WELCOME

CHROMOSOMAL ABNORMALITIES

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CHROMOSOMAL ABNORMALITIES

Numerical :

Gain or loss of one or more chromosomes

Structural :

Structural change in chromosome/s

STRUCTURAL ABERRATIONS

- **INVERSIONS**

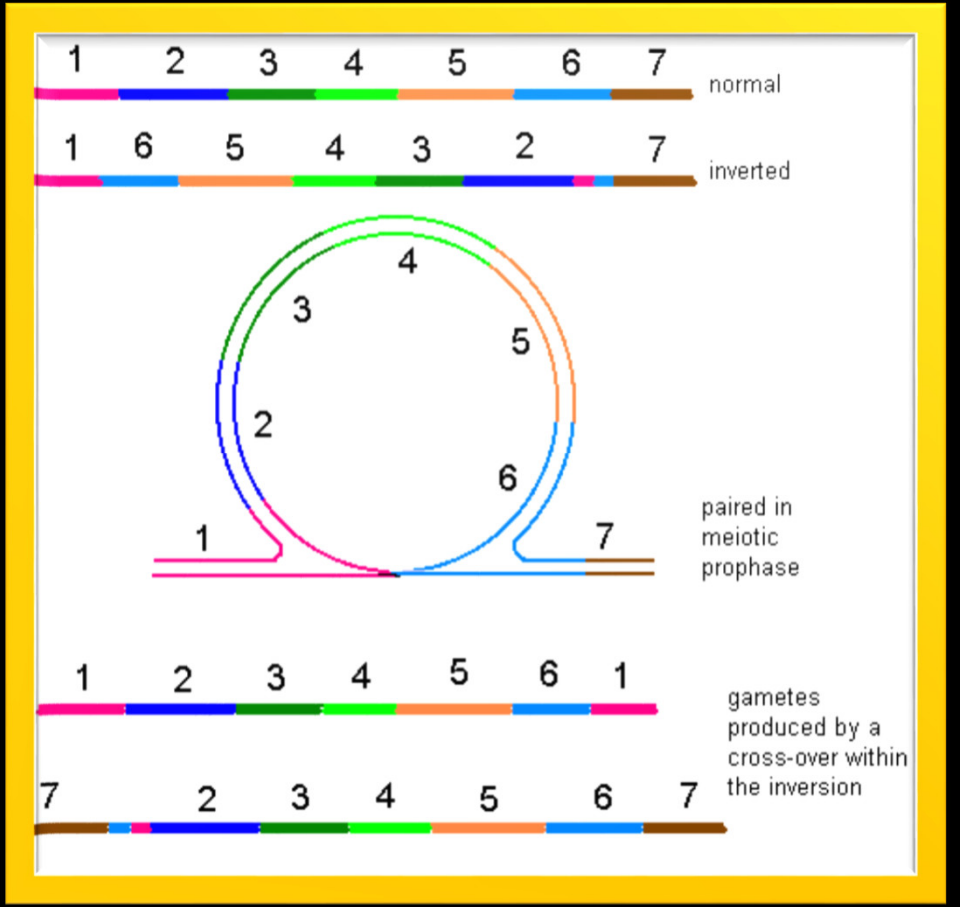
  In an inversion, a piece of chromosome has been lifted out, turned around and reinserted.

I. **PERICENTRIC INVERSION**

If this includes the centromere

II. **PARACENTRIC INVERSION**

If it excludes the centromere



STRUCTURAL ABERRATIONS

I. **PERICENTRIC INVERSION**

If this includes the centromere

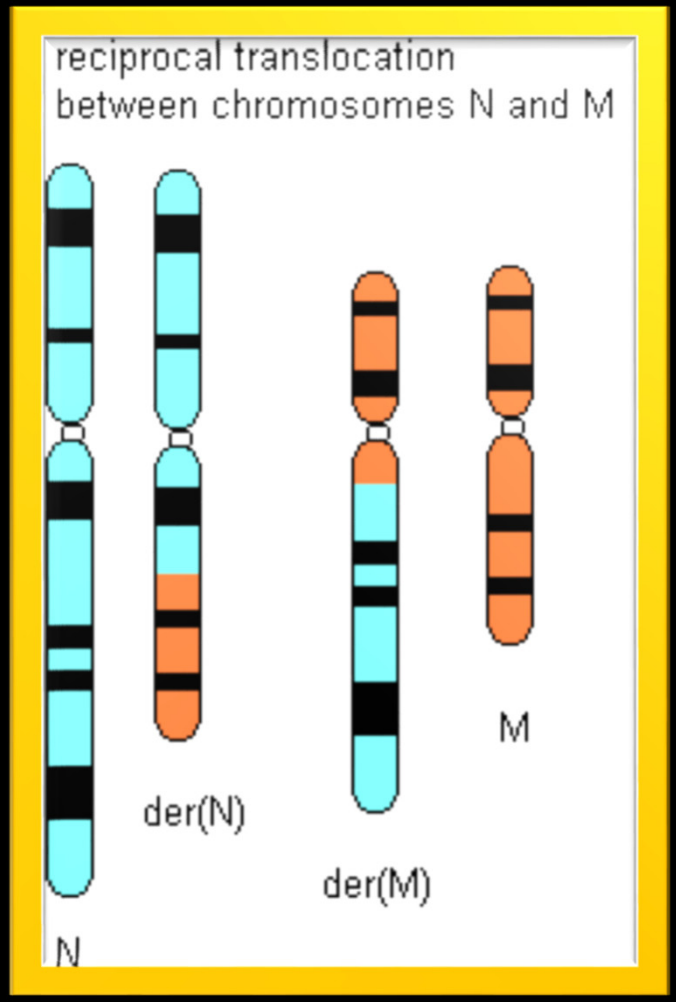
II. **PARACENTRIC INVERSION**

If it excludes the centromere

STRUCTURAL ABERRATIONS

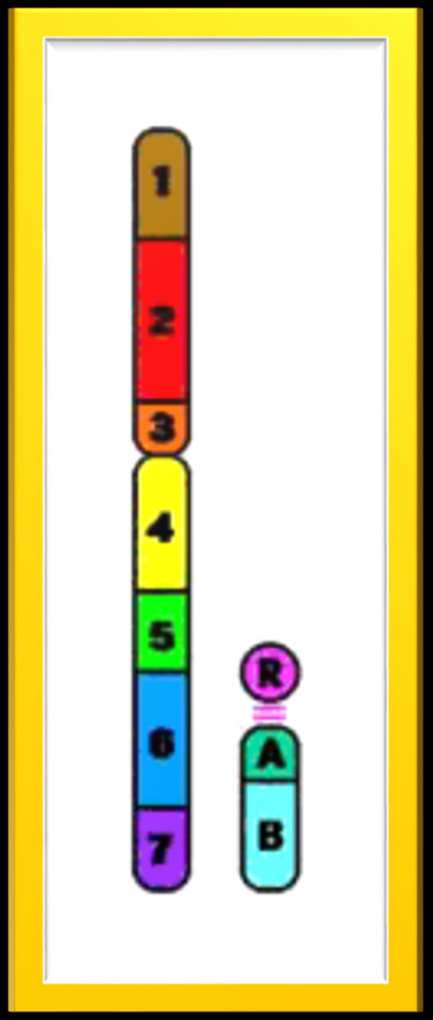
- **Translocations**

  In a balanced translocation there is no net gain or loss of chromosomal material, two chromosomes have been broken and rejoined in the wrong combination

