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A REVIEW ON MALE AND FEMALE INFERTILITY- CAUSES, TREATMENT AND FUTURE PROSPECTIVES

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ABSTRACT
The term 'medicalization' to denote the process by which certain behaviour comes to be understood as a question of health and illness, subject to the authority of medical institutions. One phenomenon that has become increasingly defined as a medical condition is infertility, usually defined in the biomedical context as the inability to conceive after 12 months of regular unprotected intercourse. The social construction of health and illness is perhaps even more striking in the case of infertility than it is for other conditions. Infertility may occur due to male, female or unexplained factors. Some causes of infertility are preventable. Treatment of infertility often involves in-vitro fertilization (IVF) and other types of medically assisted reproduction. Fertility care encompasses the prevention, diagnosis and treatment of infertility. Equal and equitable access to fertility care remains a challenge in most countries; particularly in low and middle-income contries. Fertility care is rarely prioritized in national universal health coverage benefit packages.

KEYWORDS: Infertility, Reproduction, Embryo.

INTRODUCTION
"Infertility" a small word but may abolish the forth coming generation. Approximately one in five couples has trouble conceiving a child. If a couple is unable to conceive after one year of unprotected intercourse, they are said to be subfertility. Around 40% of fertility problems originate in the women with causes including failure to ovulate and abnormalities of the fallopian tubes on uterus. In most cases the couple can be helped with assisted reproductive technologies. For around one in 10 couples investigated for infertility, no cause is found. This is known as idiopathic infertility. Many people may be infertile during their reproductive years. This may be unaware of this because they are not seeking to create a pregnancy. On any one occasion, the chance of pregnancy is just one percent (Wade et. al. 2012).

Most infertility results from physical problems in a man or woman's reproductive system. About 35% of all cases of infertility arise from problems in the man's system. About 35% arise from abnormalities in the women's system. About 20% of the time, the man and woman both have fertility problems. In 10% of cases, no cause can be found. Age often increases the risk of infertility (Mathew and Tobler 2022).

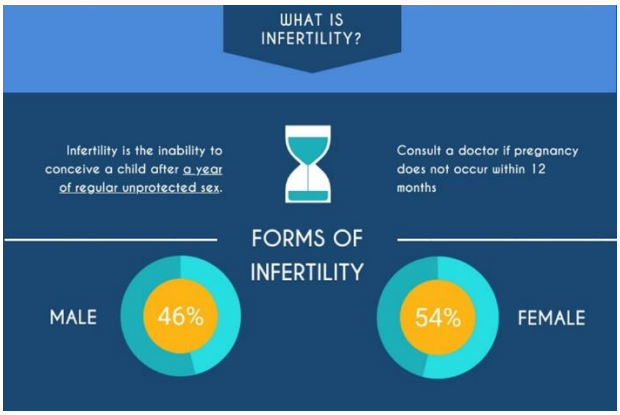

Figure 1: Forms of Infertility.

Infertility can be caused by poor sexual and life style habits that are easily remedied. Other easily treated illnesses or life style habits that may contribute to infertility are; (Nemours TeensHealth, 2023)

- Heavy use of alcohol, tobacco or drugs
- Starvation diets or anorexia in the woman.
- Tight underwear or pants in the man, which raises the crotch temperature and reduces sperm count.
- Stress. In a woman, this may cause her irregular menstruation. In a man, stress may reduce his sperm count.

Most of the problems can be resolved with medical treatment or lifestyle changes such as wearing boxer shorts, avoiding a sexual lubricant or tying some simple stress reduction methods such as physical exercise or relaxation techniques. Changing the timing of sex and the couple's sexual techniques may also increase the chance of pregnancy. Sometimes the semen from the man fails to reach the woman's cervix (Richard H. Harrison (2022).

REPRODUCTION IN WOMAN: (Kathryn (2018)
Some important hormones stimulate the reproductive system of a woman,

- Luteinizing hormone
- Follicle stimulating hormone
- Estrogen
- Progesterone

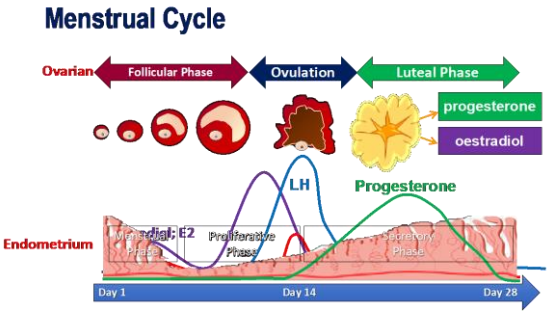

Figure 2: Menstrual cycle.

