L.4 Chromosomes anomalies

Can be classified into**:** Numerical and structural

Abnormal chromosome number:

A human karyotype is abnormal if the number of chromosomes is not 46 , or if individual chromosome have extra or missing ,or rearranged genetic material. Abnormal chromosomes account for at least 50% of spontaneous abortions. Therefore most embryos and fetuses with abnormal chromosomes stop developing before birth.

The set of 46 chromosomes present in each somatic cell is referred to as diploid, or 2n , number of chromosomes. Similarly, the set of 23 chromosomes (n) is the haploid set. Together these normal conditions are referred to as the **euploid** condition.

Polyploidy:

Is the multiple of the parental chromosome number (or a cell with extra set of chromosomes). Abnormalities in the number of haploid chromosome sets can arise in several ways:

1- Errors in meiosis during gamete formation

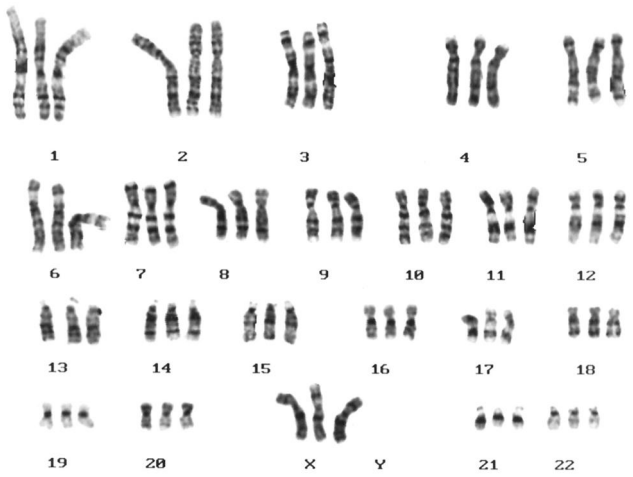
2- Errors in mitosis following fertilization

3- Events at fertilization.

Polyploidy sometimes occurs through a process called endoreduplication ,in which cytokinesis fails to occur in the last stage of cell of mitosis , the result will be gametes that contain the diploid instead of haploid number of chromosomes. Fusion between this unbalanced gamete and a normal gamete will produce a triploid zygote .

A diploid gamete can also arise through meiotic errors. An error in meiosis I can result in the failure of homologous chromosomes to separate, producing diploid gamete after meiosis II. Alternatively, in meiosis II, if all the chromosomes move to the same pole after centromere separation, diploid gamete will also result. Another event that can result in polyploidy is **dispermy**, the simultaneous fertilization of a haploid egg by two haploid sperm. The result is triplody zygotes. Triploids account for 17% of spontaneous abortions, very rarely, an infant survives as long as a few days

with defects in nearly all organs(figure 3). Certain human cells may be polyploidy such as liver cells, has some tetraploid (4n) and even octaploid (8n).



The karyotype of triploid individual

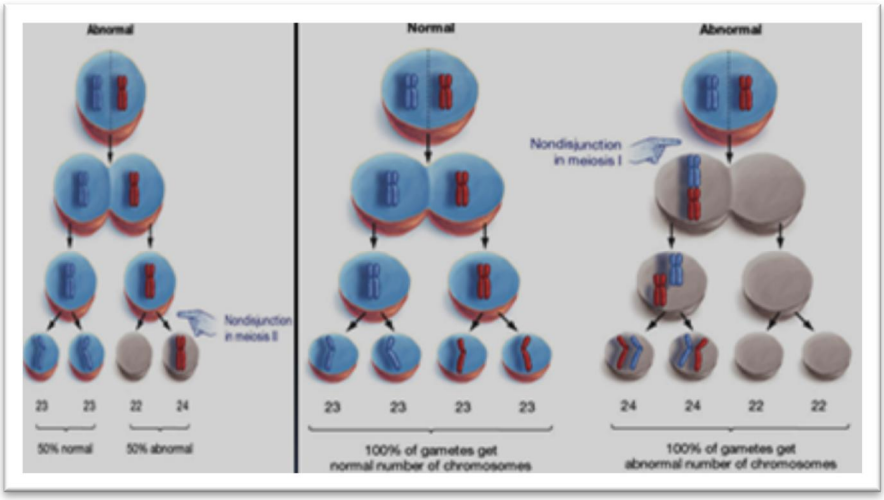
Aneuploidy

Is the addition or deletion of individual chromosomes from the normal diploid set of 46 . Most autosomal aneuploidies are spontaneously aborted. Those that survive have specific syndromes, with symptoms depending upon which chromosomes is missing or extra.

