Basics of Infertility

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Dedication

To my great mother.

Acknowledgement:

To all medical researchers who are working to promote the life of man, through the gate of knowledge.

Introduction

Infertility definitions

Clinical definitions:

- Infertility is "a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse."… (WHO-ICMART glossary1).
- "Infertility is the inability of a sexually active, non-contracepting couple to achieve pregnancy in one year. The male partner can be evaluated for infertility or subfertility using a variety of clinical interventions, and also from a laboratory evaluation of semen."

Demographic definitions of infertility:

- An inability of those of reproductive age (15-49 years) to become or remain pregnant within five years of exposure to pregnancy.
- An inability to become pregnant with a live birth, within five years of exposure based upon a consistent union status, lack of contraceptive use, non-lactating and maintaining a desire for a child.

Epidemiological definition of infertility:

(For monitoring and surveillance) Women of reproductive age (15–49 years) at risk of becoming pregnant (not pregnant, sexually active, not using contraception and not lactating) who report trying unsuccessfully for a pregnancy for two years or more.

Infertility as a disability

Disability: Infertility generates disability (an impairment of function), and thus access to health care falls under the Convention on the Rights of Persons with Disability. An estimated 34 million women, predominantly from developing countries, have infertility which resulted from maternal sepsis and unsafe abortion (long term maternal morbidity resulting in a disability). Infertility in women was ranked the 5th highest serious global disability (among populations under the age of 60).

Primary infertility:

When a woman is unable to ever bear a child, either due to the inability to become pregnant or the inability to carry a pregnancy to a live birth she would be classified as having primary infertility. Thus women whose pregnancy spontaneously miscarries, or

whose pregnancy results in a still born child, without ever having had a live birth would present with primarily infertility.

Secondary infertility

When a woman is unable to bear a child, either due to the inability to become pregnant or the inability to carry a pregnancy to a live birth following either a previous pregnancy or a previous ability to carry a pregnancy to a live birth, she would be classified as having secondary infertility. Thus those who repeatedly spontaneously miscarry or whose pregnancy results in a stillbirth, or following a previous pregnancy or a previous ability to do so, are then not unable to carry a pregnancy to a live birth would present with secondarily infertile.

Male infertility

Up to 15 percent of couples are infertile. This means they aren't able to conceive a child even though they've had frequent, unprotected sexual intercourse for a year or longer. In up to half of these couples, male infertility plays a role.

Male infertility is due to low sperm production, abnormal sperm function or blockages that prevent the delivery of sperm. Illnesses, injuries, chronic health problems, lifestyle choices and other factors can play a role in causing male infertility.

Not being able to conceive a child can be stressful and frustrating, but a number of male infertility treatments are available.

Symptoms:

The main sign of male infertility is the inability to conceive a child. There may be no other obvious signs or symptoms. In some cases, however, an underlying problem such as an inherited disorder, hormonal imbalance, dilated veins around the testicle, or a condition that blocks the passage of sperm causes signs and symptoms.

Although most men with male infertility do not notice symptoms other than inability to conceive a child, signs and symptoms associated with male infertility include:

•Problems with sexual function — for example, difficulty with ejaculation or small volumes of fluid ejaculated, reduced sexual desire or difficulty maintaining an erection (erectile dysfunction)

•Pain, swelling or a lump in the testicle area

•Recurrent respiratory infections

•Inability to smell

•Abnormal breast growth (gynecomastia)

•Decreased facial or body hair or other signs of a chromosomal or hormonal abnormality

•Having a lower than normal sperm count (fewer than 15 million sperm per milliliter of semen or a total sperm count of less than 39 million per ejaculate.

Causes:

You must produce healthy sperm. Initially, this involves the growth and formation of the male reproductive organs during puberty. At least one of your testicles must be functioning correctly, and your body must produce testosterone and other hormones to trigger and maintain sperm production.

•Sperm have to be carried into the semen. Once sperm are produced in the testicles, delicate tubes transport them until they mix with semen and are ejaculated out of the penis.

•There needs to be enough sperm in the semen. If the number of sperm in your semen (sperm count) is low, it decreases the odds that one of your sperm will fertilize your partner's egg. A low sperm count is fewer than 15 million sperm per milliliter of semen or fewer than 39 million per ejaculate.
•Sperm must be functional and able to move. If the movement (motility) or function of your sperm is abnormal, the sperm may not be able to reach or penetrate your partner's egg.

Medical causes:
Problems with male fertility can be caused by a number of health issues and medical treatments. Some of these include:
•**Varicocele**:
A varicocele is a swelling of the veins that drain the testicle. It's the most common reversible cause of male infertility. Although the exact reason that varicoceles cause infertility is unknown, it may be related to abnormal testicular temperature regulation. Varicoceles result in reduced quality of the sperm.
Treating the varicocele can improve sperm numbers and function, and may potentially improve outcomes when using assisted reproductive techniques such as in vitro fertilization.
•**Infection**:
Some infections can interfere with sperm production or sperm health or can cause scarring that blocks the passage of sperm. These include inflammation of the epididymis (epididymitis) or testicles (orchitis) and some sexually transmitted infections, including gonorrhea or HIV. Although some infections can result in permanent testicular damage, most often sperm can still be retrieved.
•**Ejaculation issues**:
Retrograde ejaculation occurs when semen enters the bladder during orgasm instead of emerging out the tip of the penis. Various health conditions can cause retrograde ejaculation, including diabetes, spinal injuries, medications, and surgery of the bladder, prostate or urethra.
Some men with spinal cord injuries or certain diseases can't ejaculate semen, even though they still produce sperm. Often in these cases sperm can still be retrieved for use in assisted reproductive techniques.
•**Antibodies that attack sperm:**
Anti-sperm antibodies are immune system cells that mistakenly identify sperm as harmful invaders and attempt to eliminate them.
•**Tumors:**
Cancers and nonmalignant tumors can affect the male reproductive organs directly, through the glands that release hormones related to reproduction, such as the pituitary gland, or through unknown causes. In some cases, surgery, radiation or chemotherapy to treat tumors can affect male fertility.
•**Undescended testicles:**

In some males, during fetal development one or both testicles fail to descend from the abdomen into the sac that normally contains the testicles (scrotum). Decreased fertility is more likely in men who have had this condition.

•Hormone imbalances:

Infertility can result from disorders of the testicles themselves or an abnormality affecting other hormonal systems including the hypothalamus, pituitary, thyroid and adrenal glands. Low testosterone (male hypogonadism) and other hormonal problems have a number of possible underlying causes.

•Defects of tubules that transport sperm:

Many different tubes carry sperm. They can be blocked due to various causes, including inadvertent injury from surgery, prior infections, trauma or abnormal development, such as with cystic fibrosis or similar inherited conditions.

Blockage can occur at any level, including within the testicle, in the tubes that drain the testicle, in the epididymis, in the vas deferens, near the ejaculatory ducts or in the urethra.

•Chromosome defects:

Inherited disorders such as Klinefelter's syndrome — in which a male is born with two X chromosomes and one Y chromosome (instead of one X and one Y) — cause abnormal development of the male reproductive organs. Other genetic syndromes associated with infertility include cystic fibrosis, Kallmann's syndrome and Kartagener's syndrome.

•Problems with sexual intercourse:

These can include trouble keeping or maintaining an erection sufficient for sex (erectile dysfunction), premature ejaculation, painful intercourse, anatomical abnormalities such as having a urethral opening beneath the penis (hypospadias), or psychological or relationship problems that interfere with sex.

•Celiac disease:

A digestive disorder caused by sensitivity to gluten, celiac disease can cause male infertility. Fertility may improve after adopting a gluten-free diet.

•Certain medications:

Testosterone replacement therapy, long-term anabolic steroid use, cancer medications (chemotherapy), certain antifungal medications, some ulcer drugs and certain other medications can impair sperm production and decrease male fertility.

•Prior surgeries:

Certain surgeries may prevent you from having sperm in your ejaculate, including vasectomy, inguinal hernia repairs, scrotal or testicular surgeries, prostate surgeries, and large abdominal surgeries performed for testicular and rectal cancers, among others. In most cases, surgery can be performed to either reverse these blockage or to retrieve sperm directly from the epididymis and testicles.

<u>Environmental causes:</u>

Overexposure to certain environmental elements such as heat, toxins and chemicals can reduce sperm production or sperm function. Specific causes include:

•Industrial chemicals:

Extended exposure to benzenes, toluene, xylene, pesticides, herbicides, organic solvents, painting materials and lead may contribute to low sperm counts.

•Heavy metal exposure:

Exposure to lead or other heavy metals also may cause infertility.

•Radiation or X-rays:

Exposure to radiation can reduce sperm production, though it will often eventually return to normal. With high doses of radiation, sperm production can be permanently reduced.

•Overheating the testicles:

Elevated temperatures impair sperm production and function. Although studies are limited and are inconclusive, frequent use of saunas or hot tubs may temporarily impair your sperm count.

Sitting for long periods, wearing tight clothing or working on a laptop computer for long stretches of time also may increase the temperature in your scrotum and may slightly reduce sperm production.

Health, lifestyle and other causes:

Some other causes of male infertility include:

•Illicit drug use:

Anabolic steroids taken to stimulate muscle strength and growth can cause the testicles to shrink and sperm production to decrease. Use of cocaine or marijuana may temporarily reduce the number and quality of your sperm as well.

•Alcohol use:

Drinking alcohol can lower testosterone levels, cause erectile dysfunction and decrease sperm production. Liver disease caused by excessive drinking also may lead to fertility problems.

•Tobacco smoking:

Men who smoke may have a lower sperm count than do those who don't smoke. Secondhand smoke also may affect male fertility.

•Emotional stress:

Stress can interfere with certain hormones needed to produce sperm. Severe or prolonged emotional stress, including problems with fertility, can affect your sperm count.

•Weight:

Obesity can impair fertility in several ways, including directly impacting sperm themselves as well as by causing hormone changes that reduce male fertility.

Certain occupations including welding or those involving prolonged sitting, such as truck driving, may be associated with a risk of infertility.

