Journée Jean Cohen
Paris Novembre 2013

Le Mot Du Président

L’Etat de la France et AMP

Au Début…

Les Visionnaires

Evidence-based medicine and its application in clinical preimplantation embryology

Jacques Cohen [a,*], Mina Alikani [b]

Reproductive BioMedicine Online (2013) 27, 547–561

Table 1 The use of preclinical animal research and systematic reviews in clinical embryology technologies.

Procedure	*Year first introduced clinically*	*Animal studies*	*Status today*	*RCT efficacy controversy*	*Systematic reviews*	*Systematic review conclusions*		
						Implantation	*Pregnancy*	*Live Birth*
IVF/embryo transfer	1976	Yes	In use	No	No		–	
Slow Freezing	1983	Yes	In decline	No	No		–	
PZD	1988	Yes	Not in use	Yes	No		–	
SUZI	1989	Yes	Not in use	Yes	No		–	
Assisted hatching	1990	Yes	In use	Yes	Yes	No conclusion	Increased[a]	Unchanged[a]
Co-culture	1989	Yes	Limited use	Yes	Yes	Increased	Increased	No conclusion
PGD	1990	No	In use	No	No		–	
PGS	1991	No	In use	Yes	Yes	FISH combined with day-3 biopsy—decreased		
ICSI	1992	No	In use	No	No		–	
Blastocyst transfer	1998	Yes	In use	Yes	Yes	No conclusion	No conclusion	Increased
Low oxygen culture	1999	Yes	In use	Yes	Yes	Increased	Increased	Increased
Embryo vitrification[b]	2002	Yes	In use	Yes	Yes	Increased	Increased	Increased
IVM	1996	Yes	Limited use	Yes	No		–	
Embryo glue	2002	Yes	In use	Yes	No		–	
IMSI	2001	No	In use	Yes	Yes	Increased	Increased	No conclusion
PICSI	2006	No	In use	Yes	No		–	

ICSI = intracytoplasmic sperm injection; IMSI = intracytoplasmic morphologically selected sperm injection; IVM = in-vitro maturation; PGD = preimplantation genetic diagnosis; PGS = preimplantation genetic screening; PICSI = physiological intracytoplasmic sperm injection; PZD = partial zona dissection; SUZI = subzonal insemination.

[a] See Tables 2 and 3.

[b] Versus slow freezing.

Et Depuis ? Questions Posées :

- Qualité de la Pratique
- Comparaisons Internationales
- Organisation de la Pratique
- Financement de la Pratique
- Utilisation et Indications de l'AMP
- Contexte Professionnel, Réglementaire et Politique

Qualité De La Pratique – Comparaisons Internationales

Réalité ou non d'une exception française

Human Reproduction, Vol.28, No.9 pp. 2318–2331, 2013
Advanced Access publication on July 9, 2013 doi:10.1093/humrep/det278

human reproduction

ORIGINAL ARTICLE *ESHRE pages*

Assisted reproductive technology in Europe, 2009: results generated from European registers by ESHRE†

A.P. Ferraretti*, V. Goossens, M. Kupka, S. Bhattacharya, J. de Mouzon, J.A. Castilla, K. Erb, V. Korsak, and A. Nyboe Andersen, The European IVF-monitoring (EIM)‡, Consortium, for The European Society of Human Reproduction and Embryology (ESHRE)

Table I ART in European countries in 2009.

	IVF clinics in the country		Treatment cycles								Cycles/million[a]	
	Total	Reporting	IVF	ICSI	FER	ED	IVM	PGD	FOR	All	Women 15–45	Population
France	106	106	21 123	35 111	17 153	641	54	393		74 475	6022	1153
All	1179	1005	135 621	266 084	104 153	21 604	1334	4389	4278	537 463	5455	1067

Table II Results after ART in 2009.

Country	Initiated cycles IVF + ICSI	IVF			ICSI			FER			ART infants[a]	ART infants per national births (%)
		Aspirations	Pregnancies per aspiration (%)	Deliveries per aspiration (%)	Aspirations	Pregnancies per aspiration (%)	Deliveries per aspiration (%)	Thawings FER	Pregnancies per thawing (%)	Deliveries per thawing (%)		
France		21 123	23.9	18.9	35 111	26.4	20.8			13.3	16 074	1.9
All[b]	348 111	126 793	28.9	20.6	256 651	28.7	19.3	77 799	20.9	13.3	109 239	

Table III Number of embryos transferred and deliveries after ART in 2009.

Country	IVF + ICSI								FER		
	Transfers	1 embryo (%)	2 embryos (%)	3 embryos (%)	4+ embryos (%)	Deliveries	Twin (%)	Triplet (%)	Deliveries	Twin (%)	Triplet (%)
France	47 822	27.1	61.8	10.3	0.8	11 292	18.0	0.3	2287	9.9	0.3
All[a]	340 799	24.2	57.7	16.9	1.2	72 327	19.4	0.8	13 369	12.7	0.3

Table IV IUI-H or IUI-D semen in 2009.

Country	IUI-H						IUI-D					
	Cycles	Deliveries	Deliveries (%)	Singleton (%)	Twin (%)	Triplet (%)	Cycles	Deliveries	Deliveries (%)	Singleton (%)	Twin (%)	Triplet (%)
France	52 851	5044	9.5	89.5	10.2	0.3	3890	612	15.7	88.9	10.8	0.3
All[a]	162 843	11 015	8.3	88.9	10.4	0.7	29 235	2455	13.4	89.2	10.3	0.5

Update on the comparison of assisted reproduction outcomes between Europe and the USA: the 2002 data

Norbert Gleicher, M.D.,[a,b] *Andrea Weghofer, M.D., Ph.D,*[a,c] *and David Barad, M.D., M.S.*[a,d]

Fertility and Sterility® Vol. 87, No. 6, June 2007

TABLE 3

Pregnancy rates per oocyte retrieval and per embryo transfer in nondonor cycles.

	Europe	Change from 2001, %	U.S.	Change from 2001, %
Oocyte retrievals (n)	241,107		75,519	
Embryo transfers (n)	218,475		69,857	
Pregnancies (n)	64,277		29 423	
Per retrieval (%)	26.7[a]	+0.5	39.5[a]	+1.3
Per transfer (%)	29.4[a]	+1.5	42.1[a]	+1.5

[a] $P<.0001$.

Gleicher. ART outcomes in Europe and the USA. Fertil Steril 2007.

TABLE 2

Number of embryos transfered.

	Percentage of patients			
No. of embryos	Europe	Change from 2001, %	U.S.	Change from 2001, %
1	13.7	+1.3	6.7	+0.5
2	54.8	+3.1	31.6	+4.3
3	26.9	−3.9	33.6	−0.9
≥4	4.7	−1.1	28.1	−3.8

Gleicher. ART outcomes in Europe and the USA. Fertil Steril 2007.

Factors affecting success rates in two concurrent clinical IVF trials: an examination of potential explanations for the difference in pregnancy rates between the United States and Europe

Valerie L. Baker, M.D.,[a] *Clarence E. Jones, Ph.D.,*[b] *Barbara Cometti, Ph.D.,*[b] *Fred Hoehler, Ph.D.,*[c] *Bruno Salle, M.D., Ph.D., D.Sc.,*[d] *János Urbancsek, M.D.,*[e] *and Michael R. Soules, M.D.*[f]

Fertility and Sterility® Vol. 94, No. 4, September 2010

TABLE 4

Pregnancy outcomes in the US and European trials.

Variable	US	Europe	*P* value
Gestational sac	46.7%	30.3%	.004
Fetal heartbeat	43.4%	29.7%	.016
Live birth	38.2%	27.6%	.064
Multiple birth	37.9%	22.5%	.126
Implantation rate	35.4%	16.5%	<.001
Successful implantation rate	25.9%	14.0%	.001

Notes: The denominator for the clinical pregnancy and live birth rates is all treated patients (n = 152 for US, n = 145 for Europe). Multiple birth rates were calculated by dividing the number of patients with a multiple live birth by the total number of patients with a live birth (n = 58 for US, n = 40 for Europe). Implantation rate was calculated by dividing the number of gestational sacs by the number of embryos transferred. Successful implantation rate was calculated as the number of babies born divided by the total number of embryos transferred (n = 309 for US, n = 357 for Europe).

