Polish Collection of Chromosomal Translocations

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and

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1st Central and Eastern European Summit on Preconception Health and Prevention of Birth Defects

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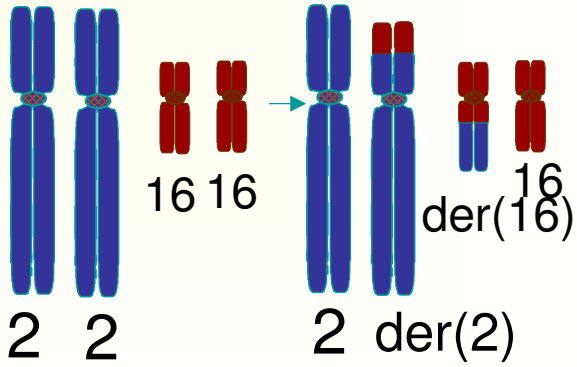
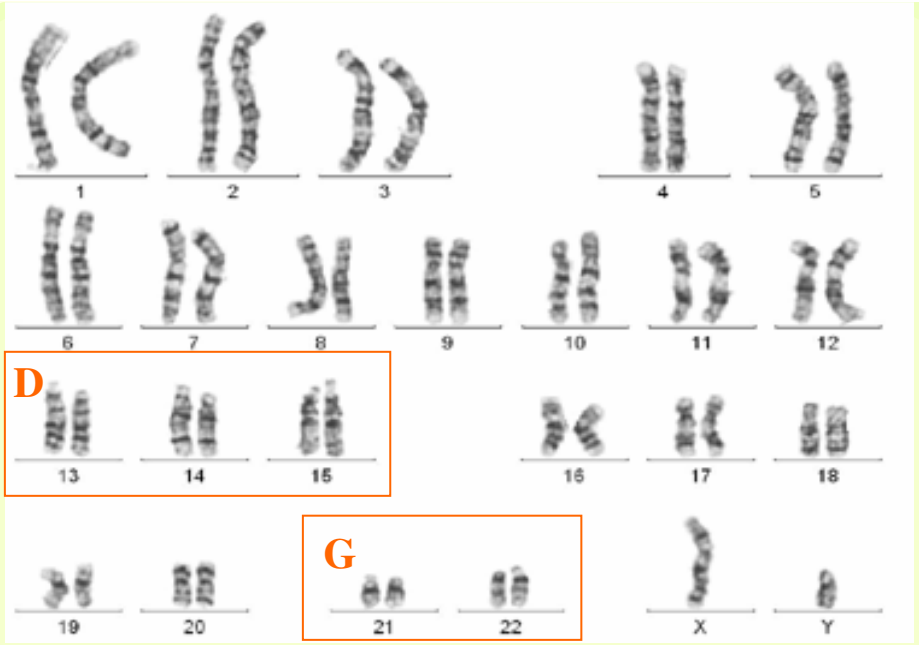
Chromosome translocations (CT)

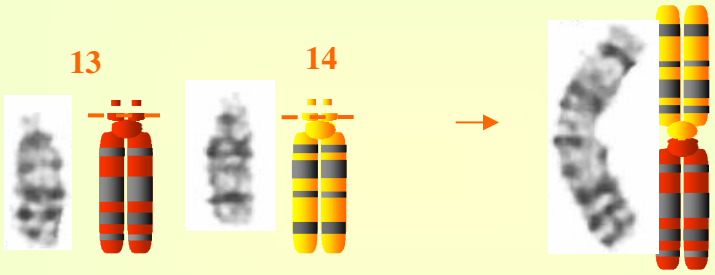
- ***Chromosome translocations (CT) represents of the most common chromosomal structural aberrations in man with frequency 1:600 in newborn population***



Heterologic pairs of chromosomes are involved in the origin of chromosome translocation

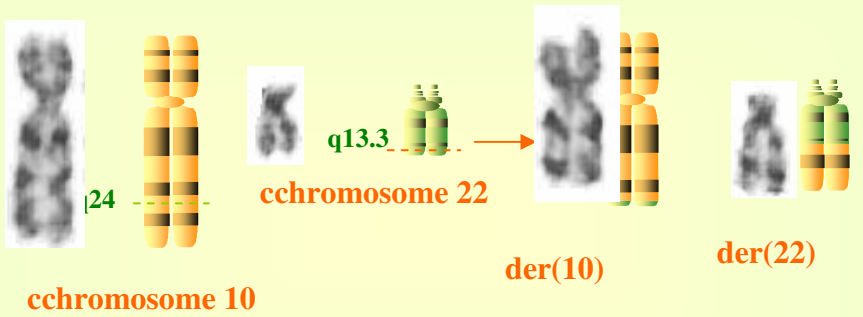


Robertsonian



der(13;14)(p11.2;p11.2)

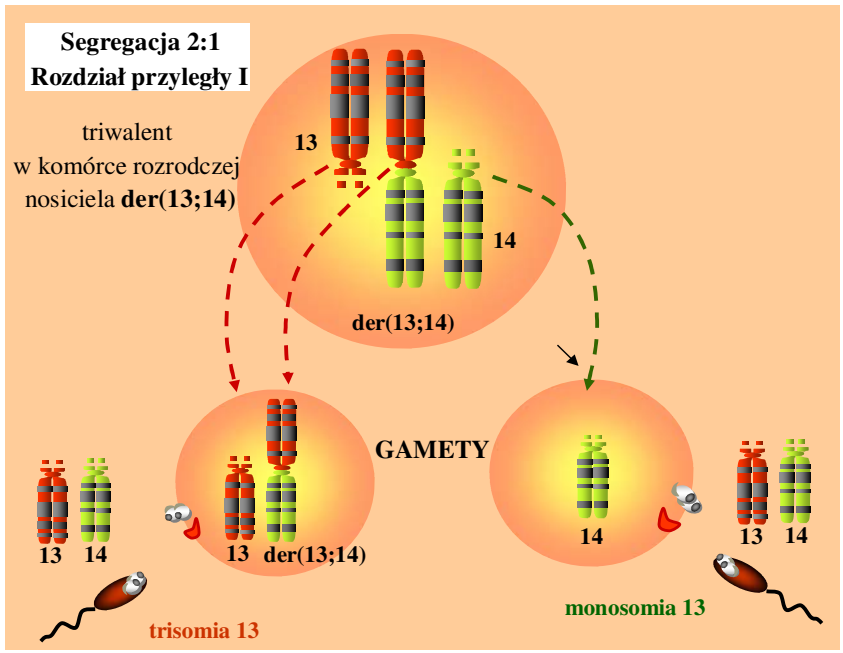
Non Robertsonian – Reciprocal



t(10;22)(q24;q13.3)

Meiotic malsegregation

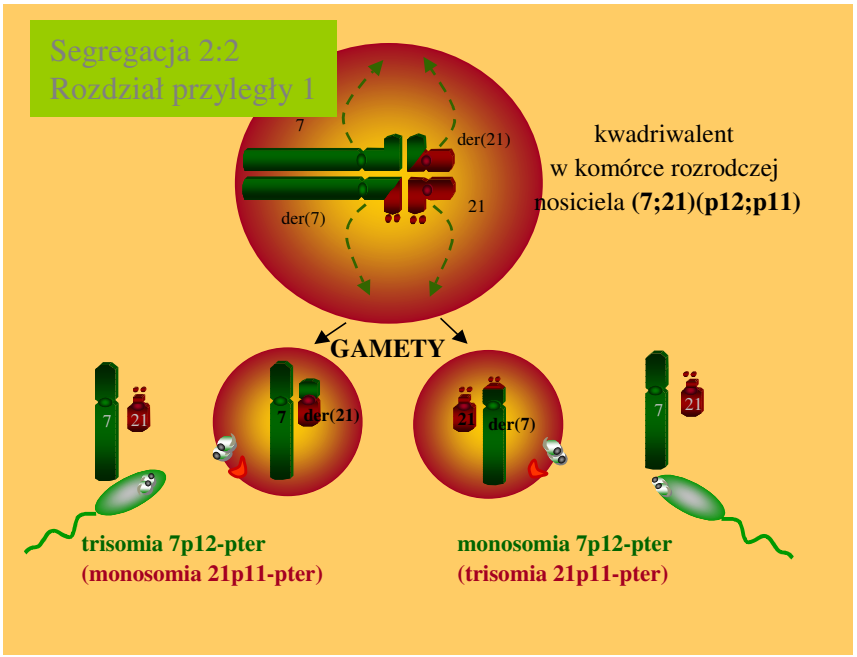
RobCT



der(13;14)

clinical effect on progeny due to different unbalanced karyotype in gametes is producing by meiotic malsegregation of chromosomes involved in the actual chromosome translocation.

ReciprocalCT



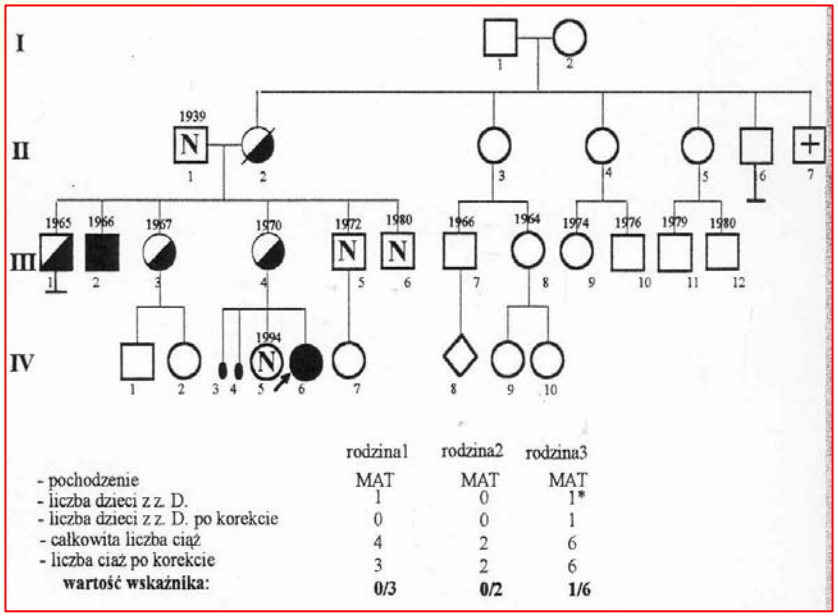
t(7;21)(p12;p11)

Clinical effects RCT

- ***Dependent on survival rate of unbalanced embryo/fetus/child***
- ***the malformed offspring*** *at birth and at prenatal diagnosis,*
- *miscarriages,*
- *stillbirths*

early deaths of newborn

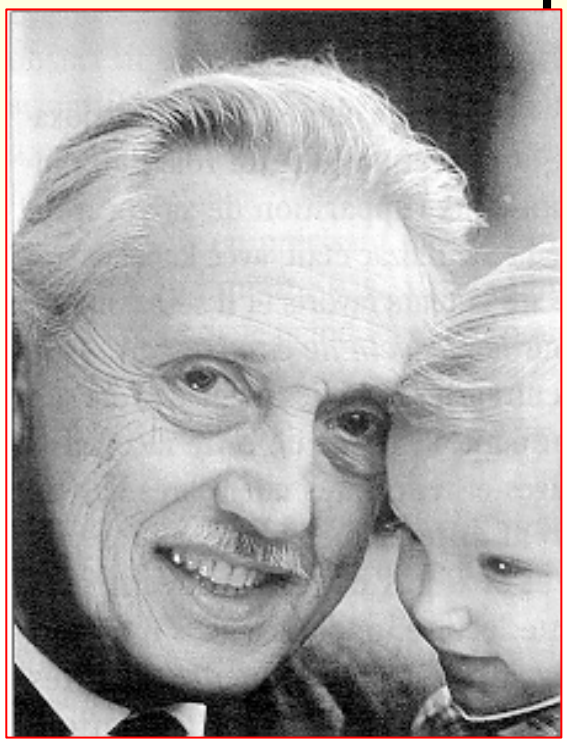
have been observed



	rodzina1	rodzina2	rodzina3
- pochodzenie	MAT	MAT	MAT
- liczba dzieci z z. D.	1	0	1*
- liczba dzieci z z. D. po korekcie	0	0	1
- całkowita liczba ciąż	4	2	6
- liczba ciaż po korekcie	3	2	6
wartość wskaźnika:	**0/3**	**0/2**	**1/6**

Interchromosomal effect

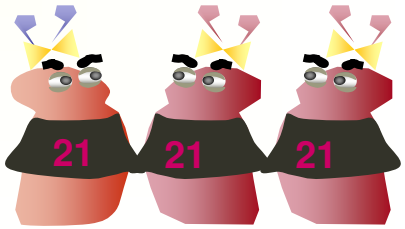
the presence of structural reorganizations could have an effect on the segregation of other chromosome pairs during meiosis



Lejeune 1961

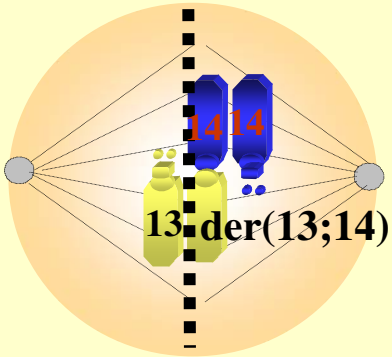
der(13;14)

?

