Chromosome pathology

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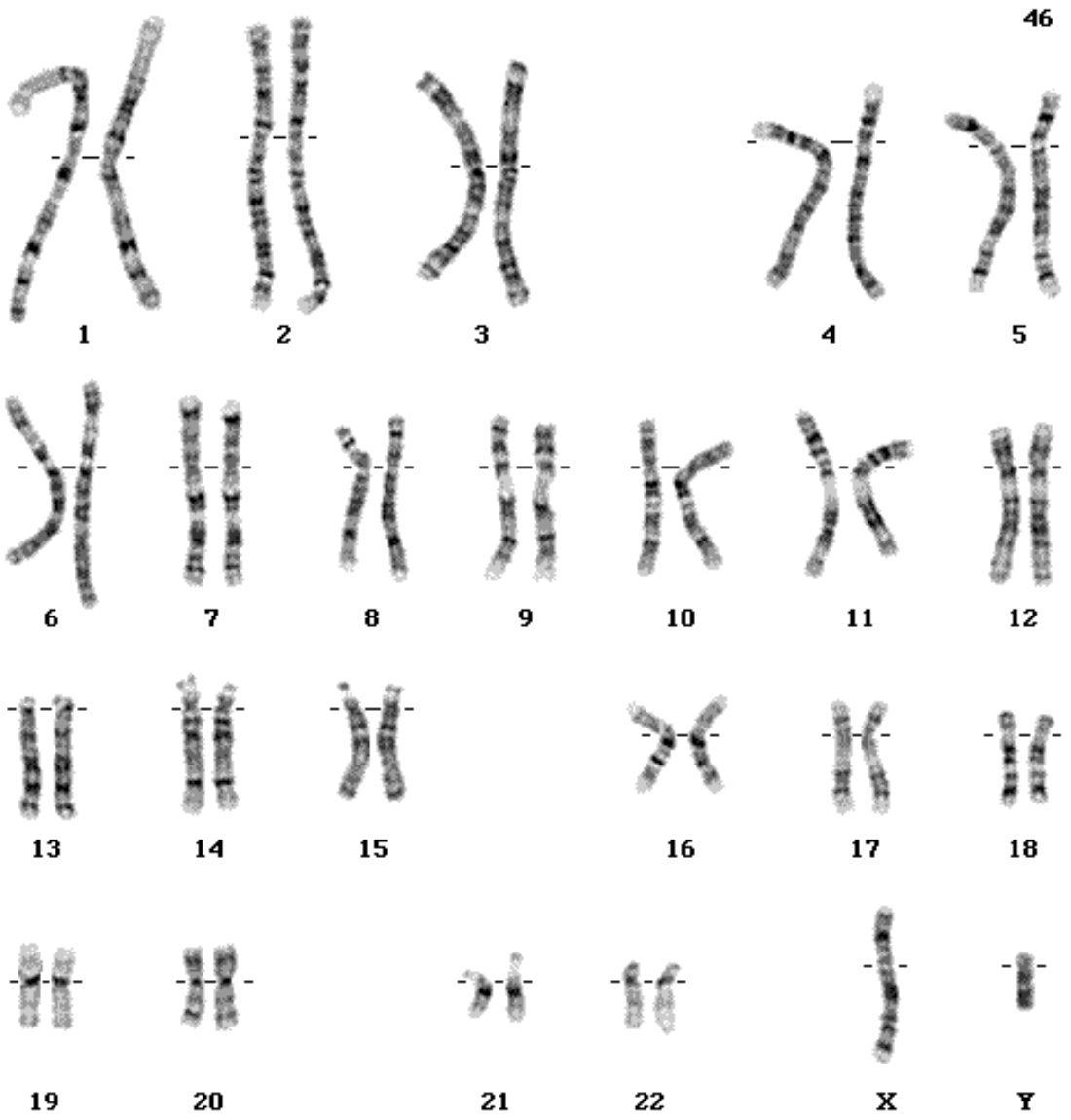
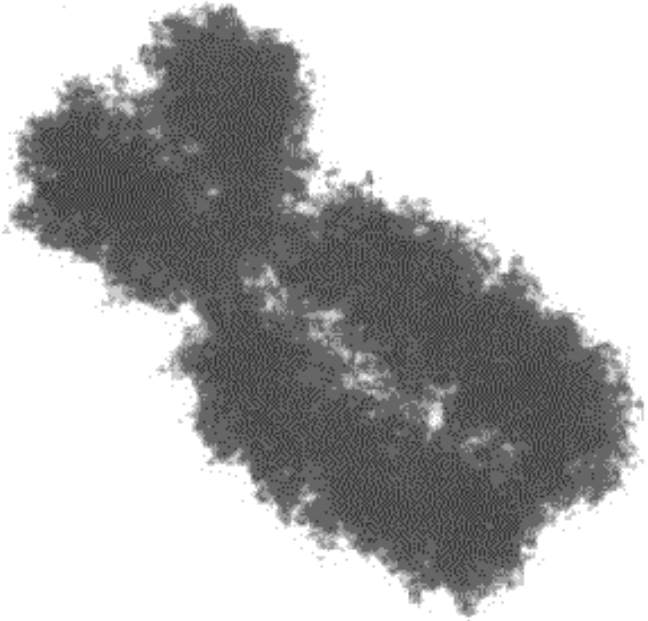
Cytogenetics is the study of chromosomes and the related disease states caused by abnormal chromosome number and/or structure.

