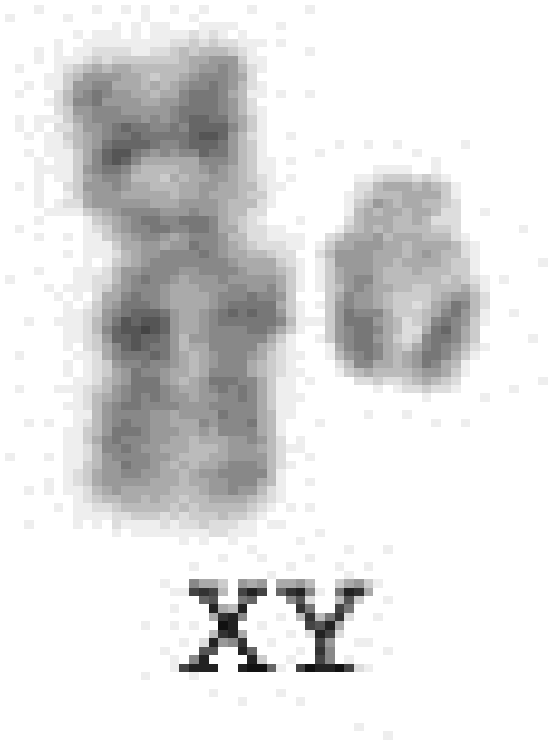
Learning Objectives

1-Know what is Single gene diseases?

2- Have an Idea about multifactorial diseases.

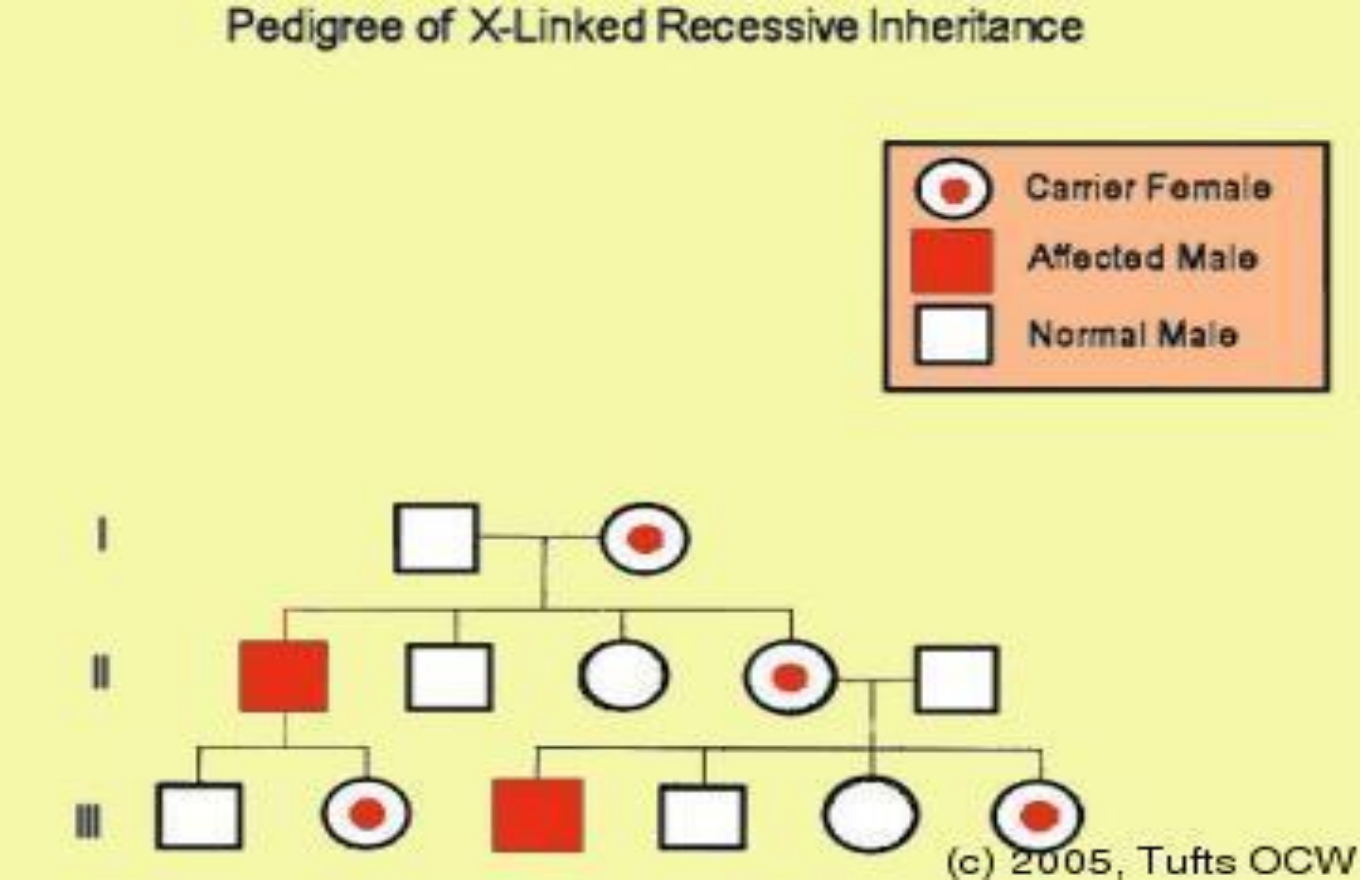
3- Define cytogenetic diseases and what are the types?

