Pericentric inversion of chromosome 9: back to epidemiological field work.

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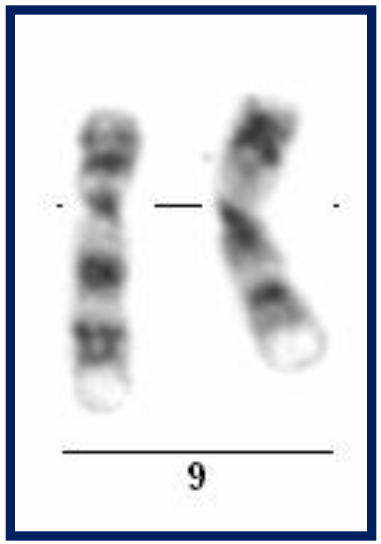
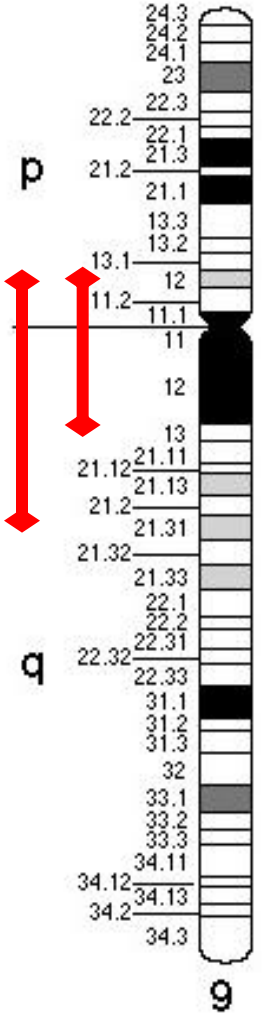
Pericentric inversion of chromosome 9

- Described for the first time in 1972 (Wahrman et al, 1972)
- Considered to be a **clinically insignificant** heterochromatine variant of the human karyotype (ISCN 2009)
- Relative common finding (1-4 % of general population)
- At least two major cytogenetic variants of the inv(9) exist:
  - inv(9)(p12q13)
  - inv(9)(p12q21)



- However, on the molecular-cytogenetic level (FISH studies), at least six different variants exist (Starke et al, 2002)
- inv(9) is repeatedly mentioned in association with various clinical diagnoses, especially with **reproduction failure**



Questions and hypotheses

- How common is the inv(9) in the Czech Republic?
- Is there any possible association between inv(9) and reproduction failure (or other diagnose)?
- Should the inv(9) carriers be accepted as gamete donors?

- **Hypotheses:**
  - The inv(9) is very common finding in the Czech Republic.
  - The inv(9) has no clinical significance and is not associated with any clinical diagnose.

- **Proposed type of study:**
  - Retrospective epidemiological analysis of inv(9) carriers

Data sources 1

- **National Registry of Congenital Anomalies of the CZE:**
  - Includes all diagnoses from the ICD-10 Q00-Q99 group
  - All cases identified up to 15th year of age of affected individual are included

- **However…**
  - There is no specific ICD-10 code for inv(9)
  - A lot of inv(9) cases are identified **after** the 15th year of age
  - Many specialists do not consider inv(9) to be harmful so they do not report it at all

- **The National Registry couldn‘t be used this time**

Data sources 2

- **Cytogenetic databases and archives in:**
  - **General University Hospital (Prague)**
    (Antonin Sipek jr., Romana Mihalova, Ales Panzcak)
  - **Thomayer University Hospital (Prague)**
    (Antonin Sipek, Vladimir Gregor, Jiri Horacek)
  - **Pronatal Sanatory (Prague)**
    (Antonin Sipek, Vladimir Gregor, Petr Lonsky, Vladimir Sobotka)
  - **Gennet (Prague)**
    (Jiri Horacek, David Stejskal)