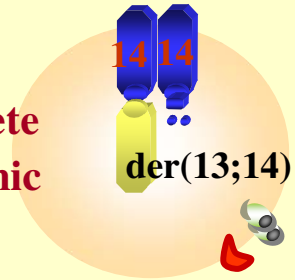


Clinical effect of UPD (Uniparental Parental disomy)

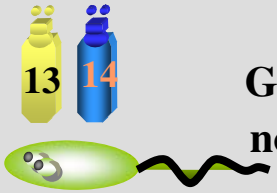
45,XX,der(13;14)



Gamete
Disomic

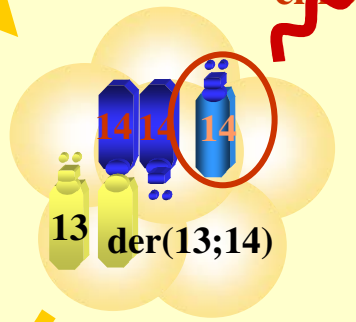


46,XX



Gamete
normal

Loss of
paternal
chromosome

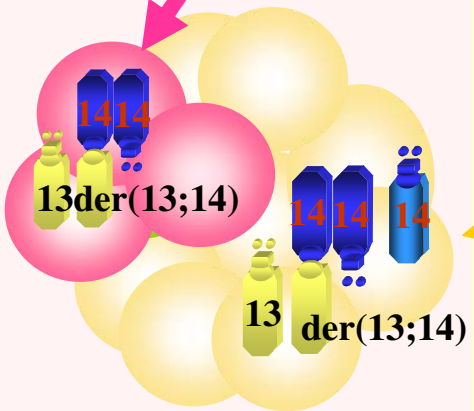


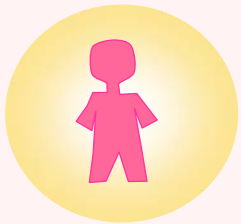
Trisomy14

Trisomy rescue – paternal chromosome 14 is missing

–

UPD14 MAT





FETUS
withUPD14 Mat

ANY trisomy rescue
TRISOMY 14
fetus/ placentA

Uniparental disomy 14 - (UPD) 14

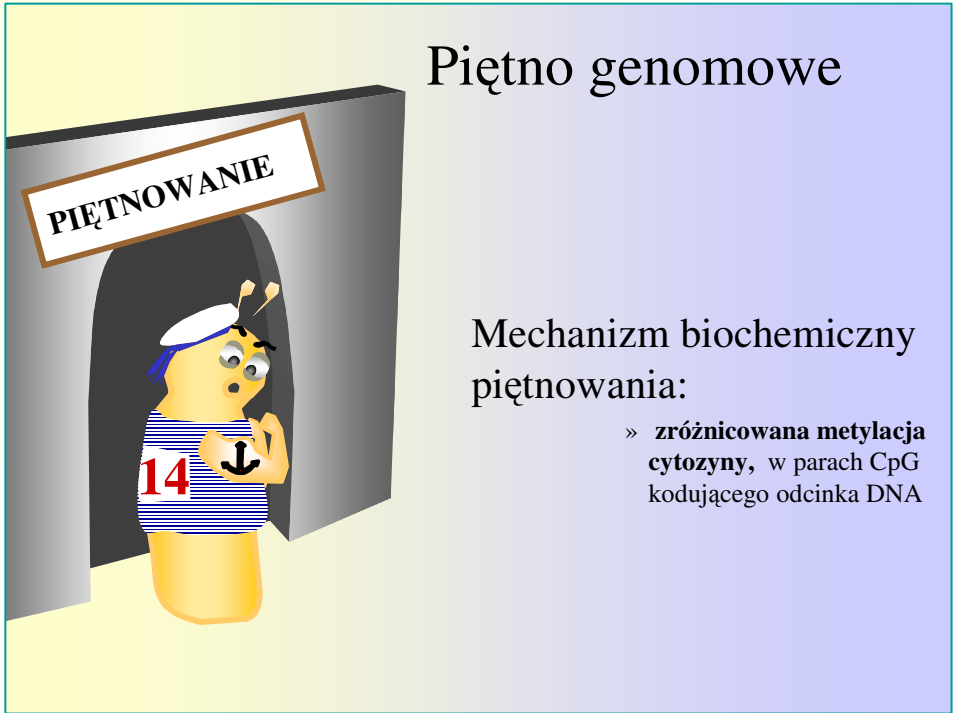
One of the consequence of aneuploidy 14 repair

is **chromosomal disomy 14**

resulted in a **distinct phenotype**

The superexpression or missing of imprinted genes

is basis of clinical effect.



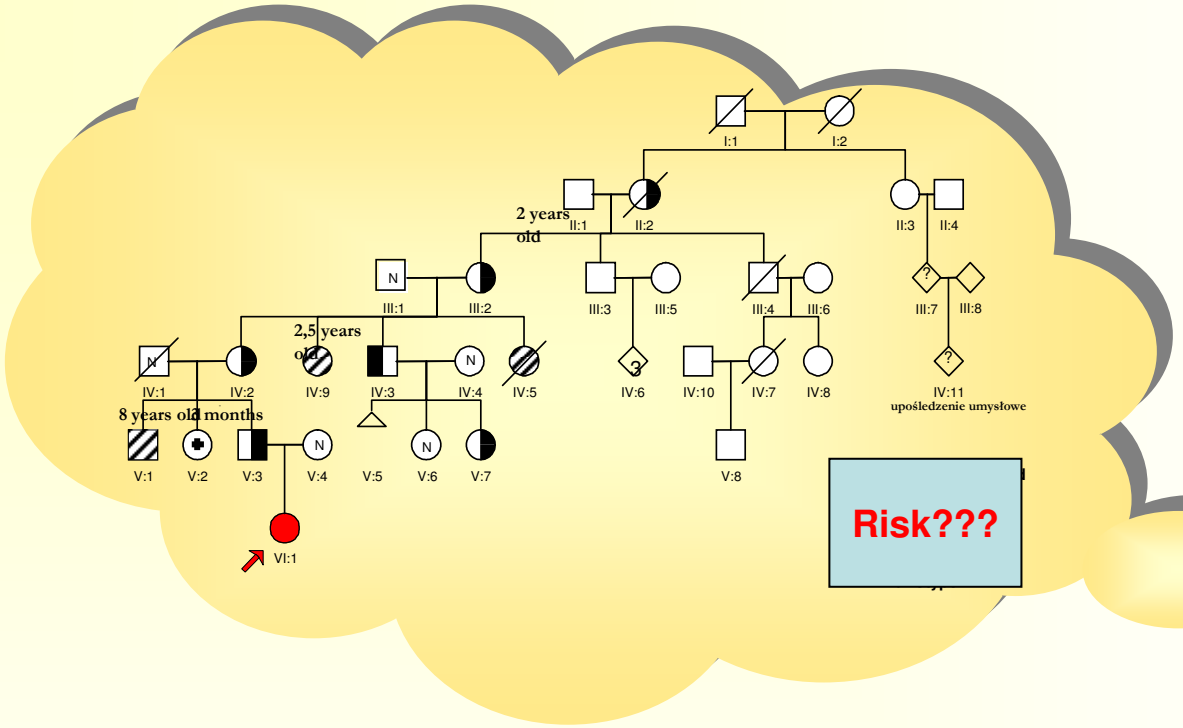
Clinical effect of RCT

- *genetic contents of imbalance – survival rate*
- *UPD effect on particular chromosome regions*
- *the X chromosome inactivation spreading to the autosomal segment and/or generating functional imbalance in particular sets of RTC*
- *effect position of breakpoint region*
- *interchromosomal effect*
- *others*

Families with RCT may be ascertained by

- ***unbalanced progeny***
  - ***at birth, or***
  - ***at prenatal diagnosis***
- ***miscarriages***
- ***stillbirth/early newborn deaths***
- ***by chance (!)***

All are interested in their assesment
of probability of occurrence
of different types
of unfavorable pregnancy outcomes



It can be done on the basis
of segregation analysis
of their actual pedigrees constructed
using empirical data
(clinical and cytogenetic results) as each
chromosomal translocation is individual
risk factor of reproductive failures

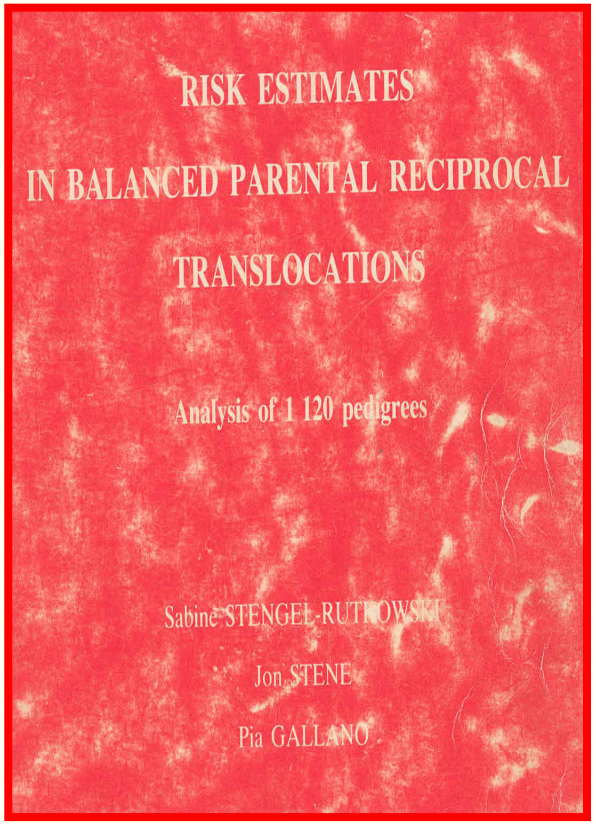
probability of occurrence of different types of unfavorable pregnancy outcomes

The empiric probabilities
for different types
of unbalanced progeny at birth
or for other types of unkaryotyped,
unfavorable pregnancy outcomes

can be obtained for many RCT

In spite of the great number of pedigrees (1120 pedigrees) elaborated by Stengel-Rutkowski et al] the number of observations in some subgroups of RCT is small and hence the probability estimation is not very accurate.

In addition a new empirical data for survival rate of unbalanced progeny for each time of prenatal development (PGD, Sperm) tof gether with progression of knowledge by new techniologies of molecular cytogenetics (FISH, Microarray, MLPA) used now for identification of chromosome rearrangement.



