

# ESHRE PGD Consortium data collection VI: cycles from January to December 2003 with pregnancy follow-up to October 2004

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**The sixth report of the ESHRE PGD Consortium is presented, relating to cycles collected for the calendar year 2003 and follow-up of the pregnancies and babies born up to October 2004. Since the beginning of the data collections, there has been a steady rise in the number of cycles, pregnancies and babies reported. For this report, 50 centres participated, reporting on 2984 cycles, 501 pregnancies and 373 babies born. Five hundred and twenty-nine cycles were reported for chromosomal abnormalities, 516 cycles were reported for monogenic diseases, 137 cycles were reported for sexing for X-linked diseases, 1722 cycles were reported for preimplantation genetic screening (PGS) and 80 cycles were reported for social sexing. Data VI is compared to the cumulative data for data collections I–V.**

*Key words:* PGD/preimplantation genetic screening/fluorescence in-situ hybridization/PCR/ESHRE PGD Consortium

## Introduction

Since 1999, the ESHRE PGD Consortium has reported on a regular basis on the current practice of PGD, as reported by their members (ESHRE PGD Consortium Steering Committee, 1999, 2000, 2002; Sermon *et al.*, 2005; Harper *et al.*, 2006). The data analysed previously included referral and clinical data on the patients consulting for PGD, the cycles they underwent, the pregnancies that ensued from these cycles and the babies born.

Because the analysis of the referral and clinical data was biased by several factors, e.g. the underreporting of couples who did not come through for PGD, this analysis is left out for the current report.

## Materials and methods

Data were collected using a FileMaker Pro 5 database consisting of files for cycle records, frozen cycle records, pregnancies and babies. A first general round of correction was carried out, requesting corrections from participating centres, followed by a more in-depth correction by expert co-authors. Cycles with insufficient data, e.g. with no cycle or patient identification or no clear indication, cycles from the

wrong time period, or reported after the closure of the collection period, were eliminated from the calculations.

## Results

The membership has increased steadily, and while in the first report data on sixteen centres were included (ESHRE PGD Consortium Committee, 1999), that figure has now increased to 50. This has also led to a steady increase in the number of cycles reported, from 392 in the first report to 3929 in the current report.

The results are represented in tables according to a now set layout. Accompanying text is limited to the minimum, and seven tables are only available in an electronic version: Supplementary Table IIc with the list of abnormal karyotypes, Supplementary Table IIIc with the list of X-linked diseases for which sexing was carried out, Supplementary Table IVc with the list of monogenic diseases for which PGD was carried out, Supplementary Tables VIIIa (data I–V) and VIIIb (data VI) with the complications of pregnancy and Supplementary Tables XIIa (data I–V) and XIIb (data VI) with the congenital malformations and the neonatal complications.

An overview of all cycles collected previously in data collections I–V can be found in Table Ia, whereas an overview of the current data collection can be found in Table Ib.

### PGD cycles for chromosomal abnormalities

Tables IIa and IIb summarize the 1207 and 529 cycles collected for data collection I–V and VI, respectively. Overall, there was very little difference between the two data collections. Reciprocal translocation was the most frequent class of chromosome aberration; ICSI was the predominant mode of fertilization; acid Tyrodes with cleavage aspiration was the predominant sampling method. A global average of 14.3 and 14.0 cumulus oocyte complexes (COCs) per oocyte retrieval (OR) cycle was collected for the I–V and VI data collections, respectively; the fertilization rate (74 and 70%), the proportion

of successfully biopsied embryos which gave a diagnosis (91 and 92%), the proportion of successfully biopsied embryos with a transferable result (25 and 25%) and the clinical pregnancy rate per OR (15 and 14%) were similar.

The relatively low pregnancy rates are likely to reflect that the low proportion of embryos with a transferable result limits the choice of embryo for transfer (24% of embryos biopsied for all classes of chromosome aberration and only 17% of embryos for reciprocal translocation cycles in particular for the data collection VI).

### PGD cycles for sexing for X-linked diseases

Table IIIa summarizes data I–V and Table IIIb summarizes the data from collection VI for sexing only for X-linked disease using the PCR or fluorescent in-situ hybridization (FISH).

**Table Ia.** Overall cycle data collection I–V

Indication	PGD	PGS	PGD-SS	Total
Cycles to OR	2868	3078	254	6200
Number infertile	994	2894	41	3929
Female age	33	36	35	34
Cancelled after OR before IVF/ICSI	6	0	0	6
ART method				
IVF	369	511	113	993
ICSI	2444	2501	128	5073
IVF + ICSI	3	13	0	16
Frozen	9	4	5	18
Frozen and ICSI	14	5	5	24
Frozen and IVF	0	0	1	1
Cancelled ICSI	3	0	0	3
Unknown	18	44	0	62
Unknown and frozen	2	0	2	4
Cancelled after OR	161	128	14	303
Cycles to PGS/PGD	2701	2950	240	5891
FISH	1577	2950	143	4670
PCR	1124	0	97	1221
Zona breaching				
AT drilling	1703	1808	19	3530
Laser drilling	856	1000	112	1968
Mechanical	128	77	109	314
Unknown	14	65	0	79
Biopsy method				
Polar body biopsy	25 <sup>1</sup>	178 <sup>1</sup>	0	203 <sup>1</sup>
Cleavage aspiration	2576 <sup>1</sup>	2481 <sup>1</sup>	130	5187 <sup>1</sup>
Cleavage extrusion	85	224	110	419
Cleavage flow displacement	2	16	0	18
Unknown	16	52	0	68
Embryology				
COC	38955	38561	3291	80807
Inseminated	33353	32839	2772	68964
Fertilized	24239	23323	1891	49453
Biopsied	18368	17549	1589	37506
Successfully biopsied	17998	17232	1505	36735
Diagnosed	15833	15036	1367	32236
Transferable	6085	5353	652	12090
Transferred	4380	4460	449	9289
Frozen	793	687	149	1629
Clinical outcome				
Cycles to ET	2173	2188	192	4553
hCG positive	656	702	78	1436
Positive heart beat	514	534	59	1107
(clinical pregnancy rate % per OR/% per ET)	18/24	17/24	23/31	18/24
Implantation rate data V only (fetal hearts/embryos transferred %)	15	17	14	16

ART, assisted reproduction techniques; AT, acid Tyrode's; COC, cumulus oocyte complexes; ET, embryo transfer; FISH, fluorescent in-situ hybridization; OR, oocyte retrieval; PGS, preimplantation genetic screening.

PGD column includes PGD for chromosome abnormalities, sexing for X-linked disease and PGD for monogenic disorders.

<sup>1</sup>Four cycles had polar body biopsy and cleavage stage biopsy.

**Table Ib.** Overall cycle data collection VI

Indication	PGD	PGS	PGD-SS	Total
Total number of cycles	1182	1722	80	2984
Number infertile	501	1473	1	1975
Female age	33	37	38	35
Cycles cancelled before OR	133	9	1	143
Cycles to OR	1047 <sup>1</sup>	1713	79	2839
Cycles cancelled before ART	2	0	0	2
ART method				
IVF	97	124	5	226
ICSI	902	1558	71	2531
IVF + ICSI	17	15	0	32
Frozen + ICSI	26 <sup>1</sup>	10	1	37
Frozen + IVF	2	0	0	2
Unknown and frozen	1	0	2	3
Unknown	2	6	0	8
Cancelled post OR	89	45	1	135
Cycles to PGS/PGD	958	1668	78	2704
FISH	537	1668	71	2276
PCR	421	0	7	428
Zona breaching				
AT drilling	441	716	0	1157
Laser drilling	474	870	1	1345
Mechanical	43	82	77	202
Biopsy method				
PB biopsy	11	185	0	196
Cleavage aspiration	847	1409	1	2257
Cleavage extrusion	75	74	77	226
Blastocyst	25	0	0	25
Embryology				
COC	14490	20666	1220	36376
Inseminated	12272	16867	949	30088
Fertilized	8458	11815	644	20917
Biopsied	6254	9496	478	16228
Successfully biopsied	6156	9413	461	16030
Diagnosed	5507	8795	445	14747
Transferable	2065	3193	113	5371
Transferred	1326	2277	92	3695
Frozen	240	454	20	714
Clinical outcome				
Cycles to ET	709	1283	47	2039
hCG positive	237	409	20	666
Positive heart beat	185	311	15	511
Clinical pregnancy rate (% per OR/% per ET)	18/26	18/24	19/32	18/25
Number of fetal heartbeats	223	384	21	628
Implantation rate (fetal heartbeats/100 embryos transferred %)	17	17	23	17

ART, assisted reproduction technique; AT, acid Tyrode's; COC, cumulus oocyte complexes; FISH, fluorescent in-situ hybridization; OR, oocyte retrieval; PGS, preimplantation genetic screening.