Risk factors:

Risk factors linked to male infertility include:

•Smoking tobacco
•Using alcohol
•Using certain illicit drugs
•Being overweight

•Having certain past or present infections
•Being exposed to toxins
•Overheating the testicles
•Having experienced trauma to the testicles
•Having a prior vasectomy or major abdominal or pelvic surgery
•Having a history of undescended testicles
•Being born with a fertility disorder or having a blood relative with a fertility disorder
•Having certain medical conditions, including tumors and chronic illnesses, such as sickle cell disease.
•Taking certain medications or undergoing medical treatments, such as surgery or radiation used for treating cancer. [2]

Male Infertility Complications:

- Hydrocele formation is the most common complication reported after non-microsurgical varicocelectomy, with an average incidence of about 7% Hydroceles form secondary to ligation of the testicular lymphatics. At least half of all post-varicocelectomy hydroceles grow to a size that produces sufficient discomfort to warrant surgical hydrocelectomy. The effect of hydrocele function on spermatogenesis and fertility is unknown. Theoretically, large hydroceles may impair testicular function by insulating the testis and preventing normal thermoregulation. Use of the operating microscope has essentially eliminated the development of hydroceles following varicocelectomy.
  Testicular artery ligation is also a common complication of non-microsurgical varicocelectomy although its true incidence is unknown. Injury or ligation of the testicular artery may cause testicular atrophy, impaired spermatogenesis, or both. Animal studies indicate that testicular atrophy occurs anywhere from 20% to 100% of the time following testicular artery ligation. In humans, Penn, et al. reported a 14% incidence of frank testicular atrophy, when the testicular artery was purposefully ligated during renal transplantation. Optical magnification and/or the use of a fine tipped Doppler probe facilitate identification and preservation of the testicular artery.

  The incidence of varicocele recurrence following surgical repair varies from 1% to 45%. The incidence of recurrence depends upon the type of procedure performed and the use of magnification. Venographic studies have shown that recurrent varicoceles are caused by periarterial, parallel inguinal, midretroperitoneal, gubernacular and transcrotal collateral veins. The only approach equipped to deal with these vessels is the inguinal or subinguinal microscopic technique with delivery of the testis. Using the microsurgical technique at Cornell, we have reviewed our results of over 3000 men who underwent microsurgical varicocelectomy, the couples' pregnancy rate was 43 % after one year and 69% after 2 years compared to 17% in couples with men who declined surgery and had hormone treatment or used insemination. There have been only 25 recurrences (0.9%), 5 hydroceles (0.2%), no testicular atrophy, and a 1% incidence of inadvertent unilateral (one side only) testicular artery ligation. [3]
- Stress :

Infertility can result in extreme mental and psychological stress. It can result in family discord, low confidence and relationship difficulties

- Financial stress:
  Infertility can cause severe burden financially since, there may be requirement for assisted reproductive techniques including IVF (test tube baby) which is an expensive procedure.
- Surgery:
  Certain causes of male infertility may require surgery. [4]

Diagnosis of male infertility:

An initial male fertility examination includes a medical history, physical examination, general hormone tests and one or more semen analyses, which measure semen volume as well as sperm number, ability to move spontaneously and quality of motion.

Medical History

Initial questions may include:

•A review of past medical history, prior surgeries and medications used

•A discussion of family history of infertility or birth defects

•A careful review of social history and occupational hazards to evaluate potential exposure to hazardous substances that could impact fertility.

Physical Examination

Next, you will receive a thorough physical examination to evaluate the pelvic organs — the penis, testes, prostate and scrotum.

Laboratory Tests

Laboratory tests may include:

Laboratory tests may include:

•**Urinalysis** — these can indicate the presence of an infection.

•**Semen Evaluation** — the evaluation assesses sperm motility or movement, the shape and maturity of the sperm, the volume of the ejaculate, the actual sperm count and the liquidity of the ejaculate.

•**Hormonal Tests** — Hormonal tests evaluate levels of testosterone and FSH (follicle-stimulating hormone) to determine the overall balance of the hormonal system and specific state of sperm production. Serum LH and prolactin are other hormonal tests that may be done if initial testing indicates the need for them.

If a diagnosis is not obvious after the initial evaluation, further testing may be required. One or more of the following tests may be recommended:

•**Seminal Fructose Test** — to identify if fructose is being added properly to the semen by the seminal vesicles.

•**Post-ejaculate Urinalysis** — to determine if obstruction or retrograde ejaculation exists.

•**Semen Leukocyte Analysis** — to identify if there are white blood cells in the semen.

•**Kruger and World Health Organization (WHO) Morphology** — to examine sperm shape and features more closely.

•**Anti-sperm Antibodies Test** — to identify the presence of antibodies that may contribute to infertility.

•**Sperm Penetration Assay (SPA)** — to confirm the sperm's ability to fertilize.

•**Ultrasound** — to detect varicoceles (varicose veins) or duct obstructions in the prostate, scrotum, seminal vesicles and ejaculatory ducts.

•**Testicular Biopsy** — to determine if sperm production is impaired or a blockage exists.

•**Vasography** — to check the structure of the duct system and identify any obstructions.

•**Genetic Testing** — to rule out underlying mutations in one or more gene regions of the Y chromosome, or to test for cystic fibrosis in men missing the vas deferens.

After the diagnostic evaluation is completed, treatment may involve medical or endocrinologic treatment, surgical correction or a decision to manipulate or process sperm to achieve a pregnancy. (5)

Prevention:

Should there be an actual physical problem such as a congenital condition in which the vas deferens is missing, it is not possible to prevent infertility. However for infertility issues caused by sperm production problems due to addiction, infections and other reversible conditions, treatment will help cure male infertility.

Only lifestyle-related problems that cause male infertility can be prevented by taking better care of the body. The prevention of male fertility problems that are caused by lifestyle issues can be managed by living a healthier life. Below are some suggestions:

Avoid Being Overweight:

Excess weight has often been associated with sperm production problems. To prevent this from becoming an issue, maintain a healthy weight as per your body type.

Overcome Additions to Alcohol, Smoking and Drugs:

Addictions tend to disrupt the proper functioning of biological processes. Anything in excess can become an addiction and, therefore, one must monitor their intake.

Maintain an Optimum Testicular Temperature:

Wearing tight clothes can affect the circulation of blood in the genital region and raise the temperature of the testicles. Higher testicular temperature has been associated with infertility by affecting sperm production.

Avoid Mobile Phone and Laptop Radiation:

Electronic gadgets emit low levels of radiation which can affect sperm production. Ensure that you do not sit with the laptop directly on your lap for long periods of time. Also keep your mobile phone in your shirt pocket rather than in the pant pocket or hooked to your belt.

Eat Nutritious Food:

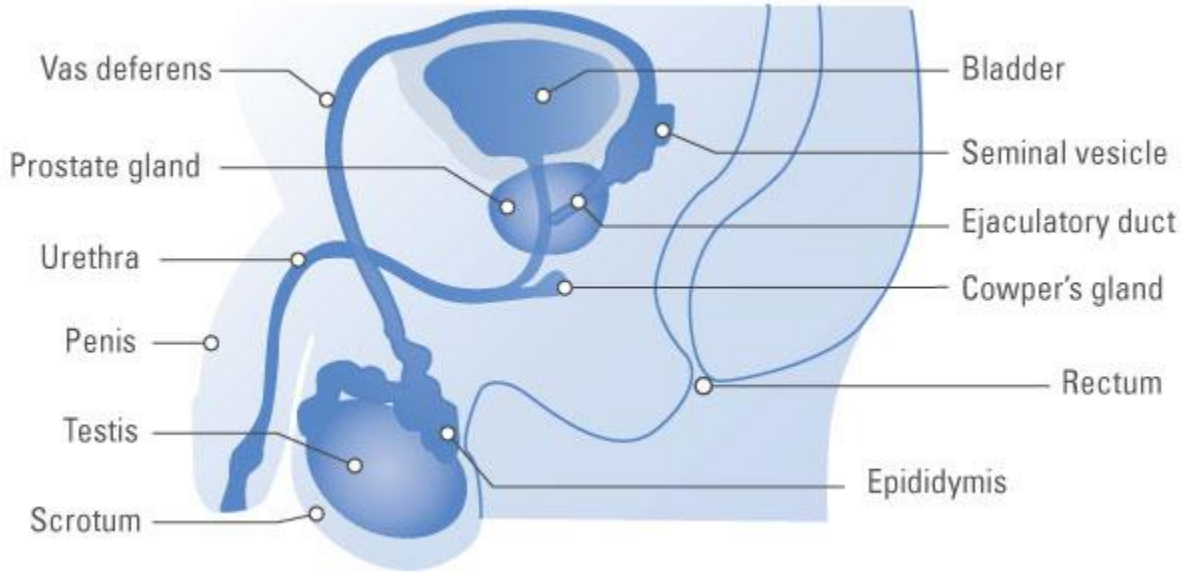
A lack of nutrients, zinc and vitamin C in particular, can cause problems in sperm production. Ensure that you eat a healthy and balanced diet and take supplements if the food is not supplying you with proper nutrition.

Exercise to Maintain High Immunity:

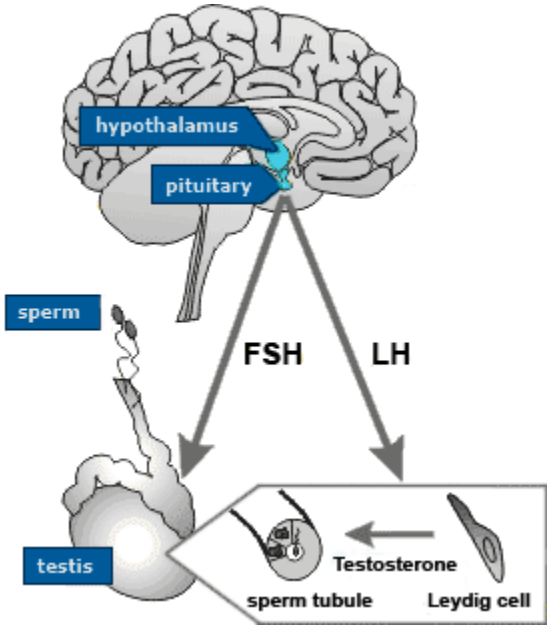
Infections and inflammations may completely stop the production of healthy sperm. Exercising regularly is a means by which you can ensure a healthy immune system. (6)

Male reproductive system

The male reproductive system is made up of the testes, a system of ducts (tubes) and other glands that open into the ducts. The brain plays an important part in the control of the male reproductive system.



The pituitary gland and the hypothalamus, located at the base of the brain, control the production of male hormones and sperm. Luteinizing hormone (LH) and follicle stimulating hormone (FSH) are the two important messenger hormones made by the pituitary gland that act on the testes.