SEX LINKED DISEASES



3-X- linked recessive disorders:

- Manifest in males.
-Affected male does not transmit the disease to his sons, but all his daughters will be carriers.
- Carrier women can transmit the disease to 50% of her sons.
- Best known examples are hemophilia A, G6PD deficiency, and diabetes insipidus.

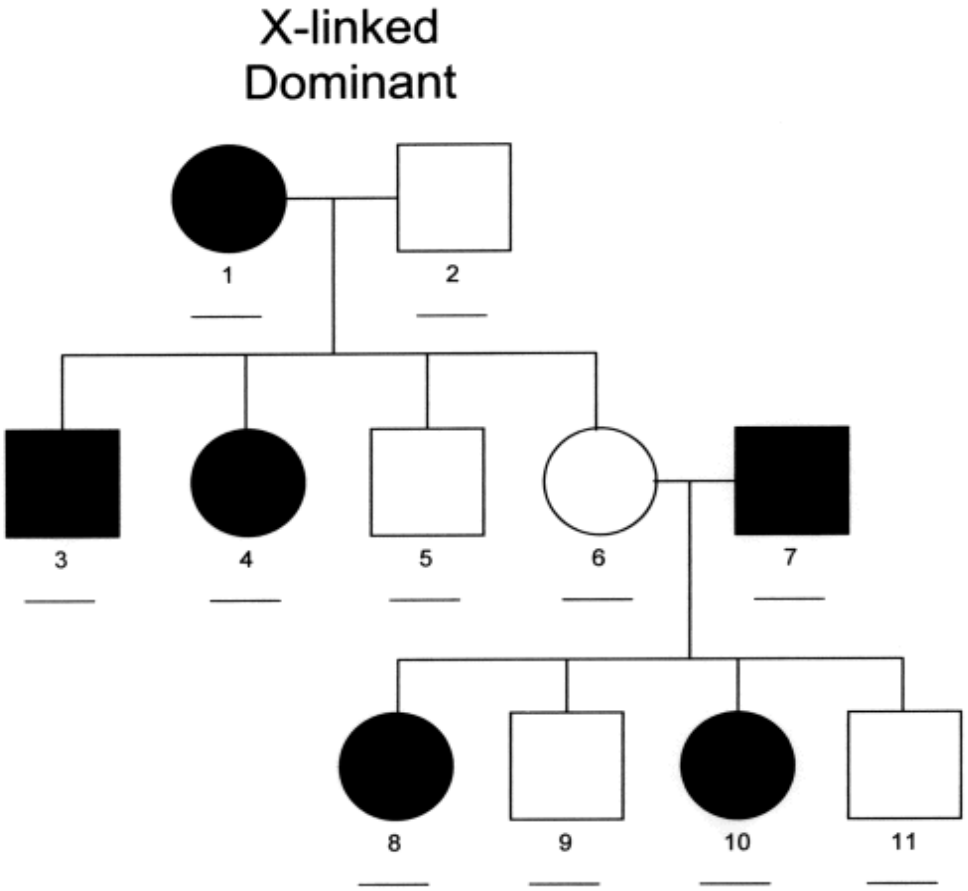

Pedigree of X-Linked Recessive Inheritance
Carrier Female
Affected Male
Normal Male
I
II
III
(c) 2005, Tufts OCW

A female is presented with an x-linked recessive disorder

EXPLAIN HOW?

