



A Brief Review on *in vitro* Fertilization

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ABSTRACT

In vitro fertilization (IVF) is the advanced and miraculous process by which the egg is fertilized by the sperm outside the body or a coined as the In-vitro. The advanced clinical treatment for the In-vitro fertilization (IVF) infertility when previously; other methods of assisted reproductive technology had been failed. The first successful birth of the "test tube baby" name was, Louise Brown, was born in 25 July, 1978 in London as the result of the natural cycle In-vitro fertilization (IVF). Robert G. Edwards, the physiologist who was developed the treatment, was awarded the Nobel Prize in Physiology Medicine in 2010. This procedure involves also monitoring and stimulating of woman's ovulatory process to remove the ovum or ova from the woman's ovaries and to let the sperms fertilize those eggs in artificial fluid medium in a laboratory. The fertilized egg or zygote is cultured for 2–6 days in an artificial growth medium and then, it is transferred to the mother's uterus with the intention of the establishing a successful pregnancy as to have the obvious benefit of boosting the odds of getting the pregnant. Especially, in the stressful and unhealthy urban life style In-vitro fertilization (IVF) is very helpful for women with blocked fallopian tubes or for men with have low sperm count and it led to conceiving of babies and in turn, their births with successful as well as expecting of survival rate which are the coined with a colloquial term "test tube babies."

Keywords: IVF, *In-vitro* fertilization, gonadotropin releasing hormone (GnRH), human, human chorionic gonadotropin (HCG), ovarian hyperstimulation, ova retrieval, infertility.

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INTRODUCTION

In vitro fertilization (IVF) is practically a household word today. But it was not so long ago, it was the mysterious procedure for the infertility that produced what were then known as "test-tube babies." Louise Brown, is born in England in 1978, was the first such baby to be conceived outside her mother's womb.

Unlike the simpler process of the artificial insemination -- in which the sperm is placed in the uterus and conception is happens otherwise in normally -- IVF involves combining eggs and sperm outside the body in a laboratory. Once the embryo or embryos forms, they are placed into the uterus. IVF is the complex and it is expensive procedure; only about 5% of couples with infertility seek it out. However, since its introduction in the U.S. in 1981, 1.9% of all babies in the U.S. are born through IVF and other assisted reproductive technologies (ART).

In-vitro fertilization (IVF) was a mysterious procedure for infertility which was previously coined as "test-tube babies." Louise Brown was the first test tube baby who was born in 25 July, 1978 in England and to be conceived

outside her mother's womb via simpler process of artificial insemination in which sperm is placed in the uterus. This conception was further preceding as In-vitro fertilization (IVF) which involves the fertilization of the eggs and the sperm outside the body in a laboratory and once the embryo or embryos are form, they are then placed in the uterus. IVF: In-vitro fertilization is the complex and expensive procedure too with only about 5% of the couples with infertility seeks it out. However, since its introduction was started in the U.S. in 1981, and In-vitro fertilization (IVF) has resulted in the birth of more than 200,000 babies. In-vitro fertilization (IVF) may be the treatment option if woman's fallopian tubes are missing or blocked, having severe endometriosis, man with low sperm counts, artificial or intrauterine insemination failed, having continued unexplained infertility for a long time, couple wants to avoid the any inherited disorders before the conceiving, failed tubal ligation reversal surgery in women. There are five basic steps in the IVF and embryo transfer process which include the collection of ova, collection of sperms, monitoring as well as stimulating the development of healthy ovum ova in the ovaries, the fusion of nurtured ova and desired sperms in the laboratory by providing the appropriate environment for fertilization & early embryo growth and finally followed by transferring the embryos into the uterus which are sequentially given below:

Step 1 of IVF: To control the ova maturation fertility medications are prescribed and to increase the chance of the collecting multiple ova during menstrual cycle referred to as ovulation induction. Multiple ova are the desired



because some of ova will not develop or the fertilize after retrieval and ovum development is monitored by the using ultrasound as well as the urine or blood test samples are examined to check the hormone levels.

Step 2 of IVF: The retrieving of ova do the follicular aspiration are retrieved through the minor surgical procedure by using the ultrasound imaging to the guide a hollow needle through the pelvic cavity which removes the ova from the ovaries.

Step 3: By ejaculation sperm is usually obtain is prepared for getting the fusion with the ova.

Step 4 of IVF: The sperm and the ova are placed into the incubators by insemination which is located in the laboratory which is enabled to fertilization, the lower probability of the fertilization was found in some cases, intracytoplasmic sperm injection (ICSI) may be done. The ova are the monitored to confirm the fertilization and cell division are taking place and it was considered as embryos after successful fertilization.

Step 5 of IVF: Into the woman's uterus the embryos are usually transferred from one to six days later, but in the most cases the transfer occurs between the two to three days following egg retrieval. At this stage, the fertilized egg has developed into the two-to-four cell embryo. The transfer process involves the speculum which is inserted into the vagina to expose the cervix. A predetermined number of embryos are suspended in fluid and gently placed through a catheter into the womb. These steps are followed sequentially under regular monitoring followed by all required blood tests and potential ultrasounds to determine by the successful implantation as well as finally desired occurrence of pregnancy.

