

IMMATURE OOCYTE INCIDENCE: CONTRIBUTING FACTORS AND EFFECTS ON INTRACYTOPLASMIC SPERM INJECTION CYCLES

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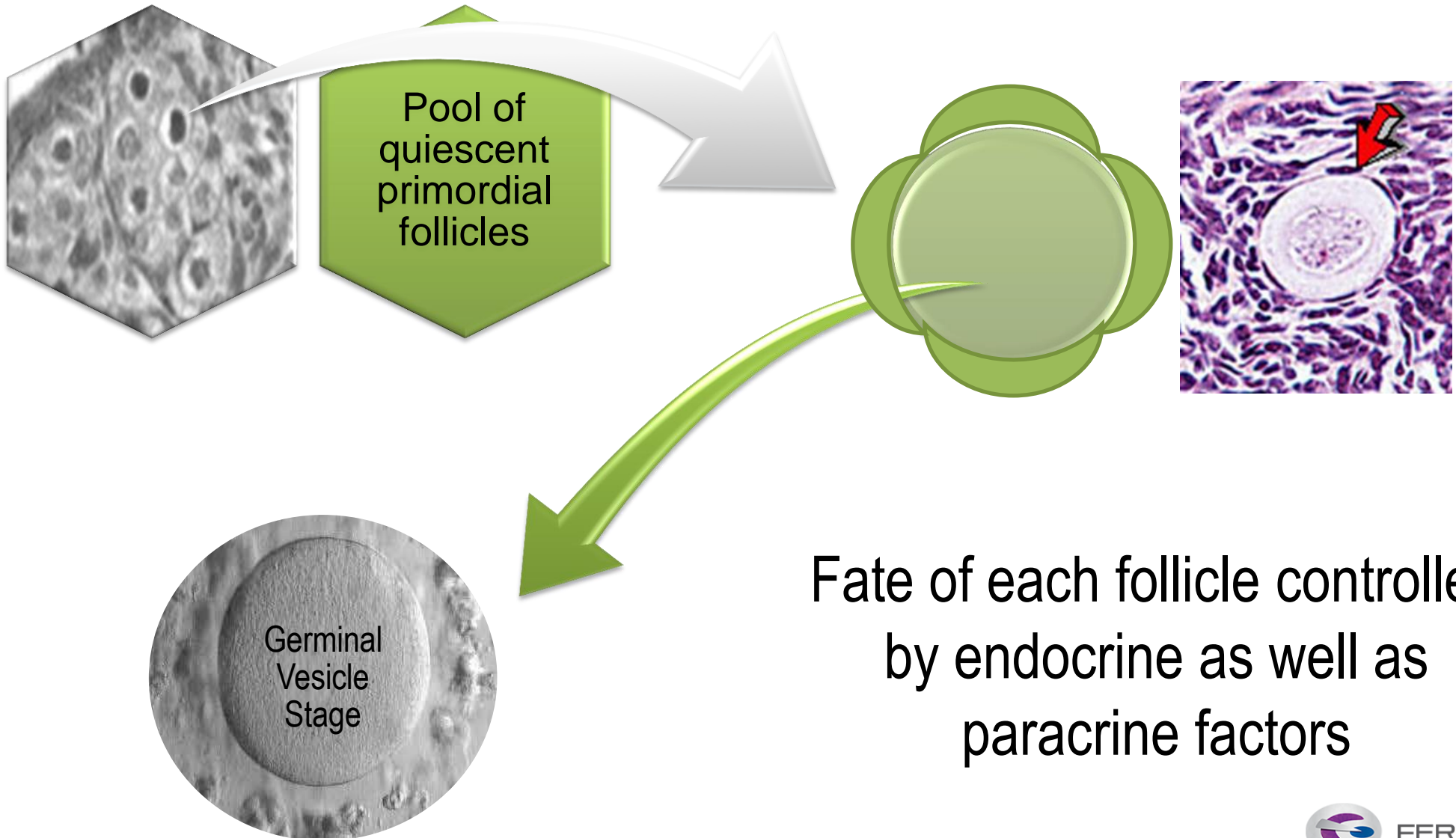
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INTRODUCTION



INTRODUCTION

POOL OF
PRIMORDIAL
FOLLICLES

400 mature during a
woman's lifetime

18 weeks pregnancy
($6-7 \times 10^6$ oocytes)

At birth
($1-2 \times 10^6$ oocytes)