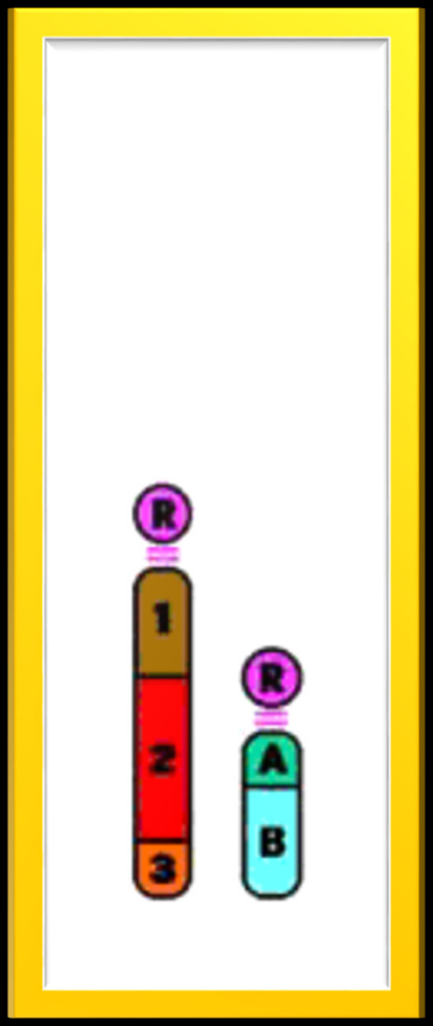


STRUCTURAL ABERRATIONS

- **Reciprocal translocation**

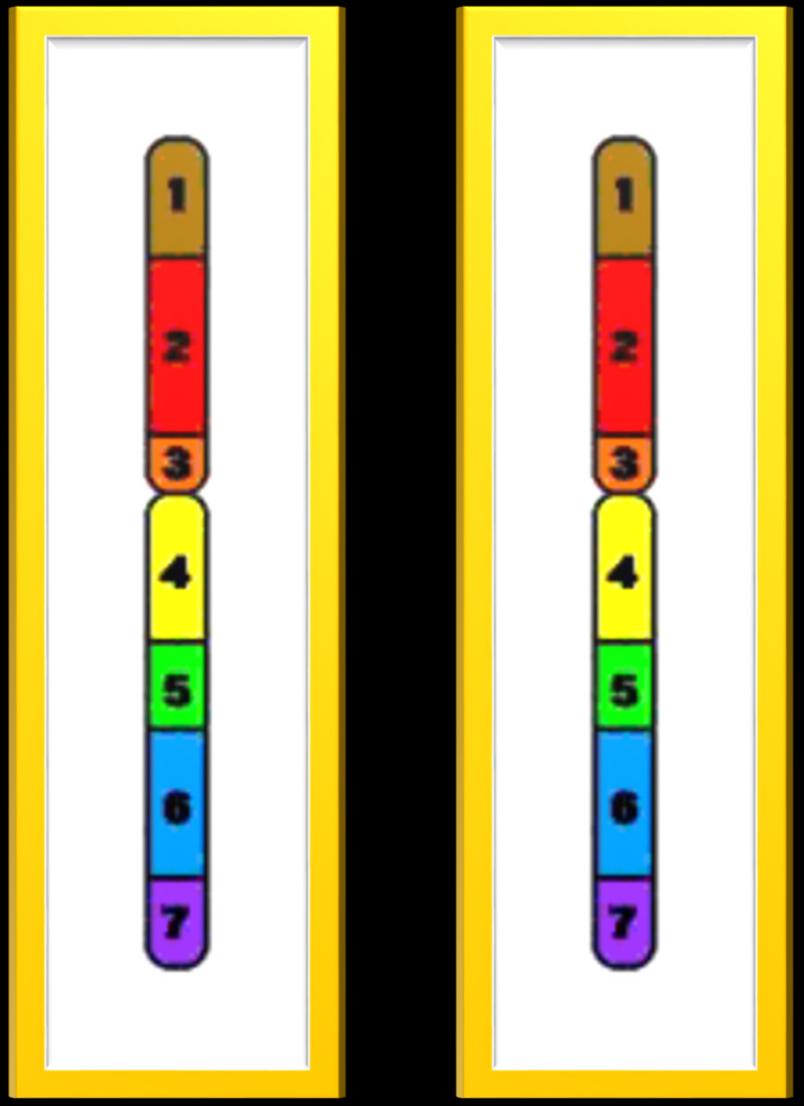


- **Robertsonian translocation**



UNBALANCED REARRANGEMENTS

- **Deletions**
  - Deletions may either be either interstitial or terminal. If big enough to be visible a deletion must be removing many genes and will probably give rise to a severe phenotype
  - An example of an interstitial deletion is Williams syndrome mentioned in an earlier lecture.
  - A well known recurrent terminal deletion involves the loss of material at the end of the short arm of chromosome 5. It causes “Cri di Chat” syndrome.



DELETION

- **Terminal Deletion –**

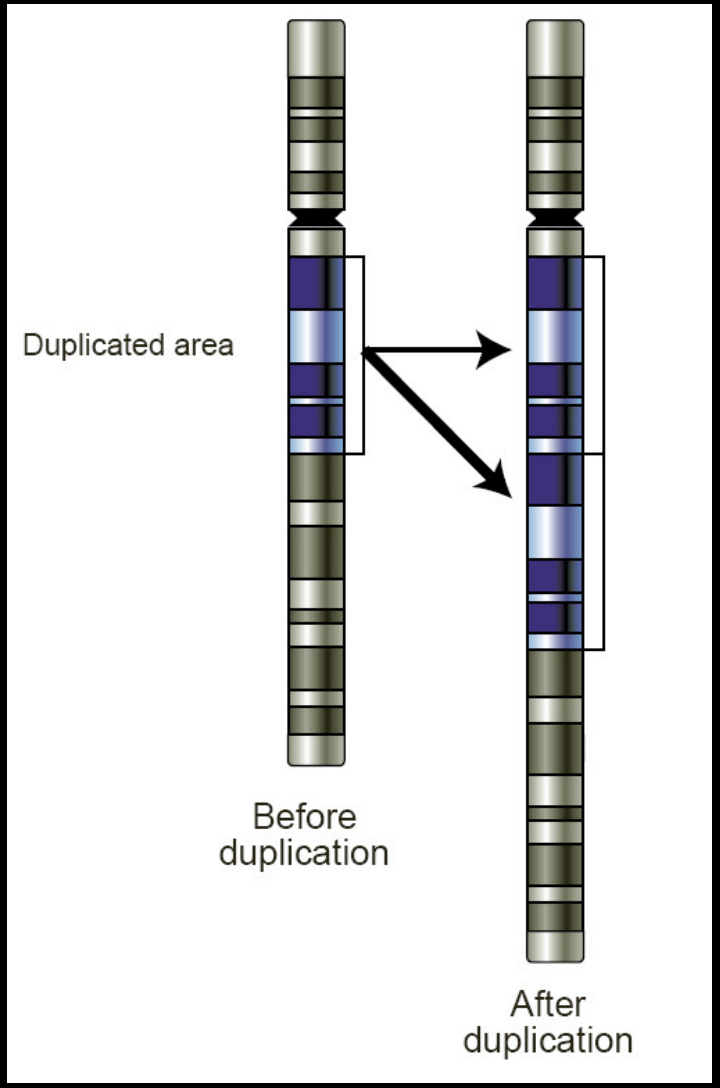
  A deletion that occurs towards the end of a chromosome.

- **Intercalary Deletion / Interstitial Deletion**

  A deletion that occurs from the interior of a chromosome.