ROLE OF GONADOTROPIN-RELEASING HORMONE (GnRH) IN IN-VITRO FERTILIZATION (IVF)

Ovarian hyperstimulation is the stimulation to induce development of multiple follicles of the ovaries which starts with response prediction of age, antral follicle count and level of antimalaria hormone. This resulting prediction of the poor or the hyper-response to the ovarian hyperstimulation determines the protocol and dosage for the ovarian hyperstimulation

Ovarian hyperstimulation also includes suppression of spontaneous ovulation by using gonadotropin releasing hormone (GnRH) agonist the protocol to know the day when the hyperstimulation treatment is started and the expected day of later oocyte retrieval can be chosen to the confirm adapted personal choice to the spontaneous onset of the previous menstruation.

Gonadotropin-releasing hormone (GnRH) mediated natural and mild In-vitro fertilization cycles (IVF)

Gonadotropin-releasing hormone (GnRH) mediated natural and mild cycle of the IVF there are the two methods. Natural IVF cycle is performed using no medication for the ovarian hyperstimulation, while drugs

for the ovulation suppression may still be used with gonadotropin releasing hormone (GnRH) antagonist protocol so that the cycle initiates from natural mechanisms. Mild IVF cycle is done with the help of small dose of ovarian stimulating drugs for a short duration during menstrual aimed to be produce 2–7 ova and resulting in the production of healthy embryos. Basically, this quality is advanced method appears to reduce life-threatening complications and also side-effects for the women and can be cheaper than conventional IVF method with significantly reduced risk of multiple gestation and ovarian hyperstimulation syndrome (OHSS).

Human chorionic gonadotropin (HCG) triggered ova maturation and retrieval in In-vitro fertilization (IVF)

When the ovarian follicles have reached a certain degree of development lead to induction of final oocyte maturation by injecting human chorionic gonadotropin (HCG) coined as "trigger shot." human chorionic gonadotropin (HCG) acts as an analogue of luteinising hormone and ovulation would occur between 38 and 40 hours after a single human chorionic gonadotropin (HCG) injection. But usually, the ovum retrieval is performed between 34 to 36 hours after human chorionic gonadotropin (HCG) injection just prior to rupturing of follicles. Human chorionic gonadotropin (HCG) injection confers a risk of ovarian hyperstimulation syndrome. Using a gonadotropin releasing hormone (GnRH) agonist instead of human chorionic gonadotropin (HCG) eliminates the risk of ovarian hyperstimulation syndrome (OHSS), but with a delivery rate of approximately 6% less than with human chorionic gonadotropin (HCG). The ova are retrieved from the patient using a transvaginal technique called transvaginal oocyte retrieval by involving an ultrasound-guided needle piercing the vaginal wall to reach the ovaries. Through this needle follicles can be aspirated and the follicular fluid is passed to an embryologist to identify ova which is common to remove ova in the range of 10 to 30.

Ova and sperm preparation in In-vitro fertilization (IVF)

The identified ova are stripped of surrounding environment and prepared for fertilization in the laboratory. An oocyte selection may be performed prior to fertilization to select ova with optimal chances of successful pregnancy. In the meantime, semen is prepared for fertilization by removing inactive cells from seminal fluid, called sperm washing. If semen is being provided by a sperm donor, it will usually have been prepared for treatment before being frozen, quarantined and thawed to make it ready for use.

Co-incubation of sperm and ovum in In-vitro fertilization (IVF)

In the ratio of approximately 75,000:1 the sperm and the egg are incubated together in a culture media in order for the actual fertilization to take place. In most cases, ova will be fertilized during co-incubation and will show two pronuclei. In certain situations, such as low sperm count or



motility, a single sperm may be injected directly into the ova using intracytoplasmic sperm injection (ICSI). The fertilized ova is transferred into a special growth medium and left untouched for 48 hours until the ovum consists of six to eight cells.

Embryo culture for In-vitro fertilization (IVF)

After ovum retrieval Embryos are cultured at 6 to 8 cell stages. In many Canadian, American and Australian programmes and meeting on IVF: In-vitro fertilization, it was discussed that embryos are placed into an extended culture system with a transfer done at the blastocyst stage at around five days after retrieval, especially if many good-quality embryos are still available on day third.

Embryo selection for In-vitro fertilization (IVF)

With high quality grading methods to interpret oocyte and embryo quality advanced laboratories have developed. The morphological scoring system is the best strategy for the selection of embryos to optimize pregnancy rate. Since 2009, the first time-lapse microscopy system for IVF was approved for clinical practice and morpho kinetic scoring systems has implemented to improve pregnancy rates further.

Embryo transfer for In-vitro fertilization (IVF)

Embryos are failed by the embryologist based on the number of cells in most of the times, evenness of growth and degree of fragmentation. The number of embryos to be transferred depends on how much number of them are available which actually, depends on the age of the woman and other related health and diagnostic factors. The embryos which are judged to be the "best" are transferred to the patient's uterus through a thin plastic catheter which goes through her vagina and cervix. Several embryos may be passed into the uterus to improve chances of implantation and pregnancy too.

Adjunctive medication in In-vitro fertilization (IVF)

Luteal support is the administration of medication of progesterone, progestins or gonadotropin releasing hormone (GnRH) agonists to increase the success rate of implantation and early embryogenesis to complementing and supporting the function of the corpus luteum. The live birth rate is significantly higher with progesterone for luteal support in IVF cycles with or without intracytoplasmic sperm injection (ICSI). The outcome of its co-treatment with gonadotropin releasing hormone (GnRH) agonists further improves by 16% live birth rate with 95% confidence interval. On the other hand, growth hormone or aspirin as adjunctive medication in IVF have not showed fairly good evidence of its overall benefit ¹.