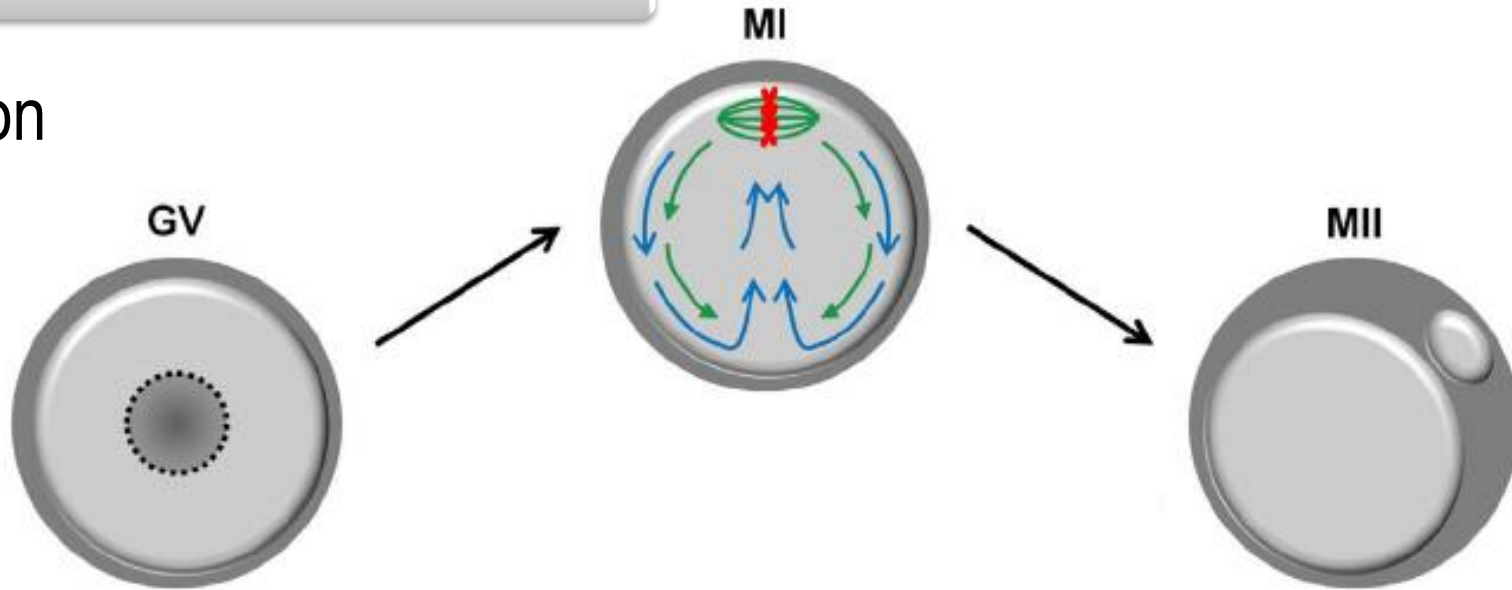
Puberty
(300 000 oocytes)

Menopause
< 1000

INTRODUCTION

✓ Oocyte maturation

Nuclear
maturation



Cytoplasmic
maturation

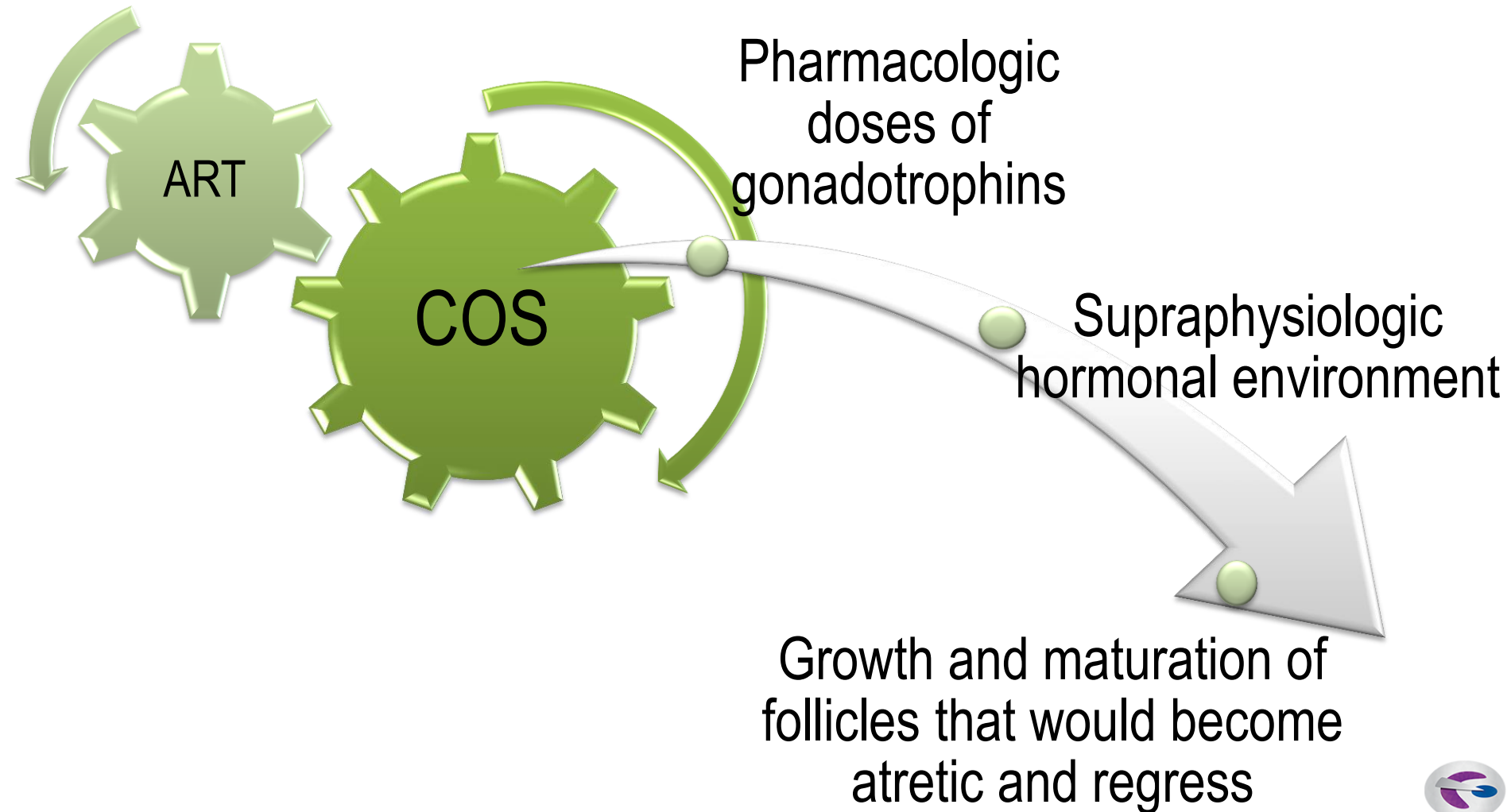
- Cytoplasmic enzymes
- mRNAs
- Organelles
- Metabolic substrates

