



# "FERTILIDAD DESPUÉS DE LOS 40"

1ER CURSO UNIVERSITARIO DE POSTGRADO DE  
FORMACIÓN EN CLIMATERIO. AAPEC.

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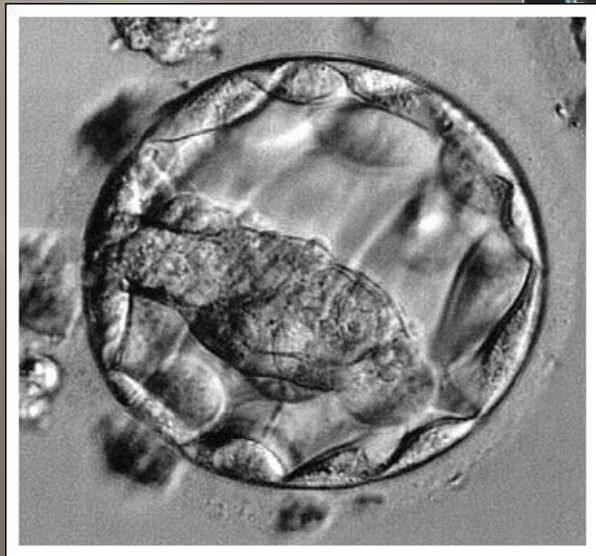
*Fertilidad después de los 40 años tiene múltiples focos de análisis.....*



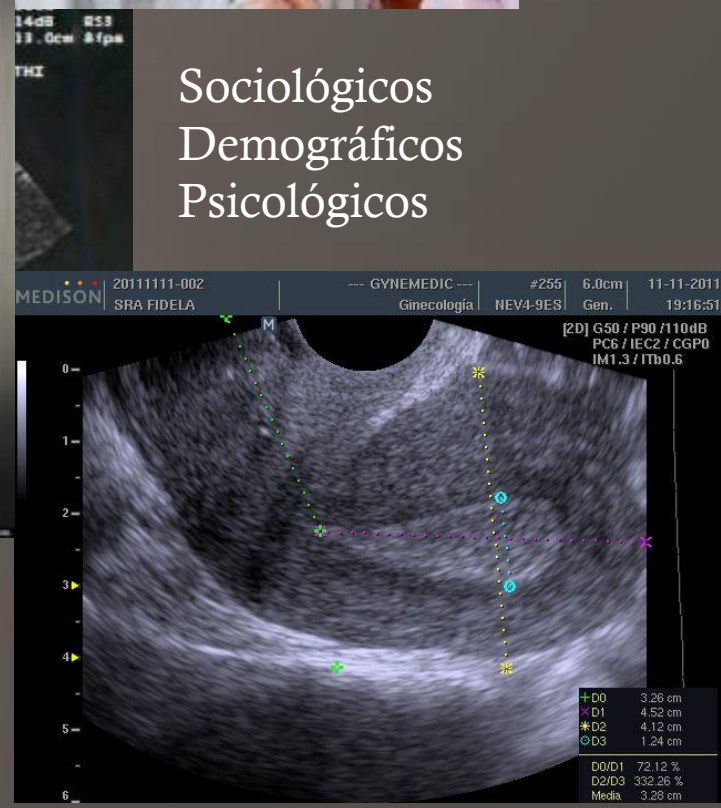
Biológicos



Sociológicos  
Demográficos  
Psicológicos



Económicos....



# TENDENCIA FASHION.....?





# TENDENCIA SOCIOCULTURAL.....?



# Edad & Fertilidad Femenina



- Ageing Ovárico
- Ageing Uterino
- Resultados materno-fetales de los embarazos en edad materna avanzada.

Feb/08

*"I may only do this one time, so I want this moment to be as big as it can be. I want the biggest bang"*

Hally Berry

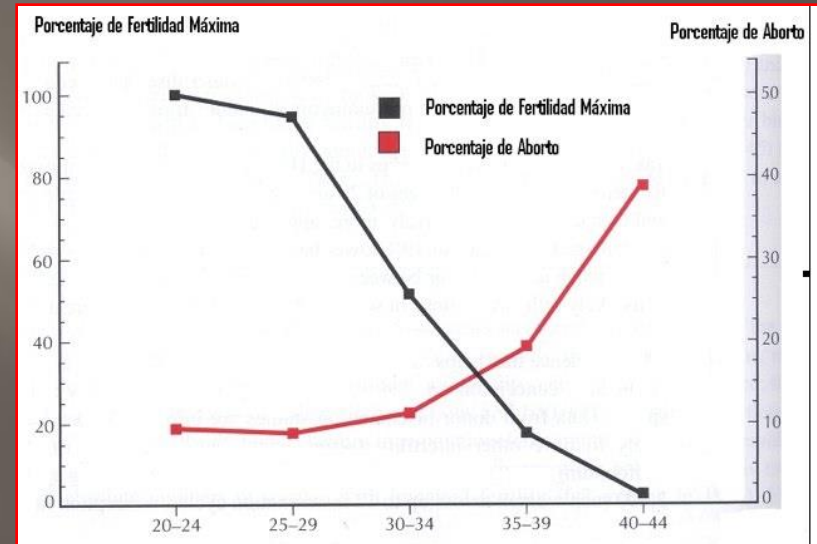
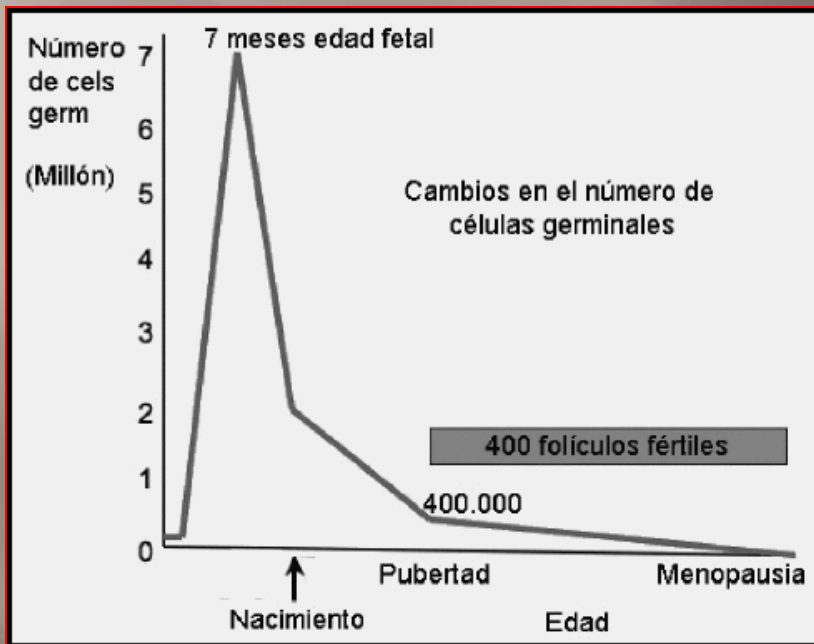


