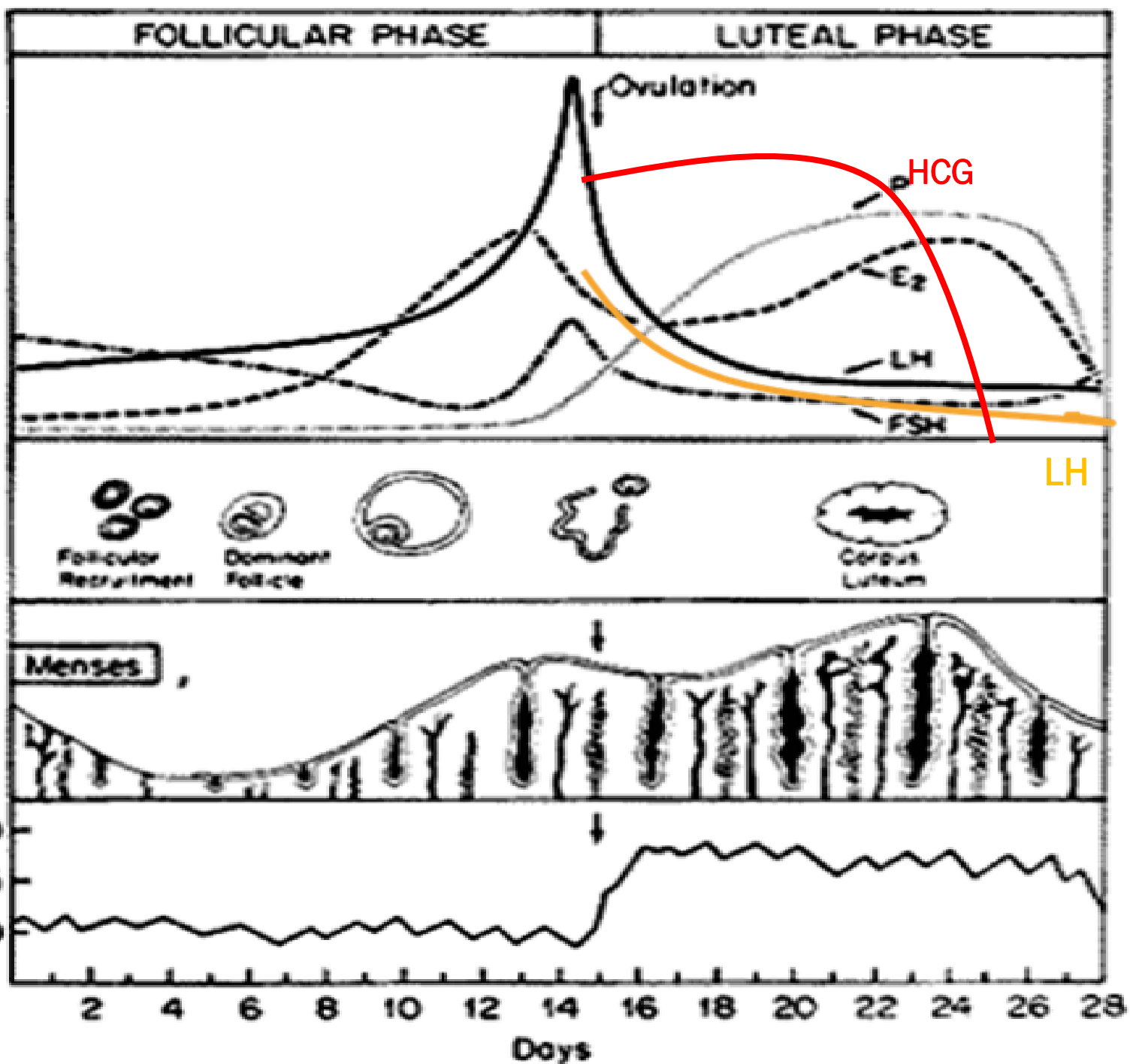


**A NOVEL METHOD OF LUTEAL
SUPPLEMENTATION WITH
RECOMBINANT LH,
WHEN A GNRH-AGONIST IS USED INSTEAD
OF HCG FOR OVULATION TRIGGERING.**

