



Welcome



IV INTERNATIONAL WORKSHOP

ON

OPTIMIZING INFERTILITY

TREATMENTS

Sao Paulo, Brazil

September 3 - 6, 2003

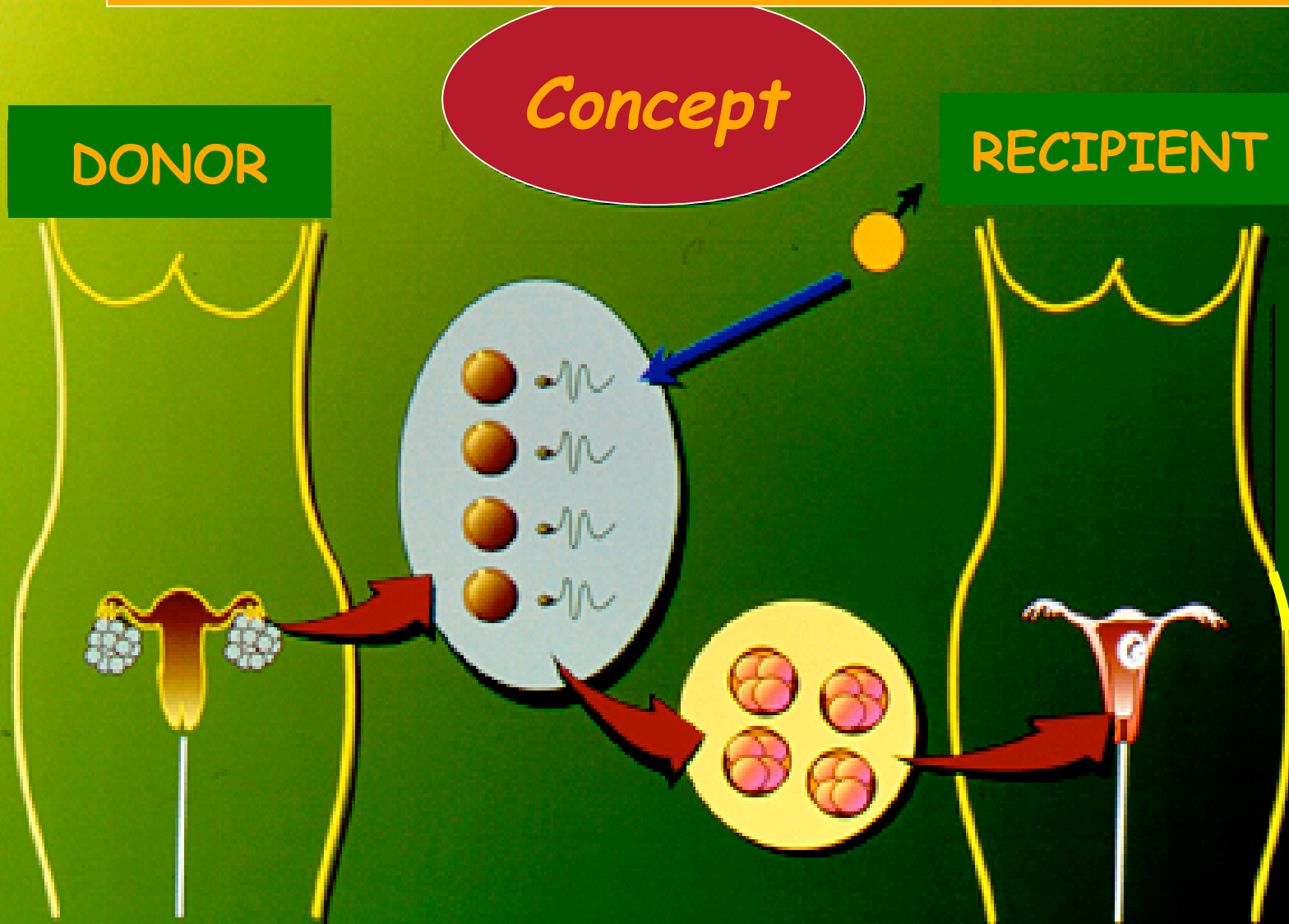
Visit www.seronosymposia.org



*Oocyte donation 2003
Experience over 6000 cycles*

*Prof. Antonio Pellicer
Instituto Valenciano de Infertilidad (IVI)
University of Valencia, Spain*

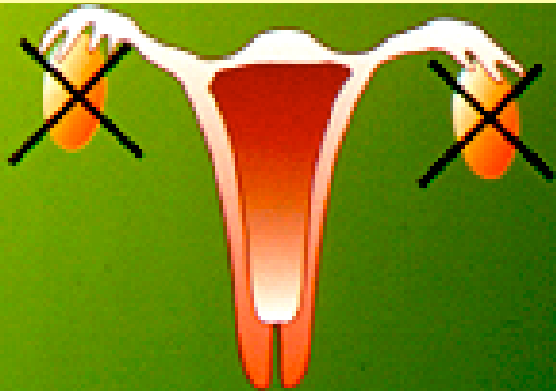
OVUM DONATION



OVUM DONATION

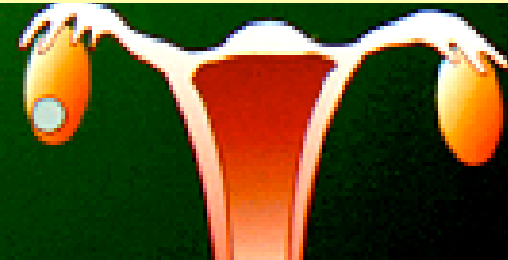
Concept

Without ovarian function



- POF
- Menopause

With ovarian function



- Low response
- Advanced age
- Severe endometriosis
- Implantation failure
- Recurrent miscarriage



March 1990 – May 2003

January 1993 – May 2003



OBJECTIVES

- ┌ *To analyze the scientific impact of OD*
- ┌ *To discuss the overall results of OD in our program*
- ┌ *To determine the effect of age on outcome*
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- *To describe the impact of OD in donors*

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OVUM DONATION

Lessons Learned

- Effect of age on the reproductive system
 - Cano et al, Fertil Steril 64: 584, 1995
 - Guanes et al Fertil Steril 66: 265, 1996
 - Gallardo et al, Fertil Steril 66: 260, 1996
- Influence of high E2 levels on implantation
 - Simón et al Hum Reprod 10: 2432, 1995
 - Pellicer et al, Fertil Steril 65: 1190, 1996
 - Simón et al, Fertil Steril 70: 234, 1998
 - Valbuena et al, Fertil Steril 76: 962, 2001

OVUM DONATION

Lessons Learned

- The oocyte as a cause for implantation failure and recurrent miscarriage
 - Remohí et al, Fertil Steril 67: 717, 1997
 - Remohí et al, Hum Reprod 11: 2048, 1996
- Pathophysiology of endometriosis-associated infertility
 - Simón et al Hum Reprod 9: 725, 1994
 - Pellicer et al, Hum Reprod 10: 91, 1995
 - Pellicer et al, Fertil Steril 69: 1135, 1998
 - Pellicer et al, Fertil Steril 70: 524, 1998
 - Diaz et al, Fertil Steril 74: 31, 2000
 - Garrido et al, Fertil Steril 76: 568, 2001