# Ageing Ovárico



POOL DE FOLÍCULOS PRIMORDIALES FINITO

CALIDAD & CANTIDAD



El concepto de reserva ovárica limitada en cuanto a cantidad y calidad de ovocitos es el mas importante dogma de la reproducción humana natural y asistida. Últimos hallazgos lo han puesto en discusión pero aun es considerado como la verdad absoluta.

# Ageing uterino

- ❖ *Menor tasa de embarazo/implantación.*
- ❖ *Mayor tasa de aborto.*
- ❖ *Peores resultados perinatales.*





# Ageing Uterino & resultados



## Clinical factors affecting endometrial receptiveness in oocyte donation cycles

Sérgio Reis Soares, M.D.,<sup>a</sup> Juan Antonio Garcia Velasco, M.D.,<sup>b</sup> Manuel Fernandez, M.D.,<sup>b</sup>  
Ernesto Bosch, M.D.,<sup>b</sup> José Remohí, M.D.,<sup>b</sup> Antonio Pellicer, M.D.,<sup>b,c</sup> and Carlos Simón, M.D.<sup>b</sup>

<sup>a</sup>IVI-Lisboa, Avenida Infante Dom Henrique, 333-H, 1800-282, Lisboa, Portugal; <sup>b</sup>Instituto Universitario IVI, Universidad de Valencia, Valencia; and <sup>c</sup>Hospital Universitario Dr. Peset, Valencia, Spain

Fertility and Sterility® Vol. 89, No. 3, March 2008

- ✚ Edad de la mujer receptora.
- ✚ Índice de masa corporal.
- ✚ Hábito del tabaco.
- ✚ Preparación endometrial.
- ✚ Presencia de hidrosalping y endometriosis-adenomiosis.



**TABLE 1****Factors influencing endometrial receptiveness in oocyte donation cycles.**

	Cutoff point	PR	MR	MPR	References
Recipients age (y)	>45	↓	↑		Yaron et al. (4), Moomjy et al. (5), Legro et al. (6), Paulson et al. (7), Noyes et al. (8), Cano et al. (9), Toner et al. (10), Soares et al. (1)
BMI (kg/m <sup>2</sup> )	>30	↓	↑		Wattanakumtornkul et al. (17), Styne-Gross et al. (18), Bellver et al. (19), Bellver et al. (20)
Endometrial priming Thickness		No effect			Noyes et al. (8), Soares et al. (11), Garcia-Velasco et al. (23), Shapiro et al. (24), Abdalla et al. (25), Borini et al. (26), Remohí et al. (27), Coulam et al. (28)
Serum E <sub>2</sub> levels		No effect			Noyes et al. (8), Soares et al. (11), Garcia-Velasco et al. (23), Michalas et al. (31), Remohí et al. (34)
Duration (wk)	>7	↓			Soares et al. (11), Michalas et al. (31), Yaron et al. (32), Younis et al. (33), Remohí et al. (34), Borini et al. (35)
Oral vs. transdermal Progesterone		No available data No effect			Daya et al. (48), Manno et al. (49), Lightman et al. (50), Gibbons et al. (51)
Pituitary suppression		No effect			Simon et al. (53), Dal Prato et al. (54), El-Toukhy et al. (55)
Smoking habit Hydrosalpinx	>10/day	↓ ↓		↑	Soares et al. (65) Camus et al. (68), Andersen et al. (69), Strandell et al. (70), Strandell et al. (71), Meyer et al. (72), Bildirici et al. (73), Seli et al. (74), Johnson et al. (75), Stadtmayer et al. (76), Hurst et al. (77)
Endometriosis		No effect			Simón et al. (85), Sung et al. (86), Díaz et al. (87)
Adenomyosis		No available data			

Note: PR = pregnancy rate; MR = miscarriage rate; MPR = multiple pregnancy rate.

Source: Clinical factors relevant to egg donation. *Fertil Steril* 2008.





J Hum Reprod Sci. 2012 Sep;5(3):252-7.

**A study of recipient related predictors of success in oocyte donation program.**

Gupta P, Banker M, Patel P, Joshi B. Department of Reproductive, Medicine and Endoscopy, The Pulse Women Hospital Pvt. Ltd. Ahmedabad, Gujarat, India.

**Table 1: Clinical pregnancy, implantation rate and ongoing pregnancy rates relative to the age of recipients**

Age of recipient (years)	Clinical pregnancy rate (%)	Ongoing pregnancy rate %	Implantation rate %	Singleton/twin/triplet (S/tw/tri)	Miscarriage rate
<35	29/79 = 36.70 <sup>a</sup>	28/79 = 31.64 <sup>b</sup>	45/229 = 19.65 <sup>c</sup>	16/10/3	1/29 = 3.4 <sup>d</sup>
35-39	34/81 = 41.97 <sup>a</sup>	31/81 = 38.37 <sup>b</sup>	58/235 = 24.68 <sup>c</sup>	14/16/4	3/34 = 8.8 <sup>d</sup>
40-44	25/78 = 32.05 <sup>a</sup>	20/78 = 24.64 <sup>b</sup>	25/228 = 12.28 <sup>c</sup>	15/10/0	5/25 = 20 <sup>d</sup>
≥45	7/32 = 21.87 <sup>a</sup>	6/32 = 18.75 <sup>b</sup>	12/91 = 13.18 <sup>c</sup>	3/3/1	1/7 = 14.8 <sup>d</sup>
*P value	0.209	0.001	0.001	NA	0.195

\*P = non significant for a and d, significant for band c


.....This might be due to **reduced uterine blood flow** with increased age.[6,7] or a **decreased sensitivity to progesterone effects**. [8] Histologic, ultrastructural, and biochemical changes like subepithelial extracellular matrix deposition, stromal angiosclerosis, which become more common with age.[2,6] .....

