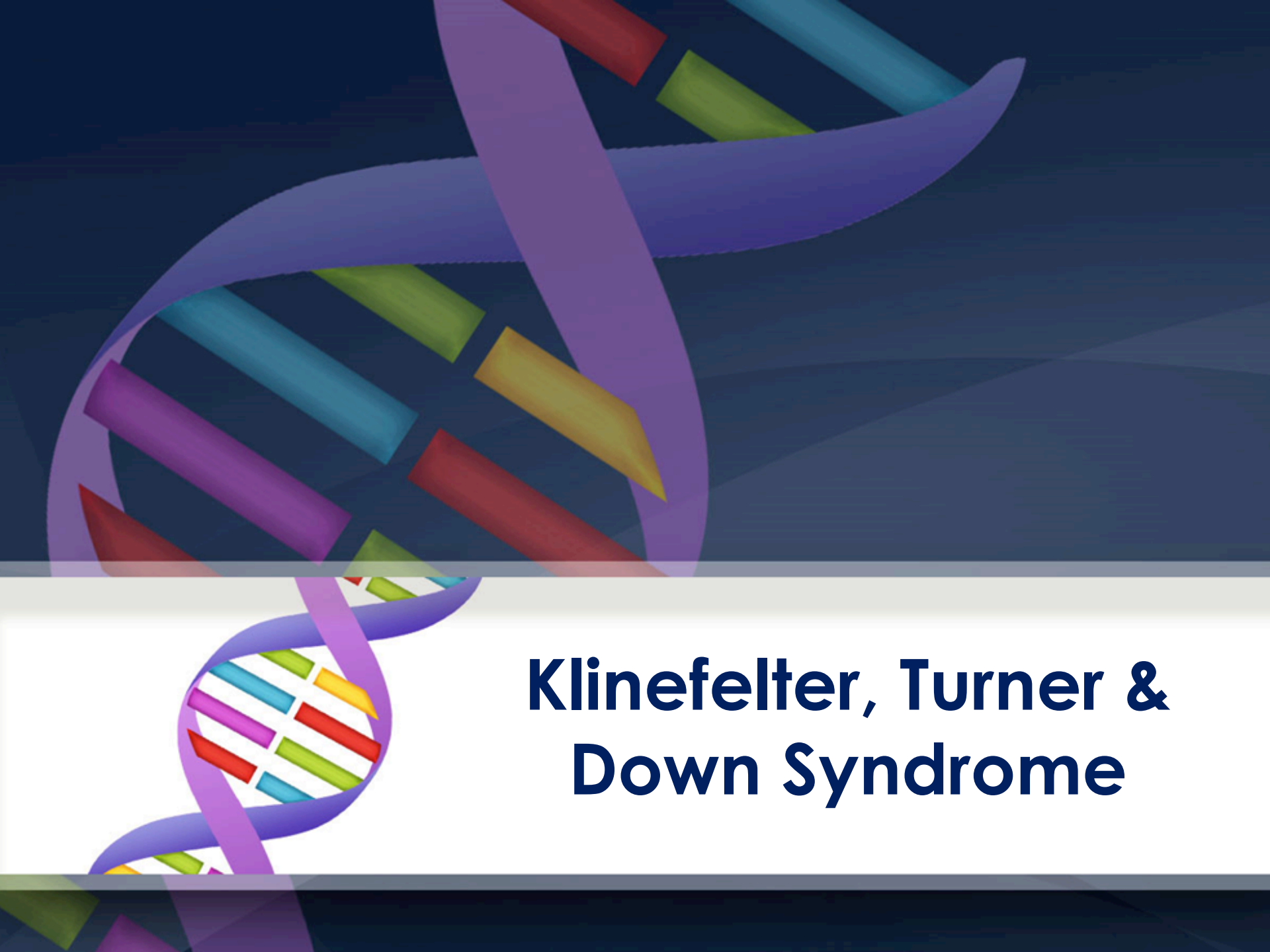
