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## Introduction

**The year two thousand and sixteen** marks the thirtieth year of the Assisted Reproduction Programme at Queen Mary Hospital.

A total of 568 assisted reproduction treatment cycles were initiated in 534 couples during this period. The numbers of treatment cycles and of patients were lower than those in 2015. This could be attributed to the laboratory closure for renovation work in the early part of the year. The number of frozen-thawed embryo transfer cycles was lower for similar reasons. The mean numbers of embryos replaced were 1.5 and 1.6 per transfer in conventional IVF and ICSI cycles respectively, which was similar to the previous year, and we continued to promote elective single embryo transfer in selected patients with better prognosis. The mean number of embryos replaced in frozen-thawed embryo transfer cycles was 1.5 per transfer. This year, our multiple pregnancy rates were 14.8% and 8.6% in conventional IVF and ICSI cycles respectively, and there was no higher order multiple pregnancy resulted.

Similar to last year, women who were younger than 35 years in their first treatment cycle and had at least two good quality embryos were encouraged to have elective single embryo transfer. The pregnancy and ongoing pregnancy rate per transfer were 49.0% and 43.8% respectively whereas the corresponding rates in non-elective single embryo transfer cycles were 22.6% and 17.0% respectively. Those with at least 6 cleaving embryos 2 days after egg collection were also counselled for extended culture.

In 2016, preimplantation genetic diagnosis was performed in 39 cycles in 38 women at risk of having babies with serious chromosomal or genetic disorders.

In December 2016, Our Unit celebrated the 30<sup>th</sup> anniversary of our assisted reproduction programme.

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### Team Photo:



**Front Row:** (Left to Right)

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**Second Row:** (Left to Right)

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**Back Row:** (Left to Right)

Mr. Milton CHAN, Mr. Tommy CHAN, Mr. T.M. CHEUNG, Dr. David CHAN, Dr. Kevin LAM, Mr. Leo CHEUNG, Ms. Connie CHAN

## Work-Load Statistics

Table 1: Workload Statistics I

No. of Cycles	IVF	Natural cycle IVF	Oocyte donation	Sperm donation	Vitrified oocyte	ICSI	MESA	TESE	IVM	PGD	TOTAL
Initiated Cancelled	284 12 (4.2%)	6 2 (33.3%)	1 0 (0%)	2 0 (0%)	3 0 (0%)	214 0 (0%)	11 0 (0%)	7 0 (0%)	0 -	40** 0 (0%)	568 14 (2.5%)
With Oocyte Retrieval	272 (95.8%)	4 (66.7%)	1 (100%)	2 (100%) <sup>#</sup>	-	214 (100%)	11 (100%)	7 (100%)	-	39 (100%) <sup>#</sup> *	550 (97.5%) <sup>#</sup> *
With Embryo Transfer	196 (69.0%)	1 (16.7%)	0 (0%)	2 (100%)	3 (100%)	149 (69.6%)	8 (72.7%)	3 (42.9%)	-	1 (2.5%)	363 (63.9%)

("IVF": Conventional IVF-ET; "IVM": In vitro maturation; "ICSI": ICSI with ejaculated sperm; "MESA": MESA + ICSI; "TESE": TESE + ICSI; "PGD": Preimplantation genetic diagnosis)

( ) % of initiated cycles

<sup>\*</sup>denominator does not include FET cycles

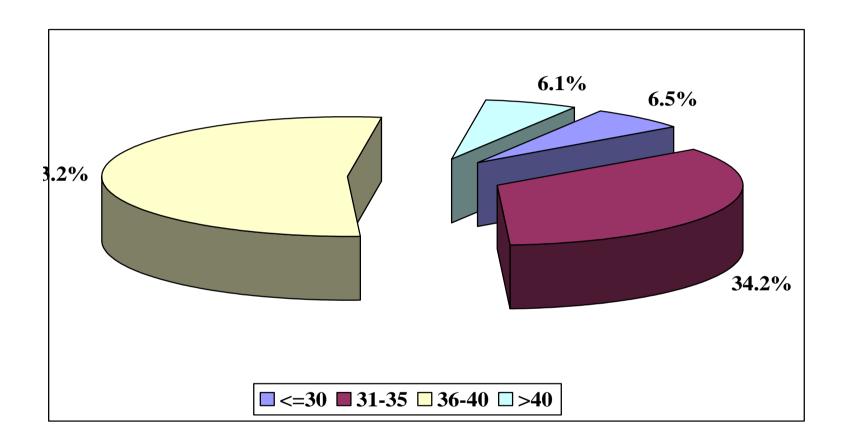
<sup>\*\*39</sup> fresh + 1 FET

<sup>\*</sup>vitrified oocyte cycles are excluded

**Table 2: Workload Statistics II** 

No. of cycles	IVF	Natural cycle IVF	Oocyte donation	Sperm donation	Vitrified oocyte <sup>#</sup>	ICSI	MESA	TESE	IVM	Fresh- PGD	TOTAL
Without Oocyte Retrieved	4 (1.5%)	2 (50.0%)	0 (0%)	0 (0%)	0 (-)	0 (0%)	0 (0%)	0 (0%)	-	0 (0%)	6 (1.1%)
Without insemination	1 (0.4%)	0 (0%)	0 (0%)	0 (0%)	0 (-)	6 (2.8%)	0 (0%)	4 (57.1%)	-	0 (0%)	11 (2.0%)
Without Normal Fertilization	17 (6.3%)	1 (25.0%)	0 (0%)	0 (0%)	0 (-)	9 (4.2%)	0 (0%)	0 (0%)	-	0 (0%)	27 (4.9%)
Without Normal Cleavage	2 (0.7%)	0 (0%)	0 (0%)	0 (0%)	0 (-)	0 (0%)	1 (9.1%)	0 (0%)	-	0 (0%)	3 (0.5%)
Without embryos suitable for transfer	2 (0.7%)	0 (0%)	0 (0%)	0 (0%)	0 (-)	0 (0%)	0 (0%)	0 (0%)	-	10 (25.6%)	12 (2.2%)
With ET Postponed	50 (18.4%)	0 (0%)	1 (100%)	0 (0%)	0 (-)	50 (23.4%)	2 (18.2%)	0 (0%)	-	28 (71.8%)	131 (23.8%)
Without Embryo Transfer	76 (27.9%)	3 (75.0%)	1 (100%)	0 (0%)	0 (-)	65 (30.4%)	3 (27.3%)	4 (57.1%)	-	38 (97.4%)	190 (34.5%)