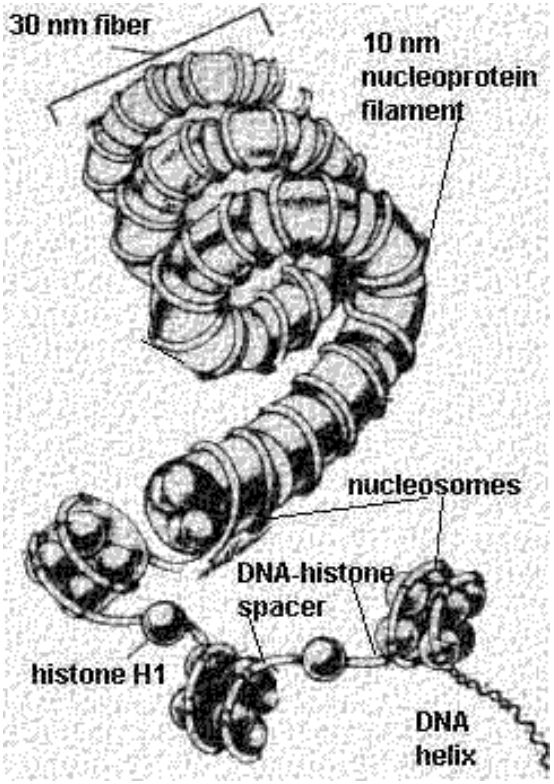


Normal human somatic cells have 46 chromosomes (diploid number): 22 pairs, or homologs, of autosomes (chromosomes 1-22) and two sex chromosomes Females carry two X chromosomes (46,XX) while males have an X and a Y (46,XY).

What Are chromosomes?