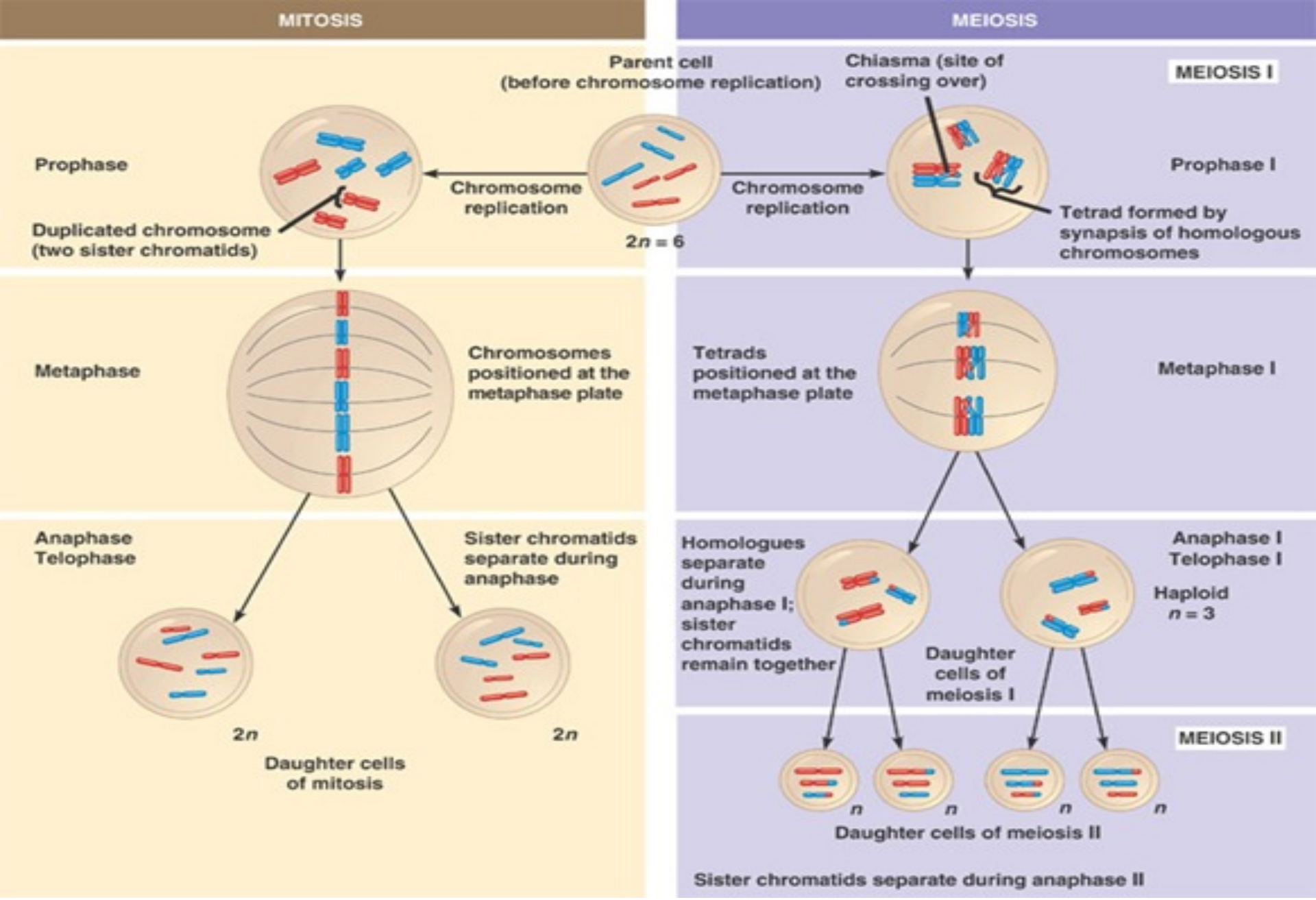


