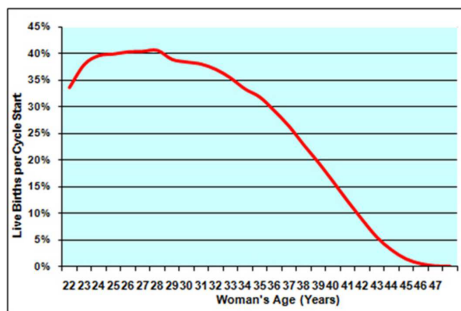




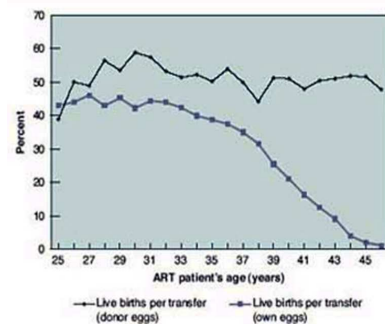
Preimplantation aneuploidy testing: when is necessary ?

Katerina Vesela

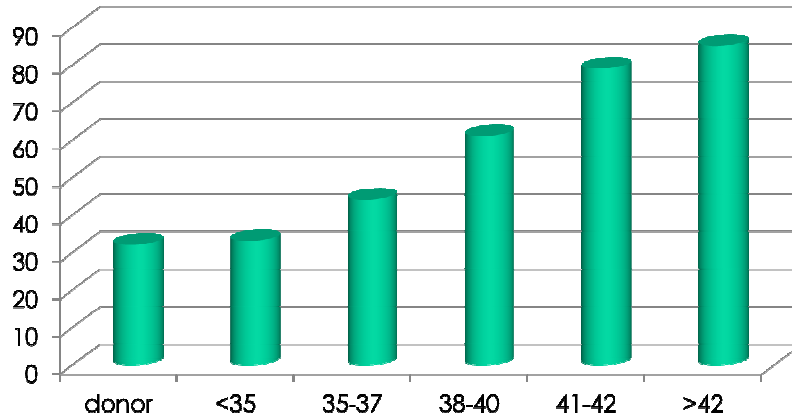
Identification and elimination of embryo aneuploidy is a clinical imperative



Live Births per Transfer for ART Cycles Using Fresh Embryos from Own and Donor Eggs, by ART Patient's Age, 2002

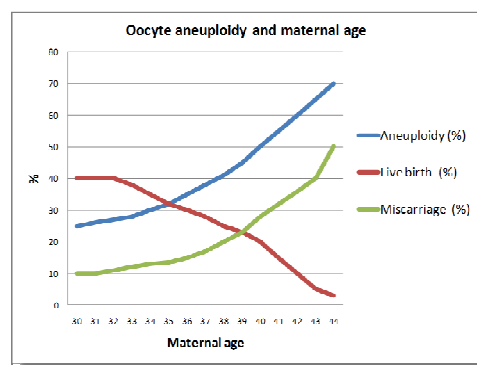
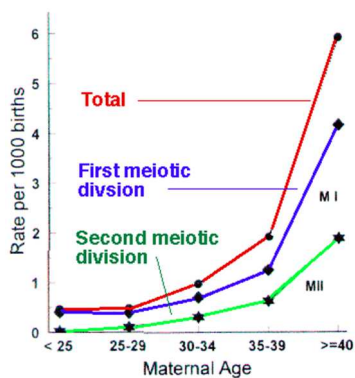


Aneuploidy and maternal age



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Aneuploidy and miscarriage versus maternal age



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Multicenter study on implantation of euploid embryos – biopsy day 3 versus day 5. Harton and al, 2013

Day 3 Biopsy			Day 5 Biopsy		
Age	Implantation (+ Sac)	Aneuploidy Rate	Age	Implantation (+ Sac)	Aneuploidy Rate
30-34	40.6 (73/180)	53.1 (530/999)	30-34	51.1 (119/233)	31.7 (306/966)
35-37	43.6 (44/101)	68.2 (420/616)	35-37	54.2 (65/120)	44.2 (237/536)
38-40	42.1 (59/140)	73.7 (659/894)	38-40	47.2 (59/125)	43.1 (324/751)
41-42	31.6 (18/57)	85.8 (460/536)	41-42	40.4 (19/47)	76.3 (200/262)
P Value	NS	<0.001	P Value	NS	<0.001

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Blastocyst time formation and aneuploidy

Age Groups	Aneuploidy Rate (%)		
	D5 Blastocyst	D6 Blastocyst	p value
donor	29 (n=217)	38 (n=88)	0.17
<35	24 (n=229)	46 (n=128)	0.00*
35-37	37 (n=139)	53 (n=100)	0.02*
38-40	55 (n=160)	68 (n=124)	0.04*
41-42	76 (n=80)	84 (n=45)	0.36
>42	76 (n=42)	93 (n=51)	0.04*