The testes (testis: singular) are a pair of egg-shaped glands that sit in the scrotum next to the base of the penis on the outside of the body. The testes make sperm and the male sex hormone testosterone. It takes about 70 days for sperm to become mature and able to fertilize an egg.

When released from the testes, the sperm spend two to 10 days passing through the epididymis where they gain the vital ability to swim strongly (become 'motile'), and to attach to and penetrate (get into) the egg.

At orgasm, waves of muscle contractions transport the sperm, with a small amount of fluid, from the testes through to the vas deferens. The seminal vesicles and prostate contribute extra fluid to protect the sperm. This mixture of sperm and fluid (the semen) travels along the urethra to the tip of the penis where it is ejaculated (released). [7]

Treatment of male infertility

Other than the inability to conceive within a stated period of time or the inability to deliver a live-born infant, in most cases, infertility has no other outward symptoms.

The evaluation of a man's fertility includes looking for signs of hormone deficiency, such as increased body fat, decreased muscle mass, and decreased facial and body hair. The evaluation also includes questions about the man's health history, including past injury to the testicles or penis, recent high fevers, and childhood diseases such as mumps. Physical examination allows for the identification of problems such as infection, hernia, or varicocele. A health care provider may also ask a man to provide a semen sample to assess the health and quality of his sperm. Other tests may include measurement of hormones in the blood, a biopsy of the testicle, or genetic screening.

Treatments for male infertility may be based on the underlying cause of the problem, or in the case of no identified problem, evidence-based treatments that improve fertility may be recommended. Treatments include surgery to correct or repair anatomic abnormalities or damage to reproductive organs, use of medical procedures to deliver sperm to the woman, fertilization of the egg in a laboratory, and using a third party for donating sperm or eggs and/or carrying a pregnancy. Medication can treat some issues that affect male fertility, including hormone imbalances and erectile dysfunction. Surgery can be effective for repairing blockages in the tubes that transport sperm. Surgery can also be used for repair of varicocele.2 Assistive reproductive technologies, such as in vitro fertilization, can be effective if other treatments do not restore fertility. [8]

Female infertility

Infertility is defined as trying to get pregnant (with frequent intercourse) for at least a year with no success. Female infertility, male infertility or a combination of the two affects millions of couples in the United States. An estimated 10 to 18 percent of couples have trouble getting pregnant or having a successful delivery.

Infertility results from female factors about one-third of the time and male factors about one-third of the time. The cause is either unknown or a combination of male and female factors in the remaining cases.

Female infertility causes can be difficult to diagnose. There are many available treatments, which will depend on the cause of infertility. Many infertile couples will go on to conceive a child without treatment. After trying to get pregnant for two years, about 95 percent of couples successfully conceive. [9]

Normal aging reduces a woman's ability to become pregnant. As a woman grows older, ovulation—the process of forming and releasing an egg—becomes slower and less effective.

Aging begins to reduce fertility as early as age 30. Pregnancy rates are very low after age 44. This is true even when fertility medications are used.

Symptoms:

The primary symptom of infertility is difficulty getting pregnant. Various causes of infertility may result in additional symptoms.

Any of the following problems may cause infertility:

• Infrequent ovulation. When your periods do not come every month, you have infrequent ovulation.

Common causes of infrequent ovulation include:

•Body stresses such as:

◦Eating disorders

◦Unusually ambitious exercise training

◦Rapid weight loss

◦Low body weight

◦Obesity

•Some hormonal abnormalities such as:

- Pituitary-gland problems
- Adrenal-gland problems
- Polycystic ovary syndrome

- Thyroid problems

Hormonal abnormalities can delay or prevent the ovaries from releasing an egg. Symptoms that suggest a hormone abnormality include:

◦Unexpected weight loss or gain

◦Fatigue

◦Excessive hair growth or hair loss

◦Acne

◦Ovarian cysts. Cysts in the ovary can cause pelvic pain. They also can interfere with the normal
• Scarring in the fallopian tubes. This can prevent pregnancy by stopping the egg from traveling into the uterus. Process of ovulation.

Damage can result from:

◦A previous surgery

◦A previous ectopic (tubal) pregnancy

◦Endometriosis

◦Pelvic inflammatory disease (PID). PID is a bacterial infection in the pelvis. It often scars, damages or blocks the fallopian tubes.

•Abnormalities in the shape or lining of the uterus, such as fibroid tumors or uterine polyps. These conditions also can cause:

◦Heavy menstrual bleeding

◦Pelvic pain

◦Enlargement of the uterus

Scar tissue can develop within the uterus as a complication of:

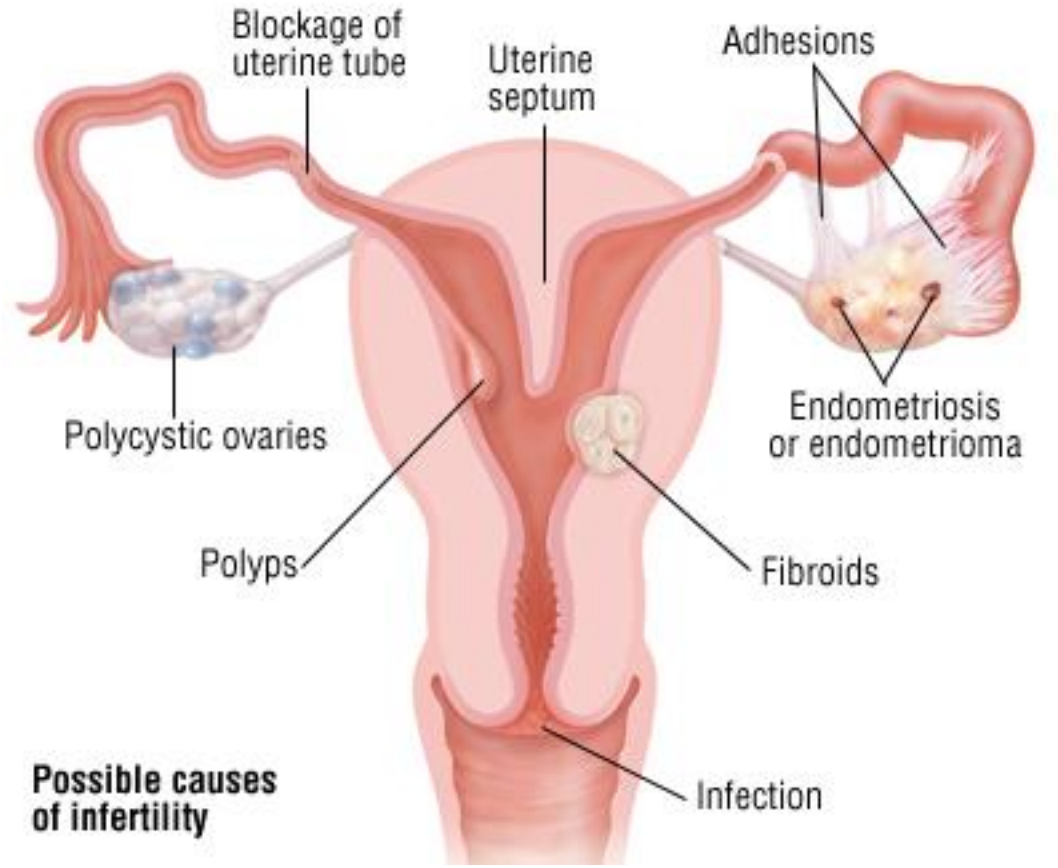
•Uterine infections

•Miscarriages

•Abortions

•Surgical procedures such as a dilation and curettage (D&C).

Such scar tissue can lead to infrequent periods or minimal menstrual flow [10].



Causes of female infertility:

Ovulatory disorders are one of the most common reasons why women are unable to conceive, and account for 30% of women's infertility. Fortunately, approximately 70% of these cases can be successfully treated by the use of drugs such as Clomiphene and Menogan/Repronex. The causes of failed ovulation can be categorized as follows:

(1) Hormonal Problems

These are the most common causes of anovulation. The process of ovulation depends upon a complex balance of hormones and their interactions to be successful, and any disruption in this process can hinder ovulation. There are three main sources causing this problem:

• Failure to produce mature eggs

In approximately 50% of the cases of anovulation, the ovaries do not produce normal follicles in which the eggs can mature. Ovulation is rare if the eggs are immature and the chance of fertilization becomes almost nonexistent. Polycystic ovary syndrome, the most common

disorder responsible for this problem, includes symptoms such as amenorrhea, hirsutism, anovulation and infertility. This syndrome is characterized by a reduced production of FSH, and normal or increased levels of LH, estrogen and testosterone. The current hypothesis is that the suppression of FSH associated with this condition causes only partial development of ovarian follicles, and follicular cysts can be detected in an ultrasound scan. The affected ovary often becomes surrounded with a smooth white capsule and is double its normal size. The increased level of estrogen raises the risk of breast cancer.

• Malfunction of the hypothalamus

The hypothalamus is the portion of the brain responsible for sending signals to the pituitary gland, which, in turn, sends hormonal stimuli to the ovaries in the form of FSH and LH to initiate egg maturation. If the hypothalamus fails to trigger and control this process, immature eggs will result. This is the cause of ovarian failure in 20% of cases.

• Malfunction of the pituitary gland

The pituitary's responsibility lies in producing and secreting FSH and LH. The ovaries will be unable to ovulate properly if either too much or too little of these substances is produced. This can occur due to physical injury, a tumor or if there is a chemical imbalance in the pituitary.

(2) Scarred Ovaries

Physical damage to the ovaries may result in failed ovulation. For example, extensive, invasive, or multiple surgeries, for repeated ovarian cysts may cause the capsule of the ovary to become damaged or scarred, such that follicles cannot mature properly and ovulation does not occur. Infection may also have this impact.

(3) Premature Menopause

This presents a rare and as of yet unexplainable cause of anovulation. Some women cease menstruation and begin menopause before normal age. It is hypothesized that their natural supply of eggs has been depleted or that the majority of cases occur in extremely athletic women with a long history of low body weight and extensive exercise. There is also a genetic possibility for this condition.

(4) Follicle Problems

Although currently unexplained, "unruptured follicle syndrome" occurs in women who produce a normal follicle, with an egg inside of it, every month yet the follicle fails to rupture. The egg, therefore, remains inside the ovary and proper ovulation does not occur.