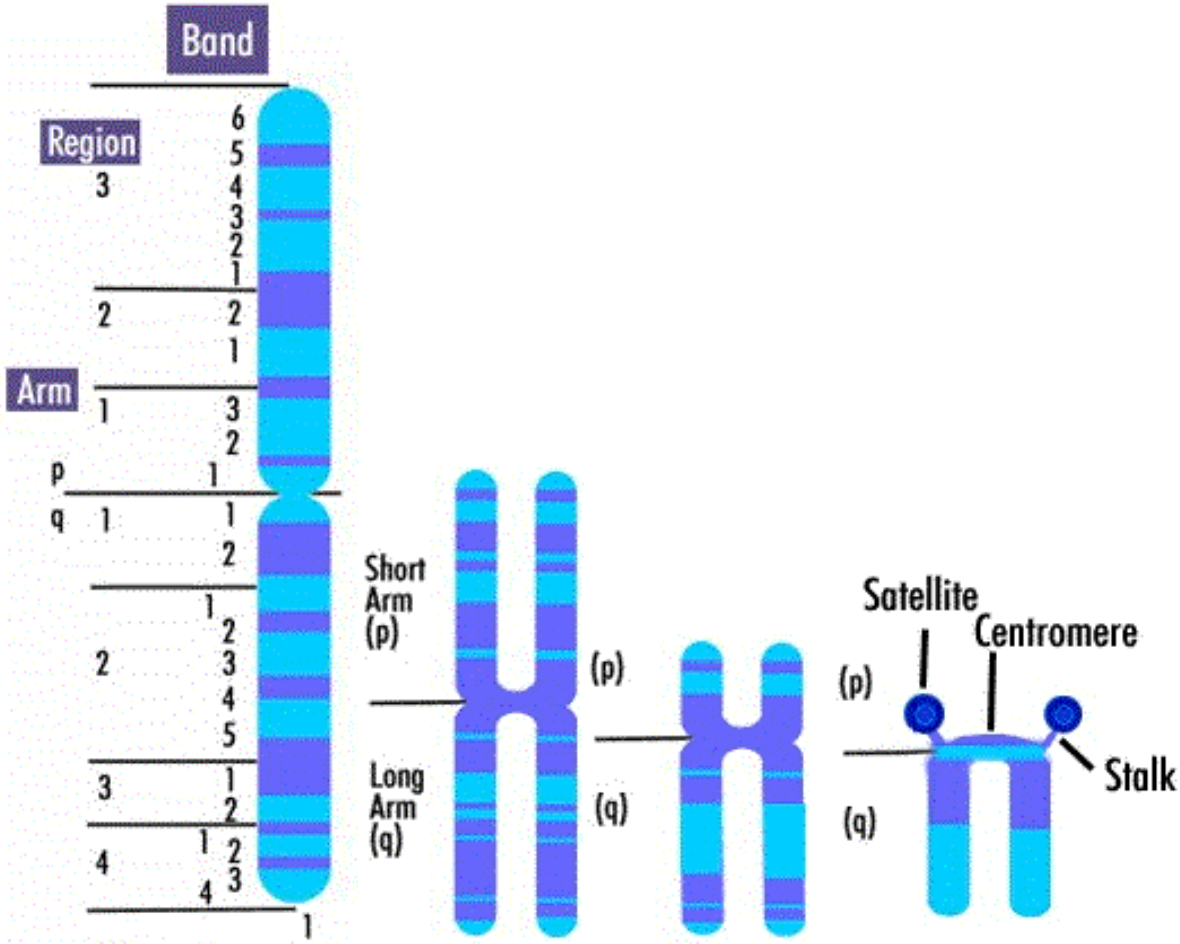
Chromosomes are complex structures located in the cell nucleus, they are composed of DNA, histone and non-histone proteins, RNA , and polysaccharides. They are basically the "packages" that contain the DNA.





Chromosome Morphology

They all have a short arm and long arm separated by a primary constriction called the centromere (location of spindle attachment). The stalks contain genes which code for ribosomal RNA.Each band is numbered (specific banding patterns) to aid in describing rearrangements.



Chromosome Analysis

Peripheral blood, bone marrow, amniotic fluid, and products of conception can be used. Sample log-in and initial setup:

- •Tissue culture (feeding and maintaining cell cultures)
- •Addition of a mitotic inhibitor to arrest cells at metaphase.
- •Harvest cells. hypotonic solution followed by a series of fixative solutions.

Preparation of slides :

The most common staining treatment (to produce a banding pattern specific to each chromosome) is called G-banding. Typically 15-20 cells are scanned and counted with at least 5 cells being fully analyzed and 2 cells karyotyped (to compare band-for-band with it's homolog). This allows for the detection of subtle changes in chromosome structure. It is necessary to examine this many cells in order to detect clinically significant mosaicism (Sometimes individuals are found who have both normal and abnormal cell lines).

Chromosome Abnormalities

Two basic types: numerical and structural. (Both types can occur simultaneously).

Numerical abnormalities involve the loss and/or gain of a whole chromosome(s) and can include both autosomes and sex chromosomes. Chromosome loss monosomy has a greater effect on an individual than does chromosome gain trisomy.