Baker. Comparison of 2 IVF trials (US, Europe). Fertil Steril 2010.

TABLE 2

Comparison of baseline characteristics in the US and European trials for those volunteers who received at least one dose of FSH.

	US	Europe
Number of patients treated	152	145
Completed study	135	135
Canceled prior to hCG[a]	11	3
Canceled after retrieval[b]	6	7
Age[c]	34.6 (3.1, 25.6–39.9)	30.4 (3.8, 21.5–39.4)
BMI	23.6 (3.13, 18.3–30.0)	23.5 (3.38, 17.0–33.0)
Duration of infertility (years)[c]	3.1 (2.3, 0.3–14.0)	4.0 (2.1, 1.0–13.0)
Previous pregnancies	40.1%	31.7%
Prior IVF cycle[c]	9.2%	37.9%
Prior IUI cycle[c]	52.6%	11.0%
Male factor infertility[c]	50.0%	96.6%
Tubal factor infertility	21.1%	24.1%
Baseline FSH	6.4 (1.5, 0.7–10.0)	6.0 (2.2, 1.1–19.3)
Baseline estradiol (pg/mL)[c]	41.2 (19.3, 10–126)	68.4 (57.2, 11–325)
Prolactin (ng/mL)[c]	12.8 (7.1, 1–43)	19.3 (22.6, 1–228)
Endometrial thickness at baseline (mm)[c]	3.4 (1.1, 1.3–8.0)	4.1 (1.3, 1.0–9.0)

Notes: When means are expressed, standard deviation and range are listed in parentheses. BMI = body mass index.

[a] Reasons for cancellation in the US study prior to hCG included risk of OHSS (n = 1), uterine polyp (n = 1), poor ovarian response (n = 9). Reasons for cancellation in the European study prior to hCG included risk of OHSS (n = 1) and poor ovarian response (n = 2).

[b] Reasons for cancellation in the US study after oocyte retrieval included no oocytes retrieved (n=1), risk of OHSS (n = 1), no fertilization (n = 3), and no progression of embryo (n = 1). Reasons for cancellation in the European study after oocyte retrieval included risk of OHSS (n = 3), no fertilization (n = 3) and no progression of embryo (n = 1).

[c] Denotes statistically significant difference between studies ($P \leq .05$).

Baker. Comparison of 2 IVF trials (US, Europe). Fertil Steril 2010.

TABLE 3

Treatment variables in the US and European trials.

	US	Europe
Days of FSH treatment[a]	9.4 (1.5, 3–13)	10.7 (1.5, 8–18)
Total FSH dose (IU)[b]	2,678 (871, 900–5,550)	2,439 (793, 1,275–5,850)
Daily FSH dose (IU)[a]	282 (59, 142–427)	224 (47, 113–419)
Total number follicles[a]	21.2 (10.4, 4–67)	13.5 (4.7, 5–30)
Number follicles ≥15 mm	10.0 (5.0, 0–34)	11.0 (4.5, 0–30)
Cancellation prior to hCG[c]	7.2%	2.1%
Intramuscular hCG (not SQ)[a]	50.4%	73.9%
Total oocytes retrieved[a]	16.7 (9.3, 0–54)	11.5 (5.2, 0–32)
2 PN on day 1[a,e]	10.5 (5.5, 0–29)	6.2 (3.2, 1–17)
Total embryos (including fertilization noted on day 2)[a,e]	10.5 (5.2, 1–26)	7.2 (3.9, 1–19)
Fertilization rate (2 PN/oocytes exposed to sperm)	66.6%	70.1%
Embryos transferred[d,e]	2.3 (0.6, 0-5)	2.6 (1.0, 0–4)
Embryos frozen[a,e]	3.8 (3.9, 0–21)	2.1 (3.1, 0–17)
Day of embryo transfer[a]	3.5 (0.9, 2–6)	2.7 (0.7, 2–6)

Notes: Data are expressed as mean with standard deviation and range in parentheses. All other *P* values are >.05.

[a] $P < .001$.

[b] $P = .014$.

[c] $P = .053$.

[d] $P = .003$.

[e] Means are based on patients with at least one embryo (n = 136 US, n = 139 Europe).

Baker. Comparison of 2 IVF trials (US, Europe). Fertil Steril 2010.

A comparison of live birth rates and cumulative ongoing pregnancy rates between Europe and North America after ovarian stimulation with corifollitropin alfa or recombinant follicle-stimulating hormone

Robert Boostanfar, M.D.,[a] Bernadette Mannaerts, M.Sc.,[b] Samuel Pang, M.D.,[c] Manuel Fernandez-Sanchez, M.D.,[d] Han Witjes, Ph.D.,[b] and Paul Devroey, M.D., Ph.D.,[e] on behalf of the Engage Investigators

Fertility and Sterility® Vol. 97, No. 6, June 2012

Main clinical outcome including ongoing pregnancy rate and live birth rate after transfer of fresh embryos and cumulative pregnancy rate after transfer of fresh and frozen-thawed embryos per treatment group and continent.

	Corifollitropin alfa		rFSH		*P* value[a]	
	NA	EU	NA	EU	Treatment effect	Continent effect
Mean (SD) duration of stimulation (d)	9.4 (1.4)	9.8 (1.5)	9.0 (1.2)	9.4 (1.3)	<.01	<.01
Mean (SD) of total rFSH dose (IU) from day 8 onward	372.9 (279.6)	443.8 (320.6)	322.6 (236.5)	379.4 (277.8)	<.01	<.01
Mean (SD) no. of follicles ≥11 mm on day of hCG	16.4 (7.3)	15.5 (6.6)	14.5 (6.6)	13.2 (5.3)	<.01	<.01
Mean (SD) no. of oocytes	14.4 (8.7)	12.9 (7.6)	13.3 (7.5)	11.6 (5.6)	<.01	<.01
Mean (SD) no. of good-quality embryos	5.3 (4.6)	3.4 (3.7)	5.1 (4.4)	3.5 (3.0)	.62	<.01
Mean (SD) no. of fresh embryos transferred	1.9 (0.3)	1.5 (0.5)	1.9 (0.3)	1.5 (0.5)	.67	<.01
Single ET, %, n/N	7.6%, 28/368	47.7%, 145/304	11.1%, 42/380	45.7%, 148/324		
Mean (SD) no. of frozen embryos transferred	2.2 (0.8)	1.5 (0.5)	2.1 (0.6)	1.5 (0.6)	.61	<.01
Single ET, %, n/N	12.1%, 8/66	50.0%, 67/134	11.7%, 7/60	51.6%, 64/124		
Implantation rate of fresh embryos, n, mean (SD)	368, 39.6% (41.0%)	304, 32.1% (42.0%)	380, 36.8% (39.8%)	324, 26.7% (39.8%)	.07	<.01
Ongoing pregnancy rate after transfer of fresh embryos, %, n/N	45.4%, 182/401	31.5%, 112/355	45.7%, 184/403	29.4%, 102/347	.75[b]	<.01[b]
Ongoing pregnancy rate after transfer of fresh embryos, per ET, %, n/N	49.4%, 182/368	36.8%, 112/304	48.4%, 184/380	31.5%, 102/324	.28[c]	<.01[c]
Multiple pregnancies, %, n/N	34.6%, 63/182	17.9%, 20/112	28.8%, 53/184	12.7%, 13/102	.13[b]	<.01[b]
Live birth rate after transfer of fresh embryos, %, n/N	39.2%, 157/401	31.5%, 112/355	39.2%, 158/403	28.8%, 100/347	.63[b]	<.01[b]
Live birth rate after transfer of fresh embryos, per ET, %, n/N	42.7%, 157/368	36.8%, 112/304	41.6%, 158/380	30.9%, 100/324	.23[c]	.55[c]
Cumulative pregnancy rate after transfer of fresh and frozen embryos, %, n/N	53.1%, 213/401	40.6%, 144/355	51.9%, 209/403	36.9%, 128/347	.37[b]	<.01[b]

Note: ET = embryo transfer; other abbreviations as in Table 1.