Causes of Poorly Functioning Fallopian Tubes:

Tubal disease affects approximately 25% of infertile couples and varies widely, ranging from mild adhesions to complete tubal blockage. Treatment for tubal disease is most commonly surgery and, owing to the advances in microsurgery and lasers, success rates (defined as the number of women who become pregnant within one year of surgery) are as high as 30% overall,

With certain procedures having success rates up to 65%. The main causes of tubal damage include:

(1) Infection

Caused by both bacteria and viruses and usually transmitted sexually, these infections commonly cause inflammation resulting in scarring and damage. A specific example is Hydrosalpnix, a condition in which the fallopian tube is occluded at both ends and fluid collects in the tube.

(2) Abdominal Diseases

The most common of these are appendicitis and colitis, causing inflammation of the abdominal cavity which can affect the fallopian tubes and lead to scarring and blockage.

(3) Previous Surgeries

This is an important cause of tubal disease and damage. Pelvic or abdominal surgery can result in adhesions that alter the tubes in such a way that eggs cannot travel through them.

(4) Ectopic Pregnancy

This is a pregnancy that occurs in the tube itself and, even if carefully and successfully overcome, may cause tubal damage and is a potentially life-threatening condition.

(5) Congenital Defects

In rare cases, women may be born with tubal abnormalities, usually associated with uterus irregularities.

Endometriosis:

Approximately 10% of infertile couples are affected by endometriosis. Endometriosis affects five million US women, 6-7% of all females. In fact, 30-40% of patients with endometriosis are infertile. This is two to three times the rate of infertility in the general population. For women with endometriosis, the monthly fecundity (chance of getting pregnant) diminishes by 12 to 36%. This condition is characterized by excessive growth of the lining of the uterus, called the endometrium. Growth occurs not only in the uterus but also elsewhere in the abdomen, such as in the fallopian tubes, ovaries and the pelvic peritoneum. A positive diagnosis can only be made by diagnostic laparoscopy, a test that allows the physician to view the uterus, fallopian tubes, and pelvic cavity directly. The symptoms often associated with endometriosis include heavy, painful and long menstrual periods, urinary urgency, rectal bleeding and premenstrual spotting. Sometimes, however, there are no symptoms at all, owing to the fact that there is no correlation between the extent of the disease and the severity of the symptoms. The long term cumulative pregnancy rates are normal in patients with minimal endometriosis and normal anatomy. Current studies demonstrate that pregnancy rates are not improved by treating minimal endometriosis.

Other Factors:

(1) Other variables that may cause infertility in women:

At least 10% of all cases of female infertility are caused by an abnormal uterus. Conditions such as fibroid, polyps, and adenomyosis may lead to obstruction of the uterus and Fallopian tubes.

• Congenital abnormalities, such as septate uterus, may lead to recurrent miscarriages or the inability to conceive.

- Approximately 3% of couples face infertility due to problems with the female's cervical mucus. The mucus needs to be of a certain consistency and available in adequate amounts for sperm to swim easily within it. The most common reason for abnormal cervical mucus is a hormone imbalance, namely too little estrogen or too much progesterone.

(2) Behavioral Factors:

It is well-known that certain personal habits and lifestyle factors impact health; many of these same factors may limit a couple's ability to conceive. Fortunately, however, many of these variables can be regulated to increase not only the chances of conceiving but also one's overall health.

- Diet and Exercise

Optimal reproductive functioning requires both proper diet and appropriate levels of exercise. Women who are significantly overweight or underweight may have difficulty becoming pregnant.

• Smoking

Cigarette smoking has been shown to lower sperm counts in men and increases the risk of miscarriage, premature birth, and low-birth-weight babies for women. Smoking by either partner reduces the chance of conceiving with each cycle, either naturally or by IVF, by one-third.

- Alcohol

Alcohol intake greatly increases the risk of birth defects for women and, if in high enough levels in the mother's blood, may cause Fetal Alcohol Syndrome. Alcohol also affects sperm counts in men.

- Drugs

Drugs, such as marijuana and anabolic steroids, may impact sperm counts in men. Cocaine use in pregnant women may cause severe retardations and kidney problems in the baby and is perhaps the worst possible drug to abuse while pregnant. Recreational drug use should be avoided, both when trying to conceive and when pregnant.

(3) Environmental and Occupational Factors:

The ability to conceive may be affected by exposure to various toxins or chemicals in the workplace or the surrounding environment. Substances that can cause mutations, birth defects, abortions, infertility or sterility are called reproductive toxins. Disorders of infertility, reproduction, spontaneous abortion, and teratogenesis are among the top ten work-related diseases and injuries in the U.S. today. Despite the fact that considerable controversy exists regarding the impacts of toxins on fertility, four chemicals are now being regulated based on their documented infringements on conception.

• Lead

Exposure to lead sources has been proven to negatively impact fertility in humans. Lead can produce teratospermias (abnormal sperm) and is thought to be an abortifacient, or substance that causes artificial abortion.

• Medical Treatments and Materials

Repeated exposure to radiation, ranging from simple x-rays to chemotherapy, has been shown to alter sperm production, as well as contribute to a wide array of ovarian problems.

• Ethylene Oxide

A chemical used both in the sterilization of surgical instruments and in the manufacturing of certain pesticides, ethylene oxide may cause birth defects in early pregnancy and has the potential to provoke early miscarriage.

• Dibromochloropropane (DBCP)

Handling the chemicals found in pesticides, such as DBCP, can cause ovarian problems, leading to a variety of health conditions, like early menopause, that may directly impact fertility. [(11)]

Polycystic ovaries syndrome:

Polycystic ovary syndrome (PCOS) is a common condition that affects how a woman’s ovaries work.

The three main features of PCOS are:

•irregular periods – which means your ovaries don't regularly release eggs (ovulation)

•excess androgen – high levels of "male hormones" in your body, which may cause physical signs such as excess facial or body hair

•polycystic ovaries – your ovaries become enlarged and contain many fluid-filled sacs (follicles) which surround the eggs (it's important to note that, despite the name, if you have PCOS you don't actually have cysts)

Polycystic ovaries contain a large number of harmless follicles that are up to 8mm (approximately 0.3in) in size. The follicles are under-developed sacs in which eggs develop. In PCOS, these sacs are often unable to release an egg, which means that ovulation doesn't take place.

It's difficult to know exactly how many women have PCOS, but it's thought to be very common affecting about one in every five women in the UK. More than half of these women don't have any symptoms.

Signs and symptoms:

If you do have signs and symptoms of PCOS, they'll usually become apparent during your late teens or early twenties. They can include:

•irregular periods or no periods at all

•difficulty getting pregnant as a result of irregular ovulation or failure to ovulate

•excessive hair growth (hirsutism) – usually on the face, chest, back or buttocks

•weight gain

•thinning hair and hair loss from the head

•oily skin or acne

PCOS is also associated with an increased risk of developing health problems in later life, such as type 2 diabetes and high cholesterol levels.

Causes of PCOS:

The exact cause of PCOS is unknown, but it often runs in families. It's related to abnormal hormone levels in the body, including high levels of insulin.

Insulin is a hormone that controls sugar levels in the body. Many women with PCOS are resistant to the action of insulin in their body and produce higher levels of insulin to overcome this.

This contributes to the increased production and activity of hormones such as testosterone. Being overweight or obese also increases the amount of insulin your body produces.

The exact cause of polycystic ovary syndrome (PCOS) is unknown, but it's thought to be related to abnormal hormone levels.

Resistance to insulin:

Insulin is a hormone produced by the pancreas to control the amount of sugar in the blood. It helps to move glucose from blood into cells, where it's broken down to produce energy.

Insulin resistance means the body's tissues are resistant to the effects of insulin. The body therefore has to produce extra insulin to compensate.

High levels of insulin cause the ovaries to produce too much testosterone, which interferes with the development of the follicles (the sacs in the ovaries where eggs develop) and prevents normal ovulation.

Insulin resistance can also lead to weight gain, which can make PCOS symptoms worse, because having excess fat causes the body to produce even more insulin.

Hormone imbalance:

Many women with PCOS are found to have an imbalance in certain hormones, including:

•raised levels of testosterone – a hormone often thought of as a male hormone, although all women usually produce small amounts of it

•raised levels of luteinizing hormone (LH) – this stimulates ovulation, but may have an abnormal effect on the ovaries if levels are too high

•low levels of sex hormone-binding globulin (SHBG) – a protein in the blood, which binds to testosterone and reduces the effect of testosterone

•raised levels of prolactin (only in some women with PCOS) – hormone that stimulates the breast glands to produce milk in pregnancy

The exact reason why these hormonal changes occur isn't known. It's been suggested that the problem may start in the ovary itself, in other glands that produce these hormones, or in the part of the brain that controls their production. The changes may also be caused by the resistance to insulin.

Genetics:

PCOS sometimes runs in families. If any relatives, such as your mother, sister or aunt, have PCOS, then the risk of you developing it is often increased.

This suggests there may be a genetic link to PCOS, although specific genes associated with the condition haven't yet been identified. [12]

Testing & Diagnosis of Female Infertility:

Infertility is a disease that, according to The Center for Disease Control and Prevention, affects more than 7.3 million Americans, or 1 in 8 couples of childbearing age.

Reproductive endocrinologists (doctors specializing in infertility) generally consider a couple infertile and eligible for treatment under the following conditions:

•If the woman is under 35 and has not conceived after 12 months of contraceptive-free intercourse.

•If the woman is over 35 and has not conceived after 6 months of contraceptive-free sexual intercourse. The reason for the shorter time-frame for women over 35, is that is more of a sense of urgency due to declining fertility. Every month counts and it is not wise wait another 6 months to prove the necessity of medical intervention.

Normally, a complete medical history and a physical exam are the first steps in diagnosing a fertility problem. After that, some of the diagnostic tests for infertility might include:

•blood tests and urine tests to check hormone levels

•a Pap smear to check the health of the cervix

•urine tests to evaluate LH surges

•a basal body temperature test, which checks whether the woman is releasing eggs from her ovaries. A woman's temperature rises slightly during the days she ovulates. The woman will chart her basal body temperature every day for a few months on a graph. She will take her temperature orally or may take her temperature vaginally with a special ultra-sensitive thermometer available at most drugstores.

