



THE CROWN
is the property of the
Cathedral of Monza

1ST EUROPEAN CONGRESS ON IN VITRO MATURATION OF HUMAN OOCYTES IN ASSISTED REPRODUCTION

The Role of Different Priming in In-Vitro Maturation

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“BIOGENESI”

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Istituti Clinici Zucchi, Monza-Italy**

IVF and IVM

Risks

Efficiency

EFFICIENCY IVM vs. IVF

- **Lower Pregnancy Rate**
- **Lower Implantation Rate**

EFFICIENCY of IVM

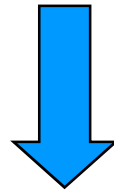
Pregnancy Rate

☹ **In the late 90s** **2-4 %**

☺ **Currently** **30-35 %**

EFFICIENCY OF IVM

Competent Oocytes
Competent Embryos



Pregnancy and Implantation Rates

Healthy Babies

IVM STARTING ISSUES

- **Selection of Women**
- **Timing of the Procedure**

IMPROVE THE RESULTS

- **Culture Conditions**
- **Gonadotrophin Priming**

GONADOTROPHIN PRIMING

In order to:

- **Increase the number of oocytes**
- **Optimize the oocyte maturation**
- **Enhance the competence of embryos**

BACKGROUND IN USING GONADOTROPHIN PRIMING

PCO/PCOS

FSH Priming

Mikkelsen AL et al. HR 2001

Lin YH et al. HR 2003

hCG Priming

Chian RC et al. FS 1999

Chian RC et al. HR 2000

NORMAL OVARIES

FSH Priming

Wynn P et al. HR 1998

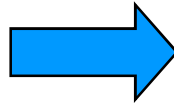
Trounson A et al. HR 1998

Mikkelsen AL et al. HR 1999

GONADOTROPHIN PRIMING IN PCO-PCOS WOMEN

FSH Priming

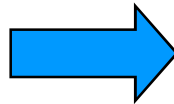
Mikkelsen AL et al. 2001



Efficient in increasing

- Maturation rate
- Pregnancy rate

Lin YH et al. 2003

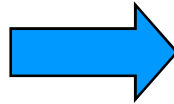


Inefficient in modifying
any Outcomes

GONADOTROPHIN PRIMING IN PCO-PCOS WOMEN

FSH Priming

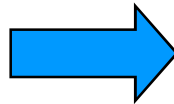
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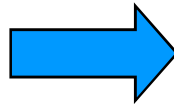


Inefficient in modifying
any Outcomes

hCG Priming

Chian RC et al. 1999

Chian RC et al. 2000



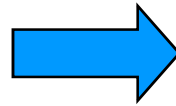
- Efficient in harvesting
Oocyte Maturation
- No effect on Pregnancy

GONADOTROPHIN PRIMING

IN WOMEN WITH NORMAL OVARIES

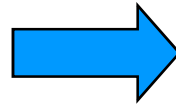
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**Efficient in harvesting
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Trounson A et al. 1998



**Inefficient in modifying
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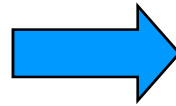
Mikkelsen AL et al. 2001

GONADOTROPHIN PRIMING

IN WOMEN WITH NORMAL OVARIES

FSH Priming

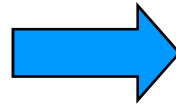
Wynn P et al. 1998



**Efficient in harvesting
Oocyte Maturation**

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**Inefficient in modifying
any Outcomes**

hCG Priming

No studies available

GONADOTROPHIN PRIMING

MAIN PROTOCOLS

PCO/PCOS

FSH Priming

**Original
Danish protocol**

hCG Priming

**Current
McGill Protocol**

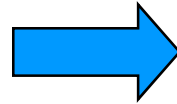
NORMAL OVARIES

**Infrequently
Eligible for IVM**

No Priming ?

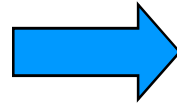
ROLE OF GONADOTROPHIN PRIMING IN IN-VITRO MATURATION

FSH Priming



**Nothing Certain
or Useless**

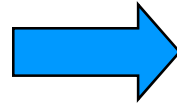
hCG Priming



**Increase Oocyte
Maturation**

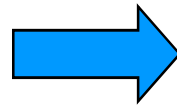
ROLE OF GONADOTROPHIN PRIMING IN IN-VITRO MATURATION