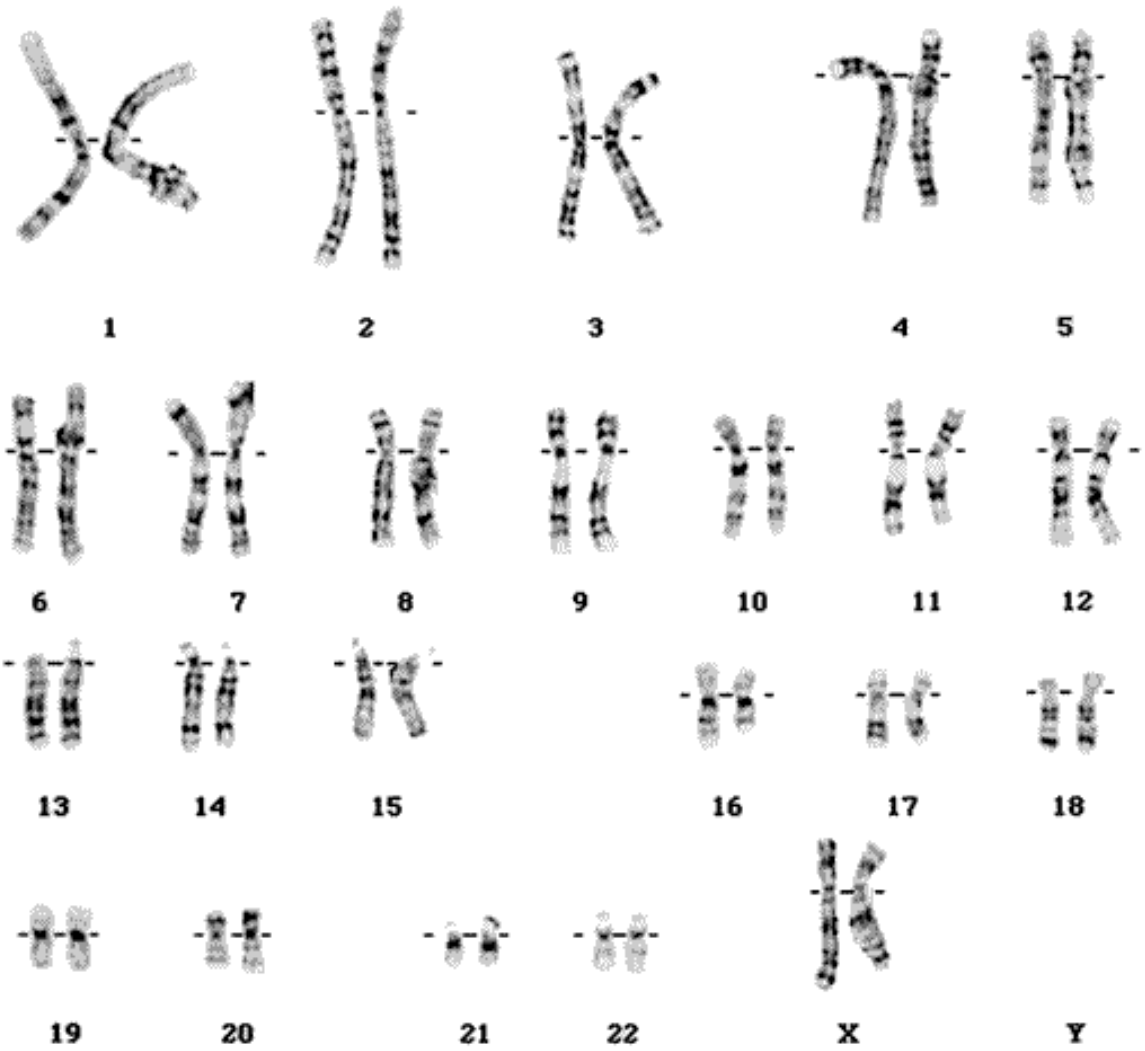
Nearly all autosomal monosomies die shortly after conception and only a few trisomy conditions (21-18-13) survive to full term. Loss or gain of an autosome has more severe consequences than loss or gain of a sex chromosome (monosomy of the X chromosome (45,X), Klinefelter Syndrome (47,XXY)).

Consequences :

- dysmorphic features
- mental retardation
- growth retardation
- internal malformations