PGD column includes PGD for chromosome abnormalities, sexing for X linked disease and PGD for monogenic disorders

<sup>1</sup>Includes two cycles with PGD on frozen embryos only. These cycles were not counted in the cycles with OR.

A total number of 137 cycles were collected in this group, with 134 cycles using FISH and three cycles using PCR.

The biopsy was successful in 98% of embryos biopsied and 92% of the embryos successfully biopsied were diagnosed. A transfer was achieved in 76% of the cycles with an average of 1.7 embryos transferred in each cycle. The overall clinical pregnancy rate was 22% per OR and 30% per embryo transfer (ET) procedure, with an implantation rate of 21%.

Supplementary Table IIIc summarizes the list of 36 indications. The most common indication was Duchenne muscular dystrophy ( $n = 33$ ; 25%), haemophilia ( $n = 25$ ; 19%), retinitis pigmentosa ( $n = 6$ ), adrenoleukodystrophy ( $n = 6$ ), Alport syndrome ( $n = 5$ ) and non-fragile X, X-linked mental retardation ( $n = 5$ ).

Overall, these data are quite unremarkable and very comparable to previous data collections (I–V). In contrast to other indication groups, the number of cycles for sexing for X-linked diseases remains stable.

#### *PGD for monogenic diseases*

Amongst PGD cycles initiated for single-gene disorders between January and December 2003, the most common autosomal recessive diseases were cystic fibrosis,  $\beta$ -thalassaemia (with or without HLA typing), spinal muscular atrophy and sickle cell anaemia. The most common autosomal dominant diseases were Huntington disease, myotonic dystrophy, adenomatous polyposis coli and Marfans syndrom. The most common specific diagnosis of X-linked diseases was for Duchenne and

**Table IIa.** PGD for chromosomal abnormalities, data collection I–V

Indication	Robertsonian translocations, male carrier	Robertsonian translocations, female carrier	Reciprocal, male carrier	Reciprocal, female carrier	Sex chromosome abnormalities	Other	Total
Total cycles	193	167	307	308	144	88	1207
Number infertile	160	70	148	102	127	41	648
Female age	34	32	33	33	34	33	32
Cycles cancelled before OR	8	5	11	12	5	4	45
Cycles to OR	185	162	296	296	139	84	1162
Cancelled after OR before IVF/ICSI	0	0	1	0	5	0	6
ART method							
IVF	9	25	39	74	14	29	190
ICSI	172	134	252	216	119	55	948
IVF + ICSI	1	1	0	0	0	0	2
Frozen	0	0	1	1	0	0	2
Unknown and frozen	0	0	0	0	1	0	1
ICSI and frozen	3	2	3	5	0	0	13
Cancelled after IVF/ICSI	11	7	19	17	7	4	65
Cycles to PGD	174	155	276	279	127	80	1091
Zona breaching							
AT drilling	126	109	203	216	68	62	784
Laser drilling	48	41	59	54	33	13	248
Mechanical	0	5	14	9	26	5	59
Biopsy method							
Polar body biopsy	1	4	0	3	0	0	8
Cleavage aspiration	170	147	264	264	127	79	1051
Cleavage extrusion	3	4	11	11	0	1	30
Cleavage flow displacement	0	0	1	1	0	0	2
Embryology							
COC	2668	2272	4490	4445	1657	1106	16638
Inseminated	2262	1885	3832	3860	1343	982	14164
Fertilized	1573	1404	2865	2945	965	679	10431
Biopsied	1029	1142	2290	2425	696	533	8115
Successfully biopsied	1003	1120	2248	2387	683	517	7958
Diagnosed	850	1013	2050	2212	614	472	7211
Transferable	328	300	450	470	289	171	2008
Transferred	258	244	385	403	202	128	1620
Frozen	14	22	11	17	19	14	97
Clinical outcome							
Cycles to ET	135	125	193	204	102	60	819
hCG positive	40	41	50	49	31	18	229
Positive heart beat	34	32	36	37	20	16	175
Clinical pregnancy rate (% per OR/% per ET)	18/25	20/26	12/19	13/18	14/20	19/27	15/21

ART, assisted reproduction technique; AT, acid Tyrode's; COC, cumulus oocyte complexes; ET, embryo transfer; OR, oocyte retrieval.

Becker muscular dystrophy, fragile X and haemophilia. PGD cycles for an additional 47 monogenic diseases were initiated in 104 cycles, included under 'other' in Table IVb, listed in Supplementary Table IVc.

An average of 13.8 oocytes were collected per OR, biopsy was successful in 98% of embryos, diagnosis was achieved in 86% of embryos successfully biopsied, and 75% of cycles to OR had an ET, with 667 embryos transferred. Overall, 20% of cycles that reached the stage of OR resulted in a clinical pregnancy (or 27% clinical pregnancy rate per ET).

As recommended (Thornhill *et al.*, 2005), 434 cycles had ICSI and 11 cycles had ICSI and frozen (two of which were just frozen embryos). Two cycles were noted as IVF and frozen and 3 cycles as IVF and ICSI. Laser drilling was used for zona breaching in 64% of biopsy cycles, with cleavage aspiration accounting for 85% of biopsy procedures. In addition 17 cycles (4%) used trophectoderm biopsy in blastocysts; representing the first time, blastocyst biopsy has been reported to ESHRE for clinical PGD cycles.

Overall, the number of PGD cycles performed for monogenic disorders between January and December 2003 represents the largest number performed in a single year so far. The assisted reproduction techniques (ART) and embryology procedures applied reflect accumulated experience and expertise, along with technological developments, e.g. laser drilling and blastocyst biopsy.

With respect to the progress and outcome of cycles, including the embryology, rates of diagnosis and clinical outcome such as clinical pregnancy and embryo implantation rates, there are no apparent changes compared to previous data collections (Table IVa and Supplementary Table IVc).

### **Preimplantation genetic screening**

The cumulative data for preimplantation genetic screening (PGS) from collections I–V are summarized in Table Va. Table Vb summarizes the data from collection VI. It is clear that the number of PGS cycles continues to rise. In last year's data collection (data

**Table IIb.** PGD for chromosomal abnormalities, data collection VI

Indication	Robertsonian translocation, male carrier	Robertsonian translocations, female carrier	Reciprocal, male carrier	Reciprocal, female carrier	Sex chromosome aneuploidy	Other	Total
Total cycles	91	60	143	159	32	44	529
Number infertile	79	34	103	95	28	24	363
Female age	33	33	34	34	33	33	33
Cycles cancelled before OR	8	9	15	17	0	9	58
Cycles to OR	83	51	128	142	32	35	471
Cancelled before ART	0	0	0	0	0	1	1
ART method							
IVF	2	4	10	40	4	4	64
ICSI	78	44	106	94	28	28	378
IVF + ICSI	1	1	2	5	0	1	10
ICSI + Frozen	1	2	8	3	0	1	15
Unknown + Frozen	0	0	1	0	0	0	1
Unknown	1	0	1	0	0	0	2
Cancelled after IVF/ICSI	10	6	15	16	3	1	51
Cycles to PGD	73	45	113	126	29	33	419
Zona breaching							
AT drilling	34	23	74	89	15	11	246
Laser drilling	38	22	34	34	13	19	160
Mechanical	1	0	5	3	1	3	13
Biopsy method							
Cleavage aspiration	70	42	96	112	29	30	379
Cleavage extrusion	3	3	13	11	0	3	33
Blastocyst	0	0	4	3	0	0	7
Embryology							
COC	1262	720	1806	1993	420	379	6580
Inseminated	1053	613	1496	1756	359	328	5605
Fertilized	703	423	989	1257	245	224	3841
Biopsied	480	324	746	948	156	179	2833
Successfully biopsied	474	323	738	933	156	177	2801
Diagnosed	432	299	674	868	143	154	2570
Transferable	170	107	117	170	70	55	689
Transferred	100	71	97	141	53	37	499
Frozen	32	6	6	8	5	4	61
Clinical outcome							
Cycles to ET	55	38	65	76	24	24	282
hCG positive	21	8	21	27	5	3	85
Positive heart beat	18	6	17	21	3	2	67
Clinical pregnancy rate (% per OR/% per ET)	22/33	12/16	13/26	15/28	9/13	6/8	14/24
Number of fetal hearts	23	6	19	23	3	2	76
Implantation rate (fetal hearts/100 embryos transferred)	23	8	20	16	6	5	15

ART, assisted reproduction technique; AT, acid Tyrode's; COC, cumulus oocyte complexes; ET, embryo transfer; OR, oocyte retrieval.