[a] *P* values of estimated odds ratios (ORs) based on model including treatment group, continent, and age group (<32 y vs. ≥32 y) as factors.

[b] *P* values of estimated ORs based on model including treatment group, continent, age group, and previous IVF cycle (yes/no) as factors.

[c] *P* values of estimated ORs based on model including treatment group, continent, age group, previous IVF cycle, and number of embryos transferred (single vs. double) as factors.

Boostanfar. Live birth rate and corifollitropin alfa. Fertil Steril 2012.

Patient characteristics per treatment group and continent (intent-to-treat group).

	Corifollitropin alfa		rFSH	
	NA	**EU**	**NA**	**EU**
Age (y)				
n	401	355	403	347
Mean (SD)	31.7 (3.3)	31.4 (3.3)	31.7 (3.3)	31.3 (3.2)
Primary/secondary infertility, n (%)				
Primary infertility	196 (48.9)	207 (58.3)	200 (49.6)	193 (55.6)
Secondary infertility	205 (51.1)	148 (41.7)	203 (50.4)	154 (44.4)
Duration of infertility (y)				
n	401	355	403	346
Mean (SD)	3.6 (2.7)	3.1 (2.1)	3.5 (2.5)	2.9 (1.7)
Previous IVF cycle, n (%)				
No	343 (85.5)	226 (63.7)	342 (84.9)	210 (60.5)
Yes	58 (14.5)	129 (36.3)	61 (15.1)	137 (39.5)
AFC stimulation day 1				
n	401	343	403	335
Mean (SD)	12.4 (4.7)	12.2 (4.4)	12.8 (4.7)	11.9 (4.1)
FSH stimulation day 1 (IU/L)				
n	358	353	350	346
Median (P5, P95)	6.2 (4.2, 9.8)	6.5 (4.1, 10.8)	6.3 (4.1, 10.0)	6.5 (4.2, 10.3)

Note: AFC = antral follicle count; P5, P95 = 5th and 95th percentiles; EU = Europe; NA = North America.

Boostanfar. Live birth rate and corifollitropin alfa. Fertil Steril 2012.

International Committee for Monitoring Assisted Reproductive Technology: world report on assisted reproductive technology, 2005

Fernando Zegers-Hochschild, M.D.,[a] Ragaa Mansour, M.D., Ph.D.,[b] Osamu Ishihara, M.D., Ph.D.,[c] G. David Adamson, M.D.,[d] Jacques de Mouzon, M.D., M.P.H.,[e] Karl G. Nygren, M.D., Ph.D.,[f] and Elizabeth A. Sullivan, M.D., M.P.H.[g]

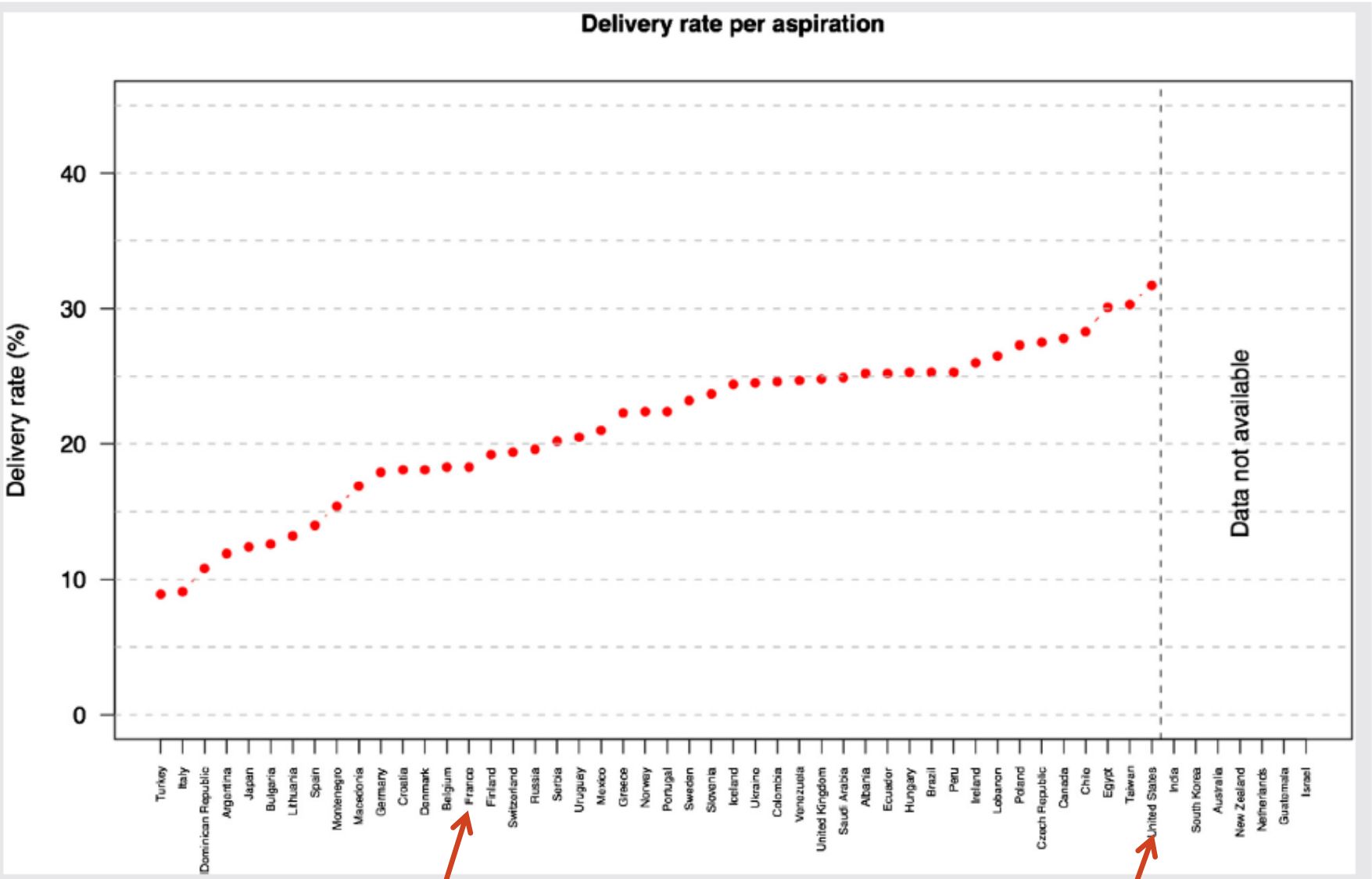
Fertility and Sterility® Vol. ■, No. ■, ■ 2013

IVF, ICSI, and FET results for 2005.

	IVF		ICSI		FET		IVF and ICSI				Total babies[a]	
							DR/Asp		Babies/Asp[b]			
Country	PR/Asp (%)	DR/Asp (%)	PR/Asp (%)	DR/Asp (%)	PR/FET (%)	DR/FET (%)	Fresh (%)	Cumul (%)[c]	Fresh (%)	Cumul (%)	Reported (n)[d,e]	Estimated (n)[e,f]
France	23.1	17.4	24.4	18.9	17.0	12.2	18.3	21.5	22.2	25.7	13,227	13,227
Total[j]	29.8	20.3	28.9	19.2	26.1	17.4	19.6	23.9	27.6	33.1	>165,836	>218,215
Region												
Asia	30.1	15.2	20.1	12.1	32.1	20.1	13.6	19.9	31.7	37.1	>8,691	>14,092
Australia/New Zealand	NA	NA	NA	NA	21.5	16.3	NA	31.6	24.9	36.4	9,355	9,355
Europe	26.9	19.0	28.5	17.0	19.7	13.5	17.7	20.8	22.5	26.9	80,956	98,337
Latin America	29.6	22.4	28.5	21.4	22.8	16.9	21.6	23.8	28.4	30.9	>8,146	>7,819
Middle East	30.5	25.6	38.2	29.5	33.4	23.2	29.4	32.2	39.7	41.8	3,345	20,578
Middle East (Israel)	NA	NA	NA	NA	216.5	0.2	NA	20.7	NA	NA	4,207	4,207
North America	40.5	32.8	38.1	30.6	35.2	27.4	31.4	38.0	42.1	50.4	51136	63,827