Red book – our „Bible”
Risk estimates in balanced parental reciprocal translocation.
Stengel-Rutkowski et al. 1988

the degree of the accuracy of the empirical risk estimation

- ***the number of informative pregnancies conceived in the case of RCT parental carriership***

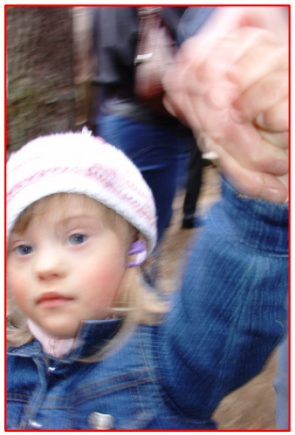
- ***the precision of identification of breakpoint position in the involved chromosomes – genetic contents of imbalance***

- *UPD effect on particular chromosome regions detection*
- *the X chromosome inactivation spreading to the autosomal segment and/or generating functional imbalance in particular sets of RTC*
- *effect position of breakpoint region evaluation*
- *interchromosome effect*

Polish Collection of ChromosomeTranslocations (PCCT)

Aim of organising of Polish Collection of Chromosome Translocations

- ***to obtain empirical data of individual RCT carriers***
- ***to improve genetic counselling***
- ***to collect clinical observations connected with chromosomal changes as a valuable resource for locating the disease gene***
- ***to collect empirical data about survival rate for different period of prenatal development***
- ***To define the lethal form of unbalanced progeny .***



Polish Collection of Chromosome Translocation (PCCT)

1990 - initiative of Commission of Human Genetics of Polish Academy of Sciences supported by Ministry of Science (prof. Janusz Limon, prof. Alina Midro)

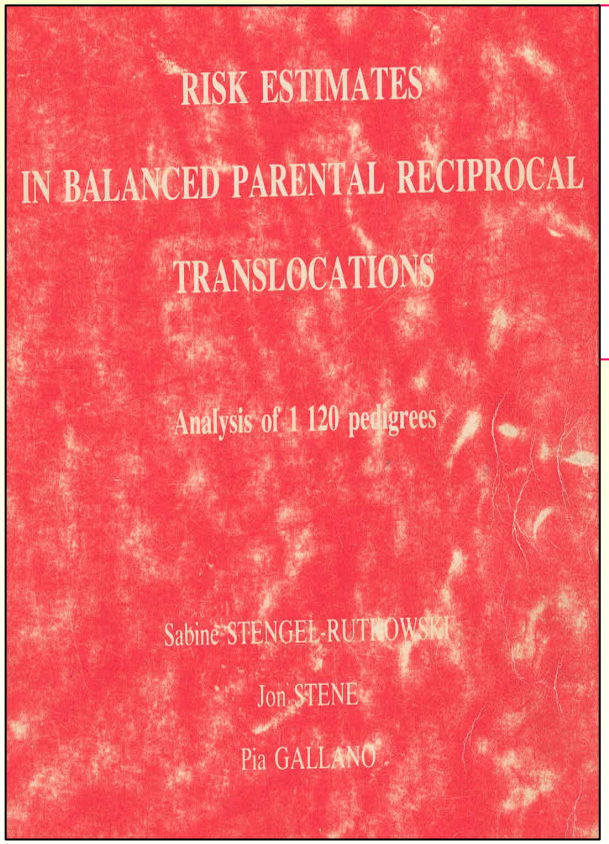
Coordinating centre:
Medical University of Białystok
Department of Clinical Genetics

Coordinator:
Prof. Dr hab. med. Alina Midro

Advisor:
Prof. Dr Sabine Stengel-Rutkowski Munchen

Co-operation Munchen – Białystok 1983-2008

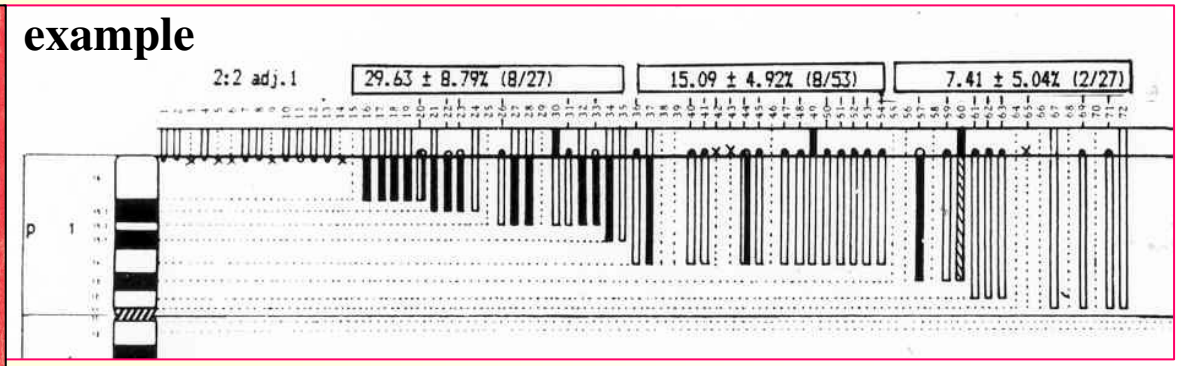
Prof. Sabine Stengel-Rutkowski



Red book – our „Bible"

Risk estimates in balanced parental reciprocal translocation. Stengel-Rutkowski et al. 1988

example



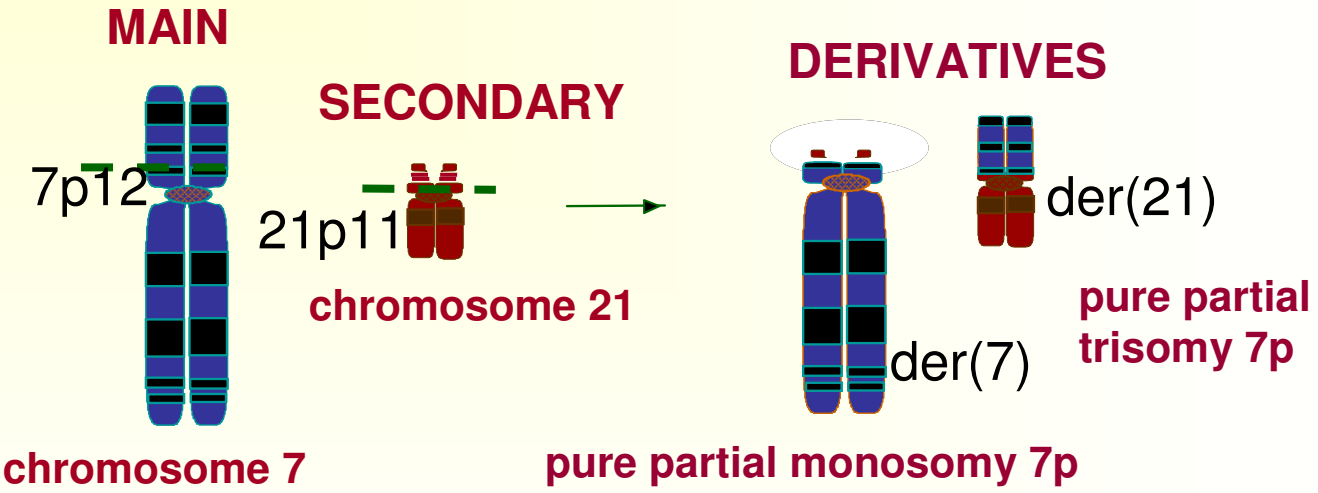
Results of risk estimates for 4p umbalances at birth

During discussion with Rector of Medical University in Białystok

Białowieża 1996

RCT at risk of single segment imbalance (acrocentric chromosome)

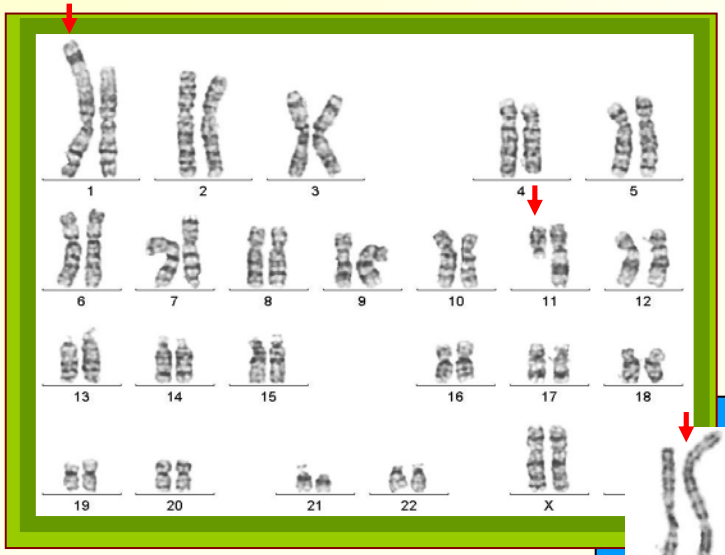
t(7;21)(p12;p11)



If one breakpoint is situated in terminal region of chromosome
mainly in the short arm of an acrocentric chromosome ,
than most types on unbalanced progeny will have „single segment imbalances ” ,
as the terminal segments and the acrocentric short arm regions have
no effect on the phenotype and survival

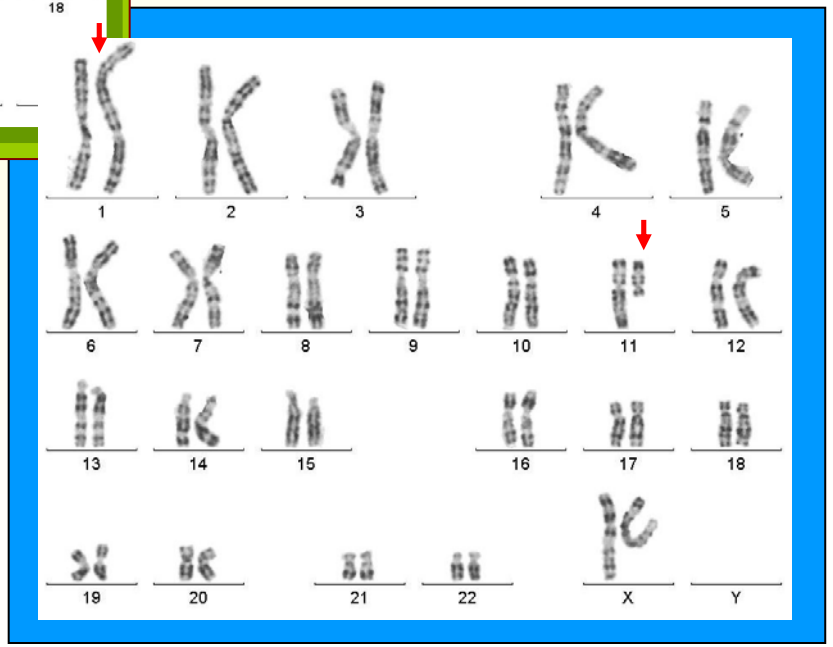
Classic evaluation of karyotype

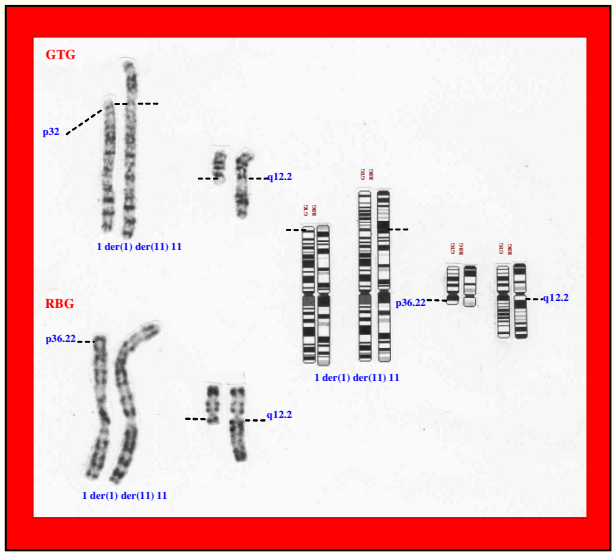
GTG



Translocation at risk for single segment imbalance?

RBG





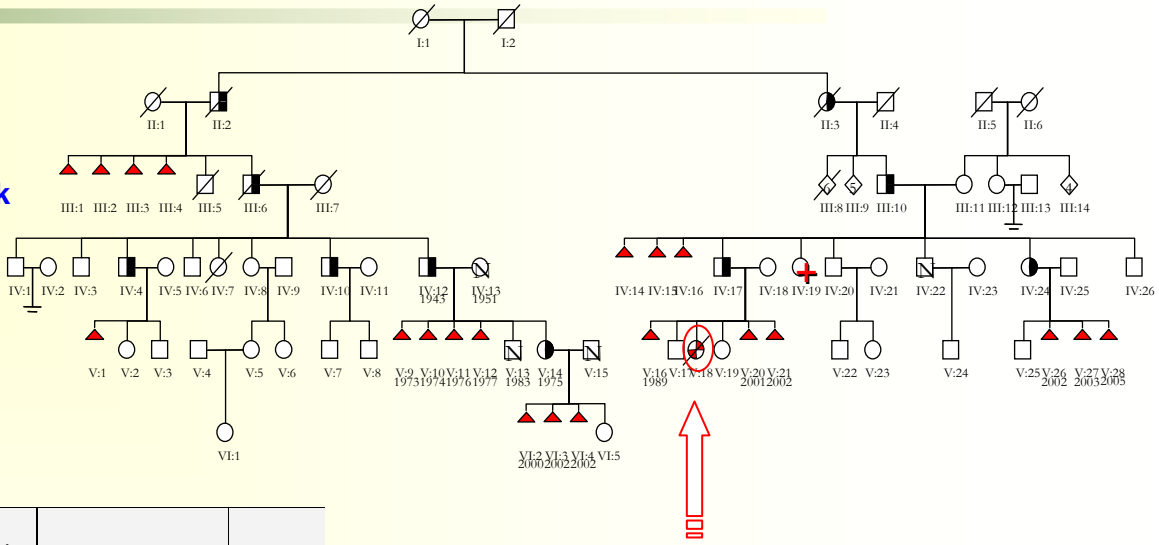
t(1;11)(p36;q12.2)

Results pedigree data

t(1;11)(p36.22;q12.2)

DIRECT ANALYSIS:

Overall risk at birth: (-/55) – not enough data
for miscarriages: 32.7±6.3% (18/55) - high risk
for stillbirth/early death: 3.6±2.5% (2/55) - low risk



Legend: MAT- maternal carrier, PAT - paternal carrierT - total number of pregnancieswith unbalanced karyotypeP - total number of miscarriage total number of pregnancyW - early deatha, b, c, n - total number of pregnancies with unbalanced, early death, total number of pregnacy after ascertainment correction

No	Carrier	Sex	Unbalanced offspring at birth[A]		Stillbirth/ early died newborn[B]		Miscarriages[C]		Pregnancies		Rate[A]	Rate[B]	Rate[C]
			T	C	T	C	T	C	Tot	Cor			
1.	V:14	MAT	-	-	-	-	3	0	4	1	-/1	-/1	0/1
2.	IV:12	PAT	-	-	-	-	4	4	6	5	-/5	-/5	4/5
3.	IV:10	PAT	-	-	-	-	-	-	2	2	-/2	-/2	-/2
4.	IV:4	PAT	-	-	-	-	1	1	3	3	-/3	-/3	1/3
5.	III:6	PAT	-	-	-	-	-	-	8	7	-/7	-/7	-/7
6.	II:2	PAT	-	-	-	-	4	4	6	5	-/5	-/5	4/5
7.	I:1; I:2	MAT/ PAT	-	-	-	-	-	-	2	1	-/1	-/1	-/1
8.	IV:17	PAT	-	-	1	1	3	3	6	6	-/6	1/6	3/6
9.	IV:24	MAT	-	-	-	-	3	3	4	4	-/4	-/4	3/4
10.	III:10	PAT	-	-	1	1	3	3	9	9	-/9	1/9	3/9
11.	II:3	MAT	-	-	-	-	-	-	12	12	-/12	-/12	-/12
Sum			-	-	1	2	21	18	62	55	-/55	2/55	18/55
Risk												3,6±2,5%	32,7±6,3%

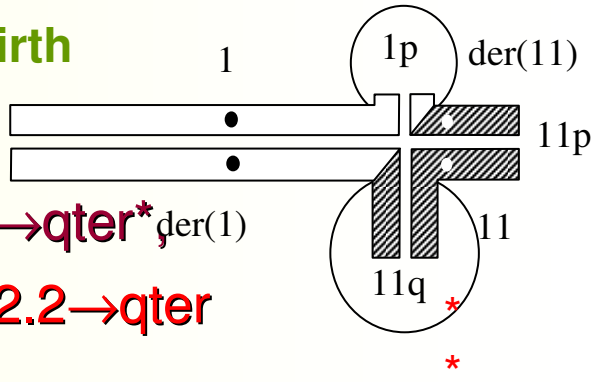
V,18 delivery at term Hydrolethalus s?(b.m 4200 g, macrocephaly, hydrocephalus external, myelomeningocoele, died after delivery)

The precise location of the breakpoint's positions was performed by FISH with the BAC clones resolution and microdeletion of 1p36.22 was found .

Hydrocephalus and 1p36.22-pter deletion has been described by Keppler –Noreuil et all J Med Genet 1995

Risk estimation

t(1;11)(p36.22;q12.2) **Survival rate at birth**



1. Risk for double segment imbalance at birth

   trisomy 1p36.22→pter and monosomy 11q12.2→qter*,

   or monosomy 1p36.22 →pter and trisomy 11q12.2→qter

   after 2:2 disjunction and adjacent-1 segregation

Direct analysis:
Overall risk at birth: (-/55) – not enough data

Indirect analysis:
No data for single segment imbalance 1p36.22-pter

2. No other form of meiotic segregation is expected in liveborn progeny of actual carriers

*not observed at birth

for miscarriages: 32.7±6.3% (18/55) - high risk
for stillbirth/early death: 3.6±2.5% (2/55) - low risk

Comment

.

To obtain more precise risk figure

It is necessary to collect more empirical data because survival rate of progeny with monosomy 1p36→pter and trisomy 11q12 →qter should be esexpected

The precise location of the breakpoint's positions should be performed by FISH with the BAC clones resolution in simitar chromosome translocation.

1993

Sabine Stengel-Rutkowski (Hrsg.)

Frühe pränatale Diagnostik
Early prenatal Diagnostics

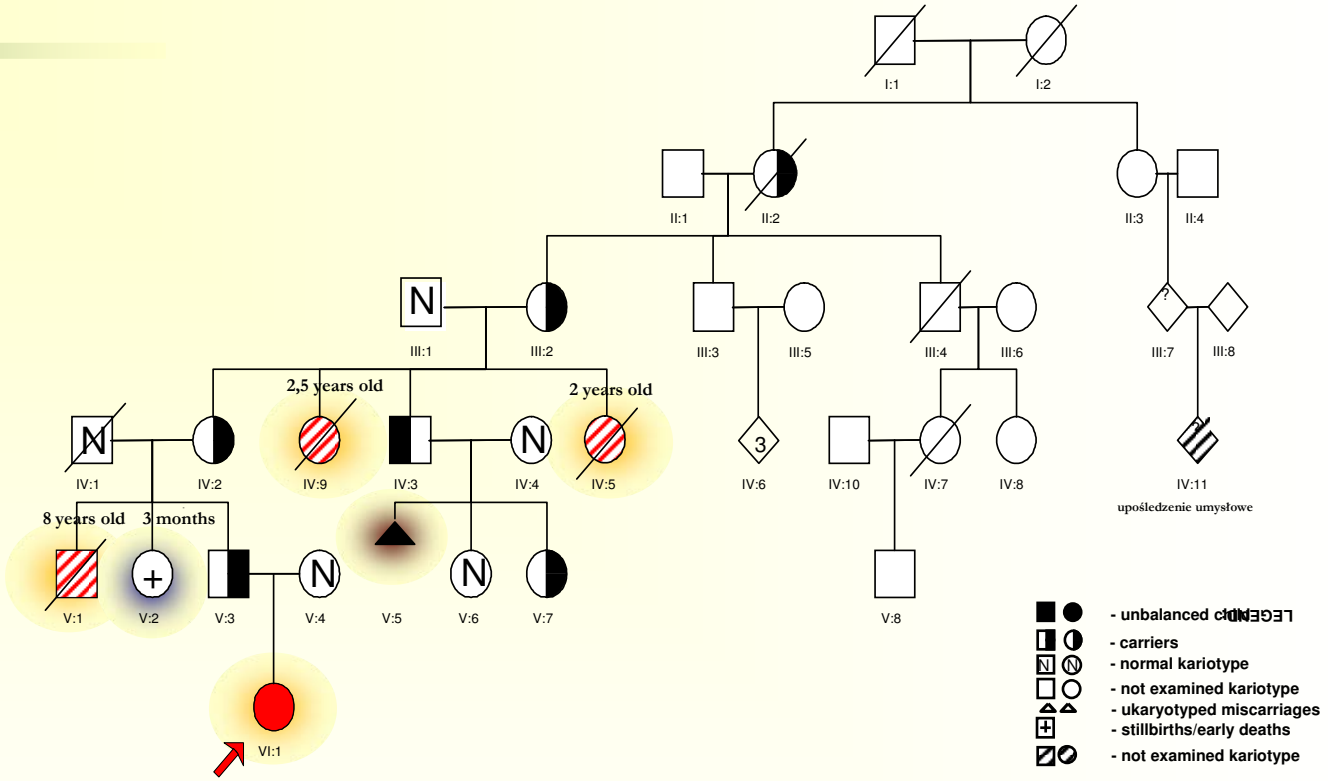
7.4 Risk estimates in reciprocal translocations. Experience obtained from the 1st trimester CVS data

by
Sabine Stengel-Rutkowski, München

a priori risk[5] at birth	1st trimenon (CVS)				2nd trimenon (AC)		at birth	
	MAT	PAT	TOTAL		TOTAL		TOTAL	
	rate	rate	rate	**risk**	rate	**risk**	rate	**risk**
high	3 / 11	0 / 1	3 / 12	**1:4**	16 / 56	**1:3,5**	93 / 529	**1:6**
medium	2 / 9	2 / 7	4 / 16	**1:4**	17 / 51	**1:3**	37 / 508	**1:14**
low	4 / 22	0 / 14	4 / 36	**1:9**	26 / 188	**1:7**	16 / 1184	**1:74**
no	0 / 3	0 / 6	0 / 9	-	0 / 57	-	0 / 217	-
unknown	0 / 5	0 / 5	0 / 10	-	0 / 0	-	0 / 0	-
TOTAL	9 / 50	2 / 33	11 / 83	**1:8**	59 / 352	**1:6**	146 / 2438	**1:17**

Table 1: Comparison of the risks for unbalanced offspring in parental balanced reciprocal translocations in data collectives from the 1st trimenon (TC/TA-CVS), the 2nd trimenon (AC) and at birth[5,6]

Risk evaluation of t(7;9)(q36.2;p21.2) …

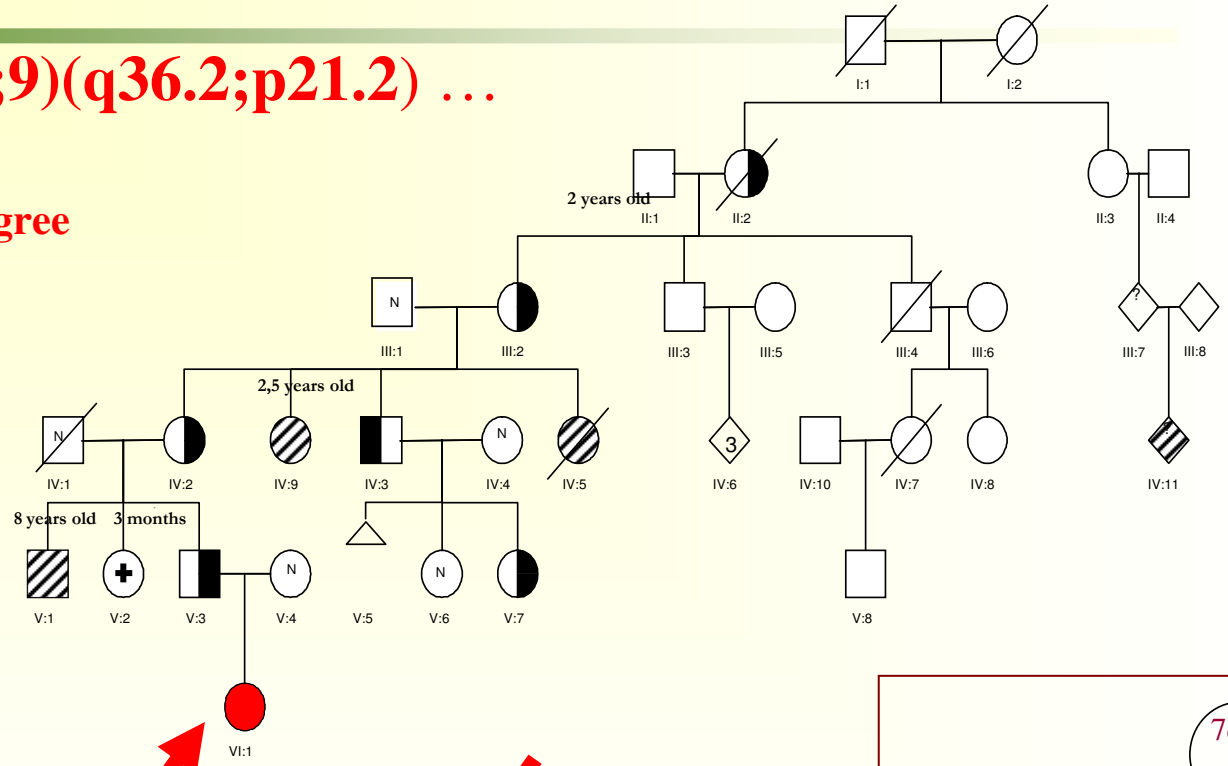


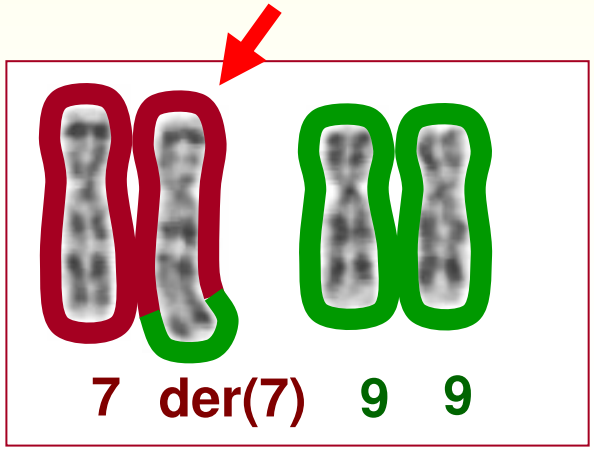
No	Pedigree position	Sex of carrier	Unbalanced progeny at birth		Miscarriages		Stilbirth/early death		Total number of pregnancy		Ratio		
			T	a	P	b	W	c	Tot	n	a/n	b/n	c/n
1	V,3	PAT	1	0	-	-	-		1	0	0/0	-/-	-/-
2	IV,2	MAT	1	1	-	-	1	1	3	2	1/2	-/2	1/2
3	IV,3	PAT	-	-	1	1	-	-	3	3	-/3	1/3	-/3
4	III,2	MAT	2	2	-	-	-	-	4	3	2/3	-/3	-/3
5	II,2	MAT	-	-	-	-	-	-	3	2	-/2	-/2	-/2
Total:			4	3	1	1	1	1	14	10			
										Total ratio:	3/10	1/10	1/10
										Risk value:	30±14,49%	10±9,49%	10±9,49%

