

# **Progesterone-primed cycles result in slower embryos without compromising implantation potential and with the advantages of oral administration and potential cost reduction: A time-lapse imaging study**

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# INTRODUCTION

INTRODUCTION

OBJECTIVE

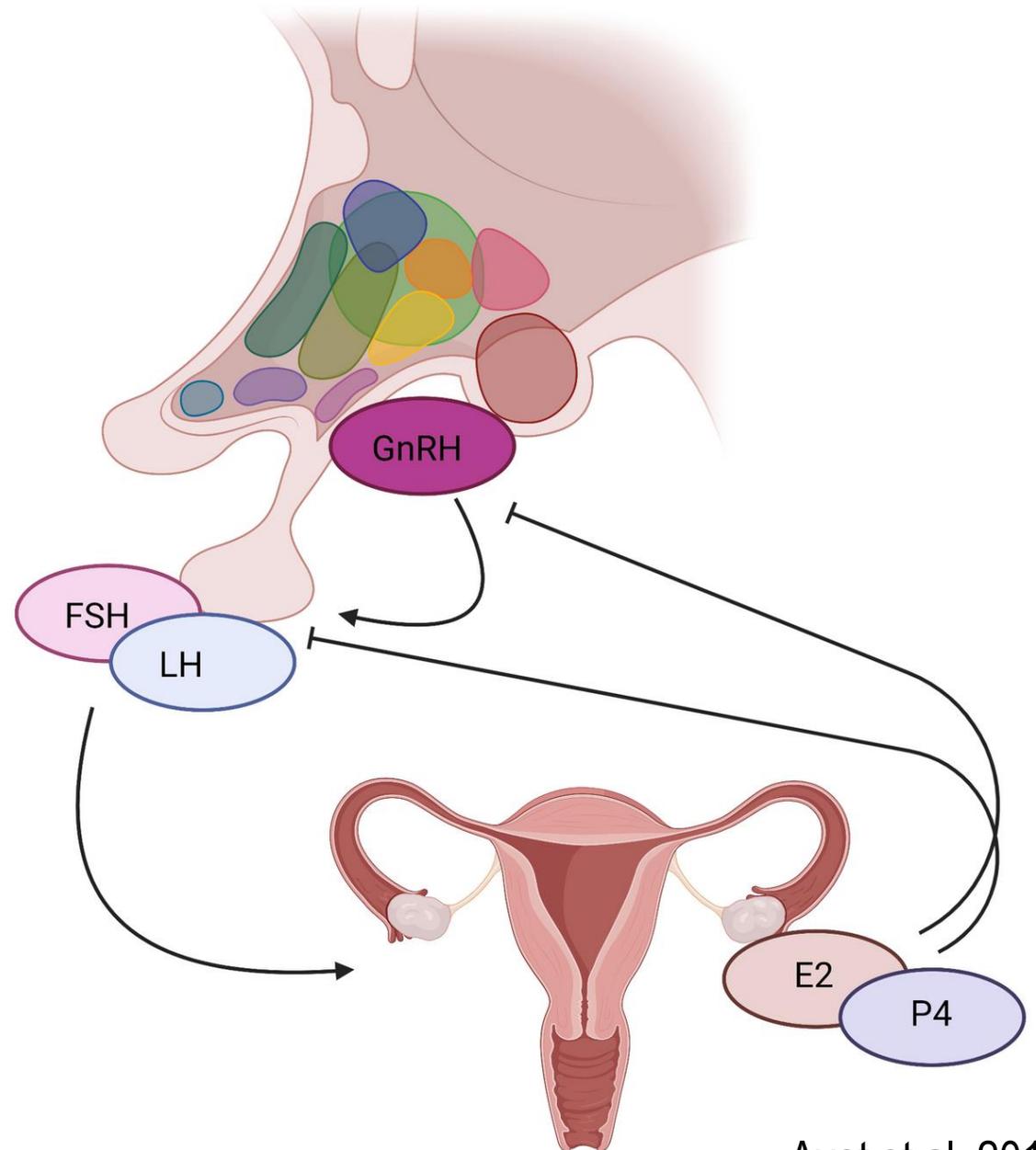