How the hormones work?
The hypothalamus, a region in the rain, first releases a hormone called gonadotropin- releasing hormone (GnRH). GnRH causes the pituitary gland to produce two more hormones- luteinizing hormone and follicle stimulating hormone. These hormones in turn to ovaries to release estrogen and progesterone.

How hormone regulate a woman's fertility

- Over a two weeks period in a woman's monthly cycle, FSH causes several follicles in the ovaries to ripen and mature.
- FSH also orders the ovaries to produce estrogen, which in turn launches the manufacturer of large amounts of LH hormone.
- LH stimulates the release of an egg from the largest follicle into the fallopian tubes – a process called ovulation.
- LH also stimulates the follicle to produce corpeus luteum- a collection of yellow tissue that produce progesterone.
- Progesterone and estrogen work together to thicken and prepare the lining of the uterus for a fertilized egg.
- Together, these hormones swell the lining of the uterus with blood, making it easier for a fertilized egg to implant itself there.

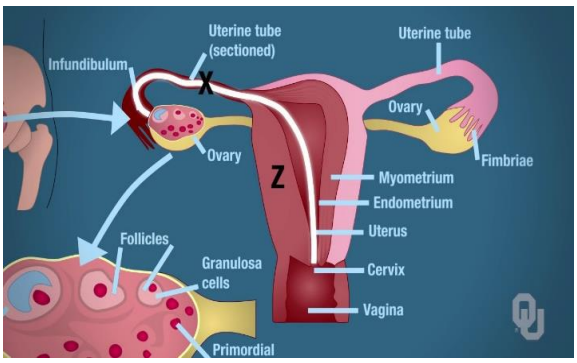

Figure 3: Female reproductive system.

How the egg is fertilized
An egg is usually fertilized by sperm within the fallopian tubes- but only if the woman has sex with a man around the time the egg is released. The sperm must penetrate the egg to fertilize it.

Sperm can survive for six days after entering a woman's vagina and can fertilize the egg at any time during this period. However, research shows that fertilization is most likely to occur two days before or on the day the egg is released. The fertilized egg then moves on the uterus where it implants and grows into an embryo and pregnancy results.

If the egg is not penetrated by sperm, it lives for 12-24 hours. The egg and the body lining of the uterus then slough off, travelling out of the uterus, the cervix and vagina- a process is called as woman's menstrual period. **(**Kathryn (2018)

REPRODUCTION IN MAN
Men have primary hormones involved in reproduction. They are follicle stimulating hormone, Luteinizing hormone and testosterone.

- In a man, the brain's hypothalamus first releases GnRh and it stimulates the pituitary gland to produce follicle stimulating hormone and luteinizing hormone.
- These hormones regulate the production of sperm and release the male hormones testosterone, all of which takes place in the male testes, located on the scrotal sac.

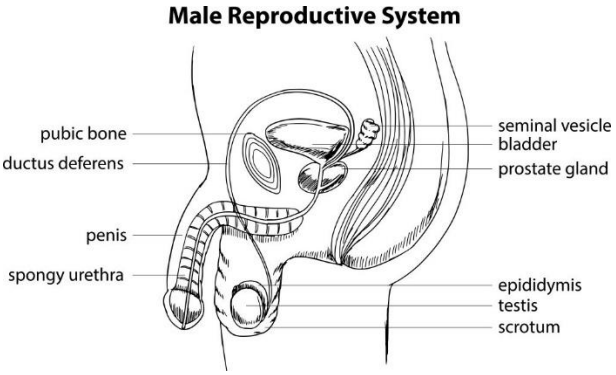

Figure 4: Male reproductive system.

Production of sperm

Sperm begin life in the testes in cells called Sertoli cells.

- At the beginning of a sperm's life cycle, hormones develop its head and tail.
- The sperm then escapes from the Sertoli cell into the epididymis, located behind the testes.
- For three weeks, a sperm travels through the epididymis in an energizing fluid containing fructose. As the sperm swims through this fluid, it matures and acquires the ability to swim and move back and forth.
- A mature sperm has a head that contains man's DNA- his genetic material and a tail that rapidly moves from side to side propelling it forward.