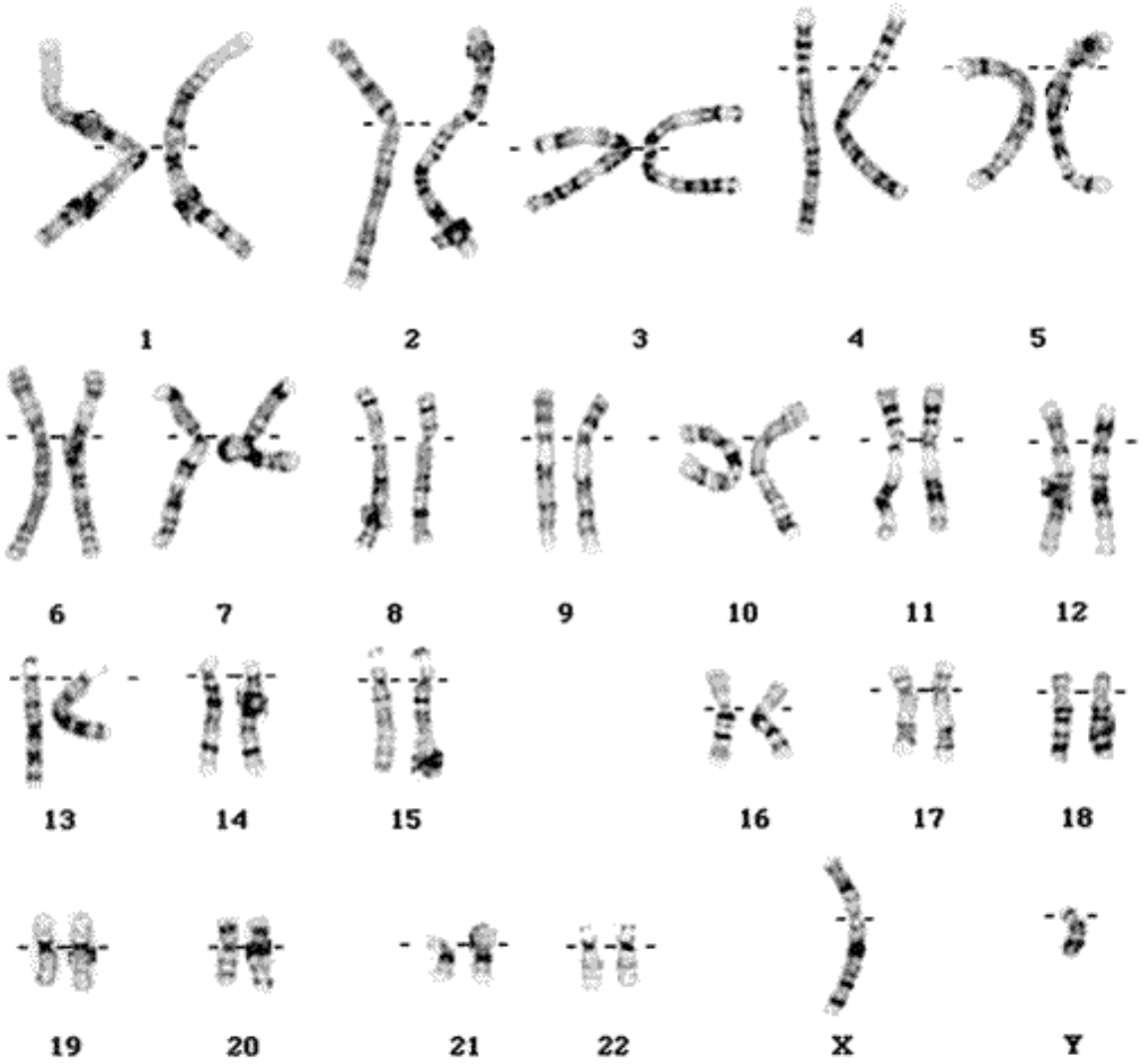
Structural abnormalities involve changes in the structure of one or more chromosomes.

- Deletions involve loss of material from a single chromosome. there is always consequences of unbalanced karyotypes even for a single band

