Cytogenetics
Chromosomal Aberrations

seminar from Physiology and Pathophysiology II

21. 3. 2023

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Chromosomes

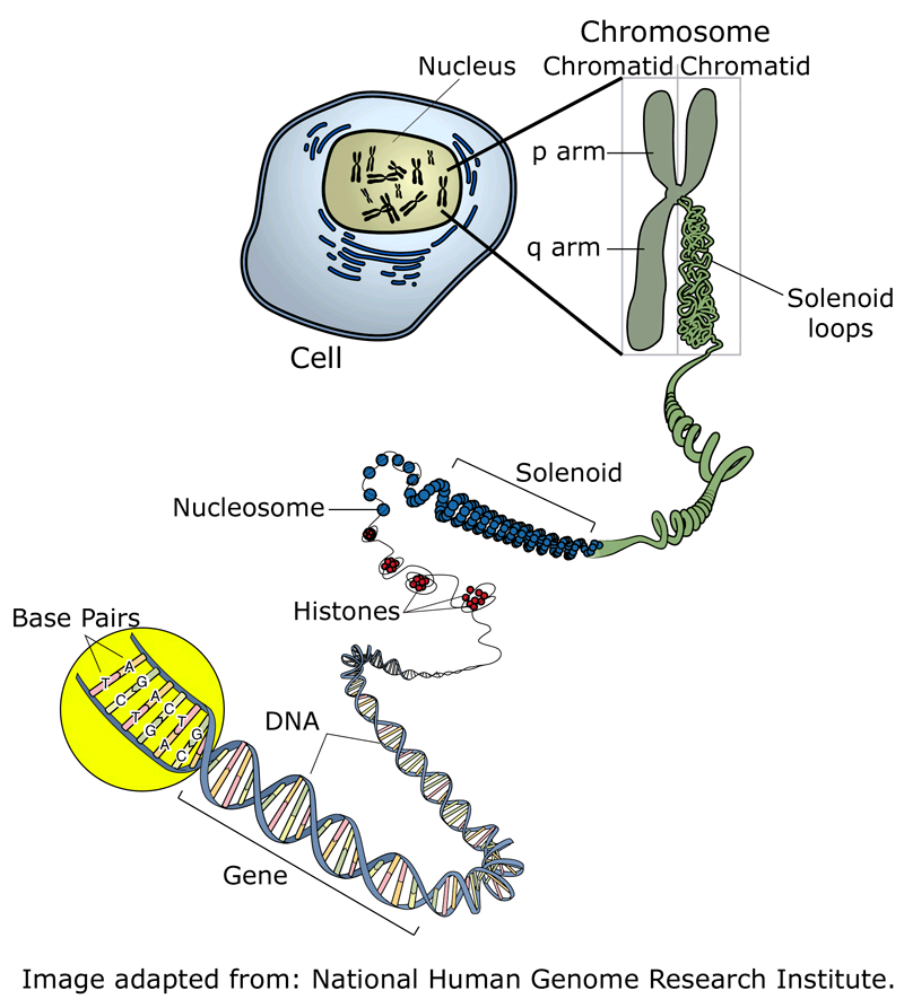
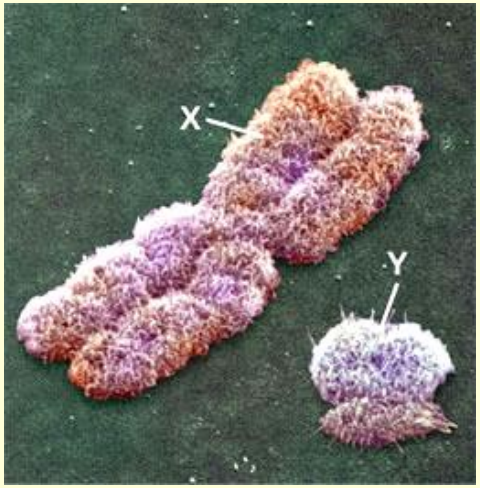
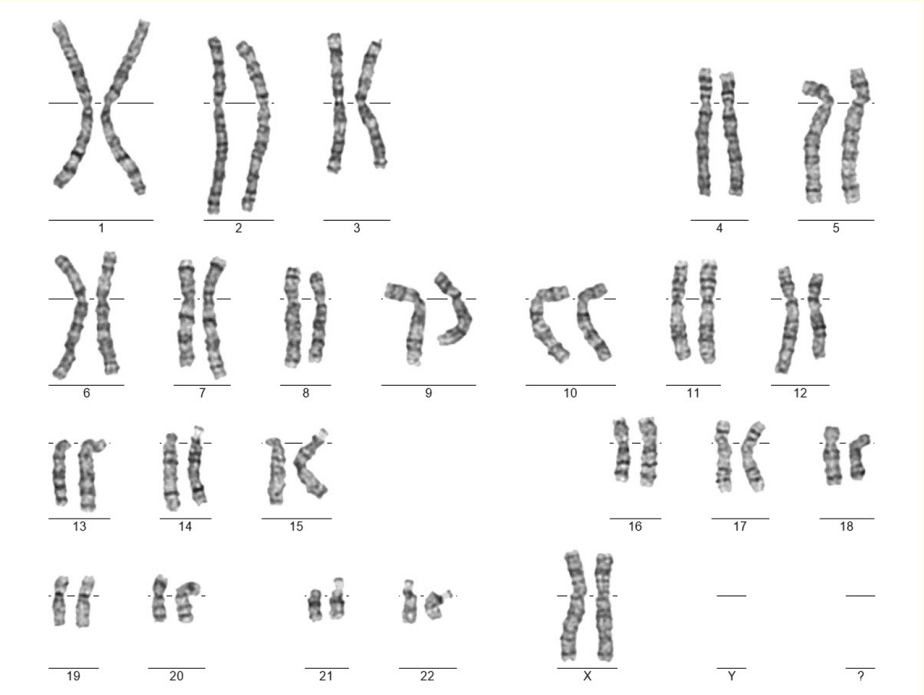