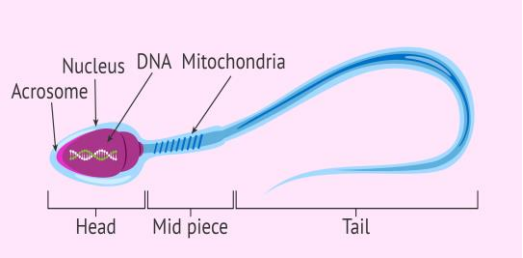

Figure 5: Structure of sperm cell.

How the sperm fertilizes egg

Of the 100 to 300 million sperm released when a man ejaculates, only about 40 survive the trip through the acidic environment of the vagina and cervix. The woman's thick cervical mucous can also be a barrier. But during ovulation, the woman's mucous thins and allows the sperm to travel more freely. After it bores through the mucous, the sperm trigger the acrosome (a special membrane located on their heads) and it dissolves and releases special enzymes. These enzymes allow the sperm to penetrate the tough coating surrounding the egg in the fallopian tubes. Only one sperm ultimately fertilizes the egg. **(**Kathryn (2018)

CAUSES FOR INFERTILITY

Infertility in a woman may stem from many causes such as hormonal deficiencies, problems in the reproductive organs and such illness. Complications from surgery and certain medications may also impair infertility. (Narjes Deyhoul, Tina Mohamaddoost and Meimanat Hosseini 2017).

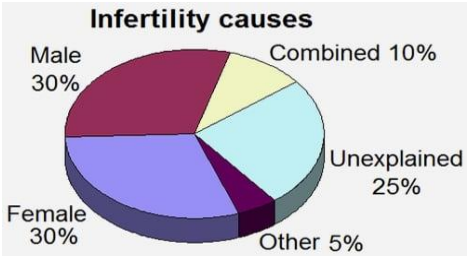

Figure 6: Statistics of infertility.

PELVIC INFLAMMATORY DISEASES (PID) – It is the most common cause of infertility in worldwide. It's an infection of the pelvis or one or more of the reproductive organs including the ovaries, fallopian tubes, cervix and uterus. Sometimes PID spreads to the appendix or to the entire pelvic area.

PID usually stems from the same bacteria that cause sexually transmitted diseases such as gonorrhoea and chlamydia. It causes 75% of fallopian tube infections. PID may also develop from bacteria that reach the reproductive organs through abortion, hysterectomy, childbirth, sexual intercourse, use of an intrauterine contraceptive devices or a ruptured appendix.

POLYCYSTIC OVARIAN SYNDROME (PCOS)- This condition affects 5 million women and is another major cause of infertility. In PCOS, the ovaries produce high amounts of male hormones especially testosterone. LH levels also remain abnormally high while FSH levels are abnormally low; thus, the follicles do not produce eggs, instead they from fluid filled cysts that eventually cover the ovaries.

PCOS not only causes infertility but also increases the risk of diabetes, cancer and even heart diseases. The symptoms are excessive facial hair, thinning hair, acne, depression, unexplained weight gain, irregular or no periods, high insulin or cholesterol readings.

OTHERS- Surgical Complications: Scar tissue left after abdominal surgery can cause problems in the movement of the ovaries, fallopian tubes and uterus resulting in infertility. Frequent abortions may also produce infertility by weakening the cervix or by leaving scar tissuethat obstructs the uterus.

Uterine muscle problems: Some women may produce weak infrequent or abnormal contractions in the uterus. During ovulation, these contractions usually push the sperm up to the fallopian tubes.

Illness: Certain diseases such as diabetes, kidney diseases or high blood pressure may cause infertility. Ectopic pregnancy and some urinary tract infections may also elevate the risk of infertility.

Medications: Many medicines such as hormones, antibiotics, anti-depressants and pain killers may bring on temporary infertility. Commonly used medications

such as aspirin and ibuprofen can also impair fertility if taken mid cycle. Acetaminophen pills can reduce the amount of estrogen and luteinizing hormones in the body, impairing fertility. (Nemours TeensHealth, 2023)

Why does a man become infertile?
The most common cause for male infertility is a problem with a sperm- either low sperm count or sperm with poor quality. It cannot move rapidly enough or in the right direction or may be abnormally shaped. (Narjes Deyhoul, Tina Mohamaddoost and Meimanat Hosseini 2017)

UNDER DEVELOPED TESTES: Usually after a mumps infection, a hernia surgery, an injury or both defects.