Papanikolaou EG, MD, PhD

Assisted Reproduction Unit “BIOGENESIS”

Thessaloniki, Greece



Endocrine
Cycle

Ovarian
Histology

Endometrial
Histology

Body
Temperature
(°C)

FOLLICULAR PHASE

LUTEAL PHASE

Ovulation

HCG

E₂

LH

FSH

LH

Follicular
Recruitment

Dominant
Follicle

Corpus
Luteum

Menses

37.0
36.5
36.0

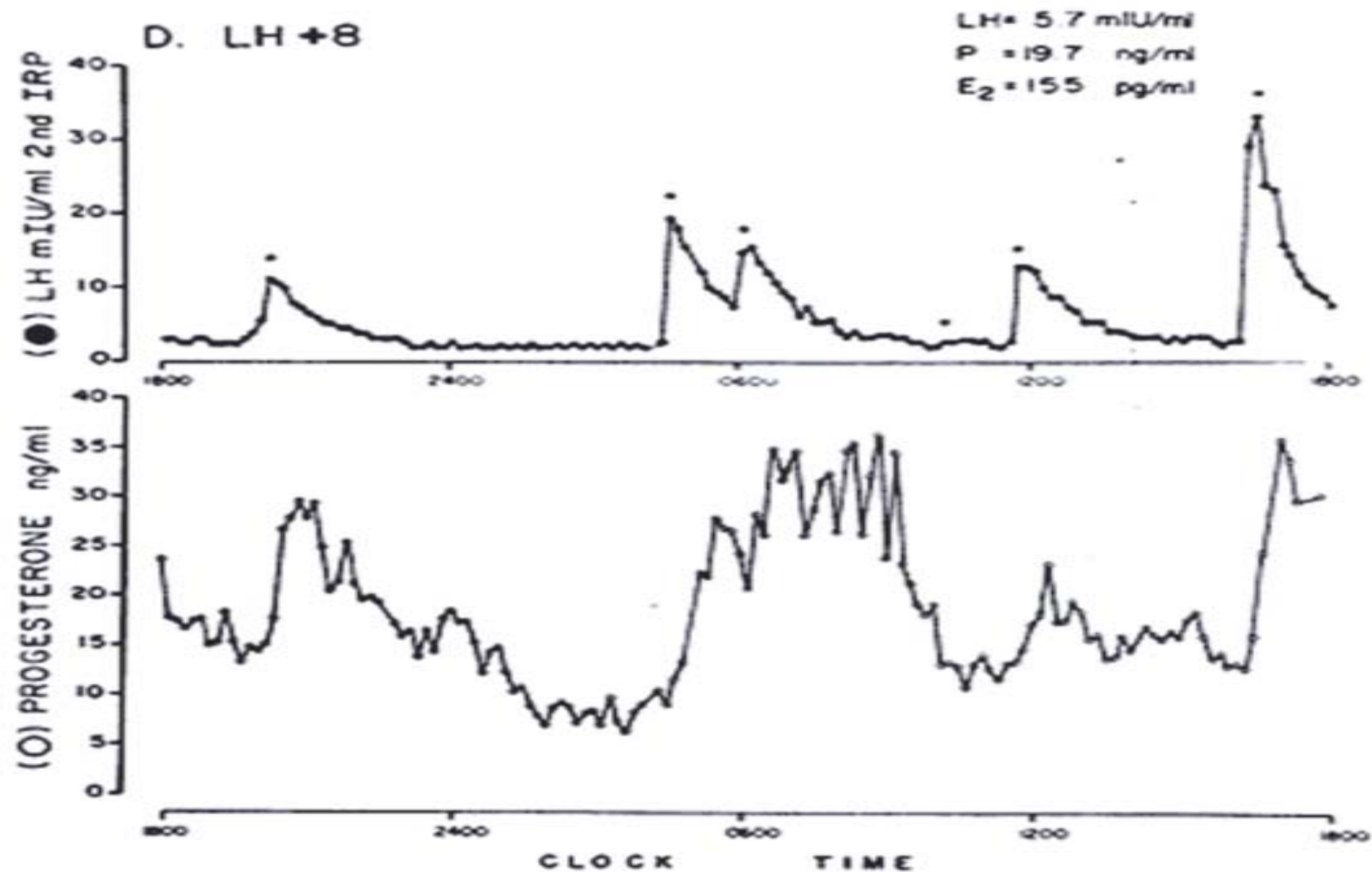
2 4 6 8 10 12 14 16 18 20 22 24 26 28

Days

Episodic secretion of LH (top) and progesterone (bottom) during the luteal phase of a woman.