TEST TUBE BABY

In 1978 The term "test tube baby" was first used with the successful birth of Louise Joy Brown in England, thanks to the development of the Assisted Reproduction Technique (ART) known as In-Vitro Fertilisation (IVF) by pioneering scientist Sir Robert Edwards and gynaecologist Dr. Patrick

Stephens. Soon after in 1983, Samuel Lee of Singapore became Asia's first test tube baby, through efforts of Prof. S.S. Ratnam and Prof. Ng Soon Chye – Sincere IVF Center's Medical Director – and his team.

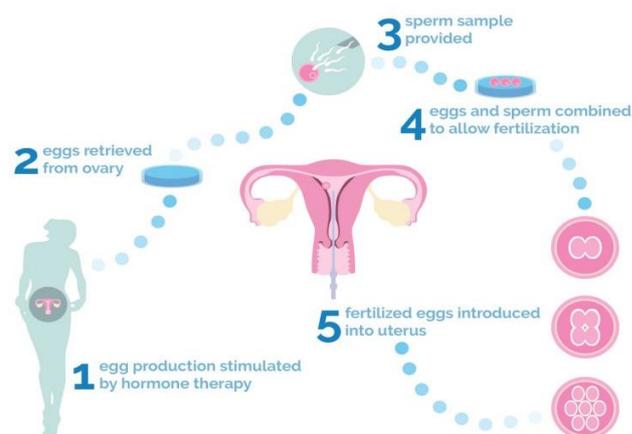
However, despite its continued popular use, the term "test tube baby" continues to cause confusion among couples seeking medical intervention for their fertility problems. Some even believe that the conception of test tube babies involves a different ART procedure from IVF or that it is a kind of Intrauterine Insemination (IUI) technique.

What Is a Test Tube Baby?

The term "test tube baby" means the child that is conceived outside a woman's body. A more complete definition specifies test tube babies as being conceived in a laboratory through the scientific process of In-Vitro Fertilisation (IVF). The use of the words "test tube" is also erroneous because, right from the beginning decades back with Edwards and Stephens, the lab instrument that they used to mix the eggs and sperm in is a Petri dish. It can be stated therefore that "test tube baby" is an oversimplified term for a child born through IVF. Hence, there is actually NO difference between IVF and test tube baby.

Test Tube Baby Step-by-Step Process

Ever since that successful attempt in 1978, numerous advancements have been made to IVF but the core procedure remains the same



Step 1: Egg production stimulated by hormone therapy

The woman is prescribed injectable hormones by GnRH and gonadotrophins prior to egg retrieval to promote the synchronous growth and maturation of the follicles inside her ovaries. Final maturation of the eggs is accomplished through the injection of HCG 36 hours before egg collection.

Step 2: Eggs retrieved from ovary

The mild sedative or anaesthetic is given to the women so that she won't feel pain or other discomforts during the egg retrieval. Using an ultrasound vaginal probe with the fine hollow needle attached to it, the fertility specialist

aspirates eggs from the woman's ovaries. These samples are promptly brought to the laboratory.

Step 3: Sperm Sample Provided

At the same day as the egg retrieval, the man is required to produce a fresh semen sample.

Step 4: Eggs and sperm combined to allow fertilisation

In a Petri dish the sperm and eggs are allowed to mixed together and then place inside an incubator for a few days. During this period, the fertility specialist checks for signs of fertilisation and monitors the growth of the embryos.

Step 5: Fertilized eggs introduced into the uterus

Two or three embryos are transferred on the day of embryo transfer into the uterus of the woman with the use of a fine catheter. To strengthen and support the uterine lining and increase the possibility of implantation she is advised to administer progesterone or HCG daily.

A common question that is asked is how painful are IVF injections?

Minimal pain and discomfort with the hormone injections most women experience, describing them as being similar to the insulin injections for diabetes. Other women claim that the more painful shots are those of progesterone because it is the oil-based and requires the use of a needle with a larger bore ².

COMPLICATIONS OF IN-VITRO FERTILIZATION (IVF) PROCEDURE

The multiple births are major complication of IVF is the risk which is directly related to the practise transferring of multiple embryos. Sometimes, multiple births are related to increased risk of pregnancy loss, obstetrical complications, prematurity, and neonatal morbidity with the potential for long term damage. Sometimes, there is risk of transferring of chronic disease such as hepatitis B to female patients and their expecting offspring by sperm during their incubation which can be brought to negligible levels as per "The Practice Committee of the American Society for Reproductive Medicine' advises that sperm washing is not necessary in IVF to prevent transmission, unless the female partner has not been effectively vaccinated. A risk of ovarian stimulation was observed as ovarian hyperstimulation syndrome (OHSS), particularly if human chorionic gonadotropin (HCG) is used for inducing final oocyte maturation which results in occurrence of swollen, painful ovaries in 30% of patients. During ovum retrieval, there is small chance of bleeding, infection, and damage during transvaginal ultrasound aspiration especially in bowel and bladder as well as difficulty in breathing, chest infection, allergic reactions to meds, or nerve damage was observed in some cases too during laparoscopy. IVF: In-vitro fertilization does not seem to be associated with an elevated risk of cervical cancer, breast cancer nor with ovarian cancer or endometrial cancer when neutralizing the confounder of infertility itself. Nor does it seem to impart any increased risk for breast cancer.