# Edad materna & resultados perinatales.



## Advanced Maternal Age and Adverse Pregnancy Outcome: Evidence from a Large Contemporary Cohort

Louise C. Kenny<sup>1</sup>, Tina Lavender<sup>2</sup>, Roseanne McNamee<sup>3</sup>, Sinéad M. O'Neill<sup>4</sup>, Tracey Mills<sup>2</sup>, Ali S. Khashan<sup>1,5\*</sup>

 PLOS ONE | February 2013 | Volume 8 | Issue 2 | e56583

### Abstract

**Background:** Recent decades have witnessed an increase in mean maternal age at childbirth in most high-resourced countries. Advanced maternal age has been associated with several adverse maternal and perinatal outcomes. Although there are many studies on this topic, data from large contemporary population-based cohorts that controls for demographic variables known to influence perinatal outcomes is limited.

**Methods:** We performed a population-based cohort study using data on all singleton births in 2004–2008 from the North Western Perinatal Survey based at The University of Manchester, UK. We compared pregnancy outcomes in women aged 40 years with women aged 20–29 years using log-linear binomial regression. Models were adjusted for social deprivation score and body mass index.

The study cohort consisted of 215,344 births; 122,307 mothers (54.19%) were aged 20–29 years, 33,966 (15.05%) were aged 30–34 years, 33,966 (15.05%) were aged 35–39 years and 7,066 (3.13%) were aged ≥40 years. Women aged ≥40 years at delivery were at increased risk of stillbirth (RR = 1.83, [95% CI 1.37–2.43]), pre-term (RR = 1.25, [95% CI: 1.08–1.55]), pre-term birth (RR = 1.29, [95% CI: 1.08–1.55]), Macrosomia (RR = 1.31, [95% CI: 1.12–1.54]), extremely low birth weight (RR = 1.40, [95% CI: 1.25–1.58]) and Caesarean delivery (RR = 1.83, [95% CI: 1.77–1.90]).

Advanced maternal age is associated with a range of adverse pregnancy outcomes. These risks are independent of parity and remain after adjusting for the ameliorating effects of higher socioeconomic status. The data from this large contemporary cohort will be of interest to healthcare providers and women and will facilitate evidence based counselling of older expectant mothers.

> riesgo de muerte fetal, pretermino, bajo peso, macrosomia, extremadamente grande para la EG, cesárea.

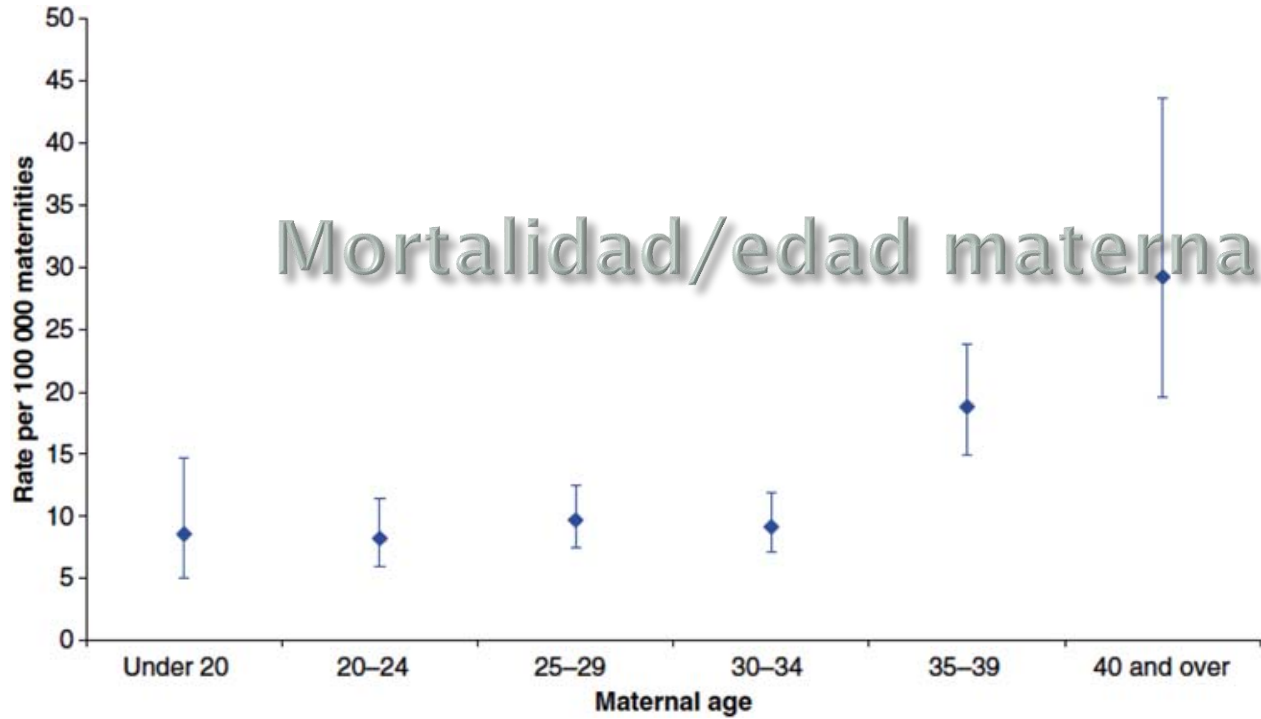


Figure 1 Maternal mortality rates by age group (years); UK: 2006–2008. Reproduced with permission from Cantwell *et al.* (2011).

*Mayor riesgo de diabetes gestacional, Preeclampsia, hemorragia postparto, obesidad, etc.*



# Association between oocyte donation and maternal and perinatal outcomes in women aged 43 years or older

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V. Tsatsaris<sup>1,2</sup>, D. Cabrol<sup>1,2</sup>, and F. Goffinet<sup>1,2</sup>

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Submitted on September 22, 2011; resubmitted on November 27, 2011; accepted on December 7, 2011

**METHODS:** This retrospective study covered all women, aged 43 or more, who gave birth between 2008 and 2010. Univariate and multivariate analyses with logistic regression models were used to compare maternal and perinatal outcomes as a function of mode of conception: without IVF, with IVF using own oocytes or with IVF and oocyte donation.