UNBALANCED REARRANGEMENTS

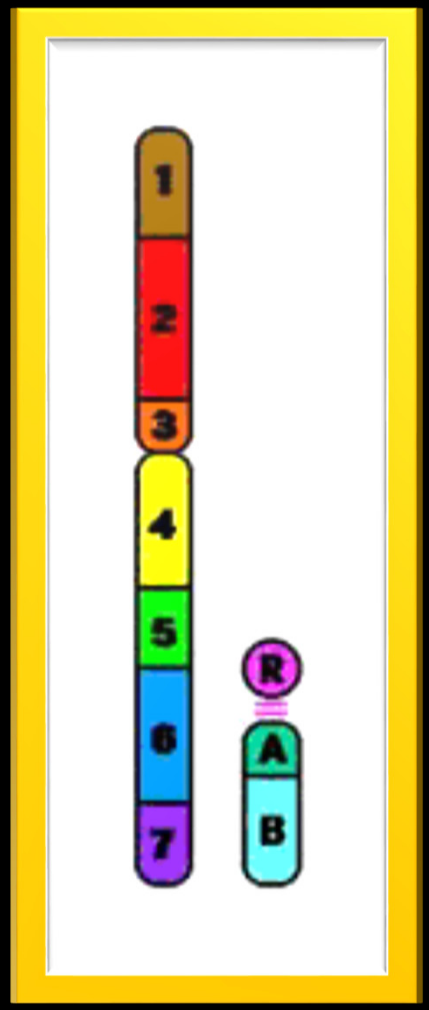
- **Duplication**
  - A part or entire chromosome may be duplicated resulting in extra genetic material.
  - Opposite of a deletion
  - Arise from an event termed unequal crossing-over that occurs during meiosis between misaligned homologous chro
  - Known human disorders include Charcot-Marie-Tooth disease type 1A which may be caused by duplication of the gene encoding peripheral myelin protein 22 (PMP22) on chromosome 17. mosomes.



UNBALANCED REARRANGEMENTS

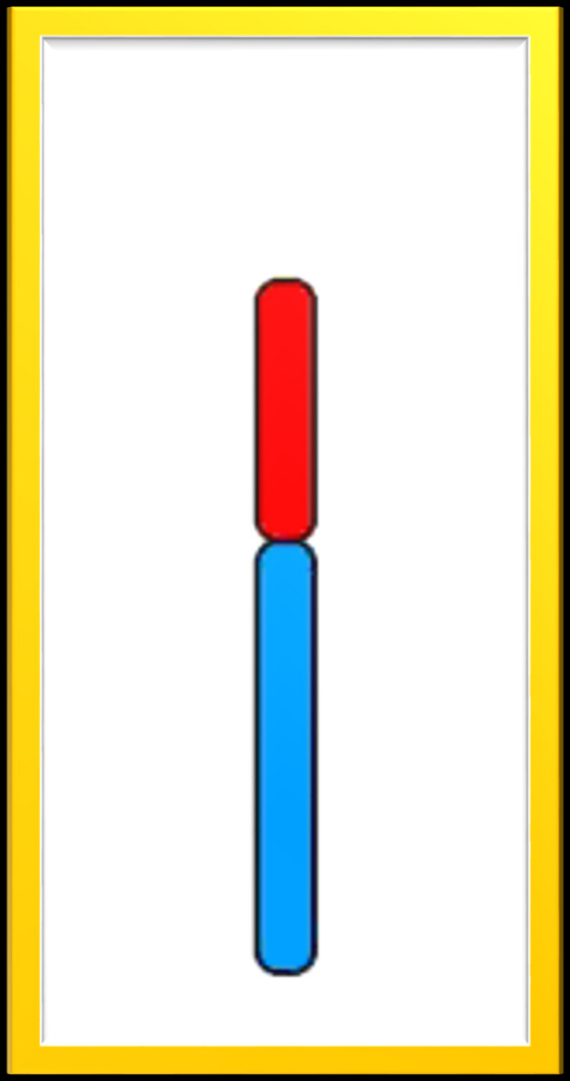
- **Insertion**

  A segment or the complete chromosome is inserted in the other chromosome



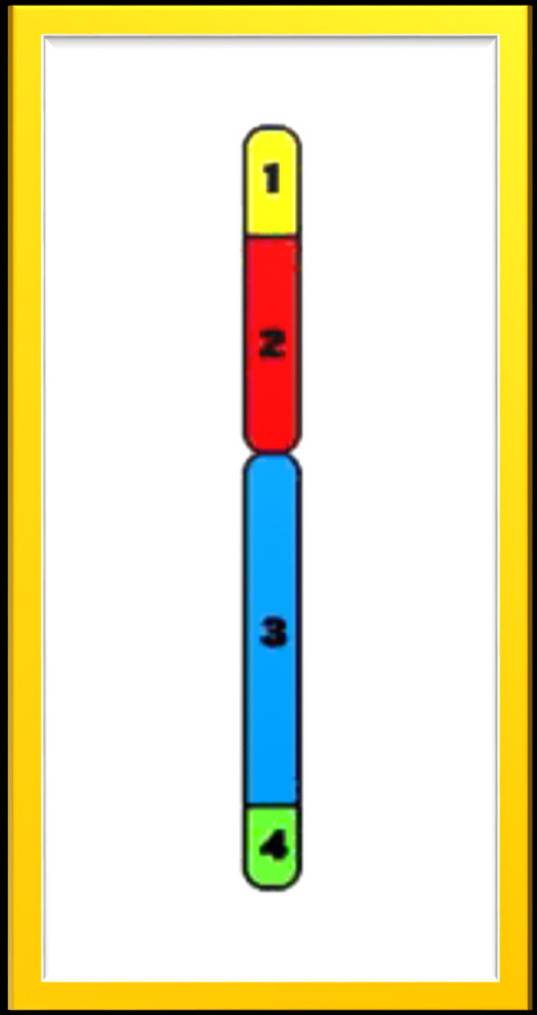
UNBALANCED REARRANGEMENTS

- **Isochromosomes**
  - A chromosome can split "the wrong way" in mitosis (or meiosis II) so that both long arms remain attached and move to one pole, and both short arms do likewise moving to the other pole.
  - The consequence is the formation of an isochromosome. These are simultaneously duplicated for the genes in the retained arm and deleted for the genes in the other.
  - The prognosis is poor except for iXq (isochromosome of the long arm of the X).



UNBALANCED REARRANGEMENTS

- **Ring chromosomes**
  - A mutation event which removes both telomeres can be repaired by sealing the ends together forming a ring chromosome.
  - This will be deleted for genes at both ends of the chromosome. The symptoms will depend on the extent of the deletion.
  - Surprisingly, ring chromosomes are mitotically stable. One might expect them to get hopelessly entangled during DNA replication and at the very least to be concatenated when the time comes to separate to the two poles. While this undoubtedly happens, it is not a frequent occurrence.



CRI-DU-CHAT SYNDROME

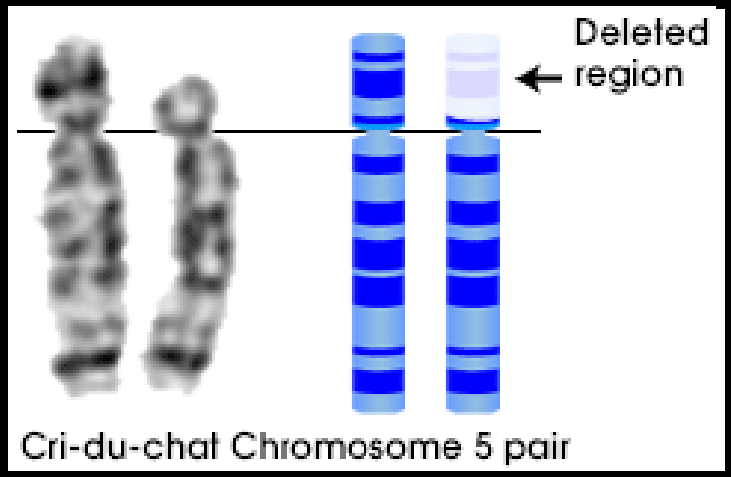
The cry is caused by abnormal larynx development, one of the many symptoms associated with this disorder.

