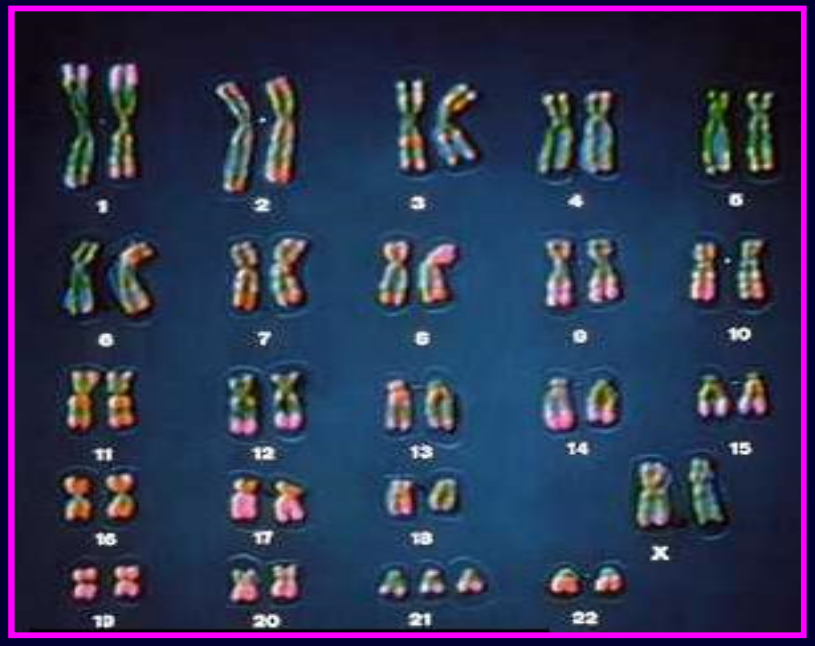
Chromosomal Aberration - Numerical



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THE INTRODUCTION

- In 1956, J. H. Tjio and A. Levan established the human chromosome number as 2n=46. This observation was confirmed by other scientists .
- In 1959, J. Lejeune and his coworkers Attributed the disorder Down syndrome to An abnormal chromosome number.
- Since that time ,many major physical and mental disorders have been linked to the Human chromosomal aberration.

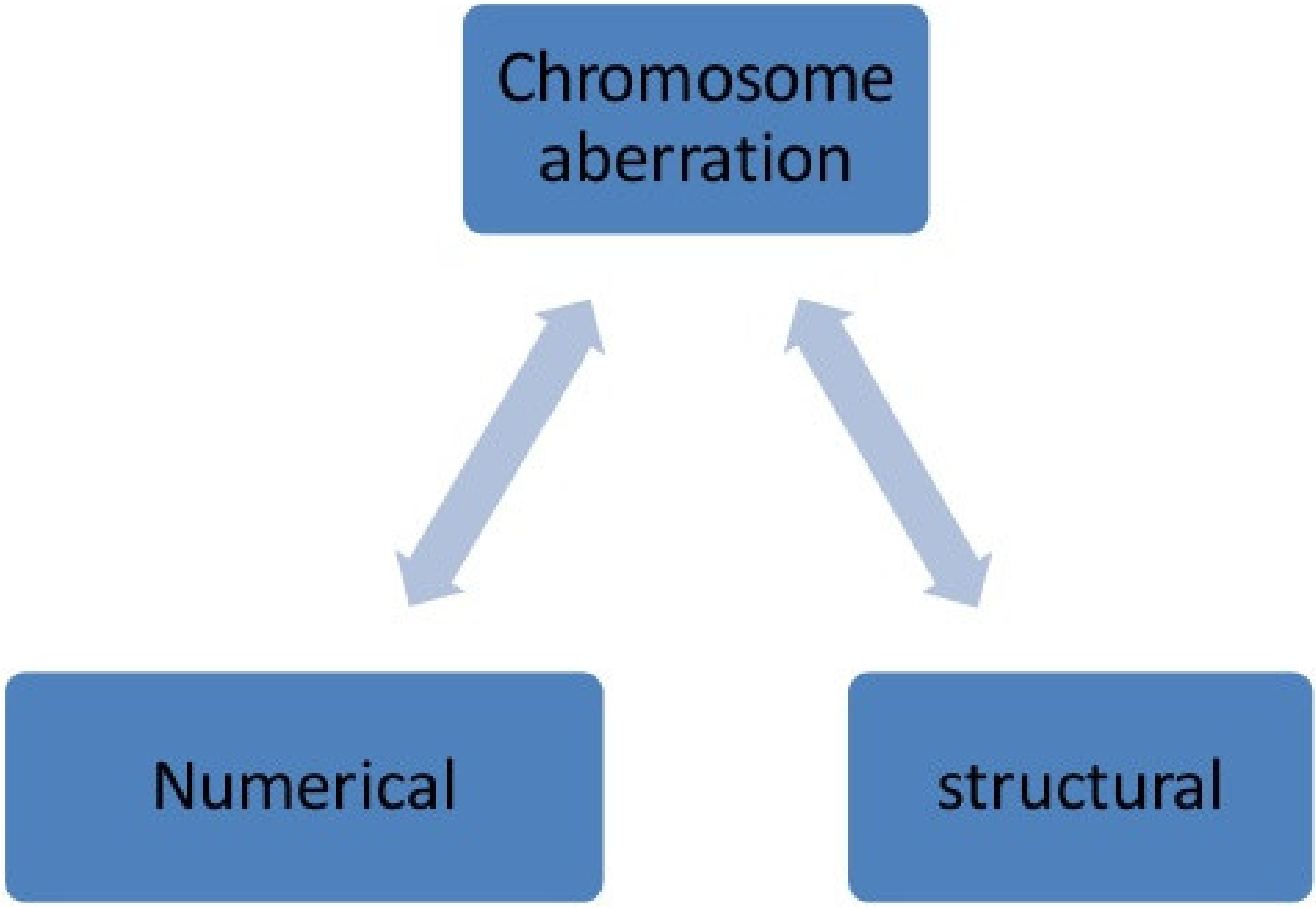
CHROMOSOMAL ABNORMALITIES

- Chromosome abnormality might be defined as changes resulting in a visible alteration of the chromosomes.
- Most chromosomal aberration are produced by disrepair of broken chromosomes, by

  improper recombinatiton or by

  malsegregation of chromosomes during mitosis or meiosis.
- Chromosomal abnormalities mostly fall into two categories:

  - Numerical chromosomal abnormality.
  - Structural chromosomal abnormality.



