

Sem – VI (UG)

CC-13: Developmental Biology

C13T: Unit -5, Implications of Developmental Biology

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In vitro Fertilization (IVF)

What is IVF?

In vitro fertilisation (IVF) is a process of fertilisation where an egg is combined with sperm outside the body, in vitro ("in glass"). The process involves monitoring and stimulating a woman's ovulatory process, removing an ovum or ova (egg or eggs) from the woman's ovaries and letting sperm fertilise them in a liquid in a laboratory. After the fertilised egg (zygote) undergoes embryo culture for 2–6 days, it is implanted in the same or another woman's uterus, with the intention of establishing a successful pregnancy.

Why it's done?

IVF is a treatment for infertility or genetic problems. Sometimes, IVF is offered as a primary treatment for infertility in women over age 40. IVF can also be done for certain health conditions:

- Fallopian tube damage or blockage:
This problem makes it difficult for an egg to be fertilized or for an embryo to travel to the uterus.
- Ovulation disorders:
If ovulation is infrequent or absent, fewer eggs are available for fertilization which reduces the chances of pregnancy.
- Endometriosis:
It occurs when the uterine tissue implants and grows outside of the uterus – often affecting the function of the ovaries, uterus and fallopian tubes.
- Uterine Fibroids:
Fibroids are benign tumours in the wall of the uterus and are common in women in their 30s and 40s. These can interfere with implantation of the fertilized egg.

- Previous tubal sterilization or removal:
If one had have tubal ligation, in which her fallopian tubes are cut or blocked to permanently prevent pregnancy – and want to conceive, IVF may be an alternative to tubal ligation reversal.
- Impaired sperm production or function:
Below-average sperm production, weak movement of sperm, or abnormalities in sperm size & shape can make it difficult for sperm to fertilize an egg. If semen abnormalities are found, it also affect in fertilization.
- A genetic disorder:
If one and his/her partner is at risk of passing on a genetic disorder to the child, he/she may be candidate for pre-implantation genetic testing – a procedure, that involves IVF. After the eggs are harvested and fertilized, they're screened for certain genetic problems. Embryos that don't contain identified problems, can be transferred to the uterus.
- Fertility preservation for cancer or other health conditions:
If one is about to start cancer treatment (radiation or chemotherapy), that could harm her fertility, IVF may be an option. Women can have eggs harvested from their ovaries and frozen in as unfertilized state for later use, or the eggs can be fertilized and frozen as embryos for future use. Women, who don't have a functional uterus or for whom pregnancy poses a serious health risk, might choose IVF using another person to carry the pregnancy (gestational carrier).

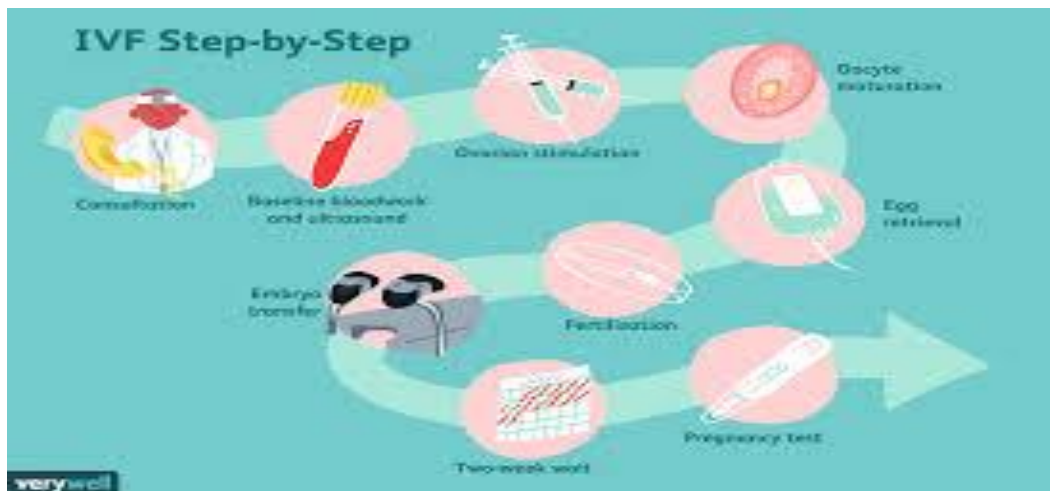
Steps involved in IVF:

IVF involves several steps – ovarian stimulation/induction, egg retrieval, sperm retrieval, fertilization and embryo transfer. One cycle of IVF can take about two to three weeks.

- Ovulation induction:
If a woman using her own eggs during IVF, at the start of a cycle she'll begin treatment with synthetic hormones to stimulate her ovaries to produce multiple eggs – rather than the single egg that normally develops each month. Multiple eggs are needed because some eggs won't fertilize or develop normally after fertilization.
In this aspect, some medications are –

- ✓ For ovarian stimulation - An injection containing FSH, LH or a combination of both. They stimulate more than one egg to develop at a time.
- ✓ For oocyte maturation - When the follicles are ready for egg retrieval (generally after 9-14 days), she has to take HCG to help the eggs mature.
- ✓ To prepare the lining of the uterus - On the day of egg retrieval or at the time of embryo transfer, the doctor might recommend that she begin taking progesterone supplements to make the lining of uterus more receptive for implantation.

Typically, she'll need 1-2 weeks of ovarian stimulation before the eggs are ready for retrieval. To determine when the eggs are ready for collection, doctor will likely perform i) vaginal ultrasound (to see the development of follicles), ii) blood tests (to measure the response to ovarian stimulation medications – oestrogen levels increase as follicles develop, progesterone levels remain low until after ovulation).