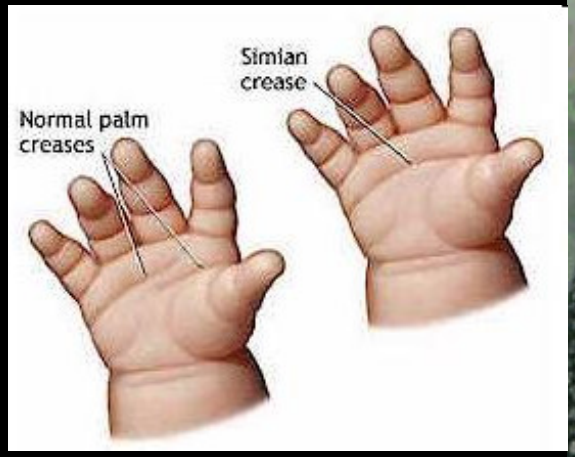
It usually becomes less noticeable as the baby gets older, making it difficult for doctors to diagnose cri-du-chat after age two.

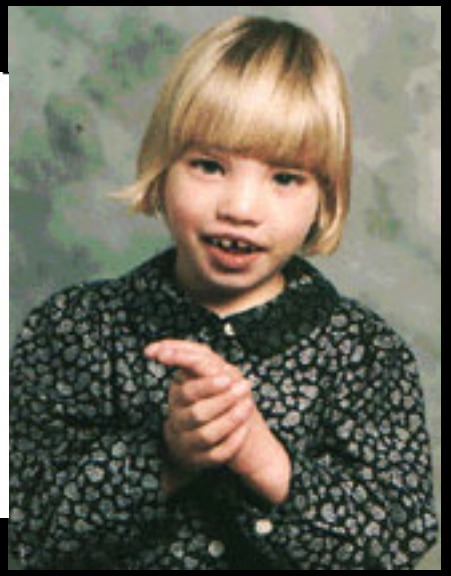
Cri-du-chat is caused by a deletion (the length of which may vary) on the short arm of chromosome 5.

Multiple genes are missing as a result of this deletion, and each may contribute to the symptoms of the disorder. One of the deleted genes known to be involved is TERT (telomerase reverse transcriptase).

This gene is important during cell division because it helps to keep the tips of chromosomes (telomeres) in tact.







WRITING KARYOTYPE INFORMATION

Abbreviation	meaning	example	description
cen	centromere		
del	deletion	46, XX, del(5)(p15.3)	Cri du chat syndrome deletion of band 5p15.3
der	derivative chromosome	der(22)	a chromosome derived from chromosome 22 and containing the chromosome 22 centromere
dup	duplication	46, XY, dup(21)(q21)	A male with a duplication of band q21 on chromosome 21
inv	inversion	46, XX, inv(9)(p12q13)	A female with a pericentric invertion on chromosome 9
mar	marker chromosome	47, XX, +mar	A female with an extra (unidentified) chromosome
mat	of maternal origin	46, XY, del(15)(q12)(mat)	A boy with Angelman syndrome
pat	of paternal origin	46,XX, del(15)(q12)(pat)	A girl with Prader-Willi syndrome
t	translocation	46, XY, t(1;2)(p21;p24)	A boy with a reciprocal translocation between band p21 on chromosome 1 and band p24 on chromosome 2
ter	the end of the chromosome arm	pter or qter	
+	gain of material	47, XY, +21	A boy with trisomy 21
-	loss of material	46, XX, 5p-	A less precise definition of the girl with Cri du chat above
/	mosaic	46,XX / 45, X	A mosaic case of Turner's syndrome

STRUCTURAL ABERRATION

1. **Deletions:** A portion of the chromosome is missing or deleted.
2. **Duplications:** A portion of the chromosome is duplicated, resulting in extra genetic material.
3. **Translocations:** When a portion of one chromosome is transferred to another chromosome.
    1. **Reciprocal translocati**on, segments from two different chromosomes have been exchanged.
    2. **Robertsonian translocation**, an entire chromosome has attached to another at the centromere - in humans these only occur with chromosomes 13, 14, 15, 21 and 22.
4. **Inversions:** A portion of the chromosome has broken off, turned upside down and reattached, therefore the genetic material is inverted.
5. **Rings:** A portion of a chromosome has broken off and formed a circle or ring. This can happen with or without loss of genetic material.
6. **Isochromosome:** Formed by the mirror image copy of a chromosome segment including the centromere.

NUMERICAL ABNORMALITIES

I. ANEUPLOIDY

Gain or loss of one or more chromosomes, but not a complete set.

A. Hyperploidy: Gain of Chromosome

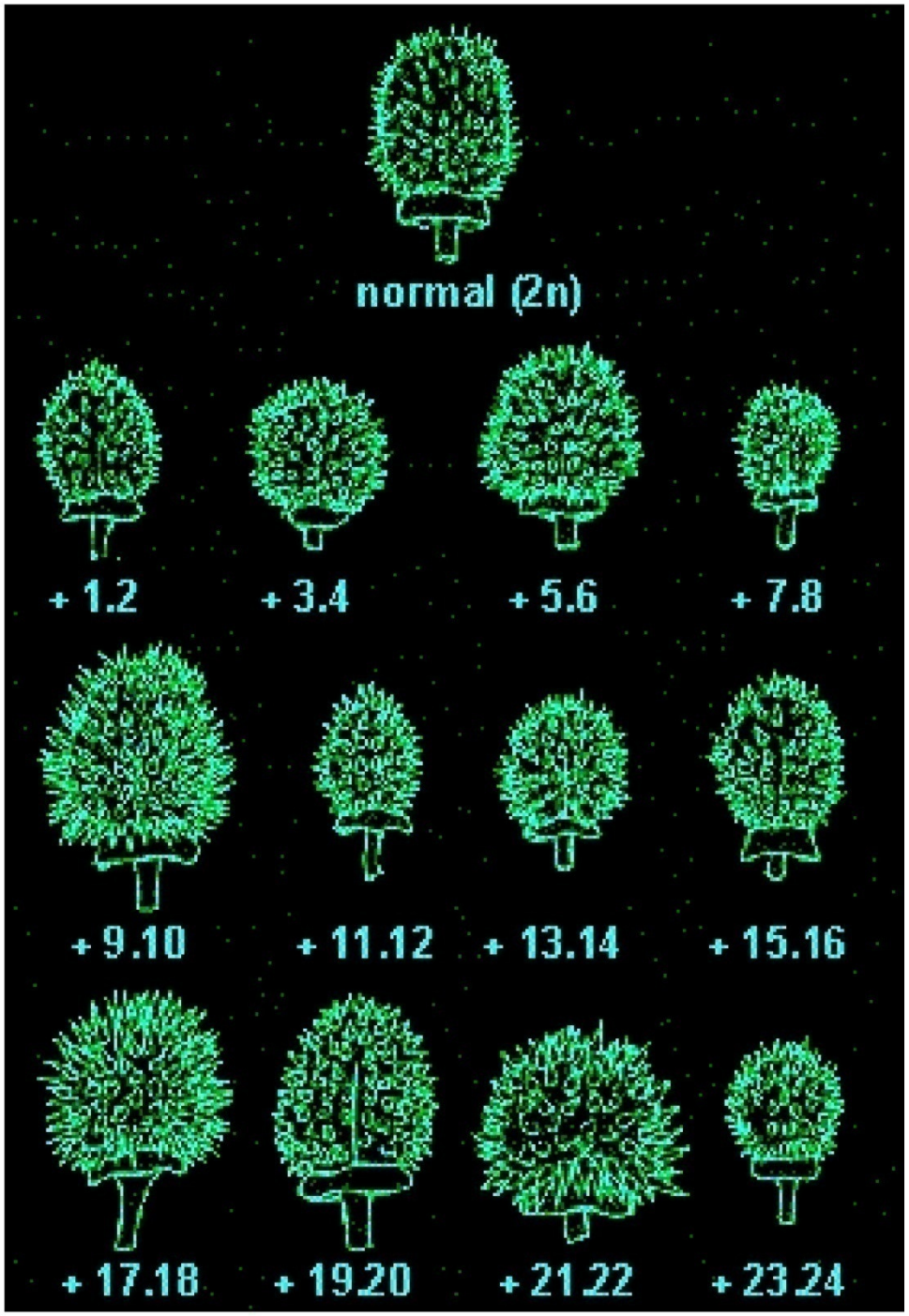
Trisomy: Gain of one chromosome in a diploid genome.