Variation in chromosome structure or number is called chromosomal aberration

Chromosomal abnormalities

constitutional

(present in all cells of the body)

Mosaic

(present in only certain cells or tissues)

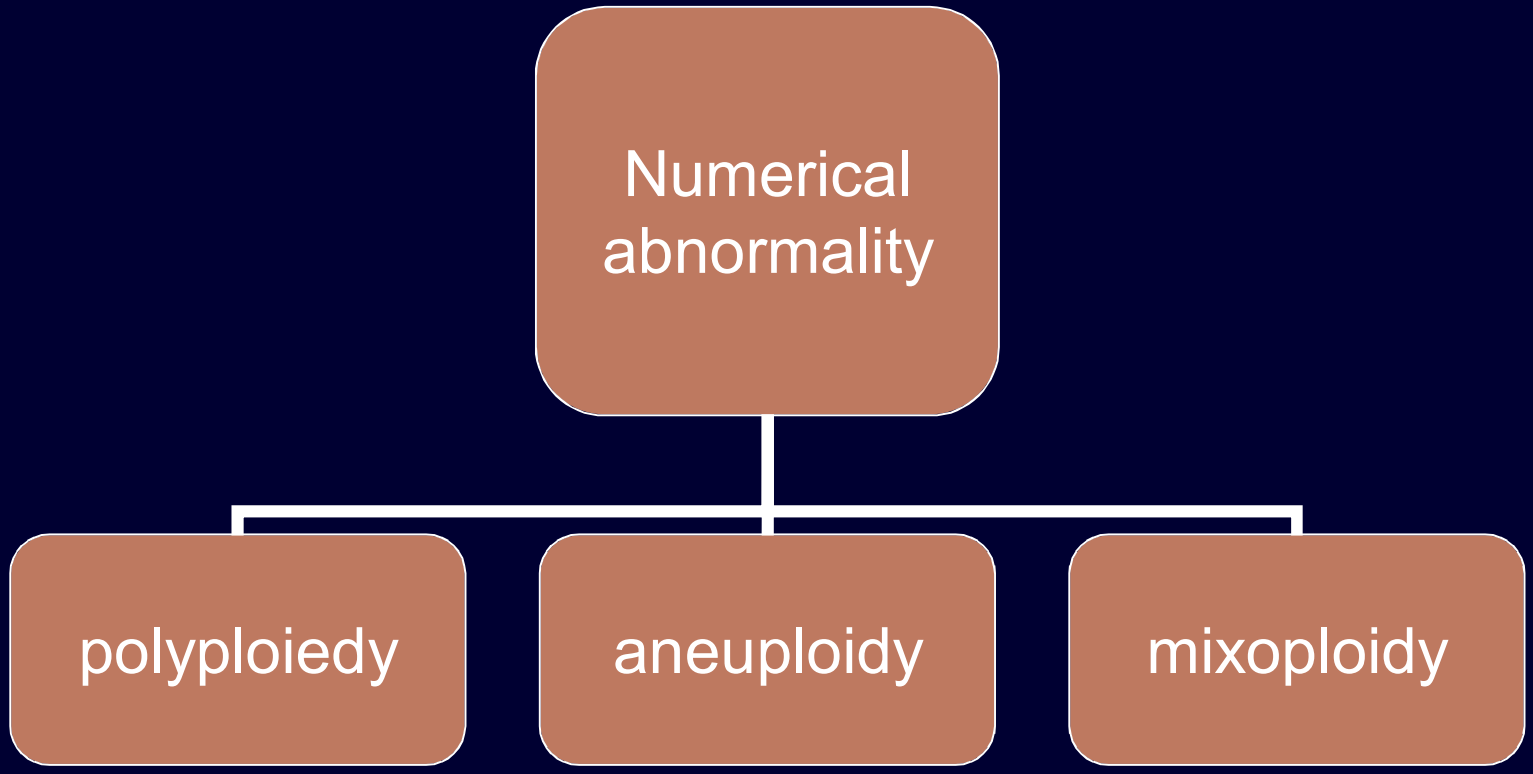
- Constitutional abnormalities must have been present very early in development.
- By contrast ,an individual with somatic abnormality is a mosaic .

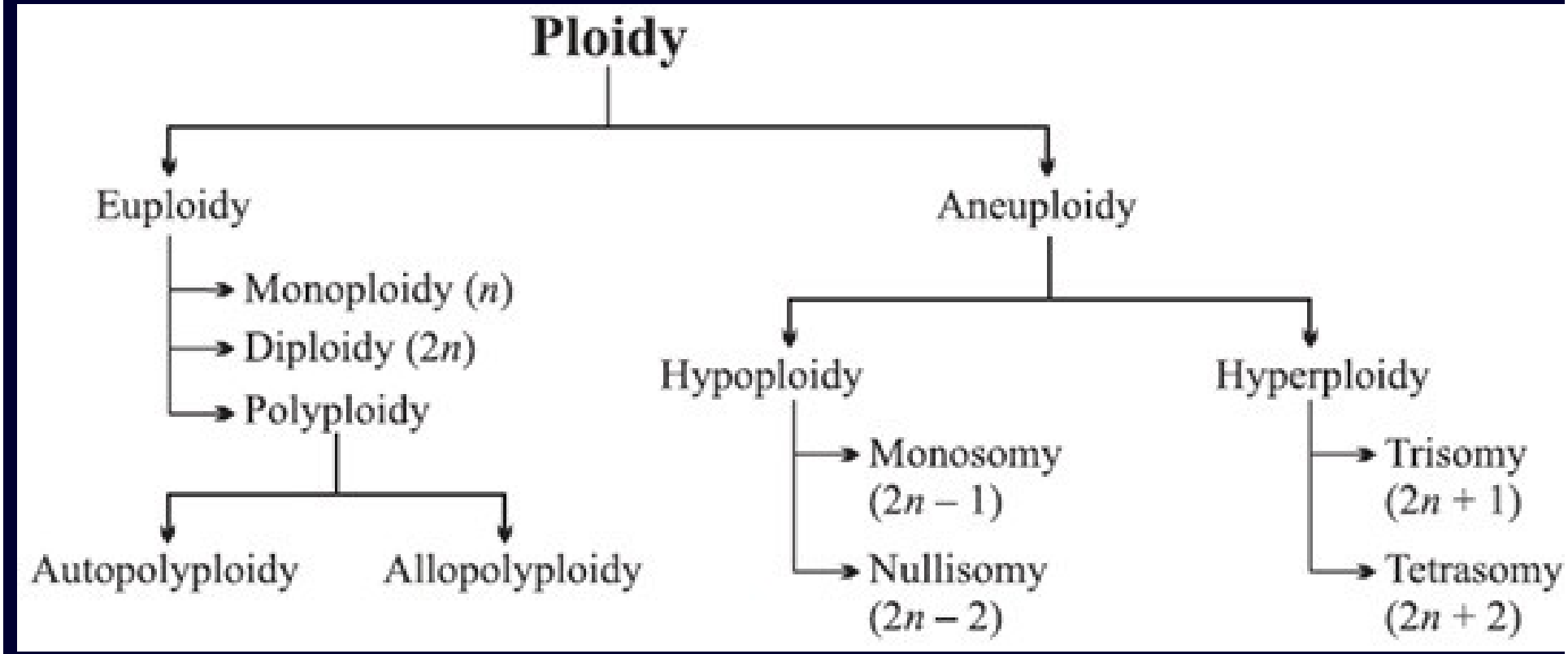
NUMERICAL CHROMOSOMAL ABNORMALITY

- This abnormality defined as addition or loss of whole chromosomes in the human cells.