OVUM DONATION

Lessons Learned

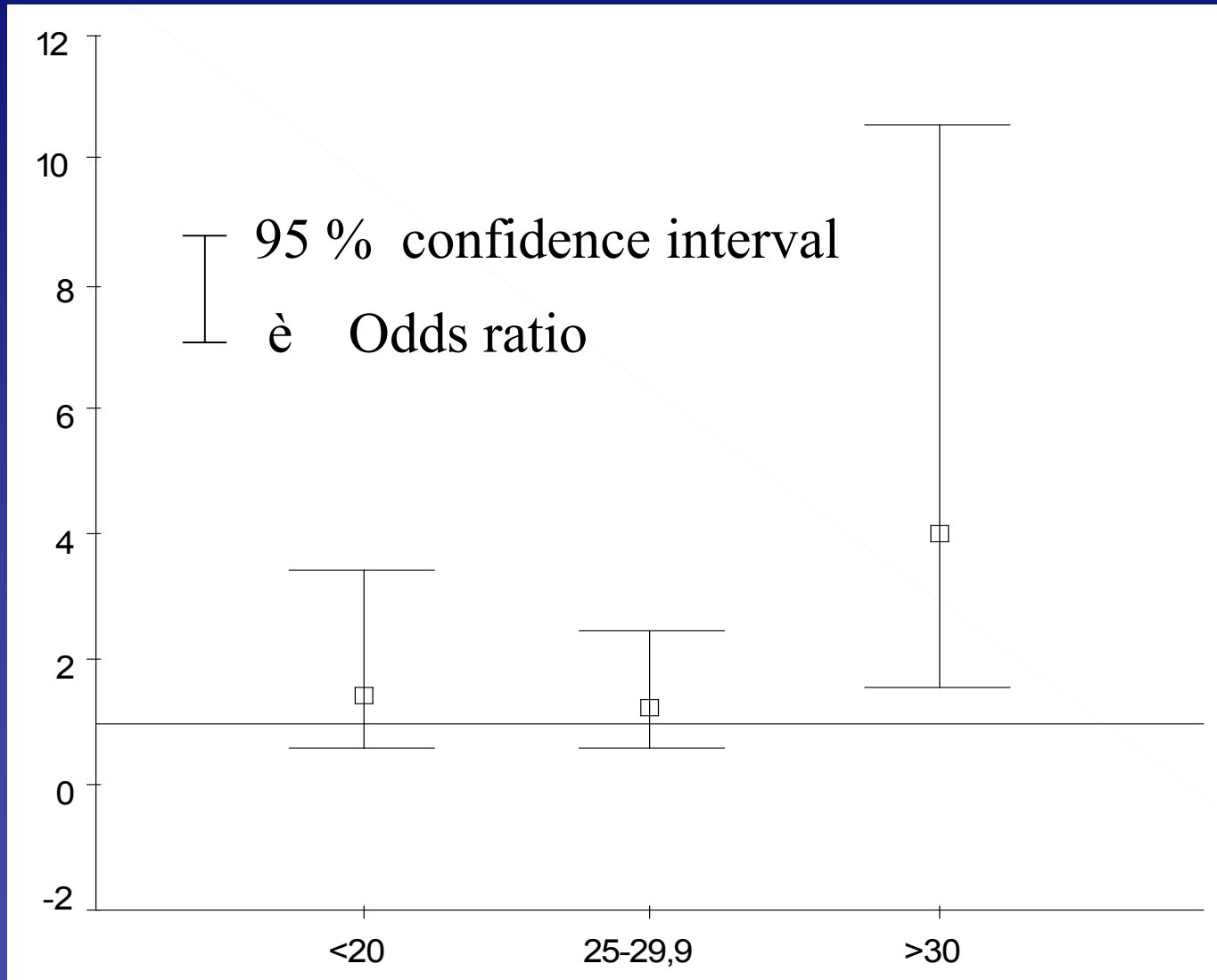
■ Obesity and spontaneous abortion

- It is not clear whether OBESITY is an independent factor causing miscarriage
- OBESITY and PCOS are frequently associated (Solomon et al, 1997) and women with PCOS miscarriage in 30-50% of cases (Balen et al, 1993; Watson et al, 1993; Nestler et al, 2002)
- Study design: A total of 712 cycles divided in four BMI groups:
 - <20
 - 20-24.9
 - 25-29.9
 - >30

Obesity and the risk of spontaneous abortion following oocyte donation

BMI groups (kg/m ²) (n)	Pregnancy (n)	Abortion rate (%)
< 20 (92)	44	18.2
20-24.9 (398)	211	13.3 ^a
25-29.9 (172)	84	15.5 ^b
≥ 30 (50)	21	38.1 ^{a,b}

Risk of abortion



BMI group (kg/m²)

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Spanish Assisted Reproduction Law (1988)

- Anonymous
- Fresh embryo transfer allowed
- VIH determination during OD cycle
 - Out of more than 3000 babies, no contamination
 - Two donors rejected because of positive test

Donors

- 18 – 35 years of age
- Informed consent
- No familiar or personal history of:
 - Genetic diseases
 - Metabolic disorders
 - Mental disorders
- VIH, Hepatitis, Syphilis ... Negative
- Donor discarded when >4 pregnancies