•an endometrial biopsy, in which the doctor removes a piece of tissue in the uterine lining. Examining this tissue will tell the physician whether eggs have been released and whether the corpeus luteum is producing enough progesterone. This test is often done if the results from the woman's basal body temperature chart are unclear.

•an ultrasound to look for fibroids and cysts in the uterus and ovaries. This test uses sound waves to picture the uterus and ovaries, causes little discomfort, and is very effective.

•a post-coital test, in which the doctor takes a sample of mucous from the woman's vagina. She must have the test during her fertile days and within 12 hours after she and her partner have sex. The test will tell the doctor if the man's sperm can survive in the woman's cervical mucus.

Further, more complex tests include one of the following:

Laparoscopy:

If the doctor suspects ovarian or fallopian tube scarring or endometriosis, a woman may undergo a laparoscopy. The doctor makes two small incisions at the pubic bone and navel, and carbon dioxide gas is injected into the stomach to enlarge it.

Then the doctor inserts a laparoscope, a long tube with lenses and a fiber optic light, into one incision and a long probe through the other opening in the skin. With the probe, the doctor can view the ovaries, fallopian tubes and uterus to check for scar tissue. In some cases, he may cut away scar tissue discovered during this operation.

The woman usually has to undergo general anesthesia for the procedure, but the risks of bleeding, infection and reaction to the anesthesia are slight.

Hysterosalpingogram:

This test checks the condition of the woman's fallopian tubes.

The doctor clamps the cervix and injects a needle filled with dye into the woman's uterus. An X-ray is taken to determine whether the dye passes through the open ends of the fallopian tubes. If the dye emerges from the end of the tubes, they are not blocked.

The test may also reveal other fertility problems, such as fibroid tumors, structural abnormalities and endometrial polyps. In some cases, the dye actually clears away blockages in the fallopian tubes, and restores the woman's fertility.

The dye is harmless and is absorbed by the woman's body after going through her tubes. The test may be uncomfortable, but is rarely painful. Unfortunately, it is noted for both false positive and false negative diagnoses. [13]

Also there are a number of diagnostic tools available to help pinpoint the cause of infertility. After a couple has undergone evaluation through a comprehensive physical exam and medical history, a fertility doctor will recommend specific diagnostic tests.

To diagnose infertility, doctors generally check the following areas: the female hormone system and ovarian reserve, the female pelvis, the vagina and cervix.

Endocrine System Tests:

The endocrine system includes all the hormone-producing glands in the body that regulate the body’s growth, metabolism and sexual development. Sometimes infertility is due to problems in the endocrine system, and the fertility specialist may perform various tests, which include:

1) Basal Body Temperature Charting (BBT):

   BBT charts help predict the time of ovulation. They can also indicate whether or not there are problems with ovulation. Higher levels of progesterone cause the body temperature to increase slightly (about 0.5F to 1F). To create a BBT chart, a woman must record her temperature every morning before getting out of bed.

   A normal BBT includes a slight increase in temperature between days 10 through 21 of the ovulation cycle.

   BBT that shows a relatively constant temperature indicates an absence of ovulation.

   There are many tests that help identify the timing of ovulation, such as Ovulation Predictor Kits (OPK) which are usually Urinary Luteinizing Hormone (uLH) tests. As a result, BBT charts are much less commonly used today than OPKs.

2) Endometrial Biopsy:

   A specialist takes a sample of the cells lining the uterus (endometrium) after ovulation occurs. They then test the sample to look for signs of inflammation, changes in the endometrium (due to ovulation), and a change in hormones. This test is usually performed about 7 to 12 days after ovulation. Today, this procedure is much less commonly performed, because it has limited ability to help with infertility diagnosis and treatment.

3) Testing for Luteinizing Hormone:

   Ovulation Predictor Kits (OPKs) detect the ovulation-triggering hormone, lutenizing hormone (LH), in the urine. Levels of LH reflect the presence or absence of ovulation. It can help a specialist time diagnostic procedures and inseminations and intercourse. OPKs are generally effective about 90% or more of the time.

4) Ultrasonography:

   Ultrasonography uses sound waves to image and closely examine the uterus, ovaries, endometrium and ovarian follicles. The imaging test can be performed via the woman's abdomen or vagina. The specialist can also use ultrasonography to look for signs of ovulation, which include:

- Smaller follicle size
- Loss of clear follicles
- Fluid in the follicle sac
- Sufficient thickness of the endometrium

   The presence of multiple small follicles may be signs of polycystic ovarian disease.

5) Testing the Health of the Ovaries:

Fertility doctors may use a combination of the following tests to check the health of a woman's ovaries and the 'supply' of eggs (ovarian reserve):

- Follicle Stimulating Hormone (FSH) test, a hormone made inside the pituitary gland. Levels of FSH increase as the number of eggs decreases. Thus, FSH levels increases with age. Levels are checked between days 2 and 4 of the woman's menstrual cycle. FSH levels below the range 10 IU/L are considered normal. FSH levels above 15 IU/L are linked with lower pregnancy rates.

- Estradiol test, a hormone produced by the ovary. Levels are checked between days 2 and 4 of the woman's menstrual cycle. Levels less than 85picograms/mL is considered healthy. While higher levels can indicate problems in ovulation, many women with a slightly abnormal result will still be able to get pregnant.
- Clomiphene Citrate Challenge Test (CCCT): A more sensitive test in which the doctor checks both FSH and estradiol levels between days 2 and 4 of the menstrual cycle. Between days 5 and 9, the woman is then given a 100mg dose of the fertility drug, clomiphene citrate. FSH levels are also checked, which should be below 10mIU/mL. The CCCT is more sensitive in picking up decreased ovarian reserve than only testing for FSH and estradiol levels alone. It is only indicated in a few patients.
- Ultrasound to determine the number of antral follicles (small follicles) in the ovaries and help diagnose decreased ovarian reserve (DOR). Usually, a woman shows signs of DOR if she has less than 8 antral follicles and the ovaries are less than 3ml in volume.
- It is important to remember that even women who experience a slightly abnormal result will often still be able to get pregnant.

  When is Ovarian Testing Performed?

  These tests are usually performed if a woman is about 33 years of age or older, or if she has other risk factors, such as: a cigarette smoker

- family history of early menopause
- ovarian or extensive pelvic surgery
- signs of premature ovarian failure
- recurrent pregnancy loss

6) Laparoscopy:

Laparoscopy is a surgical procedure that uses a thin, lighted tube (a laparoscope) to see and closely examine the uterus, fallopian tubes, ovaries and pelvic surfaces. A common sign of ovulation is the appearance of follicular cysts, which are non-harmful, fluid-filled sacs that appear on the ovaries. Follicular cysts suggest that ovulation is occurring. Laparoscopy can be very helpful in diagnosing infertility in women.

7) Other Female Endocrinology Tests:

Testing the levels of other endocrine hormones can help indicate the causes of infertility. These may include checking the levels of:

- Thyroid Stimulating Hormone, to help determine diseases of the thyroid gland
- Serum Prolactin (PRL), a hormone normally produced in large amounts during pregnancy but which can interfere with normal ovulation in a woman who is not pregnant
- Androgen hormones, particularly testosterone, which can help detect polycystic ovarian disease, a disorder in which the ovaries become enlarged and contain numerous cysts

Tests for Pelvic Disorders:

Your fertility doctor may suspect a problem within the pelvis or the tissue that lines the abdomen, uterus, bladder and rectum (peritoneum). One or more of the following diagnostic tests are likely to be used:

1) Ultrasonography and Sonohysterography:

Ultrasonography is an ultrasound-based imaging technique that helps doctors visualize the structure of organs. It is useful in detecting abnormalities in the pelvic region often associated with infertility. For example, ultrasonography can diagnose a condition called hydrosalpinges, in which the fallopian tubes are blocked by scarring (often due to previous pelvic infection). Problems in the pelvis and ovaries can also be detected using a similar technique called sonohysterography, which is a special ultrasound technique to check the inside of the uterus for abnormalities such as scar tissue, fibroids or polyps (growths attached to the inner wall of the uterus).

2) Hysterosalpingogram:

Hysterosalpingogram is a radiology procedure that examines the health of the uterus and fallopian tubes. A radio-opaque fluid is injected into the uterus and fallopian tubes and photographed via x-rays to check the shape of the uterus for fibroids, and scar tissue, and whether the tubes are blocked. It is relatively safe, simple, inexpensive and reliable test. It can cause cramping in some women.

3) Hysteroscopy:

Hysteroscopy is a minimally invasive procedure in which a fiberoptic ‘telescope’ is passed through the vagina into the uterus to examine and check for abnormalities. It can be used to find polyps, fibroids, scar tissue or other abnormalities inside the uterus.

4) Magnetic Resonance Imaging (MRI):

Magnetic resonance imaging is an imaging technique that uses a magnetic field and radio waves to develop pictures of organs inside the body. MRIs can be helpful in some situations, such as identifying lesions or rare abnormalities inside the pelvis and uterus.

5) Laparoscopy:

Laparoscopy is an out-patient surgical procedure that uses a thin, lighted tube (a laparoscope). It can also be used to look for abnormalities inside the pelvis. It is generally accurate in diagnosing infertility. It can be used to treat problems that cause infertility such as scar tissue, endometriosis, ovarian cysts, fibroids and endometriosis, a condition in which uterine lining tissue grows outside the uterus.

Tests Related to the Cervix:

Very occasionally infertility in women is related to difficulty the sperm has getting from the vagina to the inside of the uterus and fallopian tubes. This can occur because the woman's cervical mucus (which is a sticky fluid made by the endocervical canal that connects the vagina to the inside of the uterus) may not function normally as a result of surgery or other problem, or that not enough sperm are deposited at the cervix by intercourse at the right time to get pregnant. To determine if there is a problem with the cervical factor as this is called, a fertility doctor may run the following procedures or tests:

1) History of Sexual Intercourse:

Your fertility specialist will talk to you about your sexual history with your partner. Questions such as the frequency and timing of intercourse are critical. Intercourse should occur every 1.5 to 2.5 days, starting about 3 to 4 days before expected ovulation. Additional factors such as the type of lubricants that can interfere with sperm, ejaculatory problems and other issues that can affect the delivery of sperm to the cervix at the right time will be explored. This sexual history will also look carefully at your medical history, including: abnormal Pap smears, cervical or vaginal operations, and other surgeries. The lack of high quality mucus can mean the cervix has problems producing mucus or it may reflect poor timing (of sexual intercourse). Prior surgery of the cervix can also affect cervical mucus production.