INFECTIONS: Such as gonorrhoea or tuberculosis that block the ducts through which the sperm travel.

MEDICATIONS: Such as Cimitidine, Phenytoin, Methotrexate, Sulfasalazine, Cortocosteroids and Chemotherapy such as Cyclosphosphamide and exposure of some metals such as lead and pesticides.

OTHERS: Autoimmunity, retrograde ejaculation, diseases such as diabetes and multiple sclerosis, chronic prostate infections, neck, bladder and prostate surgery. Genetic defects such as germ cell aplasia and defect in Y chromosome. (Nemours TeensHealth, 2023)

TREATMENT
In woman
After the Physician has determined possible causes of the infertility, a course of treatment can plan. Sometimes simple instructions like knowing when having sex is most likely to produce a pregnancy, are all that is needed. In many cases medications are indicated while in other cases the woman may require surgery or other forms of treatment.

Drug Treatment
Clomiphene: This drug triggers the release of FSH and LH, boosting egg growth and helping the ovaries release a monthly egg. The drug is considered is safe, fairly inexpensive. Women who have PCOS or menstruate irregularly apparently benefit most from this drug. 60% of women successfully ovulate and about 30% of women become pregnant in the first three months of being on the drug. Side effects include nausea, insomnia, breast tenderness and headache.

Bromocriptine: The drug suppresses a hormone called prolactin, which if released in excessive amounts may cause a woman to stop ovulating. 90% of women on bromocriptine release egg while on the drug, considered fairly safe. Side effects include nausea, dizziness, headache and low blood pressure.

Human Menopausal Gonadotropins (HMG): This drug is comprised of hormones extracted from the urine of post-menopausal woman and contains large amounts of LH or FSH. Women have trouble ovulating, endometriosis, infertility caused by cervival problems or unexplained infertility is good drug of choice.

Luteinizing hormone releasing hormones (LH-RH): The drugs are used when the pituitary or hypothalamus gland is not producing hormones. They are also used to treat endometriosis. Most women administer these drugs themselves with a portable pump and the equipment is unwieldy and expensive. Risks include an increased chance of infections, clotting and multiple births.

Human Chorionic Gonadotropin (HCG): Chorionic gonadotropins are often prescribed with HMGs and sometimes with clomiphene, to stimulate the release of the egg. They may also use to endometriosis. Possible side effects include ovarian enlargement, ovarian cysts and multiple births.

Urofollitropin (FSH): The drug is made up of FSH taken from the urine of postmenopausal woman. It can be used with HCG to bring the release of an egg. It is an effective drug for PCOS.

Others: Antibiotics- They may cure infections in the reproductive system such as in cervix or lining of uterus and some sexually transmitted disease. Progesterone- It develops the lining of the uterus and helps a fertilized egg implant. Corticosteroids- These may be prescribed for the treatment of endometriosis. (Richard H. Harrison 2022).

Assisted Reproduction
Assisted reproduction refers to a number of advanced techniques that aid fertilization. These techniques are often used for women who have irreversible damage to their fallopian tubes or cervical mucous problems.

IVF (In-vitro fertilization)
It is one of the most well-known assisted reproduction techniques. In this method, the woman takes fertility drugs to stimulate her ovaries to produce more eggs. The Physician then retrieves one or more of the eggs by laparoscopy by passing a needle through the vaginal wall. The partner sperm is then mixed with is then mixed with the eggs in a petri dish and fertilization may takes place.

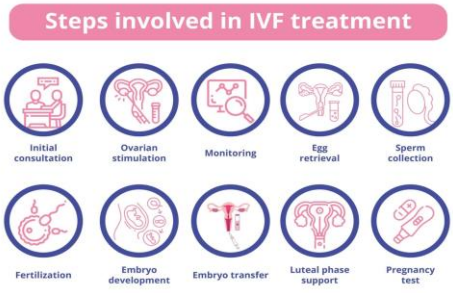

Figure 7: IVF Treatment.

