CRI-DU-CHAT SYNDROME

Partial deletion of chromosome 5

S/S

- High pitched cat like cry, a small head size , low birth weight, mental retardation and congenital heart disease.



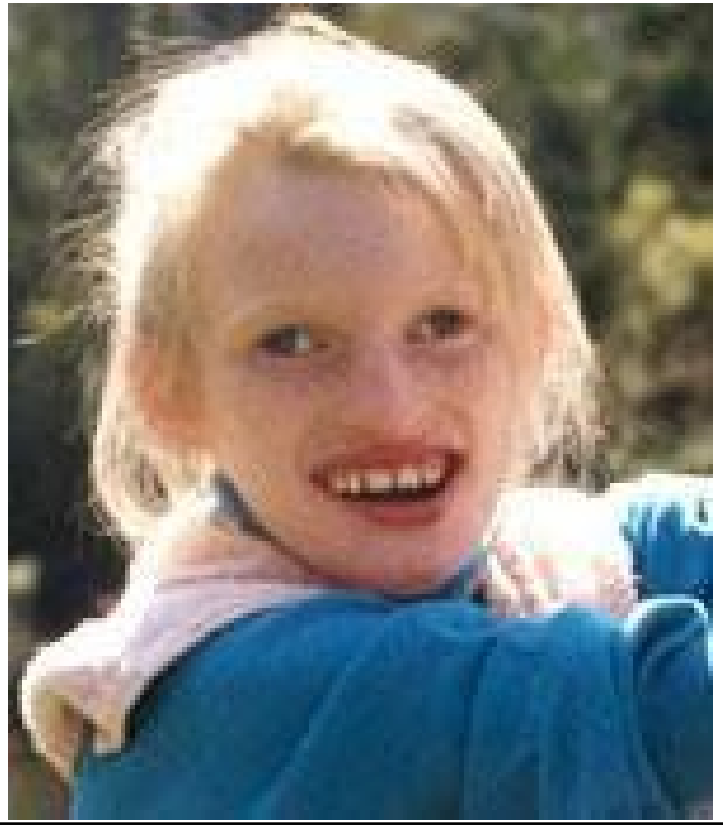
ANGELMAN'S SYNDROME

ANGELMAN'S SYNDROME

- Microdeletion (span few contiguous genes) on long arm of chromosome 15.
- **Inherited on maternal chromosome**