2) Tests for Sexually Transmitted Disease:

Doctors will test for sexually transmitted diseases, such as HIV1, Hepatitis B and Hepatitis C, Syphilis, Chlamydia and Gonorrhea. These tests are

mandatory in some States before a fertility doctor can perform Intrauterine Insemination (IUI).

3) Post-Coital Test:

   A post-coital test analyzes cervical mucus within a few hours of sexual intercourse to inspect the interaction between sperm and cervical mucus. However, in recent years, fertility doctors have stopped using the test. Many studies show it cannot help predict pregnancy. In some situations, the test can at least confirm that the sperm is near the cervix after intercourse.

4) Antisperm Antibody Tests:

   Sometimes, the woman's immune system may produce proteins that attack sperm (antisperm antibodies). Doctors can test for these proteins in the man's sperm. They can also check to see if the partner's sperm can move through a woman's cervical mucus to reach the fallopian tubes. However, these tests are now rarely performed because they do not help predict pregnancy. Fertility doctors may run this test if a male has previously undergone a vasectomy. [14]

Preventing female infertility:

Although some infertility problems are not preventable, there are actions you can take to prevent some fertility problems. Here are five keys steps you must know in how to prevent infertility for women and men.

How to prevent infertility for women:

- Avoid drugs and alcohol. For women, the rules on drinking alcohol and using recreational drugs are the same for preventing infertility as they are for men. Heavy alcohol use and drug use increase the chances of ovulation disorders and endometriosis, which can lead to infertility. If you are a smoker, stopping now may help in preventing infertility. In addition to causing damage to your cervix and fallopian tubes, smoking can bring about early menopause by aging your ovaries and draining your egg supply. Smoking also increases the risk of miscarriage.
- Try to get pregnant while you're young. The younger you are when you try to conceive, the better chance you have of preventing infertility. That's because your fertility declines after age 35 and continues to decline with each passing year. The number of eggs you produce (along with the quality of those eggs) decreases as you age. Even high-tech fertility treatments are more effective in younger women.
- Maintain a healthy weight. More tips in how to prevent infertility in women include avoiding eating disorders such as anorexia or bulimia which can hinder ovulation and cause the eggs to develop improperly. Being overweight or underweight can stop ovulation. Excessive exercise, which many women do to stay trim, can also cause

irregular periods or a total absence of periods. Cut back to moderate exercise if preventing infertility is important to you.

- Be safe in your sexual lifestyle. Practicing “safe sex” is an important key in how to prevent infertility in women. STDs can lead to pelvic inflammatory disease (PID), which can lead to infertility. Abstinence is the safest way to ensure you will not get an STD. Otherwise, stay in a monogamous relationship where you both have been tested for STDs. [15]

Can women predict their fertility?

A secular change has occurred in family planning—the mean age of mothers at first birth in Western countries is now around 29.5 years, as opposed to 25 years two decades ago. The risks of complications in pregnancy rise significantly with increasing maternal age.

How reliable are ovarian reserve tests?

Women often wish to have an idea of their potential fertility. The concentration of serum follicle stimulating hormone (FSH) measured during the first three days of menstruation is the most commonly used test of “ovarian reserve”—a term that refers to the number of oocytes in the ovary and their fertility potential. Other measurements may increase the positive predictive value of follicle stimulating hormone, including an ultrasound scan to measure ovarian volume and the number of antral follicles, serum inhibin B concentration, and anti-Mullerian hormone (AMH) concentration. It has been suggested that these tests may help determine a woman's future natural fertility, although evidence for longer term predictions is lacking and the use of ovarian reserve testing outside of the context of planning infertility treatment is unclear.

Can women protect their fertility?

Techniques have been developed for cryopreserving oocytes and ovarian tissue in women who have treatments for cancer that result in sterility. This has raised interest in the idea that women who have yet to find a partner or who wish to pursue a career could bank oocytes when young for future use. Unfortunately, however, these techniques are still relatively inefficient. To freeze oocytes, women have to undergo the same stimulation as when having in vitro fertilization, the survival rate is relatively low, and subsequent fertilization and pregnancy are not guaranteed. On average, using standard stimulation regimens, eight to 12 mature oocytes are produced per cycle, which currently provides a modest live birth rate of 18.3%—much lower than with conventional in vitro fertilization. Strips of ovarian cortex containing oocytes have been cryopreserved before giving women sterilizing chemotherapy for cancer. Up to 75% of oocytes are lost as part of the freezing, thawing, and grafting process however, so this technique should be reserved for women in whom no alternative exists, especially as a whole ovary is normally needed. [16]

Assisted reproduction methods

Assisted reproductive technology (ART) is used to treat infertility. It includes fertility treatments that handle both a woman's egg and a man's sperm. It works by removing eggs from a woman's body. The eggs are then mixed with sperm to make embryos. The embryos are then put back in the woman's body. In vitro fertilization (IVF) is the most common and effective type of ART.

ART procedures sometimes use donor eggs, donor sperm, or previously frozen embryos. It may also involve a surrogate or gestational carrier. A surrogate is a woman who becomes pregnant with sperm from the male partner of the couple. A gestational carrier becomes pregnant with an egg from the female partner and the sperm from the male partner.

The most common complication of ART is a multiple pregnancy. It can be prevented or minimized by limiting the number of embryos that are put into the woman's body. [17]

Types of assisted reproductive treatment:

Assisted reproductive treatment (ART), also known as assisted reproductive technology, refers to treatments used to assist people in achieving a pregnancy. ART covers a wide spectrum of treatments. Depending on the cause of infertility, the following types of treatment may be suggested.

- Ovulation induction:

  Ovulation induction may be used by women who are not ovulating or are not ovulating regularly. Ovulation induction involves taking a hormone medication (tablet or injection), which stimulates the production of follicle-stimulating hormone. This encourages the development of one or more follicles. When the follicles are large enough, another hormone is administered which releases the egg from the follicle. If the couple has intercourse around this time, the chances of conception are greatly increased.

- Artificial insemination :

  Artificial insemination, also known as intrauterine insemination (IUI), is used to treat women who have normal and healthy fallopian tubes, but for unknown reasons cannot conceive. This may be due to mechanical difficulties with intercourse – for example a man is not able to achieve an erection or has structural problems of the penis after trauma or surgery. Artificial insemination might also be used when semen has been frozen due to a male partner's absence or prior to cancer treatment.

  The process of AI involves insertion of a male partner's semen through the female's cervix and into the uterus at or just before the time of ovulation. AI can be performed during a natural menstrual cycle, or in combination with ovulation induction if the woman has irregular menstrual cycles. Only doctors can perform AI under the Assisted Reproductive Treatment Act 2008, although a person is not prevented from performing self-insemination. If a pregnancy is not achieved after a few AI attempts, the use of IVF or ICSI may be discussed.

- Donor conception:

  There are several ways that donor sperm, eggs or embryos can be used in ART treatments. VARTA has a range of resources to assist you.

  Donor sperm (donor insemination):

  Donor insemination (DI) may be used when:

  •a male partner does not produce sperm,

  •a male partner does not produce normal sperm, or

  •there is a high risk of a man passing on a genetic disease or abnormality to a child.

Donor insemination may also be used by single women and women in same-sex relationships. The process of donor insemination is the same as artificial insemination.

Donor eggs:

Treatment with donor eggs is possible if:

•a woman cannot produce eggs or her eggs are of low quality. This may occur due to age or premature ovarian failure (where the woman no longer produces mature eggs for ovulation).

•a woman has experienced several miscarriages, or

•there is a high risk of the woman passing on a genetic disease or abnormality to a child.

In these cases, the egg donor undergoes hormone stimulation to produce multiple eggs. When the eggs are mature they are retrieved and sperm from the recipient's partner or a donor is added to the eggs. Two to five days later, when embryos are formed, an embryo is inserted into the recipient woman's uterus. The recipient woman may take hormones in preparation for the embryo transfer, and for approximately 10 weeks after the embryos have been transferred.

Donor embryos:

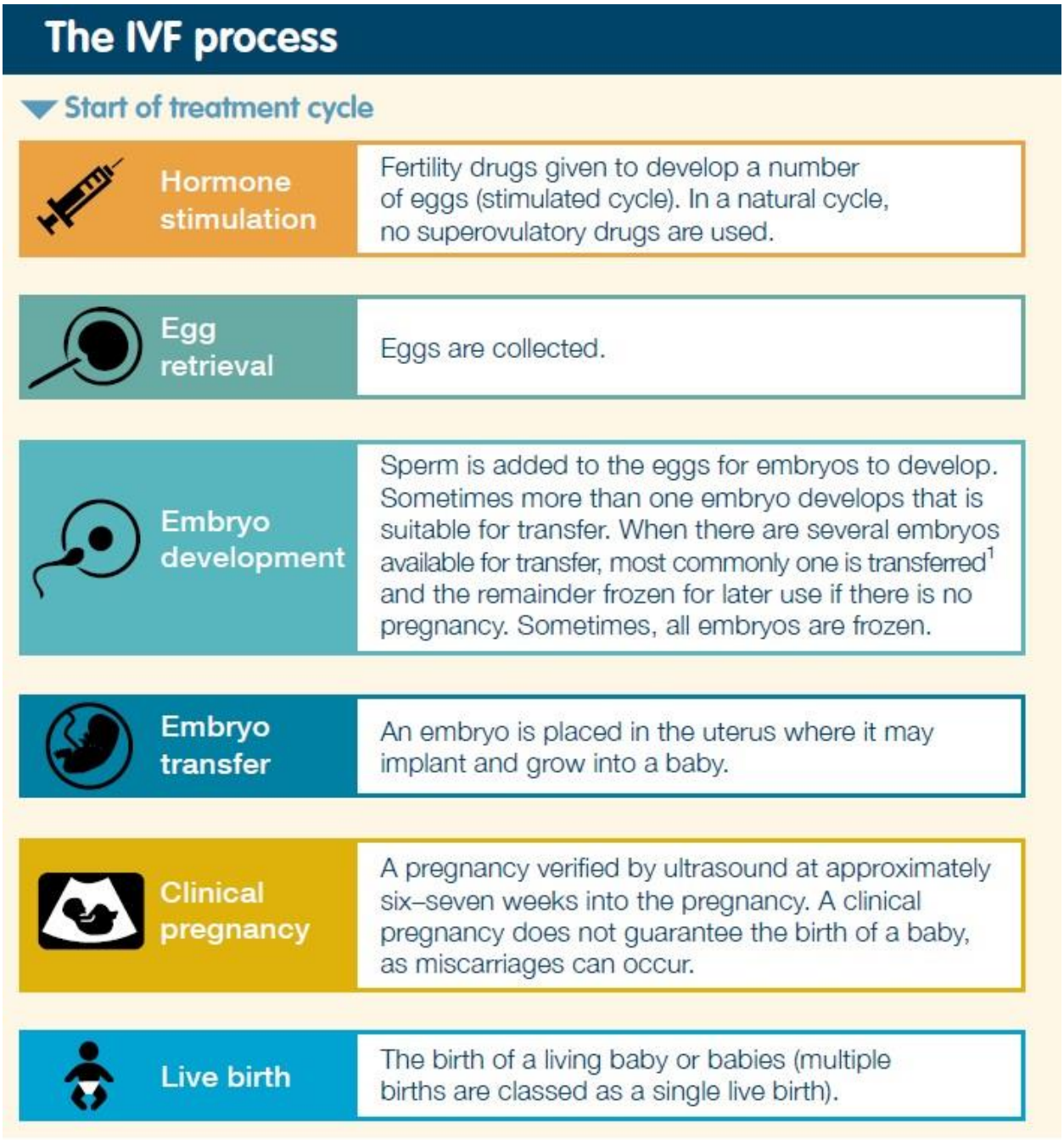
Donor embryos can be used if a person or couple requires donor sperm and donor eggs to achieve a pregnancy. Although rare, some people choose to donate frozen embryos that they no longer need (after IVF procedures, for example) for use by others undergoing IVF. When the recipient woman is ready, embryos are thawed and transferred to her uterus.