V), 1211 PGS cycles were performed (Harper *et al.*, 2006), whereas this year 1722 cycles were reported, which represents a 42% increase. The largest increase was seen in cycles for repeated implantation failures (RIF) (275–462; 68% increase) and in cycles for severe male factor (101–188; 86% increase).

As for the previous data collections, there was an underreporting of cycles that were cancelled before OR. Only 9 of 1722 cycles were reported to be cancelled, whereas in general cancellation rates are in the range of 5–10%. As a result, the outcome of PGS can only be presented as clinical pregnancy rate per OR or per ET but not per cycle started. This may partly be explained by the fact that many reporting centres only receive the blastomeres for analysis, while the IVF cycle is done elsewhere, making accurate reporting of cycles more difficult and as a result incomplete.

For data collection VI, 9496 embryos were biopsied, and a result was obtained for 8795 embryos (93% of biopsied embryos). Of 3193 embryos diagnosed as transferable (34%

of all biopsied embryos), 2277 were transferred and 454 were frozen. In total, 384 embryos implanted (17% implantation rate).

The overall clinical pregnancy rate was 18% per OR and 24% per ET. These results are similar to the results from collection V (16 and 23% clinical pregnancy rate per OR and ET, respectively). The clinical pregnancy rate per OR ranged from 9% for advanced maternal age (AMA) + recurrent miscarriage to 31% for 'other indications'. These differences in results between various indications reflect at least in part differences in patient and cycle specific data. For instance, in women treated with PGS for AMA (12% clinical pregnancy rate per OR), the mean age was 41 years and the average number of oocytes obtained per OR was 9.8. For couples treated with PGS for severe male factor (28% clinical pregnancy rate per OR), the mean age was only 33 years and the average number of oocytes obtained was 14.6.

**Table IIIa.** Sexing only for X-linked disease using PCR or FISH, data collection I–V

	FISH	PCR	Total
Total cycles	545	68	613
Number infertile	79	0	79
Female age	33	29	33
Cycles cancelled before OR	31	6	37
Cycles to OR	514	62	576
ART method			
IVF	138	10	148
ICSI	374	52	426
ICSI and frozen	1	0	1
Both IVF and ICSI	1	0	1
Cancelled after OR	28 <sup>1</sup>	1 <sup>2</sup>	29 <sup>1,2</sup>
Cycles to PGD	486	61	547
Zona breaching			
AT drilling	299	50	349
Laser drilling	163	1	164
Mechanical	24	10	34
Biopsy method			
Cleavage aspiration	478	56	534
Cleavage extrusion	8	5	13
Embryology			
COC	6787	863	7650
Inseminated	6053	662	6715
Fertilized	4322	526	4848
Biopsied	3292	431	3723
Successfully biopsied	3195	395	3590
Diagnosed	2905	305	3210
Transferable	1023	160	1183
Transferred	757	127	884
Frozen	179 <sup>3</sup>	56 <sup>4</sup>	235 <sup>5</sup>
Clinical outcome			
Cycles to ET	394	51	445
hCG positive	121	22	143
Positive heart beat	93	16	109
Clinical pregnancy rate % per OR/ET	18/24 <sup>6</sup>	26/31	19/24 <sup>6</sup>

ART, assisted reproduction technique; AT, acid Tyrode's; COC, cumulus oocyte complexes; FISH, fluorescent in-situ hybridization; OR, oocyte retrieval.

<sup>1</sup>27 embryos from two cycles frozen before biopsy due to hyperstimulation.

<sup>2</sup>20 embryos frozen before biopsy.

<sup>3</sup>11 cycles with embryos frozen without biopsy or after failed diagnosis included.

<sup>4</sup>Thirteen cycles with embryos frozen without biopsy or failed diagnosis included.

<sup>5</sup>Twenty four cycles with embryos frozen without biopsy or after failed diagnosis included.

<sup>6</sup>11 embryos transferred removed from calculations due to lack of information regarding the number of FHB in pregnancies resulting from the transfer of those embryos.

**Table IIIb.** Sexing only for X-linked disease using PCR or FISH, data collection VI

	FISH	PCR	Total
Total cycles	134	3	137
Number infertile	24	0	24
Female age	33	29	33
Cycles cancelled before OR	10	0	10
Cycles to OR	124	3	127
Cycles cancelled before ART	0	0	0
ART method			
IVF	33	0	33
ICSI	87	3	90
IVF + ICSI	4	0	4
Cancelled post OR	6	0	6
Cycles to PGD	118	3	121
Zona breaching			
AT drilling	64	2	66
Laser drilling	46	1	47
Mechanical	8	0	8
Biopsy method			
Cleavage aspiration	108	3	111

**Table IIIb.** Continued

	FISH	PCR	Total
Cleavage extrusion	9	0	9
Blastocyst	1	0	1
Embryology			
COC	1667	36	1703
Inseminated	1442	27	1469
Fertilized	1025	20	1045
Biopsied	753	20	773
Successfully biopsied	740	20	760
Diagnosed	678	20	698
Transferable	235	15	250
Transferred	150	10	160
Frozen	31	1	32
Clinical outcome			
Cycles to ET	89	3	92
hCG positive	29	2	31
Positive heartbeat	27	1	28
Clinical pregnancy rate (% per OR/% per ET)	22/30	33/33	22/30 <sup>1</sup>
Number of fetal hearts	32	1	33
Implantation rate (fetal heart beats/ 100 embryos transferred)	21	10	21

ART, assisted reproduction technique; AT, acid Tyrode's; COC, cumulus oocyte complexes; ET, embryo transfer; FISH, fluorescent in-situ hybridization; OR, oocyte retrieval. One cycle was combined FISH for sexing and HLA typing with PCR

<sup>1</sup>Four clinical pregnancies without data

### PGD cycles for social sexing

Table VIb summarizes the data from collection VI for social sexing cases using FISH and PCR. Social sexing for male embryos made up 76% of the cycles ( $n = 61$ ) while sexing for females made up 24% ( $n = 19$ ). A total of 80 cycles were collected in this group, with 79 cycles going to OR and an average of 15.4 oocytes per retrieval. The embryos in this group were mainly diagnosed using FISH (91%). The biopsy was successful in 96% of embryos biopsied and 93% of the embryos biopsied were diagnosed. A transfer was achieved in 60% of the cycles which went through PGD, with an average of 2.0 embryos transferred in each cycle. The overall clinical pregnancy rate was 19% per OR and 32% per ET, with an implantation rate [fetal heart beat (FHB)/embryos transferred] of 23%. These data are very comparable to the I–V set (Table VIa).

### Pregnancies and babies

The cumulative data for collection I–V is summarized in Tables VIIa–VIIc. It is becoming apparent that PGD babies are very comparable to ICSI babies in every respect, e.g. complications of pregnancy, characteristics at birth and major and minor malformations.