Fertilization

Early
embryonic
development

INTRODUCTION

✓ Controlled Ovarian Stimulation (COS)



INTRODUCTION

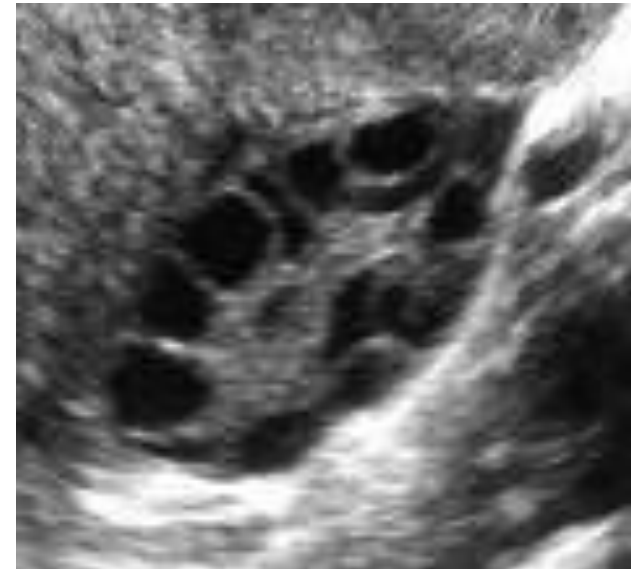
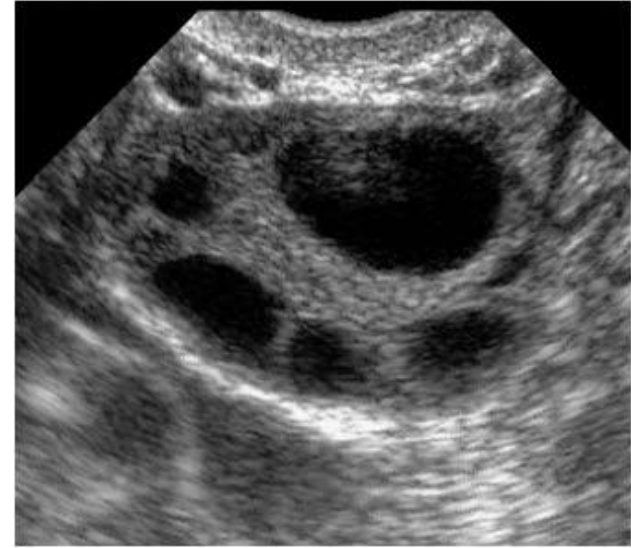
Follicular
asynchrony



