CHROMOSOMAL STRUCTURAL ABERRATIONS

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

CHROMOSOMAL ABERRATIONS

- NUMERICAL
- STRUCTURAL
  - BALANCED
  - UNBALANCED
- MIXOPLOIDY
  - MOSAICISM
  - CHIMERISM

STRUCTURAL CHROMOSOME REARRANGEMENTS

BALANCED (PHENOTYPICALLY HARMLESS):

INVERSION

TRANSLOCATION

INSERTION

UNBALANCED:

DELETION

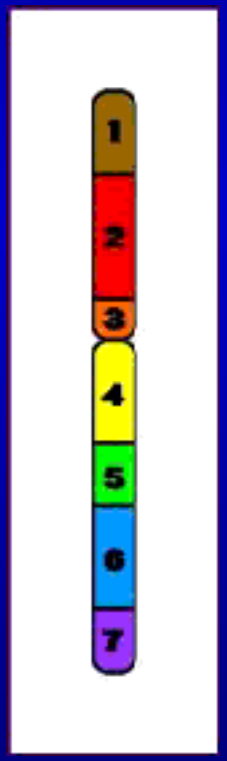
DUPLICATION

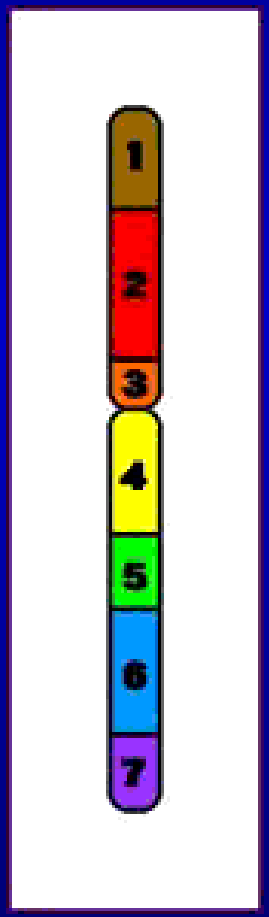
ISOCHROMOSOME

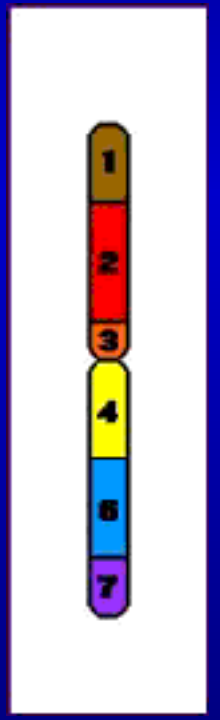
RING CHROMOSOME

DICENTRIC CHROMOSOME

DELETION
INTERSTITIAL

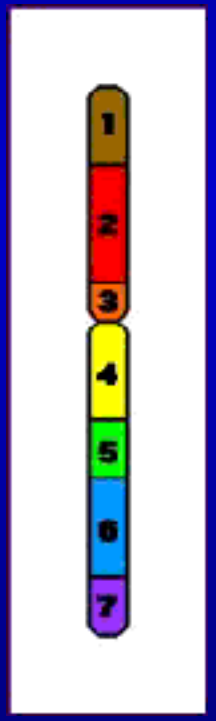


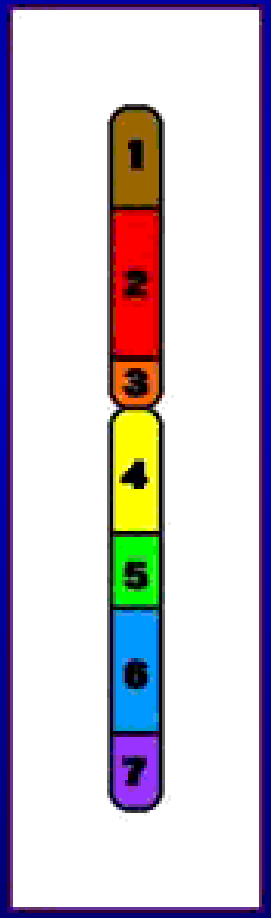


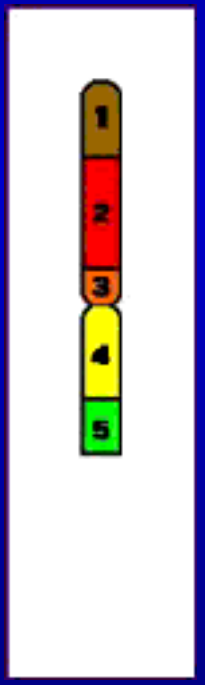