4- X- linked dominant disorders:

- Affected heterozygous women transmit disease to 50% of her sons and daughters.
- Affected men can transmit the disease to all of his daughters but none of his sons will be affected.
- Vitamin D resistant rickets is a good example.


X-linked
Dominant
1
2
3
4
5
6
7
8
9
10
11

Multifactorial disorders:

It results from the combined actions of environmental influences and 2 or more genes.

- The rate of recurrence of the disorder for the first degree relatives (parents, offspring, and siblings) is between 2-7%.
- The risk for identical twins to have a disease is 20-40%.
- The risk is increased in siblings of index case that has severe phenotypic expression of the disease. For example, siblings are at risk of 2.5%to have cleft lip if the index case has a unilateral cleft lip, but are at 6% if the index case has bilateral cleft lip.
- The greater the number of relatives to have a disease, the higher the risk for relatives to have a disease in future.
- The risk of recurrence in subsequent pregnancies depends on the outcome of previous pregnancies.

Cytogenetic Disorders:

They are group of diseases in which there are abnormal number or structure of chromosomes.

Numerical abnormalities: It means abnormal number of chromosome.

Euploidy: 46, XX or 46, XY

Haploid: 23X or 23Y

Aneuploidy means any deviation in normal number of chromosomes mainly caused by nondisjunction.

- **Mosaicism** means the presence of 2 or more cell populations in the same individual results from mitotic nondisjunction after fertilization.
- **Chimera:** fusion of two different zygotes giving rise to single embryo

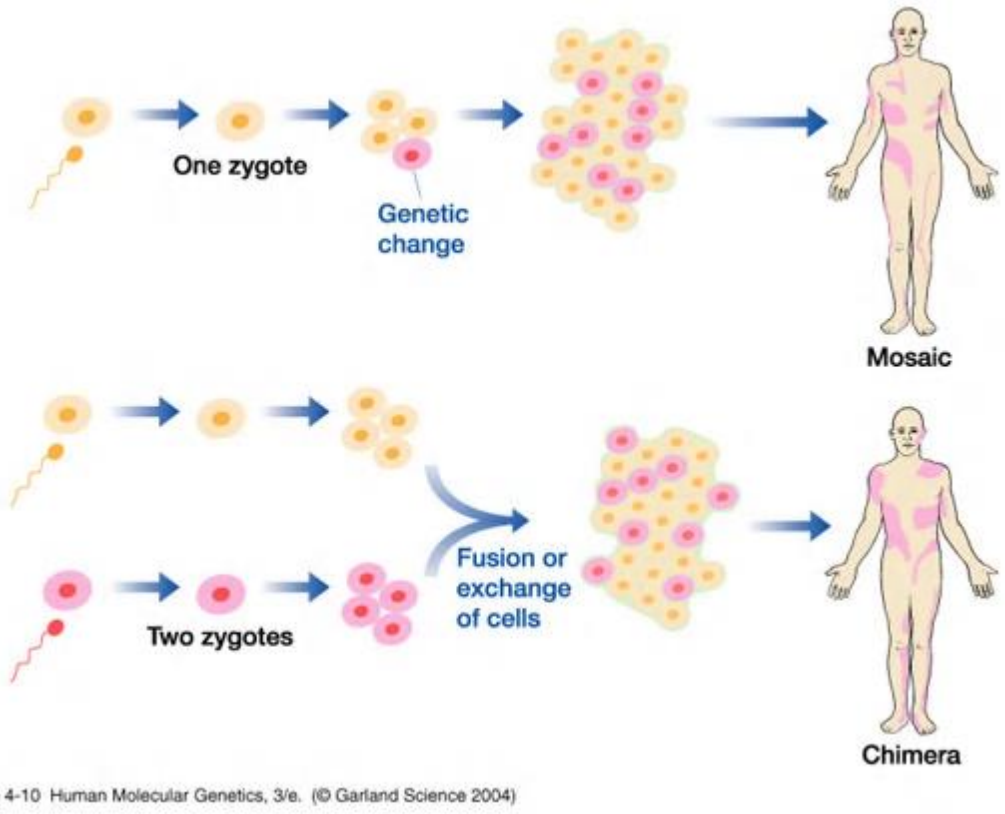


Figure 4-10 Human Molecular Genetics, 3/e. (© Garland Science 2004)