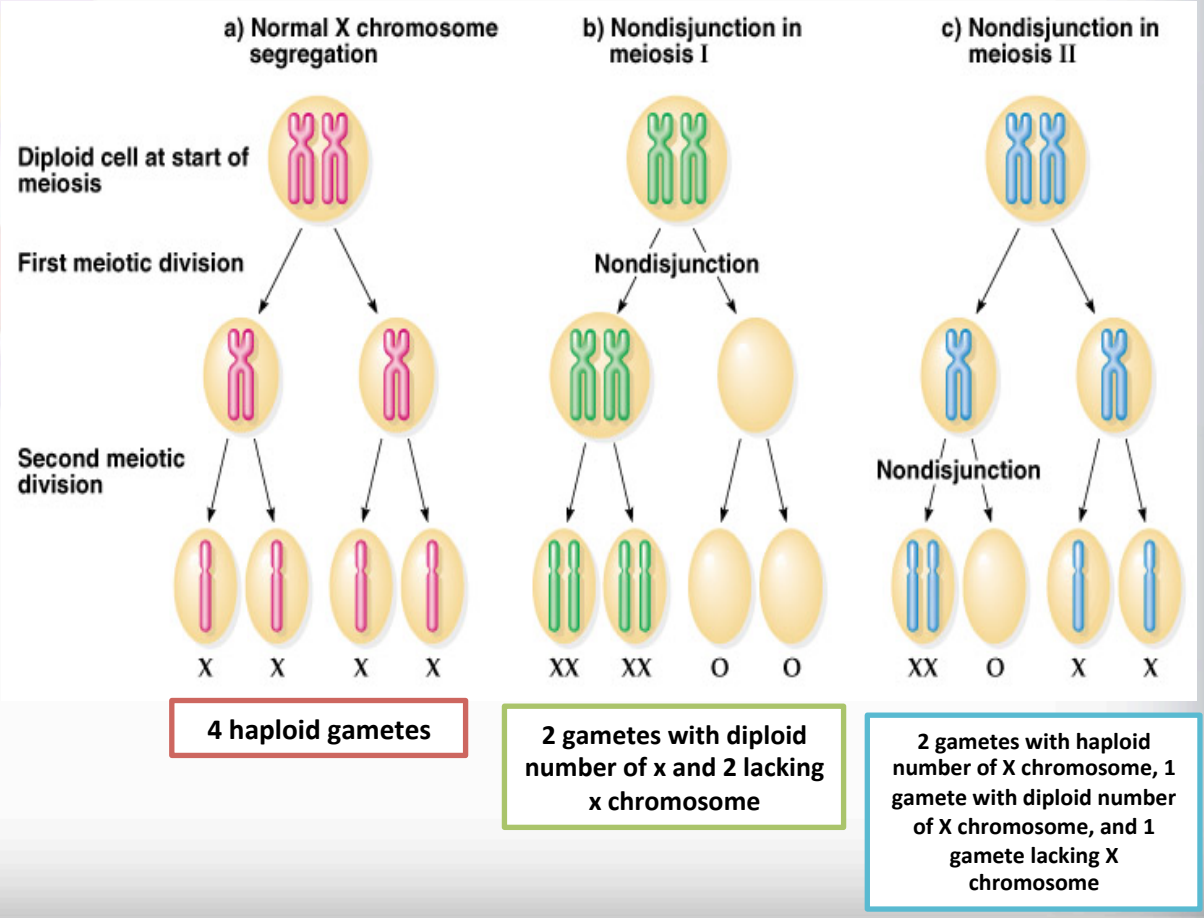
Klinefelter, Turner & Down Syndrome



A brief discussion of gamete formation, Mitosis and Meiosis: https://www.youtube.com/watch?v=zGVBAHAsjJM

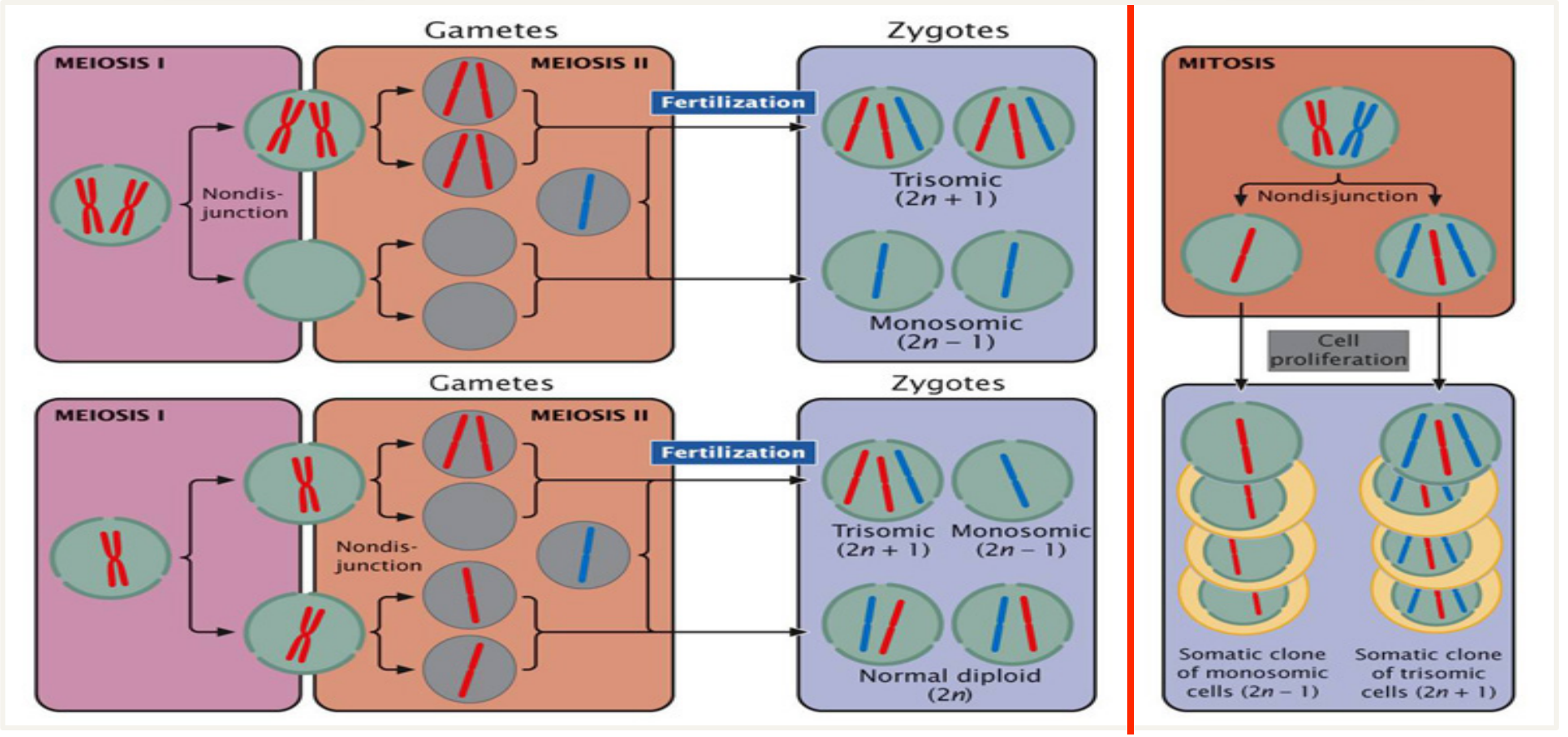
Non-disjunction in Meiosis:

- Nondisjunction "not coming apart" is the failure of a chromosome pair to separate properly during meiosis 1, or of two chromatids of a chromosome to separate properly during meiosis 2 or mitosis.
- Can effect each pair.
- Not a rare event.
- As a result, one daughter cell has two chromosomes or two chromatids and the other has none
- The result of this error is ANEUPLOIDY.



MEIOSIS

MITOSIS

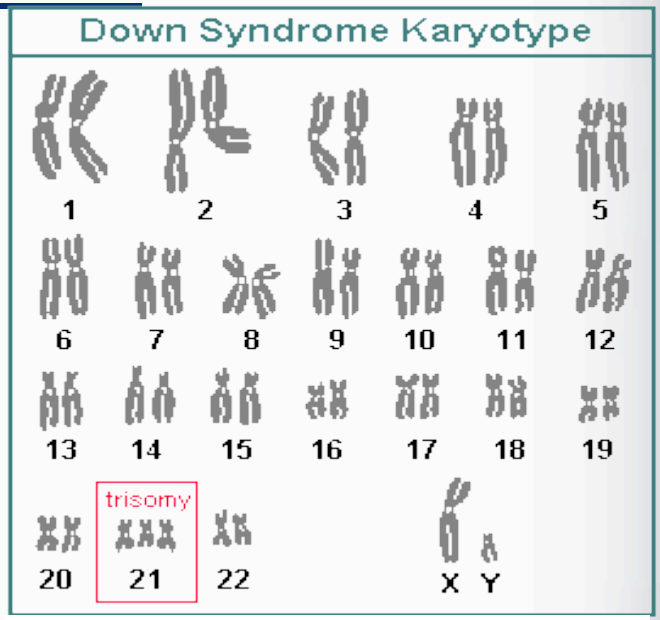


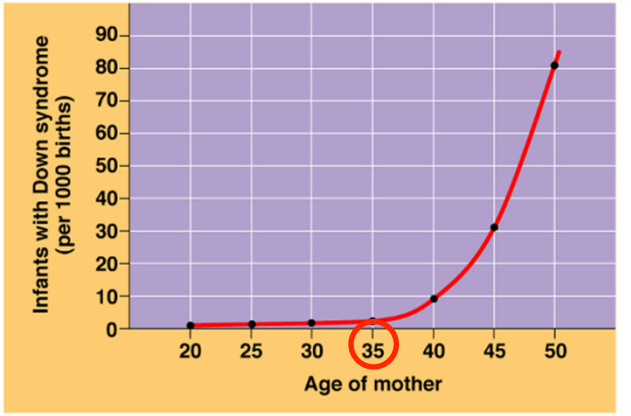
Nondisjunction at meiosis 1 = All gametes will be abnormal

Nondisjunction at meiosis 2 = Half of the gametes are normal (%50 normal and %50 abnormal)