Ectopic pregnancy may also occur if fertilized ova develop outside the uterus, usually in the fallopian tubes which increases the chance of immediate destruction of the foetus. Sometimes, negative pregnancy test after IVF is associated with an increased risk for depression in women which may be leads to be increased risk of developing anxiety disorders in some cases too but it happens rarely. Pregnancy test results do not seem to be a risk factor for depression or anxiety among men. In 2008, an analysis of the data of the National Birth Defects Study in the US was noticed that certain birth defects were significantly more common in infants conceived through IVF like septal heart defects, cleft lip with or without cleft palate, oesophageal atresia, and anorectal atresia whose mechanism of causality is still unclear with any solid evidence.

SUCCESS RATES IN IN-VITRO FERTILIZATION (IVF) IVF

Success rates are the percentage of all used IVF procedures which result in a favourable outcome depends on resulted outcome is finalized by which type of calculation used to represent the number of confirmed pregnancies called the successful pregnancy rate with number of live births called the live birth rate. Due to advancement in reproductive technology, the IVF success rates are substantially better today than they were just a few years ago (Table 1 and 2).

Table 1: The most current data available in the United States a 2009 summary was compiled by the," American Society for Reproductive Medicine" which reported the average national IVF success rates per age group using non-donor ova³.

Age of Patient	<35	35-37	38-40	41-42
Pregnancy Rate %	47.6	38.9	30.1	20.5
Live Birth Rate %	41.4	31.7	22.3	12.6

Table 2: The live birth rates using donor ova are also given by the," Society for Assisted Reproductive Technology' is given below including all age groups of patients using either fresh or thawed eggs.

Sr. No.	Fresh donor egg embryos	Thawed donor egg embryos
Live birth rate	55.1	33.8

In 2006, an average pregnancy rate of 35% Canadian clinics was reported. A French study was concluded that 66% of patients starting IVF treatment finally succeed in having a child with 40% during the IVF treatment at the centre and 26% even after IVF discontinuation due to spontaneous pregnancy only.

Success or failure factors influencing In-vitro fertilization (IVF)

Maternal age the main potential factors that influence successful pregnancy rates with live birth rates in IVF have been suggested, duration of infertility or sub-fertility, basal follicle stimulating hormonal level and number of oocytes which all are exactly reflecting ovarian function. Optimal



woman age was observed between 23–39 years at time of treatment in which pregnancy complications and more chance of infertility rate were found due to the influence of all these factors. While psychological stress was experienced during a cycle might not influence an IVF outcome, it is possible that the experience of IVF can be resulted in stress that leads to depression. The financial consequences alone of IVF can be a major issue to influence anxiety and become overwhelming too in some patients. However, for many couples, the alternative is infertility, and the experience of infertility itself can also cause extreme stress and depression as well.

BIOMARKERS MAJORLY AFFECT IN-VITRO FERTILIZATION (IVF)

Factor that affect the pregnancy chances in IVF are higher level of antral follicle count is biomarkers , anti-Müllerian hormone levels , measuring good semen quality of sperm donor by using DNA fragmentation methods e.g. by Comet assay, advanced maternal age and semen quality which increase the successful pregnancy rates while women with ovary-specific FMR1 genotypes including het-norm/low have significantly decreased pregnancy chances in IVF and progesterone elevation (PE) on the day of induction of final maturation is associated with lower pregnancy rates in IVF cycles in women undergoing ovarian stimulation using gonadotropin releasing hormone (GnRH) analogues and gonadotrophins.

OTHER FACTORS THAT INFLUENCE IN-VITRO FERTILIZATION (IVF)

Drinking, caffeine and smoking decreases the chances of successful IVF mediated live birth by 34% and increases the risk of pregnancy miscarriage by 30%. A body mass index (BMI) over 27 causes a 33% decrease rate to have live birth and pregnant women who are obese have higher rates of miscarriage, gestational diabetes, hypertension, thromboembolism during delivery, as well as leading to an increased risk of fetal congenital abnormality. Salpingectomy or laparoscopic tubal occlusion before IVF treatment increases chances for women to develop hydro salpinges after IVF. The number and quality of embryos transferred in the IVF treatment cycle as well as autoimmune disease may also play a role in decreasing IVF success rates by interfering with proper implantation of the embryo in uterus after transfer too.

FUTURE OF IN-VITRO FERTILIZATION (IVF)

Aim to achieve higher and better success rates should be achieved by transferring single selected embryo with 80% success rate despite of transferring multiple embryos to get higher chances of successful IVF which in some cases leads to multiple birth. It was followed by to do blastocyst culture embryo testing non-invasiveness, in-vitro maturation instead of transferring the blastula from the petri-dishes, to increase use of cryopreservation of the ovarian oocyte for later use to avoid wastage as an unethical practice too and use of embryonic stem cells for haplodization of cells to create gametes. These are all only

achieved by making protocols easier and simpler with minimizing the monitoring time to be used which in turn, it would be possible to make the IVF method an effective clinical practice to reach the couples of economy class of developing and underdeveloped countries too.

Test Tube Babies: Pros and Cons

The pros and cons of test tube babies are also the same as the advantages and disadvantages of the IVF.

The main advantage of IVF is that it can circumvent a number of fertility problems including...