- Some complex of symptoms such as morphological, physiological, and psychological deviations from normal can be associated with numerical abnormalities.

There are three classes of numerical abnormality:




Ploidy
Euploidy
Monoploidy (n)
Diploidy (2n)
Polyploidy
Autopolyploidy
Allopolyploidy
Aneuploidy
Hypoploidy
Monosomy (2n – 1)
Nullisomy (2n – 2)
Hyperploidy
Trisomy (2n + 1)
Tetrasomy (2n + 2)

A-POLYPLOIDY

- It means having more sets of chromosome than normal cells
- This class contains two types of abnormality:

1-Triplody:

(1-3)% of recognized human pregnancies are triploid.

The most usually cause is :two sperm fertilizing a single egg (dispermy) or the gamete may be a diploid gamete.

Triploids very seldom survive to term.

2-Tetraploidy:

Which is much rarer and always lethal, it is due to failure to complete the first zygotic division.

B- ANEUPLOIDY

- Identified as having one or more individual chromosomes extra or missing from an euploid set.
- Aneuploid can be trisomy, in other wise diploid cell is better tolerated than monosomy.

Aneuploid cells arise through two main mechanisms

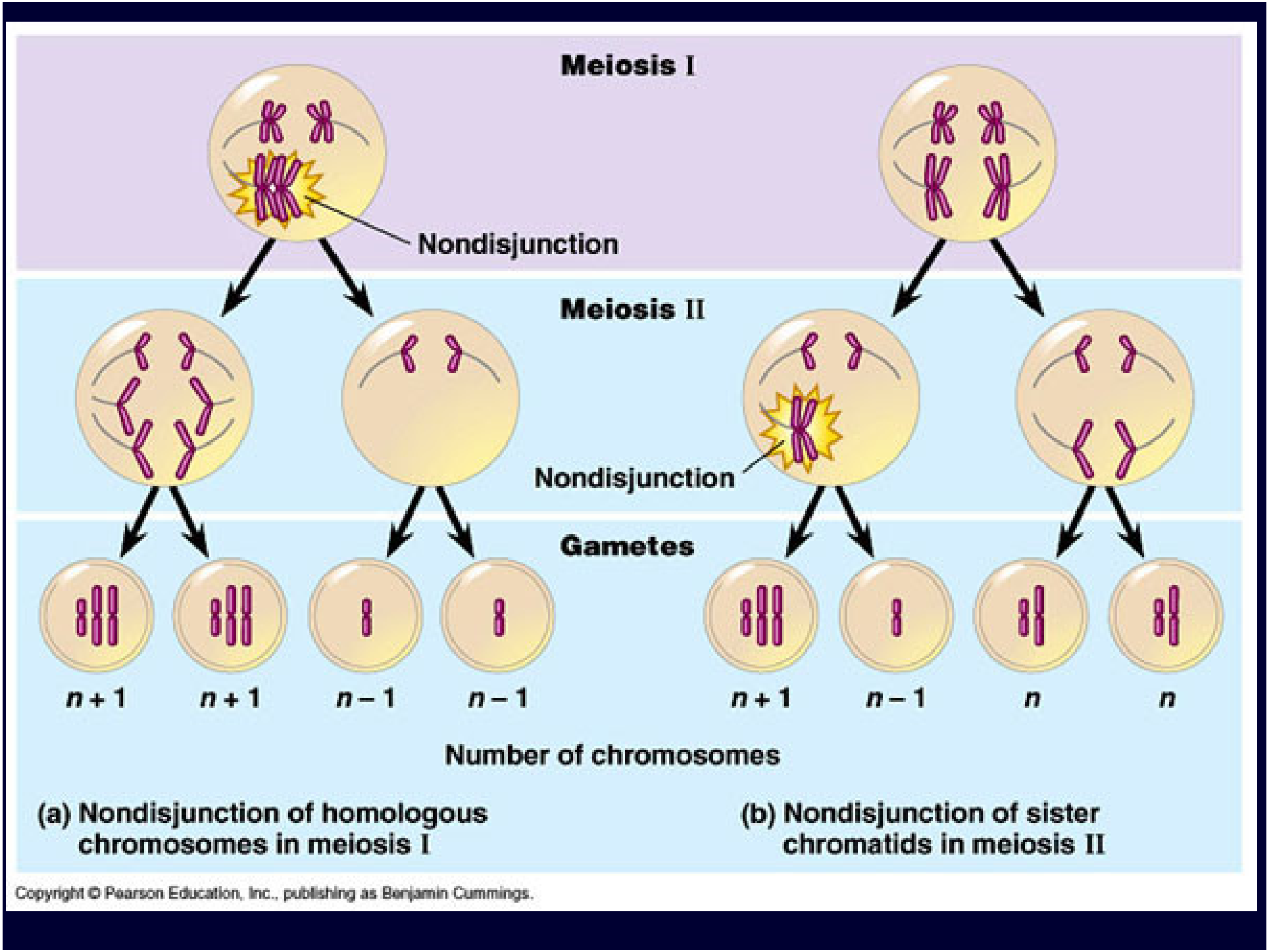
1-Nondisjunction

Failure of homologous chromosomes to separate in anaphase of *meiosis*(1) or failure of sister chromtids to disjoin on either *meiosis* (2)or at *mitosis* .