<sup>( ) %</sup> of oocyte retrieval cycles,  $\ensuremath{^{\#}}\xspace$  vitrified oocyte cycles are excluded



**Figure 1: Age Distribution of Patients** 

**Table 3: Ongoing Pregnancy Rates in Different Age Groups** 

				No. of ongoing pregnancies / No. of cycles initiated							
Age (yrs)	IVF	ICSI	Natural cycle IVF	IVM	Sperm donation	Oocyte donation*	Vitrified oocyte	MESA	TESE	PGD	Total
<= 30	3/12 (25.0%)	2/16 (12.5%)	0/0 (-)	-	0/0 (-)	0/1 (0%)	0/0 (-)	0/2 (0%)	0/0 (-)	0/5 (0%)	5/36 (13.9%)
31 - 35	33/88 (37.5%)	18/67 (26.9%)	0/0 (0%)	-	2/2 (100%)	0/0 (-)	0/1 (0%)	0/3 (0%)	0/5 (0%)	1/18 (5.6%)	54/184 (29.3%)
36 - 40	32/168 (19.0%)	22/118 (18.6%)	1/4 (25.0%)	-	0/0 (-)	0/0 (-)	0/1 (0%)	1/5 (20.0%)	0/1 (0%)	0/14 (0%)	56/311 (18.0%)
> 40	1/16 (6.3%)	0/13 (0%)	0/0 (0%)	-	0/0 (-)	0/0 (-)	0/1 (0%)	0/1 (0%)	0/1 (0%)	0/3 (0%)	1/35 (2.9%)
Total	69/284 (24.3%)	42/214 (19.6%)	1/4 (25.0%)	-	2/2 (100%)	0/1 (0%)	0/3 (0%)	1/11 (9.1%)	0/7 (0%)	1/40 (2.5%)	116/566 (20.5%)

<sup>( ) %</sup> of initiated cycles, \*no embryo transfer

# In Vitro Fertilization and Embryo Transfer~ IVF-ET

## Stimulated cycle IVF-ET

During 2016, 266 couples underwent a total of 284 conventional stimulated IVF cycles at our centre. Unexplained cause (37.3%) was the commonest indication, which was followed by tuboperitoneal problem (26.8%), male factor (11.3%) and endometriosis (8.1%). (Table 4)

**Table 4: Indications for IVF-ET** 

Indications	No of Initiated cycles	No of Pregnancies	Pregnancy Rate*	Ongoing Pregnancy Rate*
Tuboperitoneal	76 (26.8%)	23	30.3%	25.0%
Endometriosis	23 (8.1%)	9	39.1%	30.4%
Male Factor	32 (11.3%)	9	28.1%	21.9%
Unexplained	106 (37.3%)	30	28.3%	21.7%
Mixed and others	47 (16.6%)	17	36.2%	27.7%
Total	284 (100%)	88	31.0%	24.3%

<sup>\*</sup> Per initiated cycle

A total of 14 cycles (2.5%) were cancelled: 5 due to poor ovarian response, 8 due to premature luteinization and 1 due to atretic follicle. Oocytes were not obtained in 6 planned retrieval cycles and no insemination was performed in 11 cycles. There were 27 cycles without normal fertilization and 3 cycles without normal cleavage. Therefore, no embryo was transferred in these cycles. Embryo transfer was postponed in 131 cycles because of the risk of developing ovarian hyperstimulation syndrome (OHSS), high serum progesterone level or other reasons.

The **oocyte retrieval rate** was 76.1% with an average of 9.0 oocytes obtained per retrieval cycle. The **fertilization rate** was 69.3% and the **cleavage rate** was 95.4%. The oocyte retrieval rate, fertilization rate and cleavage rate were similar to the figures in previous years. The results are summarised in Table 5.

**Table 5: Results of Conventional IVF-ET** 

		per Oocyte Retrieval Cycle	per Follicle Aspirated (Oocyte Retrieval Rate)	per Oocyte Retrieved (Fertilization Rate)	per Fertilized Oocyte (Cleavage Rate)
Number of Oocyte Retrieval Cycles	272				
Number of Follicles Aspirated	3223	11.8			
Number of Oocytes Retrieved	2454	9.0	76.1%		
Number of Oocytes Fertilized	1701	6.3		69.3%	
Number of Fertilized Oocytes Cleaved	1622	6.0			95.4%
Number of Embryos Transferred	298	1.1 (1.5/ET)			
<b>Number of Pregnancies</b>	88				
Number of Embryos Frozen	615	2.3			

281 (98.9%) of our patients used a GnRH antagonist protocol. (Table 6)

**Table 6: Ovarian Stimulation Protocols Used** 

Protocol	No. of Initiated Cycles	No. of Pregnancies	Pregnancy Rate*	Ongoing Pregnancy Rate*
	V			
<b>GnRH</b> antagonist	281 (98.9%)	87	31.0%	24.2%
GnRHa (long)	2 (0.7%)	1	50.0%	50.0%
GnRHa (short)	0 (0%)	0	-	-
No GnRHa	1 (0.4%)	0	0%	0%
Total	284 (100%)	88	31.0%	24.3%

<sup>\*</sup> Per initiated cycle

All oocyte retrievals were successfully performed under transvaginal ultrasound guidance using intravenous sedation and analgesia. The degree of difficulty of embryo transfer and the corresponding pregnancy rate are shown in Table 7.