- Unexplained infertility
- Blocked fallopian tubes
- Male factor infertility (commonly done together with Intracytoplasmic Sperm Injection or ICSI)
- Older patients who desire to have a child
- Low ovarian reserve
- Polycystic Ovary Syndrome (PCOS)
- Endometriosis
- Premature Ovarian Failure

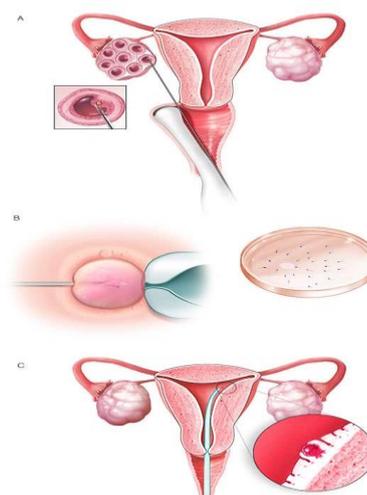
An IVF procedure is not without risks and just like with most painstaking medical procedures, it can cause emotional and mental stress on couples. In terms of costs, Singaporeans could avail of government co-funding and Medisave resources to finance the procedure.

Who Should Consider IVF Treatment?

Any couple who has been unsuccessful for a year in their attempts to have a child should consider the possibility of undergoing fertility treatments. It is very important that they consult with a fertility specialist in order for the cause of their infertility to be correctly diagnosed so that the right treatment will be given.

Here at Sincere IVF Center, our mission is to provide you with the relevant knowledge, leading edge technologies and the latest medical advancements in fertility treatment to maximise your chances of pregnancy ¹.

Overview



In vitro fertilization

In vitro fertilization (IVF) is a complex series of procedures which is used to help with fertility or prevent genetic problems and assist with the conception of a child.

Mature eggs are collected (retrieved) from ovaries and fertilized by sperm in a lab during IVF. Then the fertilized egg (embryo) or eggs (embryos) are transferred to a uterus. One full cycle of IVF takes about three weeks. Sometimes these steps are split into different parts and the process can take longer.

The most effective form of assisted reproductive technology is IVF. The procedure can be done using a couple's own eggs and sperm. Or IVF may involve eggs, sperm or embryos from a known or anonymous donor. In some cases, a gestational carrier someone who has an embryo implanted in the uterus might be used.

Depends on many factors your chances of having a healthy baby using IVF, such as your age and the cause of infertility. In addition, IVF can be time-consuming, expensive and invasive. If more than one embryo is transferred to the uterus, IVF can result in a pregnancy with more than one fetes (multiple pregnancy).

Your doctor will help you understand how IVF works, the potential risks and whether this method of treating infertility is right for you.

Why it's done?

For infertility or genetic problems In vitro fertilization (IVF) is a treatment. If IVF is performed to treat infertility, you and your partner might be able to try less-invasive treatment options before attempting IVF, including fertility drugs to increase production of eggs or intrauterine insemination a procedure in which sperm are placed directly in the uterus near the time of ovulation.

Sometimes, in women over age 40 IVF is offered as a primary treatment for infertility. IVF can also be done if you have certain health conditions. For example, IVF may be an option if you or your partner has:

- **Fallopian tube damage or blockage.** Fallopian tube damage or blockage 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.
- **Endometriosis.** Endometriosis occurs when tissue similar to the lining of the uterus 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 uterus. They are common in women in their 30s and 40s. Fibroids can interfere with implantation of the fertilized egg.
- **Previous tubal sterilization or removal.** Tubal ligation is a type of sterilization in which the fallopian tubes are cut or blocked to permanently prevent pregnancy.

If you wish to conceive after tubal ligation, IVF may be an alternative to tubal ligation reversal surgery.

- **Impaired sperm production or function.** Below-average sperm concentration, weak movement of sperm (poor mobility), or abnormalities in sperm size and shape can make it difficult for sperm to fertilize an egg. If semen abnormalities are found, a visit to an infertility specialist might be needed to see if there are correctable problems or underlying health concerns.
- **Unexplained infertility.** Unexplained infertility means no cause of infertility has been found despite evaluation for common causes.
- **A genetic disorder.** If you or your partner is at risk of passing on a genetic disorder to your child, you may be candidates for preimplantation genetic testing — a procedure that involves IVF. After the eggs are harvested and fertilized, they're screened for certain genetic problems, although not all genetic problems can be found. Embryos that don't contain identified problems can be transferred to the uterus.
- **Fertility preservation for cancer or other health conditions.** If you're about to start cancer treatment such as radiation or chemotherapy that could also harm your fertility, IVF for fertility preservation may be an option. Women can have eggs harvested from their ovaries and frozen in an 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). In this case, the woman's eggs are fertilized with sperm, but the resulting embryos are placed in the gestational carrier's uterus.

Risks

Risks of IVF include:

- **Multiple births.** IVF increases the risk of multiple births if more than one embryo is transferred to your uterus. A pregnancy with multiple fetuses carries a higher risk of early labour and low birth weight than pregnancy with a single fetus does.
- **Premature delivery and low birth weight.** Research suggests that IVF slightly increases the risk that the baby will be born early or with a low birth weight.
- **Ovarian hyperstimulation syndrome.** Use of injectable fertility drugs, such as human chorionic gonadotropin (HCG), to induce ovulation can cause ovarian hyperstimulation syndrome, in which your ovaries become swollen and painful.
- Symptoms typically last a week and include mild abdominal pain, bloating, nausea, vomiting and diarrhoea. If you become pregnant, however, your



symptoms might last several weeks. Rarely, it's possible to develop a more severe form of ovarian hyperstimulation syndrome that can also cause rapid weight gain and shortness of breath.