In fertilization occurs, the embryo is allowed to develop outside the womb for a few days. Then it is implanted in the lining of the woman's uterus with a small plastic tube. Most centres now place two to four embryos in the womb in the hope that one will burrow into the lining and begin to develop normally. The effectiveness of IVF has only 20-40% (Jeff Wang and Mark V Sauer 2022).

GIFT (Gamete Intrafallopian tube transfer)
In this method of assisted reproduction, the woman's eggs are retrieved but not fertilized. Instead, they are mixed with the man's sperm and immediately placed into the woman's fallopian tubes. The woman must have healthy tubes for GIFT to work. (Sandra Ann Carson and Amanda N Kallan 2021).

Figure 8: Gamete intrafallopian tube transfer.

ZIFT (Zygote intrafallopian transfer)
It involves placing the fertilized egg itself into the fallopian tubes. This procedure can be more successful than GIFT because the Physician has a greater chance of ensuring that the egg is fertilized. Again, the woman must have healthy tubes for ZIFT. (Sandra Ann Carson and Amanda N Kallan 2021).

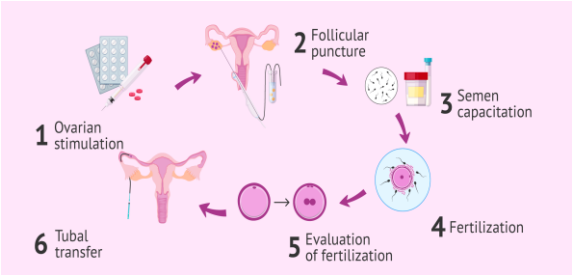

Figure 9: Zygote intrafallopian transfer.

ICSI (Intracytoplasmic sperm insertion)
In this technique, a single sperm is injected into the egg and the embryo is placed in the fallopian tube or uterus. This method is often recommended when the male partner has very few sperm or other fertilization methods are not suitable for the couple. (Sandra Ann Carson and Amanda N Kallan 2021).

Figure 10: Intracytoplasmic sperm injection.

FASIAR (Follicle aspiration, sperm injection and assisted follicular rupture)
It is one of the new methods, the Physician punctures the follicle and then remove the eggs with the syringe that also holds the sperm. This mixture is then injected back into the follicle. FASIAR may reduce the risk of multiple births than other procedures. (Jeff Wang and Mark V Sauer 2022).

IUI (Intrauterine insemination)
It is a process of introducing sperm into the uterus. The sperm are washed meaning that the sperm are separated from the semen and drawn up into an injectable device. Access to the uterus is gained via the cervix, whereby the sperm are injected directly into the uterine cavity. The sperm are then more able and more likely to their way to the fallopian tube hopefully finding an egg to fertilize. (Jo Johnson (2012).

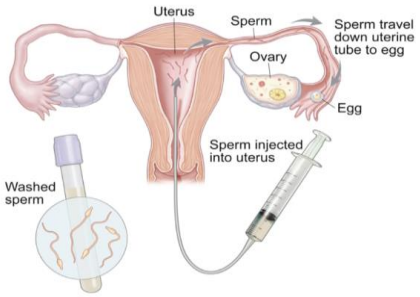

Figure 11: Intrauterine inseminations.

Potential health risks
Some of the problems associated with the use of assisted reproductive technologies include,

- Ovarian hyperstimulation syndrome
- Associated with multiple pregnancies
- Increased risk of premature labour and low birth weight
- Increased risk of caesarean delivery

In man
Drug treatment
Hormones: Though hormones can be quite successful in women, they are only occasionally effective in men. Hormone drugs include testosterone, menotropins,

GnRH medications, bromocriptine, clomiphene and human chorionic gonadotropin (HCG).

Antibiotics: These may help treat sexually transmitted diseases and other infections.

Corticosteroids: These drugs can aid men who make antibodies to reject their own sperm but they may also have serious side effects after long use.

Sildenafil (Viagra): It is a newly developed medicine for male impotence. The man takes sildenafil an hour before having sex. The medication improves blood flow to the penis resulting in an erection. (Jo Johnson 2012)

Donor insemination

Donor insemination, couples can use an external source for sperm to artificially inseminate a woman's natural ova. Couples need to understand the ramifications of obtaining donor sperm to get pregnant and how this is likely to affect their child. The ethical, legal, medical and personal aspects of this decision need to be addressed. Donor insemination carries a success rate of approximately 70-80%. (Sangeet Khanna 2012).