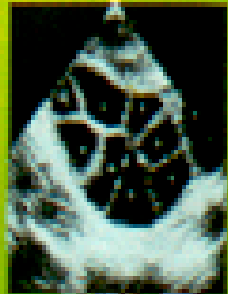
OVUM DONATION

DONOR

RECIPIENT

Procedure

1- ESTIMULACION OVARICA

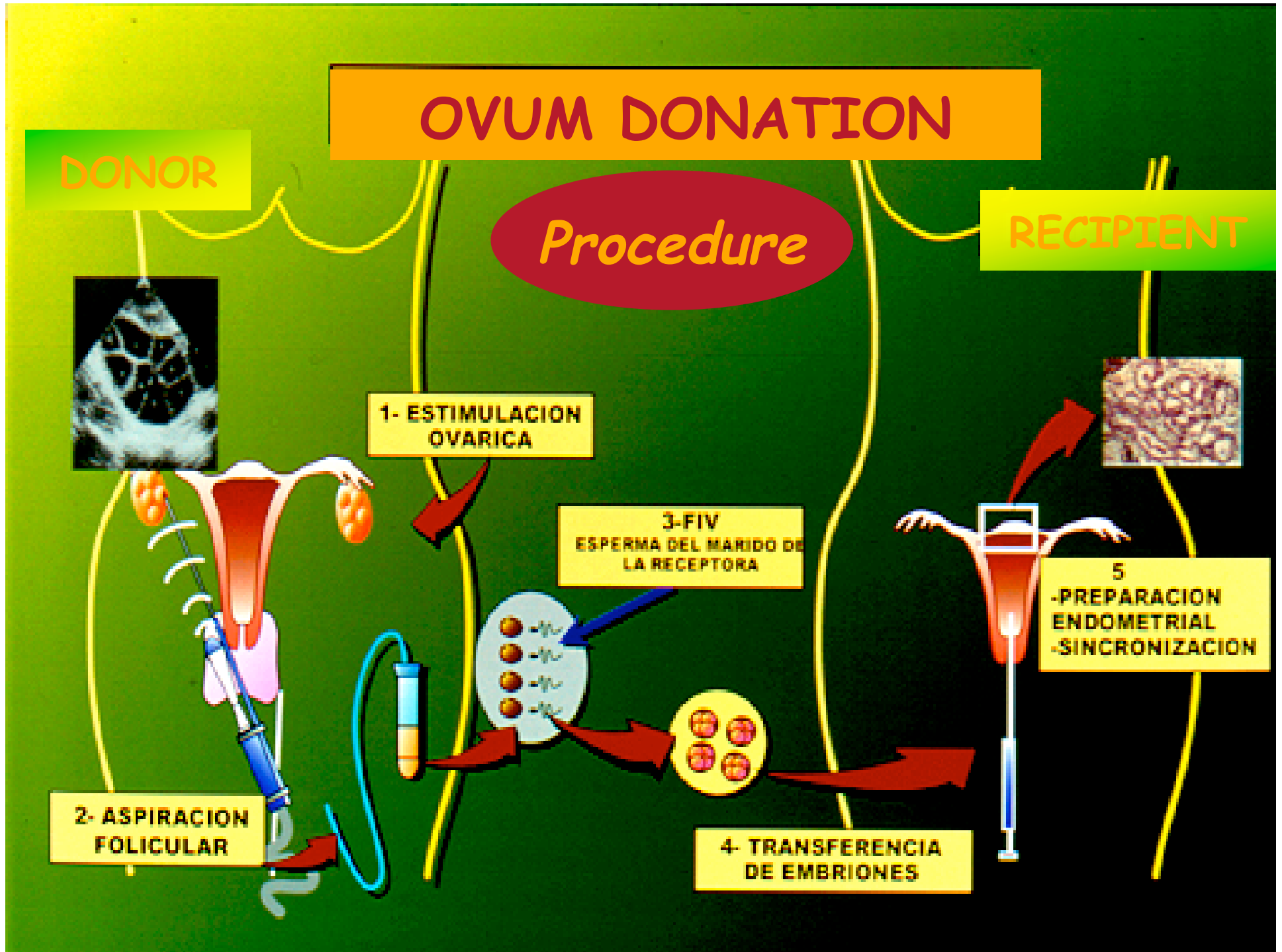


2- ASPIRACION FOLICULAR

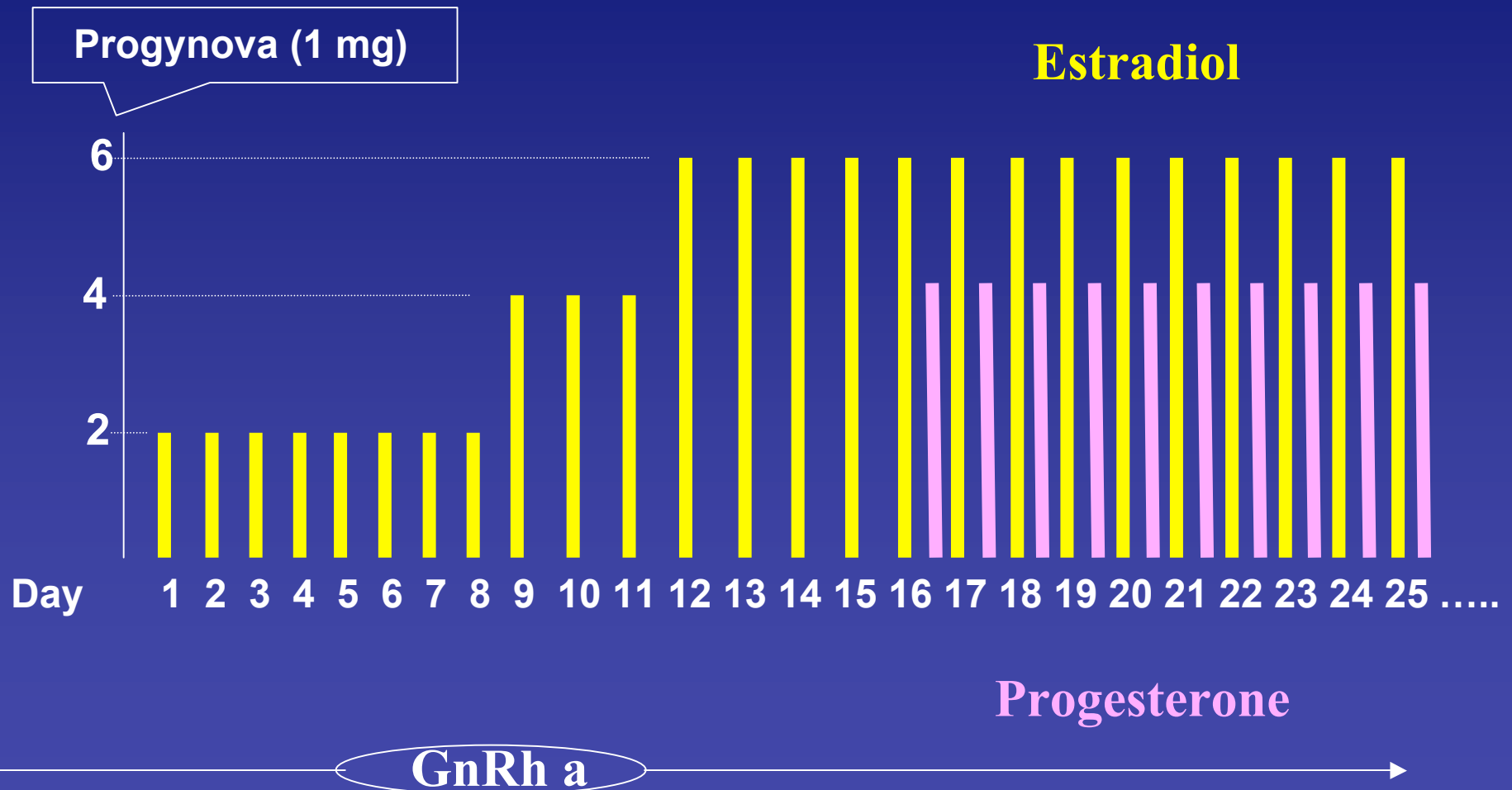
3-FIV
ESPERMA DEL MARIDO DE LA RECEPTORA

5
-PREPARACION ENDOMETRIAL
-SINCRONIZACION

4- TRANSFERENCIA DE EMBRIONES



Estradiol and Progesterone administration (Recipient)



Remohí et al. *Hum Reprod* 1995;10:1387

L. espera Imprimir Ordenar Buscar Todas

Nº historia 14620317 Edad 34 Población CUENCA Teléfono 666.518581 Observaciones telef 969233141
Fecha inicio estrógenos 2/8/2002 Tratamiento OVODON Planing Cultivo No

Especial BT AE Banco Semen mixto Semen cong si no Preferente si no Causa Dias max.