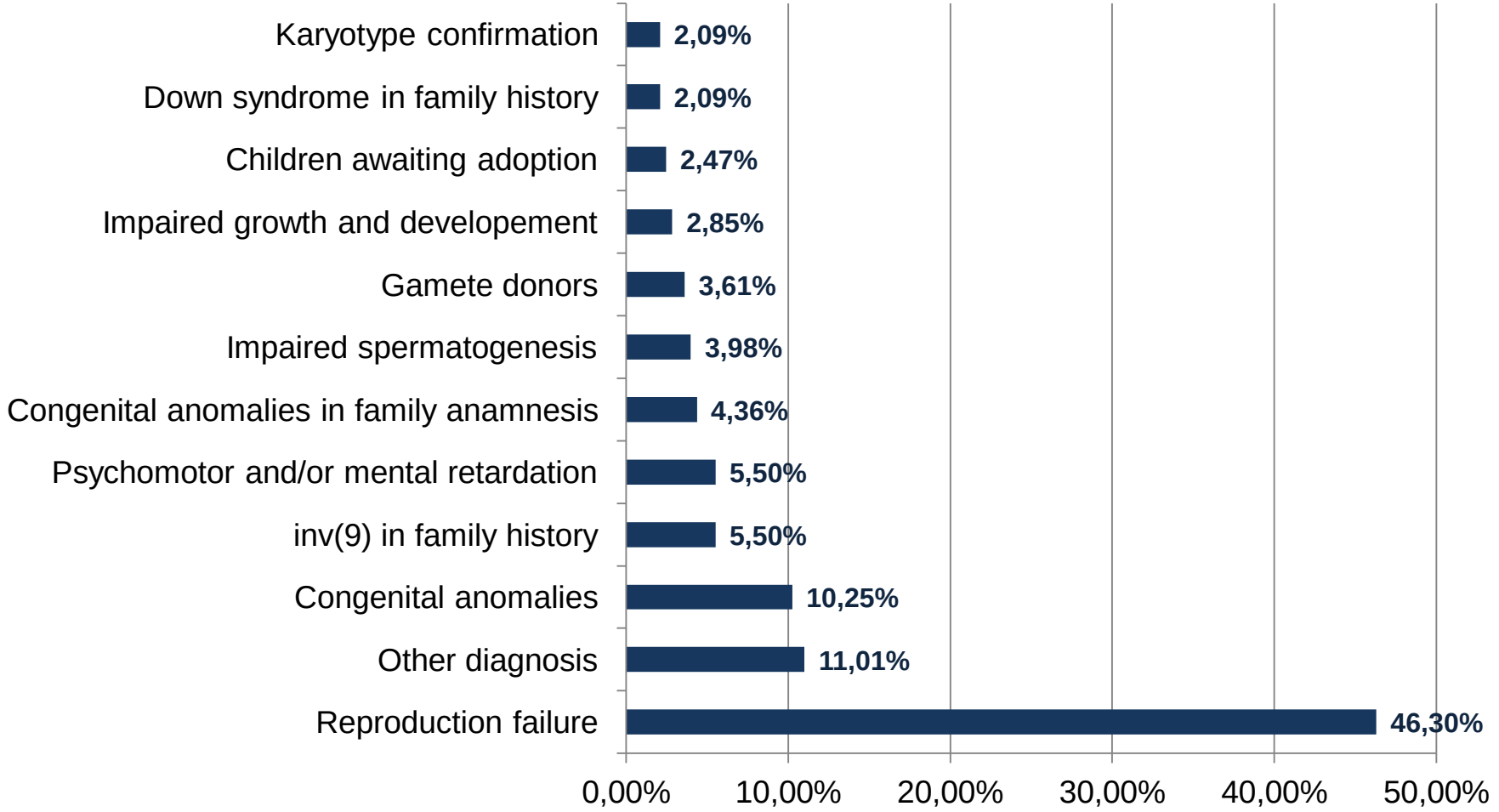
Results 1

Number of inv(9) cases in different laboratories

Laboratory	*TUH*	*GUH*	*Gennet*	*Pronatal*	*Total*
Time period	*1980-2010*	*1986-2010*	*1996-2010*	*2002-2008*	
inv(9) cases	**133**	**173**	**164**	**78**	**548**
Total cases	7884	10928	15528	4447	**38787**
Inv(9) incidence	**1.687%**	**1.583%**	**1.056%**	**1.754%**	**1.413%**
Males	67	69	78	32	**246**
Females	66	104	86	46	**302**
Sex ratio (F/M)	0.985	1.507	1.103	1.438	**1.228**

Results 2

Indication diagnoses in the whole inv(9) group (n=527)