Image adapted from: National Human Genome Research Institute.

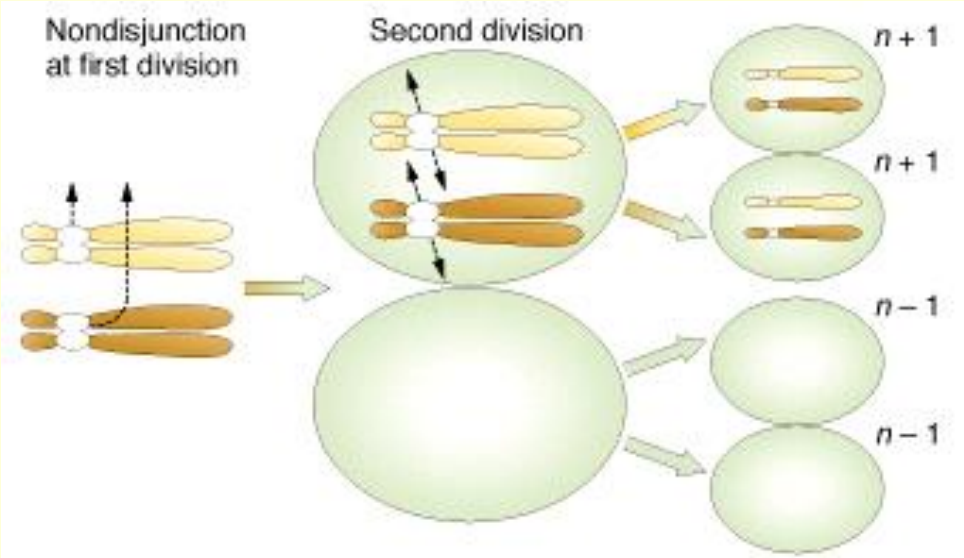


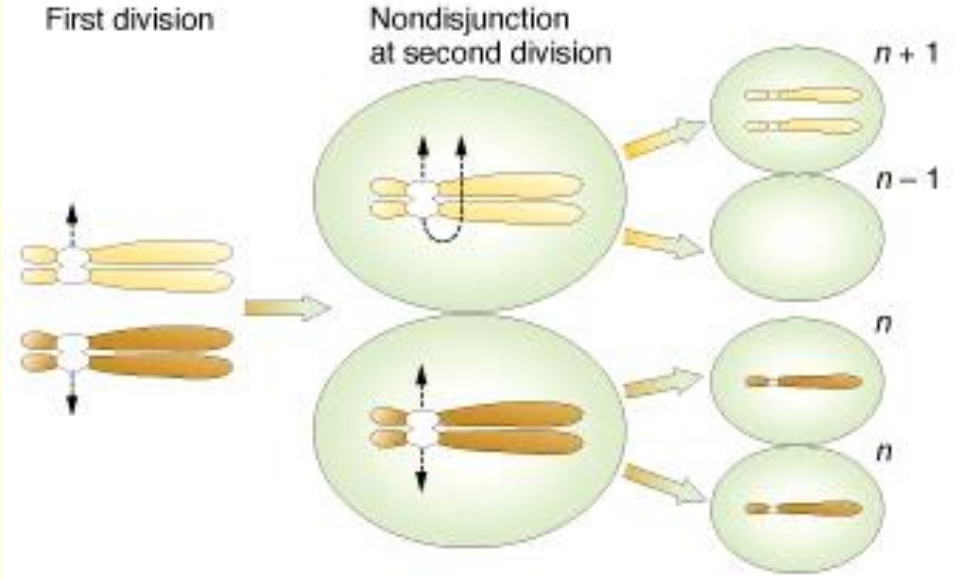
Chromosomes

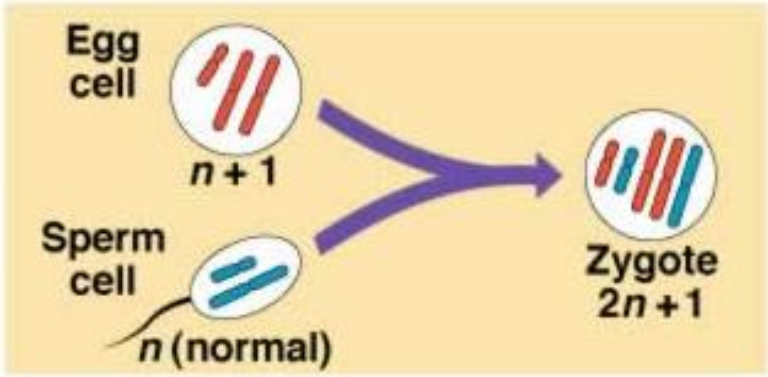
- karyotype – number and appearance of chromosomes in the nucleus
  - 22 pairs of autosomes
  - 1 pairs of gonosomes (XX/XY)
  - in women one X chromosome inactivated
    - Barr body



Nondisjunction







Chromosomal Aberrations

CONGENITAL (in gonads)

- **STRUCTURAL**
  - ❖ *with the change of genetic information*
    - deletion
    - ring chromosome
    - duplication
    - isochromosome
  - ❖ *without the change of genetic information*
    - inversion
    - insertion
    - translocation

- **NUMERIC** (*change in the number of chromosomes)*
  - aneuploidy
    - abnormal number of chromosomes (trisomy, monosomy)
  - polyploidy
    - more than two haploid (n) sets (3n = triploidy, 4n = tetraploidy)