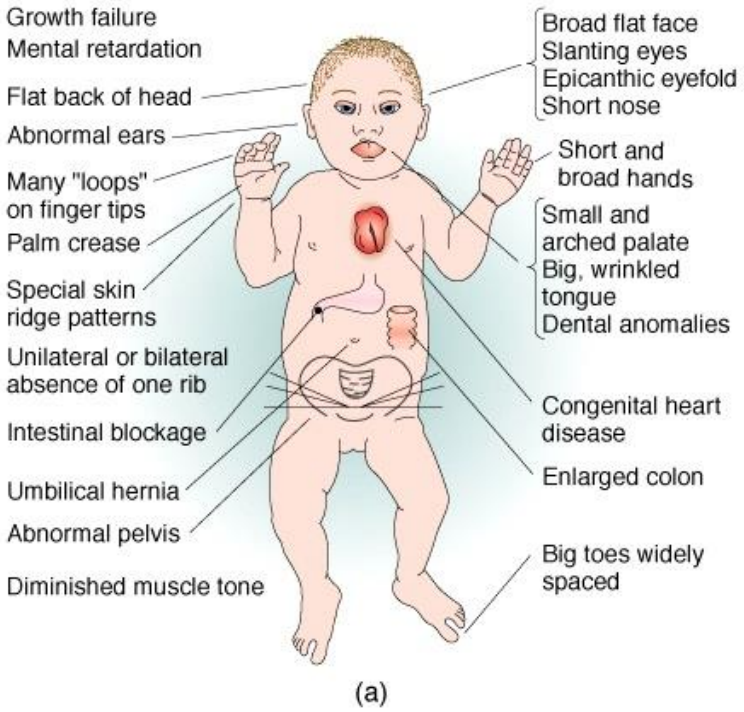
Down Syndrome

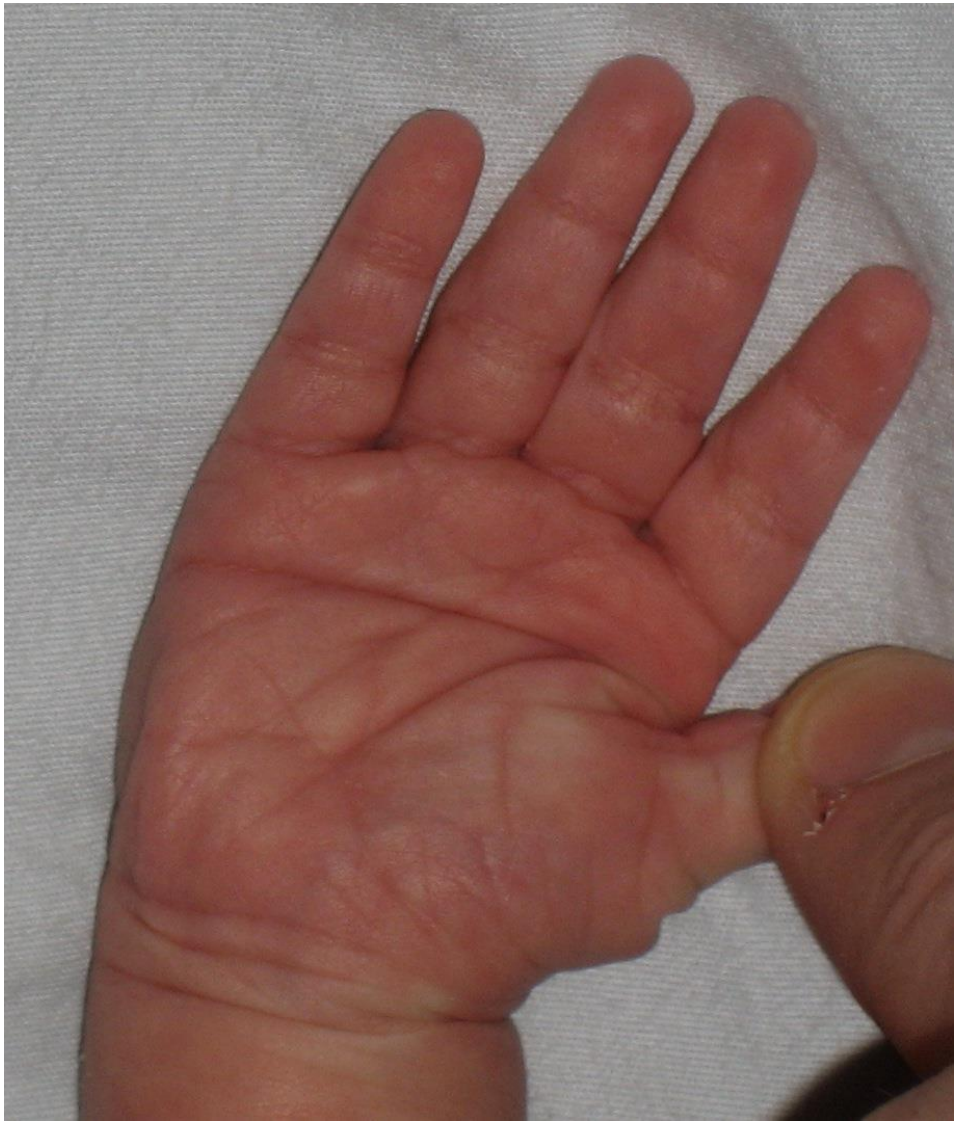
It is the most common form of chromosomal disorder and most common cause of mental retardation.