**Table 7: Difficulty of Transfer** 

Difficulty	No. of ET Cycles	No. of Pregnancies	Pregnancy Rate#	Ongoing Pregnancy Rate#
Easy	195 (99.5%)	88	45.1%	35.4%
Vulsellum	1 (0.5%)	0	0%	0%
Vulsellum & Sound	0 (0%)	0	-	-
Dilatation	0 (0%)	0	-	-
Total	196 (100%)	88	44.9%	35.2%

# Per transfer cycle

Among the 272 oocyte retrieval cycles, 5 had moderate to severe OHSS. (Table 8)

**Table 8: Complications of Conventional IVF-ET Treatment** 

Complications	No of Retrieval* Cycles
Nil	267 (98.2%)
Infection	0 (0%)
Significant haemoperitonem	0 (0%)
Moderate to severe OHSS	5 (1.8%)

There were 88 pregnancies resulting from stimulated IVF-ET cycles. The **pregnancy rate** was 31.0% per initiated cycle and 44.8% per transfer cycle (Table 9). The **miscarriage rate** was 20.5%. The **ongoing pregnancy rate** was 24.3% per initiated cycle and 35.2% per transfer cycle. The average number of fresh pre-embryos transferred was 1.5 per transfer. The **multiple pregnancy rate** was 14.8%. Thirteen sets of twins were encountered (Table 10). The **implantation rate** was 33.2%.

**Table 9: Pregnancy Rates of Conventional IVF-ET** 

	Pregnancy Rate	Ongoing pregnancy Rate
per Cycle Initiated	88/284 (31.0%)	69/284 (24.3%)
per Oocyte Retrieval Cycle	88/272 (32.4%)	69/272 (25.4%)
per Transfer Cycle	88/196 (44.8%)	69/196 (35.2%)

**Table 10: Outcome of Pregnancies** 

Outcome	Number of Cycles*			
Preclinical Miscarriage Clinical Miscarriage Ectopic Pregnancy Lost to follow up Ongoing Pregnancy	5 13 1 0	(5.7%) (14.8%) (1.1%) (0%) (78.4%)		
Total Pregnancies No. of Fetuses No. of Multiple Pregnancies	88 82 13 (14.8%)			

<sup>\*</sup>Per pregnant cycle

The outcome in relation to the number of embryos transferred is shown in Tables 11 and 12.

**Table 11: Number of Embryos Transferred & the Outcome** 

No. of Embryos	No. of ET Cycles	No. of Pregnancies	Pregnancy Rate <sup>#</sup>	Ongoing Pregnancy Rate <sup>#</sup>	Multiple Pregnancy Rate <sup>+</sup>
1 2	94 (48.0%) 102 (52.0%)	40 48	42.6% 47.1%	37.2% 33.3%	5.0% 22.9%
Total	196 (100%)	88	44.8%	35.2%	14.8%

#Per transfer cycle +Per pregnancy cycle

**Table 12: Outcome of Single Embryo Transfer** 

Elective	Average Age of Women	No. of ET cycles	Pregnancy Rate#	Ongoing Pregnancy Rate <sup>#</sup>	Multiple Pregnancy Rate <sup>+</sup>
Yes	33.6 years	58	51.7%	48.3%	3.4%
No	36.1 years	36	27.8%	19.4%	0%

**#Per transfer cycle +Per pregnant cycle** 

# Intracytoplasmic Sperm Injection~ICSI (with ejaculated sperm)

Two hundred and fourteen treatment cycles were initiated in 203 couples (excluding preimplantation genetics testing). ICSI was decided in 192 treatment cycles because of severe male factor subfertility. It was also performed in those who had either failed fertilization or poor fertilization rate (less than 30%) in a previous conventional IVF cycle. This latter group accounted for 17 of the cycles initiated (Table 13).

**Table 13: Indications for ICSI** 

Indications	No. of Initiated Cycles	No. of Pregnancies	Pregnancy Rate*	Ongoing Pregnancy Rate*
Severe male factor	192 (89.8%)	56	29.2%	21.4%
Fertilization problem	17 (7.9%)	2	11.8%	5.9%
Others	5 (2.3%)	0	0%	0%
TD: 4.1	214 (1000/)	<b>5</b> 0	27.10/	10.60/
Total	214 (100%)	58	27.1%	19.6%

<sup>\*</sup>Per initiated cycle

GnRHa antagonist protocol for ovarian stimulation was used in 213 cycles (99.5%) (Table 14) and transvaginal ultrasound-guided approach was used in 213 cycles proceeding to ovum pick-up while one was performed by the transabdominal ultrasound-guided approach.

**Table 14: Ovarian Stimulation Protocols Used** 

Protocol	No. of Initiated Cycles	No. of Pregnancies	Pregnancy Rate*	Ongoing Pregnancy Rate*
GnRH antagonist	213 (99.5%)	58	27.2%	19.7%
GnRHa (long)	0 (0%)	-	-	-
GnRHa (short)	0 (0%)	-	-	-
No GnRHa	1 (0.5%)	0	0%	0%
Total	214 (100%)	61	27.1%	19.6%

<sup>\*</sup>Per initiated cycle

Table 15: Results of ICSI

		per Oocyte Retrieval Cycle	per Follicle Aspirated (Oocyte Retrieval Rate)	per Oocyte Retrieved (Fertilizati on Rate)	per Fertilized Oocyte (Cleavage Rate)
No. of Oocyte Retrieval Cycles	214				
No. of Follicle Aspirated	2820	13.2			
No. of Oocytes Retrieved	2164	10.1	76.7%		
No. of Oocytes Fertilized	1316	6.1		60.8% (73.1% per oocyte injected)	
No. of Fertilized Oocytes	1298	6.1		5	98.6%
Cleaved					
No. of Embryos	243	1.1			
Transferred		(1.6/ET)			
No. of Pregnancies	58				
No. of Embryos Frozen	567	2.6			

Oocytes were obtained in all planned retrieval cycles and insemination was not performed in 6 cycles. Normal fertilization was not achieved in 9 cycles and all cycles had normal cleavage. Therefore, no embryo was transferred in these cycles. Embryo transfer was postponed in another 50 cycles because of the risk of developing OHSS, high serum progesterone concentration or other reasons. The fertilization rate was 73.1% per oocyte injected this year and was similar to that of last year. The mean number of embryos transferred was 1.6 per transfer and was comparable to that of conventional stimulated IVF cycles. The degree of difficulty of embryo transfer is shown in Table 16.