Figure 12: Donor sperm insemination.

Herbal Treatment

There are so many herbal supplements available on the market which claims to help fertility. The more common ones include Dong Quai, Chaste tree berries, Black Cohosh and Primrose. (Karen Bergeron Shelton 1997).

DONG QUAI

It comes from ancient Chinese herbal medicine and said to help induce ovulation because of its oestrogen-like properties. This supplement helps bind oestrogen receptors The herbal may be used in conditions which cause infertility due to oestrogen imbalance such as PCOD. It is important to discontinue the herbal supplement once pregnancy is achieved.

CHASTE TREE BERRIES

It is also known as Vitex Angus aids fertility by exerting its effect on the menstrual cycle. It works by acting on endocrine glands such as pituitary gland. This gland is responsible for the secretion of luteinizing hormone which plays a key role in inducing ovulation. This supplement also helps regulate prolactin levels which can also cause of infertility. The berries useful when used in conjugation with fertility drugs such as gonadotropins.

BLACK COHOSH

It may also be helpful when used in conjugation with gonadotropic fertility treatments since it helps reduce common side effects of such medications. This supplement is a week oestrogen which can help reduce hot flushes and other menopausal symptoms. It may help in alteration in hormonal imbalance especially oestrogen can lead to such mood changes.

PRIMPROSE

It is a type of oil which has various health benefits such as lowering cholesterol. This herbal supplement facilitates fertilization by making the cervical mucus more hospitable for sperm motility. Primrose oil works by activating prostaglandins which lead to the characteristic cervical changes.

Figure 13: Herbals such as Dong quai, Chaste tree, Black cohosh and Primrose.

Table 1: Herbal formulations used in infertility.

S.No	Treatment	Medication
1.	Internal medicines (Mohsen Akbaribazm, Nader Goodarzi, Mohsen Rahimi. 2021)	Kalingathy Thylam – 8-16 ml with 10ml of rice cold water at early morning Agathiyar Kuzhambu – 130 mg with 5gm of tender leave paste of Arasu and milk (50 ml) at early morning. Sithaathi ennai - 5 ml at early morning. Asoka Pattai Kudineer - 60 ml twice a day Kumatty Kuzhambu - 8 gm at early morning with palm jaggery (5g) Karpa sanjeevi ennai - 10 gm at early morning with luke warm water (50 ml)

		Karpakiranthi ennai - 16 ml at early morning with luke warm water (50 ml) Venpoosani Nei - 10 – 15 ml at early morning Thaneervittan Nei - 10 – 15 ml at early morning Nilakadambu chooranam - 2 g twice a day with hot water (50 ml) Amukkara chooranam - 1 – 2 g twice a day with milk (50 ml) Kumari Ilagam - 5 – 10 g twice a day Idivallathy Ilagam - 3 g twice a day Gandhaga Rasayanam - 1.3 – 2 g twice a day Maadhulai manappagu - 10 – 15 ml twice a day with hot water (50ml) Nandi mezhugu - 100 – 500 mg twice a day with palm jaggery (5 g) Rasagandhi mezhugu - 300 mg twice a day with palm jaggery (5 g) Vaan mezhugu - 50 –100 mg twice a day with palm jaggery (5 g) Vedi annabedhi chendooram-100 mg twice a day with hot water (50 ml) Arumuga chendooram - 65 –130 mg twice a day with honey (5 ml) Sangu parpam - 100 – 300 mg twice a day with water (50 ml)
2.	External medicines (Mohsen Akbaribazm, Nader Goodarzi, Mohsen Rahimi. 2021)	Oil bath may be advised twice a week with any of the following medicated oils Keezhanelli thylam Asai thylam Karisalai thylam

MEDICAL ADVANCEMENT IN THE TREATMENT OF INFERTULITY

Controlled Ovarian Hyperstimulation

Controlled ovarian hyperstimulation (COH) is performed to increase the number of oocytes available for IVF. COH involves multiple injections of gonadotropins and serial visits to the fertility clinic for the conduct of transvaginal ultrasound evaluations and the measurement of circulating hormone levels. Recent advancements in portable lower cost ultrasound devices may further simplify follicular and endometrial monitoring by way of convenient mobile facilities and potentially even self-operated endo-vaginal telemonitoring. Combined, these approaches may greatly simplify COH by rendering it less invasive and by decreasing the time commitment required. (Sandra Ann Carson and Amanda N Kallan 2021).