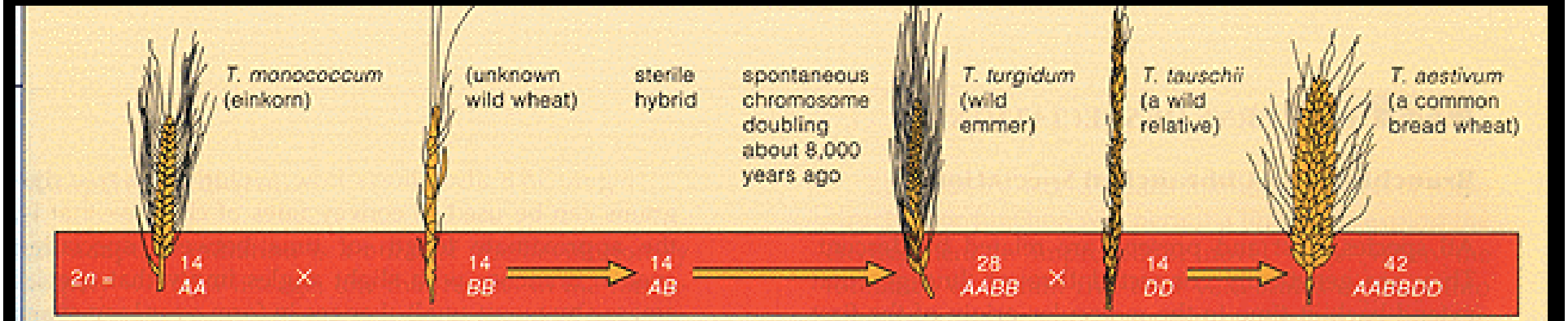
Tetrasomy: Gain of two chromosomes in a diploid genome.

B. Hypoploidy: Loss of Chromosome

Monosomy : Loss of a single chromosome from a diploid genome.

Nullisomy: Loss of a two chromosomes from a diploid genome.


normal (2n)
+ 1.2
+ 3.4
+ 5.6
+ 7.8
+ 9.10
+ 11.12
+ 13.14
+ 15.16
+ 17.18
+ 19 20
+ 21 22
+ 23 24



a About 11,000 years ago, humans start cultivating wild wheats. The species *Triticum monococcum* has diploid number 14 (two sets of 7 chromosomes, shown as 14 *AA*). It hybridizes with another species that has the same chromosome number.

b *AB* hybrid offspring are sterile but self-fertilizing; an interbreeding population of *AB* plants arises by asexual reproduction. About 8,000 years ago, by unknown events, polyploidy arises in the population. Some plants (*T. turgidum*) are tetraploid (*AABB*), with a chromosome number of 28 (two sets of 14). They are fertile. (*A* chromosomes can pair with each other, and so can *B* chromosomes, during meiosis.)

c Later, an *AABB* plant hybridizes with *T. tauschii*, a wild relative with a diploid number of 14 (two sets of 7 *DD*). Today, populations of the hybrid descendants (*T. aestivum*) provide wheat for bread. Their chromosome number is 42 (six sets of 7 *AABBDD*).

Figure 15.6 Presumed sympatric speciation in wheat through polyploidy and hybridizations. Wheat grains 11,000 years old have been found in the Near East. Diploid wild wheats still grow there.

NUMERICAL ABNORMALITIES

II. EUPLOIDY

Possession of multiples of the **haploid** set of chromosomes.

Diploidy is possession of more than two sets:

Triploid is three sets and

Tetraploid is four sets.

ANEUPLOID DISEASES

Autosomal Aneuploidy:

It contains the following syndromes:

1-Down syndromes(trisomy21).

2-Edoards syndromes(trisomy18).

3-Trisomy16.

4-patua syndromes(trisomy13).

Sex chromosomes aneuploidy contains:

1-Turner syndrome (monosomy x).

2-Klinefelter syndrome (XXY).

3-Female with trisomy x (poly-x females).

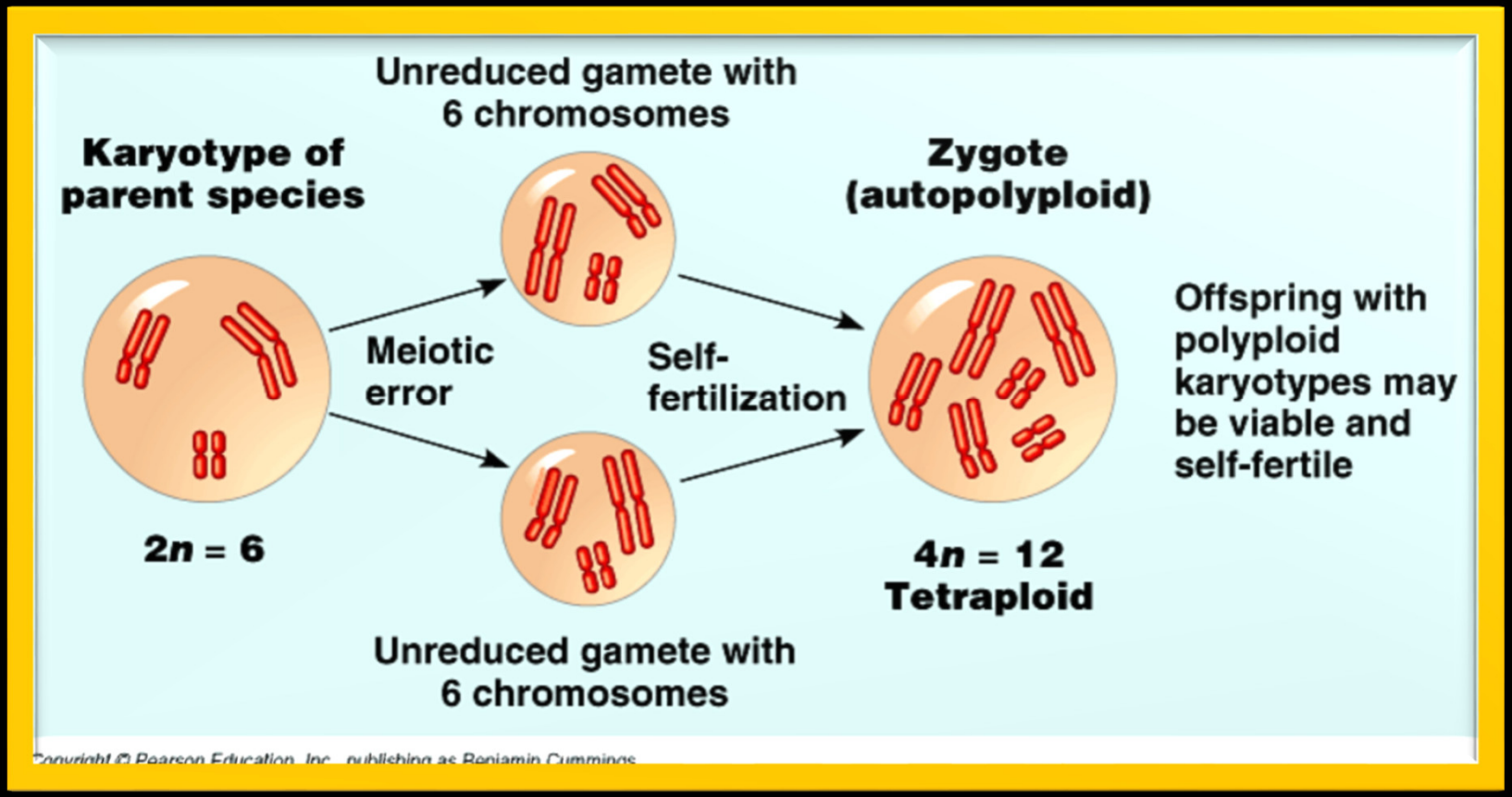
4-The xyy male.