Invitro-fertilization IVF:

IVF is used in a range of circumstances to assist with conception but is often the only means of achieving pregnancy for women whose fallopian tubes are blocked. In IVF, the woman's eggs are collected, along with sperm from the male partner or donor. The egg and sperm are left in a culture dish in the laboratory to allow the egg to be fertilized. If fertilization occurs and an embryo develops, the embryo is then placed into the woman's uterus in a procedure called an embryo transfer. Sometimes multiple embryos may develop, and they can be frozen for use in later transfer procedures.

When considering clinic success rates, you need to make sure you compare like with like, or 'apples with apples'. And, most importantly, your own personal circumstances and medical history must be taken into account when you estimate your chance of having a baby with IVF.

IVF process:



Gamete intrafallopian transfer:

GIFT was launched as a more 'natural' version of IVF. Instead of fertilization occurring in a culture dish in a laboratory, the woman's eggs are retrieved from her ovaries and inserted between two layers of sperm in fine tubing. This tubing is then fed into one of the woman's

fallopian tubes, where the egg and sperm are left to fertilize naturally. GIFT is no longer commonly used. However, it is sometimes used as an option for couples who don't want to use IVF for religious reasons, providing that the woman's fallopian tubes are functioning.

Intracytoplasmic sperm injection:

ICSI is used for the same reasons as IVF, but especially to overcome sperm problems. Essentially, ICSI follows the same process as IVF, except ICSI involves the direct injection of a single sperm into each egg to achieve fertilization.

Per-implantation genetic diagnosis:

Pre-implantation genetic diagnosis (PGD) is used to reduce the risk or avoid transmission of a genetic disease or chromosomal abnormality. PGD can be used by couples who have, or have a family history of, a genetic disease or chromosomal abnormality that they risk passing on to their children. PGD is also used for couples who have had repeated miscarriages or repeated IVF failure and also for women of advanced maternal age (generally over 36-38 years of age).

In PGD, embryos are generated through the process of IVF or ICSI and then one or two cells are removed from the embryo and are screened for a genetic condition. Embryos unaffected by a particular genetic condition may then be selected for transfer to the woman's uterus.

Surrogacy:

Surrogacy is a form of ART in which a woman (the surrogate) carries a child for another person or couple with the intention of giving the child to that person or couple after birth. VARTA has a range of resources to assist you. [18]

Assisted reproduction technology in developing countries

Sixty to 80 million people experience infertility around the world, and most of those people live in developing countries.

Infertility in developing countries is pervasive and a serious concern. Further, there is evidence that the infertility rates that are generally quoted are, in fact, underestimates.

In addition to the personal grief and suffering it causes, the inability to have children especially in poor communities can create broader problems, particularly for the woman, in terms of social stigma, economic hardship, social isolation and even violence. In some societies, motherhood is the only way for women to improve their status within the family and the community. On a practical level, many families in developing countries depend on children for economic survival. While many people, therefore, would not consider infertility a disease in itself, it can certainly be said to be a social and public health issue as well as an individual problem.

Most of the infertility in developing countries is attributable to damage caused by infections of the reproductive tract, notably gonorrhea and chlamydial infection.

Infertility services in developing countries span the spectrum from prevention to treatment. From a societal and public health standpoint, prevention is cost–effective and is considered by many governments and public health care providers to be a priority for service delivery. While prevention remains paramount, taken alone it ignores the plight of infertile couples, including those with noninfectious causes of infertility.

Assisted reproductive technologies encompasses a wide range of techniques designed primarily to aid couples unable to conceive without medical assistance. Since the birth of the first so-called ‘test-tube baby’ in 1978, more than 1.5 million children worldwide have been born following in vitro fertilization (IVF) treatment.

The term ‘assisted reproductive technology’ includes techniques such as IVF and intracytoplasmic sperm injection as well as artificial insemination. It can be defined as including all treatments that include medical and scientific manipulation of human gametes and embryos in order to produce a term pregnancy. ART raise profound moral issues.

Arguments for and against ART in developing countries:

Two key arguments are frequently used to challenge the development of new reproductive technologies in developing countries: overpopulation and limited resources.

First, the argument from overpopulation suggests that an overpopulated country should not prioritize infertility management, for the overpopulation poses a demographic problem for the country and for the global community.

The primary response to this argument is that individuals should be able to reproduce ‘if, when and as often as they wish,’ as it was stated in the definition of reproductive health adopted by the United Nation’s International Conference on Population and Development (United Nations, 1994). References in both the Universal Declaration of Human Rights and the Convention on the Elimination of All Discrimination against Women (1979) may also be interpreted to argue for a right to access to infertility treatment through ART. For, if infertile persons do not have access to ART because this would ‘contribute’ to overpopulation, why save lives in developing countries

using medical technologies, as this too would have an ‘overpopulation effect’? If it is thought that it is justified to employ medical technologies to prevent suffering, why is it not justified to use medical technologies to alleviate suffering from infertility? Distinguishing the cases requires the assumption that the harms of disease necessitate medical technology in a way that the harms of infertility do not.

The second argument, the limited resources argument, suggests that developing countries should not allocate resources for expensive technology that can benefit only a few. Proponents maintain that a country’s resources should be directed toward the prevention of infertility.

Some critics question whether ARTs are an appropriate use of limited health care resources. It has been recommended that public health policy should invest in preventing the causes of infertility and leave the establishment of new ARTs to the private sector since it is unlikely to be cost–effective in the public sector.

As Sen (1994) observes, a careful examination of governmental budgets in both developing and developed nations frequently reveals mismanagement of funds, rather than an inability to finance social and economic rights.

Others argue on the other hand, that the social, emotional, physical and economic consequences that infertile couples—and in particular, women—face justifies investing in treatment options in developing countries.

The idea that infertility treatment is not a health care priority is based on the fallacious assumption that it does not have devastating, material and life-threatening consequences. Indeed, since the consequences of infertility are so severe in developing countries, infertility treatment should assume an even higher priority in developing countries than it does in developed countries.

In some instances ART may be the only way to treat infertility, even if prevention programmes are successful.

While the affordability of ART is a problem that needs to be assessed in the specific context of a country’s needs and economic conditions, it cannot be assumed that ART is unfeasible. Rather, given the social suffering and public health harms associated with infertility, research should be directed towards finding effective, low-cost solutions to infertility and this exploration should extend to ART.

Finally, if governments cite scarce resources as the justification for not funding ART, this is a cause for governments to think creatively about infertility solutions, rather than a justification for rejecting all ART advances and development.

Public–private partnerships:

In an effort to make much needed ARTs to developing countries accessible and affordable, developing countries should look to public–private partnerships (PPPs). These partnerships can

bring technical expertise, research, equipment and supplies to low-resource settings. At the same time, PPPs can offer services at lower costs that are more realistic in developing countries. In addition, PPPs can help influence the establishment of standards, regulations and policies to safeguard the health of couples undergoing treatment.

Cooperative public and private partnerships have the potential to make infertility care affordable and to make access more just. A framework that ensures knowledge transfer through PPPs would enable domestic drug companies to manufacture their own infertility drugs, especially for those drugs whose patents have expired. Furthermore, public–private clinics may be a source of revenue that may be used to support other health care objectives.

Evidence supports the conclusion that there is a compelling need for infertility treatment beyond prevention. In many instances, ART are the last hope or the only means to achieve a child for couples. There is a heightened need for ART in developing countries. While developing countries have generally not established adequate infertility programmes, mainly due to arguments based on overpopulation and cost, some notable exceptions raise hope of successful and just implementation of ART, perhaps through PPPs. A failure to even consider examining low-cost models of ART will be to conceive of developing countries as perpetually developing, rather than developed, with respect to public health.

