DR. RUPAL N. SHAH

Your Complete Guide to Overcome Infertility

JOY OF GETTING PREGNANT

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Your Complete Guide To Overcome Infertility

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• The idea of writing of this book related to infertility treatment arose out of the day-to-day queries, confusions, myths and insecurities related to infertility and its treatment of hundreds of my childless patients that they have shared with me over the years. Thanks to a few of **my patients'** feedback stating, "Doctor, we understand this difficult treatment easily after talking to you as you speak in our words'. This gave me the idea to write a book in their own words to give them an understanding of their problems and related treatment in a better way before they start their treatment.

• My special gratitude to leading IVF specialist of India, **Dr. Jatin Shah**, for always being a great friend and a well-wisher, who spared his valuable time from his very hectic schedule to go through the material of this book and for penning down a very genuine introduction of the book.

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"This book is dedicated to
my mother – Dr. Malti Shah,
Who never ceases to amaze me;
With her ability to love, nurture
and inspire."

Dr. [illegible]

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Dr Jatin P Shah is a renowned IVF Specialist from Mumbai. His patients include superstar Shahrukh Khan and celebrity Producer - Director Karan Johar amongst others.

Introduction

It gives me immense pleasure to write an introduction to **Dr Rupal Shah's book "Joy Of Getting Pregnant"**. I have known her as a fine Infertility physician and ART specialist for a long time and know her commitment to the education of patients who are suffering from infertility.

Why is this book so important?

Human beings share an intense desire to reproduce but unfortunately, for many couples, pregnancy is often not a certainty and becomes increasingly difficult to achieve with the passage of time. Nearly 1 in 6 couples in the reproductive age group suffer from male /female /unexplained infertility. It is so common that it affects over 100 million people worldwide. Modern social trends toward delaying child bearing in order to build a career are worrying and contributory to increasing these numbers. As a result, fertility problems such as blocked or damaged fallopian tubes, ovulation failure, fibroids, endometriosis, poor sperm production and damage from sexually transmitted diseases are often revealed only when a couple in their 30s or early 40s finds out they can't conceive.

Treatment options can be perceived very differently by patients depending on their age, duration of infertility, prior treatments, causes of infertility and emotional commitment to fertility treatment. Every treatment has differences in financial cost, time duration, medical risk and emotional stress. It is impossible for patients to make appropriate choices unless they have sound knowledge of the various diagnostic tests and treatment options.

This book deals with an in-depth understanding of all the above challenges faced by the couple and how to quickly understand and accept the apparently complicated Assisted Reproductive Technologies such as IVF, ICSI, IUI. While IVF works for thousands of couples each year, there are always instances where nothing works. In such situations, the book discusses alternative parenting options such as third party Techniques (Egg /sperm /embryo donation and gestational surrogacy) and when you need to consider these. Also, the coverage is comprehensive with chapters on genetic diagnosis and future directions making the book totally updated and complete with useful information.

Very importantly, it is often difficult for patients to get correct information. While the internet has numerous advantages, patients are often overwhelmed with inaccurate and often misleading informatio on the internet, which makes matters worse for them. This is where a book like this is invaluable. **Dr Rupal** has identified and explained all the areas of concern for the infertile patient. Every chapter reflects her years of experience with patients. She has provided a balanced perspective of the pros and cons of different treatments.

In a nutshell, this book explains the facts and explores some of the dilemmas infertile couples face, giving insights into the issues you need to take into account when considering treatment options, how modern Assisted Reproductive Technologies can help, what can go wrong and what to expect.

I believe that all infertile couples will benefit from reading this very well-written and comprehensive book. This book answers all the questions infertile patients normally have and this knowledge will help them increase their chances of having a baby. Whichever clinic and whatever options you choose, we hope this book makes your journey simple, effective and worthwhile

Congratulations to **Dr Rupal Shah** on a splendid and excellent compilation.

With my sincere wishes for good reading and good luck.

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Dr Mitsu & Praful Doshi are eminent IVF Specialists at Blossom Fertility & IVF Centre and consultant Obstetritians & Gynecologists at Me & Mummy Hospital, Surat.

Foreword

It is a matter of great pleasure to present the second updated edition of this patient education book on infertility by *Blossom IVF Centre*.
This has been possible only because of our own **Dr. Rupal Shah**, from *Blossom IVF Center*, who made great efforts to make a difficult subject with the latest medical information, simple to understand for the average reader. She has a natural flair for educating patients. A lot of labour has gone into making this new english edition which is completely updated with many new chapters.
The first book **" Santan Prapti No Anand"** in Gujarati was originally meant to give some insight about infertility to our own patients who come to '*Blossom*', to make our counselling easier and to make them more knowledgeable and thereby rid them of the fear of the unknown.
The response to our first book was overwhelming and people from various parts of India started asking for this book. Also there was a demand to make it available in other languages. Other doctors and family physicians also started asking for a copy. As a result this book with many additional features and latest information is now translated into English, and in near future, it is going to be published in Hindi and Marathi languages to reach a wider population across India.
Infertilty has emerged as a very common affliction and its personal and social impact is worse than other major diseases. The frustrated couple goes from pillar to post - doctors, vaidyas, homeopaths, faith healers, temples, churches and so on.
Due to lack of scientific knowledge, the couple finds it difficult to get the benefits of modern advances in the field of infertility and keeps spending time, effort and money on repetitive and often unscientific treatments.
At *Blossom IVF Centre*, Surat, it has been '*Team Blossom*'s' endeavour to give that ultimate gift of a child to every childless couple. Not only do we use the latest scientific technology for maximum success, we are always conscious of a couple's personal, social and financial constraints.
This book is a humble step towards that larger goal. We are sure that anyone who wants to know about infertility and it's solutions will find this book extremely useful.