Terminology for Variation in Chromosome Numbers

Term	Explanation
Aneuploidy	$2n \pm x$ chromosomes
Monosomy	$2n - 1$
Trisomy	$2n + 1$
Tetrasomy, pentasomy, etc.	$2n + 2$, $2n + 3$, etc.
Euploidy	Multiples of n
Diploidy	$2n$
Polyploidy	$3n$, $4n$, $5n$, . . .
Triploidy	$3n$
Tetraploidy, pentaploidy, etc.	$4n$, $5n$, etc.
Autopolyploidy	Multiples of the same genome
Allopolyploidy (Amphidiploidy)	Multiples of different genomes

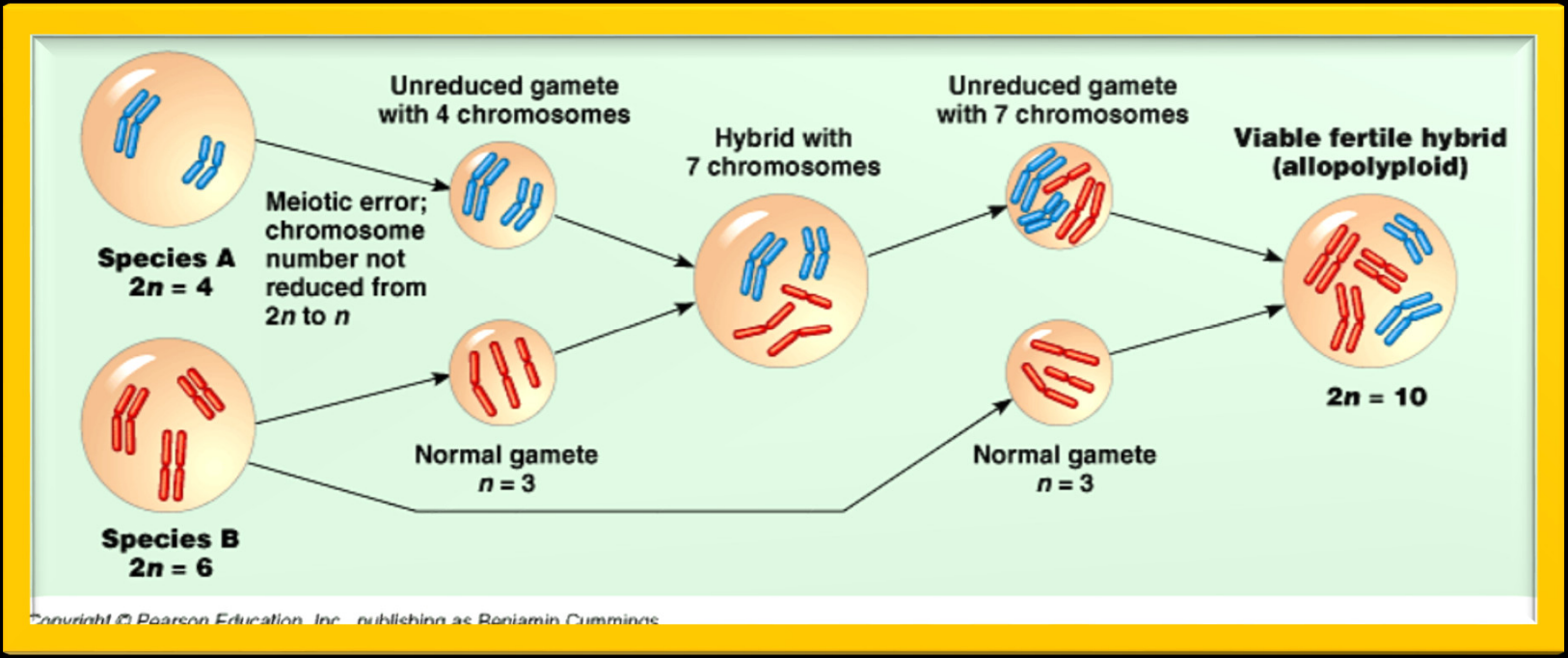
AUTOPOLYPLOID

An organism that has more than two sets of chromosomes, but all sets are derived from the same species.



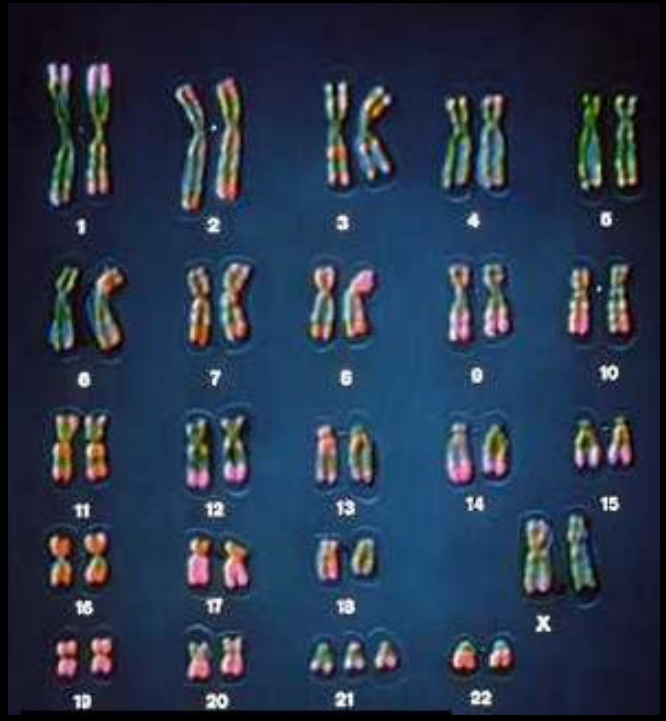
ALLOPOLYPLOID

This is the production of a polyploid species from the contributions by two different species.



DOWN SYNDROME TRISOMY,21)(47,XX OR XY+21)(

- It is a common autosomal trisomy among live –born children ,it has frequency of about 1 in 800 of live birth .
- It doesn't usually run in families and it increases with the mother age.