**RESULTS:** The study included 380 women, including 40 who had IVF without oocyte donation (10.5%) and 104 who had both (27.4%). There were 326 singleton and 54 multiple pregnancies. Overall, the complication rate was high: 8.7% pre-eclampsia, 6.1% gestational diabetes, 20.2% preterm delivery and 8.2% very preterm delivery (before 33 weeks), 44.8% Cesarean sections and 7.4% severe postpartum hemorrhage (PPH). The pre-eclampsia rate differed significantly between the groups (3.8% after no IVF, 10.0% after IVF only and 19.2% after IVF with oocyte donation,  $P < 0.001$ ). After adjustment, the risk of pre-eclampsia was significantly higher in women with donated oocytes compared with pregnant women without IVF [adjusted OR = 3.3 (1.2–8.9)]. The rate of twin pregnancy was significantly higher in women with IVF and oocyte donation (39.4 versus 15.0% with IVF only and 2.5% without IVF,  $P < 0.001$ ). Twin pregnancy was significantly associated with the risk of preterm delivery [adjusted OR = 8.9 (4.0–19.9)] and PPH [adjusted OR = 3.5 (1.3–9.5)].

**CONCLUSION:** In women aged 43 years or older, pregnancies obtained by IVF with oocyte donation are associated with higher rates of pre-eclampsia and twin pregnancies than those obtained without IVF or with IVF using their own oocytes.

**Table II Complications according to mode of conception: univariate analysis.**

	<b>No IVF (n = 236)</b>	<b>IVF without oocyte donation (n = 40)</b>	<b>IVF with oocyte donation (n = 104)</b>	<b>P</b>
Pre-eclampsia	9 (3.8)	4 (10.0)	20 (19.2)	<0.001 <sup>a</sup>
Gestational diabetes	12 (5.1)	3 (7.5)	8 (7.7)	0.494 <sup>a</sup>
Cesarean <sup>c</sup>	86 (37.9)	16 (42.1)	62 (61.4)	0.001 <sup>b</sup>
PPH	11 (4.7)	2 (5.0)	15 (14.4)	0.008 <sup>a</sup>
Preterm delivery <37 weeks <sup>c</sup>	34 (15.0)	10 (26.2)	30 (29.7)	0.006 <sup>b</sup>
Preterm delivery <33 weeks <sup>c</sup>	15 (6.6)	2 (5.3)	13 (12.9)	0.152 <sup>a</sup>
Birthweight <1000 g <sup>c</sup>	5 (2.1)	0	6 (4.2)	0.340 <sup>a</sup>
Birthweight <2500 g <sup>c</sup>	40 (17.2)	14 (31.8)	54 (38.0)	<0.001 <sup>b</sup>
IUFD <sup>d</sup>	5 (2.1)	1 (2.5)	1 (1.0)	0.728 <sup>a</sup>

IUFD, *in utero* fetal death; TOP, termination of pregnancy.

<sup>a</sup>Fisher's exact test comparing the three modes of conception.

<sup>b</sup> $\chi^2$  test comparing the three modes of conception.

<sup>c</sup>IUFD and TOP excluded.

<sup>d</sup>Onset in at least one fetus in each multiple pregnancy.

*Los autores postulan un factor inmunológico como causa de estos resultados: embrión como implante alogénico total.*

**Table I** Population characteristics according to mode of conception.

	<b>No IVF (n = 236)</b>	<b>IVF without oocyte donation (n = 40)</b>	<b>IVF with oocyte donation (n = 104)</b>	<b>P</b>
Maternal age (mean $\pm$ SD)	44.1 $\pm$ 1.4	44.0 $\pm$ 1.4	46.2 $\pm$ 2.9	<0.001
43 years (n, %)	102 (43.2)	18 (45.0)	19 (18.3)	
44 years	70 (29.7)	14 (35.0)	14 (13.5)	
45 years	35 (14.8)	2 (5.0)	14 (13.5)	
46 years	13 (5.5)	3 (7.5)	17 (16.5)	
47 years and older	16 (6.8)	3 (7.5)	40 (38.5)	<0.001
Geographic origin (n, %)				
France	118 (50.0)	24 (60.0)	70 (67.3)	
Other European countries	21 (8.9)	4 (10.0)	10 (9.6)	
Africa	66 (28.0)	6 (15.0)	12 (11.5)	
Asia	5 (2.1)	2 (5.0)	4 (3.9)	
Other	26 (11.0)	4 (10.0)	8 (7.7)	0.051
Parity (mean $\pm$ SD)	1.4 $\pm$ 1.4	0.9 $\pm$ 1.1	0.3 $\pm$ 0.6	<0.001
Nulliparity (n, %)	78 (33.2)	16 (40.0)	82 (78.9)	<0.001
Type of pregnancy (n, %)				
Singleton	230 (97.5)	34 (85.0)	62 (59.6)	
Twin	6 (2.5)	6 (15.0)	41 (39.4)	
Triplet	0	0	1 (1.0)	<0.001



# The aged uterus: multifetal pregnancy outcome after ovum donation in older women

Michal J. Simchen<sup>1,3</sup>, Adrian Shulman<sup>2</sup>, Amir Wiser<sup>2</sup>, Eran Zilberberg<sup>1</sup>, and Eyal Schiff<sup>1</sup> *Human Reproduction, Vol.24, No.10 pp. 2500–2503, 2009*

**Table I** Maternal characteristics: ovum recipient pregnant women aged  $\geq 40$  years and controls (women with twin pregnancies)

	Ovum recipient women with twins (n = 42)	Ovum recipient women with singletons (n = 83)	P-value (study twins versus study singletons)	Controls (n = 417)	P-value (study twins versus control twins)
Mean maternal age (years $\pm$ SD)	49.2 $\pm$ 4.3	49.3 $\pm$ 4.7	NS	31.6 $\pm$ 6.5	<0.001
Diabetes	13 (31%)	24 (29%)	NS	30 (7.3%)	<0.001
Hypertension	21 (50%)	35 (42%)	NS	38 (9.1%)	<0.001
Hospitalization	29 (69%)	39 (47%)	0.03	58 (13.9%)	<0.001
Cesarean delivery	41 (98%)	75 (89%)	NS	273 (65.5%)	<0.001

SD, standard deviation; NS, not significant.