FSH Priming



**Nothing Certain
or Useless**

hCG Priming



**Increase Oocyte
Maturation**

**Can these statements
endorse any choice ?**

ROLE OF GONADOTROPHIN PRIMING IN IN-VITRO MATURATION

**We are still far from comprehending
the role of priming in IVM.
The subject is still
OPEN**

We needed a new study

CLINICAL EXPERIENCE

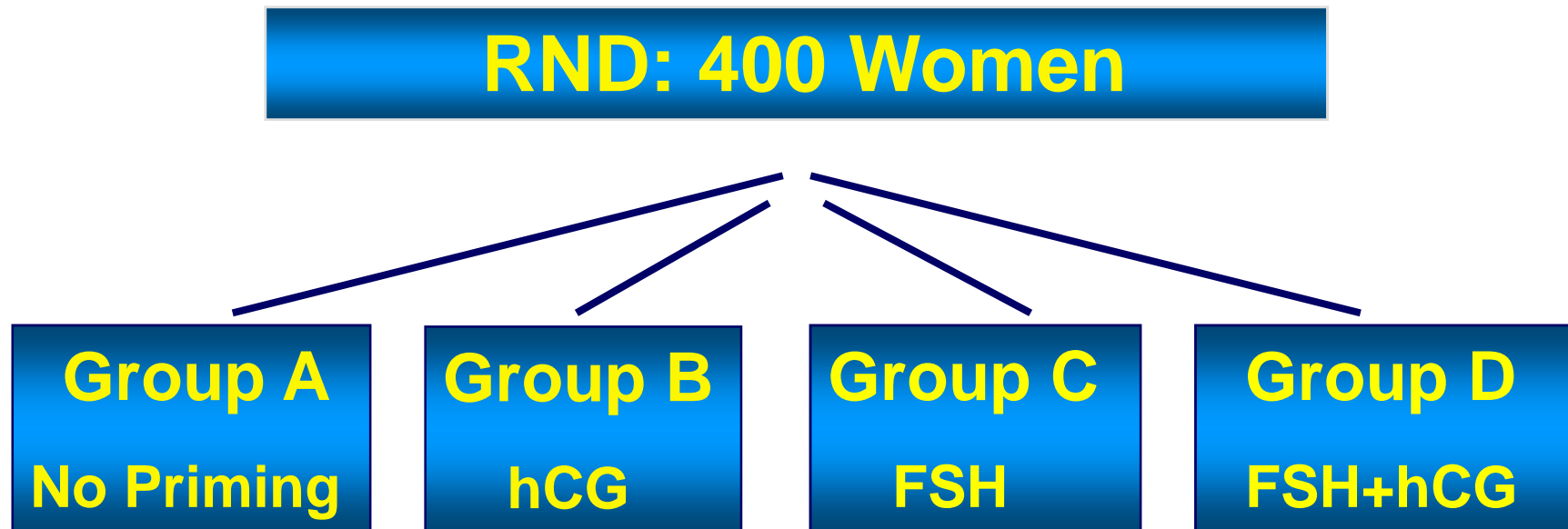
MAY 2006 – JUNE 2008

THE EFFECT OF DIFFERENT GONADOTROPHIN PRIMING IN WOMEN WITH NORMAL OVARIES: A PROSPECTIVE RANDOMIZED STUDY



Fadini R. et al.
In Press RBMO

GONADOTROPHIN PRIMING STUDY IN NORMAL WORKING OVARIES



CRITERIA OF INCLUSION

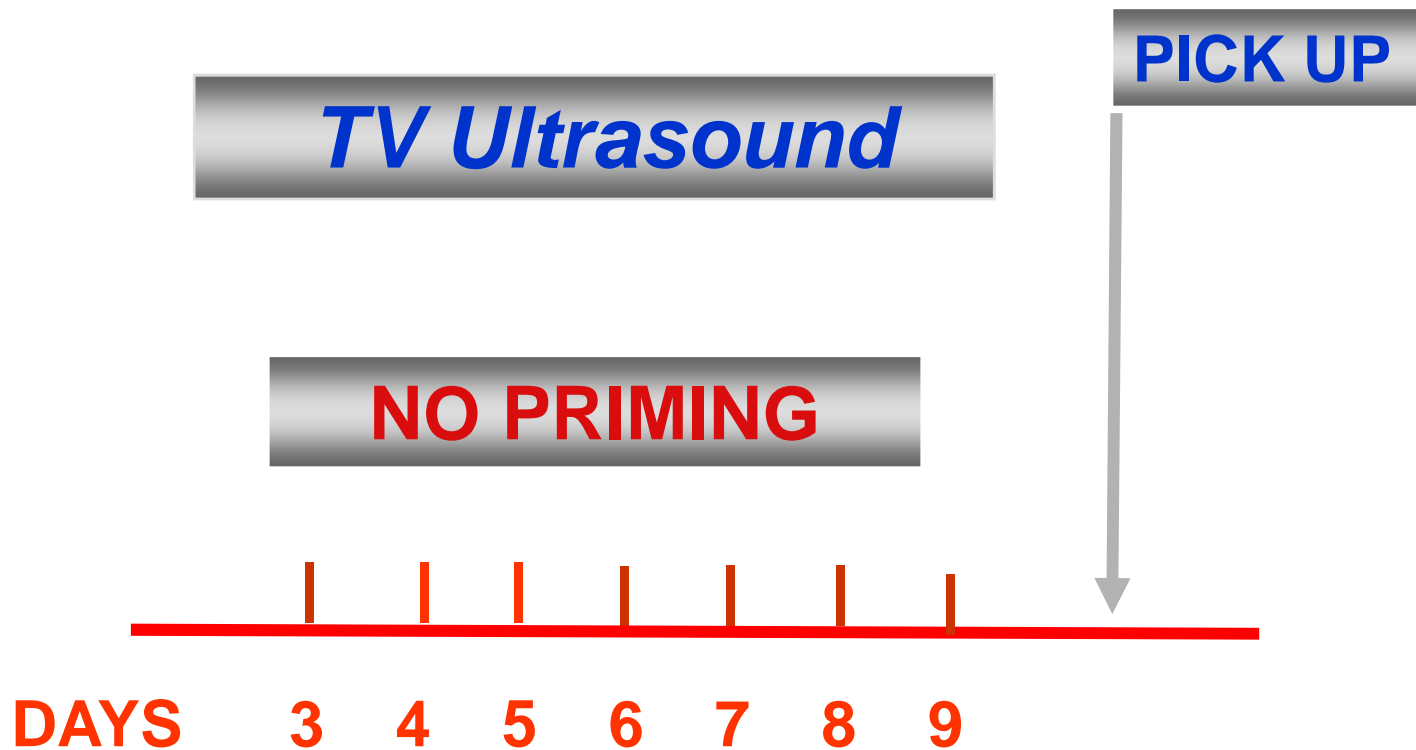
Inclusion Criteria

- Age < 38 years
- Cycle: 24-35 days

