Sheba - Academic Medical Center Hospital

Sheba Medical Center IVF Fertility Unit
Information Brochure for IVF Patients

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General Tests Required Prior to Treatment at the IVF Fertility Unit

Dear Patients,
In accordance with Ministry of Health directives, you will be required to undergo the tests listed below prior to treatment:

Female Partner:

1. **Various laboratory tests performed in preparation for a pregnancy designed to rule out any problems that might affect pregnancy or the health of the mother or fetus**
   - Blood type and Rh
   - Indirect Coombs test
   - Rubella and VDRL antibody test
   - CMV and toxoplasmosis antibody test
   - HBsAg, Hepatitis C antibody and HIV antigen tests
2. **Early screening tests that are regularly performed on women**
   - Latest gynecological exams including pap smear
   - Surgical breast exam / mammography
3. **Preliminary tests prior to general anesthesia (updated within the past 6 months)**
   - Complete blood count, clotting function, full chemistry
   - ECG for women over the age of 40
4. **Blood test for hormone profile** performed on Day 3 of the menstrual cycle
5. **Uterine imaging** based on pelvic (gynecological) ultrasound, latest hysterosalpinogram and/or hysteroscopy (observation of the uterine cavity using an optic device).
   Referral will be given by the physician if necessary.

Male Partner:
- Sperm analysis (including morphology)
- Blood tests required by Ministry of Health:

HBsAg, Hepatitis C antibody and HIV antigen tests
These tests are valid for only one year from the test date

Patients should contact the Genetics Institute at Sheba for a consultation on tests to determine whether they are carriers of common genetic diseases, in accordance with Ministry of health directives.
Telephone: 03-5303060

Hormonal Treatment for Controlled ovarian hyperstimulation

During the meeting with the physician, an individual treatment plan will be formulated

Women naturally release only one egg (or two in the case of twins) every month. In IVF treatments, the goal is to release a larger number of eggs to improve the chances of pregnancy without endangering the patient. Ovulation Induction is achieved through hormone treatments, as part of the controlled ovarian hyperstimulation protocols for IVF treatments.

In general, there are two main controlled ovarian hyperstimulation protocols: long protocol and GnRH antagonist protocol:

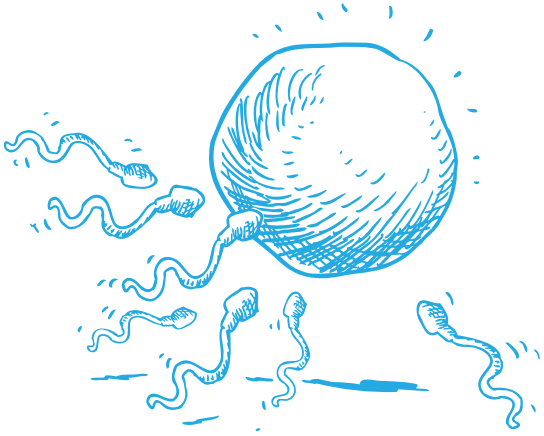
GnRH antagonist protocol:

Treatment begins on Day 2-3 of the menstrual cycle, with daily administration of follicle stimulation hormone (FSH). After 5-6 days, another injection (GnRH antagonist) is given. The antagonist is designed to prevent premature ovulation that might hinder treatment success. The combined treatment is continued until mature follicles are obtained. Once mature follicles (generally over 17mm diameter) appear, an HCG injection is administered to induce final maturation of the eggs in the follicles as well as to trigger the production and secretion of progesterone into the bloodstream.

Long treatment protocol (with GnRH agonist):

Treatment largely begins on Day 21 of the previous cycle (about one week prior to the scheduled menstruation) with administration of a GnRH agonist. The agonist, like the antagonist, is designed to prevent premature ovulation. Unlike that antagonist, however, the agonist must be administered for about two weeks prior to achieving suppression – which is identified through ultrasounds of the ovarian follicles and blood tests for hormone levels. Once hormone suppression is achieved, stimulation of the ovaries can begin in order to produce follicles (which contain the eggs).

The physician will select the ovarian induction protocol, taking into account previous response to ovulation induction protocol, woman's age, weight and basal hormonal profile.



IVF Treatment involves using a wide range of drugs:

Drugs that stimulate the ovaries to produce follicles

This group includes the following drugs:

Gonadotropins: Menogon, Menopur, Puregon, Gonal F, Pergoveris and Elonva, which work directly on follicular development and the formation of eggs in the ovary. These drugs are designed to stimulate an optimal number of follicles / eggs (about 5-15) without endangering the patients with ovarian hyperstimulation syndrome (OHSS). They are administered either subcutaneously in the abdominal region, which allows patients to inject themselves, or intramuscularly (in accordance with the physician's instructions).

Anti-estrogens: Clomiphene, Tamoxifen and Letrozole are administered in tablet form and indirectly affect follicle development.