From Filicori M, Butler JP, Crowley WF Jr. Neuroendocrine regulation of the corpus luteum in the human. J

Clin Invest. 73:1638 1984



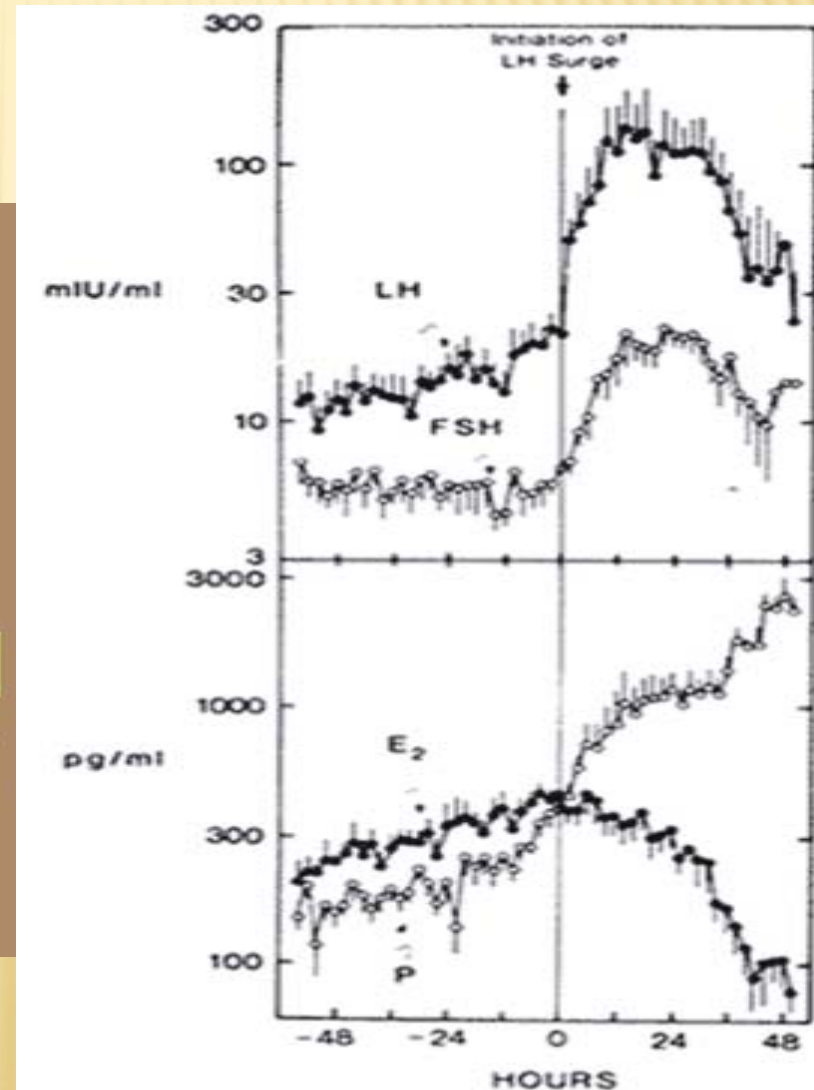
NUMBER (24 hr)	PERIODICITY (min)	AMPLITUDE (mIU/ml/min)	HALF-DURATIONS (min)	LH HALF-LIFE (min)	TOTAL DAILY SECRETION (mIU/ml/24 hr)
Early follicular 175±1.4a	80 ± 3a	0.43 ± 0.02a	6.5 ± 1.0a	131 ± 13a	49 ± 6a
Late follicular 26.9±1.6b	53 ± 1b	0.70 ± 0.03b	3.5 ± 0.9b	128 ± 12a	56 ± 8a
Midluteal 10.1±1.0c	177 ± 15 [#]	0.26 ± 0.02 ^{c#}	11.0 ± 1.1e	103 ± 7a	52 ± 4a