DELETION

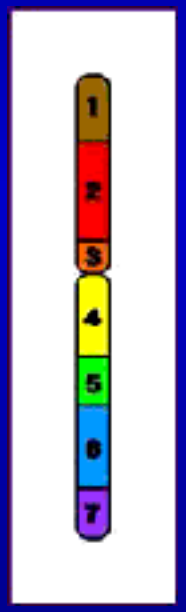
TERMINAL

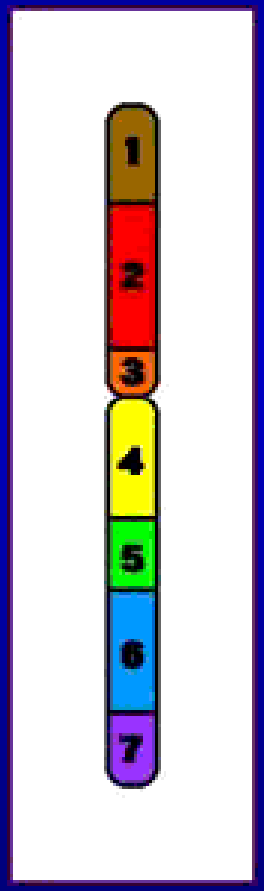


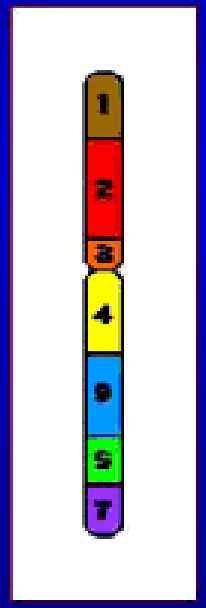




INVERSION
PARACENTRIC



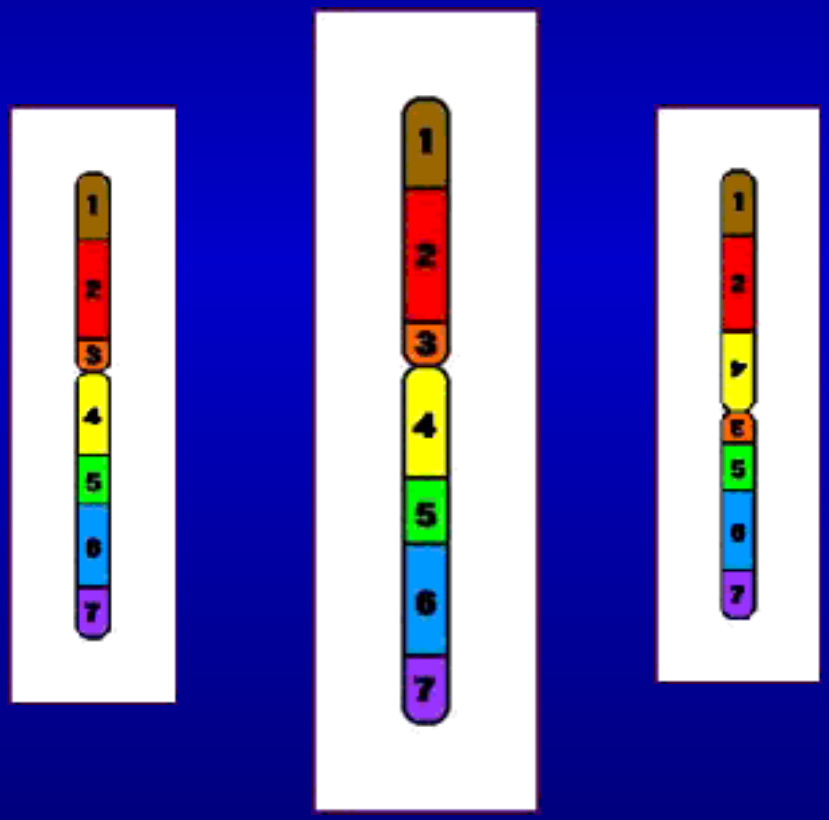




Balanced rearrangement

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

INVERSION
PERICENTRIC

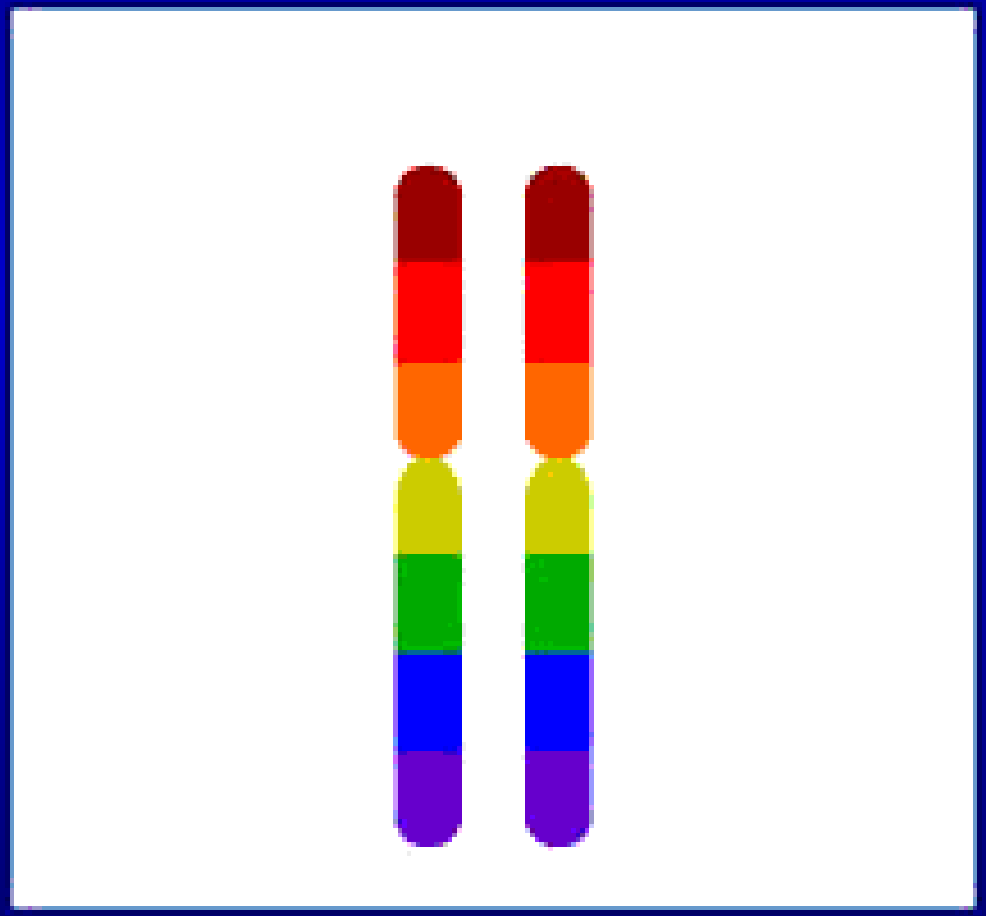


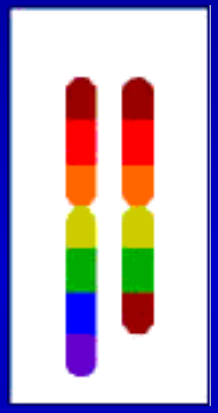
Carriers – normal phenotype

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

PERICENTRIC INVERSION

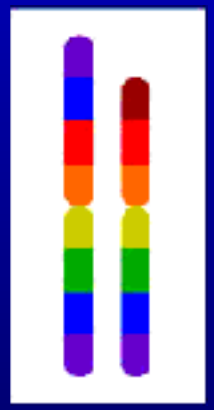
PRODUCING UNBALANCED GAMETES





PART. TRISOMY

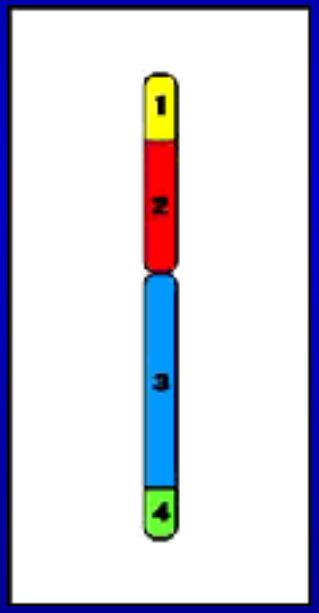
PART. MONOSOMY