Dr Mitsu P. Doshi MD (OBGYN)
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Medical Directors,
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Chapter 01

Infertility - Why?

Infertility is defined as "Failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse."
Approximately 80 - 85% of couples will conceive within one year of marriage, if they have regular unprotected sex. One in 6 couples have problems leading to infertility.
Studies indicate that out of all cases of infertility 40% are due to female conditions, 40% are due to male problems, while 20% are due to a combination of both male and female factors or unidentified factors (Unexplained Infertility).

Primary infertility

When a woman is unable to bear a child, she would be classified as having primary infertility.

Secondary infertility

It's called secondary infertility, when a woman is unable to get pregnant after having at least one pregnancy in form of miscarriage or pre-term/full-term delivery of a baby.

FEMALE INFERTILITY

There are many possible causes of infertility. Unfortunately, in about one-third of cases, no cause is ever identified.

Ovulation disorders

Problems with ovulation are the most common cause of infertility in women.

Ovulation disorders can be due to:

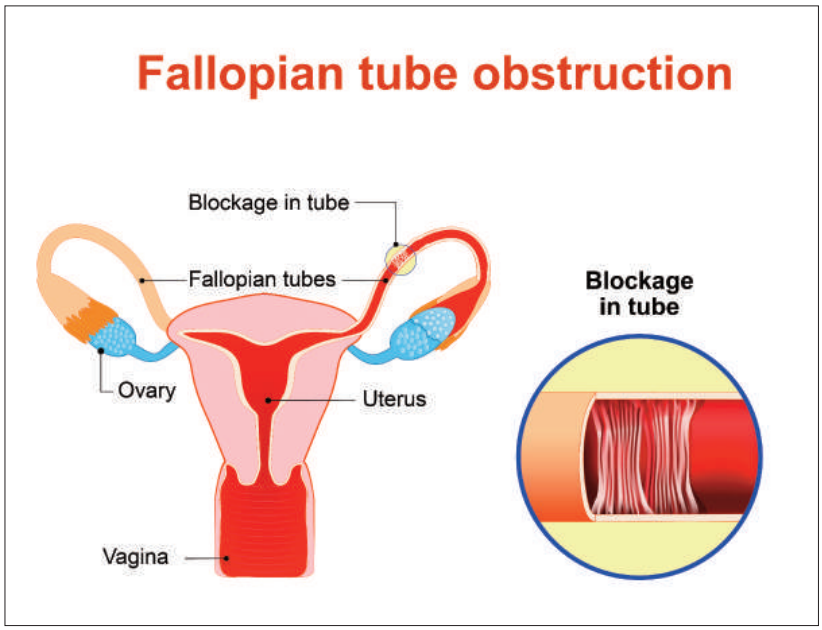
• PCOS (polycystic ovary syndrome) - A woman's ovaries function abnormally due to abnormal reproductive hormonal levels. She may also have abnormally high levels of androgen. About 5% to 10% of women of reproductive age may have this problem.
• Hyperprolactinemia - If a woman's prolactin hormone level is high, it can affect her ovulation and fertility.
• Poor egg quality /old age patients - Eggs which are damaged or having genetic abnormalities, cannot sustain a pregnancy.
• Overactive thyroid gland /Underactive thyroid gland.
• Premature ovarian failure - When a woman's ovaries stop working before she is 40.
• Patients who are on treatment for some chronic conditions, such as AIDS or cancer.

Problems in the uterus or fallopian tubes

The egg travels from the ovary to the uterus (womb), through fallopian tubes. Fertilisation of egg and sperm takes place in the fallopian tube and fertilized egg (embryo) grows in the uterus. If there is something wrong in the uterus or fallopian tubes, a woman may not be able to conceive naturally.

Causes of blocked fallopian tubes:

• Pelvic Inflammatory Disease (PID) leading to salpingitis and hydrosalpinx
• Ectopic pregnancy
• Endometriosis
• Tubal Ligation surgery
• Adhesions following abdominal surgery
• Genital Tuberculosis (still common in developing countries like India).