From Carr BR, Wilson JD. Disorders of the ovary and female reproductive tract.
In: Braunwald E, Isselbacher KJ, Petersdorf RG, et al, eds.

Harrison's Principles of Internal Medicine. 11th ed. New York: McGraw-Hill, 1987: 1818-1837.

CHANGES IN GONADOTROPINS AND OVARIAN STEROIDS AT MIDCYCLE, JUST PRIOR TO OVULATION. THE INITIATION OF LH SURGE IS AT TIME 0

HOFF JD, QUIGLEY ME, YEN SCC. HORMONAL DYNAMICS AT MIDCYCLE: A RE-EVALUATION. J CLIN ENDOCRINOL METAB. 57:792, 1983



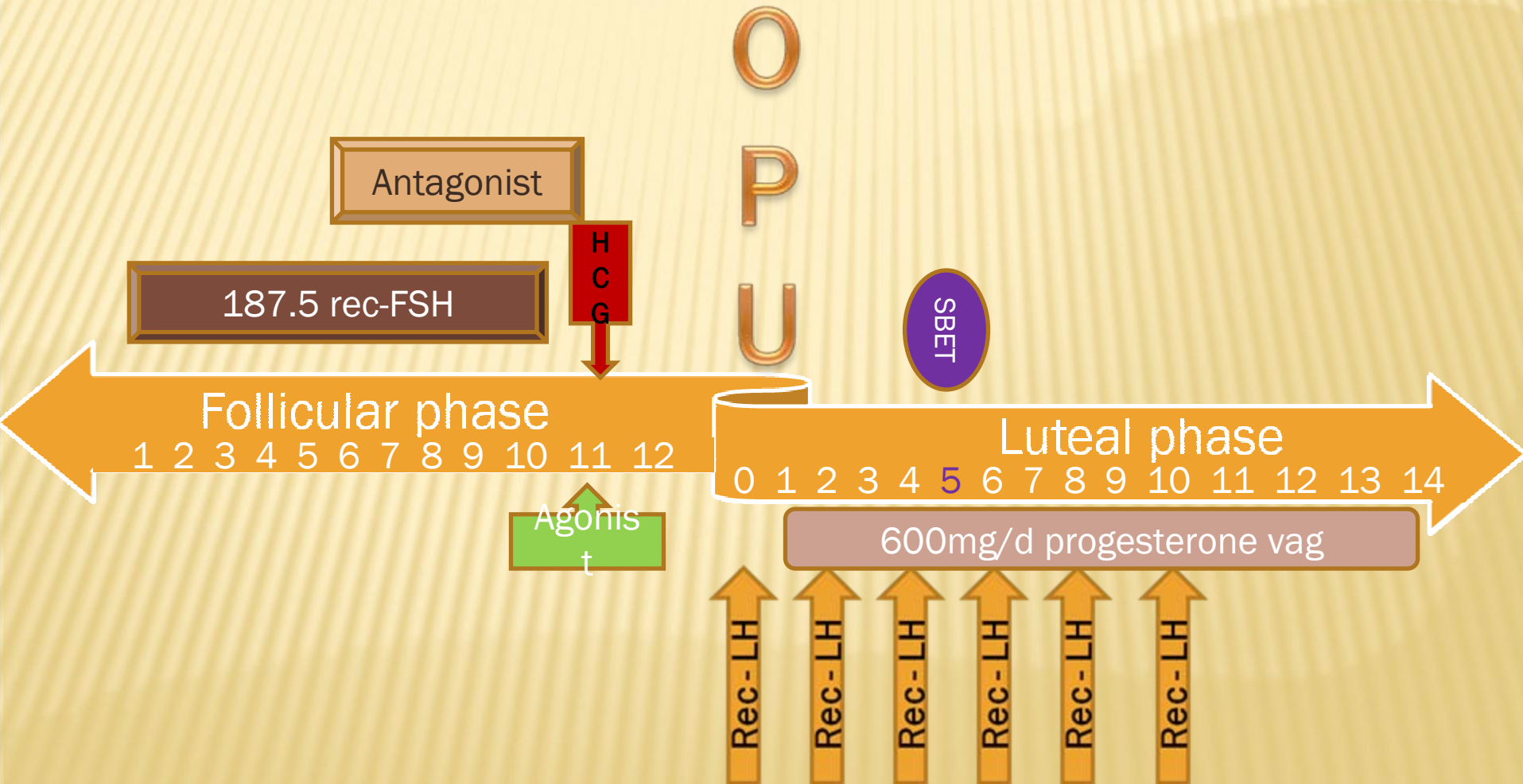