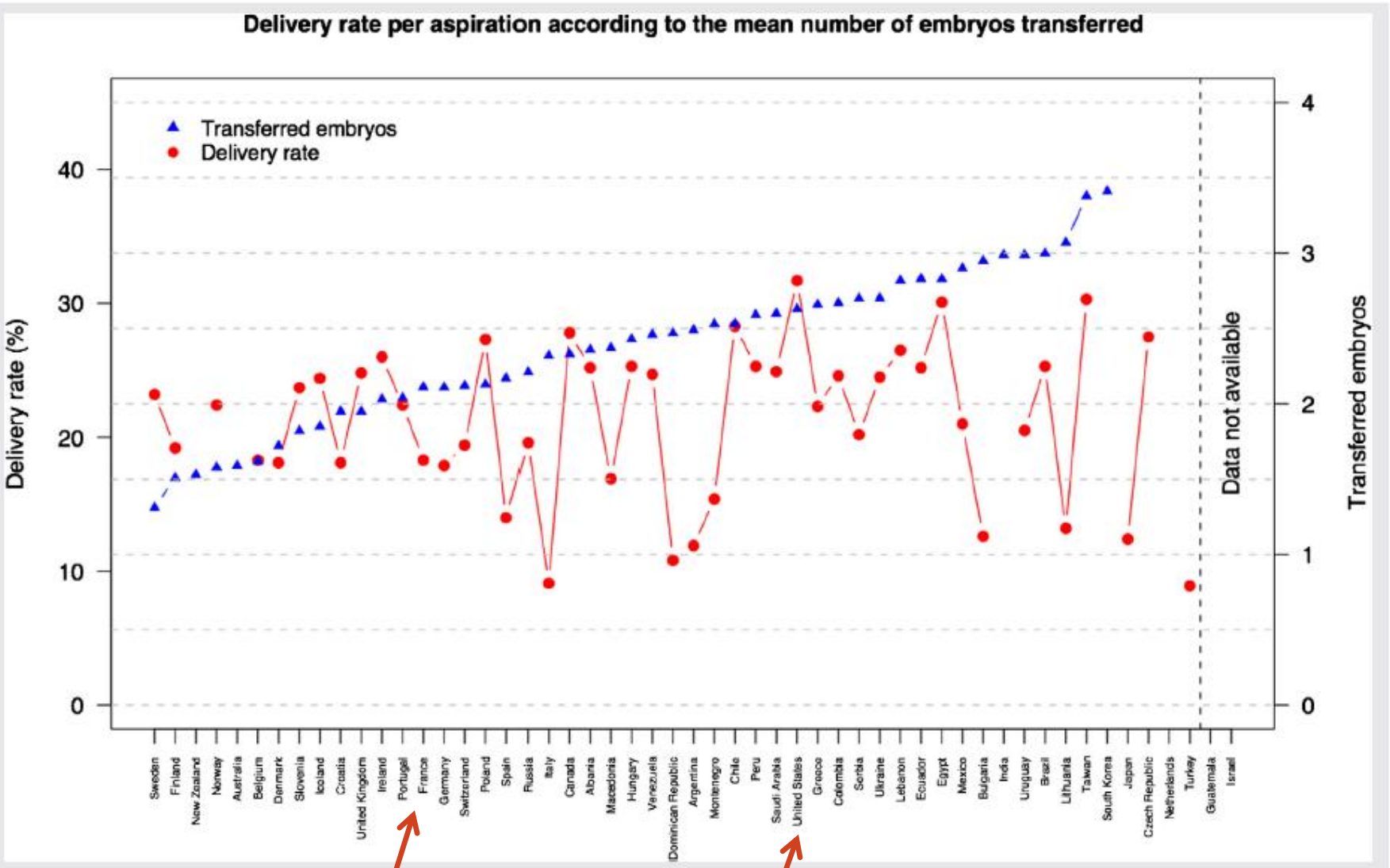
IVF and ICSI cycles: number of transferred embryos, efficacy, and safety for 2005.

	No. of transferred embryos (%)					Efficacy			Multiplicity	
Country	1	2	3	≥4	Average	PR/Asp (%)	Delivery/Asp (%)	Babies/Asp (%)[a]	Twin (%)	Triplet+ (%)
France	17.5	59.1	18.7	4.7	2.11	23.9	18.3	22.2	20.6	0.5
Total	17.5	48.3	24.4	9.8	2.29	28.5	19.7	27.6	23.6	1.5
Region										
Asia	8.4	17.6	32.4	41.6	3.22	23.2	14.3	31.7	23.9	0.6
Australia/New Zealand	44.2	53.4	2.3	0.1	1.58	27.1	21.5	24.9	14.9	0.3
Europe	20.0	56.2	21.5	2.3	2.06	27.9	17.7	22.5	21.0	0.8
Latin America	10.4	26.2	39.3	24.2	2.81	28.9	21.6	28.4	22.1	4.5
Middle East	6.5	20.7	61.1	11.7	2.81	38.0	29.4	39.7	29.4	2.8
Middle East (Israel)	NA	NA	NA	NA	NA	24.7	20.7	NA	NA	NA
North America	9.2	44.6	28.8	17.4	2.60	38.9	31.4	42.1	29.7	2.4



Delivery rate per aspiration by country.

Zegers-Hochschild. World report on assisted reproduction, 2005. Fertil Steril 2013.



Delivery rate per aspiration according to the mean number of embryos transferred by country.

Zegers-Hochschild. World report on assisted reproduction, 2005. Fertil Steril 2013.

Distribution of women's age at aspiration, IVF, and ICSI combined for year 2005.

Country	All women	Age ≤34 y, % (n)	Age 35–39 y, % (n)	Age ≥40 y, % (n)
France	55.058	57.2 (31.514)	30.0 (16.534)	12.7 (7.010)
United States	78,178	44.0 (34,389)	36.8 (28,769)	19.2 (15,020)
Region				
Asia	>20,771	59.8 (12,413)	28.2 (5,863)	12.0 (2,495)
Australia and New Zealand	24,612	42.4 (10,425)	36.3 (8,941)	21.3 (5,246)
Europe	>282,768	50.5 (142,663)	35.7 (100,968)	13.8 (39,137)
Latin America	20,463	44.9 (9,182)	36.0 (7,367)	19.1 (3,914)

Oocyte donation results for year 2005.

		Transfers				Recipient Pregnancies/transfer (%)			Deliveries (%)		
Country	Donor aspirations (n)	Total (n)	Fresh (%)	Age >40 y (%)	Embryos ≥4 (%)	Fresh	FET	Total	DR/transfer	Multiple	Babies (n)
France	NA	450	NA	NA	43.9	26.2	NA	26.2	10.7	NA	NA
United States	NA	12,726	69.0	68.9	7.9	61.5	39.7	54.7	45.8	37.6	8,181
Region											
Asia	2,182	1,785	81.7	48.9	32.7	52.0	30.0	47.9	37.1	38.5	952
Australia and New Zealand	826	1,471	48.7	61.0	0.1	33.0	19.5	26.0	19.0	17.9	331
Europe	NA	10,924	NA	39.1	4.1	42.0	NA	42.0	22.0	21.4	2,532
Latin America	NA	3,545	86.8	61.9	22.2	42.1	23.7	39.7	35.6	34.7	1,767
Middle East	15	NA	NA	NA	0.0	NA	NA	NA	NA	28.6	10
Middle East (Israel)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
North America	NA	13,136	69.1	68.6	7.9	61.1	39.3	54.3	45.4	37.5	8,355
Total	>3,023	30,861	71.0	56.8	9.7	49.1	35.0	46.5	34.3	35.8	13,947

Indications de l'AMP

- Trop tôt?
  - Expectant management
  - Scores prédictifs

Indications de l'AMP

- Trop tard ?
  - Retard à la prise en charge efficace
  - Pronostic défavorable et freins au don de gamètes

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Age-specific success rate for women undertaking their first assisted reproduction technology treatment using their own oocytes in Australia, 2002–2005

Y.A. Wang[1,4], D. Healy[2], D. Black[3] and E.A. Sullivan[1]