**Table 16: Difficulty of Transfer** 

Difficulty	No. of ET Cycles	No. of Pregnancies	Pregnancy Rate#	Ongoing Pregnancy Rate <sup>#</sup>
Fagy	146 (98.0%)	57	39.9%	28.3%
Easy	140 (90.0%)	37	39.970	20.370
Vulsellum	3 (2.0%)	1	33.3%	33.3%
Vulsellum + Sound	0 (0%)	0	-	-
Total	149 (100%)	58	39.8%	28.2%

# Per transfer cycle

There were 58 pregnancies and 42 were ongoing (Tables 17 & 18). The **multiple pregnancy rate** was 8.6%. Five sets of twins were encountered. The **implantation rate** was 25.5%. One patient (0.5%) had moderate or severe OHSS.

**Table 17: Pregnancy Rates of ICSI** 

	Pregnancy Rate	Ongoing Pregnancy rate
per Cycle Initiated	58/214 (27.1%)	42/214 (19.6%)
per Oocyte Retrieval Cycle	58/214 (27.1%)	42/214 (19.6%)
per Transfer Cycle	58/149 (39.8%)	42/149 (28.2%)

**Table 18: Outcome of Pregnancies** 

Outcome	Number of Cycles	
Preclinical Miscarriage	6	(10.3%)
Clinical Miscarriage	7	(12.1%)
<b>Ectopic Pregnancy</b>	3	(5.2%)
Ongoing Pregnancy	42	(72.4%)
<b>Total Pregnancies</b>	58	
No. of Fetuses	47	
No. of Multiple Pregnancies	5 (8.6%)	- all twins

The outcome in relation to the number of embryo transferred in shown in Table 19 and Table 20.

Table 19: Number of Embryos Transferred & the Outcome

No. of Embryos	No. of ET Cycles	No. of Pregnancies	Pregnancy Rate#	Ongoing Pregnancy Rate <sup>#</sup>	Multiple Pregnancy Rate <sup>+</sup>
1	55 (36.9%)	19	34.5%	29.1%	0%
2	94 (63.1%)	39	41.5%	27.7%	12.8%
Total	149 (100%)	58	39.8%	28.2%	8.6%

<sup>#</sup> Per transfer cycle

**Table 20: Outcome of Single Embryo Transfer** 

Elective	Average Age of Women	No. of ET cycles	Pregnancy Rate#	Ongoing Pregnancy Rate <sup>#</sup>	Multiple Pregnancy Rate <sup>+</sup>
Yes	34.7 years	38	44.7%	36.8%	0%
No	38.0 years	17	11.8%	11.8%	0%

**#Per transfer cycle** 

<sup>+</sup> Per pregnant cycle

<sup>+</sup>Per pregnant cycle

# Microsurgical Epididymal Sperm Aspiration - MESA

Nine couples underwent 11 treatment cycles in 2016. The urological team at Queen Mary Hospital performed a total of 6 MESA (including percutaneous epididymal sperm aspiration) procedures, which were arranged before ovarian stimulation or the oocyte retrieval. Indications for MESA cycles are given in Table 21.

**Table 21: Indications for MESA** 

Indications	No. of OPU Cycles	No. of Pregnancies	Pregnancy Rate*	Ongoing Pregnancy Rate*
Congenital Absence of Vas deferens	6 (54.4%)	1	16.7%	16.7%
Obstructive Azoospermia	3 (27.3%)	1	33.3%	0%
Severe male factor	1 (9.1%)	0	0%	0%
Ejaculatory problem	1 (9.1%)	0	0%	0%
Total	11 (100%)	2	18.2%	9.1%

\*Per initiated cycle

The antagonist protocol was used in all 11 cycles. Oocyte retrieval was performed under transvaginal ultrasound guidance in all 11 cycles and oocytes were obtained in all the retrieval cycles. An average of 10.5 oocytes was retrieved in these 11 cycles. The fertilization rate was 55.0% per oocyte injected (Table 22). Embryo transfer was performed in 10 cycles and embryo transfer was postponed in 1 cycle.

**Table 22: Results of MESA+ ICSI** 

		per Oocyte Retrieval Cycle	per Follicle Aspirated (Oocyte Retrieval Rate)	per Oocyte Retrieved (Fertilizati on Rate)	per Fertilized Oocyte (Cleavage Rate)
Number of Oocyte Retrieval Cycles	11				
Number of Follicles Aspirated	116	10.5			
Number of Oocytes Retrieved	78	7.1	67.2%		
Number of Oocytes Fertilized	33	3.0		42.3% (55.0% per oocyte injected)	
Number of Fertilized Oocytes Cleaved	32	2.9		11,00000)	97.0%
Number of Embryos Transferred	10	0.9 (1.3 / ET)			
Number of Pregnancies	2				
Number of Embryos Frozen	17	1.5			

No patient developed moderate to severe OHSS.

**Table 23: Pregnancy Rates of MESA + ICSI** 

	Pregnancy Rate	Ongoing pregnancy rate
per Cycle Initiated per Oocyte Retrieval Cycle per Transfer Cycle	2/11 (18.2%) 2/11 (18.2%) 2/8 (25.0%)	1/11 (9.1%) 1/11 (9.1%) 1/8 (12.5%)

There were 2 pregnancies resulting from MESA + ICSI procedures. The **pregnancy rate** was 18.2% per initiated cycle and 25.0% per transfer cycle (Table 23). The **ongoing pregnancy rate** was 9.1% per initiated cycle and 12.5% per transfer cycle. The **implantation rate** was 20.0%. There was no multiple pregnancy (Table 24).