STUDY DESIGN

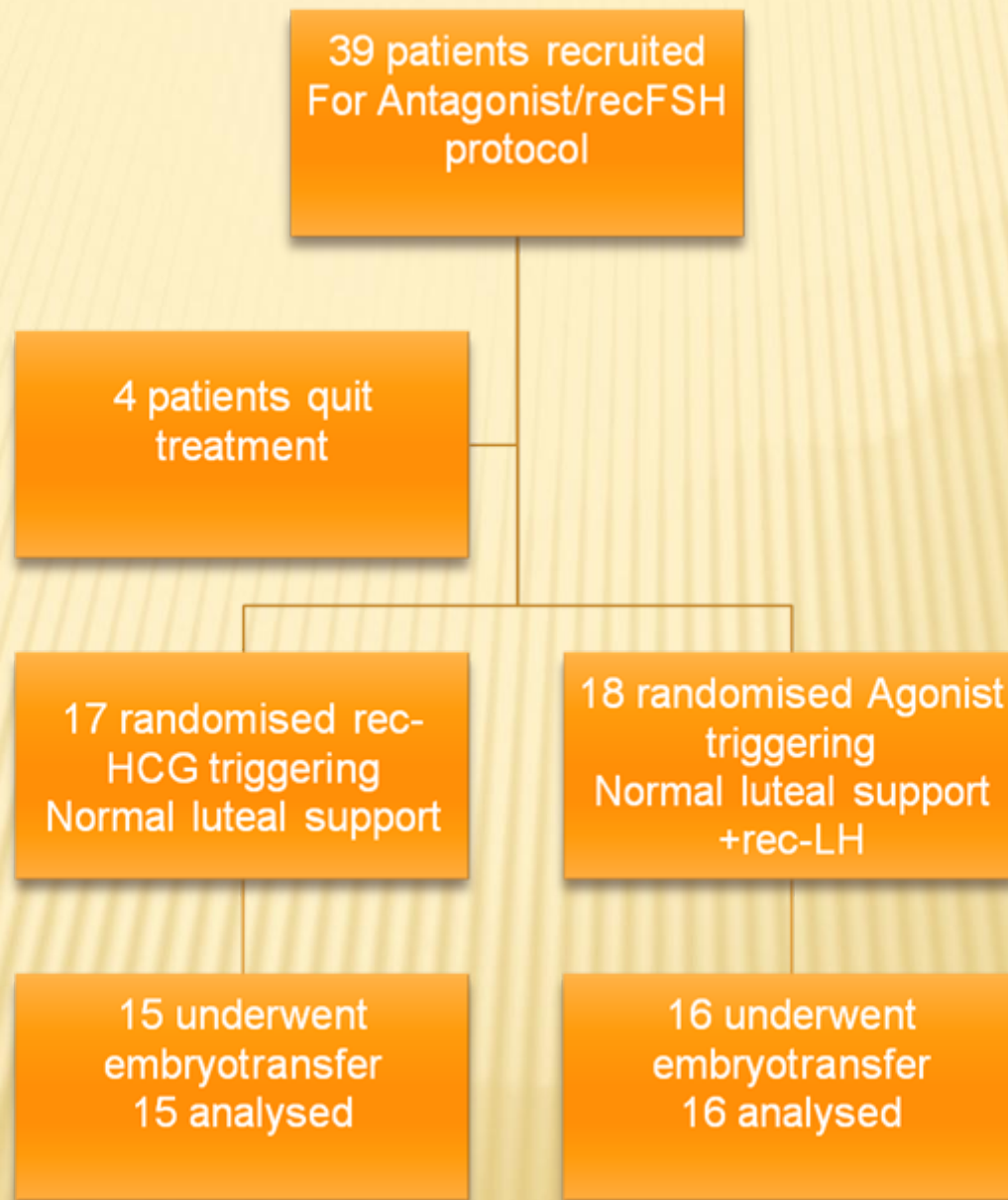
- × Prospective RCT
- × August 2005 to December 2007
- × Age less than 36 years,
- × FSH <12 mIU/ml
- × Antagonist day-6 protocol
- × Starting gonadotrophin dose fixed for five days and ranged 187.5 IU
- × 1st or 2nd IVF cycles.
- × Exclusion criteria were: (a) known endocrine disorder, (b) endometriosis stage III and IV, (c) PCO and (d) stimulation could not initiate if progesterone was higher than 1.5 ng/mL and estradiol higher than 80 pg/ml.