Nondisjunction in *meiosis*

gametes (22 or 24)chromosomes

normal gamete trisomic or monosomic zygote



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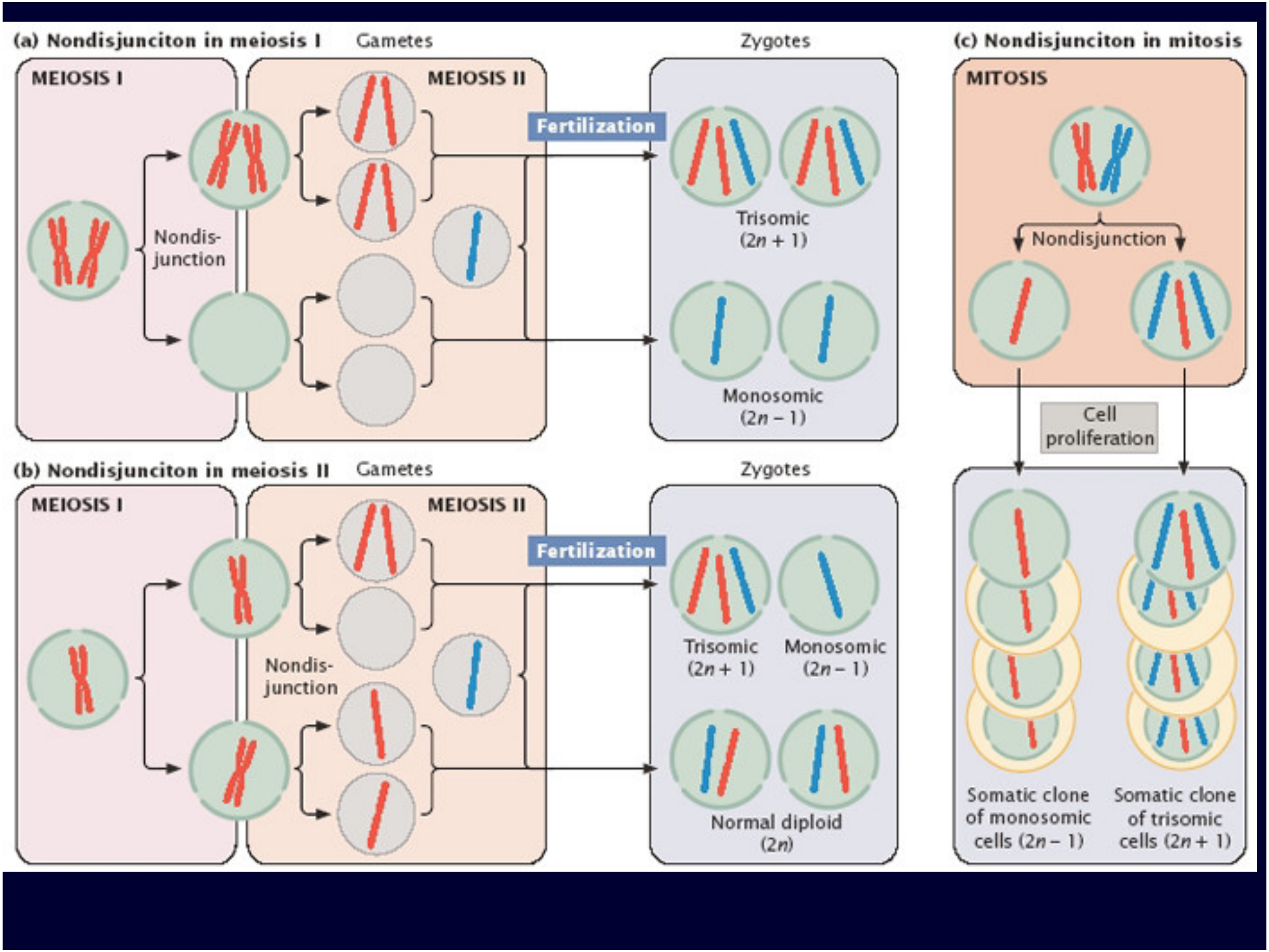
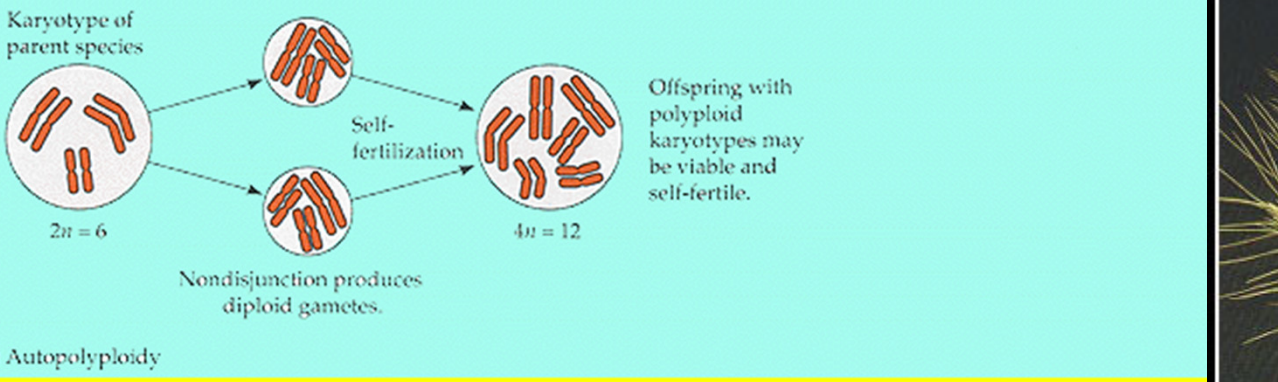
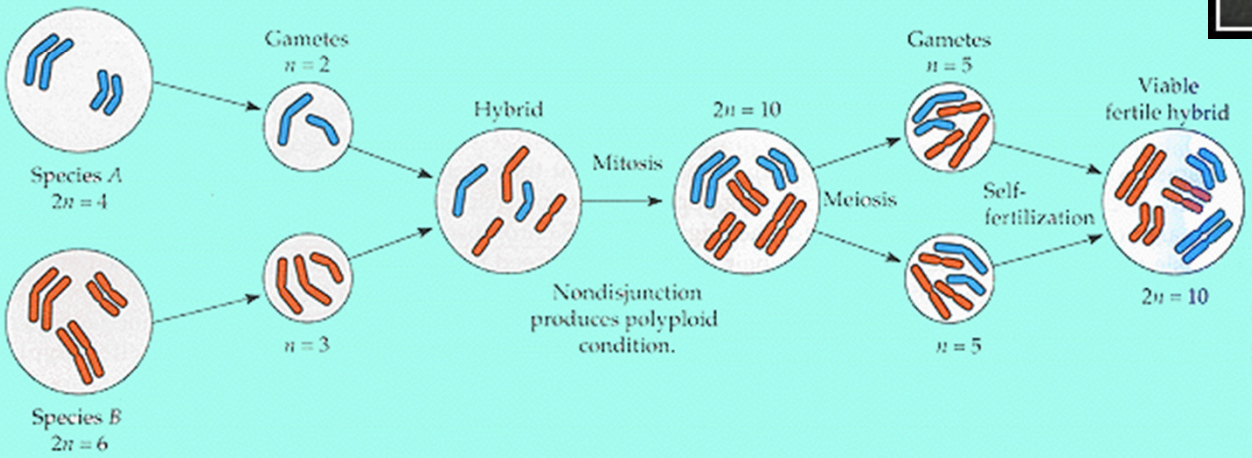
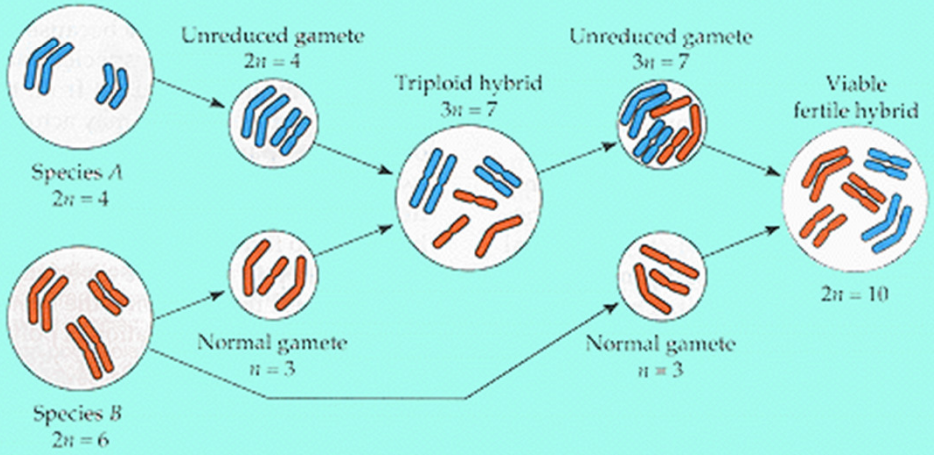