MATERIAL AND  
METHODS

RESULTS

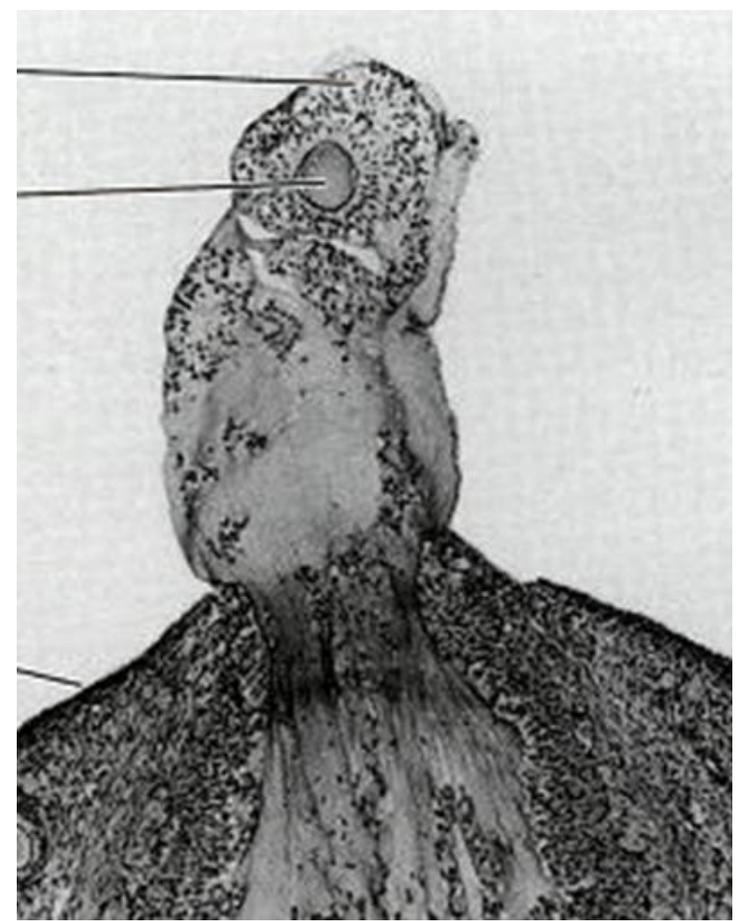
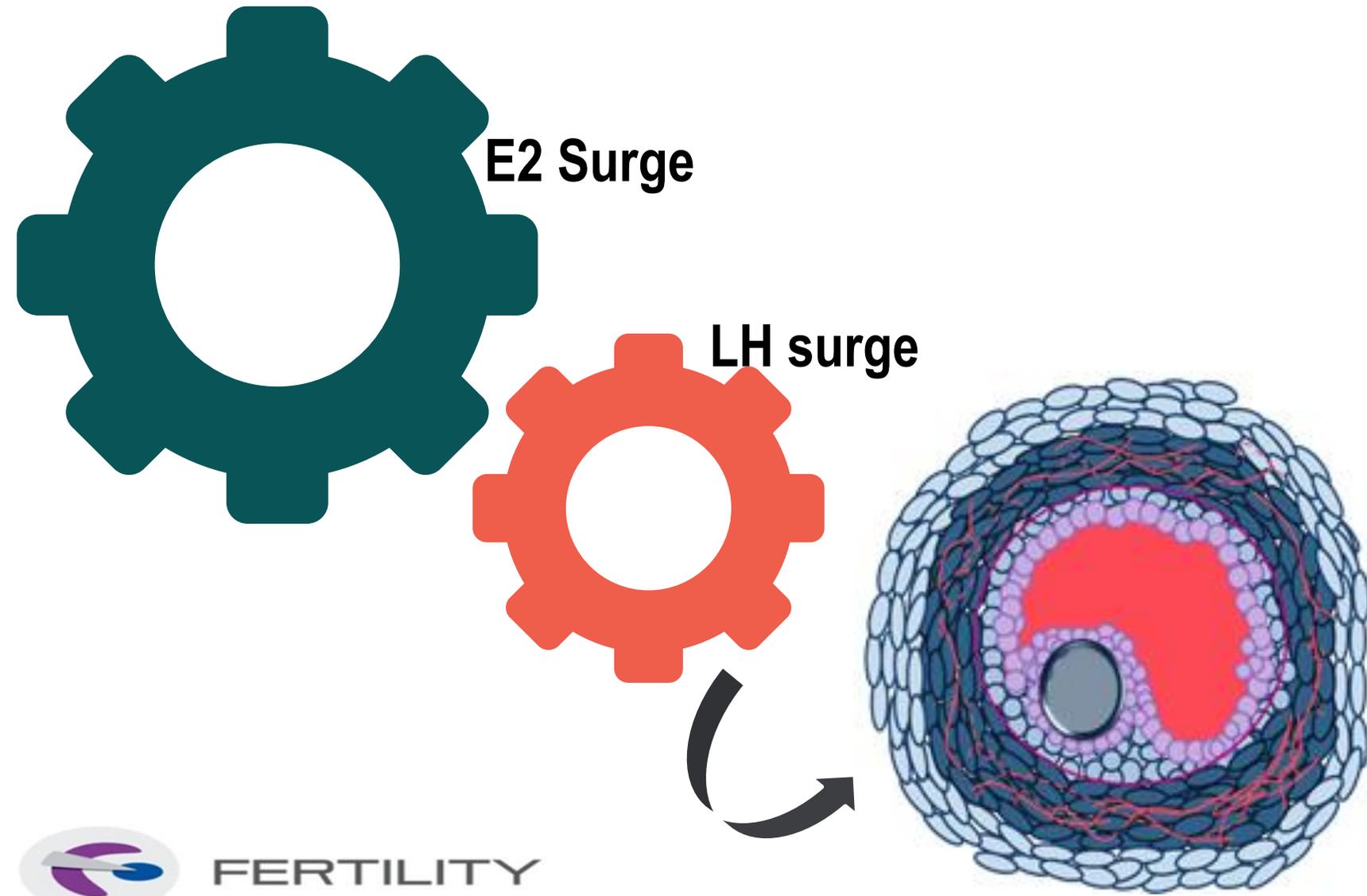
CONCLUSION

# GnRH ACTION

- ✓ GnRH activates its receptor in pituitary gonadotrophs
- ✓ Resulting in the synthesis and secretion of LH and FSH
- ✓ Both regulating gametogenesis and steroidogenesis in the gonads