STUDY DESIGN

- ✘ Primary outcome was the clinical pregnancy/implantation rate
- ✘ Secondary outcome was the incidence of OHSS

PROTOCOL





RESULTS

	Standard protocol rec-HCG triggering (n=17)	Luteal rec-LH protocol Agonist triggering (n=18)	Statistics
Age (mean \pm SEM)	30.6 \pm 0.7	30.1 \pm 0.7	0.12
Days of stimulation	9.6 \pm 0.9	9.6 \pm 1.0	0.9
Total FSH dose (IU)	1767.7 + 187	1808 \pm 209	0.5
COCs retrieved	13.8 \pm 0.4	11.7 \pm 0.5	0.3
2PN embryos	8.3 \pm 0.9	7.9 \pm 1.0	0.08
Blastocyst transferred	1	1	
Embryos cryopreserved	1.2 \pm 0.6	1.4 \pm 0.8	0.8
OHSS occurrence	0	0	0.8

Pregnancy rates per protocol analysis

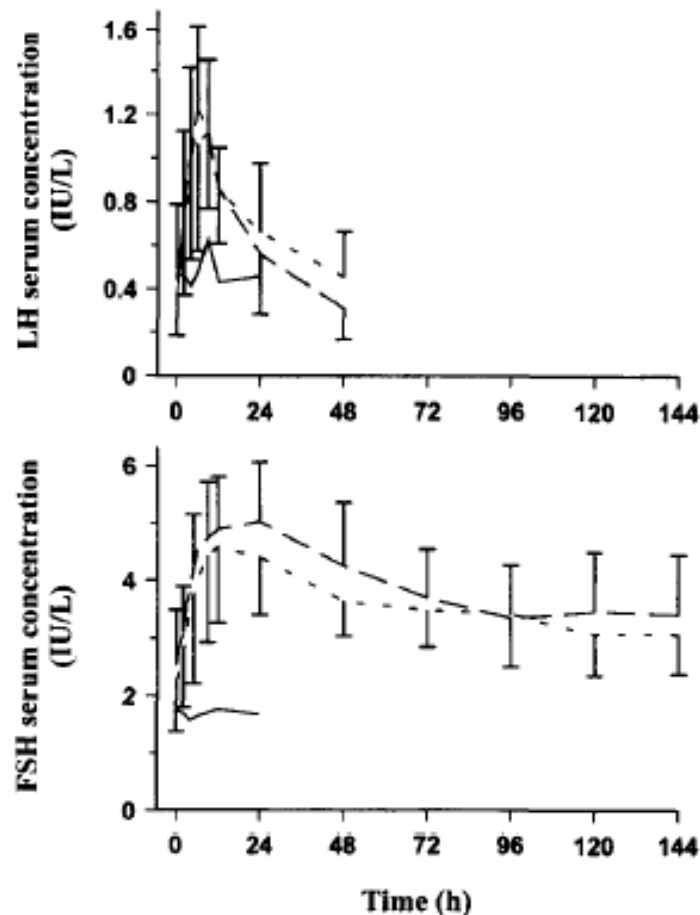
	Standard (n=15)	Rec-LH luteal (n=16)
Positive HCG test rate	40.0% (6)	31.3% (5)
Clinical/Implantation rate	26.7% (4)	25.0% (4)