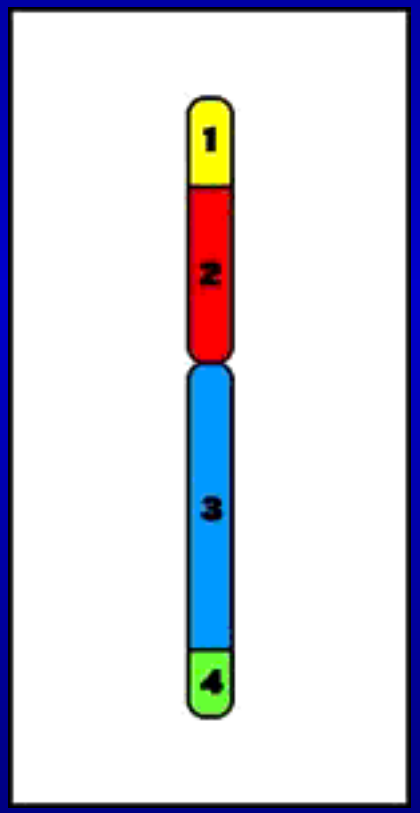


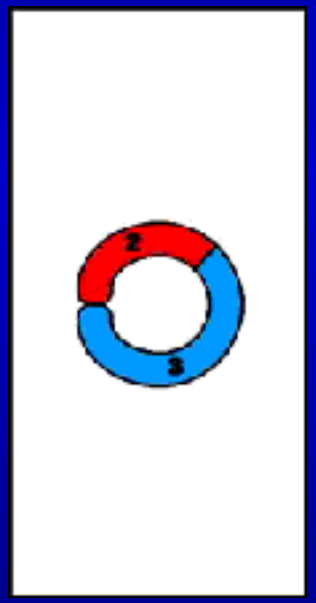
PART. TRISOMY

PART. MONOSOMY

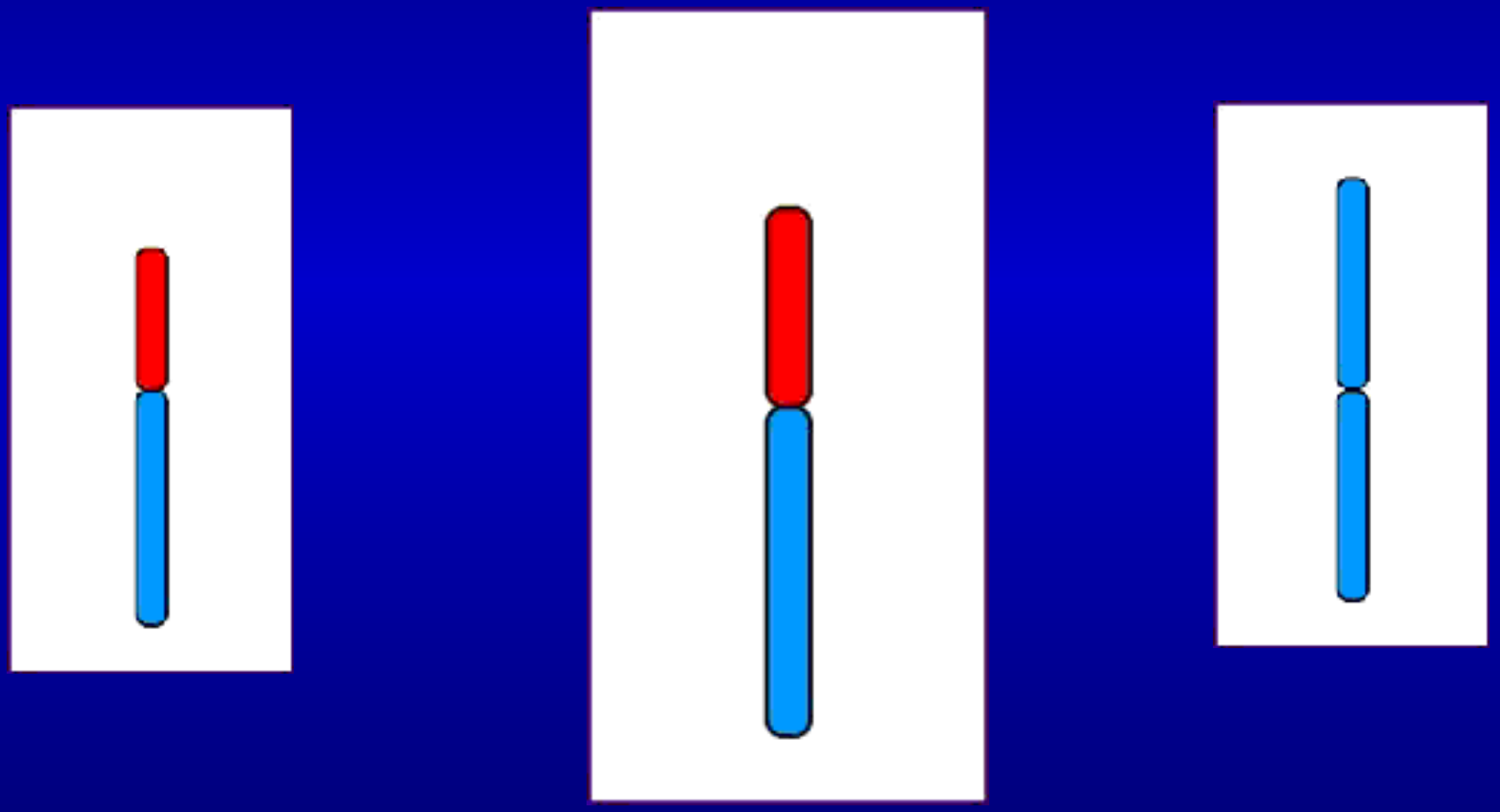
RING CHROMOSOME





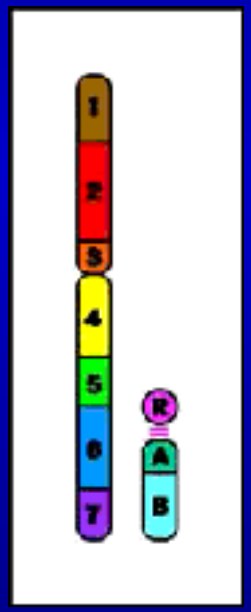


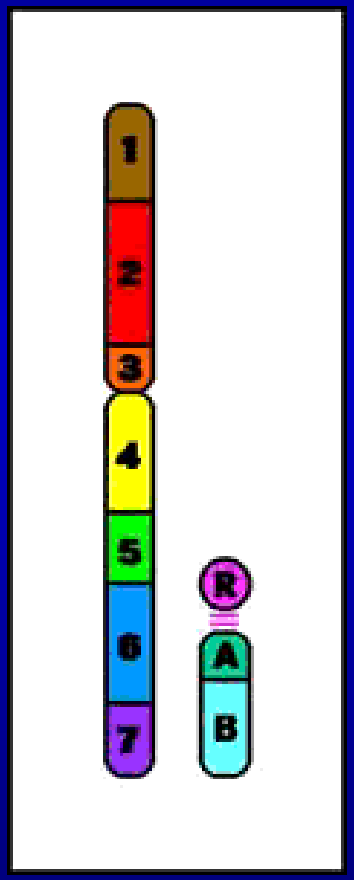
ISOCHROMOSOME

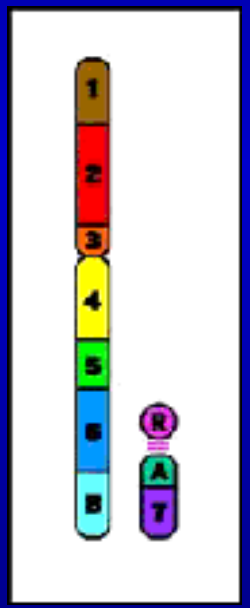


TRANSLOCATION

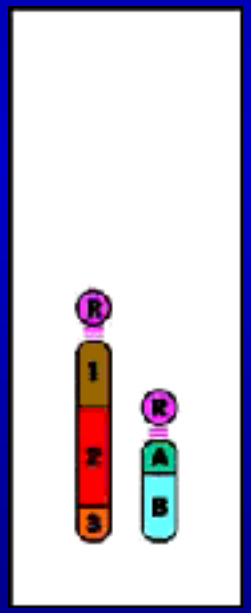
RECIPROCAL

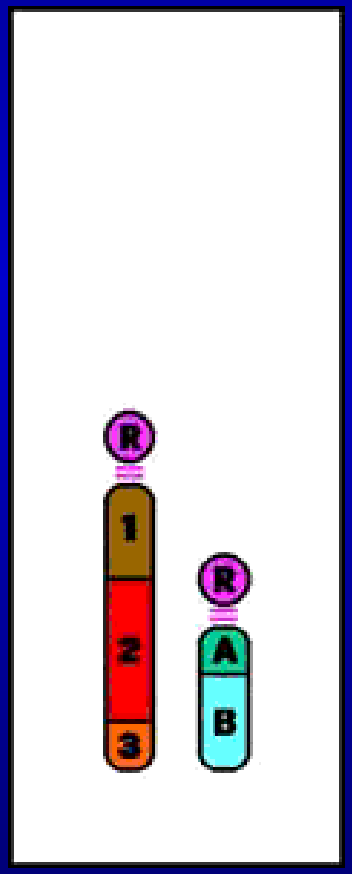


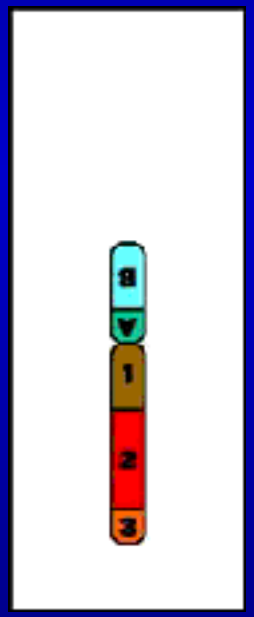




TRANSLOCATION
ROBERTSONIAN (CENTRIC FUSION)







INTERNATIONAL CYTOGENETIC NOMENCLATURE ISCN – 1995, 2005

(examples of symbols and abbreviations)

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?)