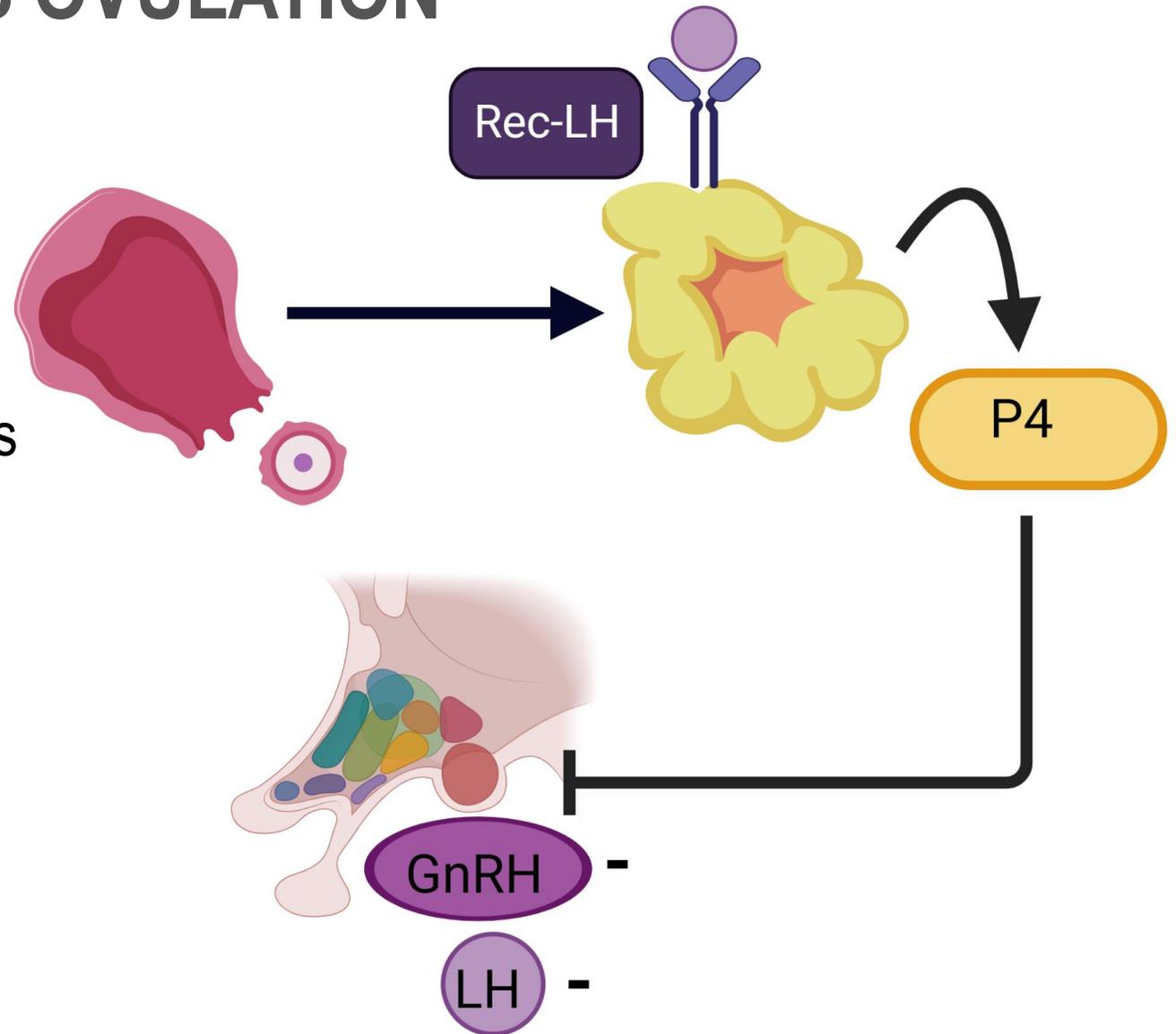


# OVULATION



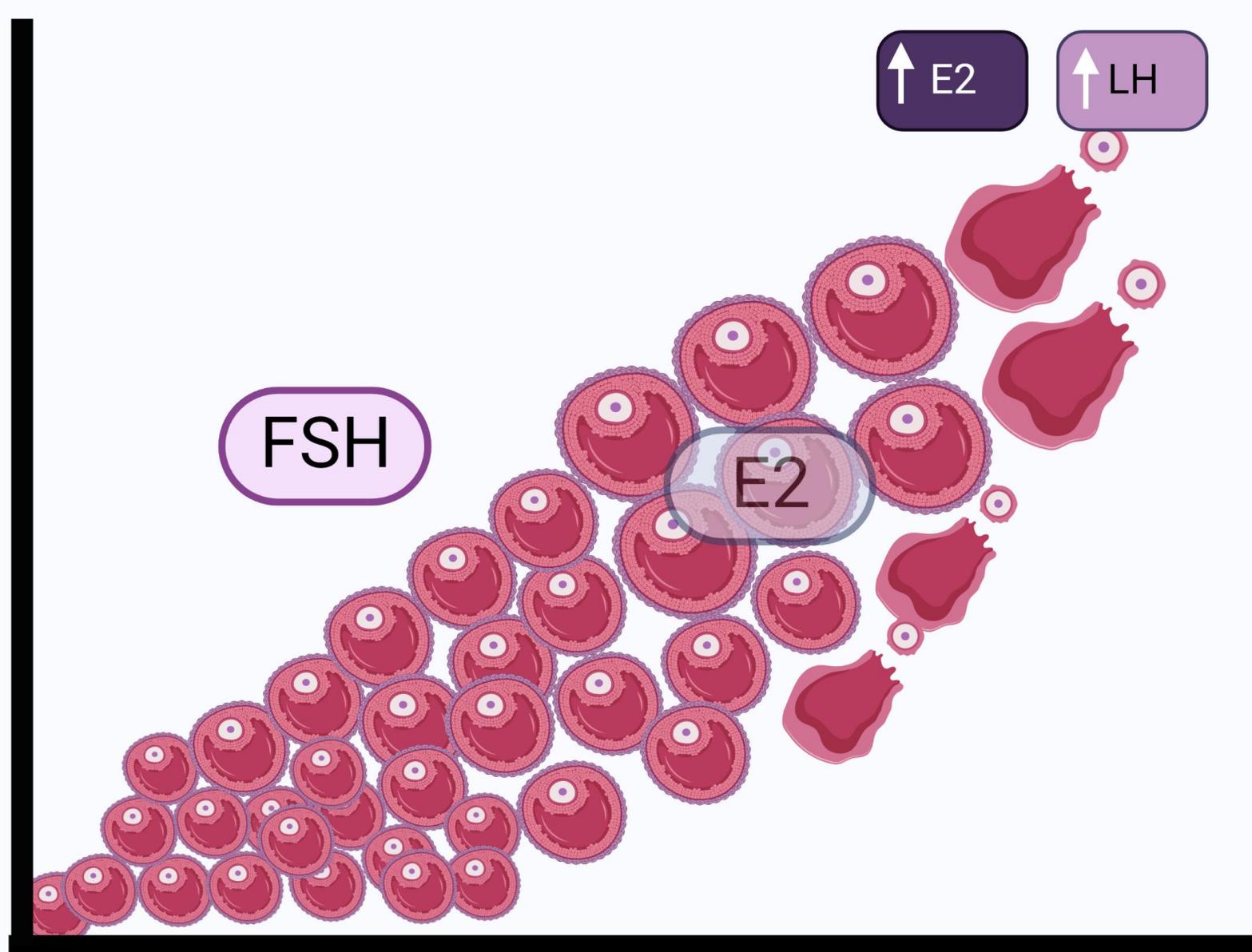
# PROGESTERONE INHIBITS OVULATION

- ✓ During the luteal phase, progesterone produced by the corpus luteum inhibits pulsatile GnRH and LH secretion and therefore inhibits ovulation