TABLE 4. Summary of treatment results

Treatment arm Parameters examined	5,000 IU		15,000 IU		30,000 IU		15,000 + 10,000 IU		P (linearity)
	rhLH (n = 39)	u-hCG (n = 34)	rhLH (n = 39)	u-hCG (n = 41)	rhLH (n = 26)	u-hCG (n = 22)	rhLH (n = 25)	u-hCG (n = 24)	
No. of follicles >10 mm	14.03 ± 5.32	16.44 ± 6.95	15.17 ± 8.34	15.46 ± 6.75	14.23 ± 5.61	14.00 ± 4.90	°	°	0.3007
No. of oocytes retrieved	10.23 ± 4.70	11.74 ± 6.27	11.84 ± 7.53	11.78 ± 6.75	12.62 ± 6.22	10.82 ± 5.70	°	°	0.1702
Oocytes in metaphase II	85.5%	77.8%	90.8%	88.6%	57.6%	84.5%	°	°	0.183
No. of oocytes inseminated	9.82 ± 4.74	11.26 ± 5.73	11.63 ± 7.52	11.57 ± 6.57	12.38 ± 6.25	10.55 ± 5.74	°	°	0.1687
No. of embryos	5.42 ± 3.33	7.00 ± 4.68	6.65 ± 5.02	6.36 ± 4.68	7.67 ± 4.34	6.33 ± 5.19	°	°	0.0983
No. of embryos transferred	2.39 ± 0.60	2.48 ± 0.85	2.58 ± 0.65	2.52 ± 0.62	2.78 ± 0.80	2.67 ± 0.73	°	°	0.4310
Implantation rate	6.0 ± 0.16%	15.0 ± 0.31%	6.0 ± 0.19%	9.0 ± 0.24%	11.0 ± 0.26%	3.0 ± 0.09%	19.0 ± 0.33%	17.0 ± 0.33%	0.1373
Pregnancy (total)	15.4% (n = 6)	26.5% (n = 9)	10.3% (n = 4)	24.4% (n = 10)	23.1% (n = 6)	13.6% (n = 3)	32.0% (n = 8)	37.5% (n = 9)	0.2689
Clinical pregnancy	10.3% (n = 4)	23.5% (n = 8)	7.7% (n = 3)	14.6% (n = 6)	15.4% (n = 4)	13.6% (n = 3)	28.0% (n = 7)	25.0% (n = 6)	0.1479
Live birth	5.1% (n = 2)	17.6% (n = 6)	7.7% (n = 3)	12.2% (n = 5)	15.4% (n = 4)	4.5% (n = 1)	20.0% (n = 5)	16.7% (n = 4)	0.0606
Cryopreserved embryos	4.42 ± 2.65	6.81 ± 3.67	7.93 ± 4.18	4.90 ± 3.24	6.27 ± 2.96	4.80 ± 3.19	5.75 ± 2.49	9.89 ± 3.22	0.2645
Cryopreserved embryos transferred	3.42 ± 1.83	5.67 ± 2.65	3.50 ± 1.84	3.27 ± 1.49	3.00 ± 1.41	2.17 ± 0.98	2.50 ± 0.71	4.75 ± 2.43	0.9092
Pregnancy from cryopreserved embryos (total)	16.7% (n = 2/12)	0.0% (n = 0/9)	50.0% (n = 5/10)	27.3% (n = 3/11)	62.5% (n = 5/8)	33.3% (n = 2/6)	0.0% (n = 0/2)	0.0% (n = 0/8)	°
Clinical pregnancy from cryopreserved embryos	8.3% (n = 1/12)	0.0% (n = 0/9)	40.0% (n = 4/10)	27.3% (n = 3/11)	50.0% (n = 4/8)	16.7% (n = 1/6)	0.0% (n = 0/2)	0.0% (n = 0/8)	°
Live birth from cryopreserved embryos	8.3% (n = 1/12)	0.0% (n = 0/9)	30.0% (n = 3/10)	18.2% (n = 2/11)	12.5% (n = 1/8)	0.0% (n = 0/6)	0.0% (n = 0/2)	0.0% (n = 0/8)	°

