

Modified Natural Cycle (MNC) – mild stimulation IVF

Modified Natural Cycle (MNC) IVF treatment is a form of IVF where the treatment is carried out within the natural menstrual cycle but involves the use of fewer fertility medication. This approach can help to reduce the risk of spontaneous ovulation, the side effects while maintaining a reasonably good success rate.

This treatment has a better success rate compared to the natural cycle IVF while retaining many of its benefits.

In 2017, A multicentre randomized trial concluded that a mild ovarian stimulation strategy in women with poor ovarian reserve undergoing IVF leads to similar ongoing pregnancy rates as a conventional ovarian stimulation strategy (1)

Why choose Natural Cycle IVF?

1. Lower doses of fertility drugs and shorter treatment times:

Natural Cycle IVF generally uses lower doses of fertility medications leading to fewer risks and side effects. Larger doses of hormone medications are used during conventional IVF treatment to stimulate the ovaries to produce multiple eggs (on average around 10 eggs per cycle in women with average ovarian reserve). The treatment cycle may also be prolonged by nearly two weeks due to suppression of the ovaries – leading to unpleasant menopausal symptoms.

2. Reduced side effects and better implantation of embryos:

MNC Cycle IVF is associated with less chances of OHSS. It is also associated with less side-effects (such as less chances of headaches, hot flushes, bloating, mood changes or other concerns relating to pituitary down regulation).

The main risks of conventional IVF include: Ovarian Hyperstimulation Syndrome (OHSS), changes to the lining of the womb reducing the likelihood chances of embryo implantation (changing the implantation window), and a potential increase in chromosome abnormalities in both eggs and embryo.

3. Reduced cost of treatment:

MNC Cycle IVF is less expensive as compared to conventional IVF treatments as it requires less doses of the expensive fertility medications.

4. Improved egg quality:

Naturally selected eggs have potentially fewer chromosomal abnormalities. This would increase the chances of having embryos with normal chromosomes.

5. MNC Cycle IVF patients can repeat their treatment resumed in consecutive cycles as compared to stimulated IVF cycles which required around 3 months break between cycles.

Who can have MNC IVF treatment:

MNC IVF is particularly appropriate for patients at increased risk of ovarian hyperstimulation syndrome, poor responders, and those wishing to avoid supernumerary embryo production (2). This includes the following groups:

- 1) Women with polycystic ovarian syndrome and high levels of Anti-Müllerian Hormone.
- 2) Women with reduced ovarian reserve and low (AMH) and high levels of Follicle Stimulating Hormone (FSH)
- 3) Women who have had a poor response to conventional IVF (e.g. produced fewer than three eggs).
- 4) cancer patients if fertility drugs might make their condition worse. For example, breast cancer patients may be unable to take certain drugs that would increase their oestrogen levels if their cancer is sensitive to oestrogen (3)
- 5) You may also hold religious beliefs which mean you don't want any leftover eggs or embryos to be destroyed or frozen (3)

What is the success rate for natural cycle IVF?

The success rate of MNC IVF in patients with adequate ovarian reserve is generally good and comparable to conventional IVF treatment.

The success rate in patients with reduced ovarian reserve is generally low (around 8 - 10% in different studies), meaning that 8 - 10 women out of one hundred will get pregnant in a natural cycle. The lower success rate is linked to the nature of the patients receiving treatment and the lower likelihood of obtaining an egg in each cycle. Recent studies concluded that in advanced-age and poor responders, MNC-IVF, which is a more patient-friendly approach, could be a reasonable alternative (4).

What happens when I go into hospital for egg collection?

Your stay in the hospital is usually for just a day. You will be asked to come to the Assisted Reproduction Unit at 8 am.

On the morning of the operation you should not have anything to eat or drink unless you are advised otherwise. You should have a bath or shower. **DO NOT** use any deodorant, perfumes, make-up, or nail varnish when you come into hospital.

What do I need to bring into hospital with me?

You will need to bring the following items with you:

- Dressing Gown.
- Slippers.
- Towel.
- Flannel and Soap.
- Toothbrush and Toothpaste.

- Comb or Hairbrush.

Please do not bring any valuables into hospital with you.

How is the egg collected?