- **Miscarriage.** The rate of miscarriage for women who conceive using IVF with fresh embryos is similar to that of women who conceive naturally — about 15% to 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 a blood vessel. Risks are also associated with sedation and general anaesthesia, if used.
- **Ectopic pregnancy.** About 2% to 5% of women who use IVF will have an ectopic pregnancy — when the fertilized egg implants outside the uterus, usually in a 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, no matter how the child is conceived. More research is needed to determine whether babies conceived using IVF might be at increased risk of certain birth defects.
- **Cancer.** Although some early studies suggested there may be a link between certain medications used to stimulate egg growth and the development of a specific type of ovarian tumour, more-recent studies do not support these findings. There does not appear to be a significantly increased risk of breast, endometrial, cervical or ovarian cancer after IVF.
- **Stress.** Use of IVF can be financially, physically and emotionally draining. Support from counsellors, family and friends can help you and your partner through the ups and downs of infertility treatment.

How you prepare?

The Centers for Disease Control and Prevention and the Society for Assisted Reproductive Technology provide information online about U.S. clinics' individual pregnancy and live birth rates.

A clinic's success rate depends on many factors. These include patients' ages and medical issues, as well as the clinic's treatment population and treatment approaches. Ask for detailed information about the costs associated with each step of the procedure.

Before beginning a cycle of IVF using your own eggs and sperm, you and your partner will likely need various screenings, including:

- **Ovarian reserve testing.** To determine the quantity and quality of your eggs, your doctor might test the concentration of follicle-stimulating hormone (FSH), oestradiol (estragon) and anti-Mullerian hormone in

your blood during the first few days of your menstrual cycle. Test results, often used together with an ultrasound of your ovaries, can help predict how your ovaries will respond to fertility medication.

- **Semen analysis.** If not done as part of your initial fertility evaluation, your doctor will conduct a semen analysis shortly before the start of an IVF treatment cycle.
- **Infectious disease screening.** You and your partner will both be screened for infectious diseases, including HIV.
- **Practice (mock) embryo transfer.** Your doctor might conduct a mock embryo transfer to determine the depth of your uterine cavity and the technique most likely to successfully place the embryos into your uterus.
- **Uterine exam.** Your doctor will examine the inside lining of the uterus before you start IVF. This might involve a sonohysterography — in which fluid is injected through the cervix into your uterus — and an ultrasound to create images of your uterine cavity. Or it might include a hysteroscopy — in which a thin, flexible, lighted telescope (hysteroscope) is inserted through your vagina and cervix into your uterus.

Before beginning a cycle of IVF, consider important questions, including:

- **How many embryos will be transferred?** The number of embryos transferred is typically based on age and number of eggs retrieved. Since the rate of implantation is lower for older women, more embryos are usually transferred — except for women using donor eggs or genetically tested embryos.
- Most doctors follow specific guidelines to prevent a higher order multiple pregnancy, such as triplets or more. In some countries, legislation limits the number of embryos that can be transferred. Make sure you and your doctor agree on the number of embryos that will be transferred before the transfer procedure.
- **What will you do with any extra embryos?** Extra embryos can be frozen and stored for future use for several years. Not all embryos will survive the freezing and thawing process, although most will.
- Having frozen embryos can make future cycles of IVF less expensive and less invasive. Or, you might be able to donate unused frozen embryos to another couple or a research facility. You might also choose to discard unused embryos.
- **How will you handle a multiple pregnancy?** If more than one embryo is transferred to your uterus, IVF can result in a multiple pregnancy — which poses health risks for you and your babies. In some cases, fetal reduction can be used to help a woman deliver fewer babies with lower health risks. Pursuing fetal



reduction, however, is a major decision with ethical, emotional and psychological consequences.

- **Have you considered the potential complications associated with using donor eggs, sperm or embryos, or a gestational carrier?** A trained counsellor with expertise in donor issues can help you understand the concerns, such as the legal rights of the donor. You may also need an attorney to file court papers to help you become legal parents of an implanted embryo.

What you can expect?

IVF involves several steps — ovarian stimulation, egg retrieval, sperm retrieval, fertilization and embryo transfer. One cycle of IVF can take about two to three weeks. More than one cycle may be needed.

Ovulation induction

The start of an IVF cycle begins by using synthetic hormones to stimulate the ovaries to produce multiple eggs — rather than the single egg that typically develops each month. Multiple eggs are needed because some eggs won't fertilize or develop normally after fertilization.

Several different medications may be used, such as:

- **Medications for ovarian stimulation.** To stimulate your ovaries, you might receive an injectable medication containing a follicle-stimulating hormone (FSH), a luteinizing hormone (LH) or a combination of both. These medications stimulate more than one egg to develop at a time.
- **Medications for oocyte maturation.** When the follicles are ready for egg retrieval — generally after eight to 14 days — you will take human chorionic gonadotropin (HCG) or other medications to help the eggs mature.
- **Medications to prevent premature ovulation.** These medications prevent your body from releasing the developing eggs too soon.
- **Medications to prepare the lining of your uterus.** On the day of egg retrieval or at the time of embryo transfer, your doctor might recommend that you begin taking progesterone supplements to make the lining of your uterus more receptive to implantation.

Your doctor will work with you to determine which medications to use and when to use them.