Different COS
protocols

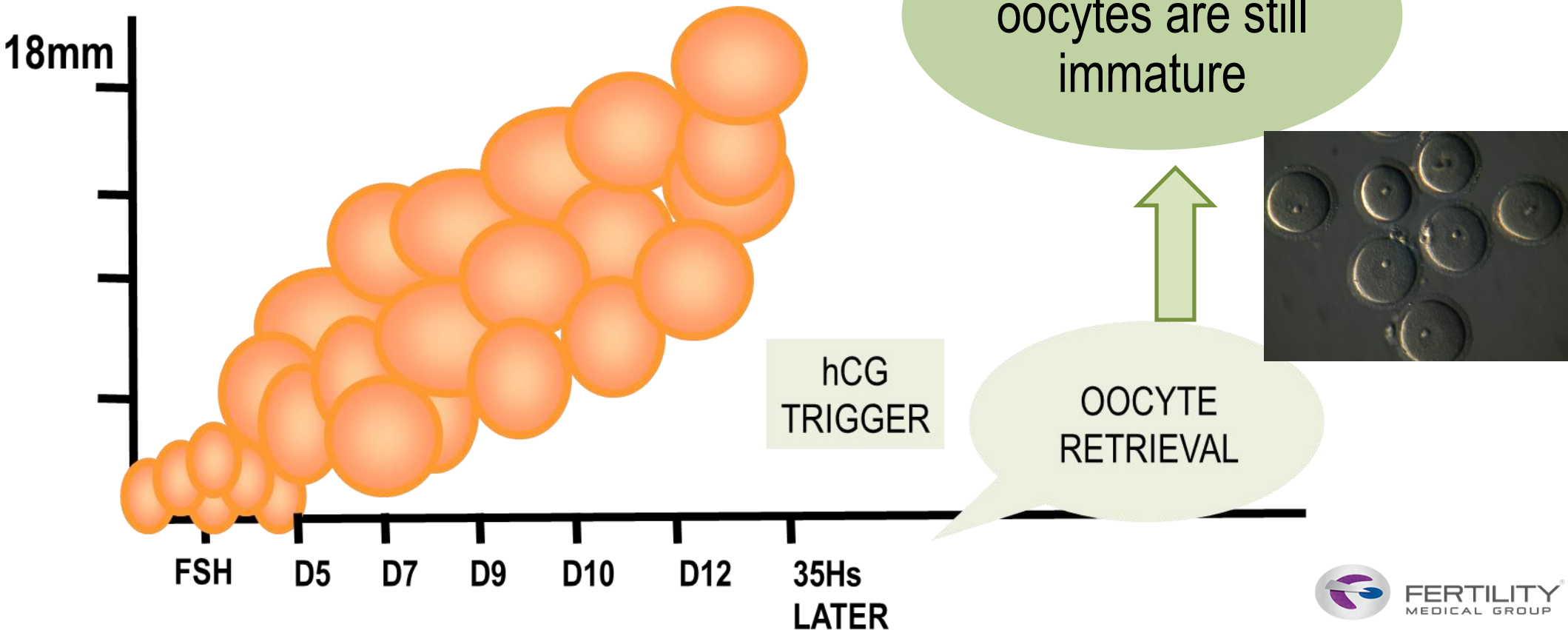


Variations in
oocyte number
and quality

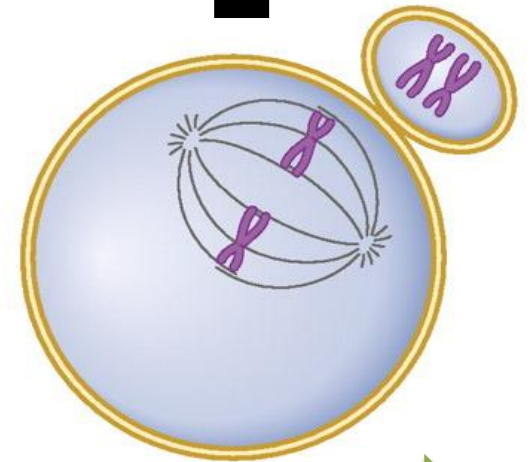
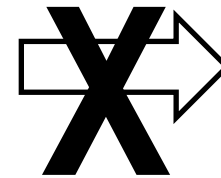
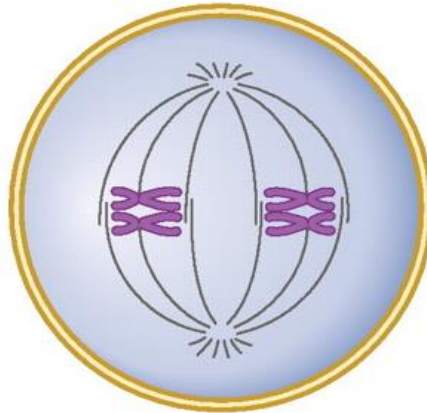
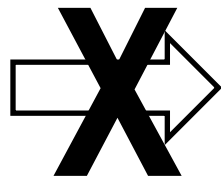
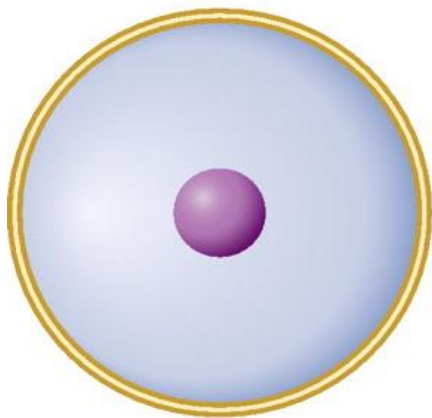
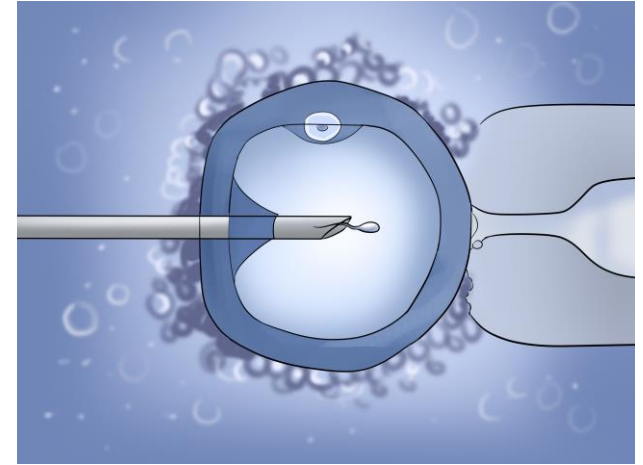