For IVF/ICSI, the egg is collected using ultrasound. A vaginal scan is performed to locate the follicle, and a needle is inserted into the follicle. The fluid from inside the follicle is drained into a sterile tube via a needle attached to a suction pump. The embryologist then examines the fluid under the microscope to find the egg. The egg is placed into a labelled dish and placed into an incubator.

Is the procedure painful?

The egg collection is performed after giving you some sedation and pain relief. Sedation relieves anxiety and helps you to relax. Most women describe minimal discomfort during the egg collection, and many don't remember much about it afterwards. Cramping and a small amount of vaginal bleeding can occur after the procedure. You can take Paracetamol tablets for pain relief, but you must wait 4 hours between doses, and must not take more than 8 tablets in a 24-hour period. If your pain is not relieved by Paracetamol, contact the medical staff using the emergency contact number.

When is the sperm sample collected?

Around the time of egg collection, your partner will be asked to produce a fresh sample of sperm. This is usually provided at the hospital. A private room is provided for this. We recommend that you do not have intercourse for 3-4 days prior to the egg collection.

If you have any worries about producing your sperm sample in the hospital, it might be possible to produce it at home and bring it to the assisted reproduction unit within 45 minutes of production. Please discuss this with the nurses and the embryology teams in advance.

The sperm sample is stored for a short time before the sperm are washed and spun at a high speed. This is so the healthiest and most active sperm can be selected. The semen is prepared by the embryologist and the egg is fertilised by either IVF or ICSI. It is placed in an incubator overnight. The egg is examined the following day for signs of successful fertilisation.

When will I know if the eggs have fertilised?

The Embryologist will contact you between 9:00am & 10:00am the day after egg collection. This is to find out whether the egg has fertilised and if it is suitable for replacement.

Failure of the egg to fertilise or not to develop sufficiently means that the procedure failed, and your cycle will have to be discontinued. The Unit Counsellor will be available for you and your partner if you wish to see her. Please ask the nurses to arrange this for you. Another appointment will be made for you to see the Consultant.

When is the embryo replaced?

The embryologist will check your embryos every day after your egg collection and will grade them. We will try to replace the embryo (s) on the fifth day following egg collection if they have divided and considered suitable for transfer by the embryology team.

How is the embryo replaced?

The procedure feels similar to a smear test and causes very little discomfort. No anaesthetic is needed. You will be asked to come to the assisted reproduction unit on the morning of the embryo replacement. You can have your breakfast before coming into hospital, and again we request that you wash with simple soap and avoid perfumes and deodorants.

The embryo is placed into the womb using a long, thin plastic tube which is passed through the cervix (neck of the womb). You will be given a scan during the procedure and you will need to have a full bladder for this. The procedure takes approximately 30 minutes.

You will be taken back to the ARU from theatre and you can get dressed and go home.

References:

- 1) Youssef, M. A. et al. (2017) 'A mild ovarian stimulation strategy in women with poor ovarian reserve undergoing IVF: a multicenter randomized non-inferiority trial.', *Human reproduction (Oxford, England)*, 32(1), pp. 112–118. doi: 10.1093/humrep/dew282.s
- 2) Ho JR, Paulson RJ. Modified natural cycle in in vitro fertilization. *Fertil Steril.* 2017 Oct;108(4):572-576. doi: 10.1016/j.fertnstert.2017.08.021. PMID: 28965551.
- 3) IVF options | Human Fertilisation and Embryology Authority (hfea.gov.uk): [IVF options | Human Fertilisation and Embryology Authority \(hfea.gov.uk\)](https://www.hfea.gov.uk/ivf-options/)
- 4) Drakopoulos P, Romito A, Errázuriz J, Santos-Ribeiro S, Popovic-Todorovic B, Racca A, Tournaye H, De Vos M, Blockeel C. Modified natural cycle IVF versus conventional stimulation in advanced-age Bologna poor responders. *Reprod Biomed Online.* 2019 Oct;39(4):698-703. doi: 10.1016/j.rbmo.2019.05.009. Epub 2019 May 16. PMID: 31383604.

Modified Natural Cycle (MNC) Schedule of Treatment.

PLEASE READ THIS INFORMATION CAREFULLY.