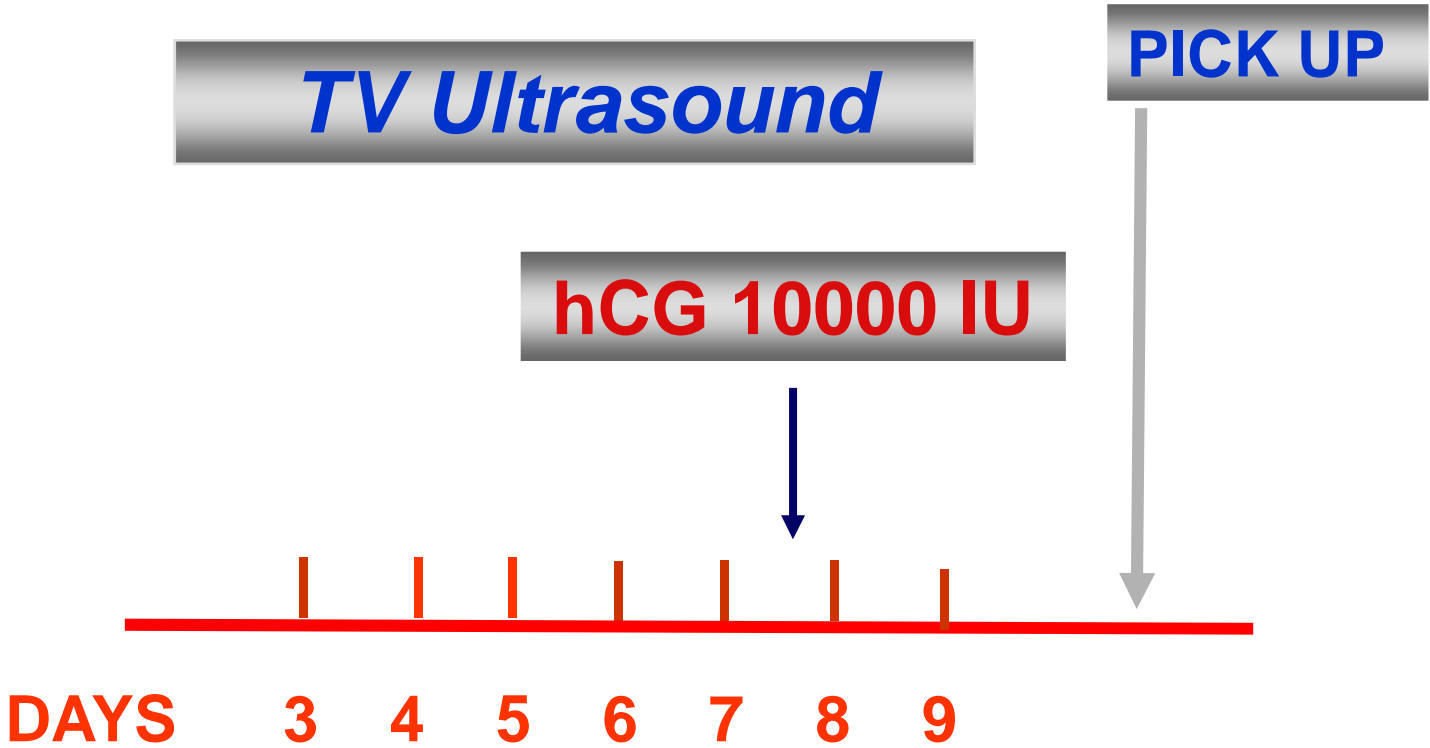
Exclusion Criteria

- FSH Basal Levels ≥ 10 mIU/ml
- PCO or PCOS
- Endocrine Abnormalities

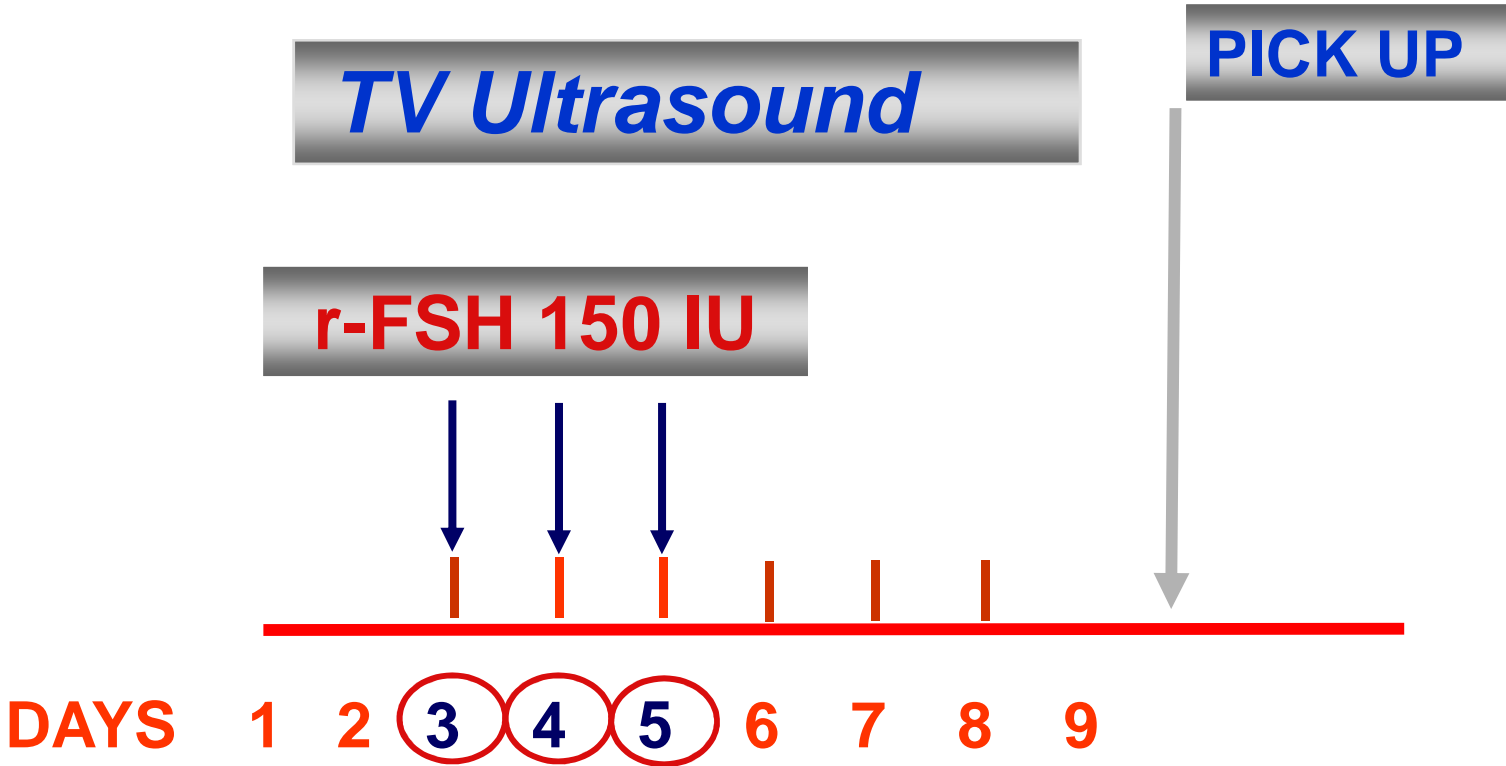
PROTOCOL: Group A



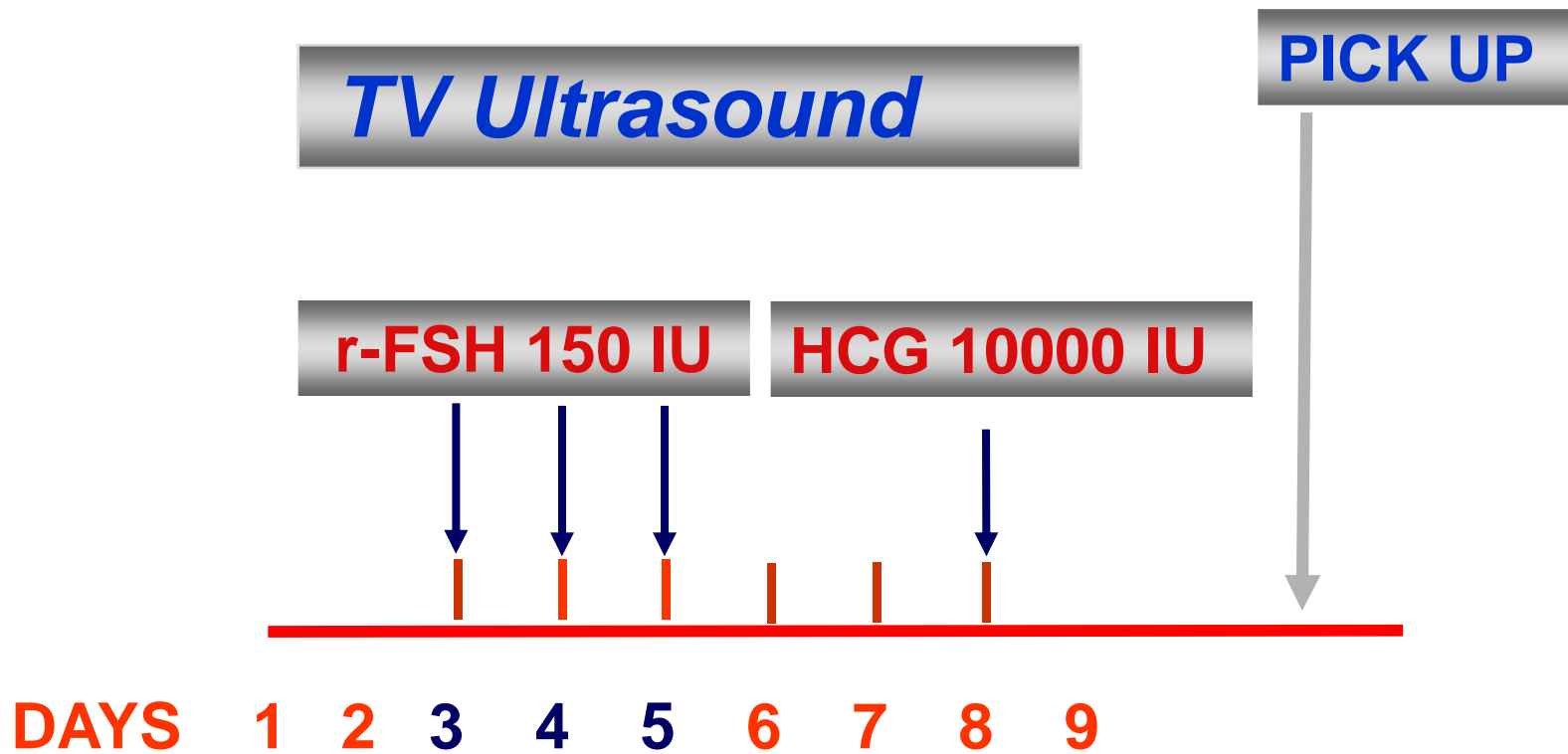
PROTOCOL: Group B



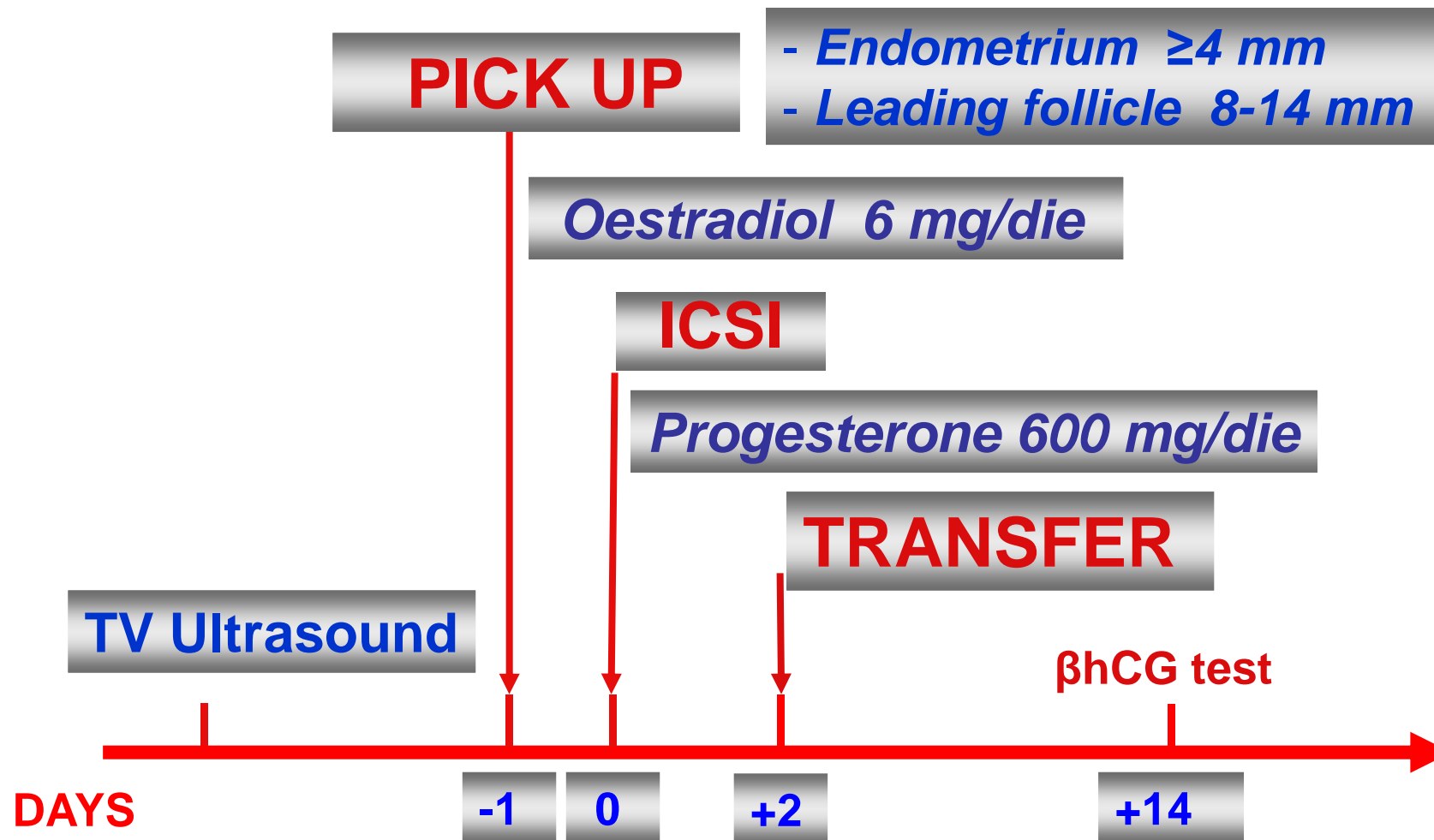
PROTOCOL: Group C



PROTOCOL: Group D



PROTOCOL



SUBJECT FEATURES

	TOT Mean±SD	NO Priming	HCG Priming	FSH Priming	FSH+hCG Priming
Age	33.2±3.1	33.1±2.9	33.1±4.3	33.1±4.3	33.6.5±2.6
BMI	21.8±2.9	21.9±2.8	21.6±2.6	22.1±3.2	21.5±3
E2	35.9±14.2	35.1±14.4	32.2±14.2	37.7±15.3	37.0±13.8
FSH	6.1±1.5	6±1.6	6.1±1.3	6.2±1.4	6.1±1.5
AFC	8.8±3.7	8.8±3.3	8.9±4.1	9±3.9	8.4±3.7

No difference among the groups

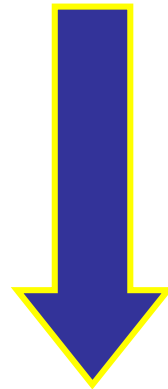