(a) Nondisjunciton in meiosis I
Gametes
Zygotes
(c) Nondisjunciton in mitosis
MEIOSIS I
MEIOSIS II
MITOSIS
Fertilization
Nondis-
junction
Trisomic
(2n + 1)
Monosomic
(2n – 1)
Nondisjunction
Cell
proliferation
(b) Nondisjunciton in meiosis II
Gametes
Zygotes
MEIOSIS I
MEIOSIS II
Fertilization
Nondis-
junction
Trisomic
(2n + 1)
Monosomic
(2n – 1)
Normal diploid
(2n)
Somatic clone
of monosomic
cells (2n – 1)
Somatic clone
of trisomic
cells (2n + 1)



(a) Autopolyploidy





(b) Allopolyploidy

MEIOTIC NONDISJUNCTION:

Failure of two members of a chromosome pair to separate (disjoin) during meiosis so that both go to one daughter cell and none to the other.

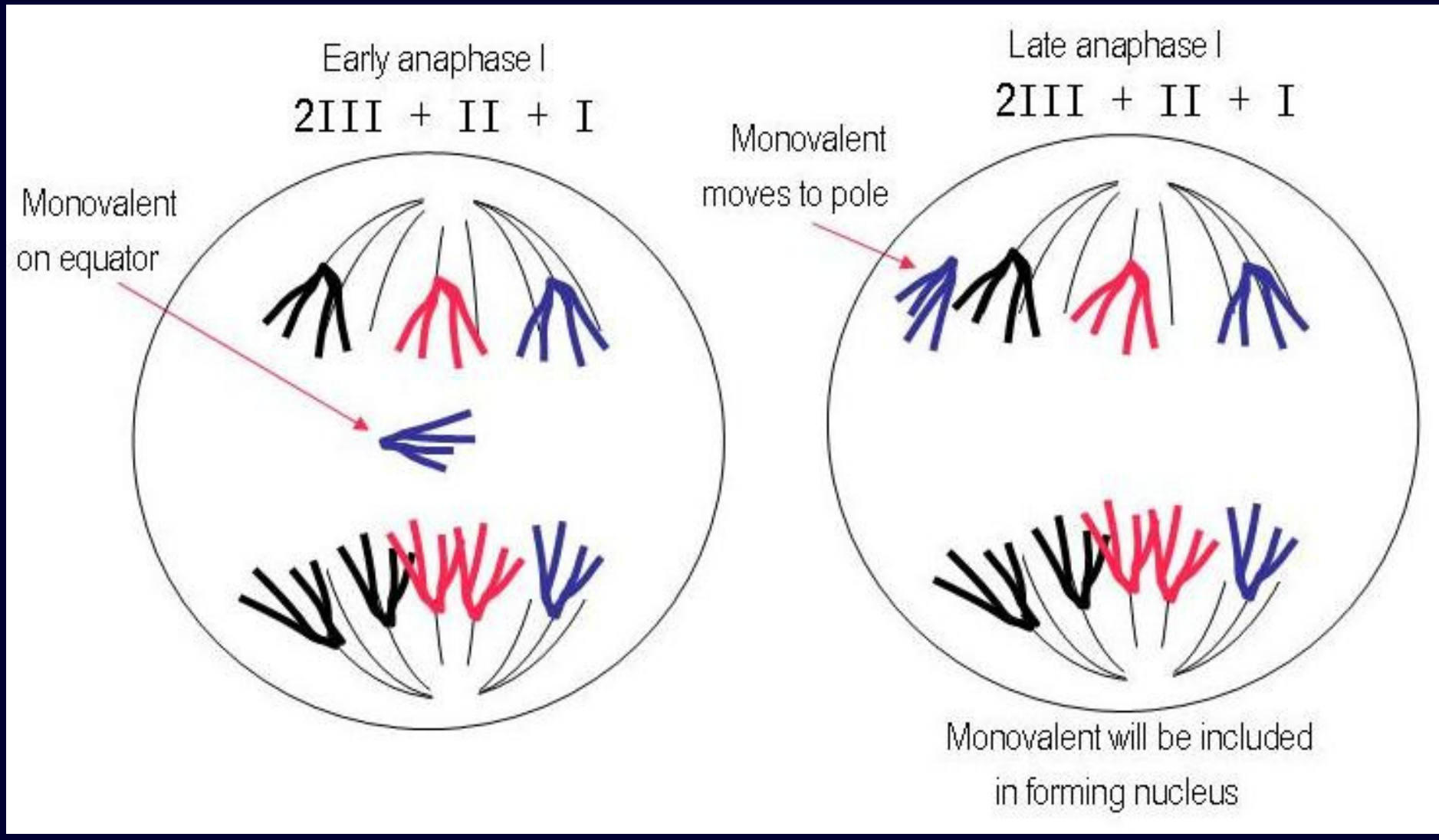
This mechanism is responsible for the extra chromosome 21 in trisomy 21 (Down syndrome)

For extra and missing chromosomes causing other birth defects and many spontaneous abortions (miscarriages).

2-ANAPHASE LAG

- failure of chromosome or chromatide to be incorporated into one of the daughter nuclei during anaphase so the chromosomes that do not enter the daughter cell nucleus are lost.