PSYCHOLOGICAL SYMPTOMS

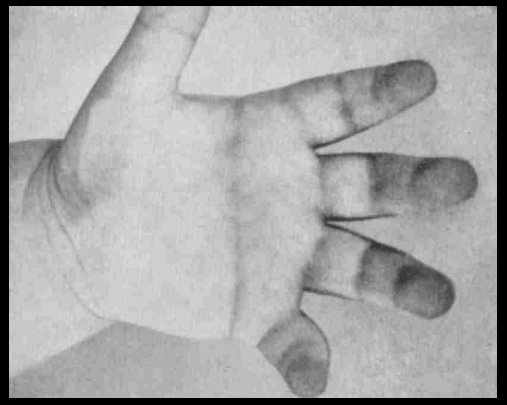
- Children with this syndrome are invariably mentally retarded.

- There is similarity between people with Alzheimer disease and adults ”over 30” with down syndrome . They share memory loss, confusion, anxiety ,and lost of ability to perform simple tasks like dressing or feeding .

The physiological symptoms

- There are of small statures due to delayed maturation of the skeletal system and their muscle tone is poor.
- They have a characteristic face appearance. It is broad and flat with a small nose ,irregular teeth, abnormally shaped ears and thick lips .
- Many of them have peculiar small fold of skin across this inner part of the eye this gives the eyes a slightly oriental look. The name “mongolism” is derived from this characteristic .

- They have large furrowed tongue.
- 40%of children with the syndrome have major heart defects.
- Defects of kidneys ,thyroid gland and Adrenal glands are so common with this syndrome.
- Some highly usual dermatoglyphic (glyphic=craving) patterns of hand creases ,fingerprints and foot prints are also associated with this syndrome.

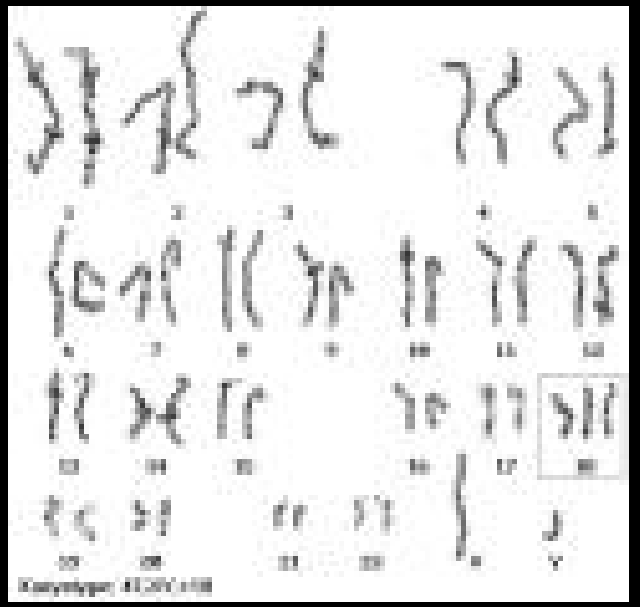


- Hipbones are abnormally shaped and the feet's little fingers often short and curved inward.
- Males have poorly developed genitals and Are invariably sterile,in females ovarian defects and irregular menstruation but fertility is possible.
- Many children learn to talk but speech is usually thick and harsh sounding ,perhaps in part because of hearing defects.

G. 1.14 Clinical photographs show several minor anomalies associ-
Brushfield spots. C, simian crease. D, wide space bet
second toes. E, short fifth finger. F, small ears.

EDWARDS SYNDROME (TRISOMY18),(47,XX OR XY+18)

- This syndrome affects about one in 4,500 Live-born children.
- Approximately 65 % of those individuals are females ,males with the syndrome are more likely to undergo spontaneous abortion.
- Karyotype:(47,XX or XY+18) means having extra 18 chromosome.



SYMPTOMS

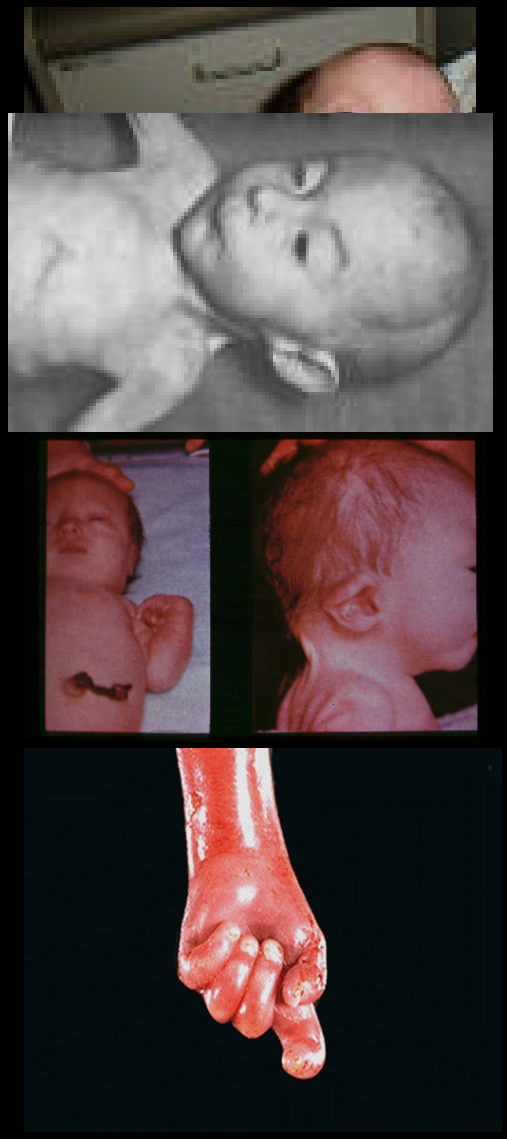
- They have multiple abnormalities including severe mental and physical retardation.

  Such as :

  1-elongated skull with low set malformed ,sometimes pointed ears ,their jaw and oral cavity is small .

  2-They carry their fingers in an abnormal position with the second finger overlapping the third.

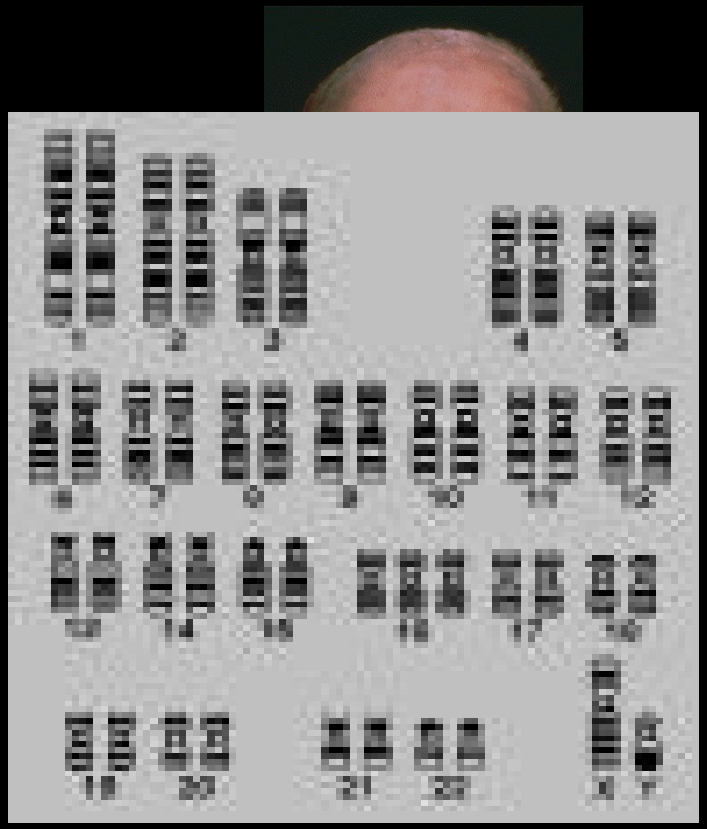
- Life expectancy of males is about 3 months ,in affected females it is about nine months.