Causa cancelación Fecha F. donación F. transfer NO transfer

Días espera: 40

Observaciones PANAS Grupo y Rh pac O Positivo Grupo y Rh pareja O Positivo

Nº historia 14617371 Edad 44 Población VALENCIA Teléfono 96/3803177 Observaciones telef MADRE ELLA movil
Fecha inicio estrógenos 4/8/2002 Tratamiento OVODON Planing Cultivo

Especial BT AE Banco Semen mixto Semen cong si no Preferente si no Causa Dias max.

Causa cancelación Fecha F. donación F. transfer NO transfer

Días espera: 38

Observaciones

Nº historia 14620366 Edad 37 Población COPENHAGEN Teléfono 00 45 39 20 Observaciones telef ESTAN HOSPEDADOS EN UNA CASA ARQUILADA. SE MARCHARAN EL
Fecha inicio estrógenos 5/8/2002 Tratamiento OVODON Planing Cultivo Co-cultivo

Especial BT AE Banco Semen mixto Semen cong si no Preferente si no Causa Dias max.

Causa cancelación Fecha F. donación F. transfer NO transfer

Días espera: 37

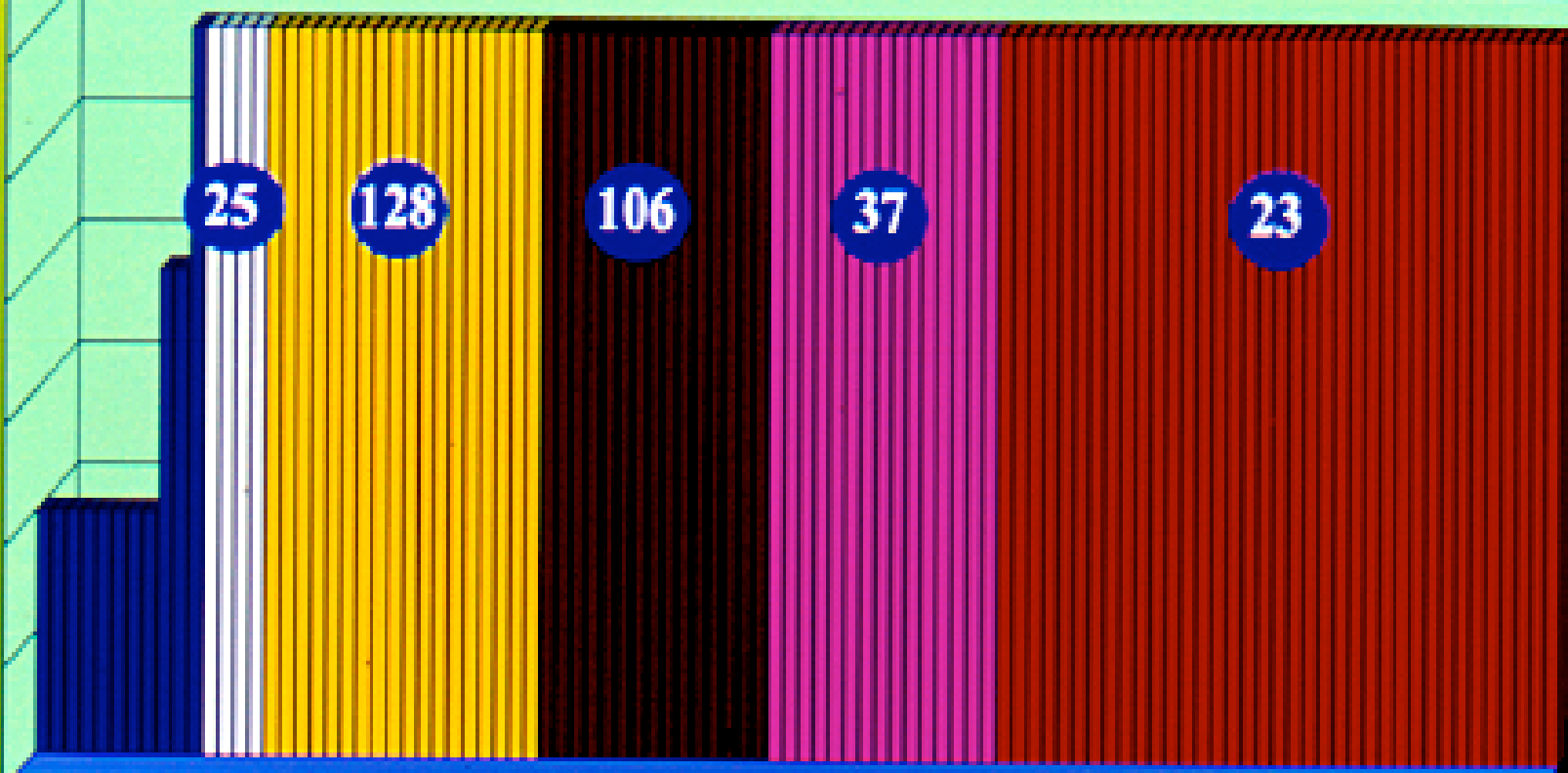
Observaciones CONSENT. OK (MJ) Grupo y Rh pac B Negativo Grupo y Rh pareja O Positivo

Nº historia 14613972 Edad 45 Población ORENSE Teléfono 988417137 Observaciones telef
Fecha inicio estrógenos 6/8/2002 Tratamiento OVODON/ICSI Planing Cultivo

Especial BT AE Banco Semen mixto Semen cong si no Preferente si no Causa Dias max.