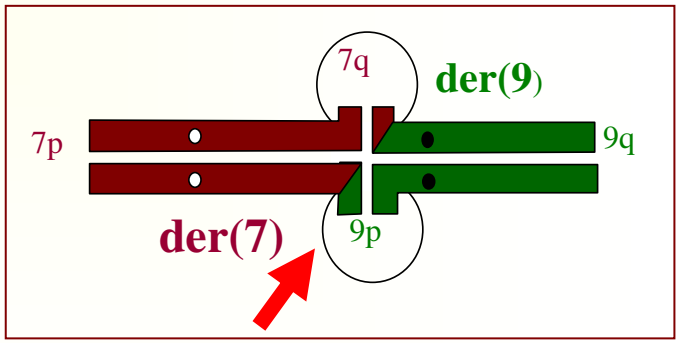
The direct segregation analyses

t(7;9)(q36.2;p21.2) …

Pedigree





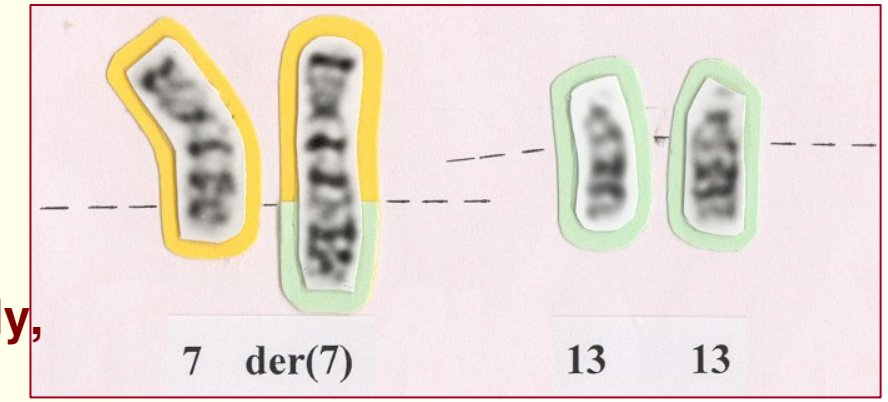


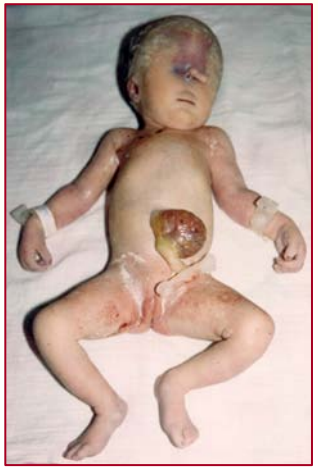
monosomy 7q36.2 → qter and trisomy 9p21.2→pter after 2:2 disjunction and adjancent-1 segregation

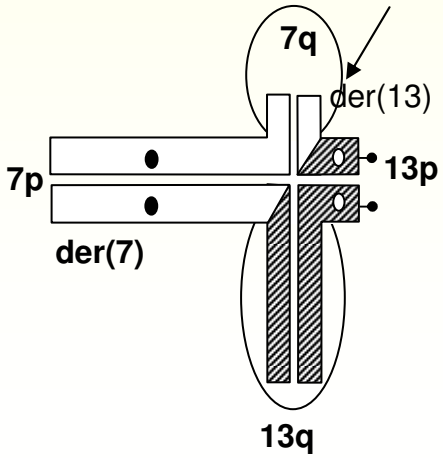
The direct segregation analyses of pedigree….

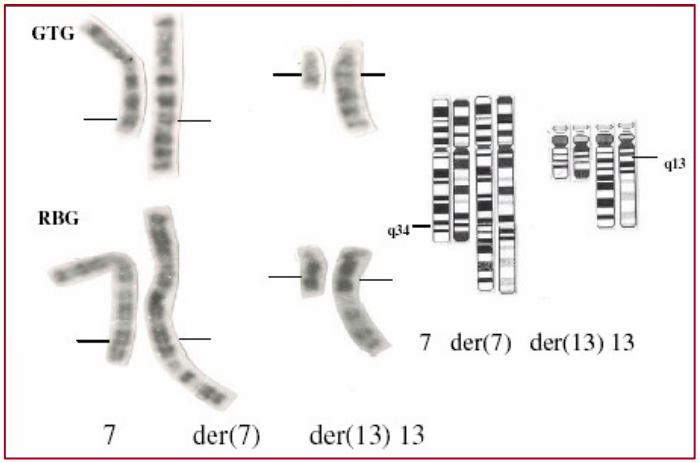
Pedigree two

The unbalanced karyotypes with monosomy 7q34→qter and trisomy 13q13→qter were detected among stillborns/early death newborns with holoprosencephaly, arrhinia, proboscis and cyclopia, omphalocele, kidney agenesis





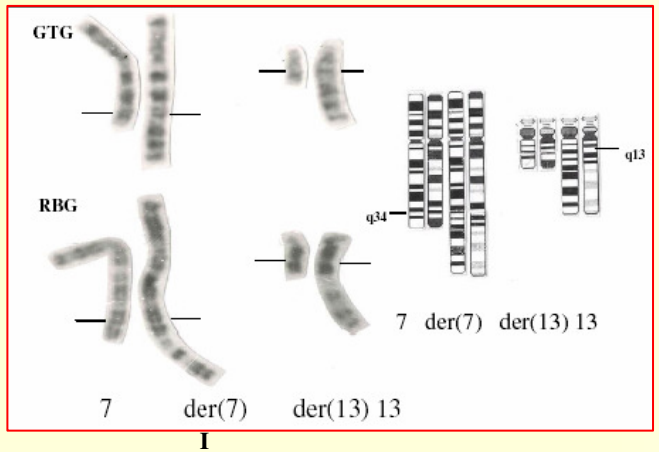




The sperm segregation pattern

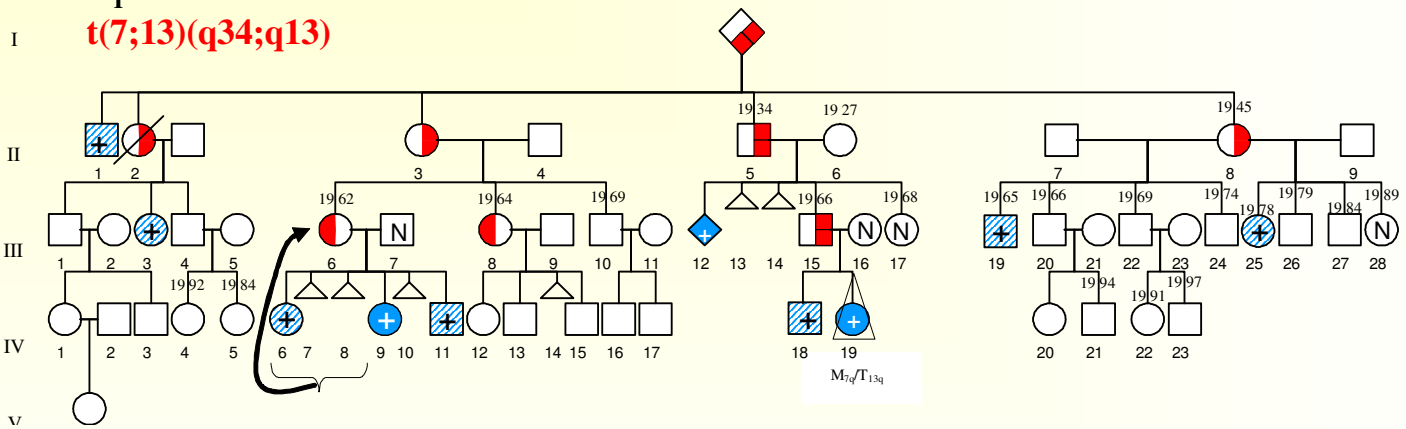
t(7;13)(q34;q13) …

- **The meiotic segregation pattern in the father of family 2 showed a rate of unbalanced spermatozoa of about 60%, with an unusual high rate (29.4%) of 3:1 segregants (i.e., 13.4% of tertiary segregation and 16% of interchange segregation). Adjacent-1 segregation followed with 23.5% and adjacent-2 with 7.2%.**



The direct segregation analyses of pedigree

t(7;13)(q34;q13)



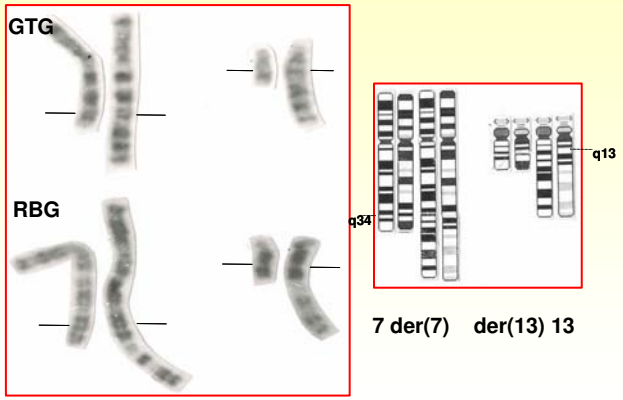
risk for stillborn/early death

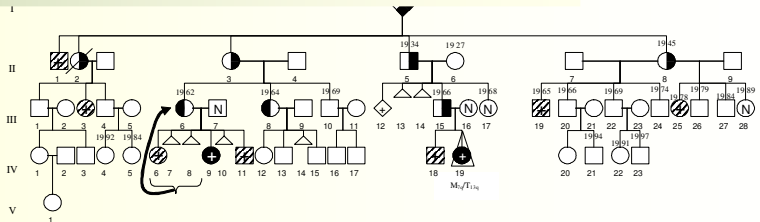
No	Carrier	Sex	Stillbirth/early died newborn[A]		Miscarriages[B]		Total Pregnancies		Rate[A]	Rate[B]
			T	C	T	C	T	C		
1	•III;6	•MAT	•3	•2	•3	•1	•6	•3	•2/3	1/3
2	•III;8	•MAT	•-	•-	•1	•1	•4	•4	•-/4	1/4
3	• III;15	•PAT	•2	•2	•-	•-	•2	•2	•2/2	-/2
4	•II;2	•MAT	•1	•1	•-	•-	•3	•3	•1/3	-/3
5	•II;3	•MAT	•-	•-	•-	•-	•3	•2	•-/2	-/2
6	•II;5	•PAT	•1	•1	•2	•2	•5	•5	•1/5	2/5
7	•II;8	•MAT	•2	•2	•-	•-	•8	•8	•2/8	-/8
8	I;1,2	?	1	1	-	-	5	4	1/4	-/4
TOTAL			10	9	6	4	36	31	9/31	4/31
RISK									29±8.2%	12.9±6.%

A. T. Midro, E. Wiland, B. Panasiuk, R Leśniewicz, M. Kurpisz. *Risk evaluation of carriers with chromosome reciprocal translocation t(7;13)(q34;q13) and concomitant meiotic segregation analyzed by FISH on ejaculated spermatozoa.*
Am J Med. Genet. 2006, 140A, (3): 245-256.

The indirect prognosis & direct segregation analysis

t(7;13)(q34;q13)





1. Direct analysis: MAT/ PAT:

overall risk at birth: no risk? (-/31)

for miscarriages: 12.9±6.02% (4/31)

for stillbirth/ early death: 29±8.2% (9/31)

for unbalanced progeny with long survival? Patau syndrome?