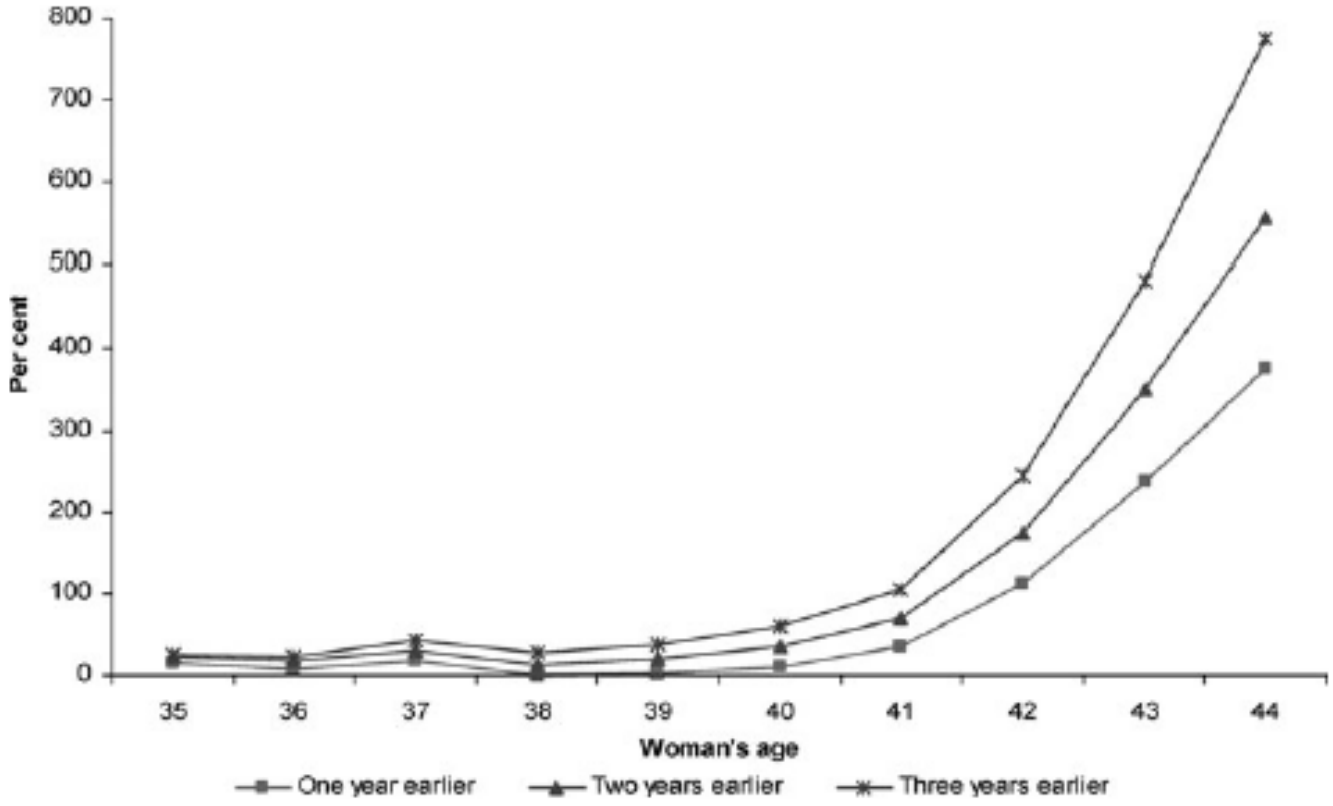

Figure 2: Percentage of extra live deliveries predicted of initiated first autologous fresh cycles in women aged 35–44 years in Australia, 2002–2005.

Indications de l'AMP

- Hétérogénéité des recommandations

J Gynecol Obstet Biol Reprod (Paris). 2010 Dec;39(8 Suppl 2):S1, S113-8.

[Management of the infertile couple].

[Article in French]

Collège national des gynécologues et obstétriciens français.

NHS
National Institute for
Health and Clinical Excellence

Fertility

Assessment and treatment for people with fertility problems

Issued: February 2013

NICE clinical guideline 156
guidance.nice.org.uk/cg156

Defining infertility

- A woman of reproductive age who has not conceived after 1 year of unprotected vaginal sexual intercourse, in the absence of any known cause of infertility, should be offered further clinical assessment and investigation along with her partner. **[new 2013]**
- Offer an earlier referral for specialist consultation to discuss the options for attempting conception, further assessment and appropriate treatment where:
  - the woman is aged 36 years or over
  - there is a known clinical cause of infertility or a history of predisposing factors for infertility. **[new 2013]**

Unexplained infertility

- Do not offer oral ovarian stimulation agents (such as clomifene citrate, anastrozole or letrozole) to women with unexplained infertility. **[new 2013]**
- Offer IVF treatment (see recommendations 1.11.1.3–4) to women with unexplained infertility who have not conceived after 2 years (this can include up to 1 year before their fertility investigations) of regular unprotected sexual intercourse. **[new 2013]**

1.1.2 Psychological effects of fertility problems

1.1.2.1 When couples have fertility problems, both partners should be informed that stress in the male and/or female partner can affect the couple's relationship and is likely to reduce libido and frequency of intercourse which can contribute to the fertility problems. **[2004, amended 2013]**

1.1.2.5 Counselling should be provided by someone who is not directly involved in the management of the individual's and/or couple's fertility problems. **[2004, amended 2013]**

1.3.2 Post-coital testing of cervical mucus

1.3.2.1 The routine use of post-coital testing of cervical mucus in the investigation of fertility problems is not recommended because it has no predictive value on pregnancy rate. **[2004]**

1.9.1 Intrauterine insemination

1.9.1.1 Consider unstimulated intrauterine insemination as a treatment option in the following groups as an alternative to vaginal sexual intercourse:

- people who are unable to, or would find it very difficult to, have vaginal intercourse because of a clinically diagnosed physical disability or psychosexual problem who are using partner or donor sperm
- people with conditions that require specific consideration in relation to methods of conception (for example, after sperm washing where the man is HIV positive)

1.9.1.2 For people in recommendation 1.9.1.1 who have not conceived after 6 cycles of donor or partner insemination, despite evidence of normal ovulation, tubal patency and semenalysis, offer a further 6 cycles of unstimulated intrauterine insemination before IVF is considered. **[new 2013]**

1.9.1.3 For people with unexplained infertility, mild endometriosis or 'mild male factor infertility', who are having regular unprotected sexual intercourse:

- do not routinely offer intrauterine insemination, either with or without ovarian stimulation (exceptional circumstances include, for example, when people have social, cultural or religious objections to IVF)
- advise them to try to conceive for a total of 2 years (this can include up to 1 year before their fertility investigations) before IVF will be considered. **[new 2013]**

1.11.1 Criteria for referral for IVF

1.11.1.1 When considering IVF as a treatment option for people with fertility problems, discuss the risks and benefits of IVF in accordance with the current Human Fertilisation and Embryology Authority (HFEA) Code of Practice. **[new 2013]**

1.11.1.2 Inform people that normally a full cycle of IVF treatment, with or without intracytoplasmic sperm injection (ICSI), should comprise 1 episode of ovarian stimulation and the transfer of any resultant fresh and frozen embryo(s). **[new 2013]**

1.11.1.3 In women aged under 40 years who have not conceived after 2 years of regular unprotected intercourse or 12 cycles of artificial insemination (where 6 or more are by intrauterine insemination), offer 3 full cycles of IVF, with or without ICSI. If the woman reaches the age of 40 during treatment, complete the current full cycle but do not offer further full cycles. **[new 2013]**

1.11.1.4 In women aged 40–42 years who have not conceived after 2 years of regular unprotected intercourse or 12 cycles of artificial insemination (where 6 or more are by intrauterine insemination), offer 1 full cycle of IVF, with or without ICSI, provided the following 3 criteria are fulfilled:

- they have never previously had IVF treatment
- there is no evidence of low ovarian reserve (see recommendation 1.3.3.2)
- there has been a discussion of the additional implications of IVF and pregnancy at this age. **[new 2013]**