Of the 666 cycles ending in a positive hCG, no pregnancy was reported in 186 cases: for 89 pregnancies, no information was given by the centres. For 89 further cycles with a positive hCG, no pregnancy was reported because there was no positive heartbeat (these are not the same as the 46 subclinical pregnancies that were reported, Table VIIb). A further eight cycles ending in a positive hCG were lost to follow-up. No cycle was reported for 21 pregnancies. This results in the reporting of 501 pregnancies. Five hundred and one pregnancies ended in 373 reported deliveries, leading to the birth of 453 babies (295 singletons, 152 twins and 6 triplets). Two pregnancies were

**Table IVa.** Cycles performed for single gene disorders using PCR, data collection I–V

Indication	Autosomal recessive				Autosomal dominant							Specific sex-linked			Other	Total
	CF <sup>3</sup>	β-Thal	SMA	SC <sup>6</sup>	EB	DM1	HD <sup>1</sup>	AP	CMT <sup>7</sup>	ACH	MS	DMD <sup>8</sup>	FRAXA	Haem		
Total cycles	324	144 <sup>5</sup>	93	27	9	203	146	10	22	7	10	43	51	18	137	1244
Number infertile	107	69	9	6	0	20	14	7	0	0	0	5	14	0	16	267
Female age	33	33	67	34	31	33	33	28	33	34	32	32	36	29	33	33
Cycles cancelled before OR	36	15	6	2	0	20	16	0	1	0	0	4	3	0	11	114
Cycles to OR	288	129	87	25	9	183	130	10	21	7	10	39	48	18	126	1130
Cycles cancelled before ART	0	0	0	0	0	3	0	0	0	0	0	0	0	0	0	3
ART method																
IVF	15	0	1	0	0	1	0	1	0	0	0	3	2	6	2	31
ICSI	268	128	81	25	9	176	127	9	21	7	10	36	44	11	118	1070
Frozen	0	1	5	0	0	0	0	0	0	0	0	0	0	1	1	8
Unknown	5	0	0	0	0	3	3	0	0	0	0	0	2	0	5	18
Cancelled after OR	14	12	6	1	0	12	5	0	2	1	0	0	4	0	7	64
Cycles to PGD	274	117	81	24	9	168	125	10	19	6	10	39	44	18	119	1063
Zona breaching																
AT drilling	167	95	43	13	8	85	46	10	2	0	8	22	13	15	43	570
Laser drilling	98	22	28	9	1	78	73	0	17	6	2	17	28	2	63	444
Mechanical	5	0	10	2	0	3	3	0	0	0	0	0	1	1	10	35
Unknown	4	0	0	0	0	2	3	0	0	0	0	0	2	0	3	14
Biopsy method																
Polar body biopsy	3 <sup>2</sup>	0	0	2	0	3	4	0	0	0	0	0	1	0	4 <sup>2</sup>	17 <sup>2</sup>
Cleavage aspiration	253 <sup>2</sup>	114	68	22	9	160	115	10	19	6	10	39	41	17	108 <sup>2</sup>	991 <sup>2</sup>
Cleavage extrusion	14	3	13	0	0	3	3	0	0	0	0	0	0	1	5	42
Unknown	6	0	0	0	0	2	3	0	0	0	0	0	2	0	3	16
Embryology																
COCs	3738	1768	1112	363	154	2220	1705	111	297	60	112	574	438	208	1807	14667 <sup>4</sup>
Inseminated	3275	1479	887	287	125	1961	1445	93	244	49	97	454	380	182	1516	12474
Fertilized	2317	951	621	194	112	1441	1038	82	196	32	79	333	276	134	1154	8960
Biopsied	1778	684	501	137	87	974	738	78	100	24	64	263	193	81	828	6530
Successfully biopsied	1759	673	498	135	87	962	723	78	99	24	63	258	192	80	819	6450
Diagnosed	1492	544	419	116	66	812	608	61	83	20	58	221	163	48	701	5412
Transferable	902	293	264	72	37	355	264	32	35	10	36	152	67	33	342	2894
Transferred	500	230	172	52	23	266	167	25	21	9	25	79	46	30	231	1876
Frozen	173	40	17	33	0	22	37	0	5	0	4	40	10	4	76	461
Clinical outcome																
Cycles to ET	239	108	77	22	8	138	102	9	11	6	10	33	29	13	104	909
hCG positive	75	42	23	6	3	37	24	3	5	0	2	11	9	6	38	284
Positive heart beat	59	34	19	4	1	29	18	1	5	0	2	10	8	5	35	230
Clinical pregnancy rate % per OR/% per ET	20/25	26/31	22/25	16/18	11/13	16/21	14/18	10/11	24/45	0/0	20/20	26/30	17/28	28/38	28/34	20/25

ACH, achondroplasia; AP, amyloid polyneuropathy; ART, assisted reproduction technique; AT, acid Tyrode's; CF, cystic fibrosis (various mutations); CMT, Charcot–Marie–Tooth disease; COC, cumulus oocyte complex; DM1, myotonic dystrophy type 1; DMD, Duchenne muscular dystrophy (specific); EB, epidermolysis bullosa; FRAXA, fragile-X syndrome; Haem, haemophilia; HD, Huntington's Disease; MS, Marfan's syndrome; OR, oocyte retrieval; SC, sickle-cell anaemia; SMA, spinal muscular atrophy; β-thal, β-thalassaemia.

<sup>1</sup>Includes nine HD with exclusion.

<sup>2</sup>Three cycles had both polar body biopsy and cleavage stage biopsy.

<sup>3</sup>Two cycles for two indications: cystic fibrosis and fragile X syndrome; cystic fibrosis and social sexing.

<sup>4</sup>Eight cycles with missing data.

<sup>5</sup>Includes three cycles of β-thalassaemia with HLA typing.

<sup>6</sup>Includes two cycles for sickle cell and β-thalassaemia.

<sup>7</sup>Includes one cycle for X-linked dominant inheritance.

<sup>8</sup>Includes one cycle for Beckers muscular dystrophy.

terminated because of an encephalocele and spina bifida diagnosed on ultrasound. Sixty-nine of 403 ongoing pregnancies (17%) presented with complications, mainly bleeding and emesis. One hundred and five of 373 pregnancies were delivered prematurely (28%), 48 singleton pregnancies (16%), 55 twin pregnancies (72%) and 2 triplet pregnancies (100%). As before, all parameters e.g. weight, length and head circumference were comparable to those of ICSI babies (Bonduelle *et al.*, 2002) and previous PGD Consortium reports (Harper *et al.*, 2006).

Seventeen babies were born with malformations (4%), eleven of which were major malformations.

Two hundred and fifty-seven of the 564 fetal sacs were tested prenatally (46%), whereas 203 of 564 fetal sacs were tested post-natally (36%). These figures cannot be added, as some fetal sacs were tested both prenatally and post-natally. Abnormalities were found in 13 instances: four prenatally, two of which ended in a termination of pregnancy (TOP) and nine post-natally. Eight abnormalities were found in miscarriage material, whereas one abnormal karyotype was found at birth.

Of the misdiagnosis: a trisomy 13 was found in miscarriage material after PGD for 45,XY,der(13;14)(q10;q10). Although difficult to trace, the centre where this misdiagnosis occurred seem to