Heterogeneity of the developing world:

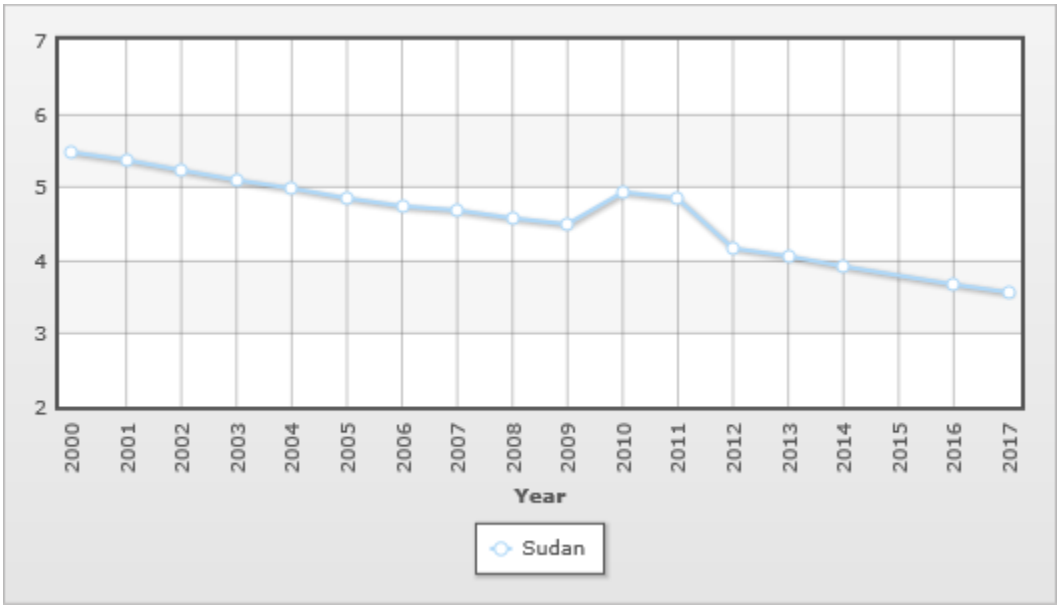
The provision of ART services in developing countries could be viewed as contradictory. Such a view may be influenced by the misconception that the developing world is homogeneous. On the contrary, developing countries are heterogeneous, varying in cultural and moral values, religions, and their pace of development. The health care infrastructure, including laboratory facilities and personnel, in some countries is substantially better positioned than in others to support the delivery of relatively sophisticated medical services. In some countries with economies in transition, an emerging middle class is already able to afford ART. In other countries, strong religious opposition to ART, on ethical rather than financial grounds, has led to little or no access to ART. Such differences are currently reflected in a wide variety of national policies toward infertility and its treatment, which, in turn, influences the options available to infertile couples. (19)

Infertility in Sudan

Total fertility rate: 3.57 children born/woman.

Definition:

This entry gives a figure for the average number of children that would be born per woman if all women lived to the end of their childbearing years and bore children according to a given fertility rate at each age. The total fertility rate (TFR) is a more direct measure of the level of fertility than the crude birth rate, since it refers to births per woman. This indicator shows the potential for population change in the country. A rate of two children per woman is considered the replacement rate for a population, resulting in relative stability in terms of total numbers. Rates above two children indicate populations growing in size and whose median age is declining. Higher rates may also indicate difficulties for families, in some situations, to feed and educate their children and for women to enter the labor force. Rates below two children indicate populations decreasing in size and growing older. Global fertility rates are in general decline and this trend is most pronounced in industrialized countries, especially Western Europe, where populations are projected to decline dramatically over the next 50 years.



Definition of Total fertility rate: This entry gives a figure for the average number of children that would be born per woman if all women lived to the end of their childbearing years and bore children according to a given fertility rate at each age. The total fertility rate (TFR) is a more direct measure of the level of fertility than the crude birth rate, since it refers to births per woman. This indicator shows the potential for population change in the country. A rate of two children per woman is considered the replacement rate for a population, resulting in relative stability in terms of total numbers. Rates above two children indicate populations growing in size and whose median age is declining. Higher rates may also indicate difficulties for families, in some situations, to feed and educate their children and for women to enter the labor force. Rates below two children indicate populations decreasing in size and growing older. Global fertility rates are in general decline and this trend is most pronounced in industrialized countries,

especially Western Europe, where populations are projected to decline dramatically over the next 50 years. [20]

Cancer and infertility

During cancer treatment, patients have important and complex issues to consider, including present and future fertility. Because many cancer treatments can damage future fertility, patients who are or will be at a childbearing age (or parents of children with cancer) should ask their cancer care team about the possible impact treatment might have on their ability to have children so they can discuss their options.

To begin, patients can ask their oncologist or other treating doctor for a referral to a reproductive endocrinologist. According to Emily S. Jungheim, MD who specializes in reproductive endocrinology and infertility at Washington University in St. Louis, patients should also ask about the possible effects their treatment could have on sexual function, reproductive function, and their future potential for having children. Woman can also ask about the possibility of premature menopause. "The options available for birth control during treatment may also be important for some," Dr. Jungheim said. "If the patient is interested and is a candidate for fertility preservation options, they should ask about the risks of these treatments, what is known about the success of these treatments, and the costs."

John Lucas, MD, assistant professor of obstetrics and gynecology at Vanderbilt University Medical Center in Nashville, said survival rates for most cancers common to young people are approximately greater than 80% and that one in 250 adults are survivors of a childhood cancer. "Patients about to undergo cancer treatment are therefore curious about how treatment will impact future fertility. Surveys indicate that 76% of cancer survivors wish to have children," Dr. Lucas explained. The impact of cancer treatment is affected by the age of the patient, the chemotherapy drugs or agents and dosages used, and the underlying cancer itself, he added.

Dr. Jungheim said that because of the different variables that must be considered, patients should be referred to reproductive specialists who can collaborate with the oncologists and other members of the cancer treatment team. In addition to the types of chemotherapy used, patients and their doctors must also consider surgical or radiation therapies when discussing how treatment will specifically affect reproductive health.

How Some Treatments Impact Reproductive Health?

Cancer treatment may affect reproductive health in a variety of ways; however, it is important to recognize that not all patients encounter fertility problems after treatment. Knowing who will have trouble is difficult. "This depends on the type of surgery performed, the type and dose of chemotherapy received, and the dose of radiation delivered and the area of the body that is irradiated. Fertility problems that do develop may be temporary or permanent." Kelvin said.

Kelvin offers a breakdown of reproductive effects based on gender:

For men and/or boys:

•Surgery of reproductive structures may result in erectile dysfunction or retrograde ejaculation, leading to the inability to release sperm naturally into the vagina.

•Radiation to the testes and some chemotherapy drugs can impair your ability to produce healthy sperm. You may recover from this after treatment; however, this may take months or even years. Predicting who will regain sperm production and who will not is difficult.

•Radiation or surgery to certain areas of the brain may reduce development of the pituitary gland hormones that stimulate sperm production.

For women and/or girls:

•Surgery may require removal of organs needed to become pregnant or maintain a pregnancy (for example, hysterectomy, and removal of ovaries).

•Radiation to the pelvis and some chemotherapy drugs may destroy eggs in the ovary, making it more difficult or impossible to become pregnant. In addition, monthly menstrual periods may stop. Menstruation may start again after some months, but some women develop premature (early) menopause. These women stop ovulating and are not able to become pregnant. Again, predicting who will be affected is difficult.

•Radiation to the pelvis may cause changes in the uterus. As a result, an embryo may not be able to implant, or the uterus may not be able to expand to hold a growing fetus. This can result in complications during pregnancy such as miscarriage, preterm (early) birth, or low birth weight babies.

•Radiation or surgery to certain areas of the brain may reduce development of pituitary gland hormones that stimulate the ovaries each month, disrupting the monthly menstrual cycle and interfering with ovulation.

Fertility Preservation:

Men:

Kelvin says fertility preservation for men involves collecting and freezing semen before beginning cancer treatment. The sperm can later be thawed and used to fertilize eggs of a partner when they are ready to start a family.

For boys who have not reached puberty, said Dr. Jungheim, testicular tissue banking is available at a handful of centers, but experts do not know how successful this procedure is. It should be done under the guidance of an institutional review board if it is going to be done, she advised.

Women:

According to Kelvin, fertility preservation for women involves collecting eggs before beginning cancer treatment, a procedure performed by a reproductive endocrinologist. The standard approach is called embryo freezing (cryopreservation).

She said the first step is to stimulate the ovaries using medication so that multiple eggs will mature. When the eggs have matured, the woman undergoes egg retrieval during an office visit. The eggs are fertilized with sperm to create embryos (in vitro fertilization). The embryos are monitored for several days and then frozen and stored. Embryos can be stored for many years. The embryos can later be thawed and transferred into that woman's uterus or into the uterus of another woman (or "gestational carrier").

Kelvin said freezing unfertilized eggs is not currently a standard treatment and is officially considered investigational.

Children with Cancer:

Even for young children, options may be available to preserve chances for reproduction, said Dr. Jungheim. For example, ovarian tissue banking is available for pre-pubertal girls, although again there is not a lot of information on how successful this technique is. "If a girl is affected, she may be a candidate at some point for a donor oocyte or donor embryo. If a young girl has radiation therapy to her pelvis, it may affect the function of her uterus and she may need a gestational carrier when she is ready for childbearing," Dr. Jungheim said.

As the effects on reproduction of some new treatments are still unfolding, and as investigational options for fertility preservation may become available or more established, it is important first and foremost to discuss this topic with your cancer care team. [21]

References

1-http://www.who.int/reproductivehealth/topics/infertility/definitions/en/

2-https://www.mayoclinic.org/diseases-conditions/male-infertility/symptoms-causes/syc-20374773

3- https://maleinfertility.org/procedures/microsurgical-varicocelectomy/complications

4-https://www.welcomecure.com/diseases/male-infertility/complications

5- https://www.ucsfhealth.org/conditions/infertility_in_men/diagnosis.html

6-https://www.news-medical.net/health/Preventing-Male-Infertility.aspx

7- https://www.andrologyaustralia.org/your-health/male-infertility/

8- https://www.nichd.nih.gov/health/topics/menshealth/conditioninfo/treatments

9-https://www.mayoclinic.org/diseases-conditions/female-infertility/symptoms-causes/syc-20354308

10- https://www.drugs.com/health-guide/female-infertility.html

11- https://web.stanford.edu/class/siw198q/websites/reprotech/New%20Ways%20of%20Making%20Babies/Causefem.htm

12-https://www.nhs.uk/conditions/polycystic-ovary-syndrome-pcos/

13- http://www.ihr.com/infertility/diagnose.html

14- https://www.arcfertility.com/patient-resources/infertility-diagnosis/

15- https://attainfertility.com/understanding-fertility/wellness-and-fertility/preventing-infertility/

16- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1988991/

17- https://medlineplus.gov/assistedreproductivetechnology.html

18- https://www.varta.org.au/information-support/assisted-reproductive-treatment/types-assisted-reproductive-treatment

19- https://academic.oup.com/eshremonographs/article/2008/1/12/619909

20- https://www.indexmundi.com/sudan/total_fertility_rate.html

21- https://www.nccn.org/patients/resources/life_with_cancer/fertility.aspx