How aneuploidy arises:

The chief causes of aneuploidy is a mistake in a meiotic division or mitotic division, leading to unequal distribution of one pair of homologous chromosomes to the daughter cells .So that one daughter cells has both or extra chromosome 2n +1 called trisomy and the other has neither chromosome or missing chromosome 2n-1 monosomy .

This kind of error is called non-disjunction (that it due to failure of mated pair to segregate).If non –disjunction occurs at 2^{nd} meiotic division produced 2 gametes containing (or lacking) 2 identical chromosome. if non-disjunction occurs at the 1^{st} meiotic division all four product are abnormal 2 having an extra chromosome (47) and 2 being deficient In mitosis can also occur after formation of the zygote. In this case halves of single chromosomes (chromatids) act as meiosis II.



In human Down's syndrome is an example for numerical aberrations:

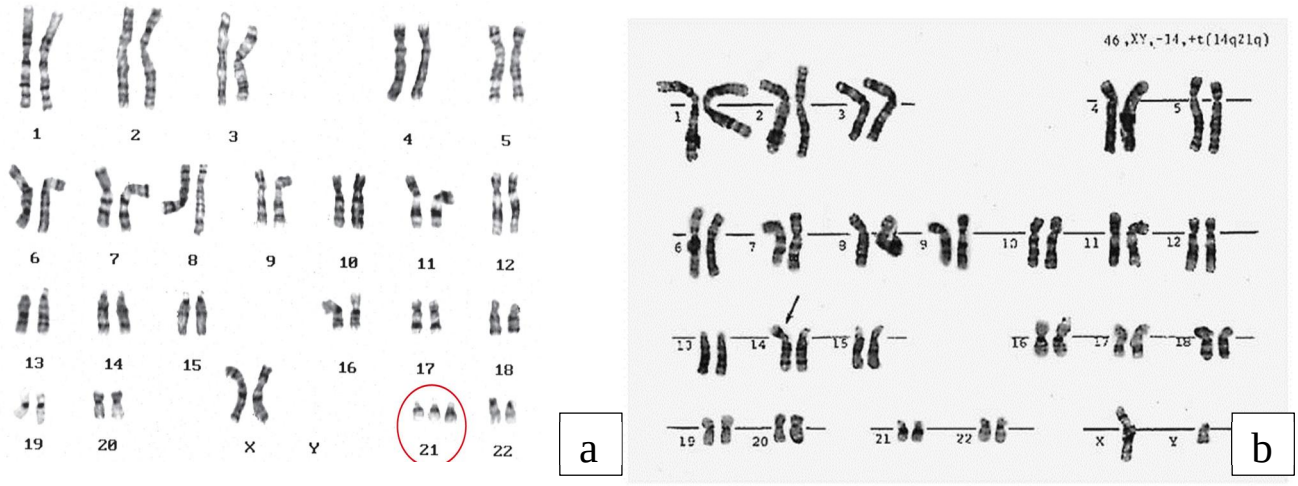
Down's syndrome:

As a case of autosomal aneuploidy .This syndrome is generally characterized by : Mental retardation, distinctive palm prints, wide, round face and an extra fold of upper eye lids. A long with an enlarged tongue make it difficult for a person to speak . Person with Down syndrome usually have 3 copies of chromosome number 21because of non-disjunction resulted a gamete with 2 copies instead one.