Mayor incidencia de Hipertensión y DBT gestacional en ambas poblaciones. Mayores tiempos de hospitalización en gemelares.

Menor peso al nacer gemelares vs gemelares de población gral.

**Table II** Pregnancy outcome for advanced age women after ovum donation (n = 42) compared with 417 controls

	Study group (n = 42)	Control group (n = 417)	P-value
Gestational age at delivery (wks $\pm$ SD)	35.19 $\pm$ 2.3	35.67 $\pm$ 2.6	0.039
Delivery $\leq 34$ weeks	15 (35.7%)	91 (21.8%)	0.06
Mean birthweight (g)	2149 $\pm$ 474	2289 $\pm$ 585	0.02
Low birthweight <2500 g	53/83 neonates (77.1%)	503/834 neonates (60.3%)	0.004
Very low birthweight <1500 g	6/83 neonates (7.2%)	78/834 neonates (9.4%)	NS
SGA	14/83 neonates (16.9%)	89/834 neonates (10.7%)	NS
At least one SGA infant	12 (28.6%)	83 (19.9%)	NS

wks, gestational weeks; SD, standard deviation; SGA, small for gestational age, birthweight less than the 10th percentile corrected for multiplicity and gender (Dollberg *et al.*, 2005); NS, not significant.



# The ageing ovary and uterus: new biological insights

S.M. Nelson<sup>1,\*</sup>, E.E. Telfer<sup>2</sup>, and R.A. Anderson<sup>3</sup>



## 1-Deterioro en el desarrollo placentario y desidualización:

- ⌘ Demostrado por estudios básicos en ratas.
- ⌘ Mayor peso placentario por hipertrofia compensatoria.
- ⌘ Reducción de los receptores de estrógeno y progesterona con incremento de la fibrosis y del colágeno.

## 2- Alteración de la función miometrial:

- ⌘ Mayor riesgo de cesárea intraparto y parto operatorio en mujeres mayores de 40 comparadas con las menores.
- ⌘ Correlación negativa entre edad materna y actividad espontánea.
- ⌘ Cambios ultraestructurales de la fibra del músculo miometrial con inclusiones citoplasmáticas, disociación de microfilamentos, destrucción mitocondrial y del Retículo endoplasmático.

*Los autores hipotizan que la exposición a ciclos de alza y caída de los esteroides sexuales es lo que lleva a un deterioro de la función miometrial / endometrial y serían la base biológica para los resultados observados en mujeres mayores de 40 años.*

# Edad & fertilidad masculina



- ❖ Fertilidad masculina natural
- ❖ Resultados de los ciclos de FIV según edad paterna.
- ❖ Asociación a patología genética o epigenética.
- ❖ Mecanismos de alteración en la fertilidad masculina.





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Review

## How to overcome male infertility after 40: Influence of paternal age on fertility



Stephanie Belloc<sup>a,1</sup>, Andre Hazout<sup>a,1</sup>, Armand Zini<sup>b,2</sup>, Philippe Merviel<sup>c,3</sup>,  
Rosalie Cabry<sup>c,3</sup>, Hikmat Chahine<sup>d,4</sup>, Henri Copin<sup>c,3</sup>, Moncef Benkhalifa<sup>c,\*</sup>

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<sup>d</sup> Andrology Unit, ForteBio Laboratory, 16 Rue Fusillés, 40100 Dax, France

- ❖ Asociación entre edad paterna y peores parámetros seminales (volumen, conteo espermático, motilidad y morfología), función endocrina y sexual.
- ❖ Menor tasa de embarazo e incremento de la tasa de aborto en embarazos espontáneos y logrados por Inseminaciones intrauterinas.
- ❖ En ciclos de FIV y Ovodonación, se observo menor porcentaje de desarrollo embrionario a 5to día en hombres mayores de 55 años. Asociado al daño del ADN espermático.
- ❖ Asociación de la edad paterna a defectos genéticos y epigeneticos.
- ❖ Estrategia medicas podrían mejorar la fertilidad masculina?

# Role of increased male age in IVF and egg donation: is sperm DNA fragmentation responsible?

Kathryn C. Humm, M.D.,<sup>a,b</sup> and Denny Sakkas, Ph.D.<sup>a</sup>

VOL. 99 NO. 1 / JANUARY 2013

- ❖ *Revisión de los efectos de la edad paterna en la fertilidad, tratamientos de fertilidad y salud de los hijos.*
- ❖ *Resultados controvertidos: pareciera que los efectos del ageing paterno se potencian o no según la edad materna.*
- ❖ *Volumen seminal seria el parámetro seminal afectado por el avance de la edad y molecularmente los mecanismos podrían ser el daño del ADN espermático, metilación del ADN espermático y estrés oxidativo.*
- ❖ *Asociación entre edad paterna y enfermedades genéticas/ epigenéticas/ multifactoriales que son foco de estudio en la actualidad.*





**TABLE 1**

**Brief overview of selected studies examining the effect of paternal age on outcomes in both natural conception and assisted reproductive technologies as well as the reported paternal age threshold of interest.**

Study	Number	Maternal age	Observed paternal age effect	Age threshold (y)
Natural conception				
Ford 2000 (11)	8,515 couples	Adjusted for maternal age	Time to conception greater in men $\geq 40$ y	$\geq 40$
Dunson 2002 (13)	782 couples	Adjusted for maternal age	Fertility lower in men $>35$ y	$>35$
Hassan 2003 (12)	2,112 pregnant women	Adjusted for maternal age and subgroup analysis of women $<25$ y	Men $>45$ y with longer time to conception	$>45$
Intrauterine insemination				
Mathieu 1995 (21)	901 cycles	Adjusted for maternal age	Pregnancy rate lower in men $\geq 35$ y	$\geq 35$
Belloc 2008 (15)	17,000 cycles	Paternal age independent of maternal age	Pregnancy rate lower in men $\geq 45$ y	$\geq 45$
Bellver 2008 (23)	2,204 cycles	Adjusted for maternal age	No effect	–
IVF and/or ICSI with autologous oocytes				
Spandorfer 1998 (25)	398 couples	Subgroup analysis of women $<35$ y	No effect	–
Klonoff-Cohen 2004 (18)	221 cycles	Adjusted for maternal age	Live birth rate lower in men $>40$ y	$>40$
De La Rochebrochard 2006 (24)	1,938 couples	Adjusted for maternal age	Likelihood of conception lower in men $\geq 40$ y	$\geq 40$
Aboulghar 2007 (53)	545 couples	Subgroup analysis of women $<40$ y	Fertilization rate lower in men $>50$ y; no effect on pregnancy rate	$>50$
Ferreira 2010 (17)	1,024 couples	Adjusted for maternal age	Pregnancy rate lower with each year of advancing paternal age in oligozoospermic men only	–
IVF and/or ICSI with donor oocytes				
Gallardo 1996 (28)	345 cycles	Donor population; not adjusted for recipient age	No effect	–
Paulson 2001 (27)	558 cycles	Donor population, not adjusted for recipient age	No effect	–
Frattarelli 2008 (19)	1,023 cycles	Donor population; not adjusted for recipient age	Live birth rate lower in men $>50$ y	$>50$
Bellver 2008 (23)	1,412 cycles	Donor population; not adjusted for recipient age	No effect	–
Luna 2009 (16)	672 cycles	Donor population; not adjusted for recipient age	Implantation rate lower in men $>60$ y	$>60$
Whitcomb 2012 (26)	1,083 couples	Donor population; adjusted for recipient age	No effect	–