INTRODUCTION

CONTROLLED OVARIAN STIMULATION



INTRODUCTION

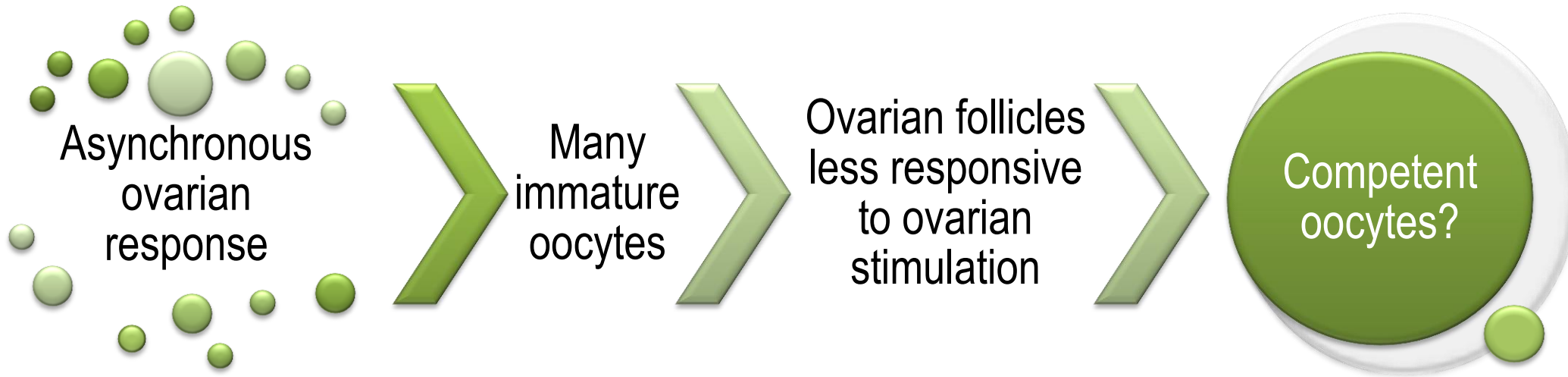


GV

MI

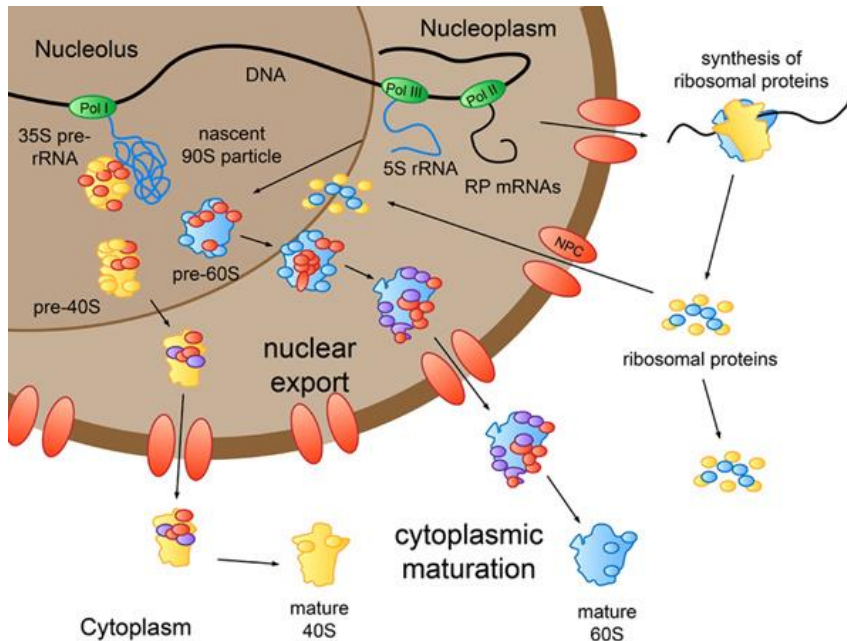
MI

INTRODUCTION



Oocytes considered mature in the same cohort may not be fully competent for fertilization and embryo development

INTRODUCTION



Cytoplasmic maturation completion

- No macroscopic markers
- No single observable factor

✓ Data about the impact of higher immature oocytes incidence in the developmental competence of the MII oocytes from the same cohort are scarce

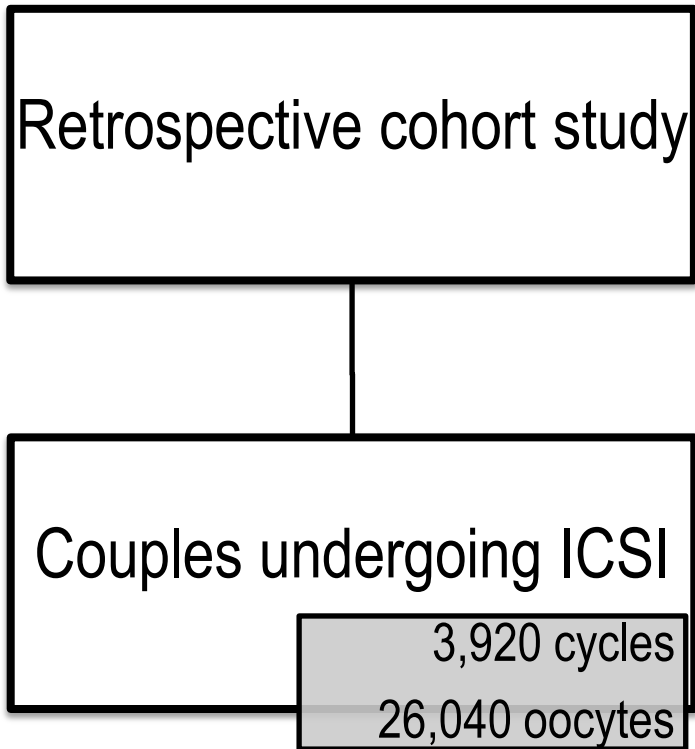
OBJECTIVE

To investigate which factors contribute to the incidence of immature oocytes

To investigate how immature oocytes impact the outcomes of mature oocytes from the same cohort

MATERIALS AND METHODS

- STUDY DESIGN



Generalized linear models

- Correlation of COS protocols and doses on immature oocyte incidence and rates

Regression models

- The effects of immature oocytes rates on ICSI outcomes

MATERIALS AND METHODS

FIRST ANALYSIS

Evaluated Variables

Total dose of FSH

COS protocol

Pituitary blockage protocol

Estradiol level on hCG trigger day

Interval between hCG and oocyte retrieval

MATERIALS AND METHODS

SECOND ANALYSIS

Evaluated
Variables

Fertilisation rate

Embryo quality on cleavage stage

Blastocyst formation rate

Implantation rate

Pregnancy rate

Miscarriage rate



MATERIALS AND METHODS

Discriminant analysis for pregnancy outcome prediction

- MI/oocyte rate
- GV/oocyte rate
- Female age
- Total FSH dose
- Number of retrieved oocytes
- Number of transferred embryos
- Endometrial thickness

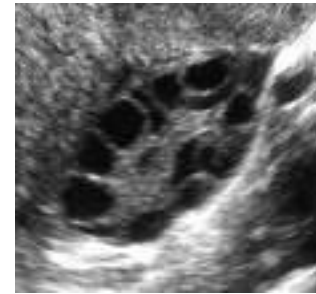
Data grouped according
with established cut-off
for MI/oocyte rate