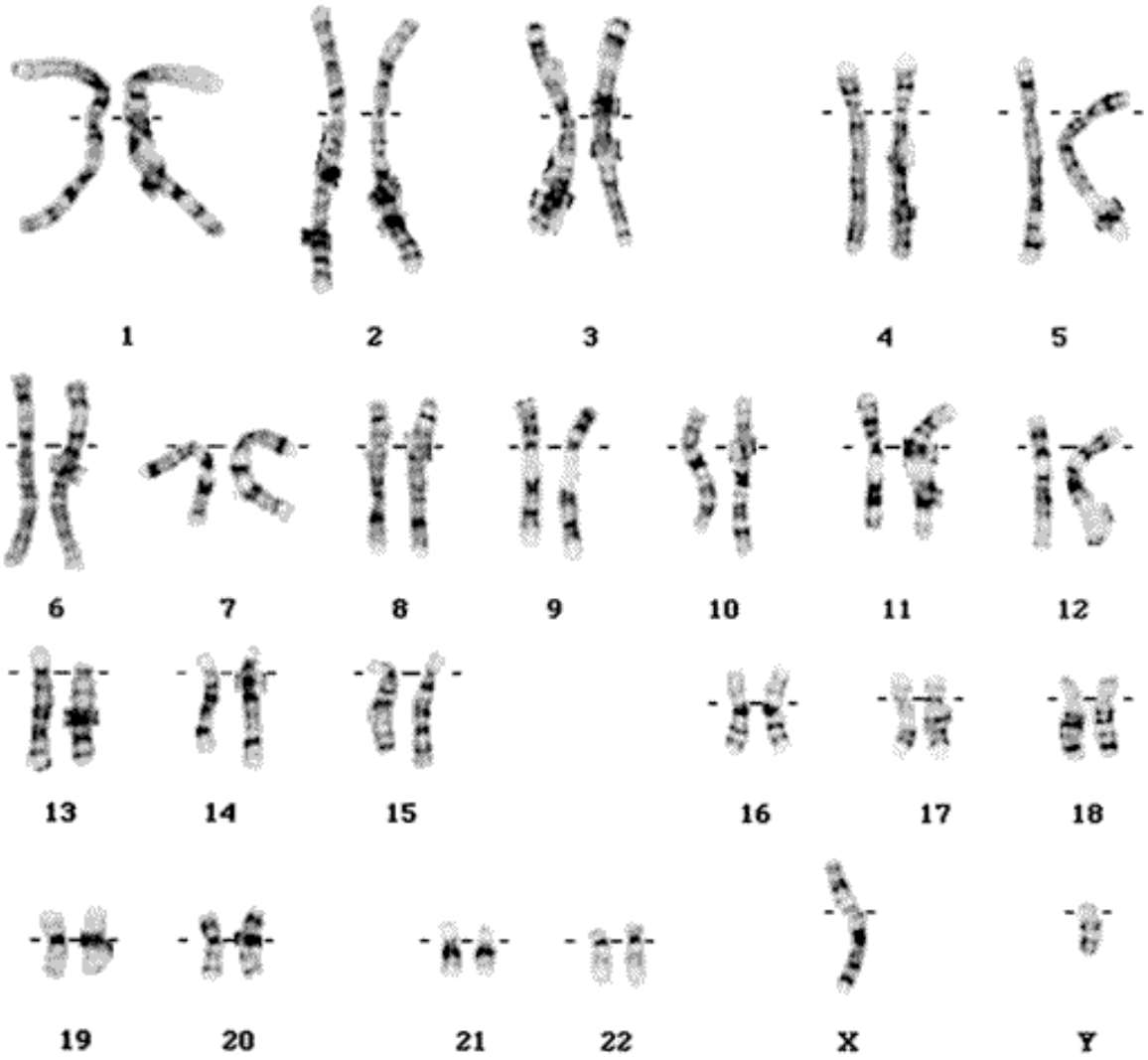


- **Inversions** occur when there are two breaks within a single chromosome and the broken segment flips 180° (inverts). There is usually no risk for problems to an individual if the inversion is of familial origin (has been inherited from a parent).

  There is a slightly increased risk if it is a de novo (new) mutation due possibly to an interruption of a key gene sequence. Although an inversion carrier may be completely normal, they are at a slightly increased risk for producing a chromosomally unbalanced embryo. This is because an inverted chromosome has difficulty pairing with it's normal homolog during meiosis, which can result in gametes containing unbalanced derivative chromosomes if an unequal cross-over event occurs.