Drugs that prevent premature ovulation

The drugs used, which are analogs of the GnRH hormone, induce reversible inhibition of the pituitary gland. The preparations used in Israel are decapeptyl, synarel and buserelin, which are GnRH agonists, and cetrotide and orgalutran, which are GnRH antagonists.

Ovulation-inducing drugs

Ovulation-inducing drugs are preparations that contain the hormone HCG (Ovitrelle or Pregnyl).

For patients undergoing ovulation induction protocol with a GnRH antagonist, who are at risk to developg ovarian hyperstimulation syndrome, ovulation can be induced with a GnRH agonist instead of HCG, thereby completely preventing the risk of OHSS.

Drugs that support the endometrial lining in preparation for implantation

These drugs contain progesterone (endometrin, utrogestan, crinone, and gestone) and occasionally estrogen (progynova and estrofem).

Side Effects of the Hormone Treatment

As previously noted, the hormone treatment given to the woman is designed to induce ovulation either when the woman fails to ovulate or in order to produce a greater number of eggs, thereby increasing the chances of pregnancy.

Side effects and complications of hormone treatment include:

1. **Sensitivity to the hormone preparations** – rare, but should any unusual effect occur, the patient should seek immediate medical care from the attending physician.

2. **Ovarian hyperstimulation Syndrome** – symptoms largely include abdominal swelling and pain, development of ovarian cysts, enlarged ovaries and even mild retention of fluid in the abdomen. In general, the side effects pass with rest and drinking large quantities of fluid. The incidence of mild ovarian hyperstimulation is 10%-25% per treatment cycle. Moderate or severe ovarian hyperstimulation are even less common and generally requires hospitalization. Moderate ovarian hyperstimulation, which occurs 5%-15% of the time, also includes nausea, diarrhea and vomiting. In addition to the aforementioned side effects, severe ovarian hyperstimulation also includes accumulation of fluid in the abdominal cavity, chest cavity and heart, which occasionally requires repeated aspiration to drain the fluid. Fluid accumulating in cavities might also result in thromboembolic complications. Other rare complications include heart failure, kidney failure and life-threatening complications. The incidence of severe ovarian hyperstimulation is 0.1%-5% per treatment cycle.

3. **Multiple embryos** – the percentage of multiple embryos in hormone treatment is relatively high, up to 30% , depending on the type of treatment. In the case of higher order multiples (three or more), selective fetal reduction might be needed due to the risks involved in multiple pregnancy. If necessary, an explanation about the procedure, risks and chances will be provided separately.

4. **Miscarriages and ectopic pregnancies** – in pregnancies achieved after ovulation induction, the incidence of miscarriages and ectopic pregnancies is slightly higher.

5. **Ovarian torsion, rupture or bleeding** – are relatively rare but occasionally require surgical intervention. On rare occasions, the ovaries might need to be removed.

6. **Other complications** – no causal link has been proven to date between ovulation induction and ovarian cancer. Pregnancy is known to provide excellent protection in lowering the incidence of malignant ovarian tumors.

In addition, hormone treatments administered to treat fertility problems may result in children with physical or mental problems, including genetic defects, or any other abnormality. The rate of these complications does not generally exceed the frequency of their occurrence in natural pregnancies.

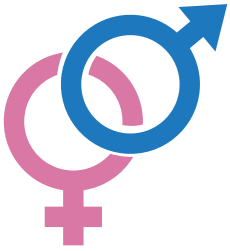
Ovarian Hyperstimulation Syndrome – Information for Patients

Definition: Ovarian Hyperstimulation Syndrome is a complication of ovulation induction treatments that is characterized by a significant enlargement of the ovaries and fluid retention in different cavities of the body.

Signs and symptoms: Ovarian Hyperstimulation Syndrome includes a wide range of clinical symptoms that are characterized by two main events: (a) significant ovarian enlargement that is attributed to the effect of FSH on maturing follicles in the ovary and (b) increased permeabilty of membranes and blood vessels, causing fluids to pass into and out of blood vessels and accumulate in third space compartments (abdominal cavity, chest, heart and subcutaneous). This fluid pathway is essentially responsible for the morbidity involved in the syndrome. Due to the movement of fluids from the intravascular compartment to the third space cavities, fluid volume begins to decline in the blood vessels. This is manifested in increased risk for blood clots, events that might result in thromboembolism. In addition, disorders in fluid and electrolyte balance might occur, as might reduction in urination to the point of kidney failure.

Risk factors for the development of the syndrome: Several conditions were found to be related to the syndrome and proposed as risk factors in its development. These conditions can be divided into primary and secondary risk factors: Primary: young age of the patient (<33 years), women who developed OHSS in the past and those suffering from polycystic ovarian syndrome. Secondary: women who during ovulation induction for IVF treatment responded with a quick or significant rise in estrogen levels, in number of follicles or in aspiration of a large number of eggs.