1.11.1.5 Where investigations show there is no chance of pregnancy with expectant management and where IVF is the only effective treatment, refer the woman directly to a specialist team for IVF treatment. **[new 2013]**

1.11.1.6 In women aged under 40 years any previous full IVF cycle, whether self- or NHS-funded, should count towards the total of 3 full cycles that should be offered by the NHS. **[new 2013]**

1.11.1.7 Take into account the outcome of previous IVF treatment when assessing the likely effectiveness and safety of any further IVF treatment. **[new 2013]**

1.11.1.8 Healthcare providers should define a cancelled IVF cycle as one where an egg collection procedure is not undertaken. However, cancelled cycles due to low ovarian reserve should be taken into account when considering suitability for further IVF treatment. **[new 2013]**

1.12.6 Embryo transfer strategies in IVF

1.12.6.1 Women undergoing IVF treatment should be offered ultrasound-guided embryo transfer because this improves pregnancy rates. **[2004]**

1.12.6.2 Replacement of embryos into a uterine cavity with an endometrium of less than 5 mm thickness is unlikely to result in a pregnancy and is therefore not recommended. **[2004]**

1.12.6.3 Women should be informed that bed rest of more than 20 minutes' duration following embryo transfer does not improve the outcome of IVF treatment. **[2004]**

1.12.6.4 Evaluate embryo quality, at both cleavage and blastocyst stages, according to the Association of Clinical Embryologists (ACE) and UK National External Quality Assessment Service (UK NEQAS) for Reproductive Science Embryo and Blastocyst Grading schematic (see figure 3). **[new 2013]**

1.12.6.5 When considering the number of fresh or frozen embryos to transfer in IVF treatment:

- For women aged under 37 years:
  - In the first full IVF cycle use single embryo transfer.
  - In the second full IVF cycle use single embryo transfer if 1 or more top-quality embryos are available. Consider using 2 embryos if no top-quality embryos are available.
  - In the third full IVF cycle transfer no more than 2 embryos.
- For women aged 37–39 years:
  - In the first and second full IVF cycles use single embryo transfer if there are 1 or more top-quality embryos. Consider double embryo transfer if there are no top-quality embryos.
  - In the third full IVF cycle transfer no more than 2 embryos.
- For women aged 40–42 years consider double embryo transfer. **[new 2013]**

1.12.6.6 For women undergoing IVF treatment with donor eggs, use an embryo transfer strategy that is based on the age of the donor. **[new 2013]**

1.12.6.7 No more than 2 embryos should be transferred during any one cycle of IVF treatment. **[2013]**

1.12.6.8 Where a top-quality blastocyst is available, use single embryo transfer. **[new 2013]**

1.12.6.9 When considering double embryo transfer, advise people of the risks of multiple pregnancy associated with this strategy. **[new 2013]**

1.12.6.10 Offer cryopreservation to store any remaining good-quality embryos after embryo transfer. **[new 2013]**

1.12.6.11 Advise women who have regular ovulatory cycles that the likelihood of a live birth after replacement of frozen–thawed embryos is similar for embryos replaced during natural cycles and hormone-supplemented cycles. **[2013]**

1.14.2 Information and counselling

1.14.2.1 Couples should be offered information about the relative merits of ICSI and donor insemination in a context that allows equal access to both treatment options. **[2004]**

1.14.2.2 Couples considering donor insemination should be offered counselling from someone who is independent of the treatment unit regarding all the physical and psychological implications of treatment for themselves and potential children. **[2004]**

Criteria for number of embryos to transfer: a committee opinion

The Practice Committee of the American Society for Reproductive Medicine and the Practice Committee of the Society for Assisted Reproductive Technology

American Society for Reproductive Medicine and Society for Assisted Reproductive Technology, Birmingham, Alabama

Recommended limits on the numbers of embryos to transfer.

	Age (y)			
Prognosis	**< 35**	**35–37**	**38–40**	**41–42**
Cleavage-stage embryos[a]				
Favorable[b]	1–2	2	3	5
All others	2	3	4	5
Blastocysts[a]				
Favorable[b]	1	2	2	3
All others	2	2	3	3

[a] See text for more complete explanations. Justification for transferring one additional embryo more than the recommended limit should be clearly documented in the patient's medical record.
[b] Favorable = first cycle of IVF, good embryo quality, excess embryos available for cryopreservation, or previous successful IVF cycle.

Practice Committee. Pharmacogenetic approach to male infertility. Fertil Steril 2013.

uary 2

Fresh Embryos From Non-Donor Oocytes

	<35	35-37	38-40	41-42	>42
Number of cycles	39721	19930	20130	10277	6033
Percentage of cycles resulting in pregnancies	46.2	38.5	29.3	19.5	9.1
Percentage of cycles resulting in live births	40.1	31.9	21.6	12.2	4.2
Reliability Range	(39.7 - 40.6)	(31.2 - 32.5)	(21.0 - 22.2)	(11.5 - 12.8)	(3.7 - 4.7)
Percentage of retrievals resulting in live births	42.9	35.2	24.8	14.5	5.3
Percentage of transfers resulting in live births	46.3	38.4	27.5	16.6	6.5
Percentage of cycles with elective single embryo transfer	11.7	6.5	1.9	0.6	0.5
Percentage of cancellations	6.4	9.5	12.7	16.3	20.7
Implantation Rate	36.0	27.3	17.5	9.4	4.0
Average number of embryos transferred	1.9	2.1	2.5	3.0	3.1
Percentage of live births with twins	30.8	26.7	21.1	14.9	10.6
Percentage of live births with triplets or more	1.2	1.3	1.3	0.7	0

Preimplantation genetic screening using fluorescence in situ hybridization in patients with repetitive implantation failure and advanced maternal age: two randomized trials

Carmen Rubio, Ph.D.,[a,b] José Bellver, M.D., Ph.D.,[a] Lorena Rodrigo, M.Sc.,[b] Ernesto Bosch, M.D., Ph.D.,[a] Amparo Mercader, Ph.D.,[a] Carmen Vidal, M.D., Ph.D.,[a] Maria José De los Santos, Ph.D.,[a] Juan Giles, M.D.,[a] Elena Labarta, M.D.,[a] Javier Domingo, M.D.,[a] Juana Crespo, M.D.,[a] José Remohí, M.D., Ph.D.,[a,b] Antonio Pellicer, M.D., Ph.D.,[a,b] and Carlos Simón, M.D., Ph.D.[a,b]

Fertility and Sterility® Vol. 99, No. 5, April 2013

Clinical outcome of the RCT study in RIF patients.

	Blastocyst (group A)	PGS (group B)	*P* value
No. of patients	43	48	–
Mean age (SD)	35.3 (2.9)	35.2 (3.5)	NS
No. of started cycles	43	48	–
Mean E_2 on the day of hCG, pg/mL (SD)	1,768.1 (567.5)	2,062.5 (1145.3)	NS
Mean stimulation days (SD)	9.9 (1.6)[a]	11.0 (2.0)	.0051
Mean previous IVF failures (SD)	3.1 (0.4)[a]	3.5 (0.8)	.0039
Mean no. of MII oocytes (SD)	9.9 (4.7)	11.0 (5.8)	NS
Abnormal/informative embryos (%)	–	152/265 (57.3)	–
No. of ETs (%)	36 (83.7)	43 (89.6)	NS
Mean embryos transferred (SD)	1.9 (0.7)	1.7 (0.6)	NS
Mean day 3 cell number (SD)	7.8 (1.3)	8.2 (1.2)	NS
Mean day 3 fragmentation degree (SD)	6.1 (4.6)	4.8 (5.0)	NS
No. of pregnancies/transfer (%)	13/36 (36.1)	27/43 (62.8)	–
No. of miscarriages (%)	1 (7.7)	4 (14.8)	NS
Ongoing pregnancy rate/transfer (%)	12/36 (33.3)	23/43 (53.5)	–
Ongoing implantation rate (%)	15/70 (21.4)	26/71 (36.6)	–
Live-birth rate/patient (%)	12/43 (27.9)	23/48 (47.9)	NS
No. of twin deliveries (%)	3 (25.0)	3 (13.0)	NS
No. of cycles with vitrified blastocyst	14	12	–
No. of thawed cycles	7	7	–
No. of ongoing pregnancies from thawed blastocyst	2	2	–
Total ongoing pregnancies/patient (%)	15/43 (34.9)	25/48 (52.1)	NS

Note: NS = no significant differences.
[a] Student's *t* test; $P < .05$.