General Linear Model followed
by Tukey post hoc

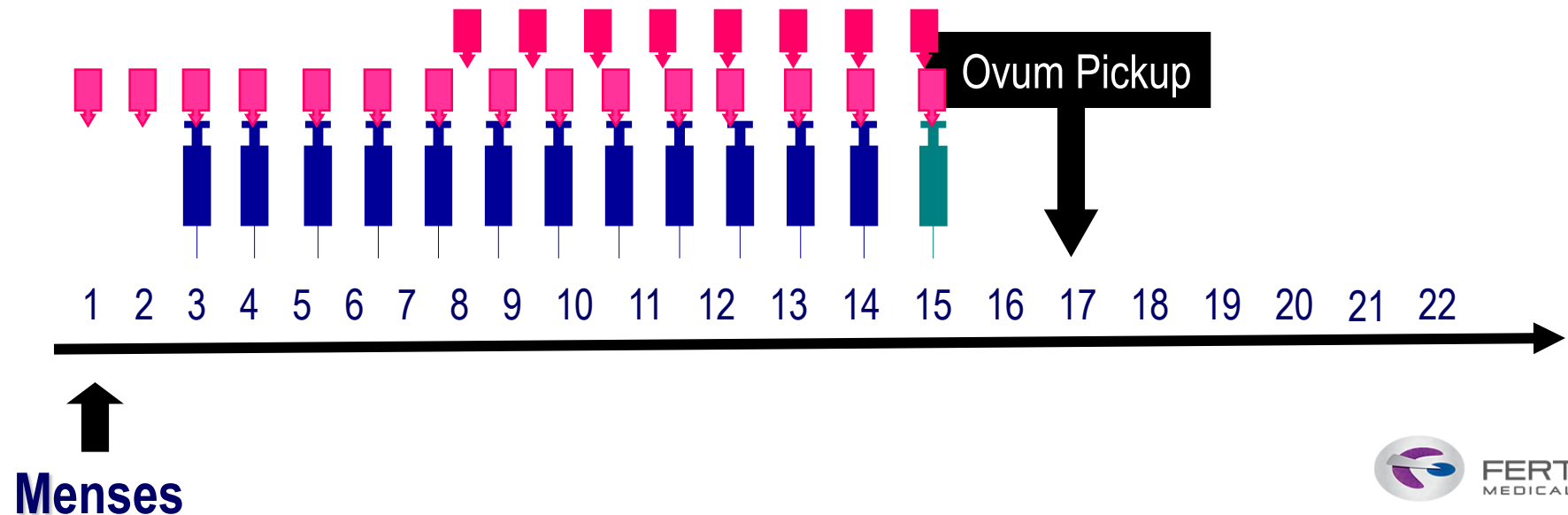
MATERIALS AND METHODS

Controlled Ovarian Stimulation

- GnRH Antagonist or Agonist
- rFSH or rFSH + rLH
- rhCG



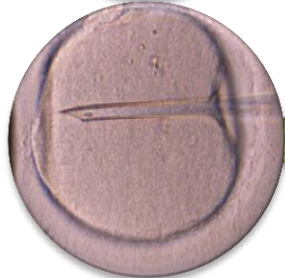
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MATERIALS AND METHODS



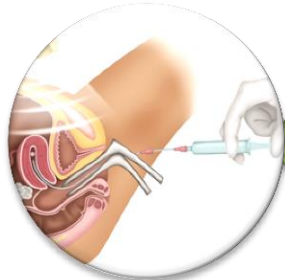
Incubation, denudation and nuclear maturation evaluation



ICSI - (Palermo et al., 1992)