# STANDARD OVARIAN STIMULATION REGIMENS

- ✓ Standard ovarian stimulation regimens use gonadotrophins to promote multifollicular development
- ✓ The rise in estradiol concentrations due to the development of multiple follicles may promote a spontaneous LH surge



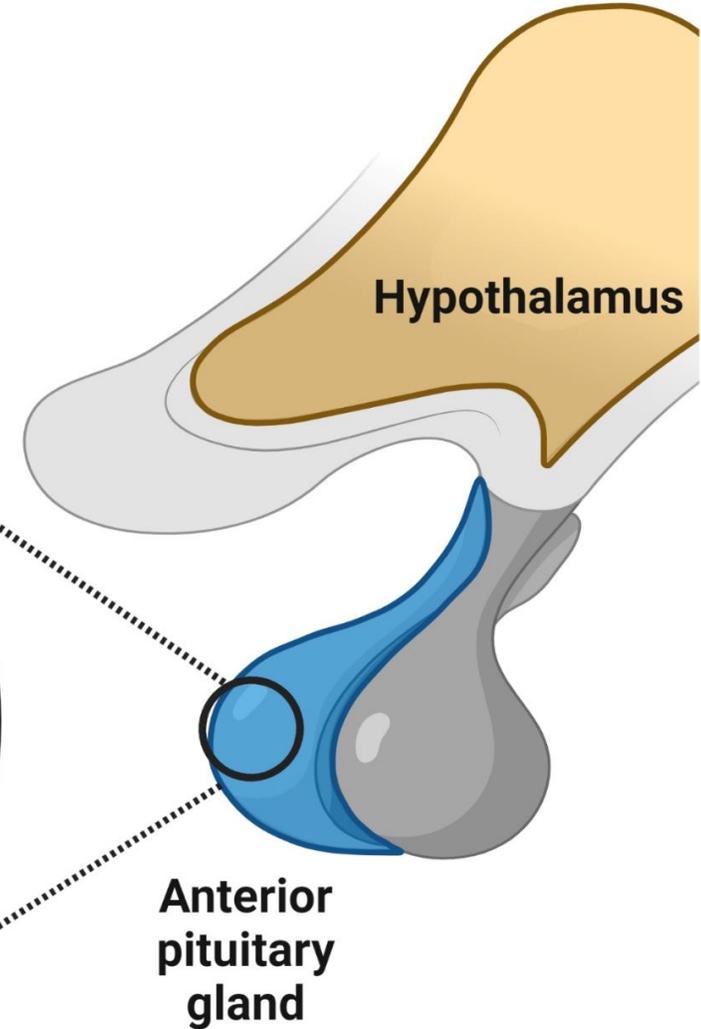
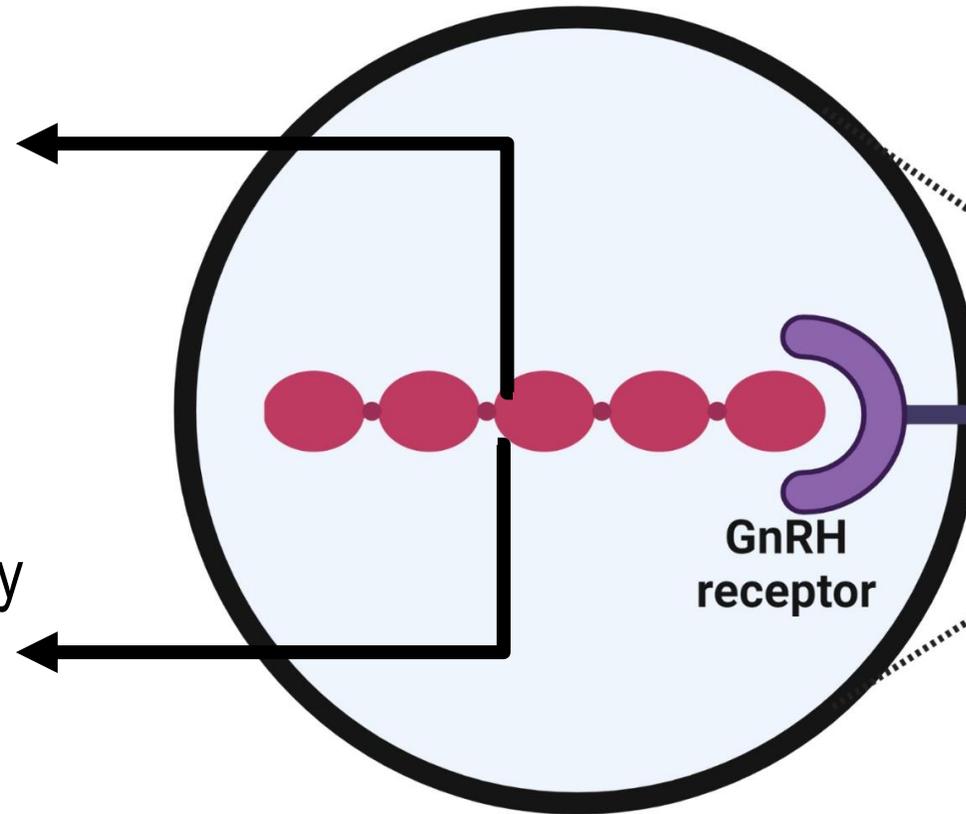
# ANALOGS OF GnRH TO PREVENT THE LH SURGE