Down's syndrome is always due to an extra chromosome but sometimes which occur due to translocation between chromosome 14 and 21. The important differences between 2 types:

1- The zygote in trisomy contain 47 chromosome with karyotype 47,+21 while in other translocation contain 46 chromosomes with 46,XY,-14,+t(14q21q) karyotype .
2- Absence of a paternal age effect in translocation Down's syndrome. But in trisomy -21 more frequently in older females.

Also Down's syndrome resulted from phenomenon called (Mosaics) has at least 2 cell lines –with different karyotype derived from a single zygote. The alteration in the karyotypes may be numerical or structural , about 1% of children have a mixture of 46 chromosomes and 47 chromosomes ,95% trisomy 21 and 4% translocation.

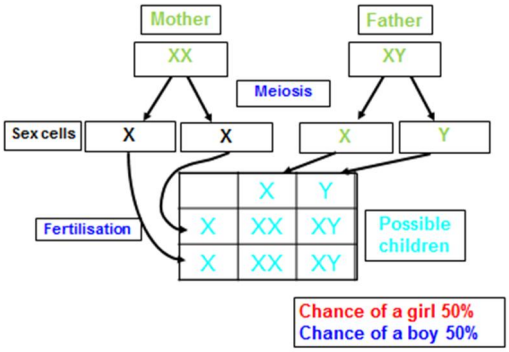


Karyotypes of Down syndrome ; a. Trisomy b. Translocation

Sex chromosome aneuploidy:

Sex- determination:

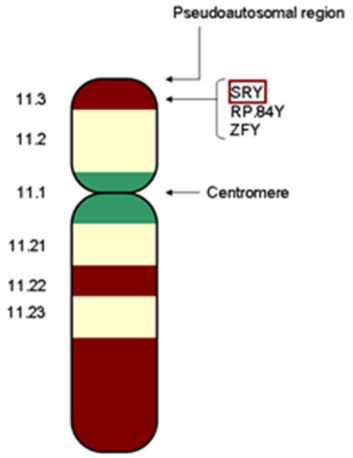
The sperm and egg carrying sex chromosome and also 22 autosomes , the offspring are either male or female ,depending on whether they receive an x or y chromosome from the male parent .In meiosis, the X and Y chromosomes separate and go into different sperm cells: ½ the sperm carry the X and the other half carry the Y. All eggs have one of the mother's X chromosomes, so when they are fertilized, ½ of the zygotes are XX (female), and ½ are XY (male) .



The Y chromosome has the main sex-determining gene on it, called SRY. About 4 weeks after fertilization, an embryo that contains the SRY gene develops testes, the primary male sex organ. The testes secrete the hormone testosterone. Testosterone signals the other cells of the embryo to develop in the male pattern. If the embryo does not have the SRY gene, it develops ovaries instead, which secrete estrogen and causes

development in the female pattern. When injected of (SRY) into normal (xx) female mice it caused them to develop as males (sterile male).

Other gene called ZFY (zinc finger) located on the Y-chromosome adjacent to SRY gene, ZFY are proteins interact with DNA, coding for testis-determining factor (ZFY gene controls the initiation of sperm cell development but not maleness) .



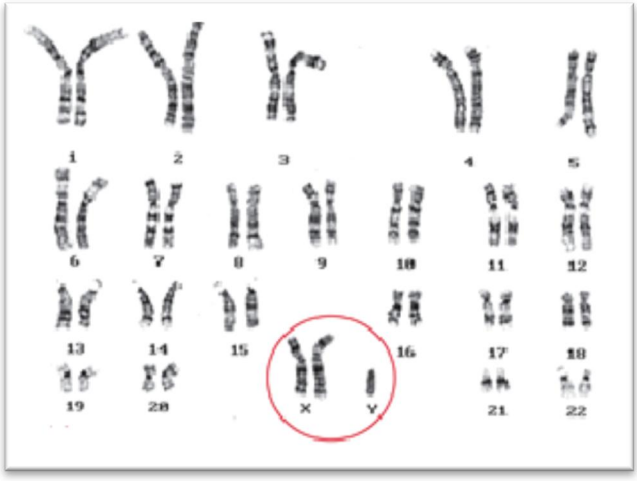
Human Y-chromosome

Non –disjunction also take place in sex-chromosomes, the abnormalities in the sex-chromosomes identified by sex chromatin (Barr body) (nx-1).Non-disjunction of sex-chromosomes during oogenesis can lead to an egg with either 2x or no x. Also non-disjunction of sex –chromosomes during spermatogenesis can result in sperm that has no sex-chromosome, both x and y,2 x chromosomes or 2Y chromosomes .