EMBRYO TRANSFER RATE

(EFFICIENCY IN COMPLETING THE PROCEDURE)



EMBRYO TRANSFER RATE (EFFICIENCY IN COMPLETING THE PROCEDURE)

379 Oocytes Collection



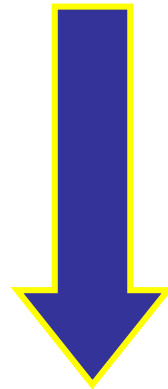
No Oocytes
No Maturation
No available Embryos

300 Embryo Transfers

	TOT	NO Priming	hCG Priming	FSH Priming	FSH+hCG Priming
ET/Rate	79 %	77 %			

EMBRYO TRANSFER RATE (EFFICIENCY IN COMPLETING THE PROCEDURE)

379 Oocytes Collection



**No Oocytes
No Maturation
No available Embryos**

300 Embryo Transfers

	TOT	NO Priming	hCG Priming	FSH Priming	FSH+hCG Priming
ET/Rate	79 %	77 %	70 %	79 %	88 %

OOCYTES COLLECTED

Mean Oocytes per Women	TOT	NO Priming	hCG Priming	FSH Priming	FSH+hCG Priming
MEAN±SD	5.2±2.8	5.3±4.2	5.3±4.1	4.8±3.4	5.4±3.5