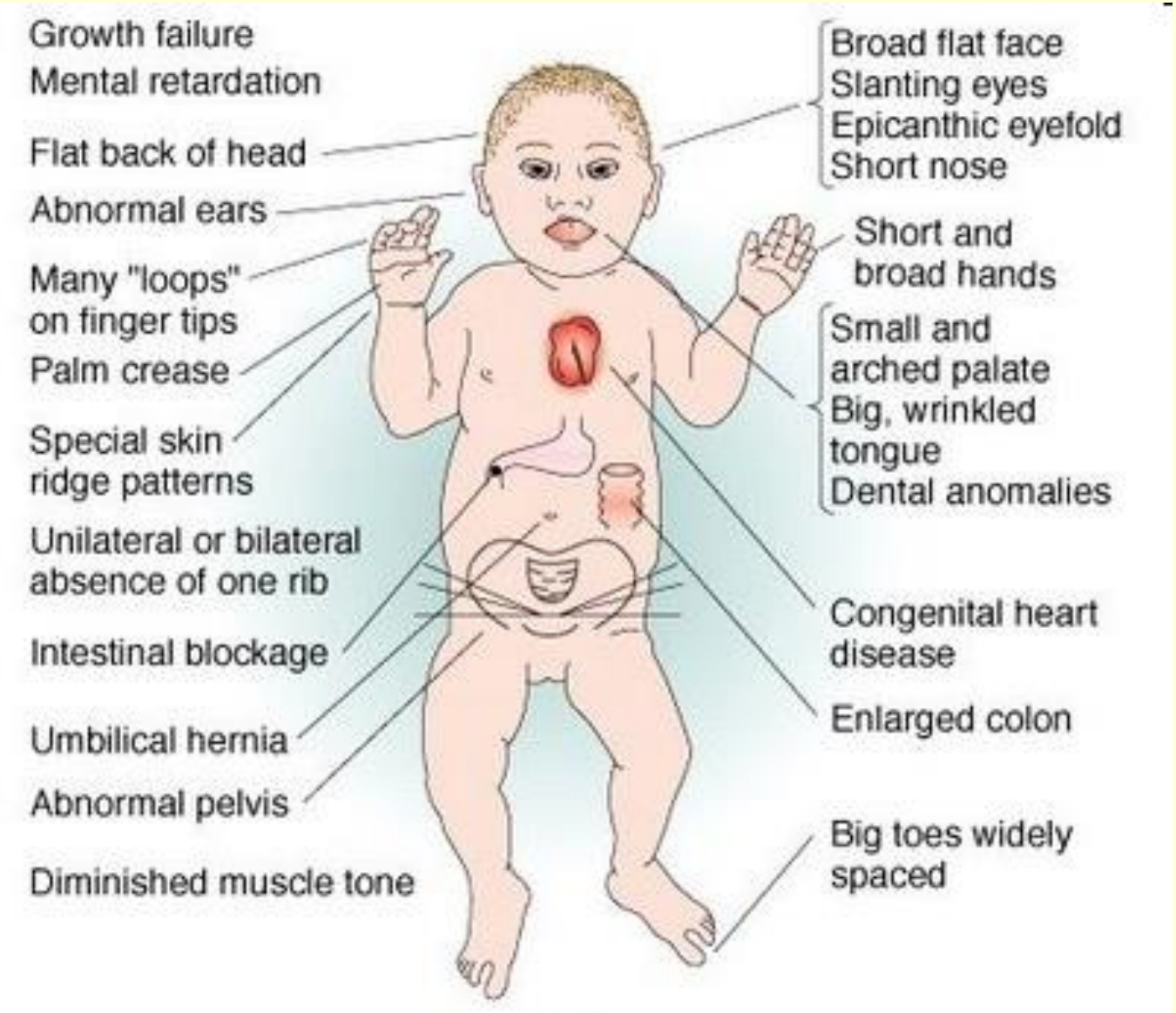
ACQUIRED (in somatic cells as an effect of mutagens)

Autosome Aberations

Down Syndrome

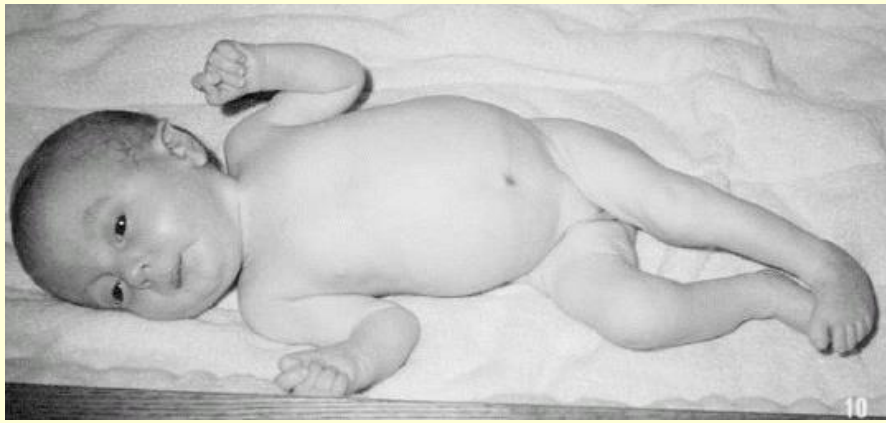
- karyotype 47, XX, +21
  or 47 XY, +21
- 93 % simple trisomy (due to older mother)
- 4 % Robertsonian translocation
- 3 % mosaicism
- 1:800 neonates