Treatment: The main treatment is conservative and designed to prevent the severe OHSS complications while reducing its duration. Close monitoring, generally outpatient, is required. Treatment includes rest, large fluid intake, pain killers and monitoring of symptoms that might indicate a progression or deterioration of the condition. Sexual relations should be avoided as it might increase the chances of ovarian torsion or rupture. Mild to moderate OHSS generally disappears on its own. If OHSS progresses to severe or life-threatening, continued treatment will be administered with the patient hospitalized.

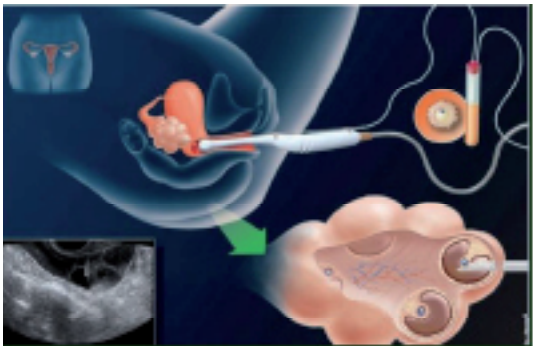


Instructions for the egg-retrieval day

- Instructions ahead of retrieval will be given by phone two days prior to the procedure.
- On the morning of the retrieval, the woman and her partner must arrive at the unit at the designated time.
- You must be in full fast beginning from midnight (no eating, drinking, smoking and gum chewing) and arrive without jewelry, makeup and nail polish.
- Avoid sexual relations two-three days prior to the scheduled egg retrieval. The partner is asked to provide a sperm sample in a sterile container. The sample should be provided at home, in a sterile cup and should be brought to the unit within one hour of donation, or alternatively, the partner should provide the sample at the hospital.
- On the egg retrieval day, you will be admitted to the hospital. The retrieval procedure is carried out under general anesthesia in an operating room of the outpatient unit. You will be hooked up to an intravenous infusion for liquids. Instructions will be given by the anesthesiologist prior to administration of the anesthesia for the egg retrieval procedure.
- Follicles are retrieved using a regular vaginal ultrasound probe. A needle attached to the probe is inserted into the follicle in the ovary through the vagina and fluid containing the egg is aspired into a special test tube. The test tube is then delivered to the laboratory adjacent to the operating room.
- In the embryology laboratory, the eggs are separated from the follicular fluid and transferred to Petri dishes containing tissue culture fluid.
- The eggs are then inseminated with the partner's sperm (by regular fertilization or micromanipulation, depending on the quality of the sperm), and are incubated for continued growth and development in a special incubator that provides similar environmental conditions as those in a human body.
- Once the eggs have been retrieved, you will remain in the recovery room and later in the gynecology outpatient department for two-four hours. Based on your condition, you will be discharged home.

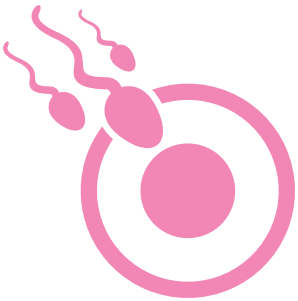
Instructions for the Patient following Egg Retrieval

- Upon your discharge from the unit following the egg retrieval, you should rest fully and drink large amounts of fluid.
- Women undergoing the retrieval under general anesthesia are not allowed to drive until the next day.
- On the retrieval day, you should rest and drink at least two liters.
- If you notice any change in your condition or experience strong abdominal pain, significant weakness or fever, you must immediate seek medical treatment at the Gynecology ER and bring your letter of discharge.
- From the day after the retrieval, you must take drugs (pills / suppositories / injections) in accordance with the unit physician's instructions, as prescribed in the discharge letter issued on the egg retrieval day.
- The day after the retrieval, you must contact the unit to find out how many eggs were fertilized and the date of the embryo transfer.
- Embryos are transferred to the woman's uterus two or three days after egg retrieval. If the decision is made to transfer blastocysts, the embryo transfer will take place on the fifth or sixth day following egg retrieval.



Instructions for After Embryo Transfer

- Once the embryos have been transferred, supportive hormone treatment designed to support embryo implantation in the uterus must continue (which includes progesterone preparations, with or without estrogen).
- Two weeks after the transfer, you will be invited to take a blood pregnancy test.
- If pregnancy is achieved, you must continue with the supportive hormone treatment. You will also be invited to repeat the test and for an ultrasound to confirm normal development of the pregnancy.
- In Week 5-6 of the pregnancy, the gestational sac is visible.
- In Week 6-7, a fetal heartbeat can be seen.
- Pregnancy follow-up at the clinic ends in Week 6-7. You will then be referred to your gynecologist for the remainder of the pregnancy.
- If, following the embryo transfer, you experience strong abdominal pain, vaginal bleeding, fever, abdominal distension or respiratory difficulties, you must visit the gynecology ER with the discharge letter, or consult the unit physician (during business hours).



Thank you for your cooperation and Good Luck!

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