No significant difference among the groups

MII (READY) OOCYTES COLLECTED

	TOT	NO Priming	hCG Priming	FSH Priming	FSH+hCG Priming
MII Collected	137	0	28	0	109
Collection Rate	6.8 %	0	5.6 %	0	20.3 %

MII (READY) OOCYTES COLLECTED

	TOT	NO Priming	hCG Priming	FSH Priming	FSH+hCG Priming
MII Collected	137	0	28	0	109
Collection Rate	6.8 %	0	5.6 %	0	20.3 %

MII OOCYTES IN-VITRO MATURED

	TOT	NO Priming	hCG Priming	FSH Priming	FSH+hCG Priming
Immature oocytes	1796	477	442	461	416
Maturation Rate	58.0 %	48.4 %			

MII OOCYTES IN-VITRO MATURED

	TOT	NO Priming	hCG Priming	FSH Priming	FSH+hCG Priming
Immature oocytes	1796	477	442	461	416
Maturation Rate	58.0 %	48.4 %	57.9 %	50.7 %	77.4 %

TOTAL MII OOCYTES AVAILABLE

	TOT	NO Priming	hCG Priming	FSH Priming	FSH+hCG Priming
MII Collected %	137 6.8 %	0	28 5.6 %	0	109 20.3 %
+					
Maturation Rate	58 %	48.4 %	57.9 %	50.7 %	77.4 %
=					
Total MII Available Percentage	1180/1796 65.7 %	231/477 48.4	284/470 60.4 %	234/461 50.7 %	431/525 82.0 %

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COMMENTS ON BIOLOGICAL OUTCOMES

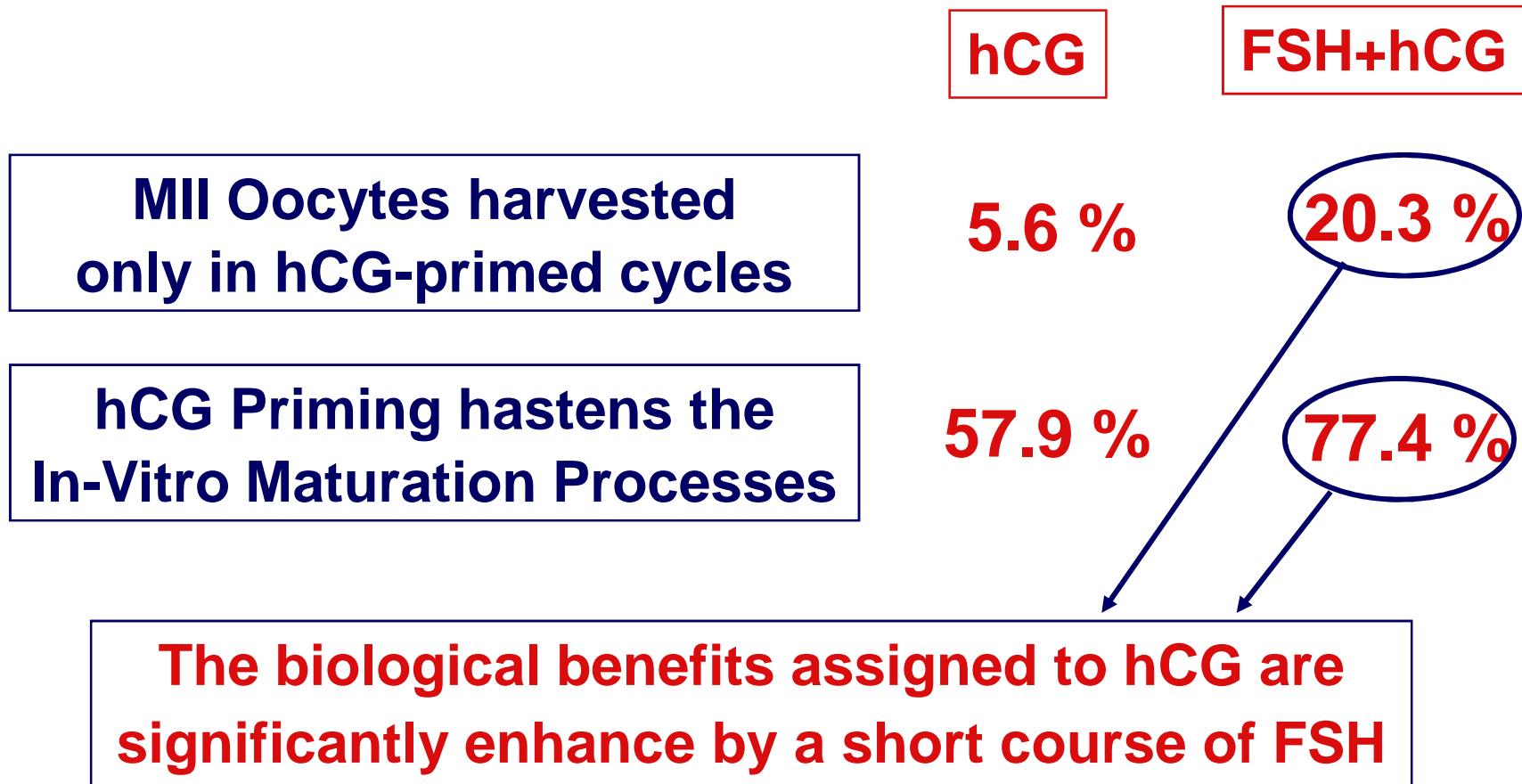
**MII Oocytes harvested
only in hCG-primed cycles**

**hCG Priming hastens the
In-Vitro Maturation Processes**

COMMENTS ON BIOLOGICAL OUTCOMES

	hCG	FSH+hCG
MII Oocytes harvested only in hCG-primed cycles	5.6 %	20.3 %
hCG Priming hastens the In-Vitro Maturation Processes	57.9 %	77.4 %

COMMENTS ON BIOLOGICAL OUTCOMES

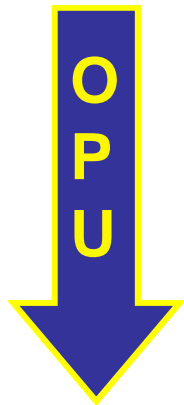


SHORT DIAGRESSION ...