Down Syndrome



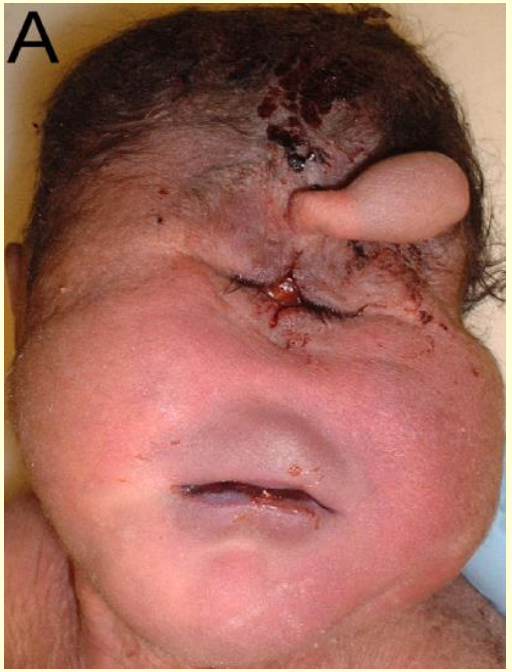
Edwards Syndrome

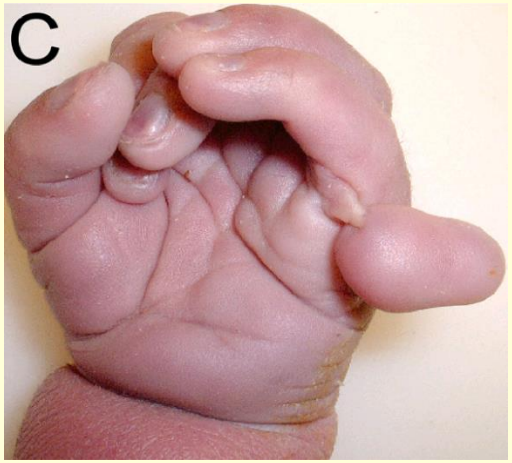
- karyotype 47, XX, +18 or 47, XY, +18
- 1:5000 neonates
- fetal growth retardation, frequent intrauterine fetal death in II.-III. trimester
- microcephaly, narrow eyelid folds, small nose, micromandible, cleft lip/palate, short neck, narrow shoulders, clenched hand with overlapped fingers
- heart defects, esophageal atresia, kidney malformations
- bad prognosis, suckling age survive only 12 % of children



Patau Syndrome

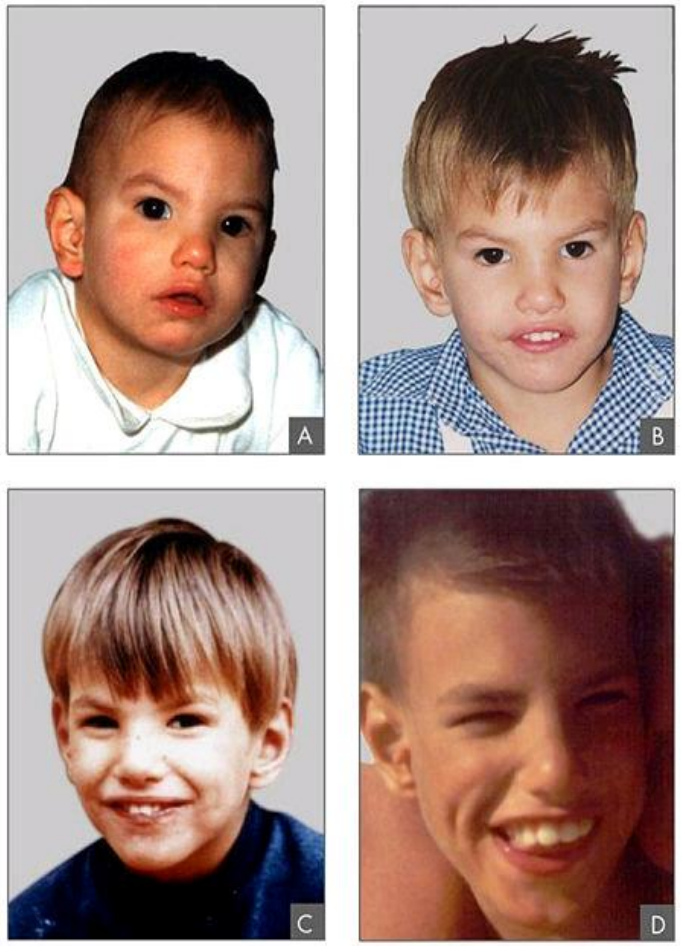
- karyotype 47, XX, +13 or 47, XY, +13
- 1:10 000–20 000 neonates
- frequent premature birth in II.-III. trimester
- microcephaly, trigonocephaly, skin defects, brain defects, low-set ears, cleft lip/palate, abnormal genitalia, kidney abnormalities, polydactyly
- more than 90% of children die within the first year of life





