CHROMOSOMAL STRUCTURAL ABERRATIONS

INSTITUTE OF BIOLOGY AND MEDICAL GENETICS OF THE 1ST FACULTY OF MEDICINE
CHROMOSOMAL ABERRATIONS

► NUMERICAL

► STRUCTURAL

  ▪ BALANCED
  ▪ UNBALANCED

► MIXOPOLOIDY
  ▪ MOSAICISM
  ▪ CHIMERISM
STRUCTURAL CHROMOSOME REARRANGEMENTS

BALANCED (PHENOTYPICALLY HARMLESS):
- INVERSION
- TRANSLOCATION
- INSERTION

UNBALANCED:
- DELETION
- DUPLICATION
- ISOCHROMOSOME
- RING CHROMOSOME
- DICENTRIC CHROMOSOME
DELETION
INTERSTITIAL
DELETION
TERMINAL
INVERSION
PARACENTRIC

Balanced rearrangement

Reduced fertility - recurrent miscarriages (gametes - acentric or dicentric chromosomes after cross-over in meiosis)
INVERSION
PERICENTRIC

Carriers – normal phenotype

Risk of producing unbalanced gametes due to cross-over and having affected children (partial trisomy and partial monosomy)
PERICENTRIC INVERSION

PRODUCING UNBALANCED GAMETES

PART.

TRISOMY

PART.

MONOSOMY

PART.

TRISOMY

PART.

MONOSOMY
RING CHROMOSOME
ISOCHROMOSOME
TRANSLOCATION
RECIPROCAL
TRANSLOCATION
ROBERTSONIAN (CENTRIC FUSION)
Normal human karyotype:  46, XX or 46, XY

Numerical aberrations:  47, XXY;  45, X;  69, XXY

+/− placed before additional or missing chromosome  47, XX, +21

Structural aberrations:

- del - deletion  46, XY, del(5)(p?)  46, X, del(X)(q?)
- t - translocation (reciprocal)  46, XY, t(2;8)(p?;q?)
- der, rob - derivative chromosome (Robertsonian translocation)  45, XX, der(14;21) n. 45, XX, rob(14;21)

46, XY, der(21;21), +21 n. 46, XY, rob(21;21), +21
TURNER SYNDROME
DELETION FORM

46,X,del(Xp)
CRI DU CHAT SYNDROME
(CAT CRY SYNDROME)

- microcephaly
- severe somatic and mental retardation
- round “moon-shaped” face (in childhood)
- hypoplastic larynx – high shrill cry (like a mewing cat)

del(5p)
PRADER-WILLI SYNDROME

NEWBORNS, EARLY INFANTS:
• severe hypotonia
• developmental delay

LATER:
• mental retardation
• overeating – extreme obesity with complications (DM, cardiovascular disorders, sleeplessness,...)
• hypogenitalism
• behavioral disorders
ANGELMAN SYNDROME

- severe mental retardation
- absent speech
- paroxysms of easily provoked laughter
- jerky movements, ataxia, stiff-legged gait
- epileptic seizures
- „happy puppet“ syndrome

del(15)(q11-13)mat
DOWN SYNDROME
TRANSLOCATION FORM

M. DOWN:
95% free trisomy of chr. 21
4-5% translocation form
(Robertsonian translocation)
<1% mosaicism
DOWN SYNDROME
TRANSLOCATION FORM

46,XY,der(14;21),+214
Analyse the karyotype of a newborn with Down syndrome features (task 17, p. 89):

Down syndrome
46,XX,der(21;21),+21
Risk: in theory 100%, empirical 100%

- **GAMETE (II. parent)**: 46,XX
- **LETHAL**: 45,XX(XY),-21 (MONOSOMY)
- **M.DOWN**: 46,XX(XY),der(21;21),+21 (TRISOMY)

- **GAMETE (I. parent)**: 46,XX
- **ZYGOTE (FETUS)**: 45,XY,der(21;21)

- **MEIOSIS**
- **PHENOTYPE KARYOTYPE**
Analyse the karyotype of a man - father of Down syndrome child, mother - 46,XX (task 16, p. 88):

- Balanced translocation
  - 45,XY,der(14;21) - father
  - 46,XX(XY),der(14;21),+21 – M. Down child
45,XY,der(14;21)

46,XX

NORMAL

BALANCED TRANSLOCATION

M.DOWM 33.3%

LETHAL
<table>
<thead>
<tr>
<th>PROBAND</th>
<th>PARENTS</th>
<th>RISK</th>
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<tbody>
<tr>
<td>47,X&lt;sup&gt;x&lt;/sup&gt;/&lt;sub&gt;y&lt;/sub&gt;,+21</td>
<td>46,X&lt;sup&gt;x&lt;/sup&gt;/&lt;sub&gt;y&lt;/sub&gt;</td>
<td>&gt; THAN POPULATION dependence on maternal age</td>
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<tr>
<td>46,X&lt;sup&gt;x&lt;/sup&gt;/&lt;sub&gt;y&lt;/sub&gt;,der(21;21),+21</td>
<td>45,X&lt;sup&gt;x&lt;/sup&gt;/&lt;sub&gt;y&lt;/sub&gt;,der(21;21)</td>
<td>100% THEORETICAL 100% EMPIRICAL</td>
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</table>
| 46,X<sup>x</sup>/<sub>y</sub>,der(D;21),+21 | 45,X<sup>x</sup>/<sub>y</sub>,der(D;21) | 33,3% THEORETICAL EMPIRICAL:  
cca 5% - father (carrier)  
cca 15% - mother (carrier) |
| 46,X<sup>x</sup>/<sub>y</sub>,der(D;21),+21 | 46,X<sup>x</sup>/<sub>y</sub>,der(21;22) | NEW MUTATION NONPATERNITY                |
| 47,X<sup>x</sup>/<sub>y</sub>,+21 | 47,X<sup>x</sup>/<sub>y</sub>,+21/46,X<sup>x</sup>/<sub>y</sub> | MOSAICISM – depends on ratio of the cell lines with normal and aberrant number of chromosome 21 |
Analyse the karyotype of a girl with severe mental and somatic retardation:

Cri du chat syndrome
46,XX,del(5p)