S/S

- Mentally retarded,
- Cannot speak



- **Prolonged periods of laughter**

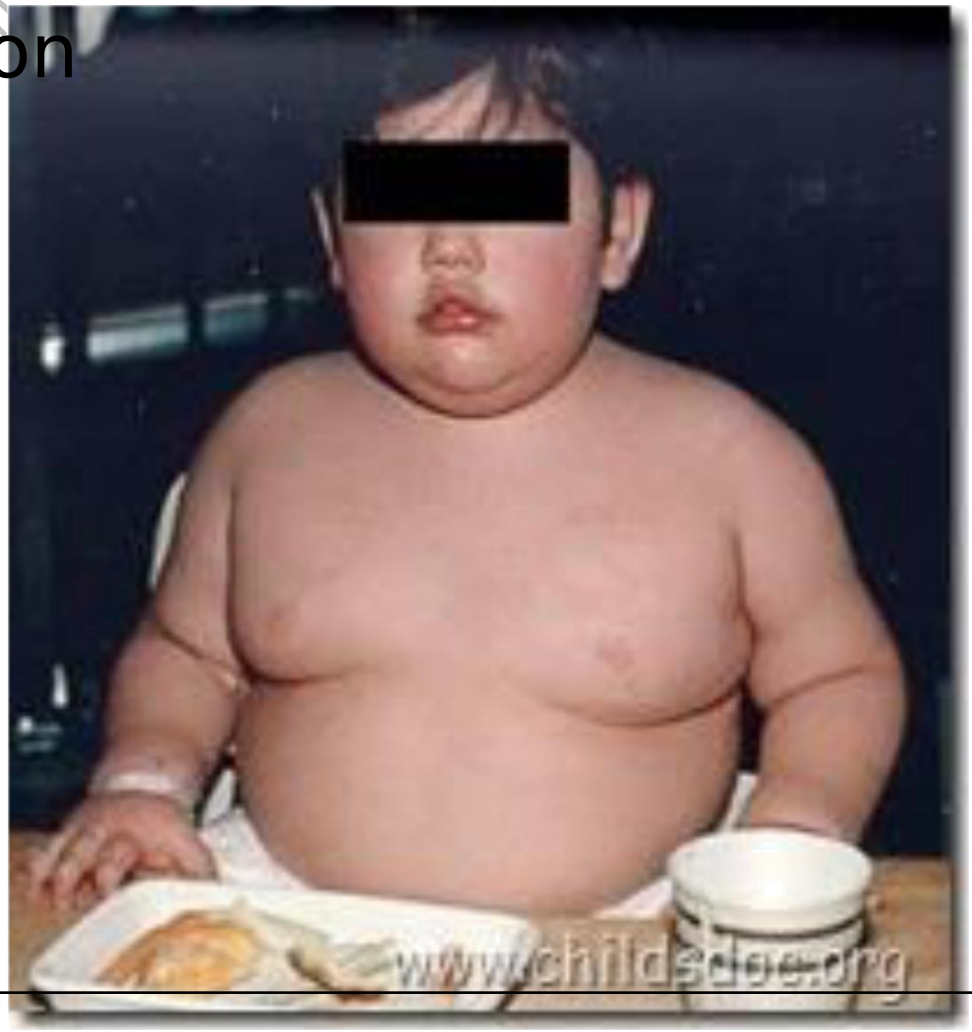
PRADER-WILLI SYNDROME

PRADER-WILLI SYNDROME

- Microdeletion occurs on long arm of chromosome 15
- **Inherited on paternal chromosome**

S/S

- Obesity
- Mental retardation
- Hypogonadism
- Cryptorchidism



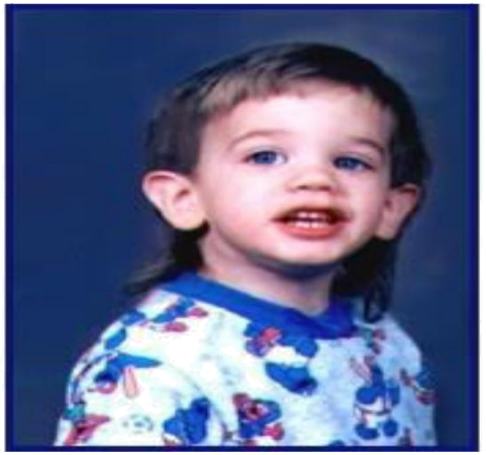
FRAGILE X SYNDROME

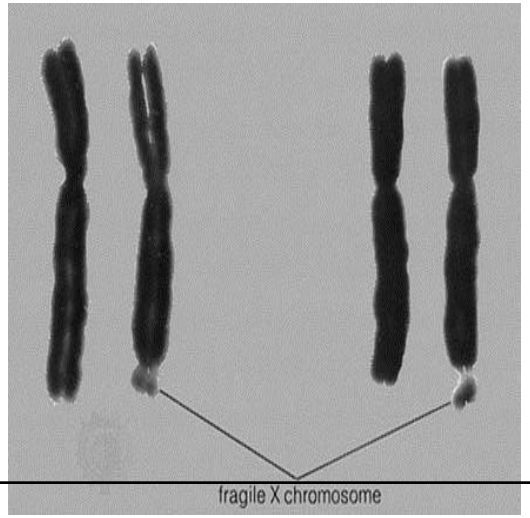
FRAGILE X SYNDROME

- Fragile X is a genetic disorder that is caused by a break or weakness on the long arm of the X chromosome.
- Syndrome occurs in 1:5000 individuals with males affected more than females.
- Is the 2nd most common inherited cause of mental retardation due to chromosomal abnormalities

S/S

Mental retardation, large ears, prominent jaw and pale blue irises





Genomic imprinting

- **These syndromes depend on whether the affected genetic material is inherited from the mother or father they are also an example of imprinting.**