- Aneuploidy can be either in sex or autosomal chromosomes thus it can be distinguished in two types:
  - Autosomal Aneuploidy.
  - Sex chromosome aneuploidy.


Early anaphase I
2III + II + I
Monovalent
on equator
Late anaphase I
2III + II + I
Monovalent
moves to pole
Monovalent will be included
in forming nucleus

- 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.

C- MIXOPLOIDY

- Includes **mosaicism** (an individual possesses two or more genetically different cell line all derived from a single zygote) and

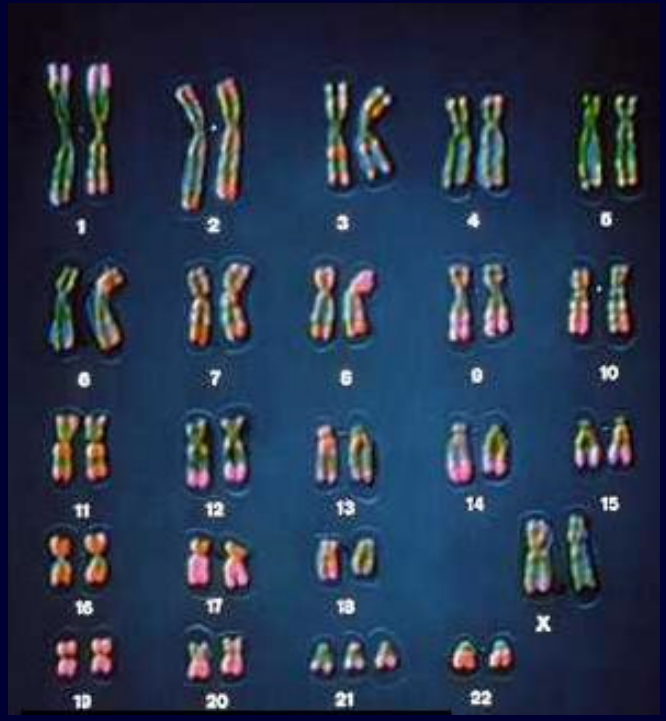
- **Chisnerism** (an individual has two or more genetically different cell lines originating from different zygotes)

Abnormalities that would be lethal in constitutional form may be compatible with life in mosaics.

AUTOSOMAL ANEUPLOIDY

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

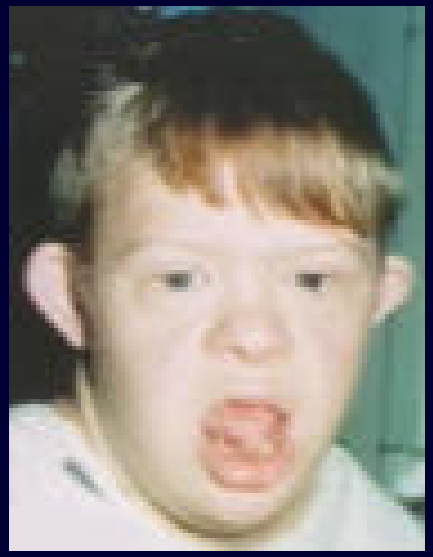
- Children with this syndrome are invariably mentally retarded.

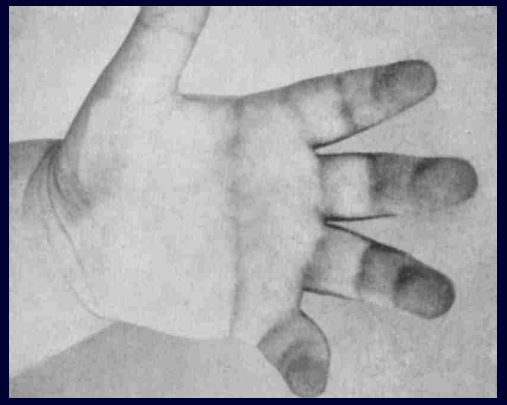
- There is similarity between people with Alzheimer disease and adults ”over 30” with down syndrome . They share memory loss, confusion, anxiety ,and lost of ability to perform simple tasks like dressing or feeding .

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.



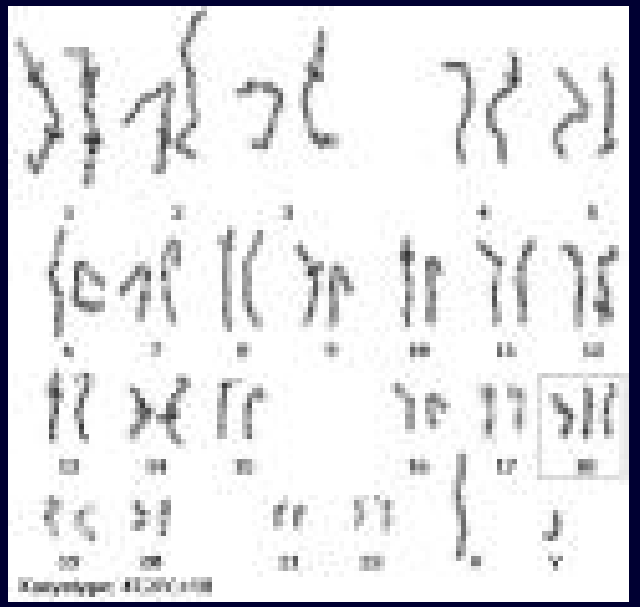


- Hipbones are abnormally shaped and the feet's little fingers often short and curved inward.
- Males have poorly developed genitals and Are invariably sterile,in females ovarian defects and irregular menstruation but fertility is possible.
- Many children learn to talk but speech is usually thick and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

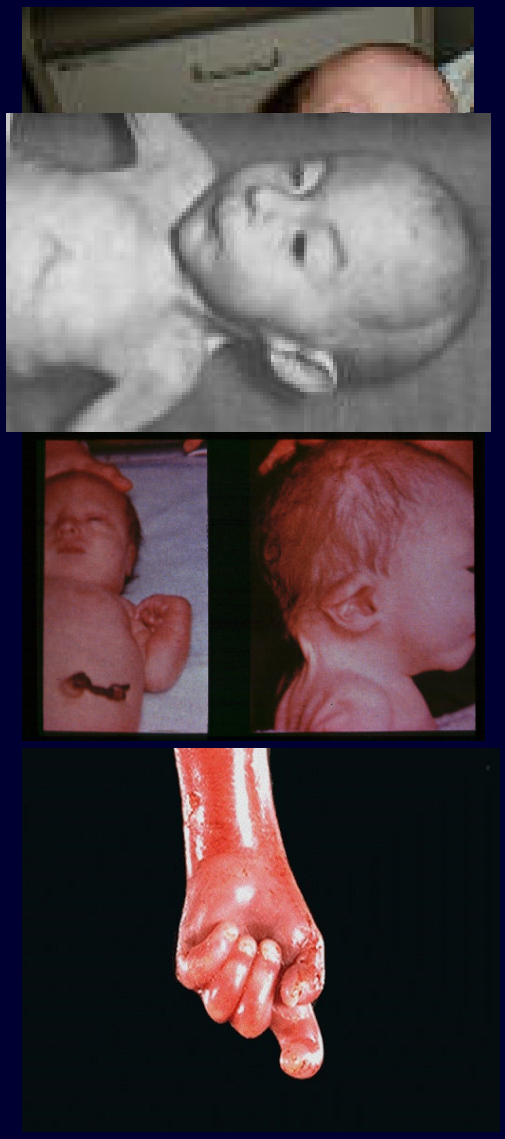
- They have multiple abnormalities including severe mental and physical retardation.