Humm. *Impact of advanced male age on ART. Fertil Steril* 2013.



Hum Reprod. 2016 Mar;31(3):582-90.

**Does age of the sperm donor influence live birth outcome in assisted reproduction?**

Ghuman NK<sup>1</sup>, Mair E<sup>2</sup>, Pearce K<sup>3</sup>, Choudhary M<sup>4</sup>.

Of 46 078 women, 84.6% (N = 38 974) underwent donor insemination treatment and the remainder, 15.4% (N = 7104), had IVF/ICSI treatment with donor sperm. The live birth occurrence decreased with increasing female age in both treatment groups; In the donor insemination treatment group, it was 11.1% in 18-34 year old women, 8.3% in 35-37 year old women and 4.7% in 38-50 year old women. The corresponding figures in the IVF/ICSI treatment group were 28.9, 22.0 and 12.9% respectively. In each of these subgroups, no evidence of declining likelihood of live birth with increasing sperm donor age was found ( $P > 0.05$ ). The miscarriage occurrence (i.e. number of miscarriages per 100 women commencing treatment) was 1.3% in 18-34 year old women, 1.9% in 35-37 year old women and 1.9% in 38-50 year old women undergoing donor insemination treatment. In the sperm donation IVF/ICSI treatment group, these figures were 5.7, 8.4 and 6.8% respectively. The results were not suggestive of any unfavourable effect of advancing sperm donor age on the odds of miscarriage occurrence ( $P > 0.05$ )



# Enfoque sociocultural del fenómeno

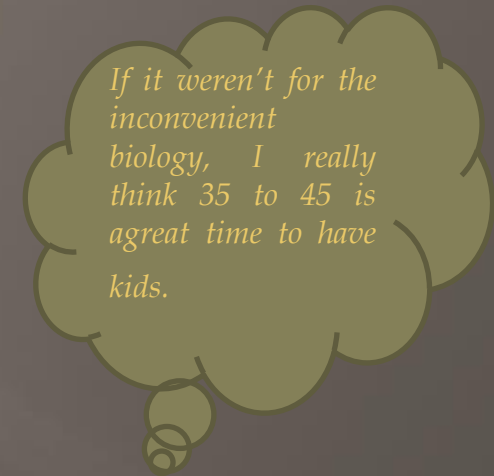
La postergación de la maternidad es un fenómeno mundial asociado a la participación de la mujer en el mundo laboral, que prioriza su carrera y sus objetivos económicos.



# 'Inconvenient biology:' advantages and disadvantages of first-time parenting after age 40 using *in vitro* fertilization

K. Mac Dougall<sup>1</sup>, Y. Beyene<sup>1</sup>, and R.D. Nachtigall<sup>1,2,\*</sup>

Human Reproduction, Vol.27, No.4 pp. 1058–1065, 2012



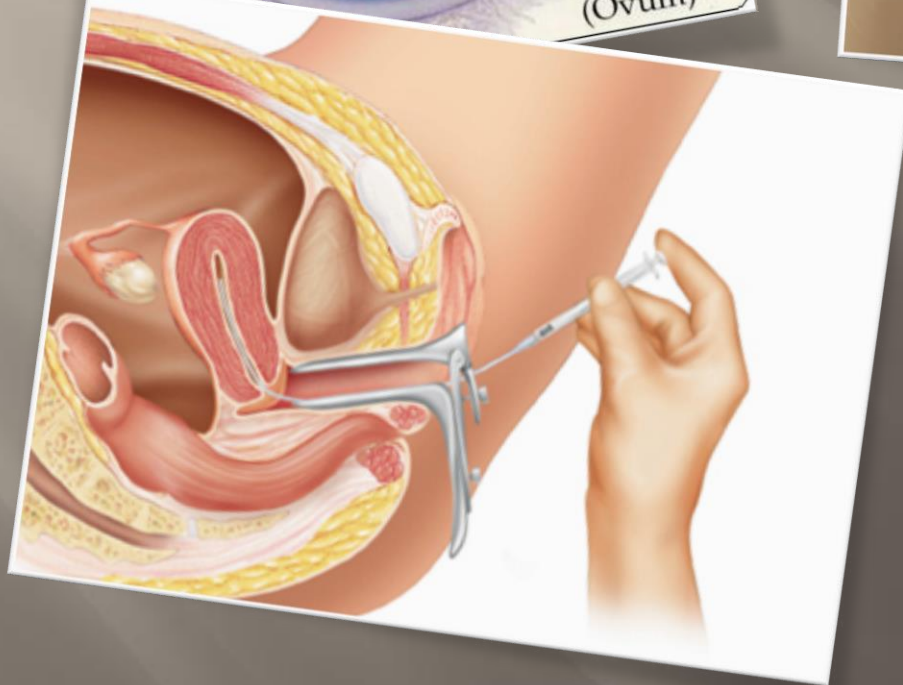
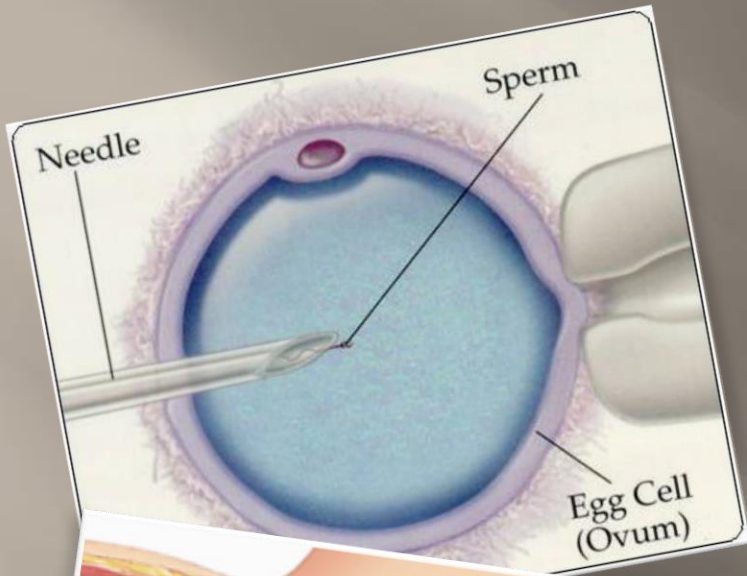
**Table II** Advantages of first-time parenting over age 40 using IVF.