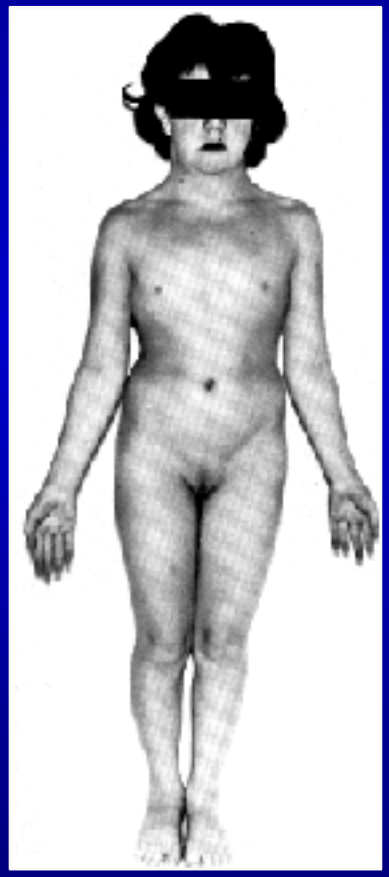
t - translocation (reciprocal) 46, XY, t(2;8)(p?;q?)

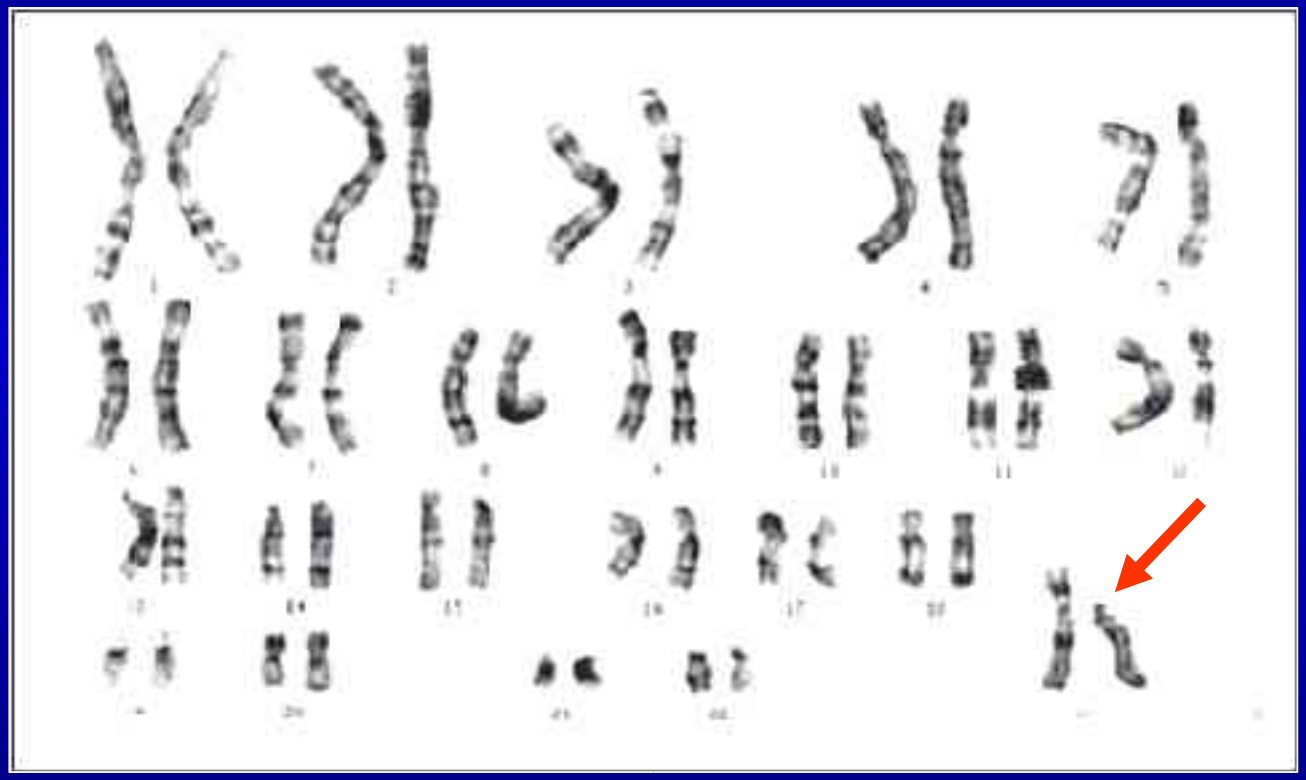
der, rob - derivative chromosome (Robertsonian translocation)

45, XX, der(14;21) n. 45, XX, rob(14;21)

46, XY, der(21;21), +21 n. 46, XY, rob(21;21), +21

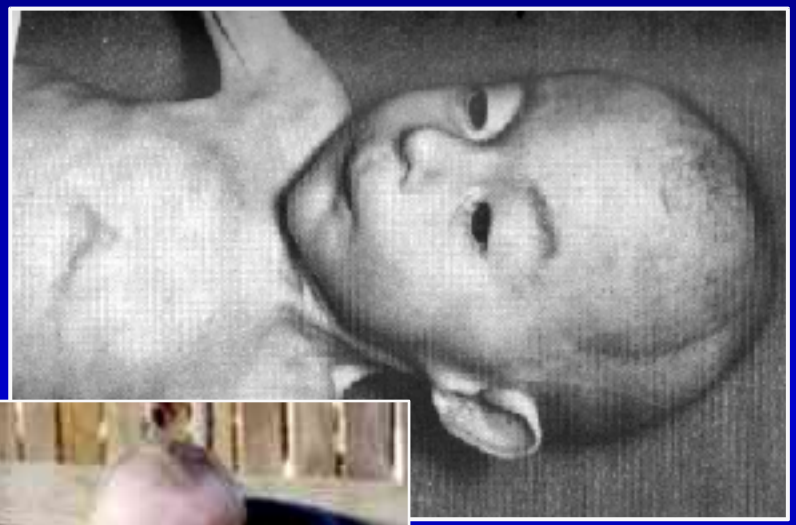
TURNER SYNDROME
DELETION FORM





46,X,del(Xp)

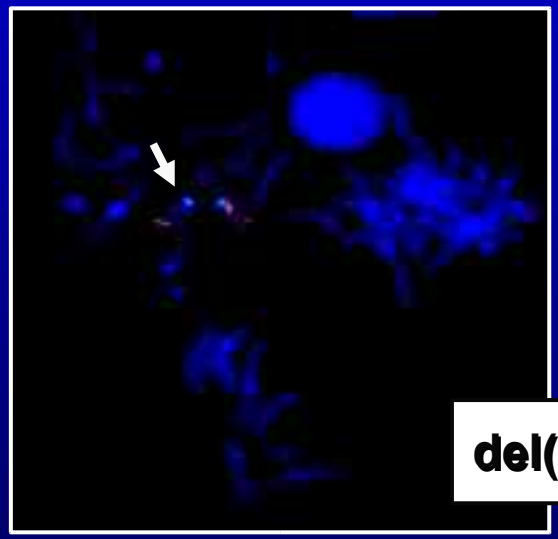
CRI DU CHAT SYNDROME
(CAT CRY SYNDROME)