Down's Syndrome

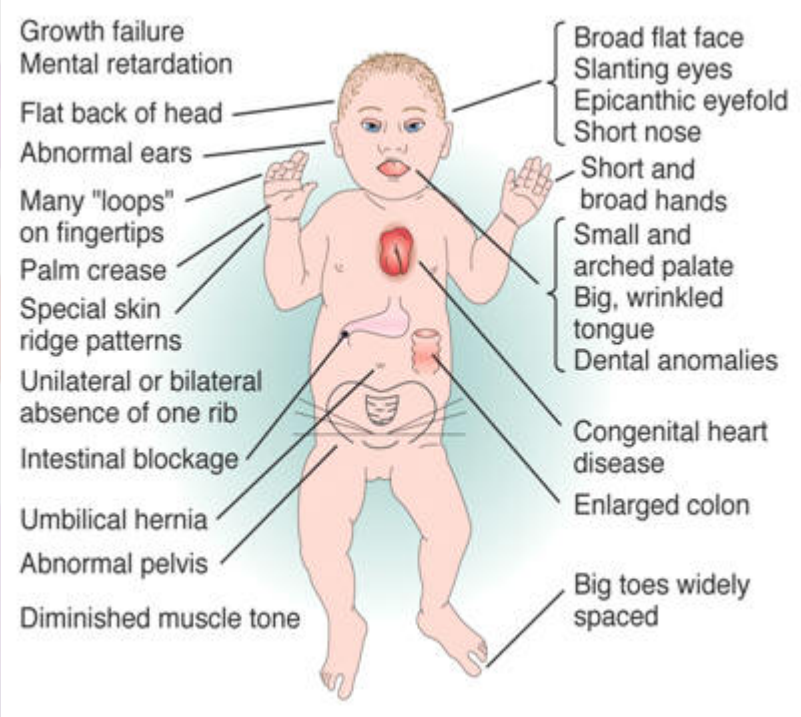
- Karyotype: 47, XY, +21
  Three copies of chromosome 21 (21 trisomy)
- The incidence of trisomy 21 rises sharply with increasing maternal age (above 37), but Down syndrome can also be the result of nondisjunction of the father's chromosome 21 (%15 of cases)
- A small proportion of cases is mosaic* and probably arise from a non-disjunction event in early zygotic division.





*"Mosaicism, used to describe the presence of more than one type of cells in a person. For example, when a baby is born with Down syndrome, the doctor will take a blood sample to perform a chromosome study. Typically, 20 different cells are analyzed. If five of the 20 are normal (46 chromosomes), while the other 15 have an extra #21 chromosome (47 chromosomes), the baby would be said to have mosaic Down syndrome."

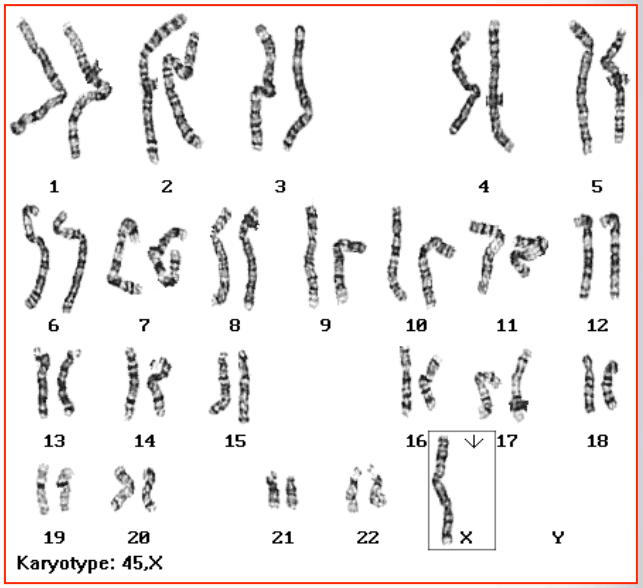
Features of Down's Syndrome



- Low muscle tone
- Rough skin
- Head and facial malformations:
  Small round face, protruding tongue
- Abnormalities of the extremities:
  Short broad hands, stubby fingers
- Developmental delays (Mental retardation)
- Heart malformations
- Increased risk of infectious diseases
- Short life span (Early death)