**Table IVb.** Cycles performed for single gene disorders using PCR, data collection VI

Indication	Autosomal recessive				Autosomal dominant				Specific sex-linked				Others	Total	
	β-thal (β-thal+HLA)				HD (HDexcl)				DMD (BMD)						FRAXA <sup>1</sup>
	CF	β-thal	SC	SMA	HD	DM1	APC	Marfan	DMD	Haem	FRAXA <sup>1</sup>				
Total n cycles	69	53 (8)	29	9	90 (8)	67	9	8	17 (4)	14	27	104	516		
Number infertile	18	22 (0)	6	2	22 (1)	10	1	0	4 (0)	5	3	20	114		
Female age	33	33 (36)	33	33	32 (29)	33	28	32	34 (26)	32	35	33	33		
Cycles cancelled before OR	5	7 (1)	5	3	14 (0)	13	0	0	0 (0)	2	4	11	65		
Cycles to OR	64	46 (7)	24	6	76 (8)	54	9	8	17 (4)	12	23	91 <sup>2</sup>	449 <sup>2</sup>		
Cycles cancelled before ART	0	0	0	0	0	0	0	0	0	0	0	1	1		
ART method															
IVF	0	0 (0)	0	0	0 (0)	0	0	0	0 (0)	0	0	0	0		
ICSI	61	46 (7)	23	6	75 (8)	51	9	8	15 (3)	11	23	88	434		
IVF + Frozen	0	0	0	0	0	2	0	0	0 (0)	0	0	0	2		
ICSI + Frozen	3	0	1	0	1 (0)	0	0	0	2 (0)	0	0	4 <sup>2</sup>	11 <sup>2</sup>		
IVF + ICSI	0	0	0	0	0 (0)	1	0	0	0 (1)	1	0	0	3		
Cancelled after ART	3	4 (0)	1	0	2 (0)	8	1	0	0 (1)	0	2	10	32		
Cycles to PGD	61	42 (7)	23	6	74 (8)	46	8	8	17 (3)	12	21	82 <sup>2</sup>	418 <sup>2</sup>		
Zona breaching															
AT drilling	18	16 (0)	6	3	27 (0)	5	6	6	6 (0)	6	7	23	129		
Laser drilling	38	26 (7)	15	3	35 (8)	41	2	2	11 (3)	6	14	56	267		
Mechanical	5	0 (0)	2	0	12 (0)	0	0	0	0 (0)	0	0	3	22		
Biopsy method															
Polar body	3	0 (0)	0	0	1 (0)	0	0	0	0 (0)	1	0	6	11		
Cleavage aspiration	52	40 (7)	17	3	56 (8)	46	6	2	15 (3)	11	17	74	357		
Cleavage extrusion	6	2 (0)	6	3	16 (0)	0	0	0	0 (0)	0	0	0	33		
Blastocyst	0	0 (0)	0	0	1 (0)	0	2	6	2 (0)	0	4	2	17		
Embryology															
COC	820	841 (81)	358	75	992 (150)	753	113	119	212 (63)	176	232	1222	6207		
Inseminated	706	716 (74)	275	60	814 (136)	629	77	67	187 (60)	149	192	1056	5198		
Fertilized	478	500 (56)	195	37	556 (98)	433	45	40	128 (37)	100	128	741	3572		
Biopsied	367	310 (42)	141	36	439 (86)	267	43	30	117 (23)	75	85	587	2648		
Successfully biopsied	366	297 (40)	141	36	432 (85)	266	42	30	111 (17)	75	85	572	2595		
Diagnosed	320	258 (39)	130	33	370 (70)	219	33	27	102 (17)	69	70	482	2239		
Transferable	184	152 (4)	82	20	172 (33)	99	18	7	75 (10)	32	29	209	1126		
Transferred	103	101 (4)	49	9	105 (14)	56	11	6	41 (8)	25	17	118	667		
Frozen	35	17 (1)	7	5	20 (7)	12	3	0	10 (0)	2	2	26	147		
Clinical outcome															
Cycles to ET	50	38 (3)	21	6	58 (8)	33	6	4	14 (3)	12	11	68	335		
hCG Positive	19	15 (1)	6	1	22 (3)	14	3	2	5 (0)	4	4	22	121		
Positive heartbeat	16	9 (1)	3	0	20 (1)	11	1	0	5 (0)	3	3	17	90		
Clinical pregnancy rate (% per OR/% per ET)	25/32	20/24 (14/33)	13/14	0/0	26/34 (13/13)	20/33	11/17	0/0	29/36 (0/0)	25/25	13/27	19/25	20/27		
Number fetal heartbeats	22	13 (3)	3	0	23 (1)	14	2	0	6 (0)	4	4	19	114		
Implantation rate (fetal hearts/100 embryos transferred)	21	13 (75)	6	0	22 (7)	25	18	0	15 (0)	16	24	16	17		

APC, Adenomatous Polyposis Coli; ART, assisted reproduction technique; AT, acid Tyrode's; BMD, Becker muscular dystrophy (specific); CF, cystic fibrosis (various mutations); COC, cumulus oocyte complexes; DM1, myotonic dystrophy type 1; DMD, Duchenne muscular dystrophy (specific); Haem, Haemophilia; HD, Huntington disease; Marfan, Marfan syndrome, FRAXA, Fragile-X syndrome; OR, oocyte retrieval; SC, sickle-cell anaemia; SMA, spinal muscular atrophy; β-thal, β-thalassaemia.

<sup>1</sup>Two cycles had both aneuploidy screening and PGD for FRAXA.

<sup>2</sup>Two cycles were on frozen-thawed embryos only, so they were not counted as cycles with an OR, but were counted as cycles going to PGD.

**Table Va.** Cycles performed for PGS, data collection I–V

Indication	AMA	AMA + miscarriage <sup>1</sup>	AMA + RIF <sup>1</sup>	Recurrent miscarriage	Recurrent IVF failure	Severe male factor <sup>2</sup>	No indication	Other	Total
Total cycles	1043	43	129	483	917	166	67	263	3111
Number infertile	990	36	114	419	893	166	63	213	2894
Female age	40	40	40	36	36	32	33	35	36
Cycles cancelled before OR	3	2	0	10	13	2	1	2	33
Cycles to OR	1040	41	129	473	904	164	66	261	3078
ART method									
IVF	197	9	33	52	143	2	16	59	511
ICSI	835	32	94	417	725	161	50	187	2501
IVF + ICSI	2	0	1	2	7	0	0	1	13
Frozen	0	0	0	0	4	0	0	0	4
Frozen and ICSI	1	0	1	1	1	1	0	0	5
Unknown	5	0	0	1	24	0	0	14	44 <sup>4</sup>
Cancelled after OR	46	3	2	9	50	9	1	8	128
Cycles to PGS	994	38	127	464	854	155	65	253	2950
Zona breaching									
AT drilling	565	18	84	333	539	59	42	168	1808
Laser drilling	386	20	42	122	266	89	18	57	1000
Mechanical	30	0	1	8	12	7	5	14	77
Unknown	13	0	0	1	37	0	0	14	65 <sup>4</sup>
Biopsy method									
Polar body biopsy	69 <sup>3</sup>	20	46	12	24	0	3	4	178 <sup>3</sup>
Cleavage aspiration	814 <sup>3</sup>	18	81	423	724	118	60	243	2481 <sup>3</sup>
Cleavage extrusion	92	0	0	27	62	36	2	5	224
Cleavage flow displacement	7	0	0	1	6	1	0	1	16
Unknown	13	0	0	1	38	0	0	0	52 <sup>4</sup>
Embryology									
COC	10907	391	1311	6663	12600	2476	836	3377	38561
Inseminated	9466	324	1116	5586	10801	1976	745	2825	32839
Fertilized	6742	192	795	3979	7738	1315	547	2015	23323
Biopsied	5406	209	739	3017	5227	971	435	1545	17549
Successfully biopsied	5325	208	733	2921	5155	958	413	1519	17232
Diagnosed	4509 <sup>5</sup>	199	710	2455 <sup>5</sup>	4782 <sup>5</sup>	804	281 <sup>5</sup>	1296 <sup>5</sup>	15036 <sup>5</sup>
Transferable	1136 <sup>5</sup>	64	229	879 <sup>5</sup>	1891 <sup>5</sup>	357	225 <sup>5</sup>	572 <sup>5</sup>	5353 <sup>5</sup>
Transferred	1358 <sup>5</sup>	49	163	720 <sup>5</sup>	1314 <sup>5</sup>	267	133 <sup>5</sup>	456 <sup>5</sup>	4460 <sup>5</sup>
Frozen	126	9	36	77	295	42	8	94	687
Clinical outcome									
Cycles to ET	677	28	96	358	643	133	60	193	2188
hCG positive	201	6	22	123	192	59	20	79	702
Positive heart beat	151	5	18	98	136	52	19	55	534
Clinical pregnancy rate % per OR/% per ET	15/22	12/18	14/19	21/27	15/21	32/39	29/32	21/28	17/24

ART, assisted reproduction technique; AT, acid Tyrode's; COC, cumulus oocyte complexes; ET, embryo transfer; OR, oocyte retrieval.

Other—includes data with two indications.

<sup>1</sup>These data were not extracted from I–IV.

<sup>2</sup>These data were not extracted from I–III.