Typically, you'll need one to two weeks of ovarian stimulation before your eggs are ready for retrieval. To determine when the eggs are ready for collection, you may have:

- **Vaginal ultrasound,** an imaging exam of your ovaries to monitor the development of follicles — fluid-filled ovarian sacs where eggs mature
- **Blood tests,** to measure your response to ovarian stimulation medications — estrogen levels typically

increase as follicles develop, and progesterone levels remain low until after ovulation

Sometimes IVF cycles need to be cancelled before egg retrieval for one of these reasons:

- Inadequate number of follicles developing
- Premature ovulation
- Too many follicles developing, creating a risk of ovarian hyperstimulation syndrome
- Other medical issues

If your cycle is cancelled, your doctor might recommend changing medications or their doses to promote a better response during future IVF cycles. Or you may be advised that you need an egg donor.

Egg retrieval

Egg retrieval can be done in your doctor's office or a clinic 34 to 36 hours after the final injection and before ovulation.

- During egg retrieval, you'll be sedated and given pain medication.
- Transvaginal ultrasound aspiration is the usual retrieval method. An ultrasound probe is inserted into your vagina to identify follicles. Then a thin needle is inserted into an ultrasound guide to go through the vagina and into the follicles to retrieve the eggs.
- If your ovaries aren't accessible through transvaginal ultrasound, an abdominal ultrasound may be used to guide the needle.
- The eggs are removed from the follicles through a needle connected to a suction device. Multiple eggs can be removed in about 20 minutes.
- After egg retrieval, you may experience cramping and feelings of fullness or pressure.
- 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 to create embryos. However, not all eggs may be successfully fertilized.

Sperm retrieval

If you're using your partner's sperm, a semen sample needs to be provided at your doctor's office or clinic the morning of egg retrieval. Typically, the semen sample is collected through masturbation. Other methods, such as testicular aspiration — the use of a needle or surgical procedure to extract sperm directly from the testicle — are sometimes required. Donor sperm also can be used. Sperm are separated from the semen fluid in the lab.

Fertilization

Fertilization can be attempted using two common methods:

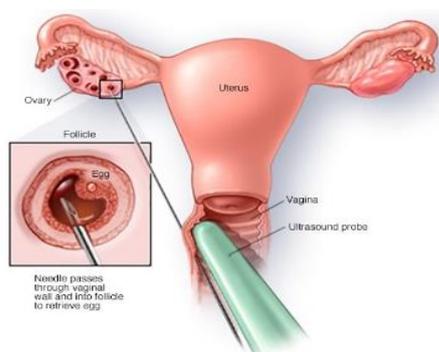


- **Conventional insemination.** During conventional insemination, healthy sperm and mature eggs are mixed and incubated overnight.
- **Intracytoplasmic sperm injection (ICSI).** In ICSI, a single healthy sperm is injected directly into each mature egg. ICSI is often used when semen quality or number is a problem or if fertilization attempts during prior IVF cycles failed.

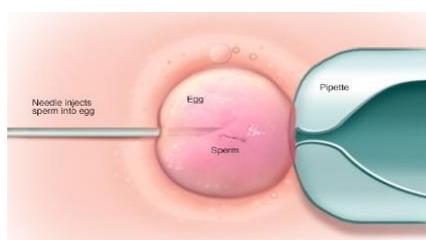
In certain situations, your doctor may recommend other procedures before embryo transfer.

- **Assisted hatching.** About five to six days after fertilization, an embryo "hatches" from its surrounding membrane (zona pellucida), allowing it to implant into the lining of the uterus. If you're an older woman, or if you have had multiple failed IVF attempts, your doctor might recommend assisted hatching — a technique in which a hole is made in the zona pellucida just before transfer to help the embryo hatch and implant. Assisted hatching is also useful for eggs or embryos that have been previously frozen as the process can harden the zona pellucida.
- **Preimplantation genetic testing.** Embryos are allowed to develop in the incubator until they reach a stage where a small sample can be removed and tested for specific genetic diseases or the correct number of chromosomes, typically after five to six days of development. Embryos that don't contain affected genes or chromosomes can be transferred to your uterus. While preimplantation genetic testing can reduce the likelihood that a parent will pass on a genetic problem, it can't eliminate the risk. Prenatal testing may still be recommended.

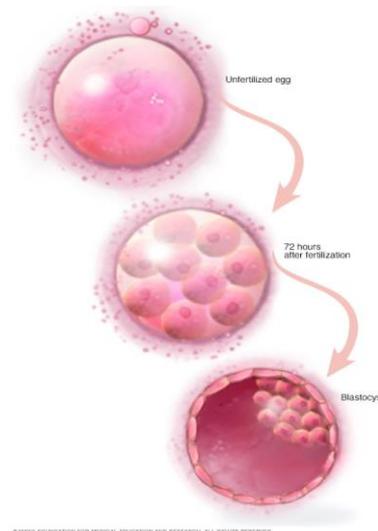
Embryo transfer



Egg-retrieval technique ³



Blastocyst ³



ICSI ³

Embryo transfer is done at your doctor's office or a clinic and usually takes place two to five days after egg retrieval.

- You might be given a mild sedative. The procedure is usually painless, although you might experience mild cramping.
- The doctor will insert a long, thin, flexible tube called a catheter into your vagina, through your cervix and into your 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 or embryos into your uterus.

If successful, an embryo will implant in the lining of your uterus about six to 10 days after egg retrieval.

After the procedure

After the embryo transfer, you can resume your usual daily activities. However, your ovaries may still be enlarged. Consider avoiding vigorous activity, which could cause discomfort.

Typical side effects include:

- Passing a small amount of clear or bloody fluid shortly after the procedure — due to the swabbing of the cervix before the embryo transfer
- Breast tenderness due to high oestrogen levels
- Mild bloating
- Mild cramping
- Constipation

If you develop moderate or severe pain after the embryo transfer, contact your doctor. He or she will evaluate you for complications such as infection, twisting of an ovary (ovarian torsion) and severe ovarian hyperstimulation syndrome.