2. Indirect analysis (prediction)

- ***At birth***

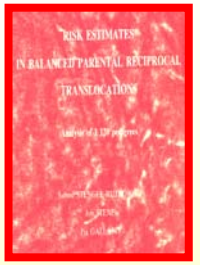
2.1. Risk for **d o u b l e** segment imbalance
monosomy 7q34→qter and trisomy 13q13→qter* or
trisomy 7q34→qter and monosomy 13q13→qter* *not observed at birth
after 2:2 segregation, adjacent – 1 disjunction

MAT/ PAT: no risk

2.2. Risk for **d o u b l e** segment imbalance, tertiary
trisomy 7q34→qter and trisomy 13q13→cen→pter or
monosomy 7q34→qter and monosomy 13q13→cen→pter
after 3:1 segregation, tertiary trisomy

segment: 7q34→qter	segment: 13q13→cen→pter
risk: <0.8 (0/63) (St-R) 2~0.4%	risk: MAT: 2.6±1.8% (2/76) (St-R)

PAT: no risk (0/40) (St-R)
MAT: 0.4%:2~0.2%

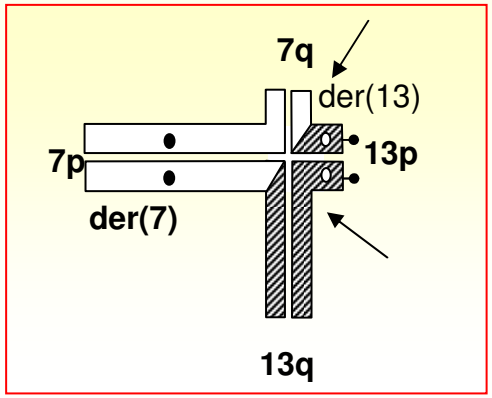


St-R 1988

2.3. Risk for interchange trisomy
after 3:1 segregation
MAT <0.2% (0/256)~0.1%
PAT: no risk 0/140 (St-R)

overall risk: MAT: 0.3%
PAT: no risk? No information

- **for miscarriages: 20-30% (ST-R)**
- **for stillbirth/ early death: 10% (ST-R)**



A. T. Midro, E. Wiland, B. Panasiuk, R Leśniewicz, M. Kurpisz. *Risk evaluation of carriers with chromosome reciprocal translocation t(7;13)(q34;q13) and concomitant meiotic segregation analyzed by FISH on ejaculated spermatozoa.*
Am J Med. Genet. 2006, 140A, (3): 245-256.

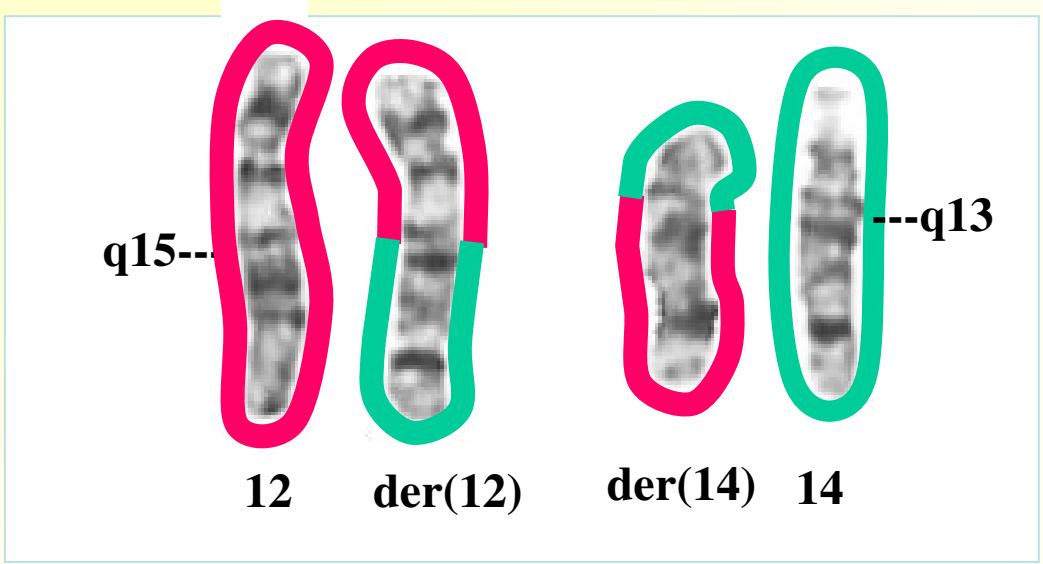
t(7;13)(q34;q13) …

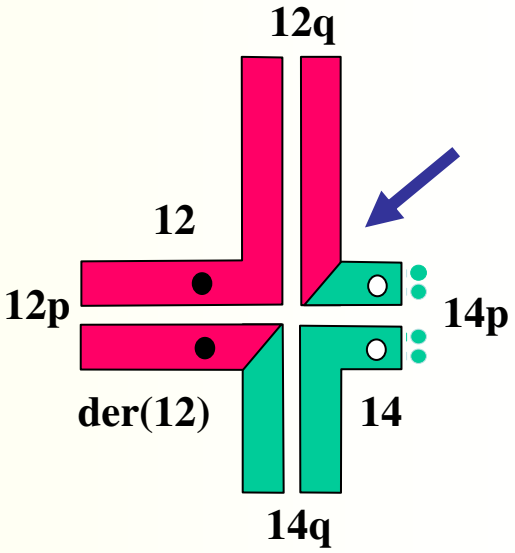
- The high rate of unbalanced gametes in comparison to the high number of stillborn/early death and miscarriages detected in the family of t (7;13) suggests a strong selection against unbalanced karyotypes.

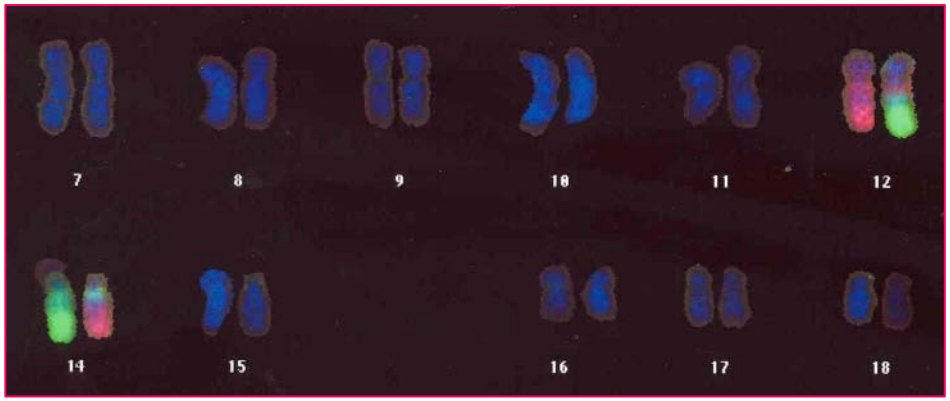
- It corresponds to a very small probability rate (about 0.3%) of viable unbalanced progeny from 3:1 meiotic segregation predicted for maternal carriers.

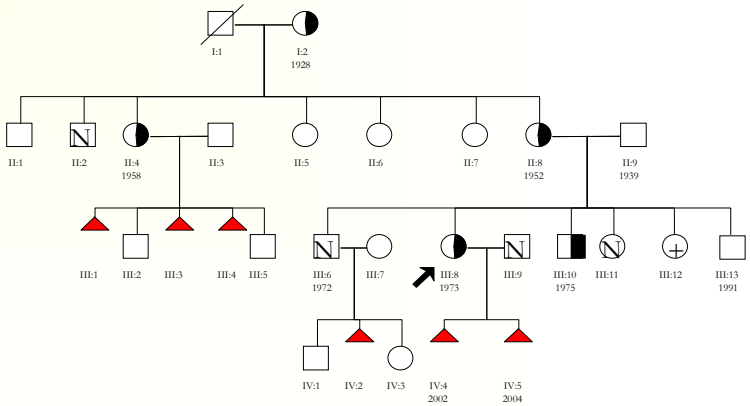
- Problem of definition of lethal malformations is still open
- (paliative care option versus termination of pregnancy with fetus with limited survival)

t(12;14)(q15;q13)









46,XX,t(12;14)(q15;q13)(wcp12+wcp14+;wcp14+wcp12)

Risk?

Results

t(12;14)(q15;q13)

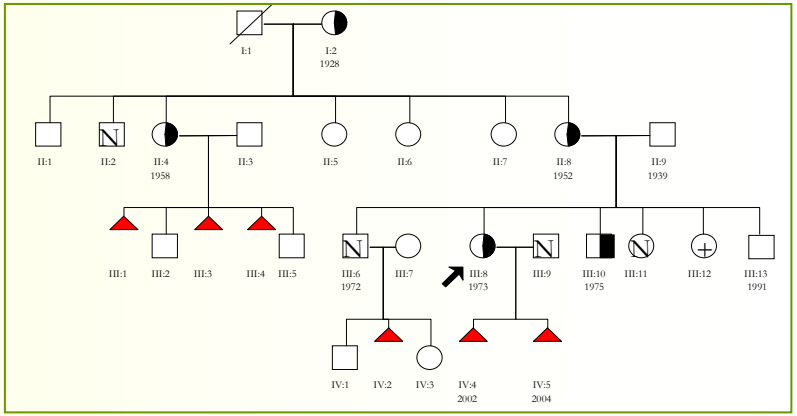


Table. The probability rates for unbalanced offspring at birth, stillbirth/ early death, miscarriages for carriers with t(12;14)(q15;q13) related to total pregnancies after ascertainment correction

No	Carrier	Sex	Unbalanced offspring at birth[A]		Stillbirth/ early died newborn[B]		Miscarriages[C]		Pregnancies		Rate[A]	Rate[B]	Rate[C]
			T	C	T	C	T	C	Tot	Cor			
1.	III:8	MAT	-	-	-	-	2	0	2	0	-/0	-/0	0/0
2.	II:4	MAT	-	-	-	-	3	3	5	5	-/5	-/5	3/5
3.	II:8	MAT	-	-	-	-	1	1	6	5	-/5	-/5	1/5
4.	I:2	MAT	-	-	-1	- 1	-	-	7	6	-/6	-/6	-/6
Total:			-	-	-	-	6	4	20	16	-/16	1/16	4/16
Risk											?	6.2%	25,0±10,8%

Overall risk at birth: (-/16) - risk?
for miscarriages: 25.0±10.8% (4/16) – high risk
for stillbirth/early death: 6.2+-6.05(1/16) - medium risk

Legend: MAT- maternal carrier, PAT - paternal carrierT - total number of pregnancieswith unbalanced karyotypeP - total number of miscarriage total number of pregnancyW - early deatha, b, c, n - total number of pregnancies with unbalanced, early death, total number of pregnacy after ascertainment correction

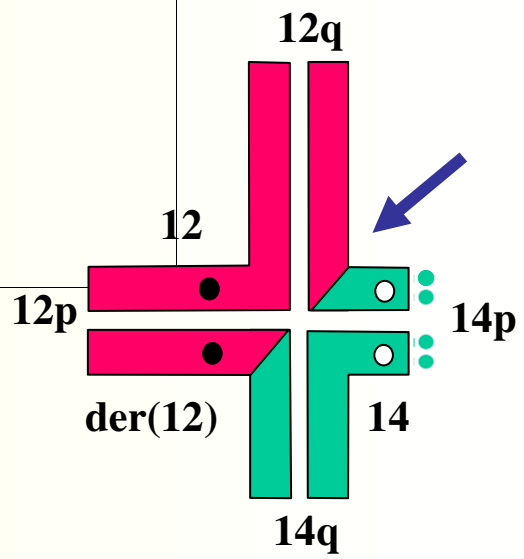
t(12;14)(q15;q13) indirect analysis

1. Risk for double segment imbalance:
   trisomy 12q15→qter and monosomy 14q13→qter* or
   monosomy 12q15→qter * and trisomy 14q13→qter
   after 2:2 disjunction and adjacent-1 segregation
   MAT/PAT: no risk

2. Risk for double segment imbalance:
   trisomy 12q15→qter and trisomy 14q13→cen→pter or
   monosomy 12q15→qter * and monosomy 14q13→cen→pter
   after 3:1 disjunction (tertiary trisomy)

* - not observed

segment: 12q15→qter	segment: 14q13→cen→pter
risk: MAT/PAT <1.50% (0/ 33):2 ~0,75%	risk: MAT: 2,63%± 2,6% (1/ 38) PAT: <0,82% (6/ 61)



Overall risk at birth:**
MAT/ PAT: 0,4%

Risk for miscarriages:
MAT/PAT: about 30%

Probability rate for UPD 14*:**
0,3% (2/341) ???

** Stengel-Rutkowski S, Stene J, Gallano. Risk estimates in balanced parental reciprocal translocations. Analysis of 1120 pedigrees. Monographie des Annales de Génétique. Paris: Expansion Scientifique Francaise, 1988.