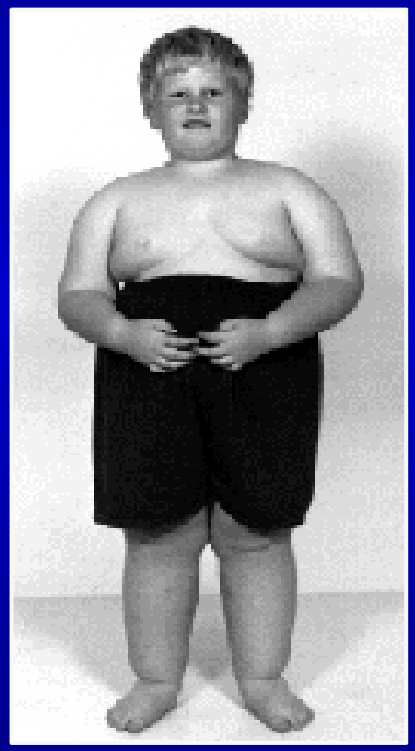
del(5p)

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

PRADER-WILLI SYNDROME



del(15)(q11-13)pat



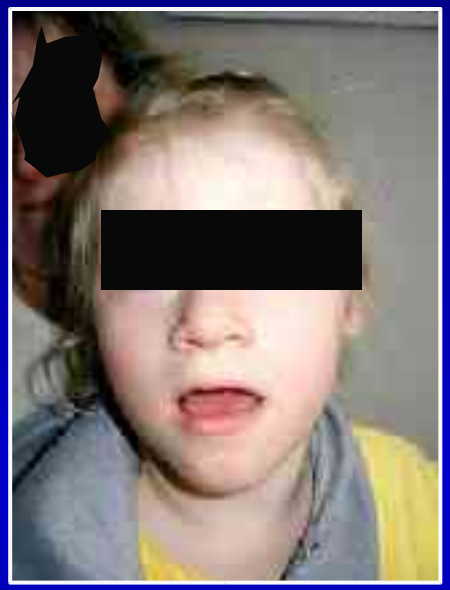
NEWBORNS, EARLY INFANTS:

- severe hypotonia
- developmental delay

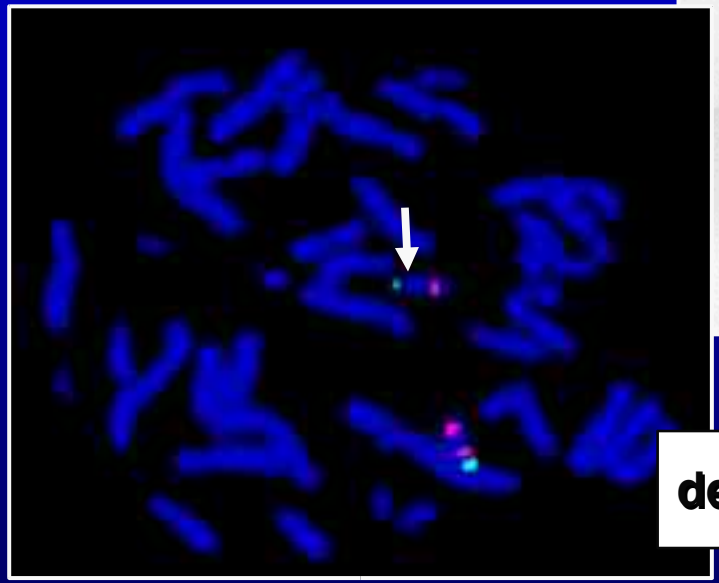
LATER:

- mental retardation
- overeating – extreme obesity with complications (DM, cardiovascular disorders, sleeplessness,…)
- hypogenitalism
- behavioral disorders

ANGELMAN SYNDROME

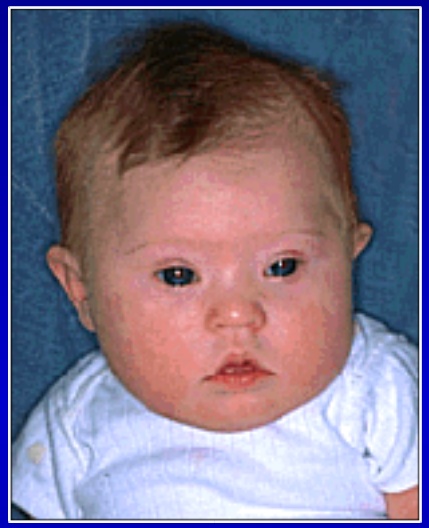


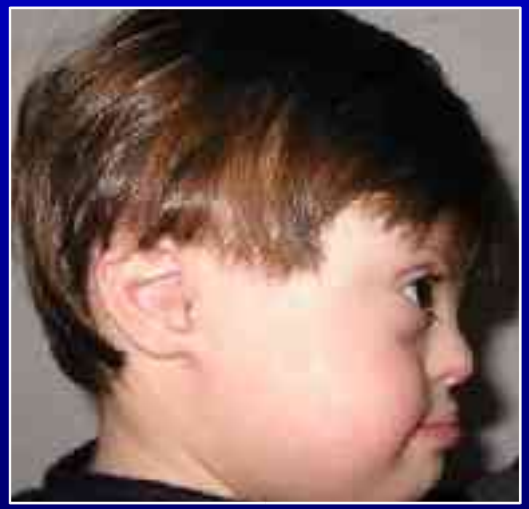
- severe mental retardation
- absent speech
- paroxysms of easily provoked laughter
- jerky movements, ataxia, stiff-legged gait
- epileptic seizures
- „happy puppet" syndrome