TRISOMY 16 (47,XX OR XY+16)

- Virtually no live –born babies having trisomy 16 are seen, cause this trisomy is often encountered in early abortuses
- Karyotype:

47 chromosome including an extra chromosome which is chromosome number 16

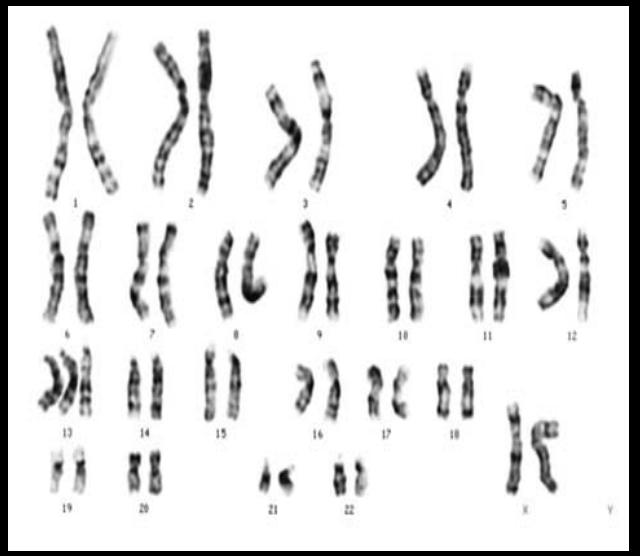


Patau's Syndrome (Trisomy 13)

- It occurs in about one in 5,000 live births.
- Affected children rarely survive more than3-4 moths after birth .
- Karyotype:

(47, XX or XY +13) Having extra 13 chromosome is the reason for that abnormality.

- Affected children are severely retarded both mentally and physically.



PHYSICAL SYMPTOMS

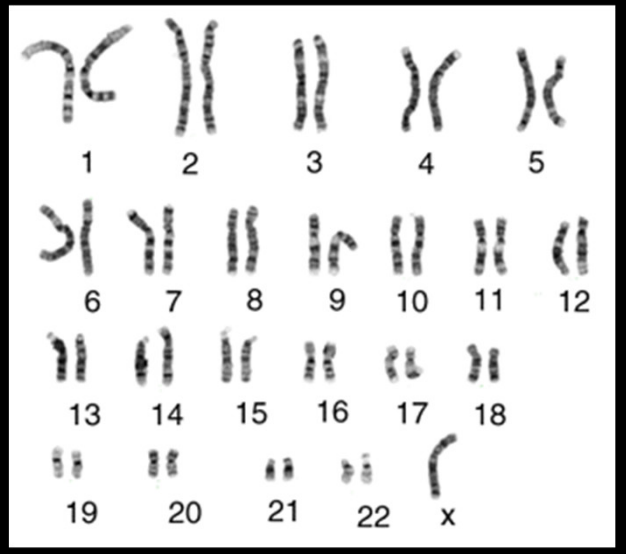
- Small skull and eyes.
- The ears are often malformed and deafness in common.
- Many have malformed thumbs and extra digits.
- 70%have heart defects.

Sex Chromosome Aneuploidy

1-Turner Syndrome (Monosomy X)

- It has Frequency of about 1 in 2,500 to 10,000 of live –borne females.
- Karyotype:

  (45, X-X) affected females with this syndrome has only 45 chromosomes, the missing chromosome is X.



Psychological and physical symptoms

- Affected women of this type are quite normal intelligence and may be rather bright, They are normal in appearance in addition to the failure of the secondary sexual Characteristics to develop. Such women:

1-tend to have short stature .

2-widely spaced nipples and a characteristic Shape of chest called a (shild chest)

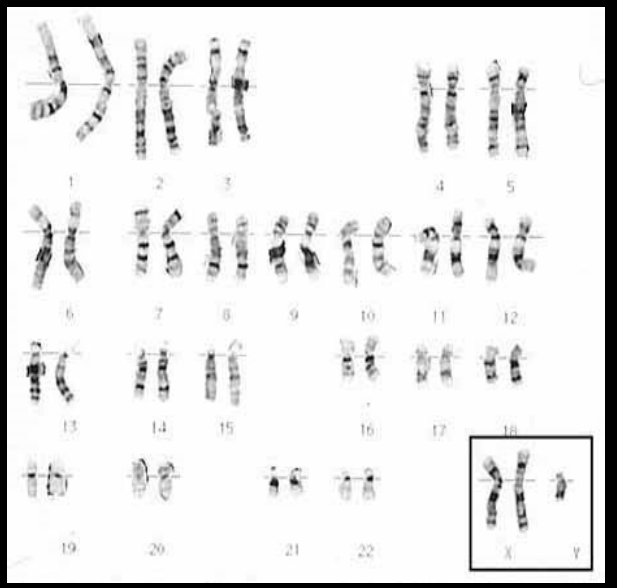
3-at birth there maybe folds of skin at a neck. Older children will usually manifest a flaring of the neck as it joins the shoulders.

4-infertility because of having primitive streak gonads that lack both germ cells and hormone-producing tissues. The oviducts, uterus, and vagina remain small and immature.

2-KLINEFELTER,S SYNDROME

- This syndrome affects about one of every 500 male berth.
- Karyotype:

  These men have two X chromosomes



- About 10%of males with klinfelter syndrome exhibit karyotypes that are different from the usuall(47,xy+x).these include(48,xy+xx),(48,xy+xy), (49,xyxxx),and(49,xy+xxy).

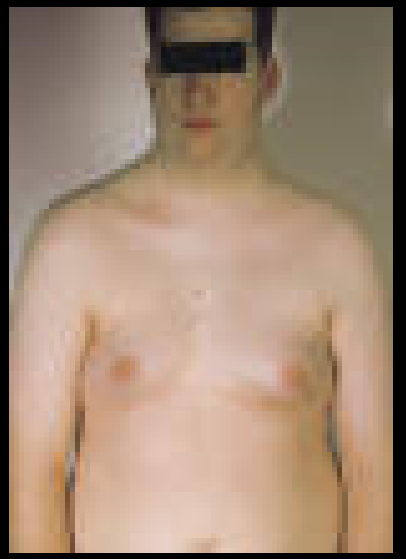
Physical and psychological symptoms

- Having more than one X will not necessarily direct development to ward femaleness, since the presence of a y along with two x's will cause the individual to develop into male.
- The individuals appears as normal bodies until the onset of puberty at this time special physical characteristic are shown such as:

1-partiall breast development.

2-sightly altered set of bodily proportion.

3-narrow shoulders and larger hips than are typical of the normal male.



NOTES

- Having the wrong number of chromosome has serious usually lethal, consequences.
- Autosomal monosomies have even more catastrophic consequences than trisomies.

- These abnormalities must be the consequence of an imbalance in the levels of gene products encoded on different chromosome at trisomies ,make a smaller change then monosomies in those levels.

- Alterlling they relative numbers of chromosomes will affect interactions between the gene products thus effecting normal development and function.
- Trisomic embryos survive longer than monosomic ones and trisomies 13,18 and 21 are compatible with survival until (birth).
- These three (chromosomes seem to be relatively poor in genes).
- Having the wrong number of chromosome has far fewer ill effects than having the wrong number of an autosomes.
- Aneuploidy mosaics are common.