*** Eggermann T., Zerres K. Uniparental disomy and robertsonian translocations. Risk estimation and prenatal testing. Mol Diagn 2003; 7(2); 113-117

Comment

We did not observe
any unbalanced offspring at birth
in large pedigree data.
We classified family with carriership of
translocation for low risk of malformed progeny
at birth (below 1%)
and high risk for miscarriages.

Comment

It is necessary to collect more empirical data because survival rate of progeny trisomy 12q12-qter with trisomy 14q13-cen-14pter should be expected.

In addition parental UPD 14 should be considered in case with chromosome 14 involved
EMPIRICAL DATA ARE Not AVAILABLE SO FAR

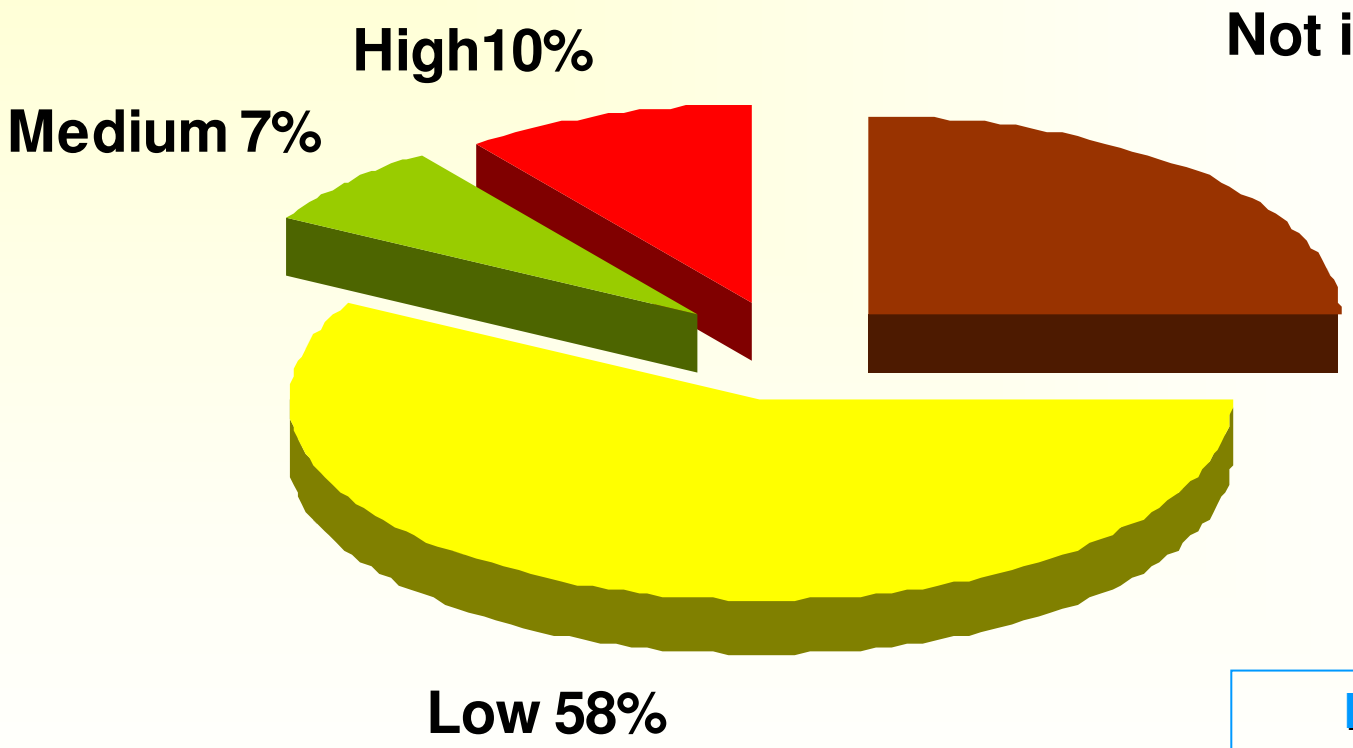
The degree of the accuracy of the risk figures estimation depends on two factors.

The first is
the number of informative pregnancies conceived in case of RCT parental carriership,
the second is
the precision of the identification of breakpoint position in the involved chromosomes.

Comments

We presented risk assesment
for the occurence of unfavorable pregnancy outcomes in the relatively large pedigrees of carriers of individual translocations.
However it was not efficient in case of two families of translocation carriership .

Polish Collection of chromosome translocations – risk group



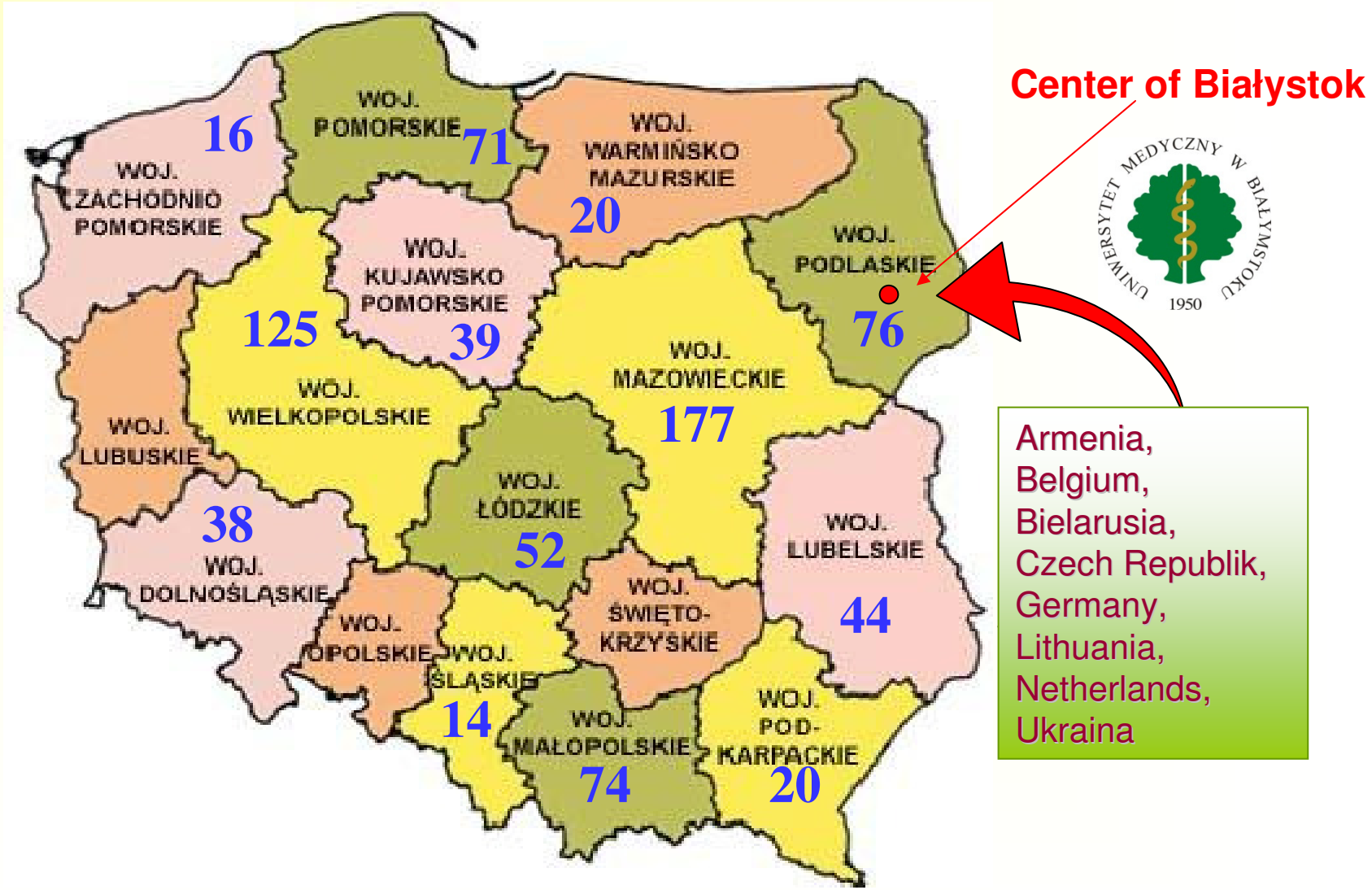
High >10%

Medium 5-10%

Low < 5%

Number of RCT 766

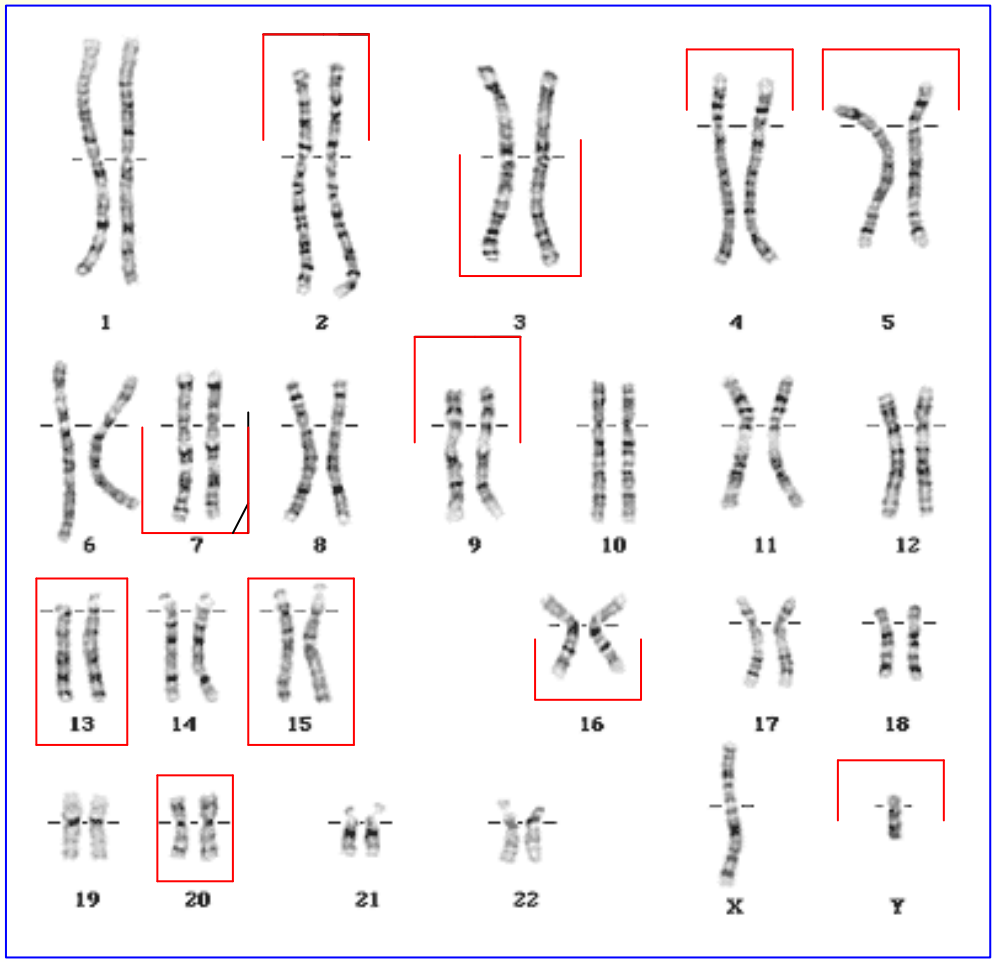
Polish Collection of Chromosomal Reciprocal Translocation