del(15)(q11-13)mat

DOWN SYNDROME
TRANSLOCATION FORM





M. DOWN:

95% free trisomy of chr. 21

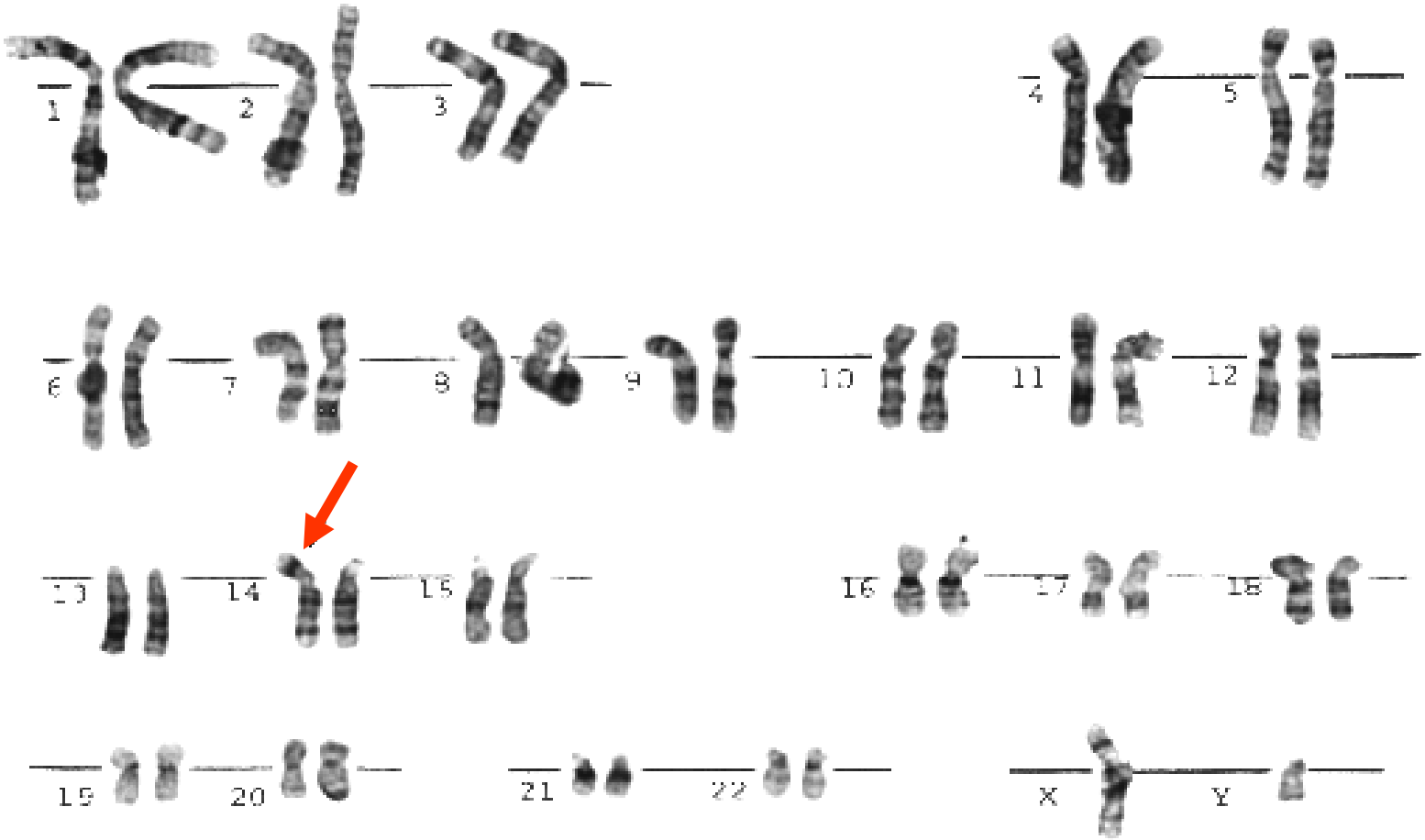
4-5% translocation form

(Robertsonian translocation)