- Translocations involve exchange of material between two or more chromosomes.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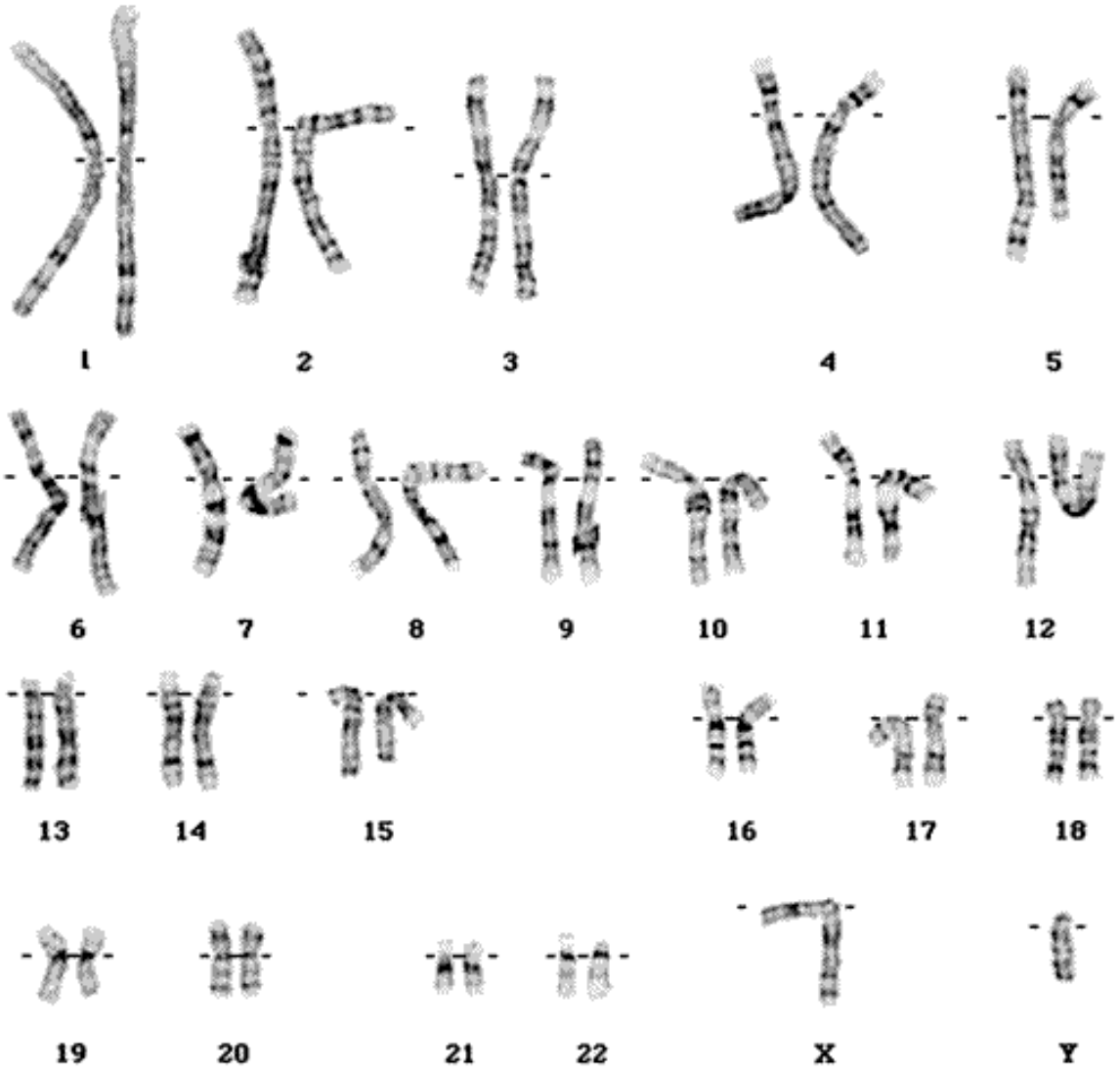


If a translocation is reciprocal (balanced) the risk for problems to an individual is similar to that with inversions: usually none if familial and slightly increased if de novo. Problems arise with translocations when gametes from a balanced parent are formed which do not contain both translocation products so an unbalanced embryo which is partially monosomic for one chromosome and partially trisomic for the other.

Klinefelter Syndrome

once in every 500 to one in every 1,000 live born males. Male with an extra X : caryotype 47,XXY., less common variations 48,XXYY; 48,XXXY; 49,XXXXY ; and XY/XXY mosaic.

Common Characteristics

- Many cases affected individuals lead healthy, normal lives with no particular medical or social questions
- Normal sexual function (erection and ejaculation)
- Testicular atrophia, azoospermia, sterility,
- Breast development in 1/3 of case,
- Incomplete masculine body build in some cases,
- Social problems more immature, shy and dependent than their brothers
- School learning problems increased risk for speech and language problems
- Testosterone therapy appears to have a positive effect except in the case of sterility.

XYY Syndrome

Men with XYY syndrome have two Y chromosomes, and the chromosome constitution 47,XYY. The frequency is approximately 1 of 1000 men. Increased height there are no special physical stigmata Physical development is otherwise normal, sex-organs are normal.

- More physically active than their brothers,
- Increased tendency for learning-problems in school,
- Intelligence is usually within the normal range