**REMARKS ON
BIOLOGICAL RESULTS**

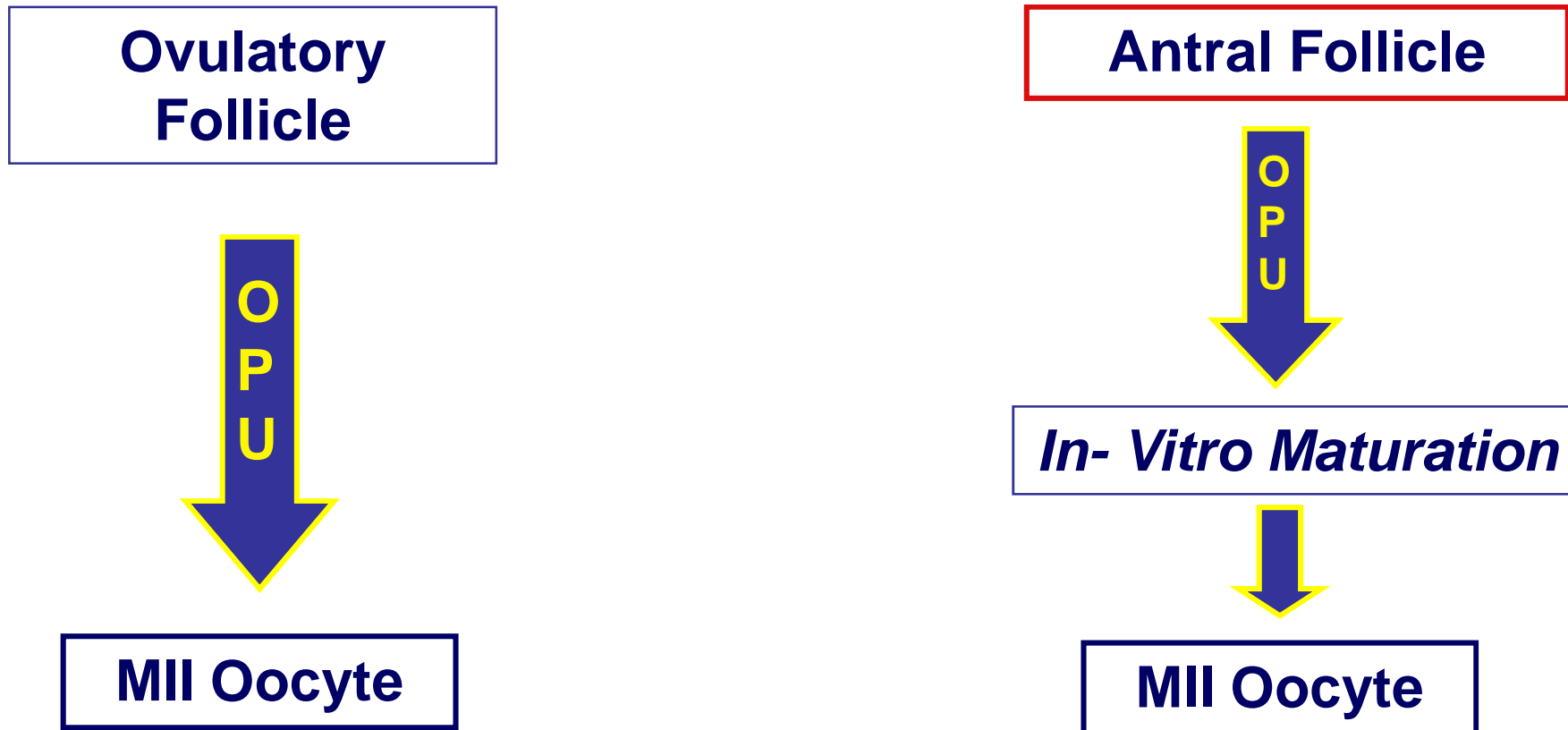
LESSON FROM PHYSIOLOGY

**Ovulatory
Follicle**

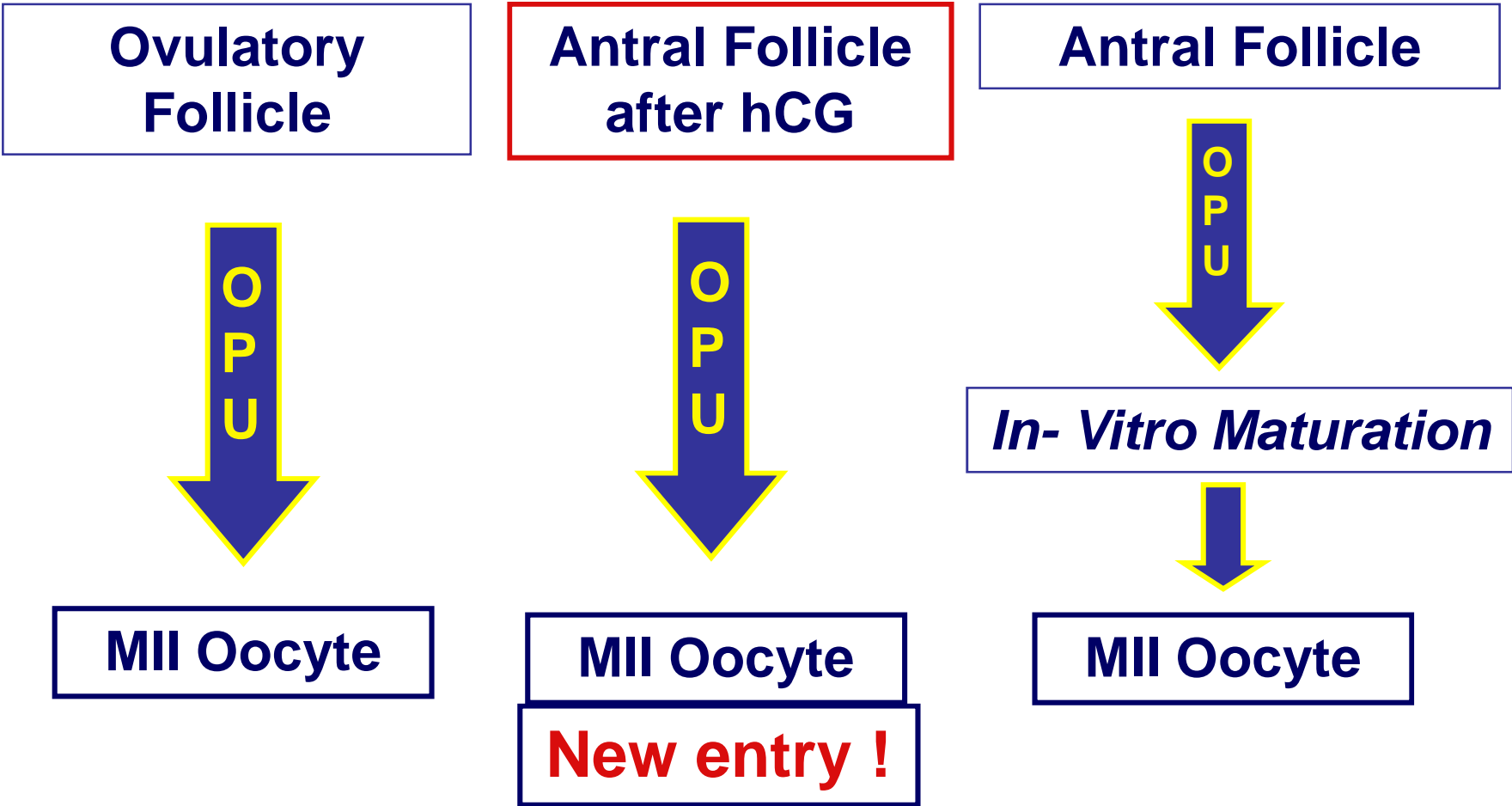


MII Oocyte

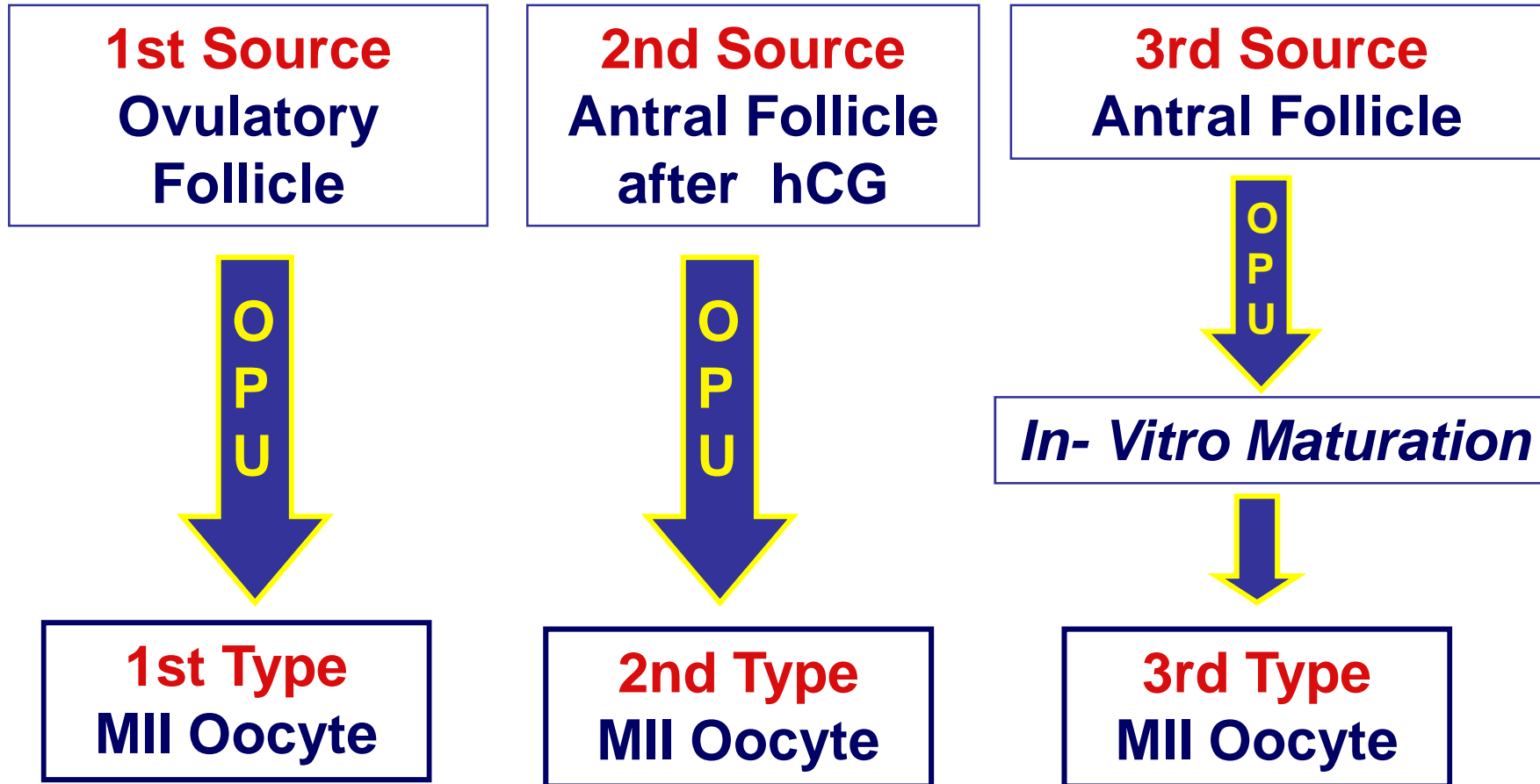
LESSON FROM ART



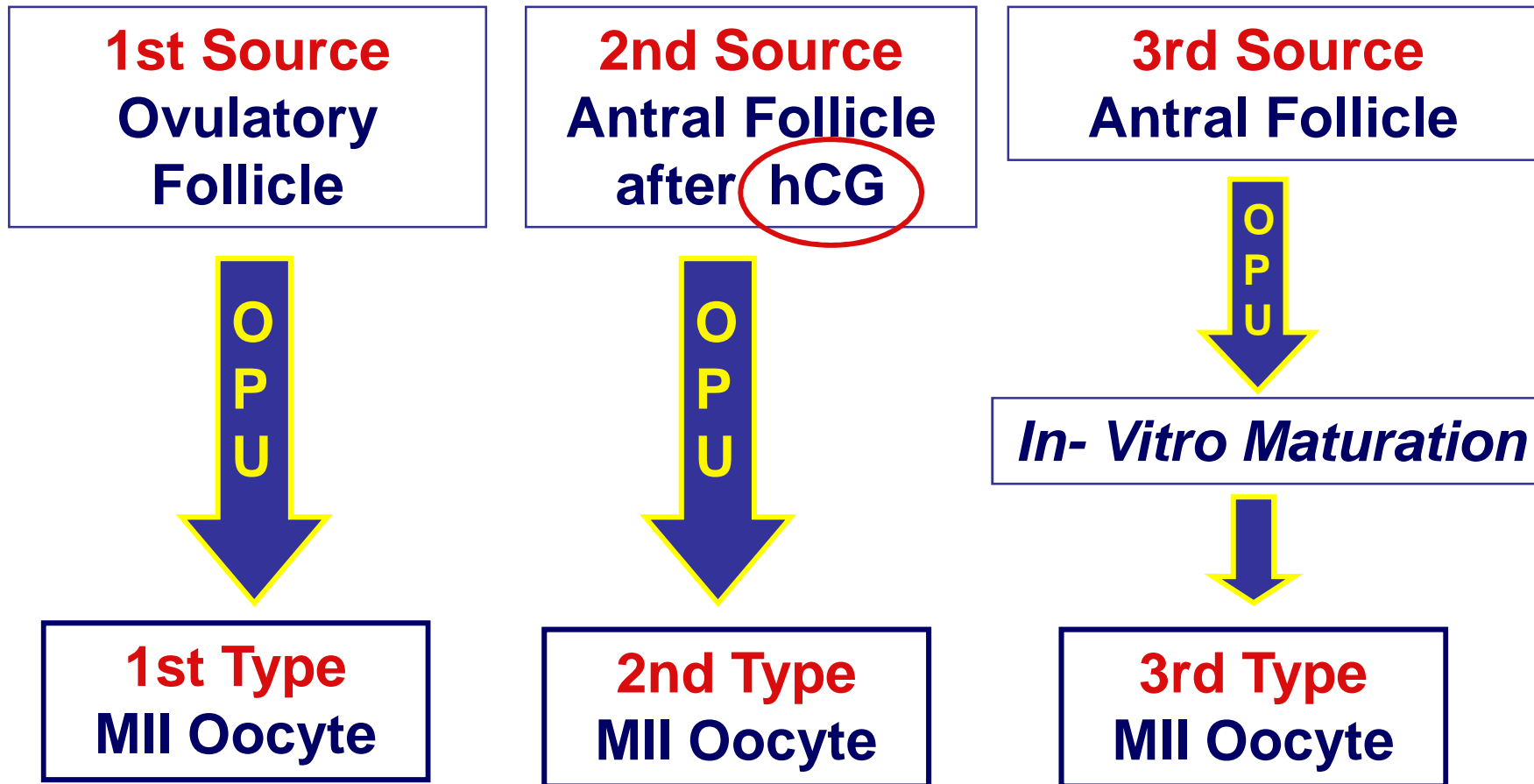
LESSON FROM ART



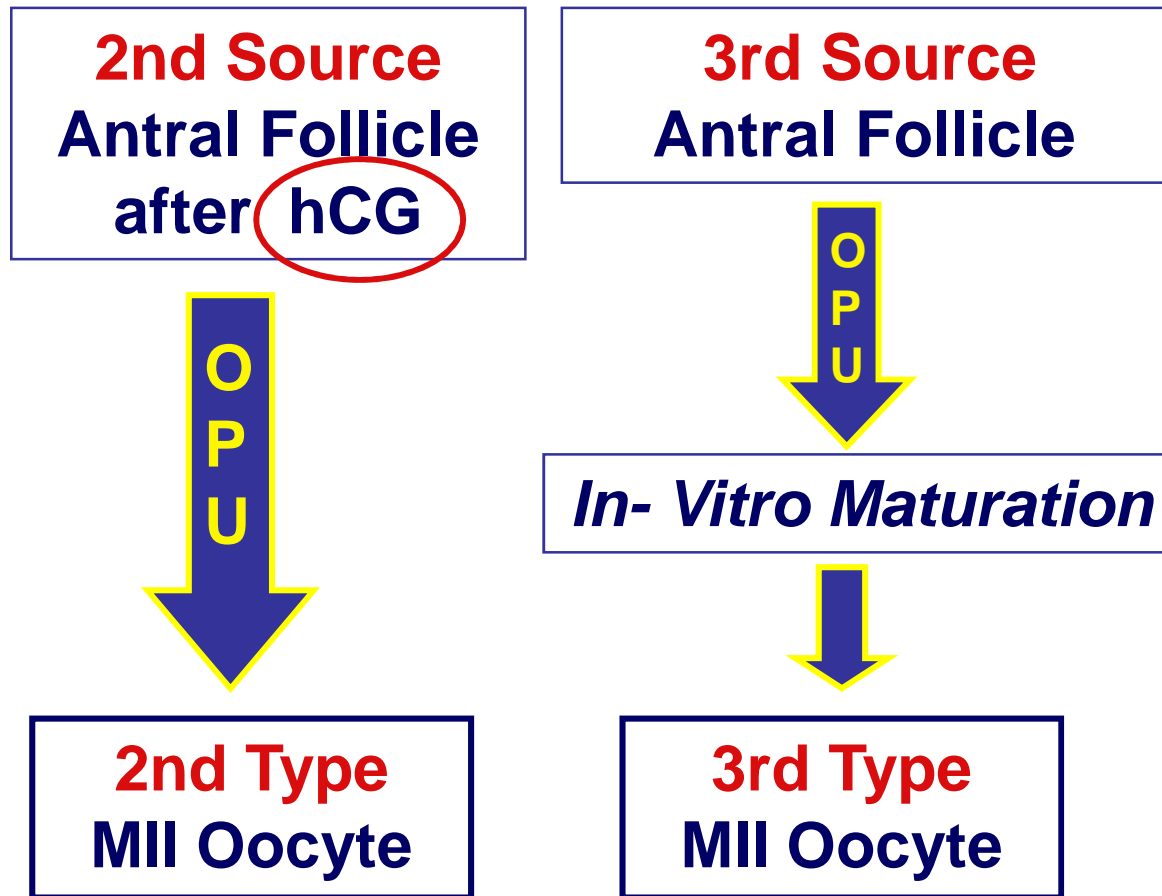
THREE TYPES OF MII OOCYTES



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FROM BIOLOGICAL REMARKS TO CLINICAL OUTCOMES

Do the *Biological benefits* assigned to
hCG or FSH priming favourably affect
Clinical outcomes ?

Pregnancy Rate

Implantation Rate

FROM BIOLOGICAL REMARKS TO CLINICAL OUTCOMES


Do the *Biological benefits* assigned to
hCG or FSH priming favourably affect
Clinical outcomes ?

Pregnancy Rate

Implantation Rate

Unexpected Clinical Outcomes !

CLINICAL OUTCOMES

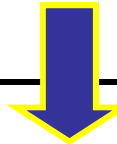


TOT	NO Priming	hCG Priming	FSH Priming	FSH+hCG Priming
-----	------------	-------------	-------------	-----------------

PR/Randomized Cycles	13.7	11.0			
PR/Oocyte Collection	14.5	11.8			
PR/Transfer	18.3	15.2			