Turner's Syndrome

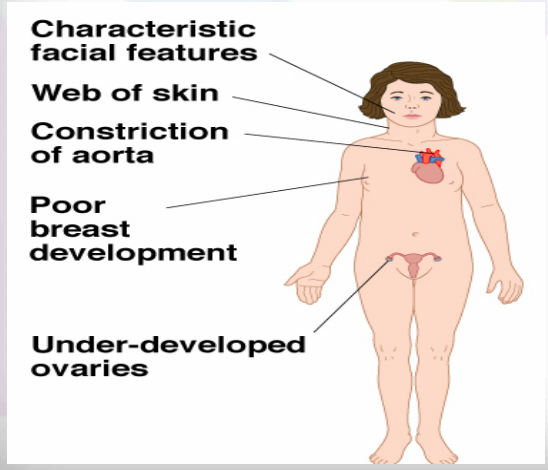
- Karyotype: Monosomy X: 45, XO
- Monosomy of sex chromosome (only one X chromosome present)
- The only viable monosomy in humans
- Occurring in 1 in 2500 phenotypic females
- NO developmental delays
- Turner syndrome is commonly treated with growth hormones, and estrogen replacement therapy.

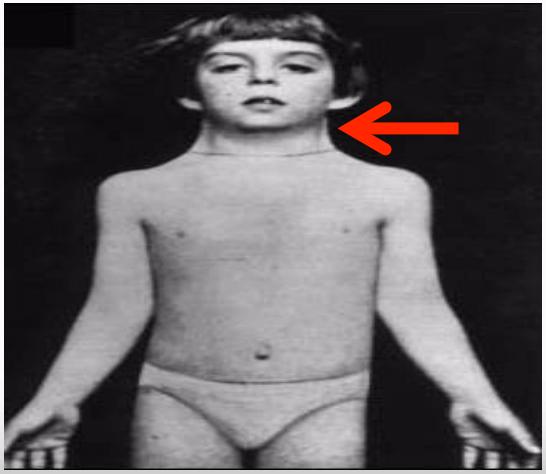


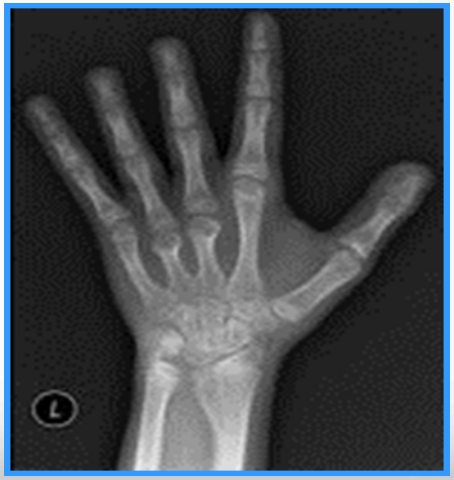
Features of Turner's Syndrome

Cardiovascular	Skeletal	Reproductive
▪ Cardiovascular constriction ▪ Bicuspid aortic valve ▪ Coarctation of the aorta ▪ Thoracic aortic aneurysm	▪ Short stature ▪ Neck Abnormalities (webbing of the neck) ▪ Osteoporosis (due to lack of estrogen) ▪ Scoliosis ▪ Short 4th metacarpal/metatarsal bone. (+ \- short 3rd & 5th)	▪ Lack of ovarian development ▪ Women with Turner syndrome are almost universally infertile. ▪ Reproductive technology can help women with Turner syndrome become pregnant