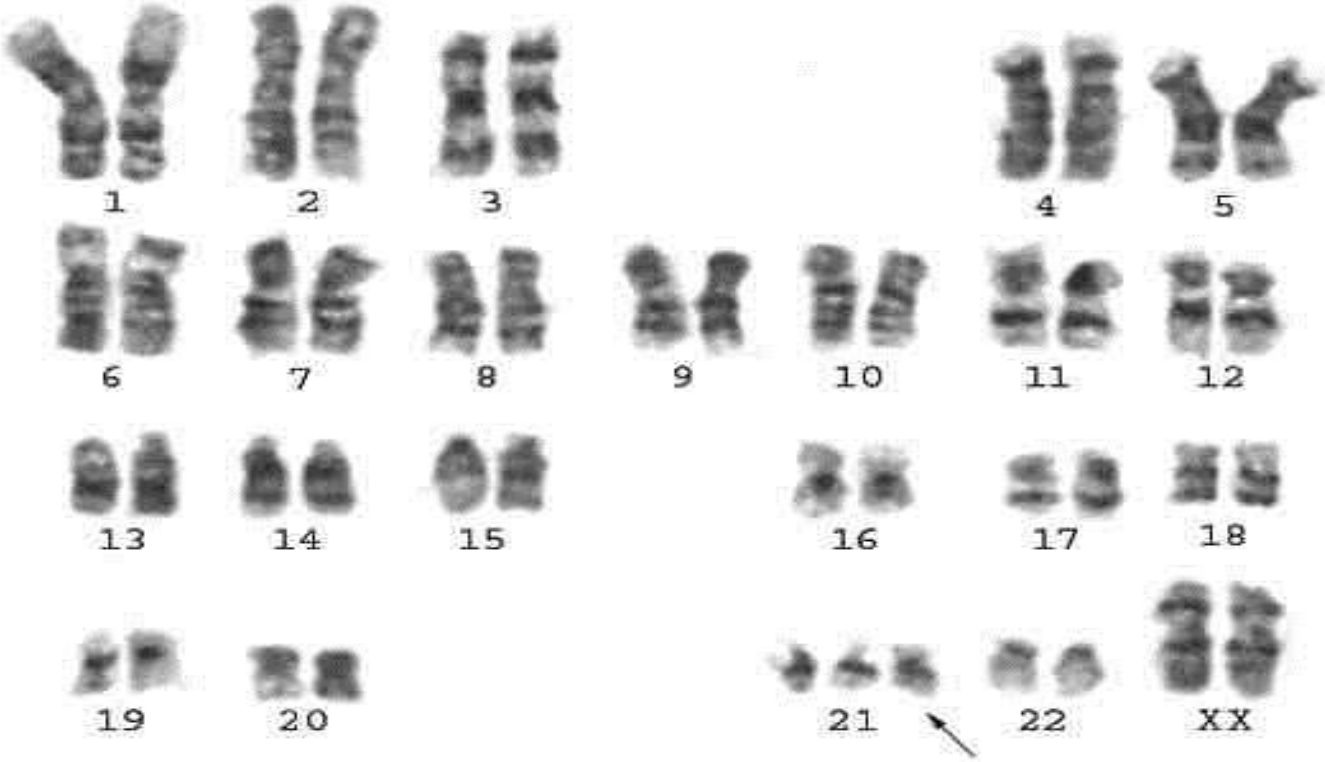
Ninety five (95%) of cases due to Trisomy 21 which occurs as a result of meiotic nondisjunction. Increased maternal age is most important factor for Trisomy 21.