Implantation Rate	10.5	9.0			
Miscarriage Rate	16.3	18.2			

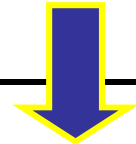
CLINICAL OUTCOMES

TOT	NO Priming	hCG Priming	FSH Priming	FSH+hCG Priming
-----	------------	-------------	-------------	-----------------



PR/Randomized Cycles	13.7	11.0		7.6	
PR/Oocyte Collection	14.5	11.8		13.7	
PR/Transfer	18.3	15.2		17.3	
Implantation Rate	10.5	9.0		10.6	
Miscarriage Rate	16.3	18.2		23.1	

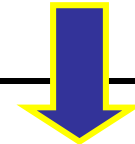
CLINICAL OUTCOMES



TOT	NO Priming	hCG Priming	FSH Priming	FSH+hCG Priming
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PR/Randomized Cycles	13.7	11.0		7.6	26.0
PR/Oocyte Collection	14.5	11.8		13.7	26.5
PR/Transfer	18.3	15.2		17.3	29.8
Implantation Rate	10.5	9.0		10.6	16.3
Miscarriage Rate	16.3	18.2		23.1	15.4

CLINICAL OUTCOMES



TOT	NO Priming	hCG Priming	FSH Priming	FSH+hCG Priming
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PR/Randomized Cycles	13.7	11.0	5.0	7.6	26.0
PR/Oocyte Collection	14.5	11.8	5.4	13.7	26.5
PR/Transfer	18.3	15.2	7.6	17.3	29.8
Implantation Rate	10.5	9.0	4.0	10.6	16.3
Miscarriage Rate	16.3	18.2	9%	23.1	15.4

COMMENTS ON CLINICAL OUTCOMES

Some good *biological benefits*, observed in FSH-primed alone cycles, disappointed the clinical results, as though the cycles needed hCG triggering

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Some good *biological benefits*, observed in FSH-primed alone cycles, disappointed the clinical results, as though the cycles needed hCG triggering

The *biological benefits* assigned to hCG priming alone are only apparent

Priming the cycles with a short course of FSH before hCG promotes the action of hCG on COC and enhances *Clinical Outcomes*

CONCLUSION ON PRIMING IN IVM

FSH

**No significant
Advantages**

hCG

**The Worst
Clinical Outcomes**

FSH+hCG

**The Best
Biological and
Clinical Outcomes**

GONADOTROPHIN PRIMING IN IVM OUR SUGGESTIONS

POLYCYSTIC SYNDROME *

FSH+hCG Priming

NORMAL OVARIES

No Priming

OR

FSH+hCG Priming

***With Irregular Menstrual Cycles**

Physicians

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B. T. Guarnieri
E. Della Morte

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