GnRH  
analogs



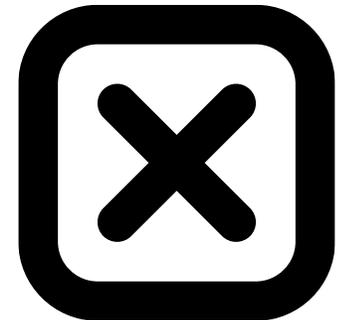
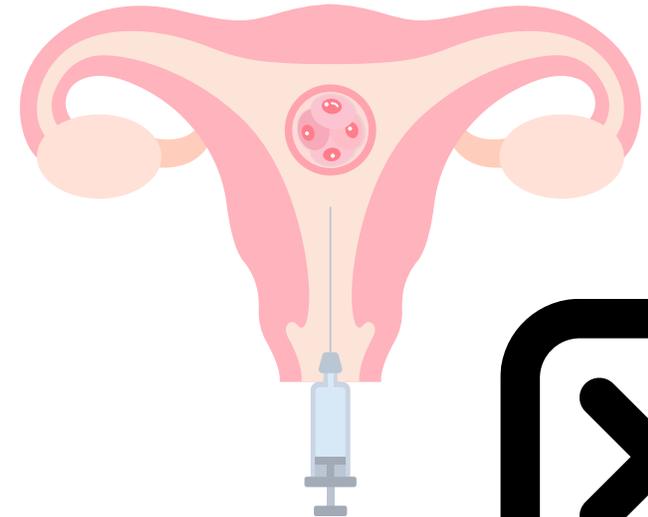
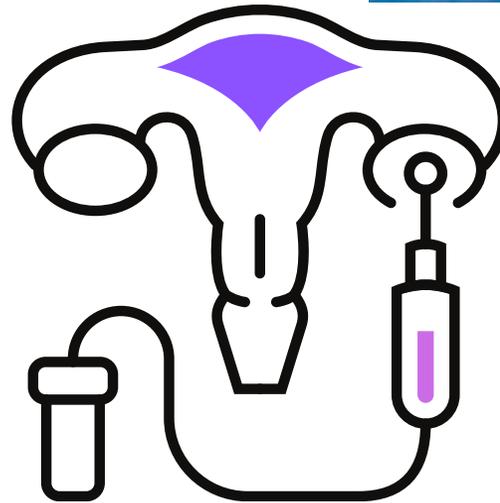
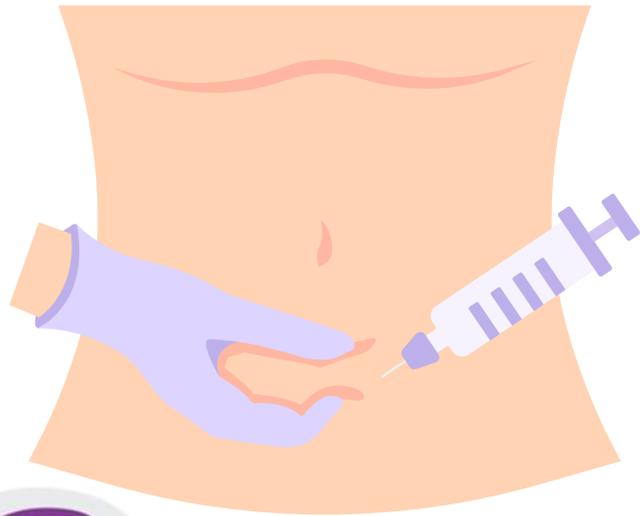
**GnRH agonists:**  
Desensitization of receptors

**GnRH antagonist:**  
Simple competitive occupancy  
of the receptor



# BREAK AWAY FROM THE STANDARD SEQUENCE: STIMULATION–RETRIEVAL–TRANSFER

- ✓ Improvements in cryopreservation techniques
- ✓ Break away from the standard sequence of stimulation–retrieval–transfer