	Women (n = 65), (%)	Men (n = 42), (%)
Emotional preparedness	72	57
Career/work flexibility	43	31
Financial security	31	36
Perception of strong Partner/ family Relationships	22	12

**Table III** Disadvantages of first-time parenting over age 40 using IVF.

	Women (n = 65), (%)	Men (n = 42), (%)
Infertility and the need for IVF	48	17
Less energy	38	26
Less lifetime with children	31	19
Smaller family size	17	2
Stigma of being 'Older Parents'	12	19





*Posibilidades terapéuticas*

## **A Randomized Clinical Trial to Determine Optimal Infertility Treatment in Older Couples: The Forty and Over Treatment Trial (FORT-T)**

**Marlene B. Goldman, Sc.D.a,b, Kim L. Thornton, M.D.c, David Ryley, M.D.c, Michael M. Alper, M.D.c, June L. Fung, Ph.D.a, Mark D. Hornstein, M.D.d, and Richard H. Reindollar, M.D.a,e**

*Fertil Steril.* 2014 June ; 101(6): 1574–81.

**Patients** – Couples with  $\geq 6$  months of unexplained infertility; female partner aged 38–42.

**Interventions** – Randomized to treatment with 2 cycles of clomiphene citrate (CC) and intrauterine insemination (IUI), follicle stimulating hormone (FSH)/IUI, or immediate IVF, followed by IVF if not pregnant.

**Main Outcome Measures** – Proportion with a clinically recognized pregnancy, number of treatment cycles, and time to conception after 2 treatment cycles and at the end of treatment.

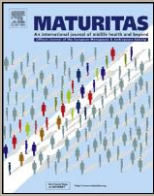
**Results** – 154 couples were randomized to receive CC/IUI (N=51), FSH/IUI (N=52), or immediate IVF (N=51); 140 (90.9%) couples initiated treatment. Cumulative clinical pregnancy

rates per couple after the first 2 cycles of CC/IUI, FSH/IUI, or immediate IVF were 21.6%, 17.3%, and 49.0%, respectively. After all treatment, 71.4% (110/154) of couples conceived a clinically recognized pregnancy and 46.1% delivered at least one live-born baby. 84.2% of all live born infants resulting from treatment were achieved from IVF. There were 36% fewer treatment cycles in the IVF arm compared to either COH/IUI arm and couples conceived a pregnancy leading to a live birth after fewer treatment cycles.

**Conclusions** – An RCT to compare treatment initiated with 2 cycles of COH/IUI to immediate IVF in older women with unexplained infertility demonstrated superior pregnancy rates with fewer treatment cycles in the immediate IVF group.







## Management of infertility in women over 40

Rosalie Cabry<sup>a,1</sup>, Philippe Merviel<sup>a,1</sup>, Andre Hazout<sup>b,2</sup>, Stephanie Belloc<sup>b,2</sup>,  
Alain Dalleac<sup>b,2</sup>, Henri Copin<sup>a,1</sup>, Moncef Benkhalifa<sup>a,\*</sup>

R. Cabry et al. / Maturitas 78 (2014) 17–21

### Resultados con IVF

- Punto de cohorte para la implementación de la técnica los 44 años.*
- Factor pronostico de embarazo y RN en casa mas importante: n de ovocitos > a 5.*
- Afianza a los marcadores de reserva ovárica como predictores del número de ovocitos a recuperar mientras que edad sigue siendo el principal factor pronostico de RN en casa.*
- No determina un esquema de estimulación ovárica como el mas apropiado, recomendando estimulación media en pacientes de pobre respuesta.*
- Estimula transferencia de mas de 3 embriones para aumentar la tasa de embarazo.*

**Table 1**

Relation between the number of collected oocytes and clinical outcome from patients over 40's after a minimum of 2-repeated IVF/ICI failure.

Number of collected complex cumulus cells	≤5 Oocytes	6-14	≥15
Average maternal age (year)	41.5 ± 1.1a	41 ± 1c	40.7 ± 0.8b
Average paternal age (year)	42.3 ± 5.7	41.7 ± 5.6	41.2 ± 5.9
Infertility duration (year)	3.4 ± 1.8d	4 ± 3.2f	5.5 ± 4e
Day 3 FSH level (UI/l)	8 ± 2.7g	6.8 ± 2.1i	6.5 ± 1.6h
<b>Number of cycles</b>	<b>181</b>	<b>260</b>	<b>59</b>
Rank of attempt	2.2 ± 1.3j	2.5 ± 1.5k	2.6 ± 1.5
Total administrated FSH (UI)	5055 ± 1545o	3667 ± 151q	2953 ± 1142p
Oestradiol the day of hCG (pg/ml)	1446 ± 363r	2101 ± 960	2685 ± 375s
Cancellation rate (%)	23.2	11.1	6.7
<b>Completed cycles via OPU</b>	<b>139</b>	<b>231</b>	<b>55</b>
Average collected cumulus	3.4 ± 1.3u	9.3 ± 2.5w	18.8 ± 3.6v
Average métaphase II	2.5 ± 1.4u	7 ± 2.9w	13.7 ± 4.4v
Fertilization rate (%)	46.4	51.6	48.9
Cleavage rate (%) 50.1	50.1	54.4	50.5
Mean transferred embryos/transfer	1.7 ± 1a'	2.2 ± 1c'	2.5 ± 1b'
<b>Clinical pregnancy/transfer (%)</b>	<b>7.9d'</b>	<b>21.7e'</b>	<b>18.7</b>
Implantation rate/embryo (%)	5	10.4	7.4
<b>Ongoing pregnancy/transfer (%)</b>	<b>3.4f'</b>	<b>11.1g'</b>	<b>10.4</b>
<b>Live birth/transfer (%)</b>	<b>2.2h'</b>	<b>10.1i'</b>	<b>6.2</b>