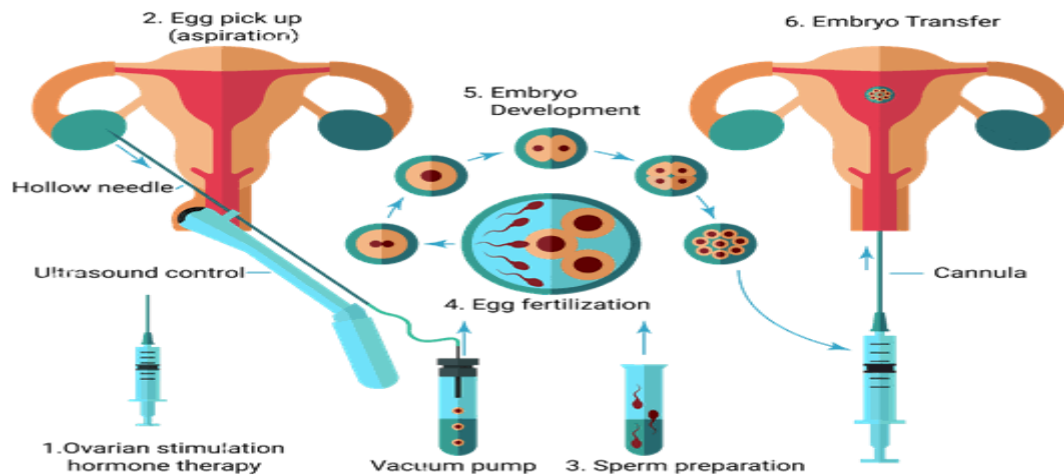
- Egg retrieval:

It can be done 34-36 hours after the final injection and before ovulation.

- ✓ During egg retrieval, she'll be sedated and given pain medication.
- ✓ Trans-vaginal ultrasound aspiration is the usual retrieval method. An ultrasound probe is inserted into the vagina to identify follicles. Then a thin needle is inserted through the vagina and into the follicles to retrieve the eggs.
- ✓ The eggs are removed from the follicles through a needle connected to a suction device. Multiple eggs can be removed in about 20 minutes.

- ✓ Mature eggs are placed in a nutritive liquid (culture medium) and incubated. Eggs that appear healthy and mature, will be mixed with sperm to attempt for fertilization. However, not all eggs may be successfully fertilized.

In Vitro Fertilization (IVF)



- Sperm retrieval:
If the woman using her partner's sperm, he'll provide a semen sample at the doctor's clinic in the morning of egg retrieval. Other methods such as testicular aspiration (use of a needle to extract sperm directly from the testicle) are sometimes required. Donor sperm can also be used. Sperms are separated from the semen fluid in the lab.
- Fertilization:
Fertilization can be attempted using two common methods:
 - ✓ Conventional insemination – during this process, healthy sperm and mature eggs are mixed and incubated overnight.
 - ✓ Intra-cytoplasmic sperm injection (ICSI) – in this process, a single healthy sperm is injected directly into each mature egg. It is often used when semen quality or number is a problem.
- Embryo transfer:
Embryo transfer is done 2-5 days after egg retrieval:
 - ✓ The woman might be given a mild sedative.
 - ✓ The doctor will insert a long, thin, flexible tube (catheter) into patient's vagina through the cervix and into the uterus.
 - ✓ A syringe containing one or more embryos suspended in a small amount of fluid, is attached to the end of the catheter.
 - ✓ Using the syringe, the doctor places the embryo(s) into the uterus.

If successful, an embryo will implant in the lining of the uterus about 6-10 days after egg retrieval.

❖ **Result:**

About 12 days – 2 weeks after egg retrieval, the doctor will test a sample of patient's blood to detect the pregnancy.

- ✓ If pregnancy occurs – the doctor will refer her to other pregnancy specialist for prenatal care.
- ✓ If pregnancy doesn't occur – she'll stop taking progesterone. The doctor might suggest steps she can take to improve the chances of getting pregnant through another cycle of IVF.

Risks:

Risks of IVF includes –

- ✓ Multiple Births: IVF increases the risk of multiple births if more than one embryo are transferred to the uterus.
 - ✓ Premature delivery and low birth weight: IVF slightly increases the risk that the baby will be born early or with a low weight.
 - ✓ Ovarian hyperstimulation syndrome: Use of injectable fertility drugs (i.e., HCG) to induce ovulation can cause ovarian hyperstimulation syndrome, in which the ovaries become swollen and painful. Symptoms include mild abdominal pain, bloating, nausea, vomiting and diarrhoea.
 - ✓ Miscarriage: The rate of miscarriage for women who conceive through IVF with fresh embryos is similar to that of women who conceive naturally – about 15% - 25%, but the rate increases with maternal age.
 - ✓ Egg-retrieval procedure complications: use of an aspirating needle to collect eggs could possibly cause bleeding, infection or damage to the bowel, bladder or blood vessel. Risks are also associated with sedation and anaesthesia, if used.
 - ✓ Ectopic pregnancy: About 2%-5% of women who use IVF will have an ectopic pregnancy (the fertilized egg implants outside the uterus, usually in the fallopian tube). The fertilized egg can't survive outside the uterus and there's no way to continue the pregnancy.
 - ✓ Birth defects: The age of the mother is the primary risk factor in the development of birth defects (i.e. septal heart defect, cleft lips with or without cleft palate, oesophageal atresia, anorectal atresia etc.). IVF, including ICSI, is associated with an increased risk of imprinting disorders including Prader – Willi syndrome and Angelman syndrome.
 - ✓ Spread of infectious diseases: Hepatitis-B, HIV etc. may be transmitted through IVF when sperms are from unknown donor.
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