Others: Diabetes, kidneys and thyroid problems

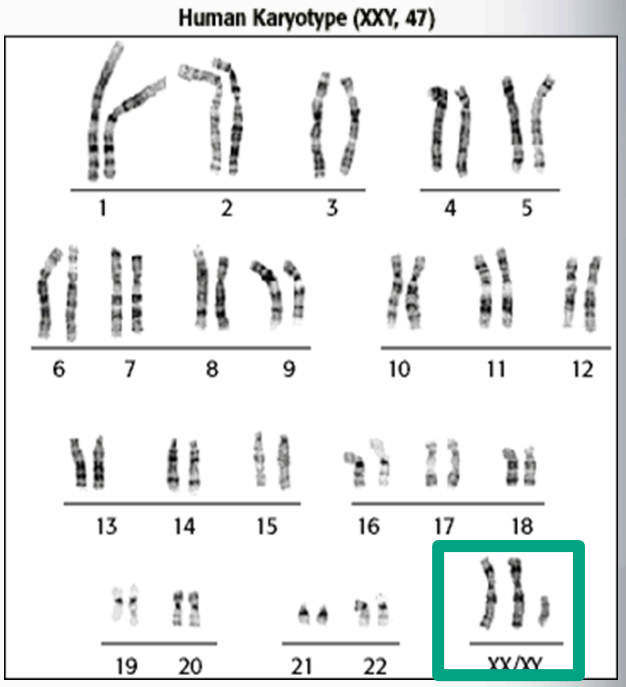






Klinefelter's Syndrome

- Karyotype: (XXY, 47) males
  Nondisjunction (23 trisomy)
- 1 in 1,100 births
- Klinefelter syndrome is a genetic condition that results when a boy is born with an extra copy of the X chromosome.
- Very rarely more extreme forms of Klinefelter syndrome occur where the patient has 48, XXXY or even 49, XXXXY karyotype.
  These individuals are generally severely retarded.
- Klinefelter syndrome often isn't diagnosed until adulthood. Most men with Klinefelter syndrome produce little or no sperm. But assisted reproductive procedures may make it possible for some men with Klinefelter syndrome to father children.



Features of Klinefelter's Syndrome

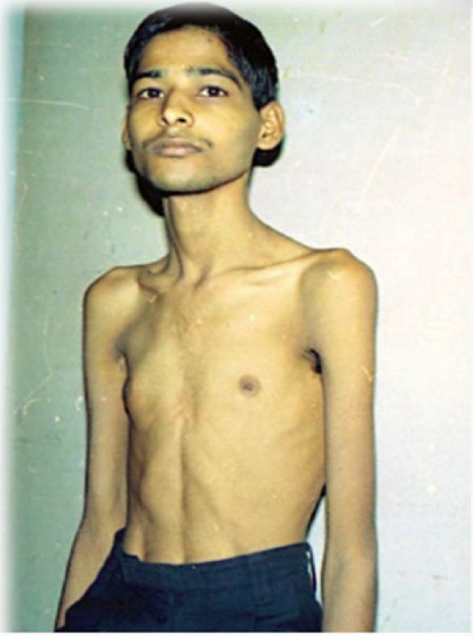
- Unusually small testes → low production of testosterone → Gynaecomastia, reduced body hair and other feminine body characteristics.

- No spermatogenesis → sterile (in some cases, testicular function is preserved)
- Low mental abilities (a slight reduction in IQ but generally they have normal intelligence)
- Delays in speech and motor skills as well as deficits in attention, auditory processing and social skills.

- Patients are taller and thinner (Reduced muscle mass) than usual with long fingers and arms
- Normal lifespan
- Brown spots (nevi)

- Increased risk of autoimmune disorders, breast cancer, osteoporosis, leg ulcers, depression, and dental problems

❖**Treatment** for these problems includes: testosterone therapy and assisted learning.



Photograph showing development of gynecomastia in
ld male after 2 months of isoniazid containing Catego
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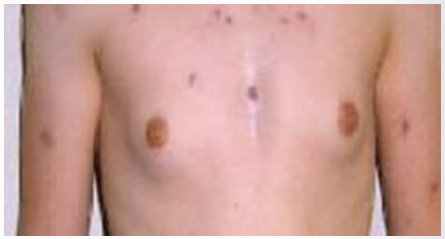


Sex chromosome unbalance is much less deleterious

- **47, XYY:**
  - ✓ May be without any symptoms.
  - ✓ Males are tall but normally proportioned.
  - ✓ 10 - 15 points reduction in IQ compared to siblings.

- **XXX females:**
  - ✓ It seems to do little harm,
  - ✓ individuals are fertile and do not transmit the extra chromosome.
  - ✓ They do have a reduction in IQ comparable (similar) to that of Kleinfelter's males.

When to do a chromosomal test

- **Prenatal:**
  A. maternal age>37yrs; Ultrasound scan changes; Family history
  B. Triple test (measuring the alpha fetoprotein (AFP), human chorionic gonadotropin (hCG), and estriol): if positive it indicates an increased risk of having diseases due to chromosomal anomalies

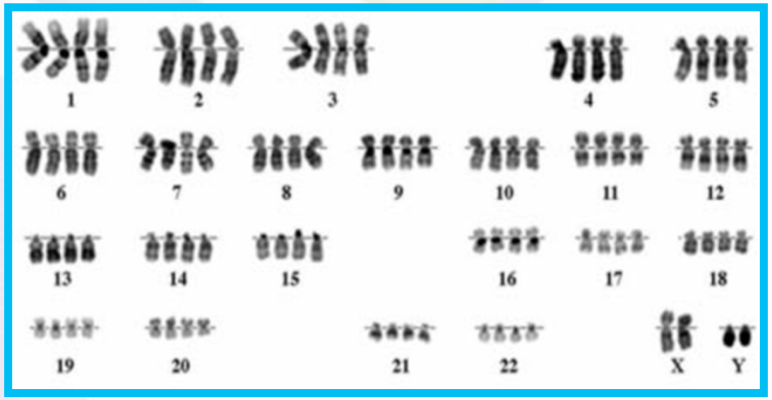
- **Postnatal:** Learning & developmental disability; growth retardation