ADMINISTRACION PROLONGADA DE ESTRADIOL

7
6
5
4
3
2
1
0



13-16 17-35 36-50 51-65 >65
NUMERO DE DIAS DE ADMINISTRACION DE ESTRADIOL

EMBARAZOS (%)	48.0	55.5	53.8	48.6	47.8	NS
ABORTOS (%)	16.7	12.7	21.1	5.6	9.1	NS

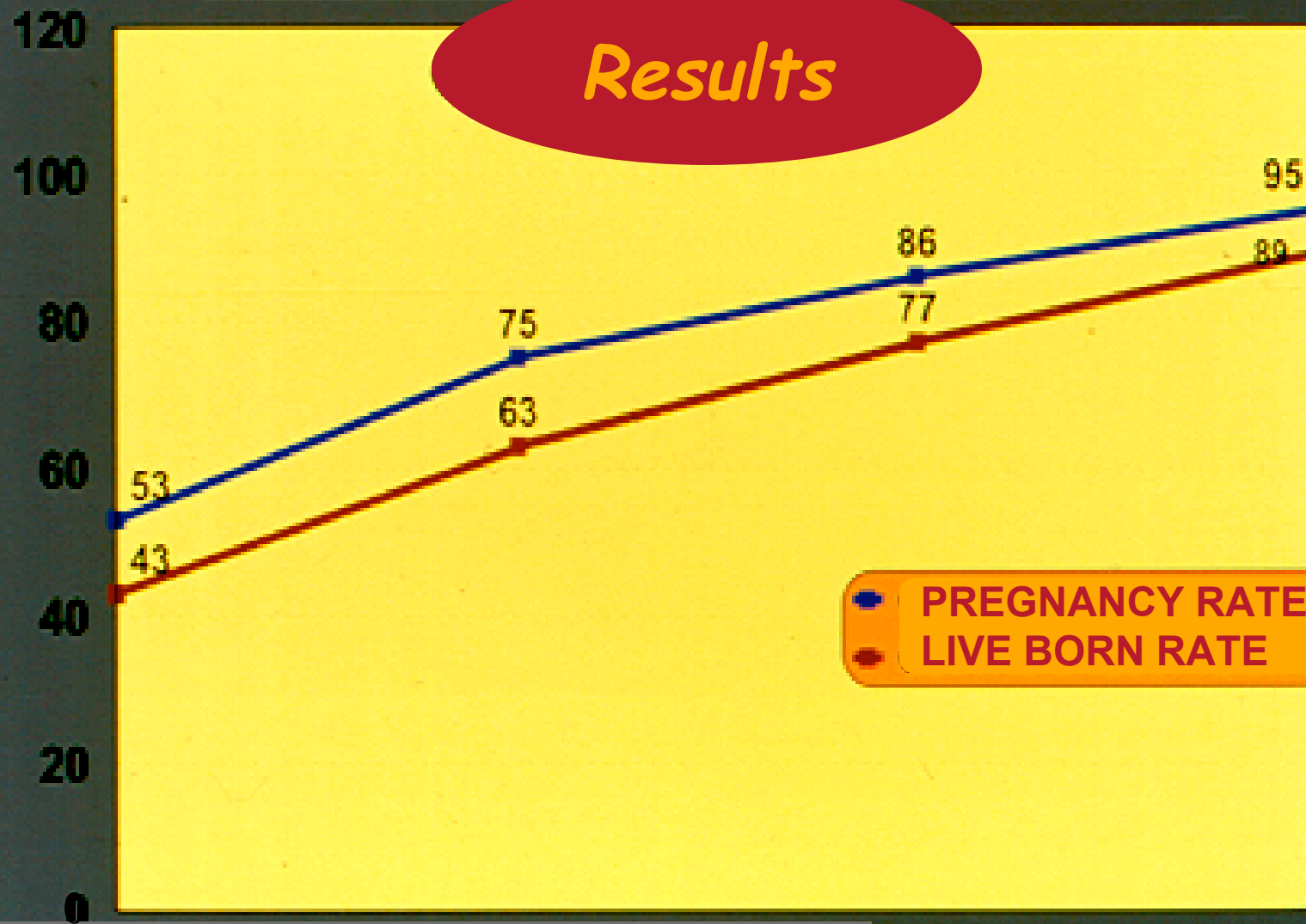
Remohí et al Hum. Reprod 10 Supl 2:84, 1995

RESULTS

CYCLES	6452
AGE	37.8 ± 5.2
OOCYTES DONATES	7.7 ± 1.8
EMBRYOS TRANSFERRED	2.6 ± 1.1
PREGNANCIES (%)	47.5
IMPLANTATION (%)	23.8
ABORTION (%)	17.8

OVUM DONATION

Results



Remohí et al. Fertil Steril 1997;67:712

3

4

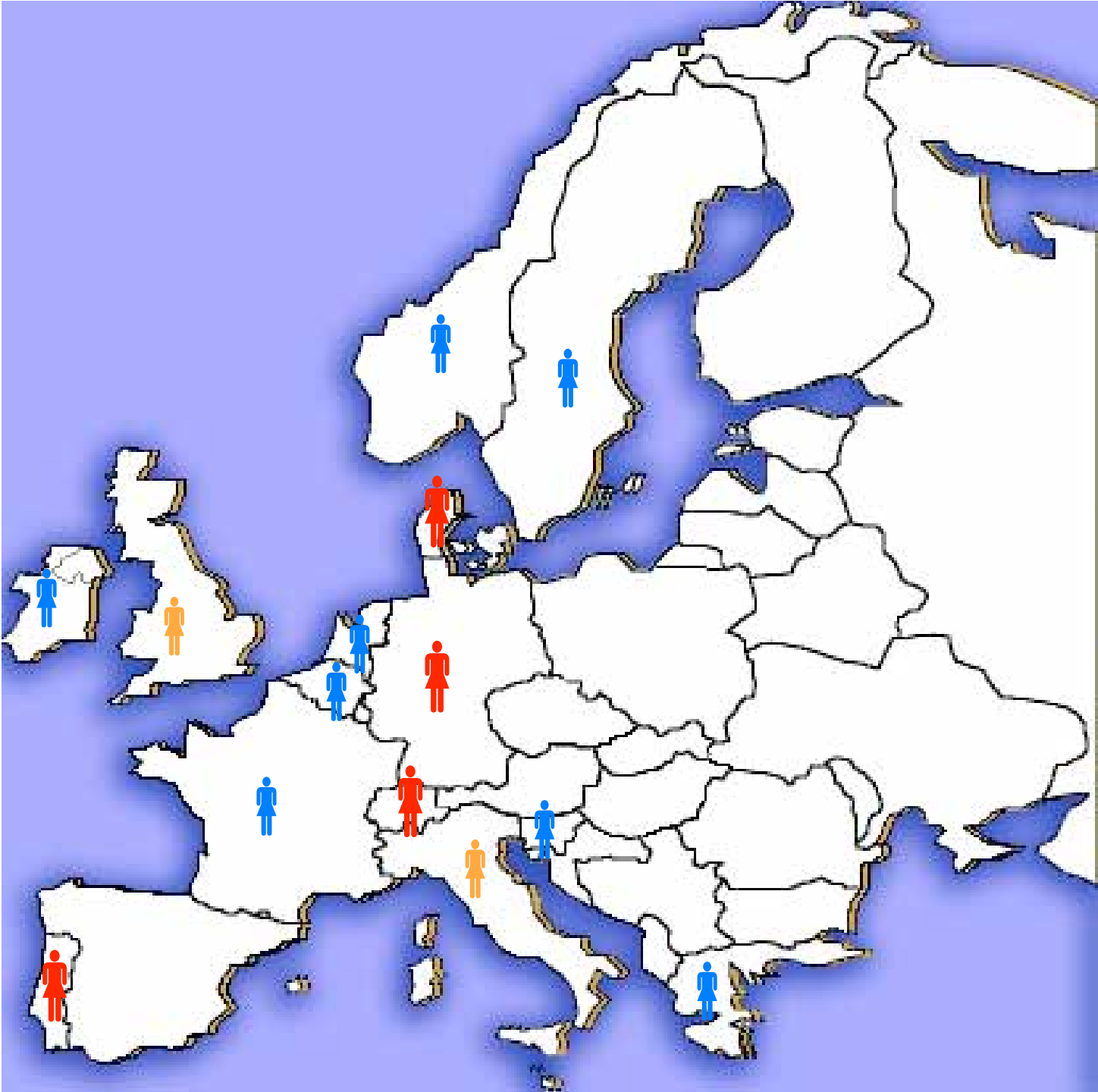
Cycles

Ovum donation last year (2002)