Results 3

Comparison of diagnoses in inv(9) and control group

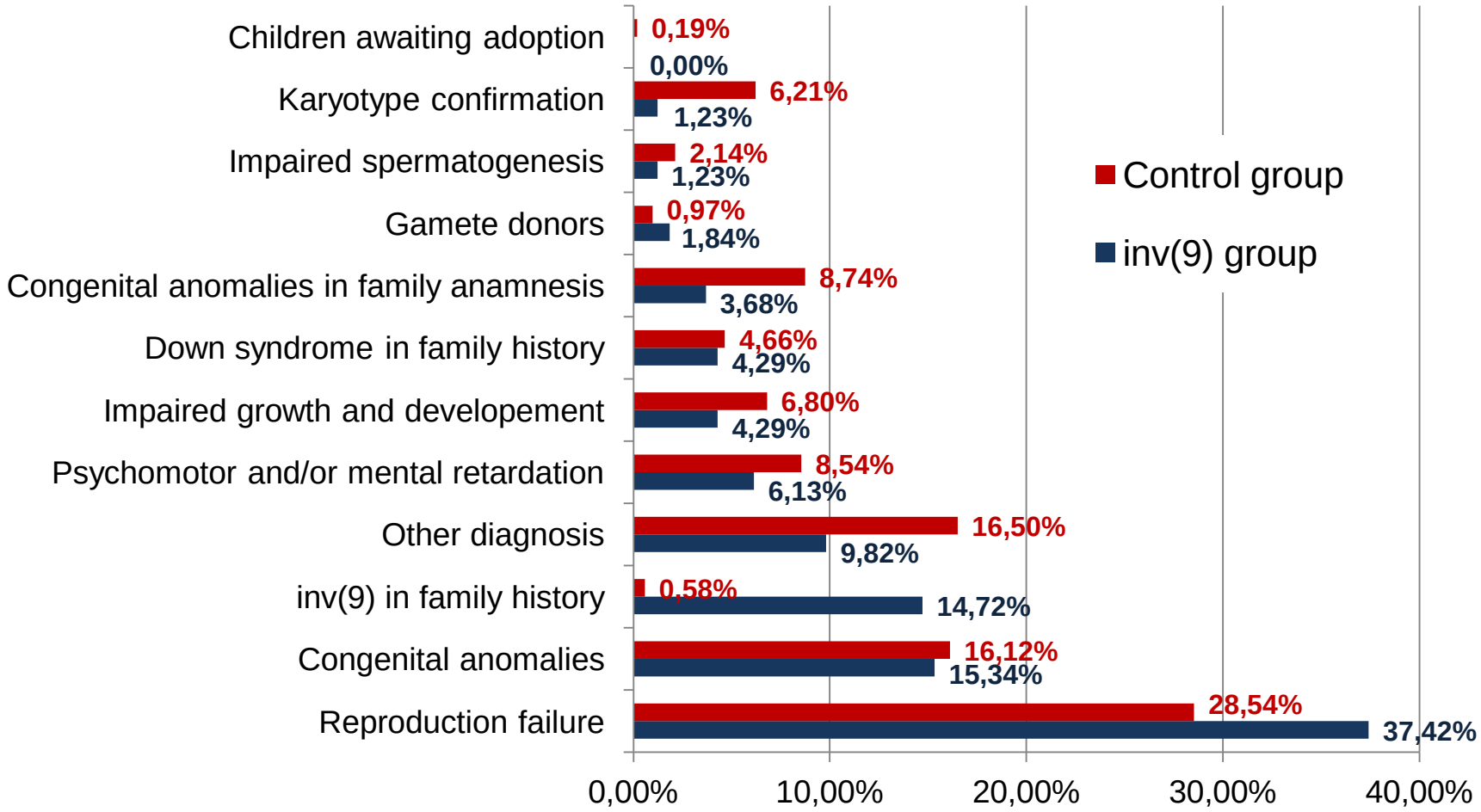
Inv(9) group (n = 163) is composed of inv(9) cases from General University Hospital

Control group (n = 515) is composed of randomly selected (*systematic sampling method*) patients with absolutely normal karyotype from General University Hospital

Reproduction failure: The difference is statistically significant ***p = 0.04***, relative risk = **1.35** (95%CI = 1.03 – 1.77)

Results 3

Comparison of diagnoses in inv(9) and control group



Results 4

Comparison of inv(9) incidence in reproduction failure and control group

Reproduction failure group (n = 761) is composed of patients (93 individuals and 334 couples) karyotyped because of idiopathic sterility between 2007 and 2009 General University Hospital

Control group (n = 855) is composed of fetuses karyotyped **solely** because of the advanced age of their mothers (35 years and over) between 2003 and 2009 in General University Hospital

Inv(9) carriers: The difference is not quite significant
p = 0.08, relative risk = **1.42** (95%CI = 1.05 – 1.94)

Results 4

Comparison of inv(9) incidence in reproduction failure and control group

	Reproduction failure group	Amniocentesis group
Patients	**761**	**855**
Males	388	413
Females	373	442
Sex ratio (F/M)	0.96	1.07
inv(9) carriers	**14**	**7**
inv(9) incidence	**1.84%**	**0.79%**
Males	7	3
Females	7	4
Sex ratio (F/M)	1.00	1.33

Results 5

Estimates of population incidence of inv(9)

	All cases	inv(9) cases	Incidence
Group	**Gamete donors - Pronatal Sanatory**		
Males	111	1	0.90%
Females	373	6	1.61%
Total	**484**	**7**	**1.45%**
Group	**Children awaiting adoption –TUH**		
Males	235	5	2.13%
Females	176	5	2.84%
Total	**411**	**10**	**2.43%**
Group	**Amniocentesis group – GUH**		
Males	413	3	0.73%
Females	442	4	0.90%
Total	**855**	**7**	**0.82%**

