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|  瑪麗醫院 QUEEN MARY HOSPITAL | Department of Obstetrics and Gynaecology | Document No. | OGRM213 |
| | Subject Information on IVF General-English | Issue Date | April 2020 |
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Information Sheet for *In Vitro* Fertilization

(I) *In vitro* fertilization (IVF)

It involves the following steps:

- (1) **stimulation of ovaries**
- (2) **egg collection**
- (3) **sperm washing and fertilization**
- (4) **embryo transfer.**

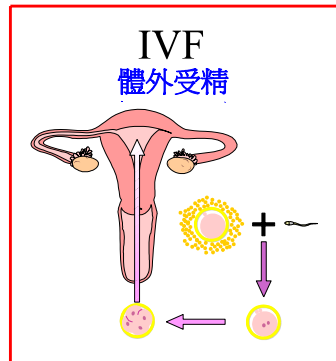


Figure 1: IVF

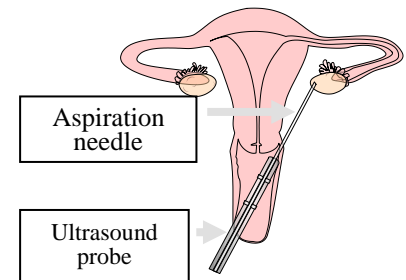



Figure 2: Egg collection

1. Stimulation of ovaries

- After the period begins, you will undergo a transvaginal scan and a blood test.
- You will then receive daily injections to stimulate the ovaries to develop multiple follicles. You can give injections yourselves.
- Antagonist is used in most patients to prevent early release of eggs.
- The ovarian response is monitored by transvaginal scanning. The scanning will usually be performed after 7-8 days of injections and subsequent scanning is arranged accordingly.
- Final maturation of the eggs will be induced when there are at least 3 follicles >17 mm in diameter.
- On average, the stimulation takes 11 days and 8-10 eggs are obtained, depending on your ovarian reserve.

2. Egg collection (Figure 2)

- The eggs will be aspirated from your ovaries about 36 hours after hCG injection in the evening, with the help of the transvaginal ultrasound scanner.
- Antibiotic as a precautionary measure will be given prior to the collection. Therefore, you should inform the doctors in advance if you have any drug allergy. A pain-killer and a sedative will be given shortly before the procedure.
- The whole procedure will usually take 30 minutes.

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3. Sperm washing and fertilization

- Your husband will have to submit a semen sample on the day of egg collection. Freezing of semen samples should be arranged in advance if he has problems to submit the sample due to various reasons.
- After the sperm washing, the sperms will be mixed with or injected into the eggs collected.

Intracytoplasmic sperm injection (ICSI)

- direct injection of a single sperm into an oocyte to assist fertilization. (Figure 3)
- indicated in couples with severe male factors or low fertilization rate (<30%) in previous cycle.
- a slight increase in the risk of sex chromosome disorder, about 1-1.5% after ICSI compared to 0.5% after natural conceptions or conventional IVF pregnancies.
- For men with no sperm in the ejaculate due to obstructive causes, sperms may be obtained by the aspiration from the distended epididymis. If the absence of ejaculated sperm is due to testicular failure, sperms can be recovered from the testicular biopsy but the success retrieval of sperm is about 40-50%.

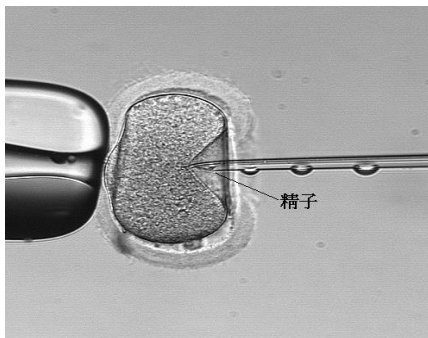



Figure 3: ICSI



Figure 4: Embryo transfer

4. Embryo transfer (Figure 4)

- You will have **ONE embryo or blastocyst replaced in each cycle**. Replacement of 2 embryos (Not blastocyst) can be considered if you :
 - Are >38 years at the time of IVF or not pregnant after 2 cycles of IVF and
 - Have no livebirth before
- After the embryo transfer, you will be given two weeks of progesterone tablets to support the luteal phase.