Cycles n	850
Age x	38.6 ± 5.0
Embr. Transfers n (%)	720 (86.3)
Oocytes n (x)	7709 (9.1 ± 2.7)
Embryos transferred x	2.4 ± 1.2
Pregnancies n (%)	395 (54.9)
Multiple pregnancy (%)	156 (39.5)
Implantation rate %	31.6
Miscarriages n (%)	50 (12.6)

Ovum donation & Co-culture July 1999 – August 2001

Cycles n	220
Age x	39.1 ± 5.3
Transfers n (%)	204 (92.7)
Previous attempts	2.3 ± 0.8
Blastocyst rate %	64.3
Blastocysts transferred x	2.4 ± 0.4
Pregnancies n (%)	126 (61.8)
Multiple pregnancies n (%)	57 (45.3)
Implantation rate %	35.4
Miscarriages n (%)	25 (19.8)



Number of ovum
Donation patientes

-  100 - 500
-  20 - 100
-  5 - 20

OD outcome in patients from 16 different European countries

Cycles n (Portugal)	610
Age x	39.1 ± 5.7
Transferences n (%)	529 (88.9)
Oocytes n (x)	5355 (8.8 ± 2.6)
Embryos transferred x	2.5 ± 1.2
Pregnancies n	265 (50.1)
Miscarriages n (%)	35 (13.2)
Implantation rate %	27.8

Germany, Denmark, Portugal, France, United kingdom, Ireland, Norway, Switzerland, Swiss, Greece, Italy, San Marino, Slovenia, Belgium, Luxemburg, Nederland.

OBJECTIVES

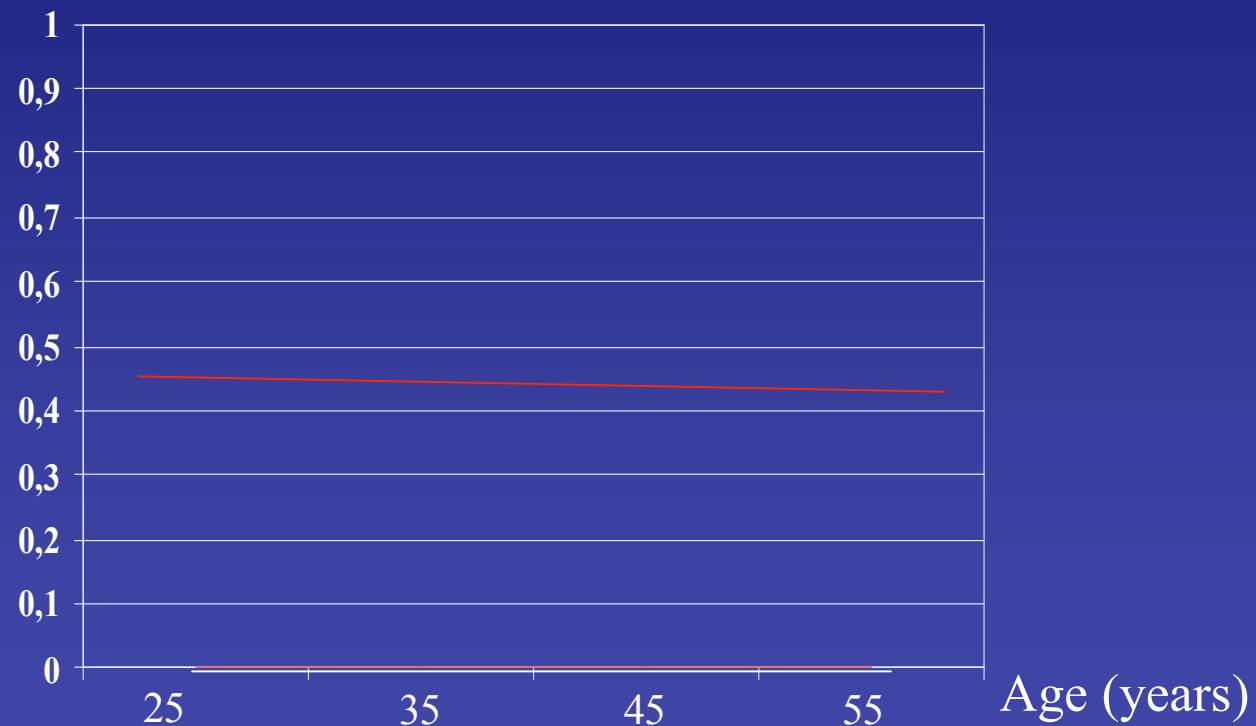
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Pregnancy rate/AGE

In a simple linear regression analysis of data related to 3089 oocyte donation cycles