<sup>3</sup>One cycle had cleavage stage biopsy and polar body biopsy.

<sup>4</sup>Several cycles had incomplete results.

<sup>5</sup>Several cycles from one centre had no information on the number of embryos diagnosed, number embryos diagnosed as transferable, but patients did have embryos transferred. In these cases, undiagnosed or abnormal embryos were transferred.

attribute it to a human error without discarding a FISH error or embryonic mosaicism, because the diagnosis was established on one cell. The trisomy 16 found in miscarriage material after PGS for AMA and RIF occurred after first polar body biopsy only, in which clearly two signals for chromosome 16 had been found. The second trisomy 16 found in miscarriage material occurred after PGS at the cleavage stage. Re-probing of the fixed blastomere clearly showed two signals for chromosome 16. Although a FISH error seems unlikely, the cause of this error (mosaicism of the embryo, human error) cannot be traced anymore.

Seventeen misdiagnoses have been reported in six reports, ten for PCR and seven for FISH. Except for one misdiagnosis for a reciprocal translocation where an inappropriate probe scheme was used (Sermon *et al.*, 2005; Mackie Ogilvie and Scriven, 2004; Kyu Lim *et al.*, 2004), the reason for the misdiagnoses is difficult to establish.

## Discussion

This sixth report of the ESHRE PGD Consortium reports on an ever-increasing number of cycles, pregnancies and babies,

**Table Vb.** Cycles performed for PGS, data collection VI

Indication	AMA	AMA + miscarriage	AMA + RIF	Recurrent miscarriage	RIF	SMF	No indication	Other	Total
Total number of cycles	478	66	197	251	462	188	43	37	1722
Number infertile	381	57	182	193	450	144	41	25	1473
Female age	41	41	40	36	34	33	33	37	37
Cycles cancelled before OR	0	2	0	1	0	0	5	1	9
Cycles to OR	478	64	197	250	462	188	38	36	1713
ART method									
IVF	27	11	8	27	22	0	24	5	124
ICSI	443	51	183	213	435	188	14	31	1558
IVF + ICSI	5	0	1	8	1	0	0	0	15
Unknown	1	0	5	0	0	0	0	0	6
ICSI + frozen	2	2	0	2	4	0	0	0	10
Cancelled post OR	18	9	0	6	7	2	3	0	45
Cycles to PGD	460	55	197	244	455	186	35	36	1668
Zona breaching									
AT drilling	186	30	105	147	149	75	4	20	716
Laser drilling	257	23	88	90	256	111	31	14	870
Mechanical	17	2	4	7	50	0	0	2	82
Biopsy method									
PB biopsy	47	13	62	5	54	0	0	4	185
Cleavage aspiration	372	41	135	232	384	179	35	31	1409
Cleavage extrusion	41	1	0	7	17	7	0	1	74
Cleavage flow displacement	0	0	0	0	0	0	0	0	0
Embryology									
COC	4707	539	1980	3211	6540	2752	437	500	20666
Inseminated	3837	446	1623	2607	5344	2202	403	405	16867
Fertilized	2638	302	1122	1890	3775	1507	285	296	11815
Biopsied	2128	280	1063	1436	3065	1080	196	248	9496
Successfully biopsied	2109	280	1045	1431	3042	1073	194	239	9413
Diagnosed	1994	265	988	1321	2842	990	171	224	8795
Transferable	614	65	314	534	1053	431	91	91	3193
Transferred	480	54	254	357	709	311	54	58	2277
Frozen	80	7	35	95	156	43	24	14	454
Clinical outcome									
Cycles to ET	297	35	155	191	380	164	31	30	1283
hCG positive	74	7	36	75	120	70	13	14	409
Positive heart beat	56	6	27	56	92	52	11	11	311
Clinical pregnancy rate (% per OR/% per ET)	12/19	9/17	14/17	22/29	20/24	28/32	29/35	31/37	18/24
Number of fetal heartbeats	65	6	29	72	118	69	11	14	384
Implantation rate (fetal heartbeats/100 embryos transferred)	14	11	11	20	17	22	20	24	17

AMA, advanced maternal age; ART, assisted reproduction technique; AT, acid Tyrode's; COC, cumulus oocyte complexes; OR, oocyte retrieval; RIF, repeated implantation failure; SMF, severe male factor.

from a still increasing number of participating centres. For this report, the referrals are not included, because it was felt from previous reports that the data were biased and incomplete. Indeed, only few centres reported all referrals, i.e. referrals for patients who did not come through for PGD because either it was technically impossible to help them, or for ethical reasons, or reasons related to IVF e.g. AMA.

An interesting feature is the relative increase in the number of PGS cycles. This reflects the fact that many IVF laboratories offer PGS, and PGS only, as an additional method to select the best embryo for transfer. The ESHRE PGD Consortium Steering Committee would like to emphasize that they feel that there is a need for large randomized controlled trials to investigate the (cost-)effectiveness of PGS for well-defined indications. Currently, there are insufficient data that demonstrate that PGS is indeed a cost-effective alternative for standard IVF (Staessen *et al.*, 2004; Twisk *et al.*, 2006).

PGD for monogenic diseases and chromosomal abnormalities have also been steadily increasing, whereas sexing (both

for X-linked diseases and for social sexing) remains stable. For the sexing for X-linked diseases, this reflects the fact that more and more specific PGD at the DNA level is offered. For social sexing, only two centres offer it, and this has remained the same for the last three reports. To be able to offer PGD for monogenic diseases or chromosomal abnormalities, a close collaboration between an IVF centre and a genetic laboratory is mandatory. The higher technical expertise needed for this type of diagnosis explains why less centres are able to offer it.

It becomes obvious that at birth PGD babies have characteristics that are comparable to those of ICSI babies. No pregnancy complication or malformation at birth is particularly occurring in the PGD population. The characteristics of the babies at birth are also comparable, and the main complication remains multiple pregnancies leading to morbidity and mortality in PGD offspring.

The ESHRE PGD Consortium has been active during the past year: the PGD Consortium guidelines for PGD and PGS were published in 2005 (Thornhill *et al.*, 2005), and recently, a

**Table VIa.** PGD for social sexing, data collection I–V

Method for sexing	FISH SS only	FISH SS + PGS	PCR	Unknown	Total
Total cycles	124	22	103	5	254
Number infertile	18	6	16	1	41
Female age	35	38	35	35	35
Cycles cancelled before OR	0	0	0	0	0
Cycles to OR	124	22	103	5 <sup>1</sup>	254 <sup>1</sup>
ART method					
IVF	104	1	5	3	113
ICSI	17	21	88	2	128
Frozen	3	0	2	0	5
Frozen and IVF	0	0	1	0	1
Frozen and ICSI	0	0	5	0	5
Unknown and frozen	0	0	2	0	2
Cancelled after OR	3		6	5	14
Cycles to PGD	121	22	97	0	240
Zona breaching					
AT drilling	9	0	10	0	19
Laser drilling	112	0	0	0	112
Mechanical	0	22	87	0	109
Biopsy method					
Cleavage aspiration	120	0	10	0	130
Cleavage extrusion	1	22	87	0	110
Embryology					
COC	1463	301	1504	23	3291
Inseminated	1421	210	1122	19	2772
Fertilized	1022	128	730	11	1891
Biopsied	876	100	613	0	1589
Successfully biopsied	802	100	603	0	1505
Diagnosed	732	83	552	0	1367
Transferable	303	24	325	0	652
Transferred	178	23	248	0	449
Frozen <sup>2</sup>	99	1	49	0 <sup>3</sup>	149
Clinical outcome					
Cycles to ET	96	14	82	0	192
hCG positive	40	4	34	0	78
Positive heart beat	38	0	21	0	59
Clinical pregnancy rate % per OR/% per ET	31/40		20/26		23/31

ART, assisted reproduction technique; AT, acid Tyrode's; COC, cumulus oocyte complexes; FISH, fluorescent in-situ hybridization; OR, oocyte retrieval.

<sup>1</sup>One natural cycle included.

<sup>2</sup>Eleven cycles with embryos frozen without biopsy or failed diagnosis included.

<sup>3</sup>Three embryos frozen without biopsy were not included.