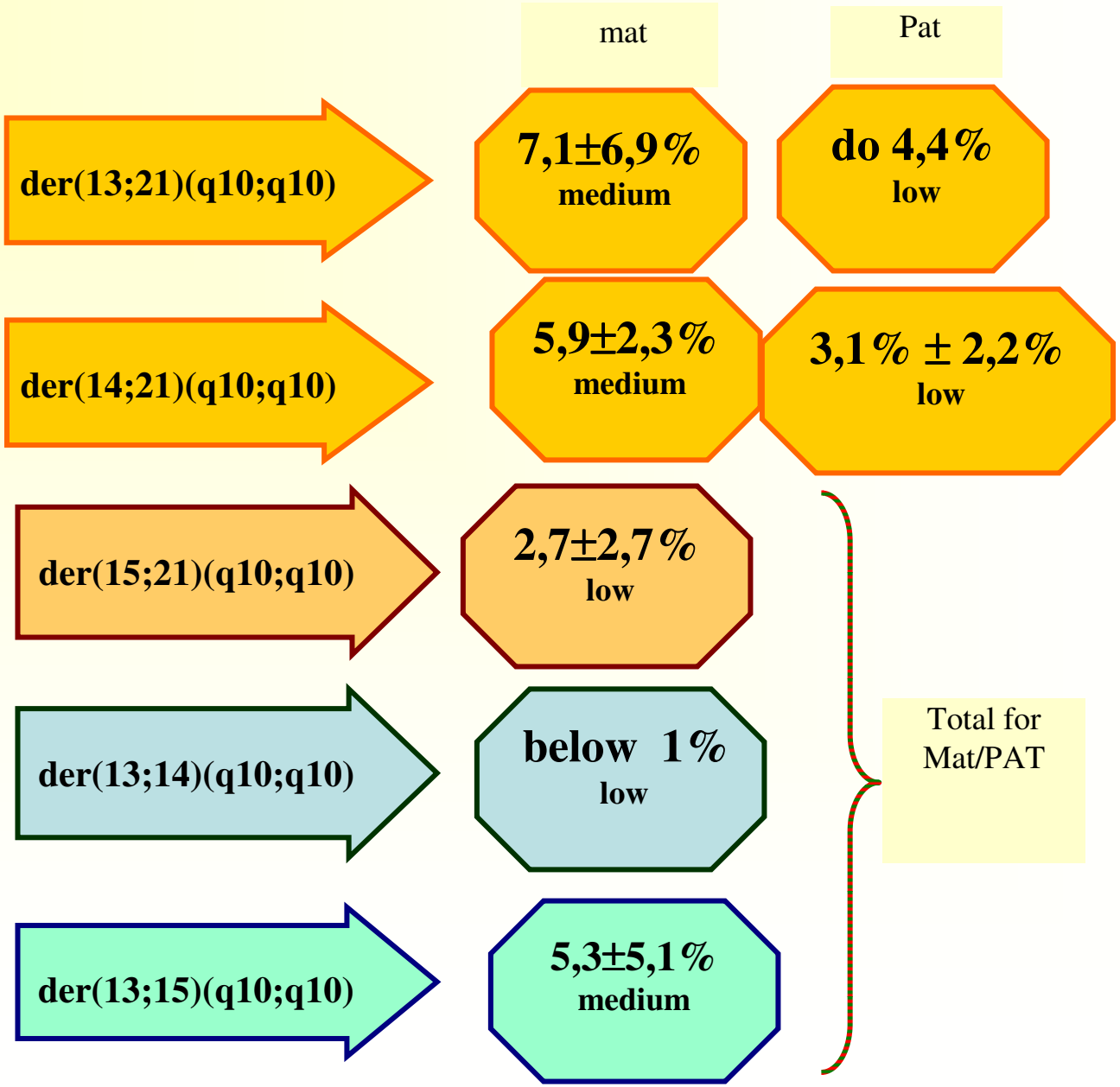
Total: **766** reciprocal chromosomal translocation from 25 Genetic centers in Poland (February 2008) and about 2000 data from other collaboratives.

Polish Collection of Chromosome Translocation

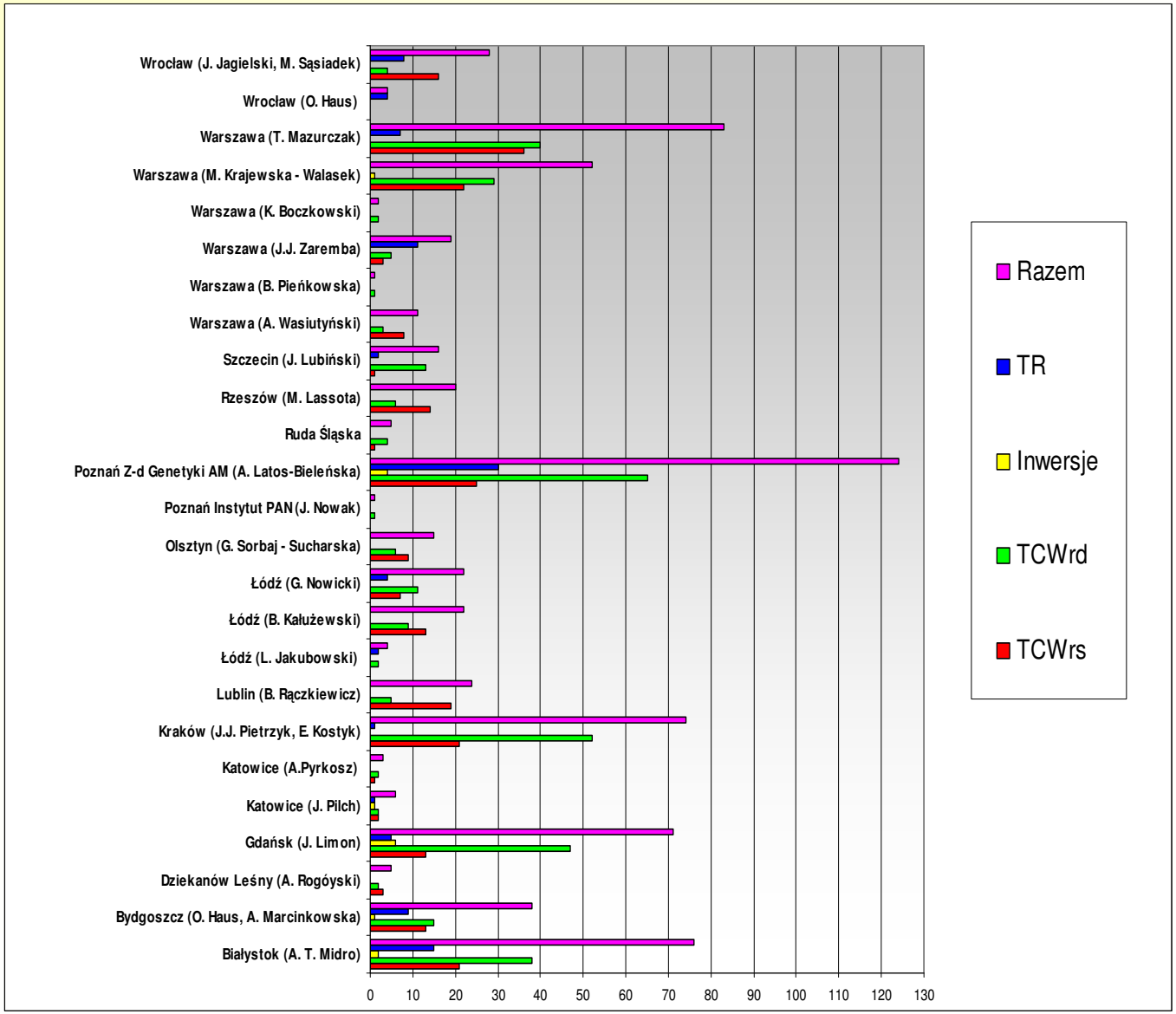
- **New risk values for RCT at risk for single segment imbalanced:**
  segments
  - **2p-pter**
  - **9p-pter**
  - **4q-qter**
  - **4p-pter**
  - **5p-pter**
  - **7q-qter**
  - **13q-qter**
  - **15q-qter**
  - **16q-qter**
  - **20q-qter**
  - **20p-pter**
  - **Xp-pter**



New risk values for Robertsonian translocations



Polish Collection of Chromosome Translocation
Collaborative data of 25 genetic centers in Poland



This study was supported by the German-Polish project BMBF POL 03/025 together with the Polish-German project KBN 5253, KBN 2 PO5A 089 27 and AMB project Nr 3 06 671

Thank You for your attention!

midro@umwb.edu.pl

Polish Collection of Chromosome Translocation

I. Risk estimation – single segment imbalance

segment 9p-pter

Midro A. T., S. Stengel-Rutkowski, M. Krajewska-Walasek, J. Szymańska, M. Lassota, R. Leśniewicz, B. Jaworowka: Different risks in two familial translocations t(9;12) with similar breakpoints. Ann Genet, 35, 1, 33-40, 1992.

segment Xp-pter

Panasiuk B., R Usinskene, E. Kostyk, A. Rybałko, B. Stasiewicz-Jarocka, B. Krzykwa, B. Krzykwa, B. Pieñkowska-Grela, V. Kucinskas, K. Michalova, A. T. Midro. Genetic counselling in carriers of reciprocal chromosomal translocations involving short arm of chromosome X. Ann Genet. 2004, 47 (1), 11-28.

segment 16q-qter

Stasiewicz-Jarocka B., Haus O., van Assche E., Kostyk E., Rybałko A., Krzykwa B., Barisic I., Marcinkowska A., Kucinskas V, B. Kałużewski, Schwanitz G. Midro A. T. Genetic counselling in carriers of reciprocal chromosomal translocations involving long arm of chromosome 16. Clin. Genet., 66 (3), 189-207.

segment 4p-pter

Panasiuk B, Leśniewicz R, Spółczyńska A, Myśliwiec M, de Die Smulders C, Sawicka A, Midro A. T. Translocation form of Wolf-Hirschhorn syndrome - assessment of recurrence rate probabilisty. Adv. Med. Sci. 2007, 52 (1), 166-170.

Polish Collection of Chromosome Translocations

II. Risk estimation – application of data base

Midro A. T., S. Stengel-Rutkowski, J. Stene: Experiences with risk estimates for carriers of chromosomal reciprocal translocations. Clin. Genet. 41, 113-122, 1992.

III. Risk estimation – double segment imbalance

Wiland E., Midro A. T., Panasiuk B., Kurpisz M. The analysis of meiotic segregation patterns and aneuploidy in the spermatozoa of father and son with translocation **t(4;5)(p15.1;p12)** and the prediction of the individual probability rate for unbalanced progeny at birth. J. Androl. 2007; 28(2): 262-272.

Midro A.T., B. Panasiuk, B. Stasiewicz-Jarocka, P.S. Iwanowski, Ch. Fauth, M. R. Speicher, R. Leśniewicz: Risk estimates for carriers of chromosome reciprocal translocation **t(4;9)(p15.2;p13).** Clin. Genet., 2000, 57(2), 153-155.

Midro A. T., E. Wiland, B. Panasiuk, R Leśniewicz, M. Kurpisz. Risk evaluation of carriers with chromosome reciprocal translocation **t(7;13)(q34;q13)** and concomitant meiotic segregation analyzed by FISH on ejaculated spermatozoa. Am J Med. Genet. 2006, 140A, (3): 245-256.

Midro A. T., S. Stengel-Rutkowski, M. Krajewska-Walasek, J. Szymańska, M. Lassota, R. Leśniewicz, B. Jaworowka: Different risks in two familial translocations **t(9;12)** with similar breakpoints. Ann Genet, 35, 1, 33-40, 1992.

Polish Collection of Chromosome Translocations

IV. Towards gene identification

A. T. Midro. K. Dêbek, A. Sawicka, D. Marcinkiewicz, M. Rogowska: Second observation of Silver-Russel syndrome in a carier of a reciprocal translocation with one breakpoints at site **17q25.** Clin. Genet, 44, 1, 53-55, 1993.

A.T. Midro, B. Panasiuk, B. Stasiewicz-Jarocka, P.S. Iwanowski, Ch. Fauth, M. R. Speicher, R. Leśniewicz: Risk estimates for carriers of chromosome reciprocal translocation **t(4;9)(p15.2;p13).** Clin. Genet., 2000, 57(2), 153-155.

Dörr, M. L. Ayala-Madriga, A. T. Midro, J. Giannakudis, I. Hansmann. Construction of a detailed physical and transcript map of the candidate region for Russel-Silver syndrome on chromosome **17q23-q24.** Genomics, 2001, 71, 174-181.

V. RCT and interstitial deletion

A. T. Midro, B. Panasiuk, Z. Tumer, P. Stankiewicz, A. Silahtaroglu, J.R. Lupski, Z. Zemanova, B. Stasiewicz-Jarocka, E. Hubert, E. Tarasów, W. Famulski, B. Zadrożna-Tołwińska, E. Wasilewska, M. Kirchhoff, V. Kalscheuer, K. Michalova, N. Tommerup. Interstitial deletion 9q22.32-q33.2 associated with additional familial translocation **t(9;17)(q34.11;p11.2)** in a patient with Gorlin-Goltz syndrome and features of nail-patella syndrome. Am. J. Med. Genet. 2004, 124 (2): 179-191.

Polish Collection of Chromosome Translocations

Robertsonian translocation der(13;14)

Engels H., Eggermann T., Caliebe A., Jelska A., Schubert R., Schüler H. M., Panasiuk B., Zaremba J., Latos-Bieleńska A., Jakubowski L., Zerres K. P., Schwanitz G. Midro A.T.

Genetic Counseling in Robertsonian Translocations der(13;14): Frequencies of Reproductive Outcomes and Infertility in 101 Pedigrees.

Am. J. Med. Genet., Part A, in press 2008.