Four% of cases are due to translocation.

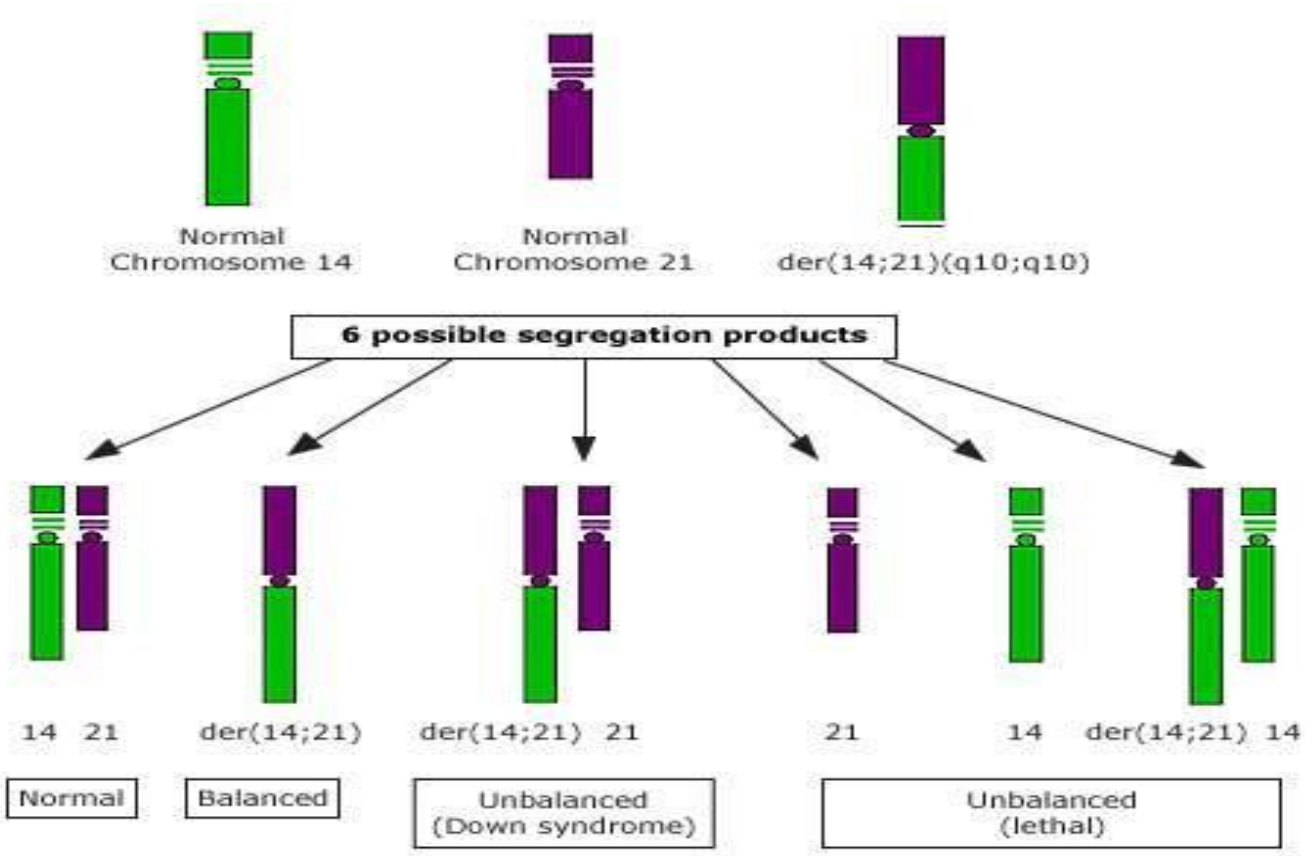
One% of cases are due to Mosaicism.