N=3089

Pregnancy rate

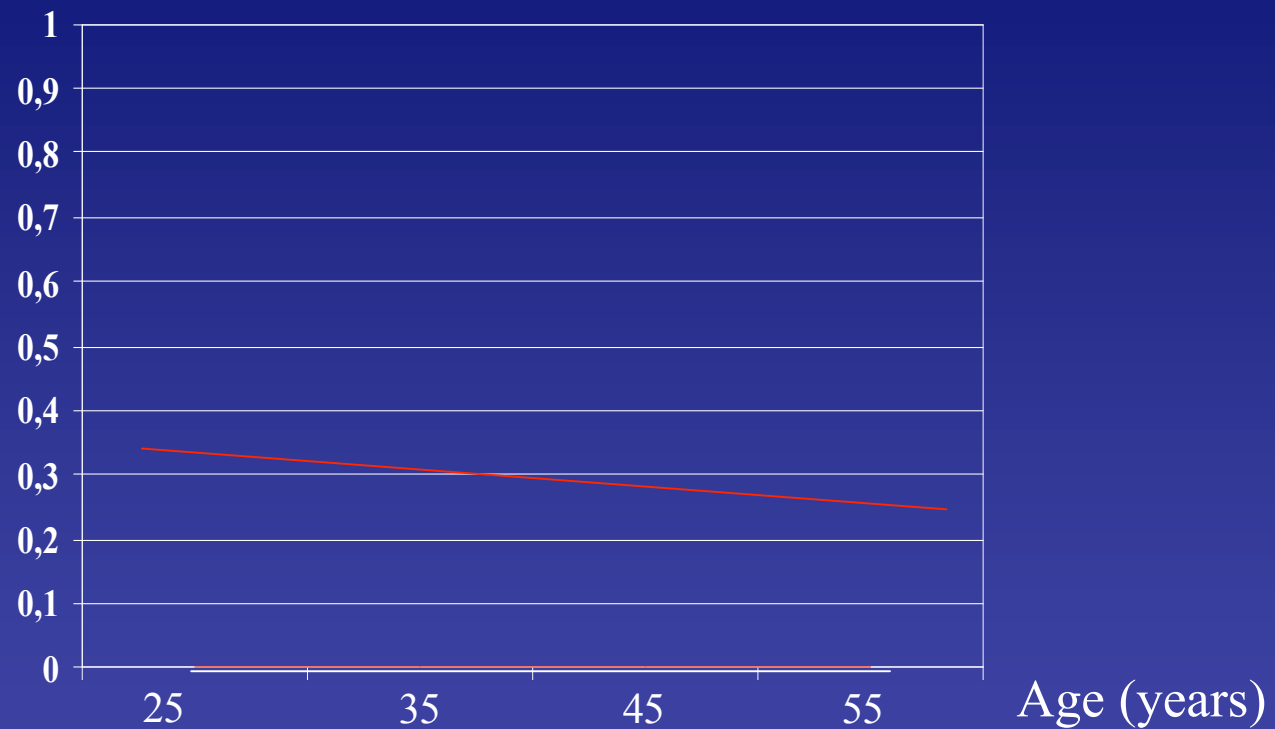


We find no statistically significant difference in pregnancy rates according to age.

Implantation rate/AGE

N=3089

**Implantation
rate**

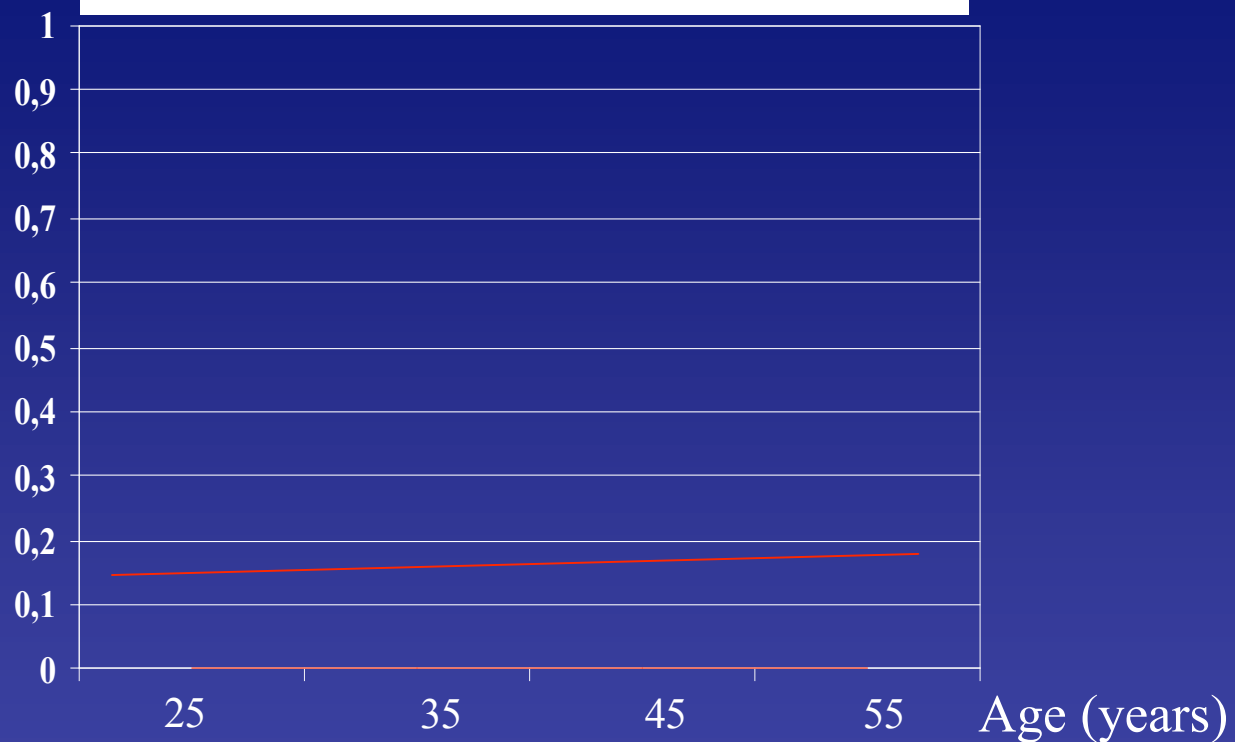


Also, no significant influence of AGE on IMPLANTATION RATE is observed.

Abortion rate/AGE

N=3089

Abortion
rate



And the ABORTION RATE is also SIMILAR in different ages.

Consequently, AGE does not determine SIGNIFICANT differences on PREGNANCY, IMPLANTATION and ABORTION rates, although results in aged women are SLIGHTLY WORSE.

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The obstetric outcome of pregnancies
obtained by

IVF/ICSI cycles (n=835)

Oocyte donation cycles (n=435)

was been compared to in our center with
the outcome of pregnancies achieved by

**natural conception (n=450, births at the
Peset University Hospital of Valencia),**

all data related to a one year period

Obstetric Outcome of OD pregnancies

	Natural conception	IVF/ICSI	Oocyte donation	P
No. of births	450	835	435	
Woman's age	35.5	35.2	35.4	NS
1st trim. hemorrhage	30/450 (6.7%)	286/835 (34.2%)	130/435 (29.9%)	<0.001
Miscarriages	45/450 (10%)	179/835 (21.4%)	103/435 (23.6%)	<0.001
Ectopic pregnancies	4/450 (0.9%)	5/835 (0.5%)	5/435 (1.1%)	NS

The incidence of 1st hemorrhage and abortion are significantly higher in AR, but there was no significant difference between both AR groups

Obstetric Outcome of OD pregnancies

	Natural conception	IVF/ICSI	Oocyte donation	p
Gest. Hypertension	27/401 (6.7%)	96/651 (14.7%)	57/327 (17.4%)	<0.001
Placenta previa	3/401 (0.7%)	29/651 (4.5%)	17/327 (5.1%)	<0.05
Abruptio placenta	4/401 (1.0%)	18/651 (2.8%)	1/327 (0.3%)	<0.05
Abnormal O'Sullivan	19/401 (4.7%)	59/651 (9.1%)	14/327 (4.3%)	<0.05

The incidence of gestational hypertension and placenta previa were also significantly higher in AR conceptions. The incidence of abruptio placenta and abnormal O'Sullivan test were only higher in IVF/ICSI gestations

Perinatal results of OD pregnancies

	Natural conception	IVF/ICSI	Oocyte donation	p
Cesarean section	111/401 (27.8%)	372/651 (57.1%)	264/327 (80.7%)	<0.001
Neonatal ICU admissions	35/401 (8.7%)	165/651 (25.3%)	64/327 (19.6%)	<0.001
Perinatal death	7/401 (1.7%)	20/651 (3.1%)	23/327 (7.0%)	<0.002

The incidence neonatal ICU admissions was higher in AR groups, as also were the incidences of cesarean section and perinatal death (both even higher in OD pregnancies).