For example in human: Klinefelter's syndrome , Turner syndrome ,

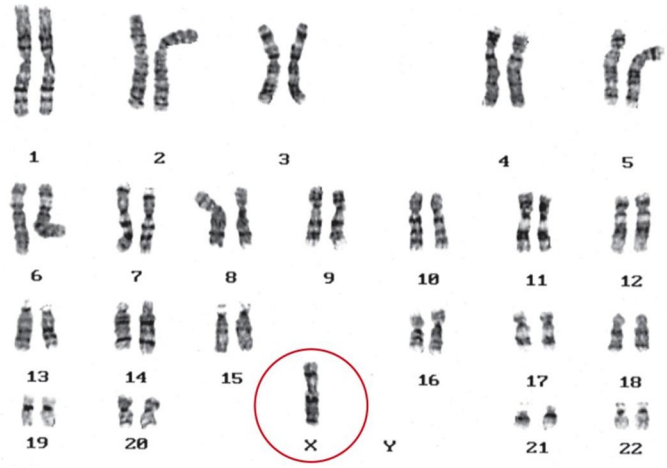
Klinefelter's syndrome (47,XXY):

About 1 in 1000 males has an extra X chromosome (47 chromosome) including a normal Y chromosome characterized by: Genitalia are undeveloped, so the person nearly sterile, Secondary sexual characters are little developed. Their limbs are longer than average, the person is usually of normal intelligence. The patient are sex-chromatin positive.



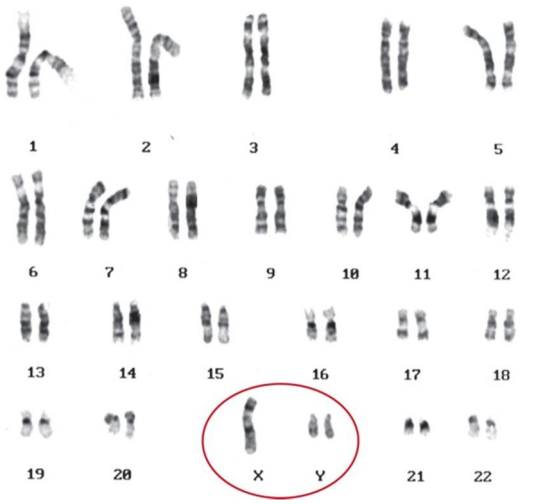
Turner's syndrome (45,XO):

The syndrome affects 1 in 2000 female birth**.** Turner's syndrome females are short stature, wide chest, webbing of neck and normal intelligence. The ovaries never become functional and lack of development of secondary sexual characteristics. Adults with turner syndrome are more likely to develop congenital cardiac and renal anomalies. Patient, with Turner's syndrome are sex-chromatin negative.



XYY or Jacobs Syndrome (47,XYY)

The man had extra copy of the Y chromosome .Males with this condition typically do not have unusual physical features and usually have normal sexual development. Signs and symptoms vary widely among affected males and may include being taller than average, adolescent acne, an increased risk of learning disabilities and delayed speech and language skills; delayed motor skills (such as sitting and walking); weak muscle tone (hypotonia) .



XXX (Triplo-X Syndrome)

About 1 in 1000 females has an extra X chromosome in each of her cells. Triple X syndrome may not cause any signs or symptoms. If symptoms do appear, they may include: Tall stature, delayed development of speech and language skills and weak muscle tone (hypotonia) .Premature ovarian failure or ovary abnormalities