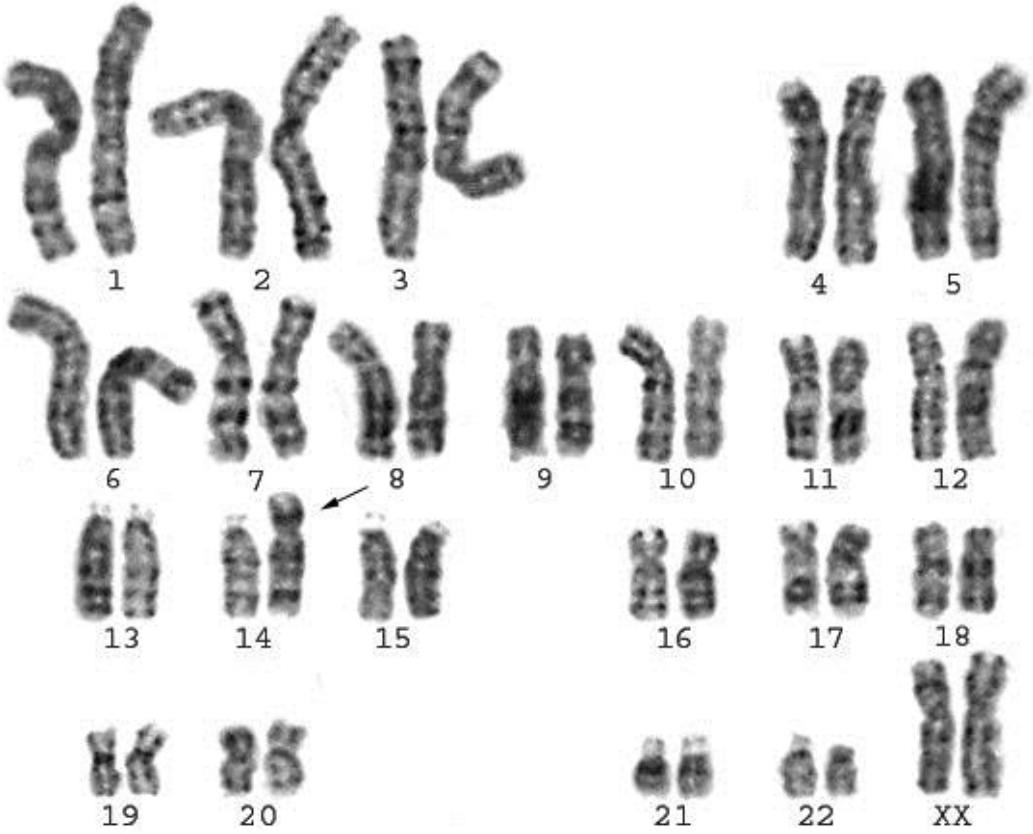

Growth failure
Mental retardation
Flat back of head
Abnormal ears
Many "loops" on finger tips
Palm crease
Special skin ridge patterns
Unilateral or bilateral absence of one rib
Intestinal blockage
Umbilical hernia
Abnormal pelvis
Diminished muscle tone
Broad flat face
Slanting eyes
Epicanthic eyefold
Short nose
Short and broad hands
Small and arched palate
Big, wrinkled tongue
Dental anomalies
Congenital heart disease
Enlarged colon
Big toes widely spaced
(a)