Rubio. PGS in RIF and AMA patients. Fertil Steril 2013.

Clinical outcome of the RCT study in AMA patients.

	Blastocyst (group A)	PGS (group B)	*P* value
No. of patients	90	93	–
Mean age (SD)	41.7 (1.0)	41.8 (0.9)	NS
No. of started cycles	128	127	–
Mean E_2 on the day of hCG, pg/mL (SD)	1,432.7 (946.9)	1661.5 (950.7)	NS
Mean stimulation days (SD)	10.7 (2.0)	11.1 (2.4)	NS
Mean no. of MII oocytes (SD)	9.2 (4.0)	9.9 (4.4)	NS
Abnormal/informative embryos (%)	–	338/485 (69.2)	–
No. of transfers (%)	74 (82.2)	70 (75.3)	NS
Mean embryos transferred (SD)	2.0 (0.6)[a]	1.6 (0.6)	<.0001
Mean day 3 cell number (SD)	7.7 (1.3)	7.3 (2.6)	NS
Mean day 3 fragmentation degree (SD)	6.6 (5.7)	7.6 (7.3)	NS
No. of pregnancies/transfer (%)	18/74 (24.3)	36/70 (51.4)	–
No. of miscarriages (%)	4 (22.2)	6 (16.7)	NS
Ongoing pregnancy rate/transfer (%)	14/74 (18.9)	30/70 (42.8)	–
Live birth rate/patient (%)	14/90 (15.5)[b]	30/93 (32.3)	*P*=.0099; OR 2.585; CI [1.262–5.295]
Ongoing implantation rate (%)	20/152 (13.1)[b]	40/114 (35.1)	–
Live-birth rate/started cycle (%)	14/128 (10.9)[b]	30/127 (23.6)	*P*=.0081; OR 0.3971; CI [0.1992–0.7916]
No. of twin deliveries (%)	3 (21.4)	10 (25.0)	NS
No. of cycles with vitrified blastocyst	18	17	–
No. of transfers of thawed blastocyst	13	9	–
No. of ongoing pregnancies from thawed blastocyst	3	1	–
Total ongoing pregnancies/patient (%)	17/90 (18.9)	31/93 (33.3)	*P*=.00297; OR 0.4658; CI [0.2356–0.9209]

Note: NS = no significant differences.
[a] Student's *t* test; *P*< .05.
[b] Two-sided Fisher's exact test; *P*< .05.

Rubio. PGS in RIF and AMA patients. Fertil Steril 2013.

OPEN ACCESS Freely available online

PLOS ONE

Global Gene Expression Profiling of Individual Human Oocytes and Embryos Demonstrates Heterogeneity in Early Development

Lisa Shaw[1,2,3☯¤a], Sharon F. Sneddon[1,2,3☯¤b], Leo Zeef[3], Susan J. Kimber[3], Daniel R. Brison[1,2*]

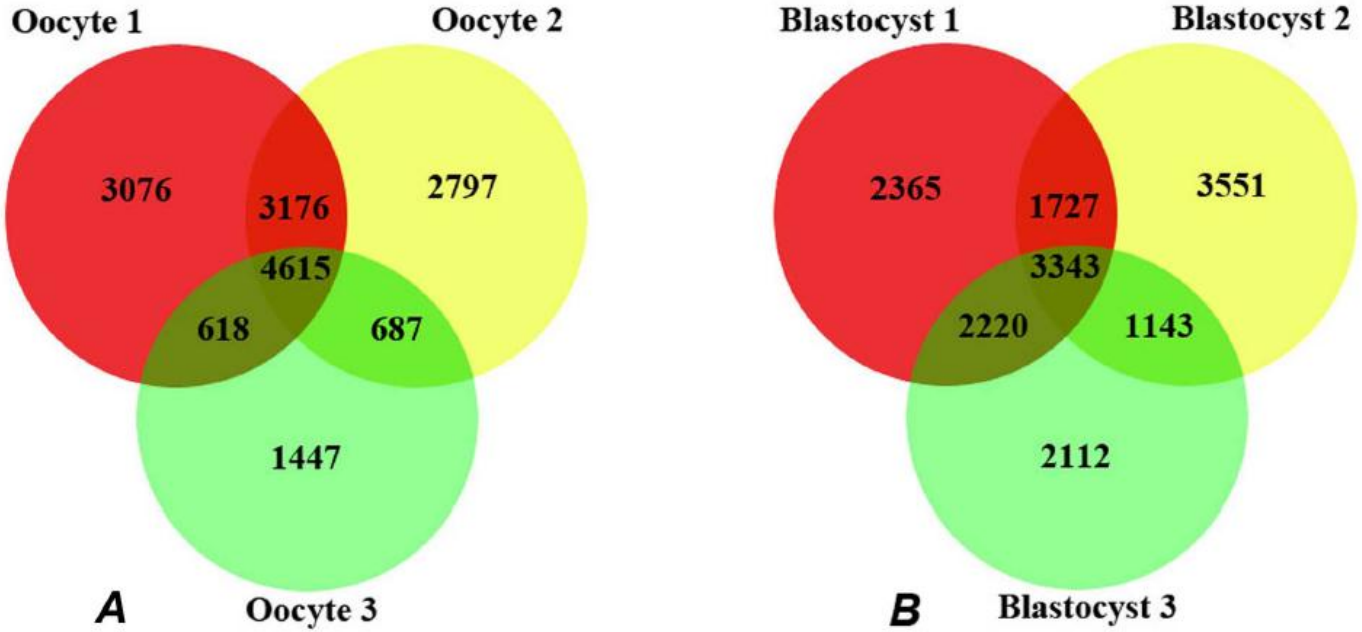

Figure 2. Venn diagrams showing the number of expressed transcripts unique and common to individual oocyte and blastocyst samples. A Individual oocytes expressed a number of transcripts that were unique to each one, relative to the remaining oocytes. Some transcripts were common between two individual samples and 4615 transcripts were common to 3/3 oocytes. Note that oocytes 1 and 2 shared more common transcripts with each other than with oocyte 3. These transcripts may not be exclusive to oocytes and may also be expressed in 1, 2 or all 4-cell embryo and blastocyst samples. B Individual blastocysts expressed a number of transcripts unique to each one. Some transcripts were common between two individual blastocysts and 3343 transcripts were common to all three samples. These transcripts may not be exclusive to the blastocyst stage and may also be expressed in 1, 2 or all oocyte and 4-cell embryo samples.

Les paradoxes français

- Une surréglementation?
- Un regard constant sur le passé?

ETAT REGLEMENTAIRE

- Inscription d'un nouveau procédé (R 2141-1) :
  - « Constitue ainsi un nouveau procédé, toute modification introduisant, compte tenu du procédé existant, une étape critique supplémentaire ou une manipulation supplémentaire des gamètes, tissus germinaux ou embryons. »

- Techniques visant à améliorer les procédés biologiques d'AMP (L2141-1, R 2141-1-5S) :
  - « La technique est autorisée si , sans constituer un nouveau procédé, elle améliore l'efficacité, la reproductibilité et la sécurité du procédé qu'elle modifie. »

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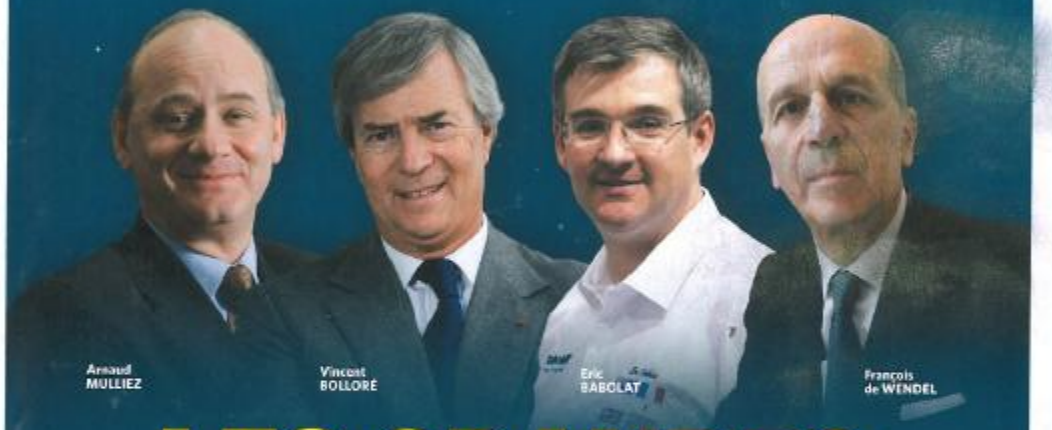
1914-2014

UN SIÈCLE APRÈS, ET SI RIEN N'AVAIT CHANGÉ ?