RESULTS

About 12 days to two weeks after egg retrieval, your doctor will test a sample of your blood to detect whether you're pregnant.

- **If you're pregnant**, your doctor will refer you to an obstetrician or other pregnancy specialist for prenatal care.
- **If you're not pregnant**, you'll stop taking progesterone and likely get your period within a week. If you don't get your period or you have unusual bleeding, contact your doctor. If you're interested in attempting another cycle of in vitro fertilization (IVF), your doctor might suggest steps you can take to improve your chances of getting pregnant through IVF.

The chances of giving birth to a healthy baby after using IVF depend on various factors, including:

- **Maternal age.** The younger you are, the more likely you are to get pregnant and give birth to a healthy baby using your own eggs during IVF. Women age 41 and older are often counselled to consider using donor eggs during IVF to increase the chances of success.
- **Embryo status.** Transfer of embryos that are more developed is associated with higher pregnancy rates compared with less-developed embryos (day two or three). However, not all embryos survive the development process. Talk with your doctor or other care provider about your specific situation.
- **Reproductive history.** Women who've previously given birth are more likely to be able to get pregnant using IVF than are women who've never given birth. Success rates are lower for women who've previously used IVF multiple times but didn't get pregnant.
- **Cause of infertility.** Having a normal supply of eggs increases your chances of being able to get pregnant using IVF. Women who have severe endometriosis are less likely to be able to get pregnant using IVF than are women who have unexplained infertility.
- **Lifestyle factors.** Women who smoke typically have fewer eggs retrieved during IVF and may miscarry more often. Smoking can lower a woman's chance of success using IVF by 50%. Obesity can decrease your chances of getting pregnant and having a baby. Use of alcohol, recreational drugs, excessive caffeine and certain medications also can be harmful.

Talk with your doctor about any factors that apply to you and how they may affect your chances of a successful pregnancy ³.

What Are the Costs of IVF?

The average cost of an IVF cycle in the U.S. costs \$12,000 to \$17,000, according to the National Conference of State Legislatures. This price will vary depending on where you live, the number of medications you're required to take, the number of IVF cycles you undergo, and the amount your insurance company will pay toward the procedure. You should thoroughly investigate your insurance company's coverage of IVF and ask for a written statement of your benefits. Although some states have enacted laws requiring insurance companies to cover at least some of the costs of infertility treatment, many states haven't.

Also be aware that some carriers will pay for infertility drugs and monitoring, but not for the cost of IVF or other artificial reproductive technology. Resolve: The National Infertility Association publishes a booklet called the "Infertility Insurance Advisor," which provides tips on reviewing your insurance benefits contract ⁴.

How long do sperm live?

The answer depends on a number of things, but the most important is where the sperm are located.

On a dry surface, such as clothing or bedding, sperm are dead by the time the semen has dried. In water, such as a warm bath or hot tub, they'll likely live longer because they thrive in warm, wet places. But the odds that sperm in a tub of water will find their way inside a woman's body and cause them to get pregnant are extremely low.

When sperm are inside women's body, they can live for up to 5 days. If you're a man and you have sex even a few days before your partner ovulates, there's chance they may get pregnant.

How many sperm do you need to get pregnant?

It takes just one sperm to fertilize a woman's egg. Keep in mind, though, for each sperm that reaches the egg, there are millions that don't.

On average, each time men ejaculate they release nearly 100 million sperm. Why are so many sperm released if it takes only one to make a baby? To meet the waiting egg, semen must travel from the vagina to the fallopian tubes, a tough journey that few sperm survive. Experts believe this process may be nature's way of allowing only the healthiest sperm to fertilize the egg, to provide the best chances of having a healthy baby.

For those sperm that complete the trip, getting into the egg, which is covered by a thick layer, is far from a sure thing ⁵.

CONCLUSION

In 25 July, 1978, Louise Brown was born in Royal Oldham Hospital, England and won the distinction of being the world's first "test tube baby" because she was conceived by thankful to miraculous clinical innovative, "IVF: In-vitro fertilization techniques' developed by British biologists. Dr. Patrick Steptoe, a gynecologist at Oldham General



Hospital, and Dr. Robert Edwards, a physiologist at Cambridge University, had been actively worked very hard for that distinction to introduce the term, "IVF: In-vitro fertilization" to the world with successful live birth of healthy baby girl. Since then, IVF has more than grown up with its increased demand in modern and urban era by adopting additional techniques, day by day, in IVF methods include ovarian hyperstimulation to retrieve multiple ova, ultrasound-guided transvaginal oocyte retrieval directly from the ovaries followed by preparation of ovum and sperm preparation for their culture as well as selection of resultant embryos before embryo transfer back into the uterus. About 10% of married couples suffer from infertility or inability to conceive a child naturally. Through the better part of the 20th century, physicians considered this a minor irrelevant problem, one that contributed overall to society by keeping the birth rate down. Use of such advanced techniques, also called assisted reproductive technology for infertility treatments has more than doubled in the last decade and accounts for 1% of all infants born in the United States each year according to the Centres for Disease Control and Prevention, Due to improved technology, the procedure has a higher success

rate than it did a decade ago and doctors now report fewer multiple births. A key reason for fewer triplets, quads and quint is that doctors began voluntarily limiting the number of embryos they implant in infertile women.

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