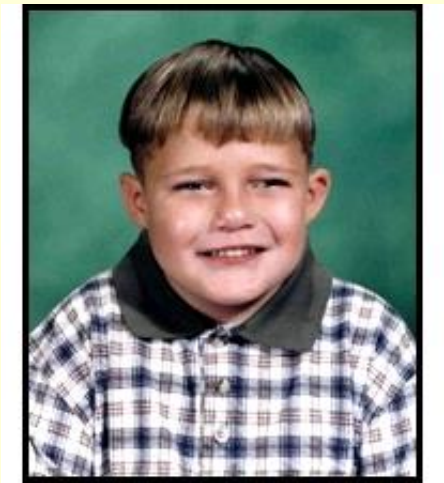
Cri du Chat Syndrome

- deletion of the part of 5. chromosome
- karyotype 46, XX, 5p- or 46, XY, 5p-
- 1:50000–100000
- characteristic cry of affected infants, which is similar to that of a meowing kitten, due to laryngomalacia
- severe growth and psychomotor retardation, hypotonia, epicanthic eye folds, heart defects



DiGeorge Syndrome

- deletion of 22. chromosome, del 22(q11)
- thymic and parathyroid gland aplasia
- severe deffect of cellular imunity
- abnormalities of calcium metabolism
- facial features (dysmorphy), heart deffects



Prader-Willi and Angelman Syndrome

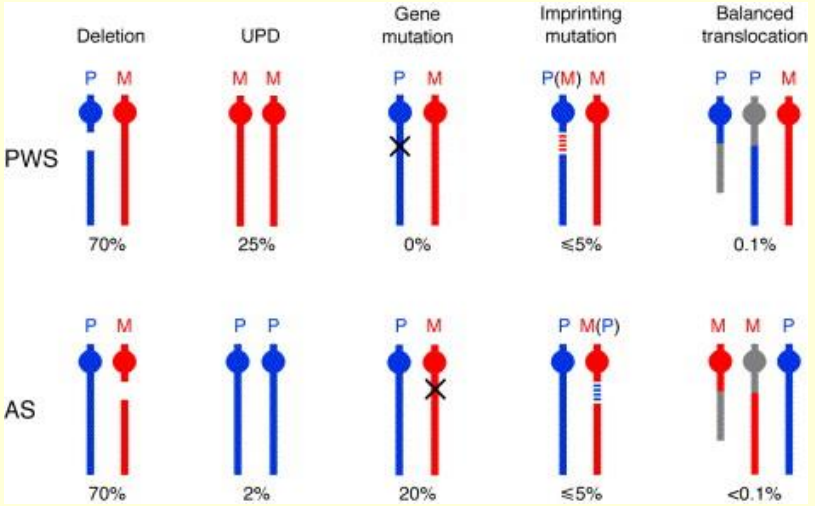
- chromosome 15q11-q13 microdeletion

Prader-Willi syndrome

- AD inheritance, parental imprinting
- mother allele is inactive, father allele has wrong expression
- hypotrophy and hypotonia, later extreme obesity, hypogenitalism