<1% mosaicism

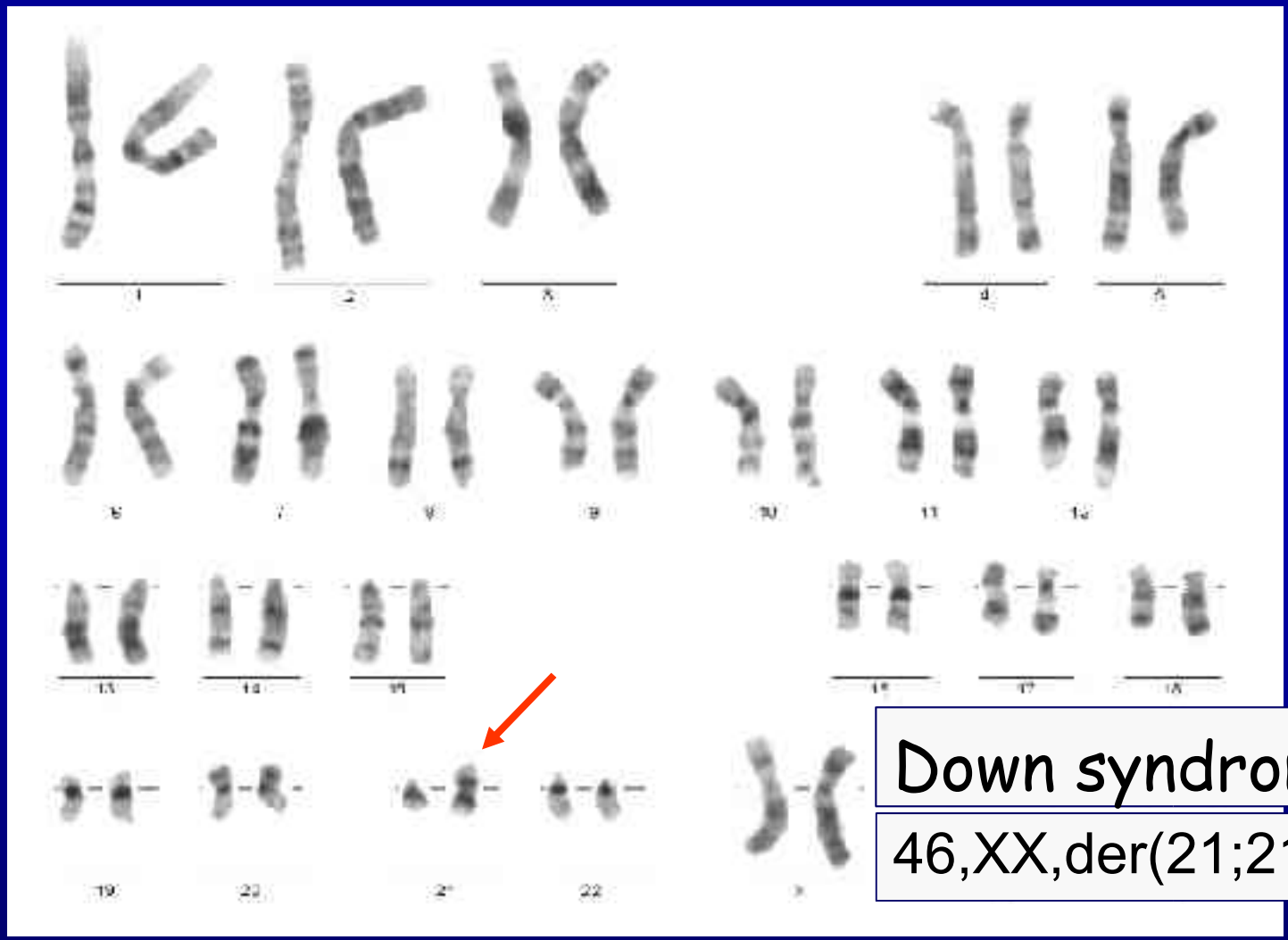
DOWN SYNDROME

TRANSLOCATION FORM



46,XY,der(14;21),+214

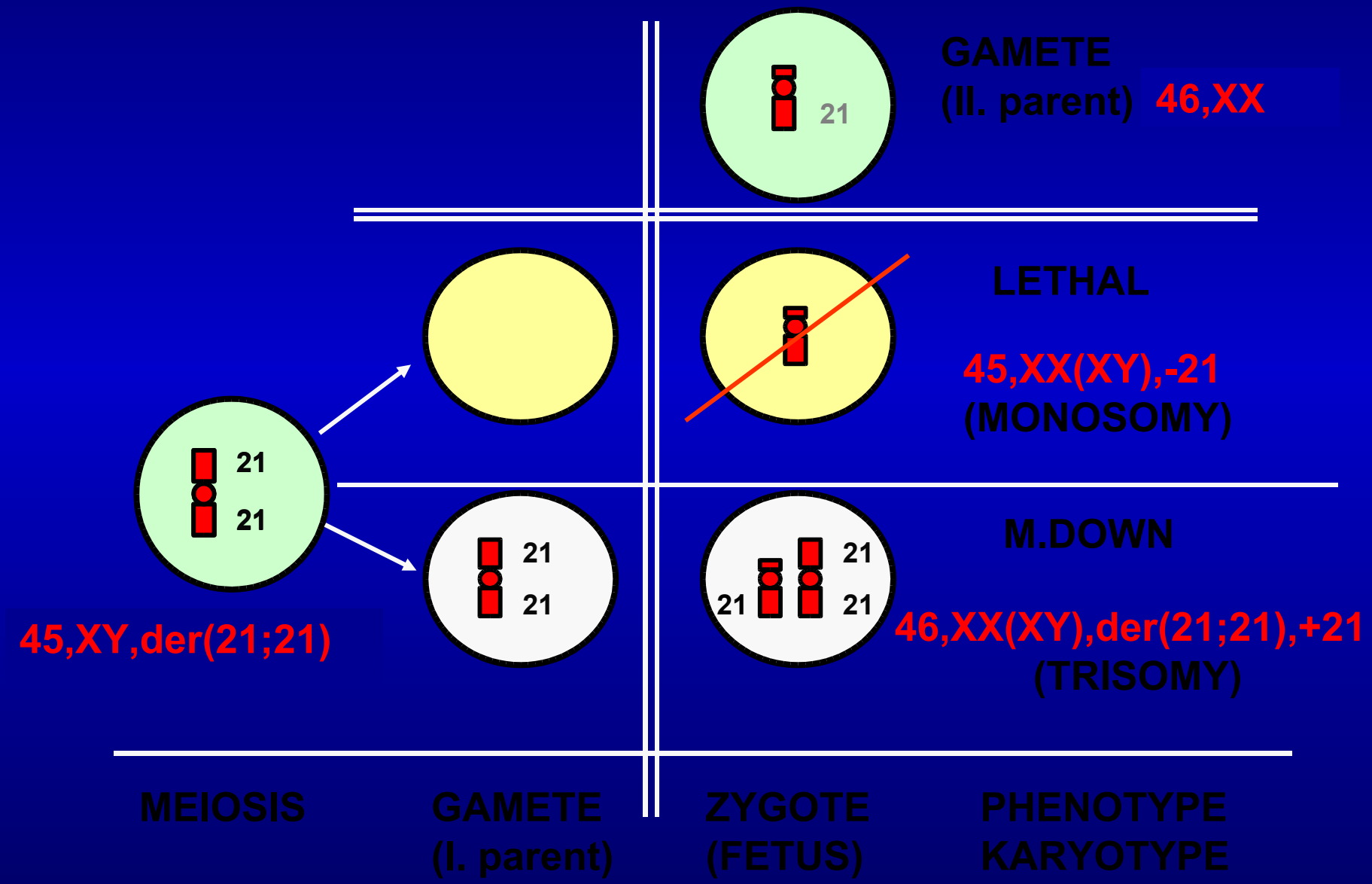
Analyse the karyotype of a newborn with Down syndrome features (task 17, p. 89):