a-c: < 0.0001; a-b: < 10<sup>6</sup>; b-c: < 0.02; d-f: < 0.03; d-e: < 0.001; f-e: < 0.01; g-i: < 10<sup>4</sup>; g-h: < 10<sup>4</sup>; j-k: < 0.05; o-q: < 10<sup>9</sup>; o-p: < 10<sup>9</sup>; r-t: < 10<sup>9</sup>; t-s: < 10<sup>9</sup>; r-s: < 10<sup>9</sup>; u-w et w-v et u-v: < 10<sup>9</sup>; a'-c': < 0.0001; a'-b': < 10<sup>4</sup>; d'-e': < 0.01; f'-g': < 0.05; h'-i': < 0.05; j'-k': < 10<sup>9</sup>.

# Ovo donación

❖ Se presenta como el tratamiento con mayores chances de éxito:

53% tasa de embarazo

42 % tasa de recién nacido vivo

94% tasa de embarazo acumulativa luego de 4 transferencias.

Remohi et al .Pregnancy and birth rates after oocyte donation. Fertil Steril 1997

❖ Influencia de la edad en la tasa de implantación que se ve reducida en mayores de 45 años.

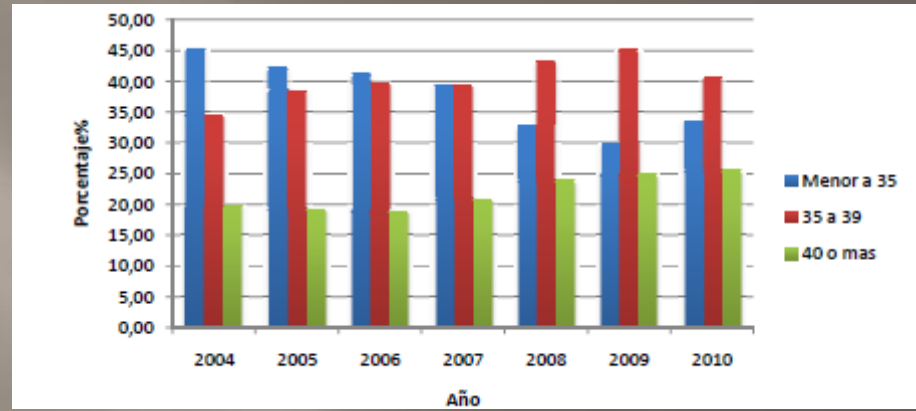
❖ Complicaciones obstétricas por encima de los 50 años rondan el 50 %

❖ punto de cohorte para la implementación de la técnica muy difícil de determinar

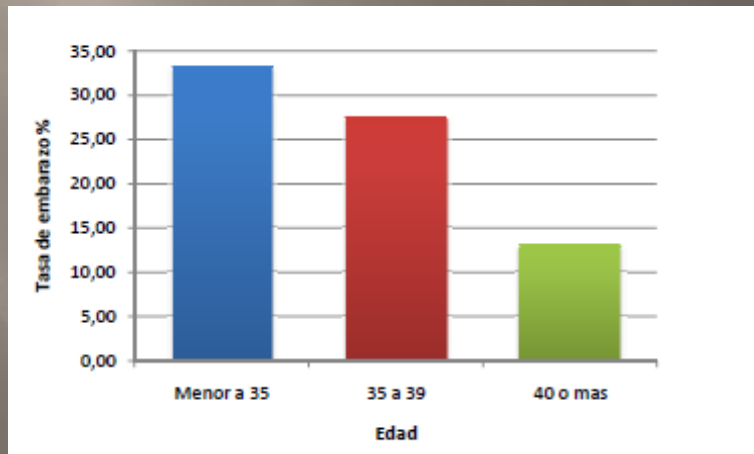
## Resultados con la Inseminación Intrauterina

*En base a resultados de distintos estudios, siendo del 10 % las mejores tasa de embarazo y mostrando un caída muy importante en esta tasa luego de los 42 años, los autores no recomiendan esta practica como primer estrategia a utilizar en pacientes por encima de 40 años.*

## Experiencia Argentina. RAFA 2004-2010.



En los primeros años (2004-2006), el grupo más prevalente era el de las mujeres menores de 35 años. Es importante resaltar que el grupo de pacientes mayores de 40 años que realizaron procedimientos de reproducción asistida fue aumentando en forma constante a lo largo del periodo analizado.



Tasa Embarazo < 35 años = 33.3%

Tasa Embarazo 35 – 39 años = 27.5%

Tasa Embarazo > 40 años = 13.1%

Las mejores tasas de embarazo en mayores de 40 años se dieron en los casos de factor masculino.



# Consideraciones éticas y legales

- ▣ Ley Nacional n° 12682 de Fertilización Asistida.
- ▣ Ley Provincial n° 14.611 de adecuación de Fertilización Asistida de la Provincia de Buenos Aires.
- ▣ Postura SAMER ante la edad de la receptora de ovo donación de 50 años o menos.



# Reseña histórica de la ovodonación.



- 1984 Inicio en el mundo de la OD (Trounson y cols).
- 1993 Argentina comienzan los ciclos de OD con pacientes que cedieron sus óvulos luego de tratamientos realizados por ellos mismos.
- 2003 comienzan a hacerse ciclos con donantes exclusivas.
- En algunos centros llega al 35 % de los tratamientos de alta complejidad.

**Tasa de embarazo de ciclos frescos: 45 %**

# ovodonacion



## Tipo de Donaciones

***Donante anónima.***

***Donante conocida.***

***Ovocitos donados por pacientes de FIV.***

***Banco de óvulos.***

## Condiciones de la Donación

***Única o compartida***

***Altruista.***

Muchas Gracias por su atension