Angelman syndrome

- father allele is inactive, mother allele has wrong expression



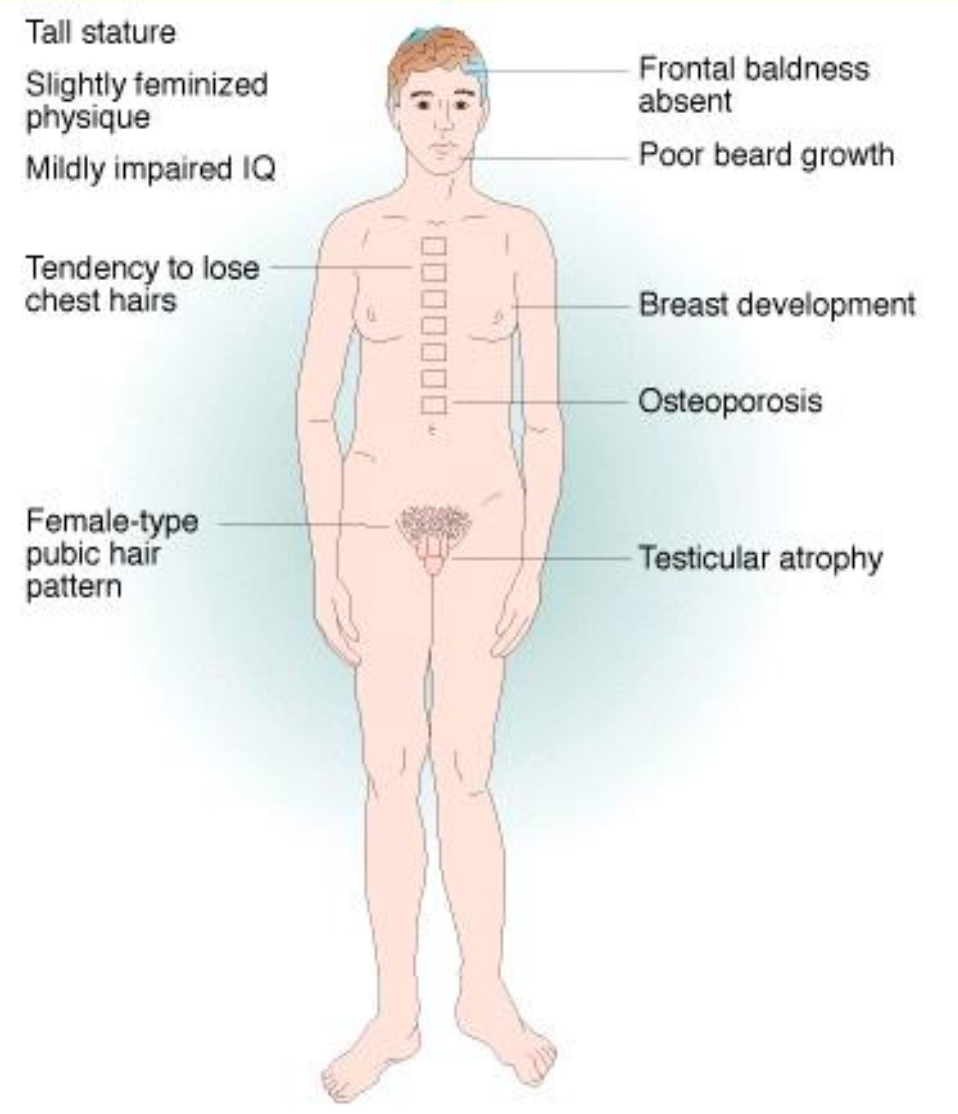
Gonosomal Aberrations

Klinefelter Syndrome

- karyotype: 47, XXY
- up to puberty normal development, can be mild psychomotor retardation, late puberty, hypogenitalism, aspermia (sterility), gynecomastia, female pattern of adipous tissue
- diabetes mellitus, varicose veins, osteoporosis