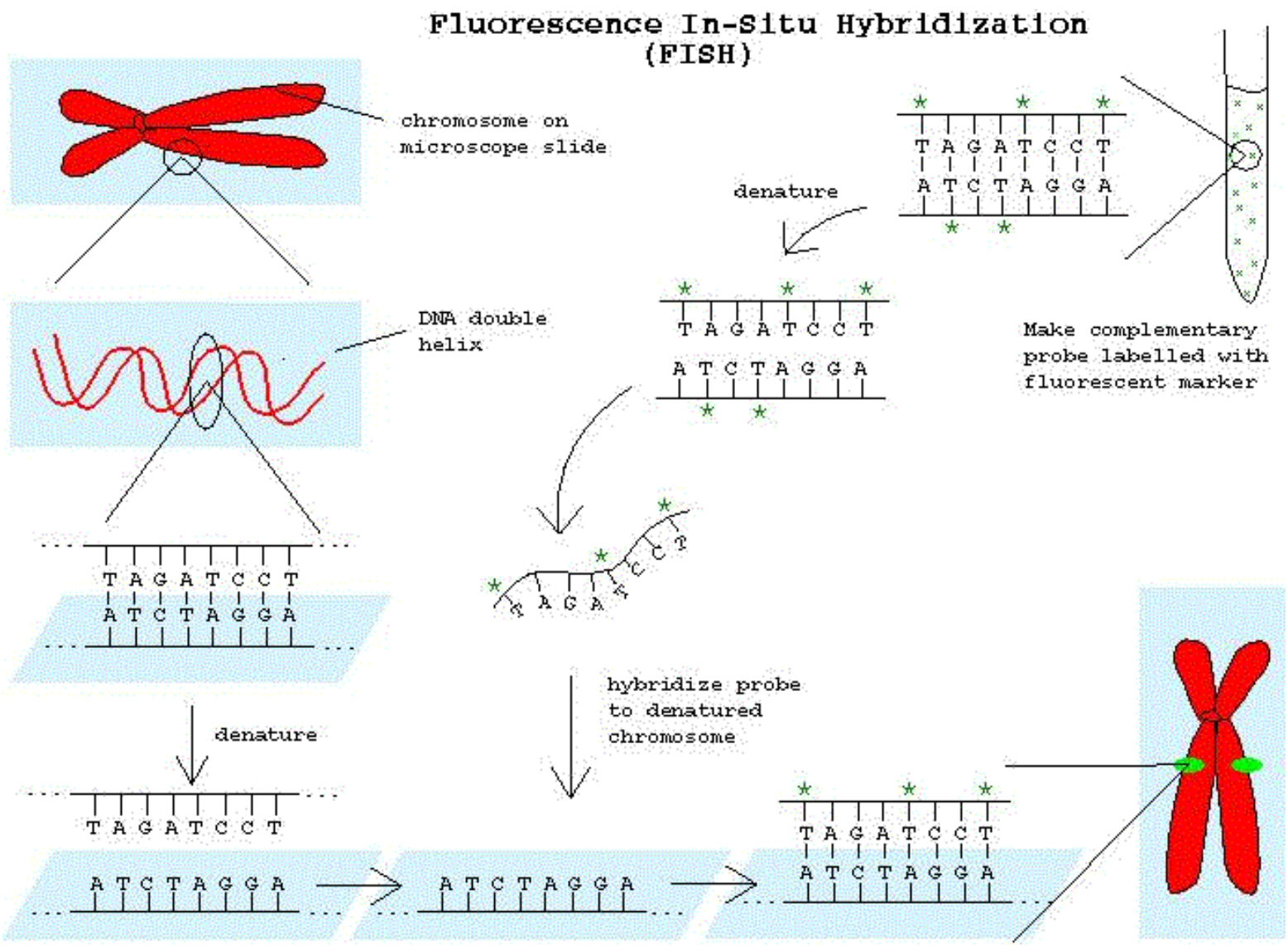
Triple X Syndrome

Women with Triple X syndrome have 3 X chromosomes and the chromosome constitution 47,XXX. The frequency is1 of 1000 women. No real stigmata connected with this syndrome. Women with Triple X usually are fertile, but they sometimes get the menopause earlier than other women. Delayed development in motor function, speech, and maturation in some cases. The average IQ for Triple X girls lies on approximately 90 compared to 100 for a control group of siblings.

Turner's Syndrome

Women with Turner's Syndrome **lack one or part of one of the X chromosomes**, that carry genes for conditions relating to the development of ovaries, sex-hormone production, and physical development in general.This relationship leads to **faulty development of the ovaries** and **sex-hormone production**, and due to this these women usually cannot get pregnant. Menstruation usually also fails to come, and usually they do not have normal development of breasts and pubic hair. Estrogen treatment should be given from the age of about 12, starting with very small doses.

The average height of Turner women is **147** cm, varying between 135 and 163 cm. Growth velocity and final height can be increased with growth hormone treatment from the age of 7.Approximately 40 % of the Turner girls have a so-called bed-neck, and in a number of cases it may be necessary to do surgery for this. 10 % have a stricture of the main artery, and approximately 12 % have other less serious heart-anomalies. The mental development of Turner girls is inside the normal area.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