**Table VIb.** PGD for social sexing, data collection VI

	FISH	PCR	Total
Total cycles	73	7	80
Number infertile	1	0	1
Female age	38	43	38
Cycles cancelled before OR	1	0	1
Cycles to OR	72	7	79
Cycles cancelled before ART	0	0	0
ART method			
IVF	5	0	5
ICSI	65	6	71
ICSI + frozen	0	1	1
Unknown + frozen	2	0	2
Cancelled post OR	1	0	1
Cycles to PGD	71	7	78
Zona breaching			
AT drilling	0	0	0
Laser drilling	1	0	1
Mechanical	70	7	77
Biopsy method			
Cleavage aspiration	1	0	1
Cleavage extrusion	70	7	77

**Table VIb.** Continued

	FISH	PCR	Total
Embryology			
COC	1066	154	1220
Inseminated	832	117	949
Fertilized	566	78	644
Biopsied	426	52	478
Successfully biopsied	409	52	461
Diagnosed	393	52	445
Transferable	78	35	113
Transferred	71	21	92
Frozen	8	12	20
Clinical outcome			
Cycles to ET	40	7	47
hCG positive	16	4	20
Positive heartbeat	12	3	15
Clinical pregnancy rate (% per OR/% per ET)	17/30	43/43	19/32
Number of fetal heartbeats	14	7	21
Implantation rate (fetal hearts/100 embryos transferred)	20	33	23

ART, assisted reproduction technique; AT, acid Tyrode's; COC, cumulus oocyte complexes; ET, embryo transfer; FISH, fluorescent in-situ hybridization; OR, oocyte retrieval.

**Table VIIa.** Evolution of pregnancy, data I–V

	Number of pregnancies	Number of fetal sacs
Pregnancies	1133	1279
FISH cycles	883/1133 <sup>6</sup>	
PCR cycles	251/1133 <sup>6</sup>	
Subclinical pregnancies <sup>1</sup>	166/1133	
Clinical pregnancies	967	1279
Singletons	694/967	694/1279
Twins	234/967	468/1279
Triplets	36/967	108/1279
Quadruplet	2/967	8/1279
Unknown	1/967	1/1279 <sup>7</sup>
First trimester loss	98/967	157/1279
Miscarriage	88/967 <sup>8</sup>	100/1279
Extrauterine pregnancy	10/967 <sup>9</sup>	11/1279
Vanishing twins/triplets		46/1279
Ongoing pregnancies >12 weeks	869	1122
Second trimester loss	26/869	36/1122
Miscarriage	18/869 <sup>2</sup>	27/1122 <sup>2</sup>
TOP after misdiagnosis <sup>3</sup>	4/869	8/1122
TOP after amniocentesis <sup>4</sup>	4/869	
Reduction <sup>5</sup>		1/1122
Reduction of multiple pregnancies		18/1122
Quadruplet to twin		4/1122
Triplet to twin		7/1122
Triplet to singleton		6/1122
Twin to singleton		1/1122
Normal evolution	843	1068
Lost to follow-up	39	51
Deliveries	804	1017
Singletons	602/804	602/1017
Twins	191/804	382/1017
Triplets	11/804	33/1017

FISH, fluorescent in-situ hybridization; TOP, termination of pregnancy.

<sup>1</sup>Subclinical pregnancy defined as pregnancy without any other clinical signs but positive serum hCG.

<sup>2</sup>One triplet: fetal reduction, followed by amniocentesis and loss of remaining twin at 16 weeks (one fetal sac counted in reduction, two in miscarriage, one second trimester pregnancy loss after miscarriage counted).

<sup>3</sup>One misdiagnosis for sexing, FISH, female fetus, indication social sexing; one misdiagnosis for beta thalassaemia, PCR; one misdiagnosis for myotonic dystrophy, PCR, one misdiagnosis after PGS, karyotype 45,X.

<sup>4</sup>TOP for abnormalities found after amniocentesis, not related to the PGD: trisomy 18, indication for PGD parent carrier of reciprocal translocation not involving chromosome 18; one polymalformation, one cystic hygroma, failed karyotype, one Turner mosaic.

<sup>5</sup>One misdiagnosis for sexing, PCR, indication Duchenne, twin pregnancy, selective termination of male fetus. Cycle done in 1996, Y-specific amplification only.

<sup>6</sup>One fetal sac was tested by FISH and PCR.

<sup>7</sup>Number of fetal heart beats not known. Counted further as 1 fetal heart beat.

<sup>8</sup>One miscarriage after amniocentesis.

<sup>9</sup>One heterotrophic gestation continued as singleton after reduction of extrauterine gestation at 6 weeks.

joint report of the European Society for Human Genetics (ESHG) and ESHRE was published (Soini *et al.*, 2006). This report discusses the interface between genetics and assisted reproductive technology regarding technical, sociological, ethical and legal issues and deals not only with PGD but also with other topics such as screening of gamete donors and reproductive tourism.

The ESHRE PGD Consortium also aims at constantly improving the data collection and its processing. A major reorganization of the database is planned, and better follow-up of data submission is now reassured by a permanent staff member at ESHRE. Quality assessment of captured FISH images is planned, as well as retrospective analysis of the children born after PGD, as a preliminary study for the long-term child

**Table VIIb.** Evolution of pregnancy, data VI

	Number of pregnancies	Number of fetal sacs
Pregnancies	501	564
FISH cycles	399	454
PCR cycles	102	110
Subclinical pregnancies <sup>1</sup>	46	
Extrauterine gestation	7	
Clinical pregnancies	448	564
Singletons	345	345
Twins	90	180
Triplets	13	39
Quadruplet	0	0
Unknown	0	0
First trimester loss	45	67
Miscarriage	44	45
Vanishing twins		21
TOP	1 <sup>2</sup>	1 <sup>2</sup>
Ongoing pregnancies (>12 weeks)	403	497
Second trimester loss	4	5
Miscarriage	3	4
TOP	1 <sup>3</sup>	1 <sup>3</sup>
Reduction of multiple pregnancies		13
Triplet to twin	4	4
Triplet to singleton	4	8
Twin to singleton	1	1
Remaining data	399	479
Singletons	321	321
Twins	76	152
Triplet	2	6
Lost to follow-up	26	26
Singletons	26	26
Twins	0	0
Triplets	0	0
Deliveries	373	453
Singletons	295	295
Twins	76	152
Triplets	2	6

FISH, fluorescent in-situ hybridization; TOP, termination of pregnancy.

<sup>1</sup>Subclinical pregnancy defined as pregnancy without any other clinical signs, but positive serum hCG.

<sup>2</sup>For encephalocele.

<sup>3</sup>For spina bifida.

**Table IXa.** Method of delivery and gestational age, data collection I–V

	Total	Singletons	Twins	Triplets
Number of deliveries	804	602	191	11
Method of delivery				
Vaginal	333	294	38	1
Caesarian	385	255	121	9
Vaginal and Caesarian	1	0	1	0
Unknown	85	53	31	1
Term at delivery				
Preterm	187	77	102	8
Term	474	420	52	2
Unknown	143	105	37	1

**Table IXb.** Method of delivery and gestational age, data VI

	Total	Singleton	Twin	Triplet
Number of deliveries	373	295	76	2
Method of delivery				
Vaginal	174	156	18	0
Caesarean	177	119	56	2
Vaginal and Caesarean	2	2	0	0
Unknown	20	18	2	0
Term at delivery				
Preterm	105	48	55	2
Term	233	217	16	0
Unknown	35	30	5	0

**Table Xa.** Confirmation of diagnosis per fetal sac, data collection I–V

Method	Result		
	N	Normal	Abnormal
Prenatal diagnosis <sup>1</sup>			
FISH			
CVS	49	49	0
Amnio	258	253	5 <sup>2</sup>
Ultrasound	98	96	2 <sup>3</sup>
Unknown	3	3	0
Total	408	401	7
PCR			
CVS	66	66	0
Amnio	47	40	7 <sup>4</sup>
Ultrasound	4	3	1 <sup>5</sup>
Unknown	2	2	0
Total	119	111	8
Post-natal diagnosis <sup>6</sup>			
FISH			
Karyo miscarriage	25	11 <sup>7</sup>	14 <sup>8</sup>
Karyo postnatal	47	45 <sup>9</sup>	2 <sup>10</sup>
Physical examination	265	263	2 <sup>11</sup>
Total	337	319	18
PCR			
Karyotype miscarriage	1	1 <sup>14</sup>	0
DNA test miscarriage	2	2	0
DNA test postnatal	24	23	1 <sup>12</sup>
Sweat test	4	4	0
Physical examination	7 <sup>15</sup>	6	1 <sup>13</sup>
Karyotype	2	2	0
Karyo + DNA	1	1	0
Unknown	1	1	0
Total	42	40	2

CVS, chorionic villus sampling; FISH, fluorescent in-situ hybridization.