**Table 24: Outcomes of Pregnancies** 

Outcome	Number of cycles
Preclinical Miscarriage	0 (0%)
Clinical Miscarriage	1 (50.0%)
Ectopic Pregnancy	0 (0%)
Ongoing Pregnancy	1 (50.0%)
Total Pregnancies	2
No. of Fetuses	1
No. of Multiple Pregnancies	0 (0%)

The pregnancy rate in relation to the number of embryos transferred is shown in Table 25.

**Table 25: Number of Embryos Transferred & the Outcome** 

No. of Embryos	No. of ET Cycles	No. of Pregnancies	Pregnancy Rate#	Ongoing Pregnancy Rate <sup>#</sup>	Multiple Pregnancy Rate <sup>+</sup>
1	6 (75.0%)	2	33.3%	16.7%	0%
2	2 (25.0%)	0	0%	0%	0%
Total	7 (100%)	2	25.0%	12.5%	0%

**#Per transfer cycle** 

+Per pregnancy cycle

## Testicular Sperm Extraction - TESE

During 2016, 7 treatment cycles were initiated in 7 couples (Table 26). The urological team at Queen Mary Hospital carried out 9 testicular sperm biopsies.

**Table 26: Indications for TESE** 

Indications	No. of OPU Cycles	No. of Pregnancies	Pregnancy Rate*	Ongoing Pregnancy Rate*
Non-obstructive Azoospermia	4 (57.1%)	0	0%	0%
Obstructive Azoospermia	1 (14.3%)	0	0%	0%
Severe male factor	2 (28.6%)	0	0%	0%
Total	7 (100%)	0	0%	0%

<sup>\*</sup> Per initiated cycle

Nine men underwent TESE. Spermatozoa were found in 4 TESE procedures. Spermatozoa could be frozen in 2 TESE procedures.

The antagonist protocol was used in all 7 cycles using TESE sperm. Oocyte retrieval was performed in 7 cycles under transvaginal ultrasound guidance. Oocytes were obtained in all the 7 cycles. An average of 8.9 oocytes were retrieved in these 7 cycles. ICSI was not performed in 4 cycles because of the absence of spermatozoa found in TESE; oocytes were obtained in all planned retrieval cycles. ICSI was performed in 3 cycles with spermatozoa retrieved from TESE procedures and the overall fertilization rate was 72.2% per oocyte injected (Table 27). Embryo transfer was performed in all the 3 cycles.

**Table 27: Results of TESE+ ICSI** 

		per Oocyte Retrieval Cycle	per Follicle Aspirated (Oocyte Retrieval Rate)	per Oocyte Retrieved (Fertilizati on Rate)	per Fertilized Oocyte (Cleavage Rate)
No. of Oocyte Retrieval Cycles	7				
No. of Follicles Aspirated	86	12.3			
No. of Oocytes Retrieved	62	8.9	72.1%		
No. of Oocytes Fertilized	13	1.9		21.0% (72.2% per oocyte injected)	
No. of Fertilized Oocytes Cleaved	13	1.9		injected	100%
No. of Embryos Transferred	4	0.6 (1.3/ET)			
No. of Pregnancies	0				
No. of Embryos Frozen	34	4.9			

There was no case of moderate to severe OHSS recorded. None of the patients got pregnant. The  $\it implantation rate = 0.0\%$ .

# Preimplantation Genetic Diagnosis - PGD

We continue to provide preimplantation genetic diagnosis (PGD) to women at risk of having babies with serious chromosomal or genetic disorders. In 2016, PGD was performed in 39 stimulated cycles and 1 frozen cycles for 37 couples and indications for PGD were shown in Table 28.

**Table 28: Summary of PGD cycles** 

				No. of embry	yo
Indication	No. of patients	No. of cycles	PGD	Normal	Replaced
Chromosomal abnormalities					
Numerical chromosomal abnormalities	1	1	2	2 (100%)	0 (0%)
Reciprocal translocation	11	11	61	16 (26.2%)	0 (0%)
Robertsonian translocation	1	1	1	1 (100.0%)	0 (0%)
α Thalassaemia	4	4	33	12 (36.4%)	0 (0%)
eta Thalassaemia	1	1	11	2 (18.2%)	0 (0%)
β Thalassaemia + HLA typing	1	1	11	2 (18.2%)	0 (0%)
Others single gene defects	13	14	63	29 (46.0%)	1 (1.6%)
Others#	6	6	29	8 (27.6%)	0 (0%)
Total	38	39	207	71 (34.3%)	1 (0.5%)

#Pre-implantation genetic screening is done for advanced maternal age, repeated implantation failure or recurrent miscarriage.

## FET after PGD/PGS

We moved to the new policy that trophectoderm biopsy were performed for all cases of PGD/PGS, and all blastocysts were frozen after biopsy; frozen-thawed transfer of the blastocysts would be arranged after the results were available for counselling. Therefore, only one fresh blastocyst transfer after PGD was performed in 2016 (for single gene defect), which resulted in an ongoing singleton pregnancy. Next generation sequencing and aCGH were used in PGS and in PGD for structural rearrangement respectively. PGS was also performed in suitable blastocysts following PGD for monogenic diseases. Each blastocyst was frozen in one straw after biopsy and patients were allowed to replace one blastocyst each time following PGD/PGS.

A total of 53 thaw cycles after PGD/PGS were initiated. Embryo transfer was not done in 1 cycle because of lysis of all frozen embryo(s) during thawing. Fifty-two frozen-thawed embryo replacements were performed.

The average number of embryos transferred per FET cycle was 1.1. There were altogether 38 **pregnancies** (73.1% per transfer) and 32 **ongoing pregnancies** (61.5% per transfer) resulting from transfer of frozen-thawed embryos. The overall **miscarriage rate** was 15.8%. The **multiple pregnancy rate** was 0%. The **implantation rate** was 60.0%.