# PROGESTERONE/PROGESTINS AS AN ALTERNATIVE TO PREVENT THE LH SURGE

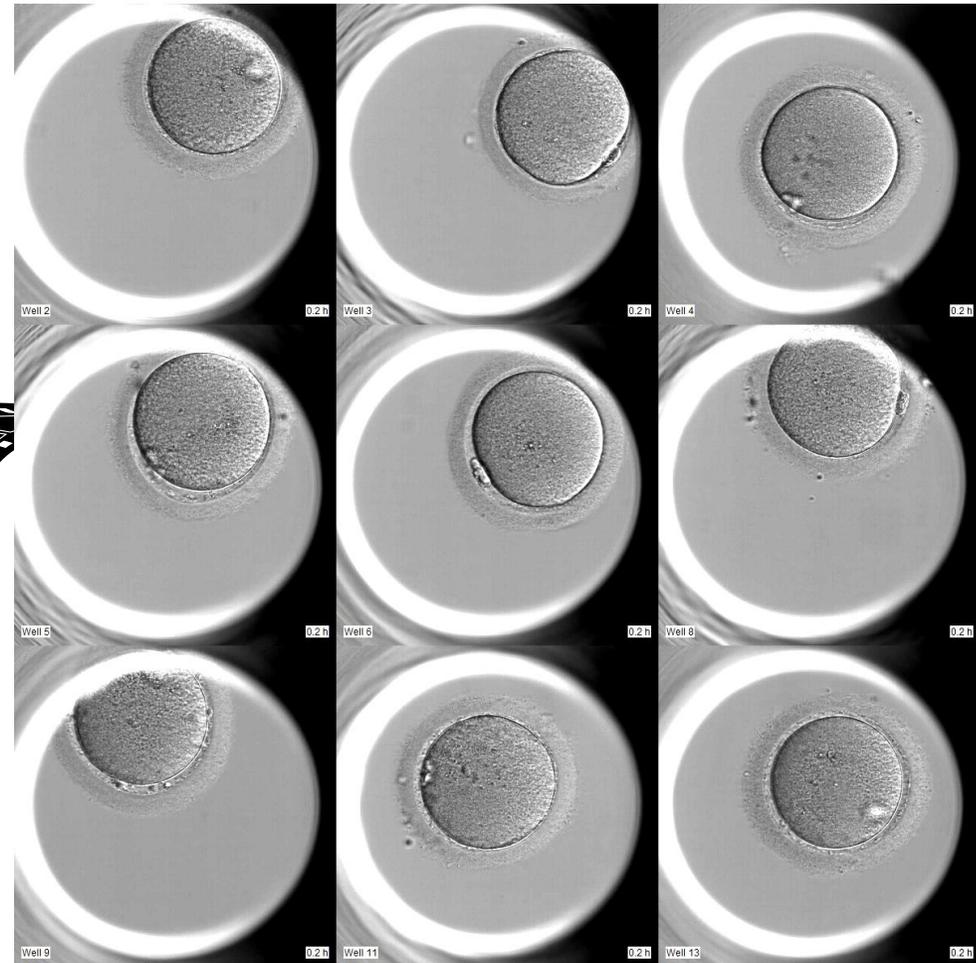
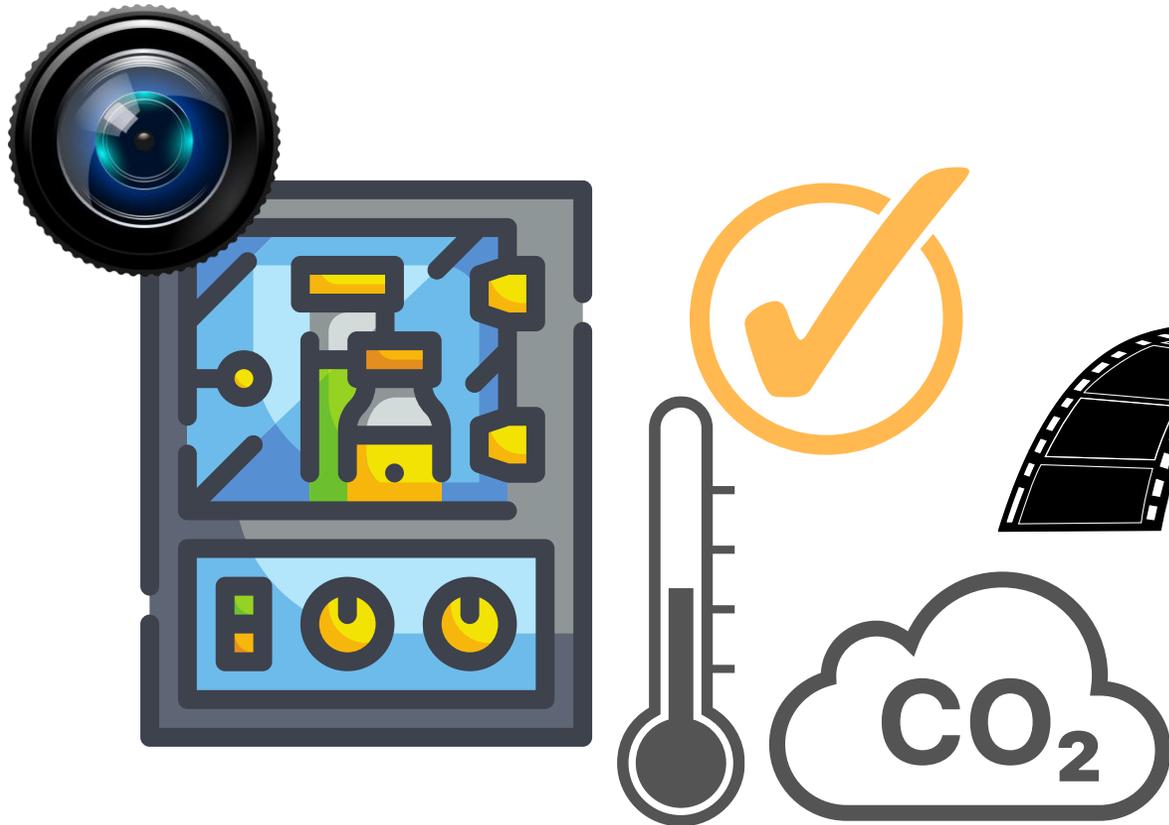
- ✓ Progesterone/progestins have been included in ovarian stimulation protocols
- ✓ Alternative to prevent the LH surge
- ✓ Advantages:
  - Oral treatment*
  - More control over LH serum levels*

**BENEFITS**



**LH**

# TIME-LAPSE IMAGING SYSTEM



# OBJECTIVE

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To investigate the impact of the use of progesterone to prevent the LH surge on embryo morphokinetics and on the outcomes of intracytoplasmic sperm injection (ICSI) cycles.