<sup>1</sup>FISH Fetal sacs tested: 408/991; PCR Fetal sacs tested: 119/289; Total prenatal testing: 527/1279 (one fetal sac had PCR and FISH at PGD).

<sup>2</sup>Two misdiagnoses: sexing, female fetus, social sexing (terminated); PGS: 45,X (terminated). Trisomy 18 after PGD for reciprocal translocation. 46,XX,t(1;5)(q43;q13)de novo after PGD for 46,XY,t(1;11)(p12;q12) (born), 45,X[10]/46,XX[55] after PGS for repeated IVF failures (TOP).

<sup>3</sup>Polymalformation on US, normal karyotype, terminated. Cystic hygroma, karyotype failed, PGD for 45,XX,der(13;21)(q10;q10).

<sup>4</sup>Six misdiagnoses: XL Duchenne (selective reduction of one affected embryo of twin pregnancy), beta-thalassaemia (terminated), myotonic dystrophy (terminated), CF (born), XL retinitis pigmentosa (born), amyloid polyneuropathy (born), 46,XX,t(8;9)(p?23;p12) de novo after PGD for Duchenne muscular dystrophy.

<sup>5</sup>Echogenic bowel at US, misdiagnosis for CF, born.

<sup>6</sup>Total FISH sacs/babies tested: 337/991; Total PCR sacs/babies tested: 42/289; Total postnatal testing: 379/1280.

<sup>7</sup>Normal karyotype in a fetus with multiple malformations, After amniocentesis with normal karyotype.

<sup>8</sup>One trisomy 3, one trisomy 15, two trisomy 16, one trisomy 22, one mosaic trisomy 22, one monosomy X, 47,XY,+D(3), one misdiagnosis, 47,XX,+der(22)t(11;22)(q23.3;q11.2)mat; parent carrier balanced translocation, 46,X,inv(Y)(p11q12); trisomy 16 after PGS with PB1 analysis; 45,XX,der(7)t(7;15)(p14;q11.2),-15de novo; 47,XX,+9, trisomy 22.

<sup>9</sup>One baby born with Fryns syndrome had a karyotype (normal result). Three twins with polymalformations had a normal karyotype.

<sup>10</sup>One misdiagnosis, trisomy 21 after aneuploidy screening,

46,XX,t(1;5)(q43;q13)de novo already seen in prenatal.

<sup>11</sup>One baby with Fryns syndrome, one baby with Prune Belly syndrome (both normal karyotype).

<sup>12</sup>One CF carrier twin pregnancy—on PGD both diagnosed as homozygote normal.

<sup>13</sup>One twin after PGD for CF: one misdiagnosis, one healthy.

<sup>14</sup>After amniocentesis.

<sup>15</sup>One baby (PGD for DMD) had FISH + PCR, diagnosis confirmed by physical examination and amnio.

follow-up. With these measures, ESHRE hopes to help IVF and genetic centres to bring PGD up to today's standards of good laboratory and clinical practice.

**Table Xb.** Confirmation of diagnosis per fetal sac, data collection VI

Method	Result			
	N	Normal	Abnormal	Unknown
Prenatal diagnosis <sup>1</sup>				
FISH				
CVS	7	7	0	
Amnio	64	61	1 <sup>2</sup>	2 <sup>3</sup>
Ultrasound	146	144	2 <sup>4</sup>	0
Total	217	212	3	2
PCR				
CVS	12	11	1 <sup>5</sup>	0
Amnio	17	17	0	0
Ultrasound	11	11	0	0
Total	40	39	1	0
Post-natal diagnosis <sup>6</sup>				
FISH				
Karyo miscarriage	17	9	8 <sup>7</sup>	
Karyo postnatal	26	25	1 <sup>8</sup>	
Physical examination	181	181	0	
Total	224	215	9	
PCR				
DNA test miscarriage	0	0	0	
Karyo miscarriage	3	3	0	
Physical examination	7	7	0	
DNA test postnatal	6	6	0	
Karyotype	4	4	0	
Sweat test	2	2	0	
Algo test	2	2	0	
Unknown	5	5	0	
Total	29	29	0	

CVS, chorionic villus sampling; FISH, fluorescent in-situ hybridization.

<sup>1</sup>FISH fetal sacs tested: 217/454; PCR fetal sacs tested: 40/110; Total prenatal testing: 257/564.

<sup>2</sup>After PGD for inversion: 46,XX/47,XXX ongoing and live birth.

<sup>3</sup>One amnio after omphalocele found on US. Mors in utero.

<sup>4</sup>One encephalocele, one spina bifida. Both TOP.

<sup>5</sup>De novo translocation 46,XX,(13;20)(q14;p11).

<sup>6</sup>FISH fetal sacs/babies tested: 183/454; PCR fetal sacs/babies tested: 20/110; Total post-natal testing: 203/564.

<sup>7</sup>45,X (PGD for 45,XX,der(13;14)(q10;q10)), 47,XX,+16 (PGS for RIF),

45,XY (no more details given, PGD for 45,XY,der(13;14)(q10;q10)),

47,XY,+9 (PGS for RM), trisomy 4 (PGS for AMA), trisomy 16 (PGS for AMA and RIF), trisomy 16 (PGS for RM). One misdiagnosis: T13 after PGD for 45,XY,der(13;14)(q10;q10).

<sup>8</sup>De novo translocation involving chromosome 20.

**Table XIa.** Data on live-born children, data collection I–V

Total children born	990	
Sex		
Male	410	
Female	535	
Unknown	45	
Mean birth weight (g)		
Singletons	3255	544
Twins	2431	304
Triplets	1756	21
Mean birth length (cm)		
Singletons	50	352
Twins	47	153
Triplets	44	6

## Supplementary materials

Supplementary data are available at <http://humrep.oxfordjournals.org/>.

**Table IIc.** Chromosomal abnormalities analysed, data VI.

**Table XIb.** Data on live-born children, data collection VI

Total children born	441
Sex	
Male	200
Female	238
Unknown	3
Mean birth weight (g)	
Singletons	3214 ( <i>n</i> = 260/295) <sup>1</sup>
Twins	2404 ( <i>n</i> = 112/152) <sup>1</sup>
Triplets	1372 ( <i>n</i> = 6/6) <sup>1</sup>
Mean birth length (cm)	
Singletons	50 ( <i>n</i> = 179/295) <sup>1</sup>
Twins	45 ( <i>n</i> = 88/152) <sup>1</sup>
Triplets	40 ( <i>n</i> = 3/6) <sup>1</sup>
Mean head circumference (cm)	
Singletons	34 ( <i>n</i> = 132/285) <sup>1</sup>
Twins	32 ( <i>n</i> = 74/150) <sup>1</sup>
Triplets	28 ( <i>n</i> = 3/6) <sup>1</sup>
Apgar scores	
Good	242/255
Poor	13/255

<sup>1</sup>Numbers between brackets indicate the number of newborns for whom information is available out of the total number of newborns.

**Table IIIc.** List of indications for which sexing has been performed, data collection VI.

**Table IVc.** List of indications under 'others' for monogenic diseases with PCR, data VI.

**Table VIIIa.** Complications in clinical pregnancies, data I–V.

**Table VIIIb.** Complications in clinical pregnancies, data VI.

**Table XIIa.** Congenital malformations and neonatal complications at birth, data collection I–V.

**Table XIIb.** Congenital malformations and neonatal complications at birth, data collection VI.

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