# Embryo / Oocyte Cryopreservation and Frozenthawed Embryo Transfer

The results of embryo cryopreservation are summarized in Table 29. There were excess embryos suitable for cryopreservation in 370 / 539 (68.6 %) of the retrieval cycles in 2016, and oocytes were cryopreserved in another 10 retrieval cycles.

Table 29: Results of Embryo / Oocyte Cryopreservation

Method of Treatment	IVF	ICSI	MESA	TESE	Others#	PGD	Total
No. of Oocyte Retrieval Cycles / Vitrified Oocytes Warming Cycles	272	214	11	7	6	39	
No. of Cycles with Embryo / Oocyte Cryopreservation	174*	157*	9	6*	5	29	380*
Total No. of Embryos / Oocytes Cryopreserved	615*	567*	17	34*	10	67	1310*
Average No. of Embryos / Oocytes Cryopreserved per Freezing Cycle	3.5*	3.6*	1.9	5.7*	2.0	2.3	3.4*
Range of Embryos / Oocytes Cryopreserved	1 – 11*	1 – 18*	1 - 4	1 – 12*	1 – 4	1 - 9	1 – 18*

\* with oocyte freezing #using vitrified-warmed oocytes, donor oocytes or donor sperm

Four hundred and twenty women planned to have replacement of frozen-thawed embryos (FET). A total of 520 thaw cycles were initiated. Embryo transfer was not done in 11 cycles because of lysis of all frozen embryo(s) during thawing. 342 frozen-thawed embryo replacements were performed in natural (spontaneous ovulatory) cycles, 30 were in clomiphene citrate-induced cycles, 135 were in total hormone replacement artificial cycles and 2 were in stimulated cycles.

The pregnancy rates of these different types of transfer cycles are shown in Table 30.

**Table 30: Outcome of FET Cycles** 

Cycle Type	Number of Cycles		Number of Pregnancies	<b>Pregnancy Rate</b>	Ongoing pregnancy rate
	2.12	<b>(5.00</b> /	1.47	42.00/	24.50/
Natural	342	67.2%	147	43.0%	34.5%
Clomid	30	5.9%	8	26.7%	23.3%
Artificial	135	26.5%	52	38.5%	28.1%
Stimulated	2	0.4%	1	50.0%	50.0%
Total	509	100.0%	208	40.9%	32.2%

**Table 31: Outcome of Pregnancies in FET** 

Outcome	No. of				
	Pregnancies	Natural	Clomid	Artificial	Stimulated
Preclinical Miscarriage	13 (6.3%)	7 (4.8%)	1 (12.5%)	5 (9.6%)	0
Clinical Miscarriage	28 (13.5%)	20 (13.6%)	0 (0%)	8 (15.4%)	0
<b>Ectopic Pregnancy</b>	3 (1.4%)	2 (1.4%)	0 (0%)	1 (1.9%)	0
Molar Pregnancy	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0
Ongoing Pregnancy	164	118	2	38	1
	(78.8%)	(80.3%)	(66.7%)	(73.1%)	(100%)
<b>Total Pregnancies</b>	208	147	8	52	1
No. of Fetuses	183	132	7	43	1
No. of Multiple	19 (9.1%)				
Pregnancies	all twins				

The average number of embryos transferred per FET cycles was 1.5. There were altogether 208 pregnancies resulting from transfer of frozen-thawed embryos. The overall **miscarriage rate** was 19.8%. The **multiple pregnancy rate** was 9.1% (Table 31). The **implantation rate** was 28.8%.

**Table 32: Number of Embryos Transferred & the Outcome** 

No. of Embryos	No. of FET Cycles	No. of Pregnancies	Pregnancy Rate#	Ongoing Pregnancy rate#	Multiple Pregnancy Rate <sup>+</sup>
1	265 (52.1%)	112	42.3%	34.7%	1.8%
2	244 (47.9%)	96	39.3%	29.5%	17.7%
Total	509 (100%)	208	40.9%	32.2%	9.1%

<sup>#</sup> Per transfer cycle + Per pregnant cycle

# Ovulation Induction and Ovarian Stimulation & Intrauterine Insemination

## **Ovulation Induction**

Twenty-seven patients underwent 64 cycles of ovulation induction by gonadotrophin therapy. The mean age of patients was 33.7 years. The cycle characteristics are detailed in Table 33. Eight cycles were cancelled (5 because of excessive ovarian response, 1 for premature LH surge and 2 for no follicular growth). Nine patients got pregnant and the pregnancy rate was 14.1% per initiated cycle. There were 6 ongoing singleton pregnancies and 1 ongoing twin pregnancy.

**Table 33: Characteristics of Ovulation Induction Cycles** 

Parameters	Mean ± Standard Deviation
Amount of gonadotrophin used (IU)  Number of follicles ≥ 14mm	$1775.6 \pm 1457.4$ $1.5 \pm 1.5$
Number of follicles ≥ 16mm	$1.1\pm0.4$
Number of follicles ≥ 18mm	$0.9 \pm 0.5$
Oestradiol on the day of hCG (pmol/l)	$1619 \pm 1004$

## Ovarian Stimulation & Intrauterine Insemination

Seventy-four patients underwent 150 cycles of ovarian stimulation by gonadotrophin or clomiphene citrate in conjunction with insemination. Seven cycles were cancelled: 1 cycle for excessive response, 2 for premature luteinisation and 4 for other reasons.

The mean age of patients was 33.6 years. The indications and cycle characteristics are shown in Tables 34 and 35 respectively. Eleven pregnancies were achieved and the **pregnancy rate** was 7.3% per cycle initiated. There were 7 ongoing singleton and 1 ongoing twin pregnancies.