# MATERIAL AND METHODS

INTRODUCTION ✓

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# DESIGNE

Matched cohort study

March 2019 – March 2021

236 freeze-all ICSI cycles

2,768 injected oocytes

Matching:  
Female age

Progesterone-primed group  
118 cycles  
1,360 embryos

GnRH antagonist group  
118 cycles  
1,408 embryos



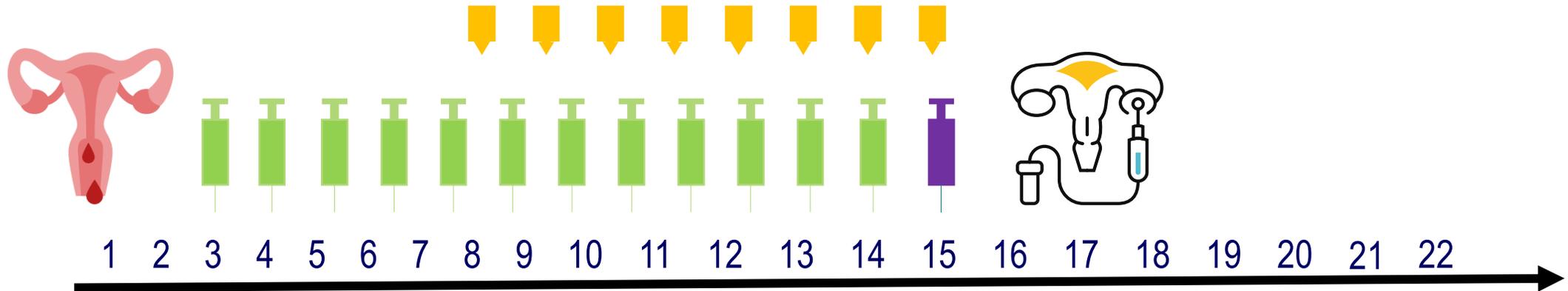
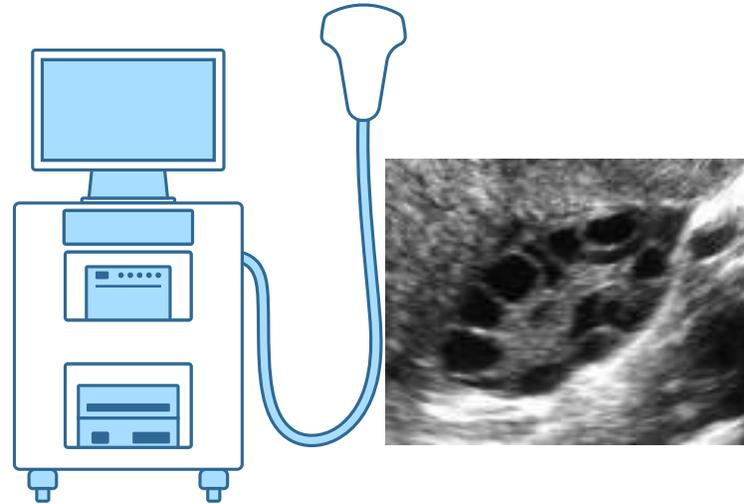
- ✓ Embryos were cultured in a TLI incubation system
- ✓ Morphokinetics and ICSI outcomes were compared between the groups

Using generalized linear models, followed by the Bonferroni post hoc test

# CONTROLLED OVARIAN STIMULATION - GNRH ANTAGONIST

GnRH antagonist

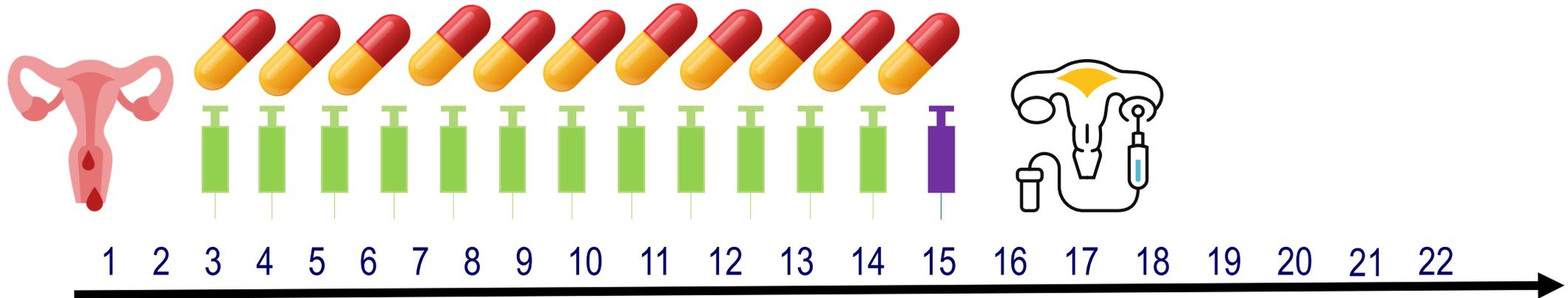
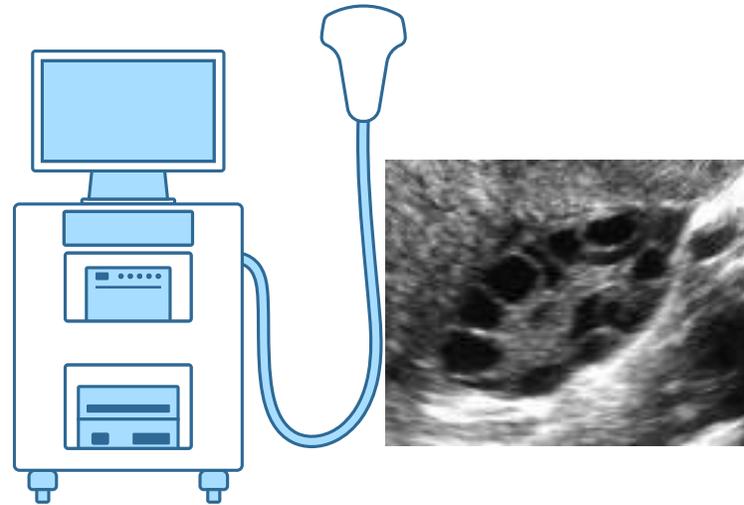
-  GnRH Antagonist
-  Recombinant FSH
-  Recombinant hCG



# CONTROLLED OVARIAN STIMULATION - GNRH ANTAGONIST

GnRH antagonist

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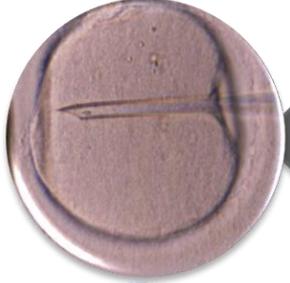


FERTILITY

# LABORATORY PROCEDURES



Incubation, denudation and nuclear maturation evaluation



Oocytes evaluated for morphology and ICSI performed according with Palermo et al (1992)



2-layered density gradient centrifugation



Embryo culture until day 5 (one or two blastocysts transferred)

# RESULTS

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## Comparison of demographic data between progestin-primed and the GnRH antagonist group