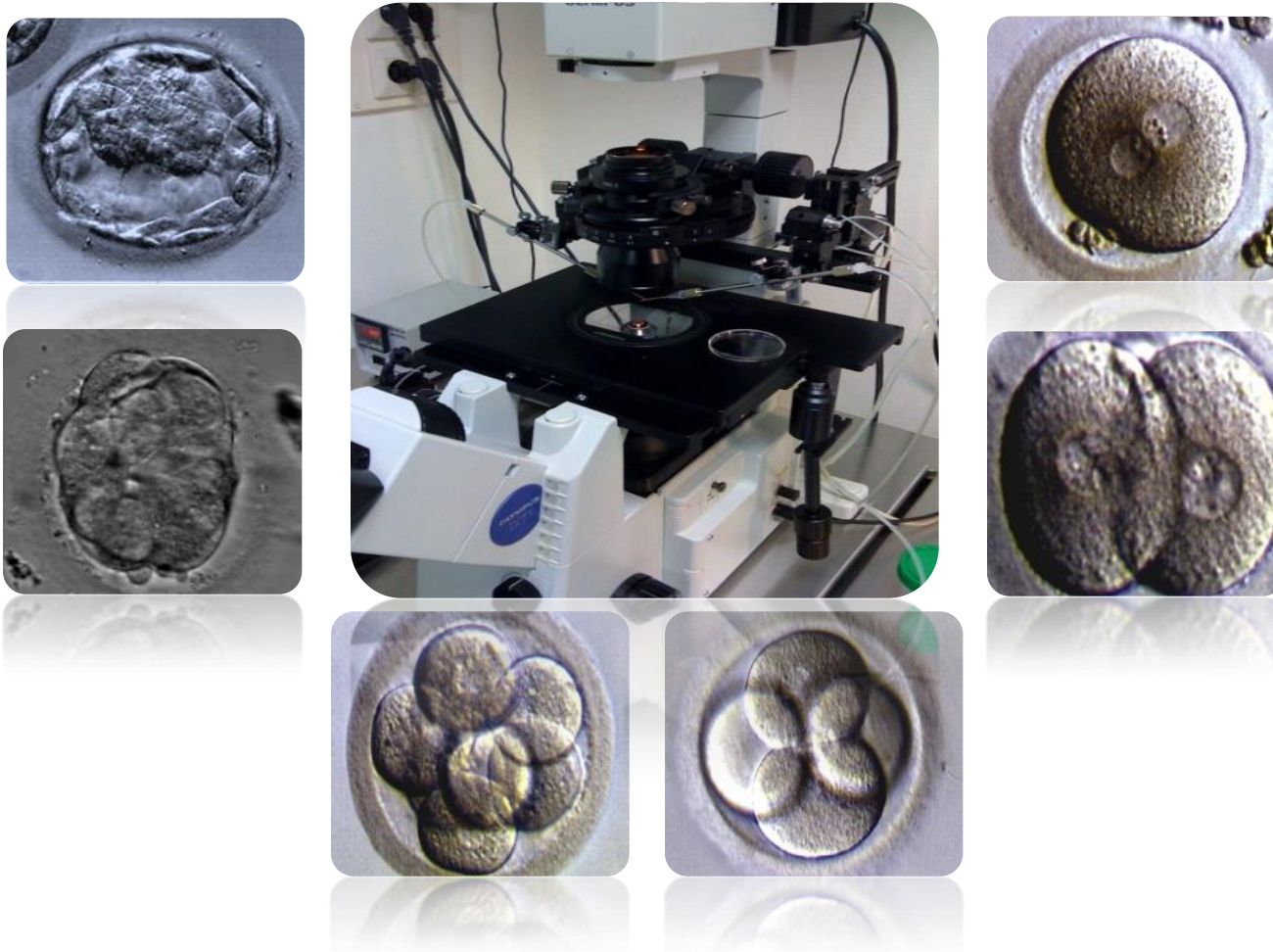
Embryo culture until day 5



One or two blastocysts transferred

MATERIALS AND METHODS

- EMBRYO MORPHOLOGY AND EMBRYO TRANSFER



RESULTS



(Pearson's $r = -0.079$ $p < 0.001$)

Each rate was evaluated separately.

RESULTS

Linear model analysis of the contributing factors for the number of immature oocytes and immature oocytes rates (n=3,920).

	GV incidence			MI incidence		
	R ²	β	p	R ²	β	p
FSH dose	0.050	-0.035	0.029	0.042	-0.046	0.004
E2 levels	0.155	0.342	<0.001	0.146	0.324	<0.001
hCG interval	0.050	-0.014	0.385	0.042	-0.015	0.368
	GV / retrieved oocytes			MI / retrieved oocytes		
	R2	β	p	R2	β	p
FSH dose	0.002	0.009	0.592	0.001	-0.009	0.567
E2 levels	0.003	0.034	0.107	0.001	0.015	0.491
hCG interval	0.003	-0.015	0.356	0.002	-0.025	0.135

RESULTS

Effect of the pituitary blockage and COS protocol on the number of immature oocytes and immature oocytes rates (n=3,920).

	GnRH antagonist			GnRH agonist		
	rFSH (n=1570)	rFSH + rLH (n=980)	p	rFSH (n=658)	rFSH + rLH (n=712)	p
MI	1.13±0.03	1.12±0.05	0.928	1.45±0.10	0.38±0.68	0.119
GV	1.33±0.05	1.36±0.08	0.731	1.46±0.14	0.40±0.93	0.263
MI/oocyte	10.75±0.36	11.33±0.59	0.405	13.40±0.91	6.32±6.19	0.147
GV/oocyte	11.01±0.36	5.93±5.40	0.042	11.52±1.12	1.86±2.10	<0.001