- **Infertility:** Recurrent miscarriage, primary infertility

Aneuploidy

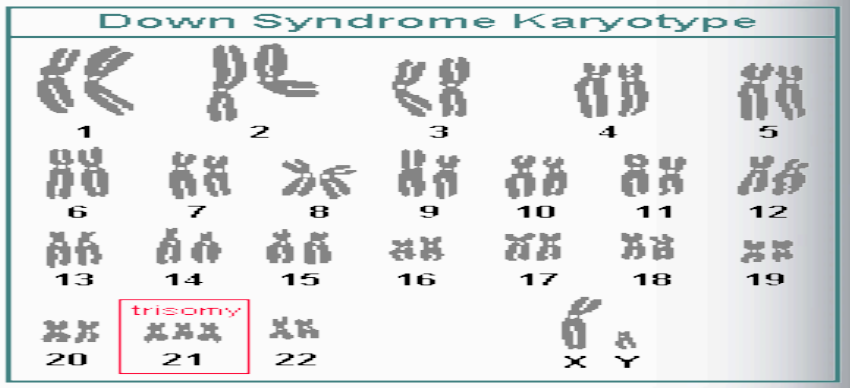
- Aneuploidy refers to a numerical change in PART OF the chromosome set.
- Aneuploidy could be:
  1. Autosomal: Trisomy 21 (Down syndrome)
  2. Sex chromosome:
     - 47XXY (Klinefelter syndrome)
     - 45X (Turner syndrome)

- Polyploidy refers to a numerical change in the WHOLE SET of chromosomes



Polyploidy

VS

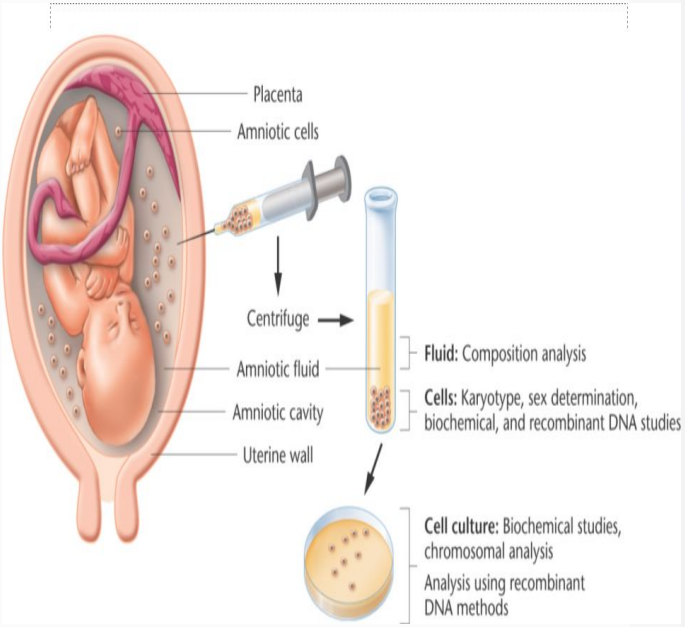


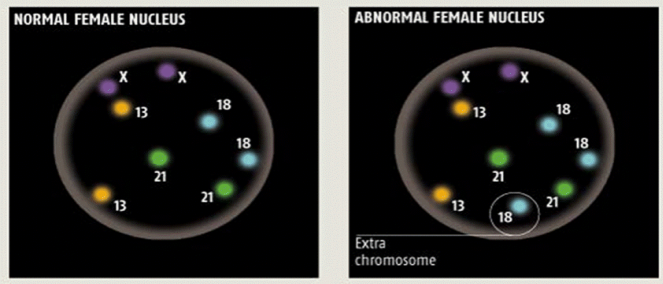
Aneuploidy

Aneuploidy Screening

1. Rapid Aneuploidy screening by FISH

- Available on amniocentesis sample
- Uncultured amniocytes
- FISH probes for X,Y, 21
- Result in 24-48 hours
- Proceed onto full karyotype (11-14 days)





2. New Techniques

A. Quantitative Fluorescence PCR: to measure number of copies of a chromosome

B. Cell-free Fetal DNA:

at 6-8 weeks of gestation. It is a non-invasive prenatal diagnostic tool for chromosomal aneuploidy. It can be used to determine the fetus sex– (look for presence of Y chromosome)

BEST WISHES!!!

Done by: Norah Alnaeim