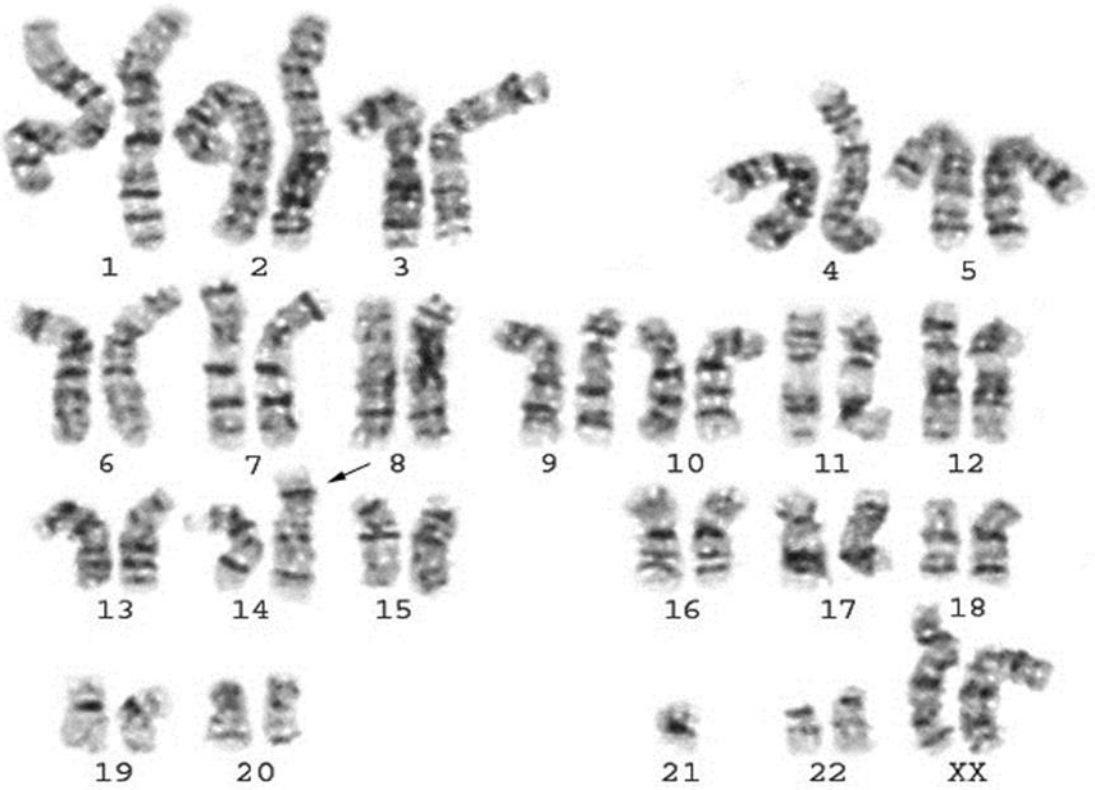


47,XX,+21

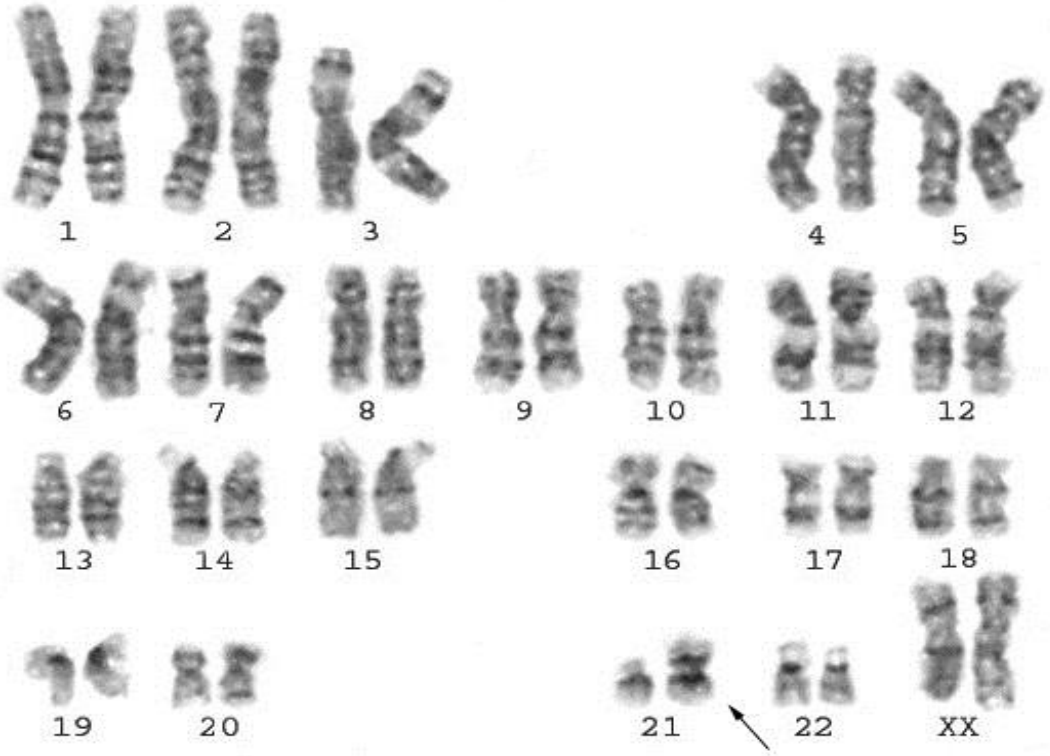

Normal
Chromosome 14
Normal
Chromosome 21
der(14;21)(q10;q10)
6 possible segregation products
14 21
der(14;21)
der(14;21) 21
21
14
der(14;21) 14
Normal
Balanced
Unbalanced
(Down syndrome)
Unbalanced
(lethal)



46,XX,t(14;21)(q10;q10),+21



45,XX,t(14;21)(q10;q10)



46,XX,+21,der(21;21)(q10;q10)