Drugs used in the Antagonist Protocol

Ovarian stimulation during MNC treatment:

Letrozole or Clomid tablets: You will start taking these tablets to simulate your ovaries to grow follicles from the second or the third day of your period. The dose and the duration of these tablets will be agreed with your consultant.

The FSH injections: (Menopur / Gonal –F or other generic injections) stimulate the ovaries to produce follicles and prepare the lining of the uterus (womb) to receive the fertilised egg. Smaller doses of these injections could be added your treatment. The dose, duration and frequency of the injections will be agreed with your consultant based on your age, previous ovarian response and your ovarian reserve. These injections are given as a subcutaneous injection (injection under the skin). You will be taught how to give this yourself or your partner can be trained to do the injection for you.

The treatment will be monitored by transvaginal (TVS) ultrasound scans to monitor the growth of the follicles. Occasionally blood testing to measure hormone levels might be required.

Whilst receiving the FSH injections, some women experience abdominal bloating, breast tenderness, increase in vaginal secretions, and if the ovaries are very swollen with a large number of follicles, some abdominal (tummy) discomfort may occur.

GnRH Antagonist (Ganirelix (Orgalutron) / Cetrotide / Fyremadel)

During normal cycles the release of an egg (ovulation) depends on a hormone made by the pituitary gland. This is called luteinising hormone (LH). The GnRH Antagonist blocks the release of this hormone so that premature ovulation (release of the eggs) and loss of the eggs cannot occur. It is given by an injection under the skin **starting on the fifth or sixth day of your period.** Side effects of the drugs include nausea, headache, injection site reactions, dizziness and malaise. Please let us know if you are concerned about any symptoms.

The antagonist drug must be given at **exactly the same time each day.** Any delay may result in early release of the ovulation hormone LH. Should this happen your cycle will be cancelled and you may place yourself at risk of complications.

The FSH and the antagonist drug are the only injections that you need to take during stimulation of the ovaries. If you have been given any other medication on your prescription, please discuss with the nurses before taking as all drugs are prescribed to be given at specific times in the treatment cycle. **Please do not stop any of your medication without obtaining advice.**

HUMAN CHORIONIC GONADOTROPHIN (HCG) (Gonasi / Pregnyl or Ovitrelle)

When the follicles are at the correct size, this drug is given as a single injection late at night to ensure that the eggs collected will be at the correct stage of maturity. It simulates the effect of LH. The timing of this drug is very important to ensure that eggs are collected at the right time. **The injection is timed to be given 34-36 hours prior to egg collection.**

When Do I Stop Taking the Injections?

The HCG is your final injection before egg collection. All other injections are stopped when this has been given.

Do I take any medications after egg collection?

You will be given hormones in the form of an injection (Lubion) and/or vaginal pessary (Cyclogest or Lutigest) following the egg collection to support the early embryo after embryo transfer and increase the chance of a successful pregnancy. This is known as “luteal phase support.” The medications are taken every day up to the day of your pregnancy test. If your test is positive you must ring the unit and collect another prescription that day. **You must not stop taking them or miss a dose.** You need to continue with them until you are 8 - 12 weeks pregnant.

Side effects could include nausea, vomiting, and swollen breasts. If you experience any side effects, speak to the doctors or nurses. Use the emergency contact number after 5pm and weekends for advice before stopping any medication.

Occasionally you may be given injections to thin the blood after egg collection, and aspirin tablets. If your pregnancy test is positive you will also need to continue taking these medicines until you are 12 weeks pregnant.

If you have any other symptoms or vaginal bleeding, you must contact us for advice.

Modified Natural Cycle IVF

Date	Day of Cycle	Day of FSH	Procedure			
	1		Phone unit and register for treatment			
	2	1	Scan	Blood tests	Start: Clomid / Letrozole Dose:	START FSH Menopur / Gonal F Dose:
	3	2				FSH
	4	3				FSH
	5	4				FSH
	6	5				FSH + START ANTAGONIST DRUG Ganirelix (Fyremadel) Cetrotide or Ovitrelle
	7	6				FSH + ANTAGONIST
	8	7				FSH + ANTAGONIST
	9	8				FSH + ANTAGONIST
	10	9				FSH + ANTAGONIST
	11	10				FSH + ANTAGONIST
	12	11				FSH + ANTAGONIST