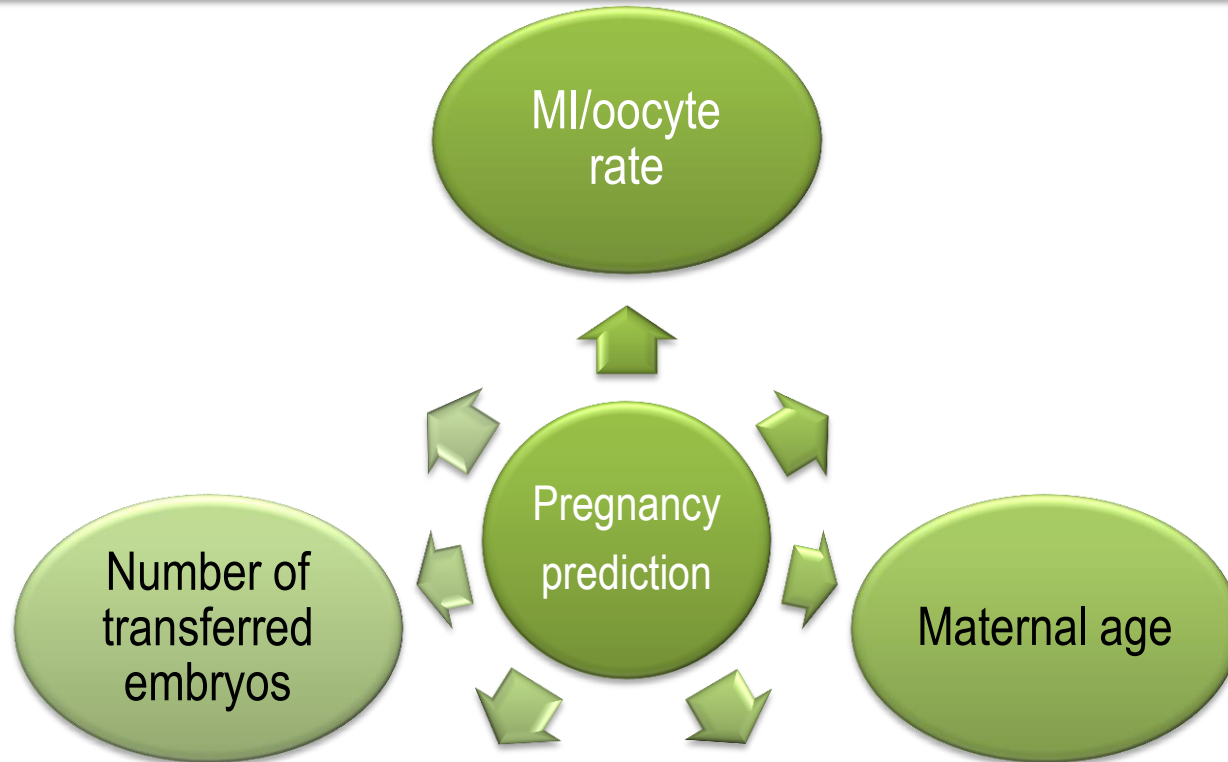
RESULTS

Regression analysis of the association between immature oocytes rate and ICSI outcomes

	MI/oocyte				GV/oocyte		
	R ²	β	p		R ²	β	p
Fertilization rate	0.035	-0.096	<0.001		0.029	-0.059	<0.001
High-quality embryos rate D2	0.014	-0.102	<0.001		0.008	-0.066	<0.001
High-quality embryos rate D3	0.020	-0.090	<0.001		0.020	-0.087	<0.001
Blastocyst rate	0.073	-0.066	<0.001		0.071	-0.053	<0.001
Implantation rate	0.059	-0.074	<0.001		0.056	-0.042	0.033
	B	OR	p		B	OR	p
Pregnancy rate	-0.011	0.989	0.002		-0.009	0.992	0.013
Miscarriage rate	0.010	1.011	0.220		0.006	0.944	0.418

RESULTS

Discriminant analysis for pregnancy outcome prediction



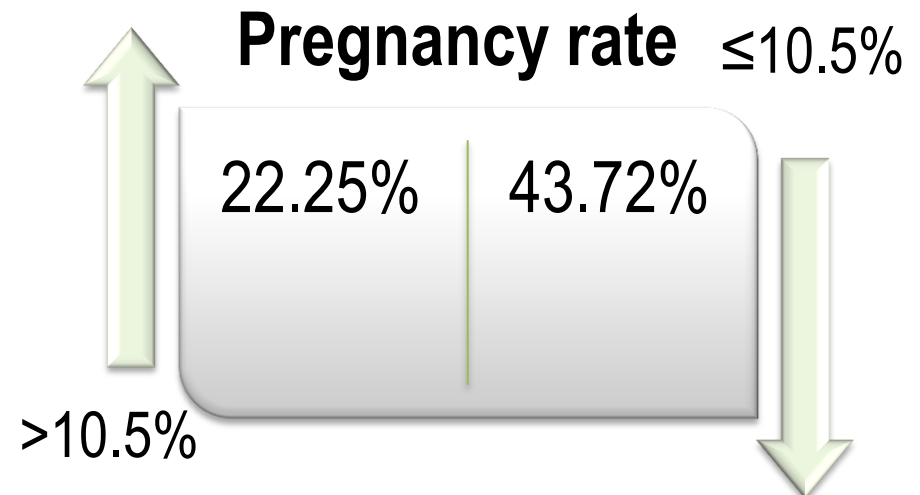
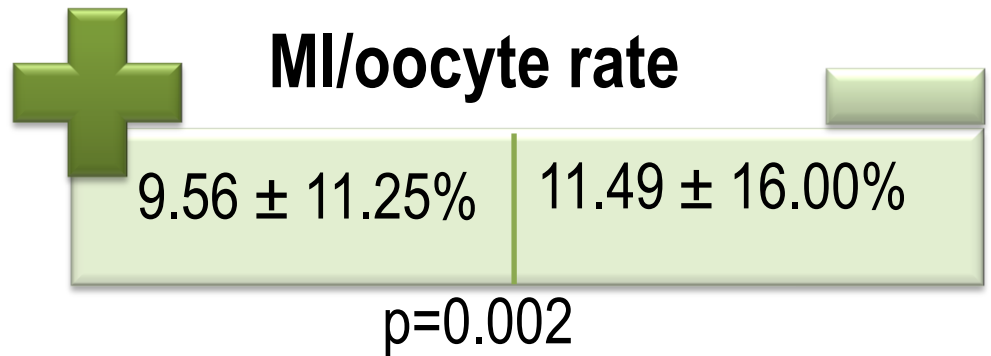
RESULTS

Discriminant analysis for pregnancy outcome prediction

66.8% of original cases

Cut-off point for MI/oocytes: 10.5%

Prediction for negative pregnancy, of 94.1%.



CONCLUSION

The immature oocyte incidence is affected by the COS protocol and gonadotrophin dose

Immature oocyte incidence negatively impacts laboratorial and clinical ICSI outcomes

WIDER IMPLICATIONS OF THE FINDINGS

The incidence of immature oocytes may reflect the competence of the whole cohort

Mature oocytes derived from cycles with higher incidence of immature oocytes may have poor embryo development and low implantation potential

These findings highlight the importance of the COS protocol and the gonadotrophin dose for the outcomes of assisted reproduction cycles



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