OBJECTIVES

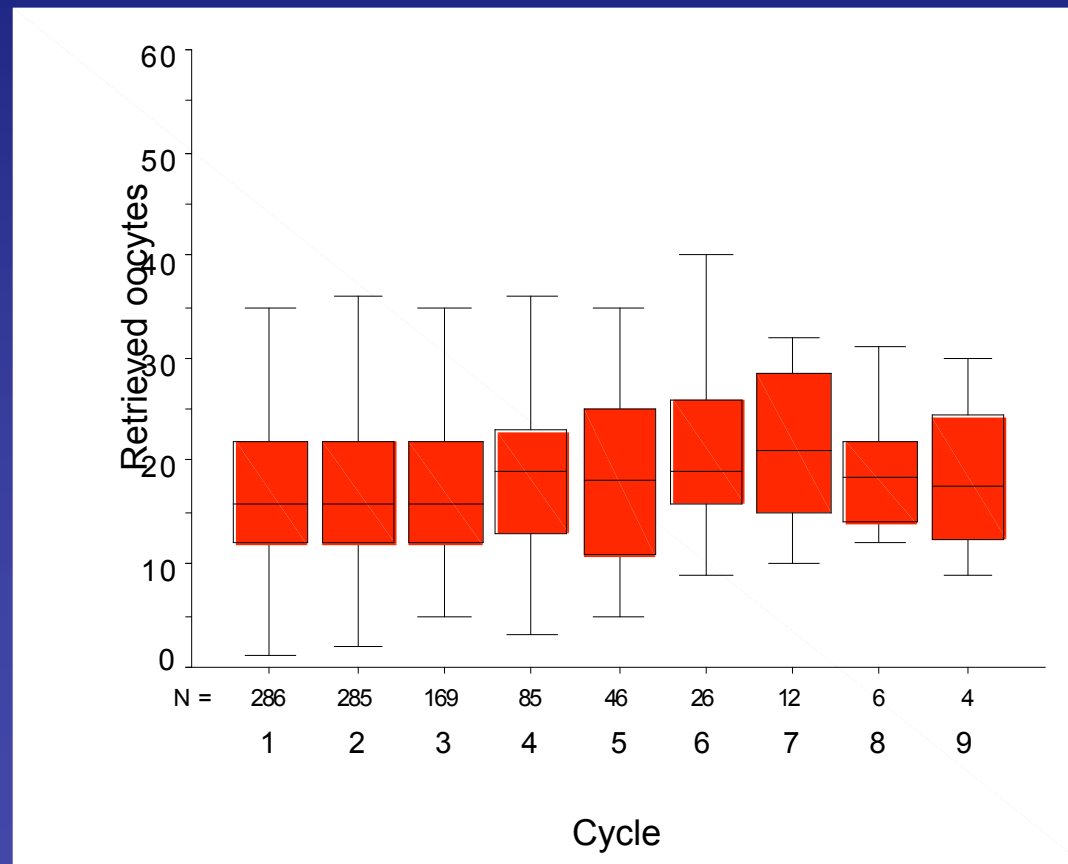
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Donors

■ Initiated cycles	2393
■ Age	25.6 _± 4.2
■ Canceled cycles	300 (12.5%)
■ Oocyte retrievals	2093
■ Oocytes/cycle	18 _± 8.8
■ Recipients/donor	1.9 _± 0.9
■ Inseminated oocytes/cycle	13.1 _± 6.5
■ Frozen zygotes	53

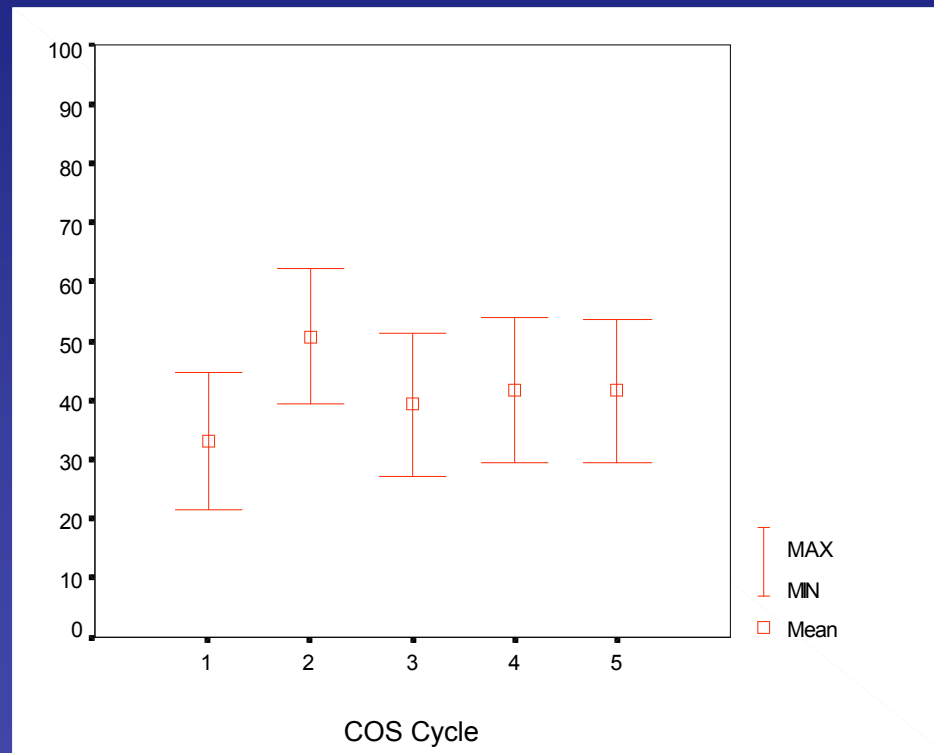
(data up to July 2002)

Median and interquartile ranges of retrieved oocytes through consecutive cycles of COH in donors.



Caligara et al. Hum Reprod

Pregnancy rate of donated oocytes through five consecutive cycles



Caligara et al. Hum Reprod

Chromosomal abnormalities in OD embryos

	Donors	Control
Number of cycles	15	11
Woman's age ^a	27.0 ± 4.8*	31.3 ± 2.1
Total dose of FSH + hMG (IU)	2578 ± 1097*	3616 ± 1325
Number of retrieved oocytes	25.9 ± 9.3	14.8 ± 7.1*
Chromosomally abnormal embryos (%)	61/108 (56.5)	25/67 (37.3)
Number of embryo transfers	12	10
Number of transferred embryos	2.1 ± 0.8	2.0 ± 1.5
Pregnancies (%)	4 (33.3)	4 (40.0)
Implantation rate	25.0	36.4
Miscarriages	0	0

*p<0.05

Reis et al. Fertil Steril 2003 (10)(In press)

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