LES GRANDES FAMILLES

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Lobby bancaire, modèle allemand, fantasme du déclin... Est-ce si nouveau ?

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TOUT CE QUI ÉTAIT MIEUX IL Y A 50 ANS

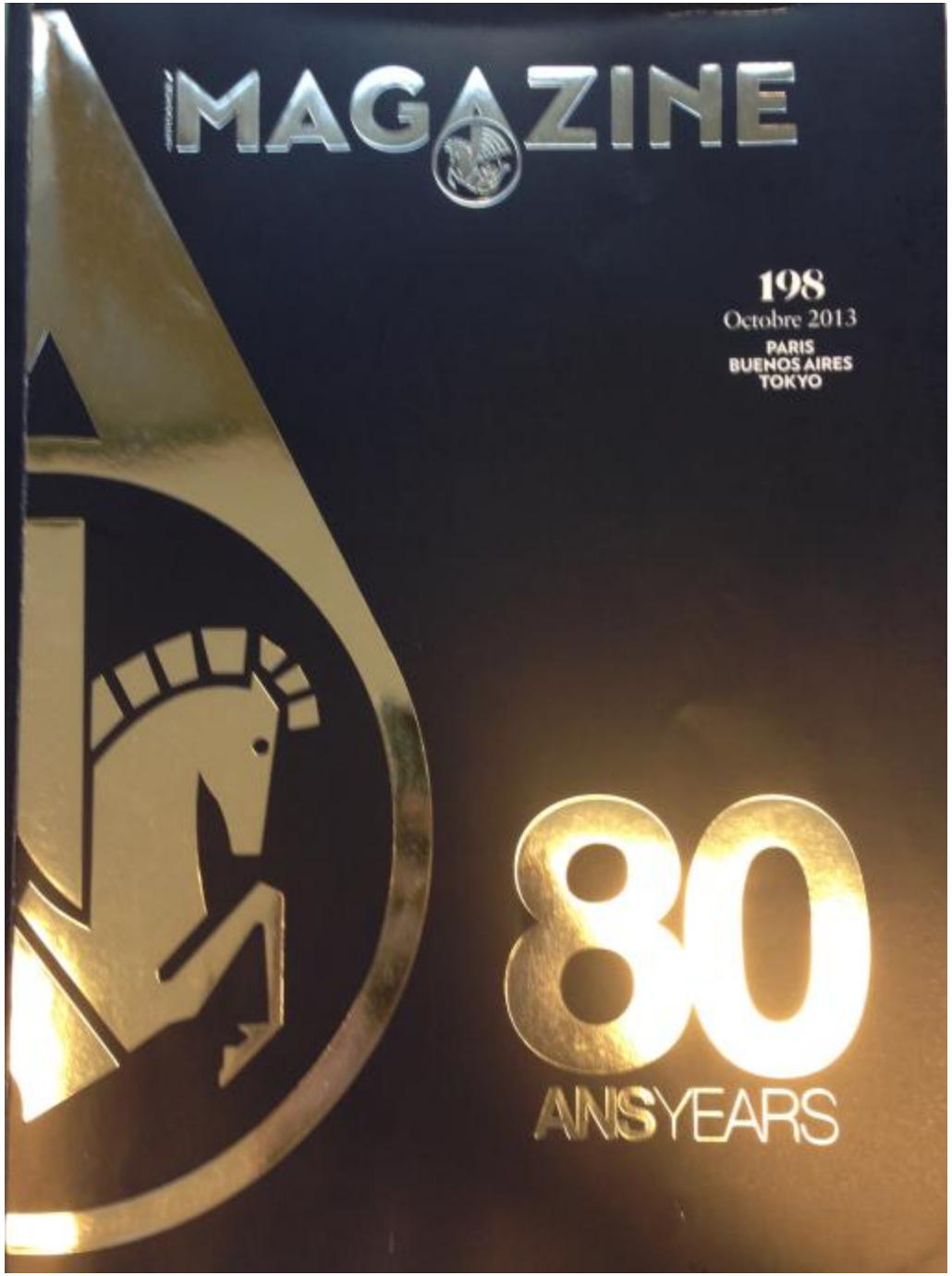
Certes, à l'époque on ne guérissait pas un cancer sur deux. Les ouvriers sniffaient de l'amiante à pleins poumons. Il n'y avait pas la pilule pour les femmes... **Mais alors pourquoi cette nostalgie ?** La rédaction de "Marianne" en explore les ressorts.

Avant, c'était simple, il n'y avait que les « vieux cons » qui disaient que c'était mieux avant. Les anciens étaient des ringards et les jeunes, des petits cons persuadés que tout était mieux maintenant et serait encore mieux demain grâce à eux. Mais ça, c'était avant. Aujourd'hui, tout le monde s'y met et les nostalgiques n'ont pas encore de poil au menton qu'ils regrettent déjà un temps qu'ils n'ont même pas connu. La voiture qui se conduit toute seule fait moins fantasmer que la mythique DS – version avec GPS, clim et lecteur DVD, tout de même. La bonne vieille culotte-gaine de mamie connaît un nouvel état de grâce. Les années 50-70 sont glorifiées : époque préférée des Français, elle supplante largement la période contemporaine et le futur (1).

Le progrès n'intéresse plus les Français. Leur truc, c'est la régression : plus de la moitié d'entre eux disent qu'ils préféreraient vivre dans le passé plutôt que dans le futur (2). Les 18-34 ans ont des circonstances atténuantes : ils constituent la première génération à vivre moins bien que leurs parents. S'ils avaient une machine à voyager dans le temps, 59 % d'entre eux opteraient pour le passé, contre seulement 37 % de leurs grands-parents de 65 ans et plus. Et la nostalgie n'est plus le monopole des réactionnaires : si 58 % des sympathisants de droite regrettent le « bon vieux temps », 48 % de ceux de gauche les rejoignent. Quand le présent est morose, que le futur n'inspire rien qui vaille, le passé se transforme en refuge douillet. Tout était tellement mieux « avant » ! Avant quoi ? On ne sait pas trop... >

LA RENAULT DAUPHINE, la voiture la plus vendue en France à la fin des années 50.

jean-philippe charbonnier / rapho / gamma


MAGAZINE
198
Octobre 2013
PARIS
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TOKYO
80
ANS YEARS

Ce plan qu'Air France ne pouvait éviter

Publié le 20-09-2013 à 14h28 - Mis à jour à 14h44

Par Caroline Michel

Les maux, qui ont conduit la compagnie aérienne a un nouveau plan de départs volontaires, sont connus

Toutes ces décisions seront-elles suffisantes ? Alexandre de Juniac, qui a souligné « le poids de l'histoire » chez Air France pour expliquer la lenteur de certains changements, en est persuadé.

Financement de l'AMP

- Mythe de l'accès égalitaire

  Versus

- Responsabilisation des couples (et des praticiens?)
- Faisabilité réelle de l'innovation

Conclusions

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Conclusions

- L'avenir sera porté:
  - Par les compétences des professionnels
  - Par l'innovation technique
  - Par un environnement réglementaire et financier adéquat

Conclusions

L'avenir dépendra :

- Des évolutions sociologiques de la famille et de la parentalité
- De leur acceptation par les politiques et les professionnels de santé
- De leur engagement : Jean Cohen et son message

NEUVIRTH VEIL…