DOSE OF REC-LH TO BE DEFINED

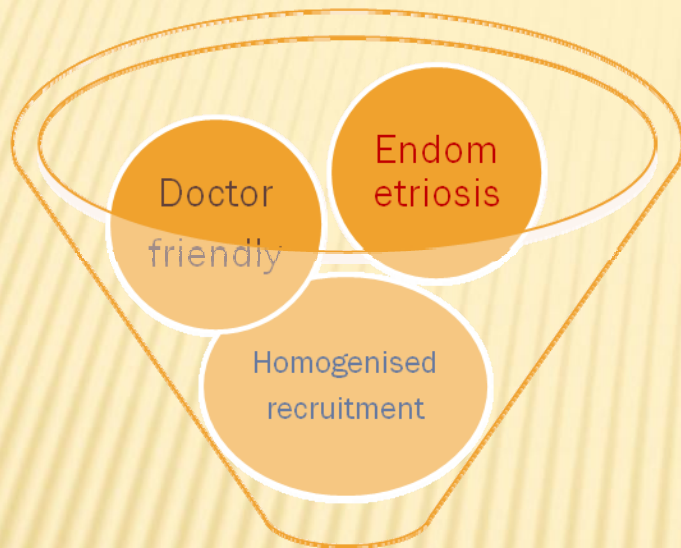
Concentrations of LH (**top**) and FSH (**bottom**) versus time during 24-hour baseline assessment (solid line) and after single SC administration of 150 IU of LH or FSH, respectively, either alone (long dashed line) or in combination (short dashed line); mean \pm 1 SD, 12 subjects (for purpose of clarity, not all error bars are displayed).



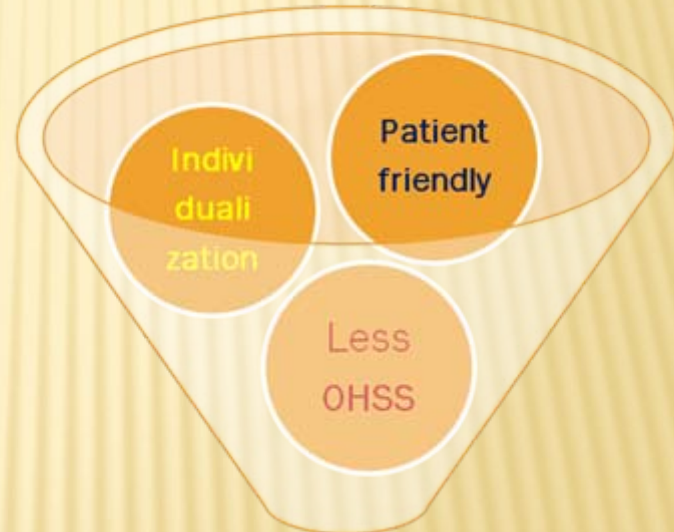
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- ✘ *P. Devroey, MD, PhD¹*
 - ✘ *W. Verpoest, MD¹,*
 - ✘ *H. Fatemi, MD, PhD¹,*
 - ✘ *Tarlatzis B, MD, PhD²,*
 - ✘ *H. Tournaye, MD, PhD¹.*

- ✘ Centre for Reproductive Medicine, Universitair Ziekenhuis Brussel, Vrije Universiteit Brussel, Laarbeeklaan101, 1090 Brussels, Belgium

SYNOPSIS



↓
Agonist



↓
Antagonist