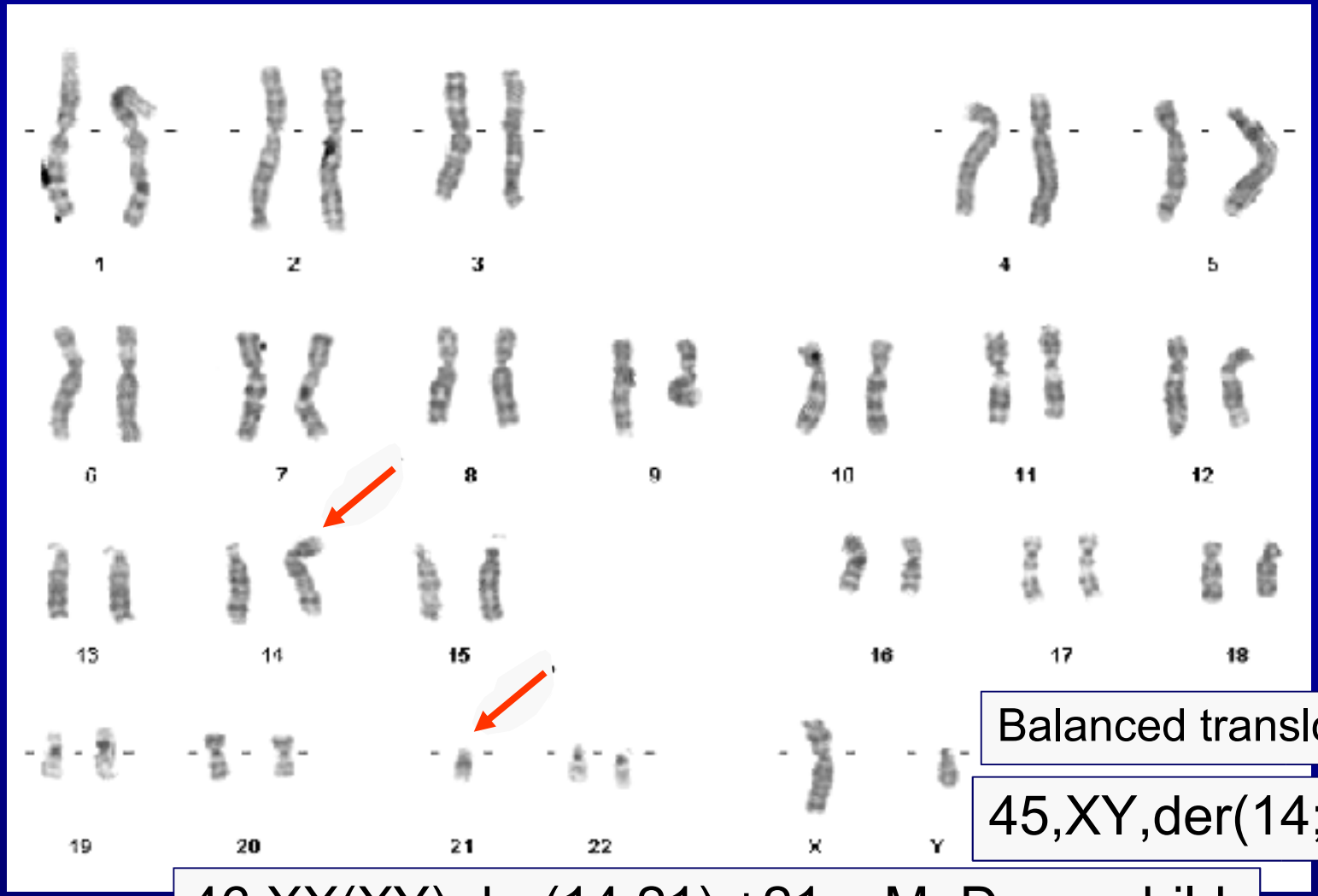
Down syndrome

46,XX,der(21;21),+21

Risk: in theory 100%, empirical 100%



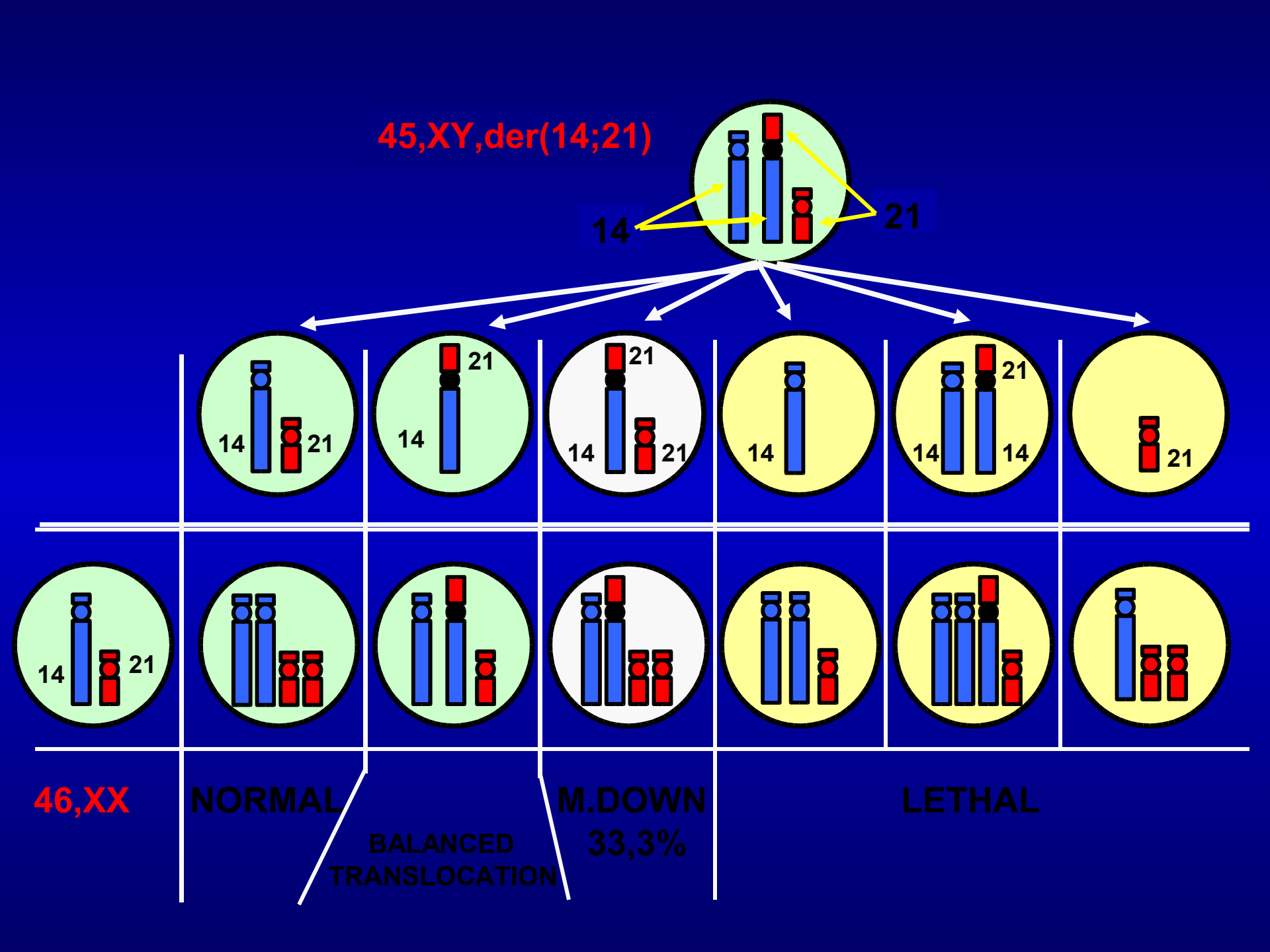
Analyse the karyotype of a man - father of Down syndrome child, mother - 46,XX (task 16, p. 88):



Balanced translocation

45,XY,der(14;21) - father

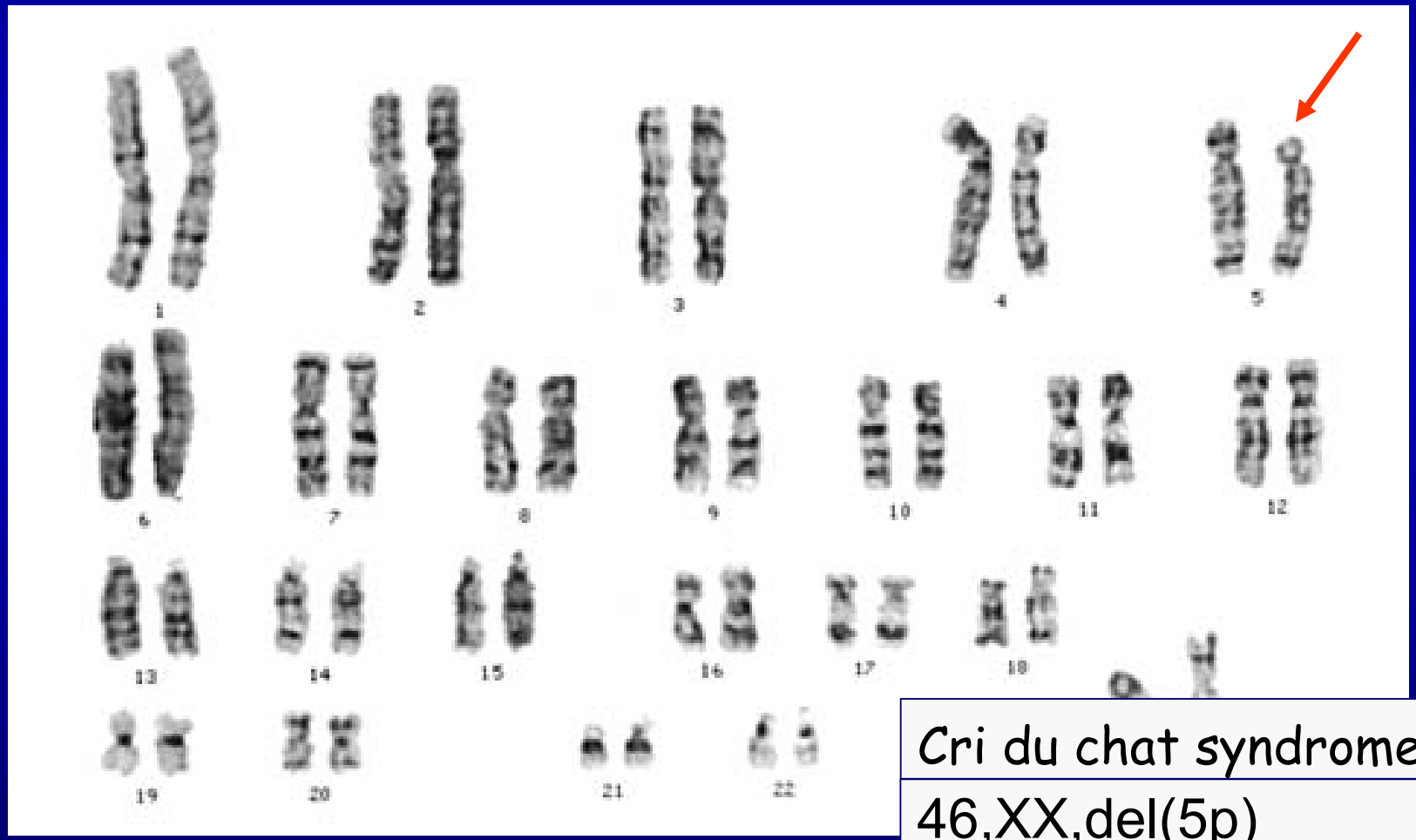
46,XX(XY),der(14;21),+21 – M. Down child


45,XY,der(14;21)
14
21
14
21
14
21
21
14
21
14
21
14
14
21
21
46,XX
NORMAL
BALANCED
TRANSLOCATION
M.DOWN
33,3%
LETHAL

MORBUS DOWN

PROBAND	PARENTS		RISK
47,$X^x/_Y$,+21	46,$X^x/_Y$	46,$X^x/_Y$	> THAN POPULATION dependence on maternal age
46,$X^x/_Y$,der(21;21),+21	45,$X^x/_Y$,der(21;21)	46,$X^x/_Y$	100% THEORETICAL 100% EMPIRICAL
46,$X^x/_Y$,der(D;21),+21 46,$X^x/_Y$+21,der(21;22)	45,$X^x/_Y$,der(D;21) 45,$X^x/_Y$,der(21;22)	46,$X^x/_Y$	33,3% THEORETICAL EMPIRICAL: cca 5% - father (carrier) cca 15% - mother (carrier)
46,$X^x/_Y$,der(D;21),+21 46,$X^x/_Y$,+21,der(21;G)	46,$X^x/_Y$	46,$X^x/_Y$	NEW MUTATION NONPATERNITY
47,$X^x/_Y$,+21	47,$X^x/_Y$,+21/46,$X^x/_Y$	46,$X^x/_Y$	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)