  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.

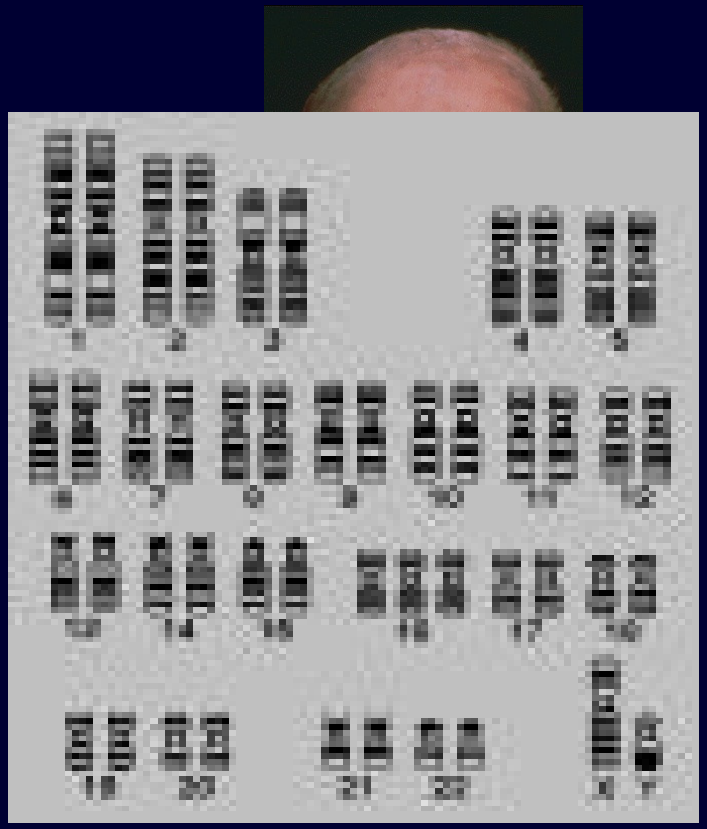
- Life expectancy of males is about 3 months ,in affected females it is about nine months.



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:

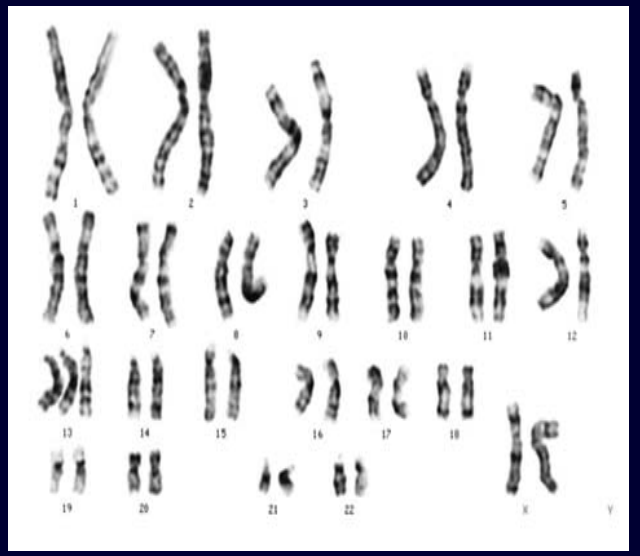
  47 chromosome including an extra chromosome which is chromosome number 16



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

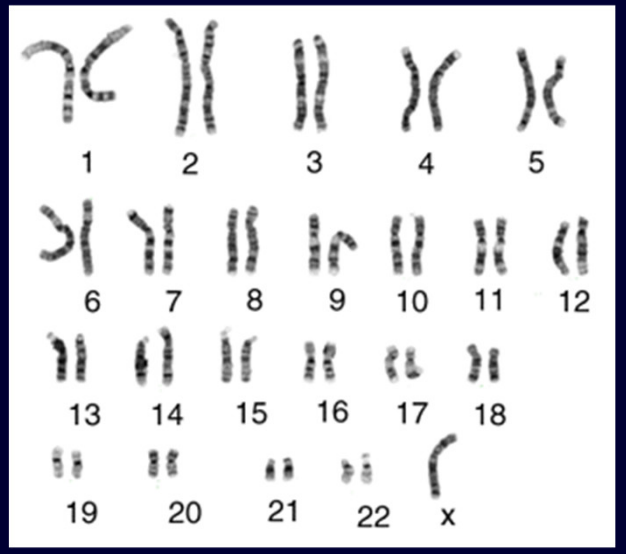
- Small skull and eyes.
- The ears are often malformed and deafness in common.
- Many have malformed thumbs and extra digits.
- 70%have heart defects.

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)

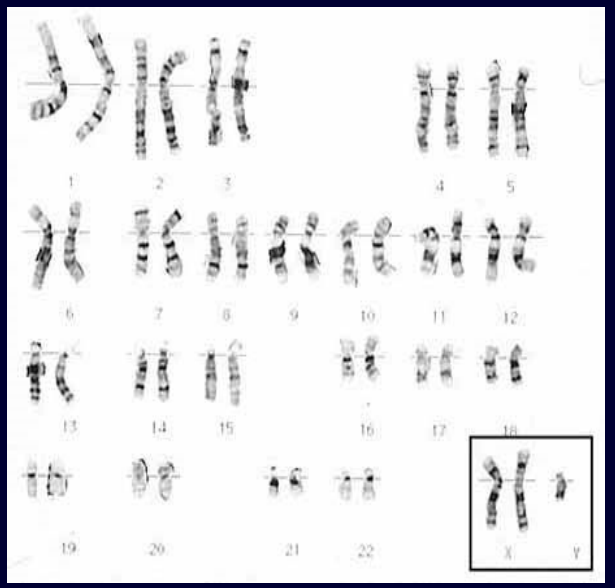
3-at birth there maybe folds of skin at a neck. Older children will usually manifest a flaring of the neck as it joins the shoulders.