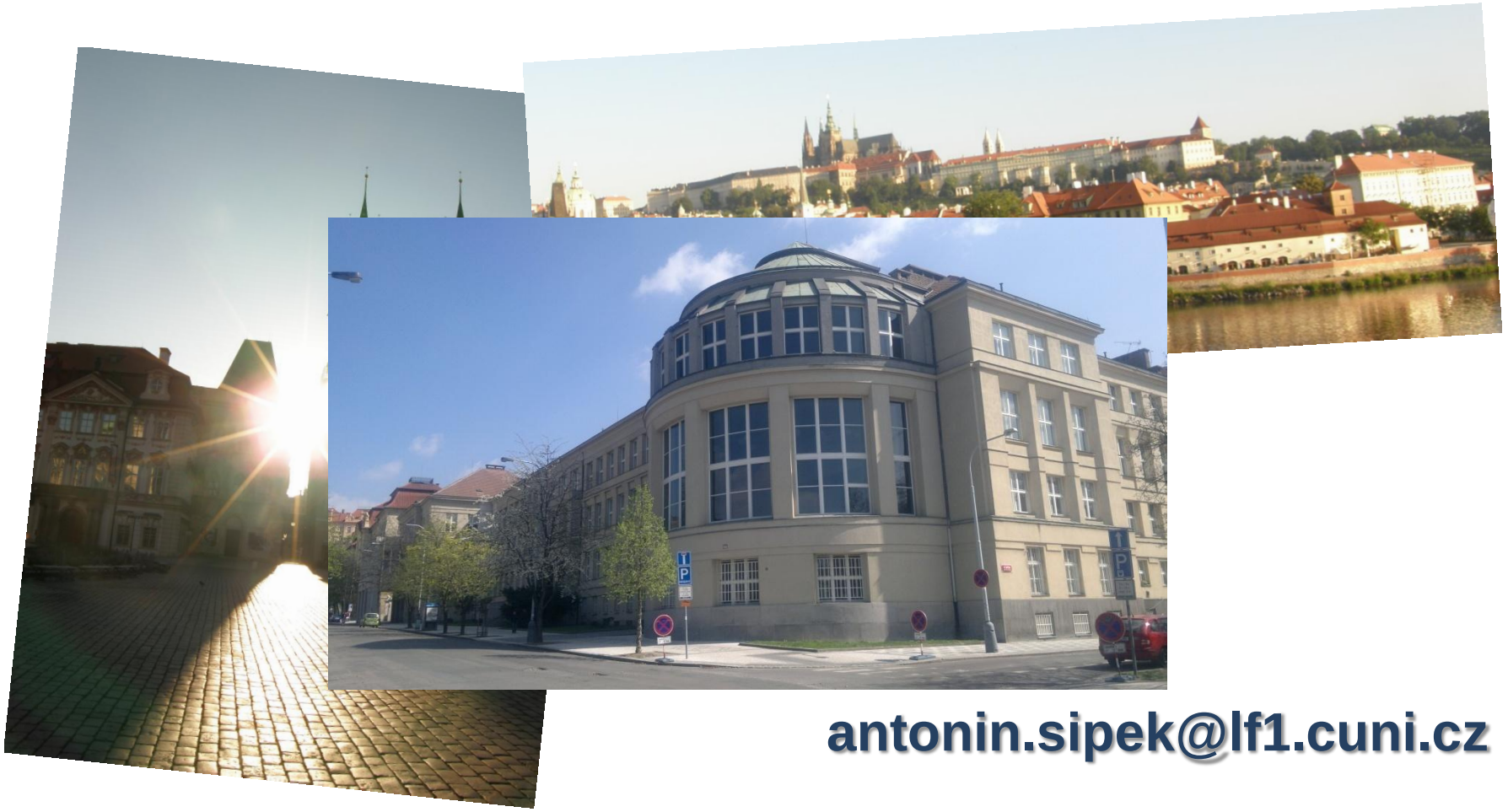
Conclusion

- **The inv(9) is relatively common finding in CZE:**
  - The laboratory incidence: 1.06% – 1.75%
  - Estimated population incidence: 0.82% - 2.43%

- **The inv(9) is an insignificant variant:**
  - We are still uncertain. It is clear, that the majority of inv(9) carriers has no trouble at all. However, the possible association of inv(9) and reproduction failure wasn‘t excluded (nor confirmed) right now.

- **More specific analyses are needed:**
  - Molecular cytogenetic methods are needed for further examination of each single case of inv(9)
  - We will try to find specific associations for specific (sub)variants of chromosome 9 heterochromatine area

Thank you for your attention!



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