Ovary transplants

Yes, ovary transplants are now possible but the whole issue of whether they are good idea was highlighted in the autumn of 2008 when a 38-year-old woman become the first ovary transplant recipient to give birth to baby. It is true that it could become possible for a woman to have one ovary removed and frozen to be transplanted later but there are much more serious reasons why this would be necessary. Many women go through the menopause early- the woman who gave birth 2009 and had suffered premature menopause at the age of 15. She had been completely infertile. Her twin who already had two children donated her sister one of her ovaries and the delicate operation was a success. She conceived the child she had longed for 20 years, just a year later. (Kathryn (2018).

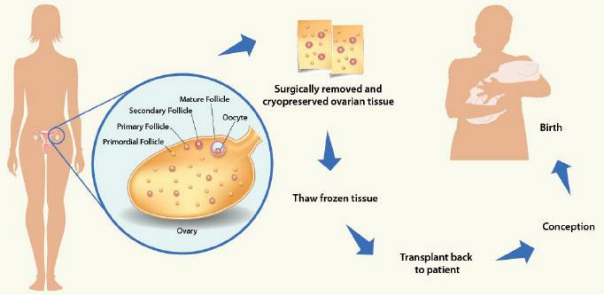

Figure 14: Ovarian transplants.

The technique is still very much in its early days but could become more routine in the future as it would help so many women. The vascular surgery needs to be done by a very experienced surgeon, as the vessels that need to be reconnected are, in some cases only a fraction of a millimetre in diameter. It is also possible to transplant strips of ovarian tissue and several women who have received this type of transplant have become pregnant successfully.

Embryo freezing

Embryo freezing or cryopreservation is one of the latest developments in the field of fertility research. This process although not common in modern society, offers mothers options for postponing pregnancy. Embryos form when a sperm penetrates the egg. With fertility treatment, this is usually done by invitro fertilisation. It is a fertility procedure where the egg is fertilized outside its natural environment. Although this technology may seem as if it came from a popular science fiction novel, it has been around since the early 1980s. In fact, the first successful cryopreserved embryo birth occurred in 1984. Despite its long existence, this technology has resulted in only a small number of live births. Limitations include

cost, ethical and moral controversy and risk of side effects (Sangeet Khanna (2010).

Figure 15: Embryo freezing.

Pre-implantation genetic screening using Aneuploidy

It is a screening test for detecting chromosomal abnormalities in the developing embryo. This special procedure helps the fertility doctor select only those embryos which exhibit no chromosomal abnormalities and transfer them to the uterus for implantation. Aneuploidy is an abnormal condition where there are variations in chromosome number. These changes can lead to the development of genetic diseases or defects which are often permanent and cannot be reversed. When undergoing fertility treatments and procedures it is highly recommended to screen for such chromosomal abnormalities so that the health and the future well being of the developing embryo. It is offered to patients who are undergoing in-vitro fertilisation and other assisted reproductive techniques. (Sangeet Khanna 2013).

CONCLUSION

Ovulation induction using gonadotropins and intrauterine inseminations has a high rate of success in most cases. However, more than one cycle of treatment is often necessary before pregnancy occurs and some women will not become pregnant despite multiple attempts. It can be difficult to deal with the emotional highs and lows of infertility treatment. This is especially true if the women have been trying to conceive for a long time and if there are any underlying problems in the couple's life. Support groups and counselling services are available at many infertilities treatment centre. The cost of infertility treatments can be high depending upon what tests are required, the type and dose of medications used and the number of cycles required to become pregnant. The average cost of FSH injection alone is between 800-1200 US Dollars. Insurance policies cover the costs of infertility treatment in some states. Less than half of the states within the US have laws requiring insurers to cover infertility treatment.

General instructions for couple are

1. Reduction of weight in overweight or obese persons.
2. Avoidance of Alcohol and heavy smoking.
3. Avoidance of tight and warm under garments.
4. Avoidance of too frequent intercourse.
5. Counselling for psychosocial evaluation.
6. Discuss- Psychology and coital problem.
7. Advice to intercourse during the time of LH surge (detected by LH test kit, one can LH surge in urine by getting a deep blue colour of dipstick. The test should be performed daily between days 12 to 16 of a regular cycle).

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