Variable		Progestin-primed	GnRH antagonist	p value
<b>Cycles</b>		118	118	
<b>Female age (years)</b>		36.7 ± 3.8	36.9 ± 5.5	0.452
<b>Male age (years)</b>		39.1 ± 6.4	38.2 ± 3.7	0.325
<b>Female BMI (kg/m<sup>2</sup>)</b>		23.5 ± 3.5	24.8 ± 3.3	0.145
<b>Total dose of FSH</b>	Follitropin alfa (UI)	2423.1 ± 1021.4	2563.5 ± 855.4	0.234
	Follitropin delta (µg)	149.4 ± 40.8.	151.3 ± 33.9	0.424

## Comparison of laboratory results between progestin-primed and the GnRH antagonist group

Variable	Progestin-primed	GnRH antagonist	p value
Aspirated follicles (n)	11.2 ± 1.2	12.7 ± 1.1	0.308
Retrieved oocytes (n)	8.2 ± 0.7	10.1 ± 0.9	0.136
Oocyte yield (%)	72.9 ± 2.3	75.7 ± 2.1	0.356
Mature oocytes (n)	6.1 ± 0.7	7.6 ± 0.6	0.135
Mature oocytes (%)	78.7 ± 2.3	73.6 ± 2.7	0.149
Fertilization (%)	70.9 ± 2.8	73.3 ± 3.2	0.573
Blastocyst formation (%)	50.3 ± 3.7	55.1 ± 4.4	0.402
Transferred embryos (n)	1.6 ± 0.6	1.5 ± 0.5	0.542

## Comparison of early morphokinetic parameters between the progestin-primed group and the GnRH antagonist group

Morphokinetic parameter (h)	Progestin-primed	GnRH antagonist	p value
Embryos	1360	1408	
tPNa	6.2 ± 0.2	7.0 ± 0.2	0.008
tPNf	24.3 ± 0.3	23.6 ± 0.2	0.142
t2	27.2 ± 0.3	26.2 ± 0.3	0.045
t3	37.5 ± 0.4	36.6 ± 0.3	0.130
t4	39.2 ± 0.4	38.8 ± 0.3	0.493
t5	50.1 ± 0.6	49.2 ± 0.5	0.316
t6	52.8 ± 0.6	52.5 ± 0.5	0.653
t7	56.4 ± 0.7	54.7 ± 0.5	0.046
t8	60.4 ± 0.8	58.7 ± 0.6	0.120

## Comparison of late morphokinetic parameters, cellular cycles and KidScore between the progestin-primed group and the GnRH antagonist group

Morphokinetic parameter (h)	Progestin-primed	GnRH antagonist	p value
Embryos	1360	1408	
tM	89.3 ± 0.8	87.1 ± 0.6	<b>0.045</b>
tSB	101.5 ± 0.8	110.8 ± 0.1	<b>0.012</b>
tB	111.0 ± 0.8	108.5 ± 0.7	<b>0.034</b>
s1	2.6 ± 0.0	2.7 ± 0.0	0.250
	1.9 ± 0.2	2.4 ± 0.2	0.172
s3	10.5 ± 0.6	10.1 ± 0.4	0.623
cc2	10.7 ± 0.2	10.3 ± 0.2	0.170
cc3	12.9 ± 0.4	12.7 ± 0.30	0.897
KIDScore	5.4 ± 0.0	5.9 ± 0.1	0.465

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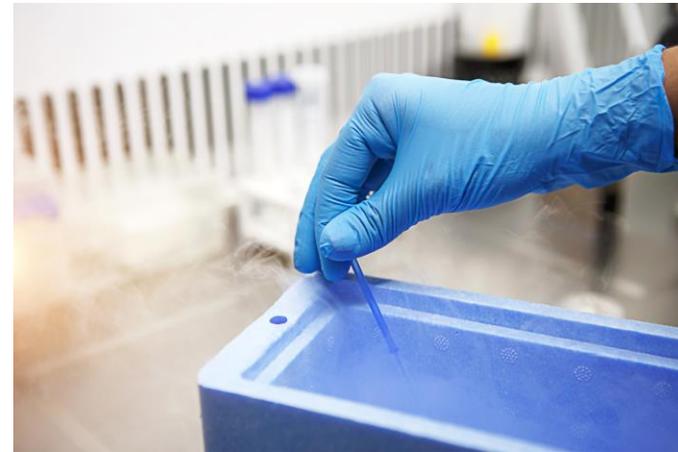
## Comparison of clinical outcomes between the progestin-primed and the GnRH antagonist group

Variable	Progestin-primed group	GnRH antagonist group	p value
Cycles	118	118	
Implantation rate (%)	64.6 ± 6.1	44.4 ± 6.3	<b>0.002</b>
Pregnancy rate (%)	64.4	49.0	0.104
Miscarriage rate (%)	2.6	8.6	0.554

# THE COST

✓ The expense for premature ovulation prevention using a GnRH antagonist was **U\$318.18**, while a total outlay of **U\$ 11.05** was sufficient to inhibit the premature LH surge during controlled ovarian stimulation using progestins

✓ However, the criopreservatin of all embryos cost ~ **U\$ 500.00**



✓ Therefore, even using progesting the Progestin + Freeze- all cycle would cost ~ **U\$ 200.00** more than the GnRH antagonist + fresh cycle



# CONCLUSION

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✓ Exogenous progesterone replaces the use of a GnRH antagonist for prevention of premature LH surge, with the advantages of oral administration and potential cost reduction.

✓ However, when there is no indication to freeze-all (no PGT, fertility preservation or cycles at high OHSS risk), the use of progestin may not be economically worthwhile.

✓ Moreover, delayed embryo transfer due to the freeze-only approach may be inconvenient for some patients.

✓ Therefore, before considering a protocol for preventing premature LH surge and ovulation in an IVF program, the pros and cons must be carefully evaluated.

**Gracias!**

**Obrigado!**

Dr. Edson Borges Jr.

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