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(II) Frozen-thawed embryo transfer (FET)

The replacement of frozen-thawed embryos can be performed in natural, letrozole or hormone replacement cycles. Please note that not all cryopreserved embryos will survive the freezing and thawing processes. The usual survival rate is more than 90%.

1. Natural cycle

If you have regular menstrual cycles, the transfer of frozen-thawed embryos will be arranged after ovulation has occurred. There is no need to give luteal phase support.

2. Letrozole cycle

If you have irregular menstrual periods, we will give you letrozole to induce ovulation. There is no need to give luteal phase support.


2. Hormone replacement cycle

If you do not ovulate with letrozole, we will use hormone replacement cycle. You will receive hormone tablets (oestrogen and progesterone) to prepare the lining of the womb for embryo replacement. The full details will be given at the beginning of the treatment.

(III) Psychosocial support

In general, patients would experience a wide range of psychosocial distress during the treatment phase, such as anxiety, stress, anger, depression, guilt, frustration, sense of loss and so on. Significant positive effects were found on those who had received the psychosocial services.

Patients with psychological problems may be referred to the medical social worker for further counselling. Please let the staff know if you need help during or after the treatment. Counseling is offered independent of the clinical decision-making process and information obtained during counseling would be kept confidential.

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(IV) Pregnancy rate


- The pregnancy rate of IVF and FET is 30-40% per cycle. It should be noted that many factors such as age of the woman, history of previous pregnancy, ovarian response and other associated factors may affect the pregnancy rate.
- There is 20-30% chance of miscarriage in early pregnancies and 4-5% chance of ectopic pregnancy. Therefore, the take-home baby rate is about 20-30% per cycle.

(V) Complications

- In general, IVF is fairly safe and the complication rate is low.
- Possible complications include:
 - multiple pregnancy (~20% when two embryos are replaced);
 - ovarian hyperstimulation syndrome (patients may develop abdominal distension, vomiting, ovarian cysts, fluid in the abdomen and the lung etc.; moderate-severe: 1-5%);
 - ectopic pregnancy (i.e. pregnancy located outside the womb; ~5%);
 - complications arising from egg collection. eg. bleeding from the ovaries and pelvic infection (rare, less than 1%);
 - fertility drugs may slightly increase the risk of ovarian cancer but the evidence is not conclusive.

(VI) Pregnancy course and obstetric outcome

- The risk of birth defects following IVF is increased by 30-40% when compared with natural conceptions. The prevalence of birth defects in natural conceptions is about 3%. Therefore, the risk of birth defects associated with IVF is about 4%.
- There is also a slight increase in the risk of sex chromosome disorder after ICSI.
- The rates of complications in pregnancy (e.g. ectopic pregnancy, miscarriage, difficulty in delivery) are similar to that in natural conception. However, there may be a 2-3 times increase in the incidence of preterm labour and small for gestational age babies even in singleton pregnancies conceived after IVF compared with those conceived spontaneously.

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(VII) Miscellaneous

1. Genetic screening for the husband


- Men with very low sperm count (less than or equal to 2 million per ml in the ejaculate) or no sperm due to testicular failure are advised to undergo tests for chromosome abnormalities and microdeletion in the Y chromosome because the chromosomal or genetic abnormalities may be transmitted to their children, if present. Patients will be charged for these tests. Please ask the staff for further details when needed.

2. Blastocyst transfer

- Embryos are usually transferred to the womb on the second day after egg collection. Embryos can now be cultured in the laboratory to the fifth day after egg collection when the embryo develops to blastocyst.
- Indicated when you have more than 3 embryos two days after egg collection.
- The transfer of blastocyst has advantages including reduction in the number of embryos to be replaced, thus reducing the risk of multiple pregnancy and the chance to select better embryos for transfer to shorten the time to pregnancy.
- Only about half of the embryos will develop into blastocysts and variation in the ability to produce blastocysts among patients is remarkable.
- Only 2% of patients will not have any development of blastocysts based on our criteria.

3. Preimplantation genetic testing (PGT)

- A method to determine the presence of chromosomal or gene defect in an embryo before transfer.
- Allows selection of normal embryos to be transferred to the patients seeking IVF and is an alternative to prenatal diagnosis.
- Indicated when the fetus is at risk of chromosomal abnormality (e.g. balanced translocation in the couple) or other major genetic diseases (e.g. Thalassaemia and some sex-linked diseases).
- Gender selection for non-medical reasons is not allowed in Hong Kong.
- When indicated, the couples will receive further details and genetic counselling before undergoing the PGT procedure.