Table 34: Indications for Ovarian Stimulation & Intrauterine Insemination

Indications	Number of Cycles
Male factors	50
Unexplained	58
Endometriosis	13
Coital	16
Anovulation	10
Mixed and Miscellaneous	3

Table 35: Cycle Characteristics of Ovarian Stimulation by Gonadotrophin & Intrauterine Insemination

Parameters	Mean ± Standard Deviation			
	<u>hMG / FSH</u> <u>Clomid</u> <u>Letrozo</u>			
Amount of gonadotrophin used (IU)	1701.4 ± 804.7	-	-	
Number of follicles ≥ 12mm	$1.5 \pm 0.8$	$1.9 \pm 0.9$	$1.3 \pm 0.5$	
Number of follicles ≥ 14mm	$1.3 \pm 0.5$	$1.5\pm0.6$	$1.1 \pm 0.3$	
Number of follicles ≥ 16mm	$1.0 \pm 0.0$	$1.3 \pm 0.5$	$0.9 \pm 0.3$	
Oestradiol on the day of hCG (pmol/l)	$1099 \pm 588$	$1709 \pm 976$	$800 \pm 445$	

## Natural Cycle Intrauterine Insemination

Eight patients underwent 15 cycles of intrauterine insemination during natural cycles because of coital problems (n=12), male factor (n=2) or unexplained infertility (n=1).

The mean age of patients was 36.5 years. One pregnancy was achieved and the **pregnancy rate** was 6.7% per cycle initiated. There was 1 ongoing singleton pregnancy.

## Artificial insemination with donor sperm

Three patients underwent 3 stimulated cycles and 1 during a natural cycle). The mean age of patients was 34.5 years. Two pregnancies were achieved and the **pregnancy rate** was 50.0% per cycle initiated. There was 1 ongoing singleton pregnancy.

# Miscellaneous Statistics

	Number
Diagnostic laparoscopy +/- chromotubation	13
Laparoscopic ovarian cystectomy	3
Laparoscopic salpingostomy	6
Laparoscopic adhesiolysis	19
Laparoscopic salpingectomy	1
Laparoscopic segmental resection	20
Laparoscopic ovarian drilling	0
Laparoscopic ablation of endometriosis	8
Salpingo-oophorectomy	0
Myomectomy	0
Diagnostic hysteroscopy	19
Hysteroscopic polypectomy	27
Hysteroscopic adhesiolysis	4
Hysteroscopic lysis of uterine septum	2
Hysteroscopic myomectomy	1
Hysteroscopic proximal tubal cannulation	1
Tubal reanastomosis	1
Semen cryopreservation for cancer patients	15

## **Outpatient Clinics**

	New	Follow-up
Subfertility Clinics	363	589
Male Infertility Clinic*	4	8
Reproductive Genetic Clinic	23	19
Recurrent Miscarriage Clinic	16	24
Private Clinic – Reproductive	291	210
Medicine		
Private Clinic – Male Infertility	16	1

<sup>\*</sup>Only those cases seen under Department of Obstetrics and Gynaecology were counted here (mainly cases requiring counselling or treatment on male endocrine problems or fertility preservation). Those requiring assessment and management by urologists were seen in the Department of Surgery and were not counted here.

## Publications and Conference Reports

### Journal articles

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- Chan M.K.D., Cheung K.W., Yung S.F., Lee V.C.Y., Li R.H.W. and Ng E.H.Y., A randomized double-blind controlled trial of the use of dydrogesterone in women with threatened miscarriage in the first trimester: study protocol for a randomized controlled trial. Trials 2016 Aug 17;17(1):408.
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- Li RWH, Wong BPC, Ip WK, Yeung WSB, Ho PC, Ng EHY. Comparative evaluation of three new commercial immunoassays for anti-Müllerian hormone measurement. Hum Reprod 2016 31(12): 2796–2802
- Liu W., NIU Z., LI Q., Pang T.K.R., Chiu C.N. and Yeung W.S.B., MicroRNA and Embryo Implantation. Am J Reprod Immunol 2016, 75: 263-271.
- Lu J., Wong R.N.S., ZHANG L., Wong R.Y.L., Ng T.B., Lee C.K.F., Zhang Y., Lao L., LIU J. and Sze C.W.S., Comparative Analysis of Proteins with Stimulating Ovarian Estradiol Biosynthesis from Four Different Dioscorea Species in vitro: Implication for Treating Menopause. Appl Biochem Biotechnol 2016;180(1):79-93
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### **Conference papers**

- Cheng H.C., Chan R.W.S., Ng E.H.Y. and Yeung W.S.B., The role of myometrium in maintaining the endometrial mesenchymal-like stem cells through secretion of matrix metalloproteinase 3. Hong Kong Society of Endocrinology Metabolism & Reproduction, Hong Kong, 20th Nov 2016. Abstract P-03, p 17.
- Cheung S.Y.C., Yiu K.W.A. and Chan S.C.S., Management of iatrogenic vesicovaginal fistula in a girl with complex congenital Mullerian and renal malformations. 18th FIJIG World Congress of Paediatric and Adolescent Gynaecology (WCPAG) 25-28 June 2016, Florence, Italy.
- Fan H.J., Wong C.K.C., Yeung W.S.B. and Lee K.F., Molecular and functional approach to delineate the effect of bisphenol analogues on the receptivity of human endometrial epithelial cells. 30th Anniversary Celebration of the HKU-QMH Assisted Reproduction Programme. 12-13 December 2016, Shenzhen, China.
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- Fan H.J., Yeung W.S.B. and Lee K.F., Bisphenol aA analogues: effect on gene activation and spheroid attachment in endometrial epithelial iIshikawa cells. 33th Annual Scientific Meeting of Hong Kong society of Endocrinology, Metabolism and Reproduction. November 2016, Hong Kong, China.
- Fan H.J., Yeung W.S.B. and Lee K.F., Effect of bisphenol aA analogues on gene regulation and spheroid attachment in endometrial epithelial iIshikawa cells. 21st Research Postgraduate Symposium, LKS Faculty of Medicine, The University of Hong Kong. December 2016, Hong Kong, China.
- Lee C.L., Yeung W.S.B. and Chiu P.C.N., Placenta-derived extracellular vesicles induce differentiation of monocyte into decidual macrophage-like phenotype. 2016 Congress of the International Society for Extracellular Vesicles. 4-7 May 2016, Rotterdam, the Netherlands.
- Lee C.L., Yeung W.S.B. and Chiu P.C.N., Soluble Human Leukocyte Antigen G5 Polarizes Decidual Macrophage Differentiation from Monocyte to Promotes Fetomaternal Tolerance