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.

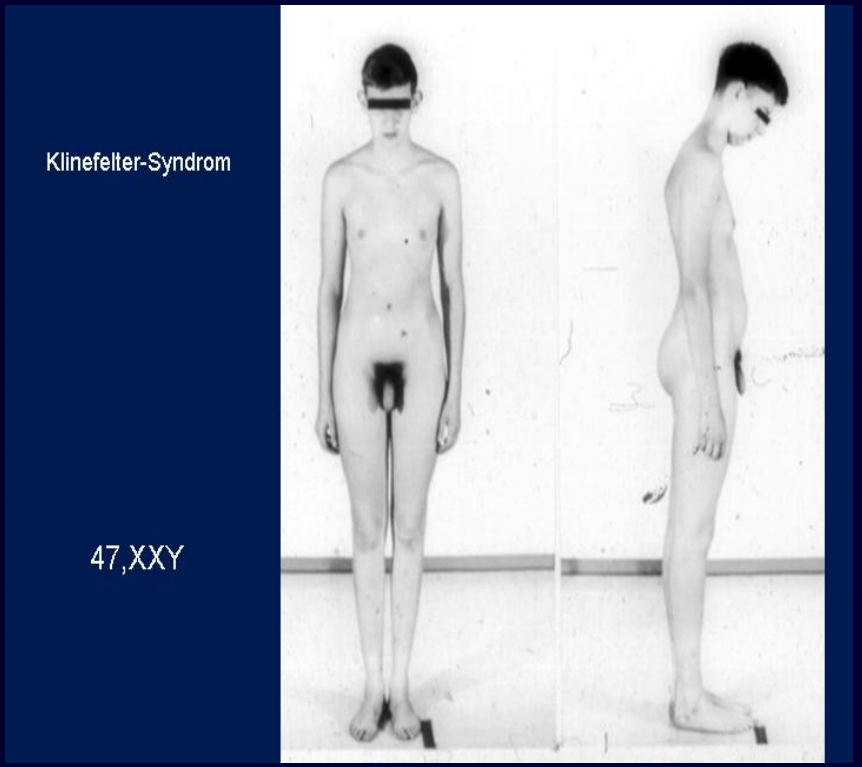
  2-sightly altered set of bodily proportion.

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

4-small testicles, the penis and scrotum are usually of normal size.

5-Infertility absence of sperms and androgens.

6-Such person maybe taller than average.

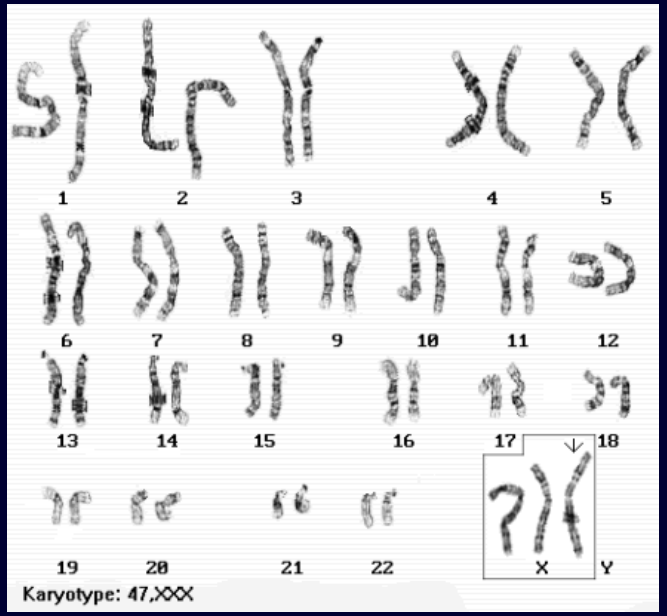


7-These individuals tend to show a slightly depressed intelligence.

- Klinefelter syndrome involving single cell lines of 48 or49 chromosomes seem to have more extreme problems of allsorts including severe mental retardations .

3-Female With (Trisomy X) And (Poly- Females)

- The frequency Of trisomy x female among new bornes is 1 in 10,000.
- They show no distinctive phenotype ,but some may have slightly lowered intelligence some of them have menstrual difficulties, many menstruate regularly and unfertile.



- Only 30 cases of 48,xxxx karyotype are found although normal in sexual development ,these female are severely retarded and also has a wide range of physical abnormality.

- Fewer 49,xxxxx females have been found in population of mentally retarded individuals.

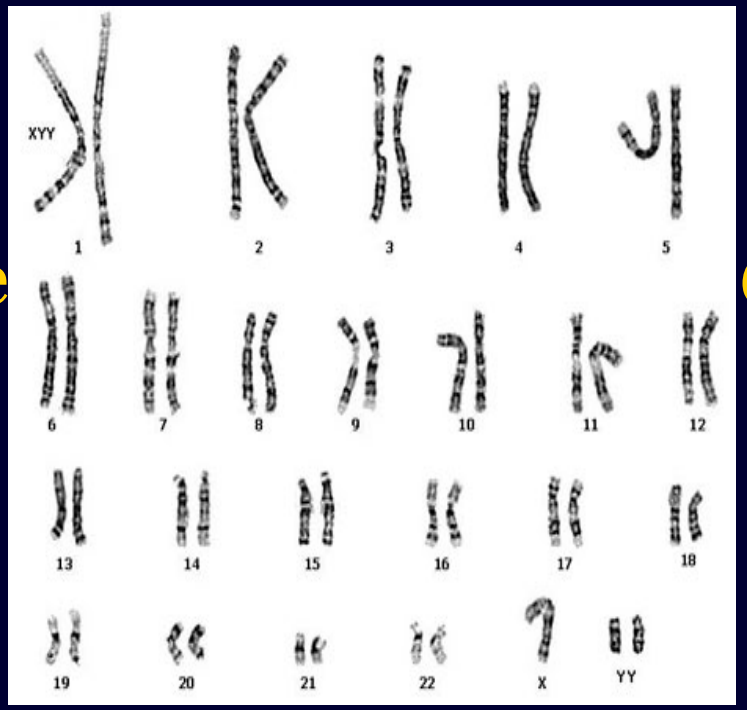
4-THE XYY MALE

- Karyotype :

  These males have 47 chromosome the extra chromosome is the y chromosome .

- Symptoms:

  1-twothirds of all affecte 6 feet tall.



2-Some of them show below –average intelligence. But they have no other distinctive Carachtristics.

Because chromosome y carries very few genes whose only important function is determine the male sex.

3-Such individuals might be innately more aggressive than normal and therefore more to run afoul of the low, a higher percentage of such men are found in prisons more than population many cases are known of xyy males who are of normal height ,intelligence and behavior.

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.