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Charges for services in assisted reproduction

A. Basic services

1. **Drugs used in IVF treatment** **\$ 4,000**
2. **Laboratory and consumable fee in conventional IVF/ET** **\$ 8,250**
3. **Intracytoplasmic sperm injection** **\$ 4,400**
4. **Semen cryopreservation for social reason (3 month storage)** **\$ 1,200**
5. **Vitrification of oocytes or embryos and 2 year storage** **\$ 4,400 for first 1-2 straws**
and then \$1,100 per straw; each contains at most 3 oocytes or 2 embryos
6. **Sperm cryopreservation for MESA/TESE and 2 year storage** **\$ 4,400**
7. **Further storage of embryos / sperm / oocytes**
 - For 3rd & 4th year **\$ 6,600**
 - For 5th & 6th year **\$ 8,800**
 - For 7th & 8th year **\$ 11,000**
 - For 9th & 10th year **\$ 11,000**
8. **Embryo thawing in frozen-thawed embryo transfer** **\$ 4,200**


B. Advanced techniques

1. **Assisted hatching by laser** **\$ 4,400**
Indications: repeated implantation failure
2. **Blastocyst culture** **\$ 2,750**
Indications:
 - a. >3 good quality embryos on Day 2

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3. Preimplantation genetic testing (PGT)

| | Tests | Charge |
|-----|---|--|
| | Pre-PGT workup | |
| 1. | On-panel monogenic diseases | \$ 4,000 |
| 2. | Category I of other monogenic diseases | \$ 15,000 |
| 3. | Category II of other monogenic diseases | \$ 25,000 |
| 4. | HLA typing optimization | \$4,000 |
| 5. | Optimization to distinguish normal from balanced <u>reciprocal translocation</u> carriers by nanopore sequencing | \$11,000 |
| | PGT treatment cycle | |
| 6. | Embryo biopsy | \$1,500 per sample |
| 7. | DNA assay for one single gene (PGT-M) | \$2,800 per sample |
| 8. | Additional DNA assay: <ul style="list-style-type: none"> • One additional gene / locus | \$ 1,000 per sample / gene |
| 9. | Next generation sequencing analysis (NGS) | \$3,000 per sample |
| 10. | Distinguish normal from balanced <u>reciprocal translocation</u> carriers | \$2,000 per cycle |
| 11. | Distinguish normal from balanced <u>Robertsonian translocation</u> carriers | 1st cycle: \$ 9,000 subsequent cycle: \$ 4,000 |
| 12. | Administrative fee for NGS | \$ 1,000 |
| 13. | <i>Express service surcharge (TAT:5 working days)</i> PGT-M PGT-A / PGT-SR PGT-M + PGT-A | per patient per cycle \$ 5,000 \$20,000 \$ 23,000 |

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Recruitment Guideline in the Hospital Authority for In-Vitro-Fertilization (IVF)

I. Background

IVF is an invasive procedure and serious complications such as ovarian hyperstimulation syndrome, risks of oocyte retrieval, ectopic pregnancy and multiple pregnancy can occur. There would also be risk usually associated with pregnancies, including abortion and congenital abnormalities. The cost effectiveness of treatment is also important. For these reasons appropriate patient selection is mandatory and a clear indication for IVF must exist for this publicly funded service.

The decision on whether to recommend IVF treatment should be based on

- (1) the likelihood that a pregnancy will occur without treatment;
- (2) the possibility that a less invasive form of treatment might be effective;
- (3) the likely outcome of IVF treatment.

II. Patient Selection Criteria

1. The female patient must not be more than 40 years of age at the time the procedure is initiated.
2. Couples must be legally married with no living child for the current marriage.
3. Couples must not have contraindications for pregnancy in terms of medical, physical and mental conditions.
4. Couples must be adequately investigated and IVF is the most appropriate treatment.
5. Clients with decreased ovarian reserve as indicated by screening test(s) will be excluded.
6. Each eligible couple will be entitled to three IVF treatment cycles within the Hospital Authority.
7. On top of the above, the individual professional team will consider other relevant factors where appropriate e.g. the underlying cause of infertility, the duration of infertility and the pregnancy history.

Hospital Authority
February 2003