☝ hormonal substitution by testosterone before puberty

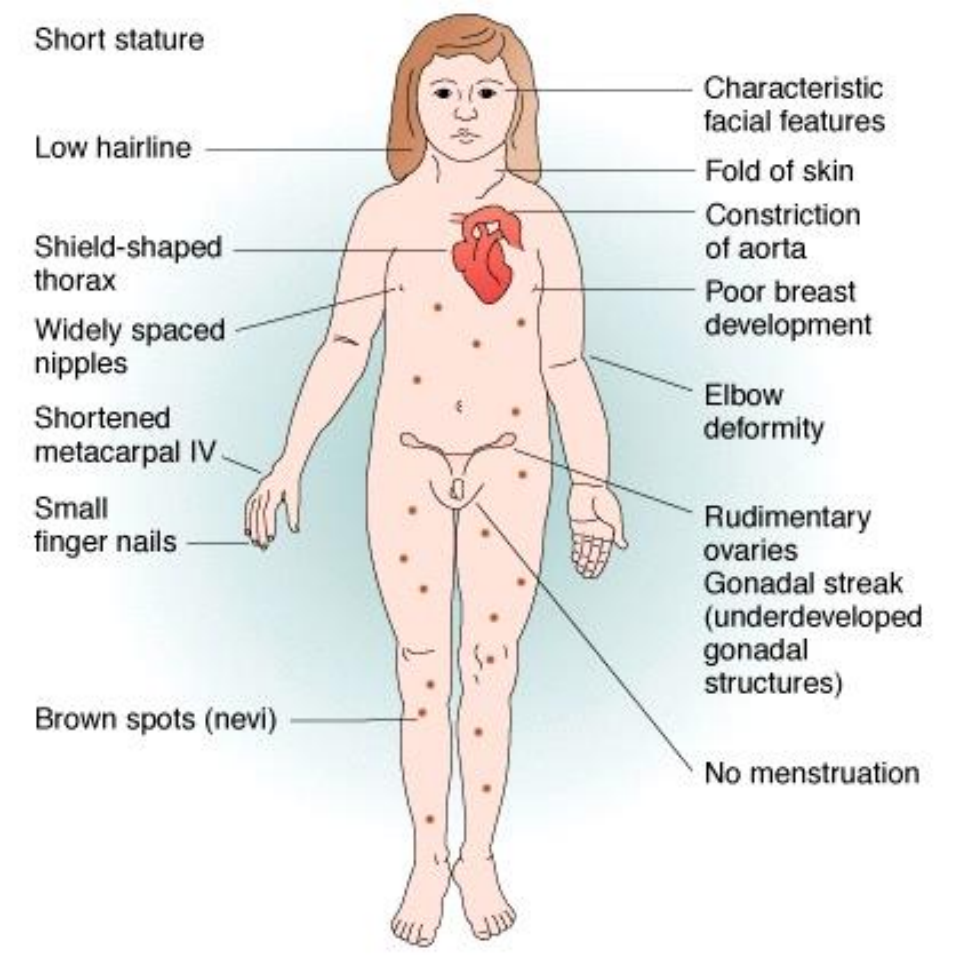
☝ fertility can´t be influenced



Turner Syndrome

- karyotype: 45, X0 monosomy X
- short stature (150–155 cm), lymphedema (swelling), low-set ears, broad chest
- reproductive sterility
- rudimentary ovaries gonadal streak
- heart and kidney defects

- hormonal substitution by estrogens and growth hormones



Prenatal Diagnostics – Methods

I. Non-invasive (screening)

- ultrasound
- maternal serum screening (TRIPLE TEST)

II. Invasive (targeted examination of high-risk women)

- amniocentesis
- chorionic villus sampling
- cordocentesis
- fetoscopy

III. Special

- detection of fetal cells in maternal blood
- preimplantation genetic diagnosis (PDG)

Ultrasound Screening

- screening of congenital diseases and malformations
- **three-phase US screening**

I. 12. w.g. – gestational age, congenital defects, number of fetuses, heart rate, anencephalus

II. 20. w.g. – congenital defects

III. 32.-34. w.g. – growth retardation, fetal position and placenta

Markers of chromosomal aberrations:

- fetal hypotrophy, urogenital abnormalities, defects of abdominal wall, heart defects, pleural effusion, hydrocephalus, early growth retardation

Biochemical Screening

- screening of aneuploidies
- necessary to know precise pregnancy duration

I. trimester

PAPP-A pregnancy associated plasma protein A

β-hCG subunit hCG

β-core hCG in urine

II. trimester

AFP α-1-fetoprotein

hCG human chorionic gonadotropin

SP1 trophoblast specific β-1 globulin

uE3 unconjugated estriol

Prenatal Diagnostics – Invasive Methods

Amniocentesis

- extraction of amniotic fluid under US control, amniocytes (from the skin, GIT, urogenital tract…) are taken
  - later: 16.-18. w.g.
  - early: 12.-14. w.g.

Cordocentesis

- blood sampling from umbilical cord after 20 w.g. transabdominal under US, fetal haemoglobin assessment (HbF)
- karyotype, Fra-X syndrome, hemoglobinopathy, metabolic disorders, fetal infections

Chorionic villus sampling

- transabdominal/transcervical under US
  - early: 10.-12. w.g.
  - later: II. a III. trimestr (placentocentesis)

Fetoscopy

- direct aspection by fetoscope, transabdominal, general anesthesia

Prenatal Diagnostics