- and Placental Development. Hong Kong Society of Endocrinology, Metabolism and Reproduction Annual Scientific Meeting. 20 Nov 2016, Hong Kong.
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- Li R.H.W., Yeung T.W.Y., Lee V.C.Y., Yeung W.S.B., Ho P.C. and Ng E.H.Y., Comparing the inter-cycle variation of serum anti-Mullerian hormone and antral follicle count measurements in predicting ovarian response before IVF, 32nd Annual Meeting, European Society of Human Reproduction and Embryology. 2016.
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- Ng E.H.Y., Can adjuvant treatments or pre-IVF procedures alter chances of pregnancy? Specialists sharing expertise, education and data, Sydney, Australia, 19-20 March, 2016.
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- Ng E.H.Y., Endometrium receptivity. Joint Meeting of the 5th Annual Scientific Meeting of the Obstetrical and Gynaecological Society of Hong Kong (ASM-OGSHK 2016) and Ovarian Club VII, Hong Kong, 21-22 May 2016.
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- Xu S., Chan R.W.S., Ng E.H.Y. and Yeung W.S.B., Characterization of Endometrial Mesenchymal-like Stem Cells Activity in Different Endometrial Layers and During the Menstrual Cycle, 49th Society for the Study of Reproduction. 2016.

## Special Event

30<sup>th</sup> Anniversary Celebration of the Assisted Reproduction Programme
In December 2016, Our Unit celebrated the 30<sup>th</sup> anniversary of our assisted reproduction programme. A scientific symposium entitled "Celebration of Life: 30 Years and Beyond" was held on 10-11 December 2018 in Hong Kong, and on 12-13 December 2018 in The University of Hong Kong – Shenzhen Hospital. This was followed by a reunion gathering on 18 December 2018 where present and past staff members, collaborators and patients met and shared the joy and fraternity.



Team members at conference



Conference faculty



Celebration gathering – cake-cutting ceremony



Celebration gathering attended by staff and patients

# **Cumulative Statistics**

**Table 36: Comparative Results of Conventional IVF-ET** 

	2016	2015	2014	2013	2012
Number of Patients	266	357	400	446	464
Number of Cycles Initiated	284	390	432	495	496
Number of Cycles Cancelled	12	21	15	28	13
Number of Cycles with Oocyte Retrieval	272	369	417	467	483
Number of Oocyte Retrieved	2454	3401	3912	4452	4067
Mean No. of Oocytes / Oocyte Retrieval	9.0	9.2	9.4	9.5	8.4
Number of Oocyte Fertilized	1701	2395	2814	2991	2834
Fertilization Rate	69.3%	70.4%	71.9%	67.2%	69.7%
Number of Cleaving Embryos	1622	2306	2705	2896	2741
Mean No. of Cleaving Embryos / Retrieval	6.0	6.2	6.5	6.2	5.7
Number of Cycles with Transfer	196	279	308	358	407
Number of Embryos Transferred	298	466	505	629	736
Mean No. of Embryos / Transfer	1.5	1.7	1.6	1.8	1.8
Range	1-2	1-2	1-2	1-2	1-2
Number of Pregnancies	88	114	133	152	175
Pregnancy Rate / Transfer	44.8%	40.9%	43.2%	42.5%	43.0%
Ongoing Pregnancy Rate / Transfer	35.2%	31.2%	33.8%	31.8%	34.6%
Number of Embryos Frozen	615	963	1226	1254	1174

Table 37: Comparative Results of ICSI (Ejaculated sperm), excluding PGT

	2016	2015	2014	2013	2012
Number of Patients	240	272	250	199	221
Number of Cycles Initiated	214	297	268	243	245
Number of Cycles Cancelled	0	1	2	0	0
Number of Cycles with Oocyte Retrieval	214	296	266	243	245
Number of Oocytes Retrieved	2164	3180	2432	2341	2285
Mean No. of Oocytes / Retrieval	10.1	10.7	9.1	9.6	9.3
Number of Oocyte Fertilized	1316	2004	1501	1423	1293
Fertilization Rate	73.1%	76.1%	61.7	74.3%	69.5%
Number of Cleaving Embryos	1298	1966	1457	1380	1268
Mean No. of Cleaving Embryos / Retrieval	6.1	6.6	5.5	5.7	5.2
Number of Cycles with Transfer	149	216	202	188	211
Number of Embryos Transferred	243	349	324	319	368
Mean No. of Embryos / Transfer	1.6	1.6	1.6	1.7	1.7
Number of Pregnancies	58	86	87	70	91
Pregnancy Rate / Transfer	39.8%	39.8%	43.1	37.2%	43.1%
Ongoing Pregnancy Rate / Transfer	28.2%	29.2%	35.6	31.4%	36.0%
Number of Embryos Frozen	567	837	698	675	561

Table 38: Comparative Results of Frozen-thawed Embryo Transfer (FET)

	2016	2015	2014	2013	2012
Number of Patients	420	532	511	436	430
Number of Thaw Cycles	520	671	640	554	555
Number of Transfer Cycles	509	660	634	538	544
Total Number of Embryos Thawed	852	1187	1196	1068	1133
Number of Embryos Replaced	753	1025	1037	930	908
Mean Number Replaced	1.5	1.6	1.6	1.7	1.7
Type of Transfer Cycle:					
Natural	342	484	458	390	360
Clomid-Induced	30	115	116	69	58
Hormone Replacement	135	59	57	77	126
Stimulated	2	2	3	2	0
Number of Pregnancies	208	271	243	210	188
Pregnancy Rate / Transfer	30.7%	41.1%	38.3%	39.0%	34.6%
Ongoing Pregnancy Rate / Transfer	22.4%	32.0%	30.6%	30.1%	24.4%