Xie et al 2014

- D6 => Significantly more aneuploidy
- Younger age groups - high percentage of aneuploidy Day 6
- Vast majority D6 blastocysts from patients >40 years aneuploid
- Blastocysts day 6 - still a very important source of chance in AMA

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Aneuploidy and FSH

Rodrigues - Purata 2014

Factor	OR	p-value
Age	1.1	<0.0001
FSHMax	1.01	0.75
FSHMax>13	0.84	0.45
FSHMax>13:Age	1.52	<0.0001

- Odds of aneuploidy increases by **10%** for each year of a woman's reproductive lifespan (OR=1.1, $p<0.0001$)
- In women with **FSH levels above 13 mIU/ml** the odds of aneuploidy increases by **50%** for each additional year (OR=1.52, $p<0.0001$) of life.

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Is PGS of blastocysts a cost effective approach in achieving a live birth? Resetkova et al 2013 & 2014

- TreeAge Pro 2013 involving 560 cycles model
- The average cost of undergoing IVF with PGS is \$25,242 with a 95% chance of achieving a live birth over three pregnancy attempts
- An average cost of \$22,776 and a cumulative success rate of 64% for IVF alone

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Is PGS of blastocysts a cost effective approach in achieving a live birth? Resetkova et al 2013 & 2014

Conclusion

- biopsy at trophectoderm stage has resulted in **increasing pregnancy rates** and **reduced miscarriage rates**, improving the effectiveness of PGS with IVF
- the addition of 23 chromosome microarray PGS to IVF is **cost effective for couples across all maternal age** groups compared to IVF alone over a wide range of probabilities and costs.

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Comparision using Time-Lapse and PGS

PRCT (Yang et al 2014)

- Prospective investigation using **sibling oocytes** for PGS with Time-Lapse
- 138 PGS patients
- Mean age 36.6 ± 2.4 years
- Randomized into two groups
 - Group A, oocytes (n = 582) were cultured in the time-lapse system and
 - Group B, oocytes (n = 581) were cultured in the conventional incubator

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Comparison of pregnancy and implantation outcomes between time-lapse (Group A) and conventional incubator (Group B), as well as the mixed embryo transfer

Parameters	Group A	Group B	Mixed	p value
Patient with SET	19	15	n/a	
Patient with DET	26	22	45	
Clinical pregnancies after SET	10	5	n/a	
Clinical pregnancies after DET	21	11	24	
Clinical pregnancy rate	71.1%	45.9%	53.3%	0.037 ^a
Implantation rate	66.2%	42.4%	47.8%	0.011 ^a
Ongoing pregnancy rate	68.9%	40.5%	48.9%	0.019 ^a
Pregnancy loss rate	3.1%	11.8%	8.3%	0.273 ^b

SET = single embryo transfer; DET = double embryo transfer; Mixed = mixed embryo transfer (one from the time-lapse system and one from the conventional incubator); ^aGroup A vs. Group B, by Chi-square analysis; ^bGroup A vs. Group B, by Fisher's exact test.

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- Data clearly demonstrate that **the combination of Time-Lapse and PGS to select competent blastocysts for transfer results in improved implantation and ongoing pregnancy rates for PGS patients**
- Time-Lapse is working in synergy with PGS but is unable to substitute PGS anyhow

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Aneuploidy in PGS cycles and PGD cycles for monogenics

Aneuploidy in **PGS** cycles

- **30-90%**

according to the age

Aneuploidy in **PGD** cycles

- **30%**

(mostly fertile couples)

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Classical PGS indications

- AMA
- RPL
- RIF
- MMF
- Other
- combinations

Average couple in REPROMEDA:

- female average age **33,8 years** (increasing in approx. 6 month every year)
- **2 and more factors of infertility**

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Do we really need any special indications and inclusion criteria to perform PGS in infertile couples ?

Near future:

Infertility and IVF treatment is an indication itself.....

Exclusion criteria – the couple doesn't wish to do so.....

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Conclusions

It's an imperative to eliminate aneuploid embryos at all ages and all types of treatment not only in AMA because:

- Time to pregnancy
- Time to Live Birth
- Avoid transferring aneuploid embryos with risk of miscarriage or TOP
- Avoid to freeze aneuploid embryos
- Avoid the increased risk of multiple pregnancy
- Cost effectiveness

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Conclusions

- Classical IVF scheme: ovarian stimulation – embryo culture - fresh embryo transfer – **ABANDONED**
 - **Pregnancy, delivery and breast feeding don't break the ovarian reserve drop off and represent a risk of delay**
- **Women > 34 years** with a reproductive wish to have more than 1 child – recommendation to **bank embryos prior to the first embryo transfer**

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Conclusions – future strategy

Biopsy all
Freeze alle
Test all

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Thank you for your attention
Thank all the REPROMEDA team for cooperation