Uterine causes:

• Uterine fibroids can distort the endometrial cavity making it difficult for implantation
• Intrauterine adhesions from previous surgery or infection of the endometrium.
• Severe defect in uterine shape/absence of uterus by birth

MALE INFERTILITY

Semen Quality

Abnormal semen is responsible for about 75% of all cases of male infertility. The following semen problems are possible:
• Low sperm count (low concentration) - Sperm count of 40 million to 300 million per mililitre is the normal range. Counts of 20 million/ML or more may be fine if motility and morphology of sperm are normal. Count below 10 million/ML is considered severe male infertility.
• No sperm (azoospermia) - when the man ejacu-

lates and there is no sperm in the semen.
• Low sperm motility- The sperm cannot "swim" or cannot do progressive movement competently.
• Abnormal sperm - The sperm has an unusual shape, making it more difficult to fertilize an egg. Sperm must be of the right shape and be able to travel rapidly and accurately towards the egg. If the sperm's morphology (structure) and motility (movement) are abnormal, it is less likely to reach the egg and fertilize it.

Causes of abnormal semen parameters

1. Testicular infection: If infections like Mumps occurs after puberty, inflammation of the testicles may affect sperm production.

2. Treatment of Testicular cancer: in form of surgery, chemotherapy or radiotherapy

WHAT CAUSES INFERTILITY?

The most common causes are:
• Ovulation problems
• Tubal infertility
• Semen related problems
• Unexplained infertility
• Egg quantity and quality problems

Less common causes:
• endometriosis
• Uterine problems
• Previous tubal ligation surgery - tied tubes
• Previous vasectomy surgery

3. Surgery: surgery on the testicles may interfere with their blood supply, thus reducing the growth and maturation of sperm. Surgery to the lower part of the bladder or prostate can lead to retrograde ejaculation.

4. Overheating the testicles: Frequent saunas, hot tubs, very hot baths, or working in extremely hot environment can raise the temperature of the testicles. Tight clothing may have the same effect on some people.

5. Ejaculation disorders: For some men it may be difficult to ejaculate properly. Men with retrograde ejaculation ejaculate semen into the bladder. If the ejaculatory ducts are blocked or obstructed the man may have a problem ejaculating appropriately.

6. Varicocele: This is abnormal dilatation and tortuosity in the veins of the scrotum that may cause impaired sperm production

7. Undescended testicle **(Cryptorchidism)***:* One (or both) testicle fails to descend from the abdomen into the scrotum during intra-uterine development of a baby.

8. Absence of the vas deferens: The duct that transports the sperm from the testicles to the penis is absent. This issue is usually associated with cystic fibrosis.

9. Hypogonadism: Male hormone Testosterone or other related hormonal deficiency can lead to impaired sperm production

10. Genetic abnormalities: A man should have an X and Y chromosome. If he has two X chromosomes and one Y chromosome **(Klinefelter's syndrome)**, there will be an abnormal development of testicles, low testosterone, and a low sperm count (sometimes no sperm at all).

Microdeletion of arm of Y chromosome and a genetic medical condition known as **cystic fibrosis** can lead to severe male infertility. Cystic fibrosis is a chronic disease that affects organs such as the liver, lungs, pancreas, and intestines. Males with cystic fibrosis commonly have a missing or obstructed vas deferens.

11. Hypospadias: The urethral opening is at the underside of the penis, instead of its tip. This abnormality is usually surgically corrected in childhood only.

12.Medical diseases: Cushing's syndrome, Diabetes, Thyroid disease.

13.Medications: Sulfasalazine used in rheumatoid arthritis, Anabolic steroids, often taken by bodybuilders and athletes, Chemotherapy (anti-cancer treatment); Illegal drugs like marijuana and cocaine, excessive smoking and alcohol consumption can also lower a man's sperm count.

Chapter 02

What is a Test Tube Baby (In Vitro Fertilization)?

Sometimes it takes more than love to make a baby…

INTRODUCTION

34 years ago, on the 23rd of July, 1978, a female child was born in Great Britain. Now, you will question "What is new about it?". There would have been many children born on that day in Britain. But, this baby was not an ordinary baby, as she was not an outcome of the conventional way, (that is "love making") of giving birth. This baby was born subsequent to the research in the infertility treatment by a scientist. Name of this baby was Louise Brown, who was born as an outcome of a scientific procedure, which is popularly known as "Test Tube Baby", and is now popular as IVF (In-Vitro Fertilization). The inventor of this procedure was a Nobel laureate Dr. Robert Edward. Because of research by Dr. Edward, couples who were not having babies now have a "ray of hope" in their life. Many millions of couples who were cursed with the darkness of infertility have found a new ray of hope to make their dreams of parenthood real.

Louise Brown, world's first IVF baby

WHAT IS A TEST-TUBE BABY?

Noble Laureate Dr. Robert Edward has developed his procedure. The couples who were not having babies now have a "light of hope" in their life. Many millions of couples who were cursed with the darkness of infertility have found a new ray of hope.

IVF basically is a procedure of Assisted Reproductive Technique (ART). "Test Tube Baby" in short can be described as "Fertilization of female ovum with male sperm, outside the body and then implantation of fertilised egg (Embryo) into the uterus of an infertile female for further growth of the baby and birth process. The primary process of IVF was carried out outside a human body in a "test tube" in the initial years of its invention, hence it is popularly known as "Test Tube Baby". This procedure is now a days, known as In-Vitro Fertilization (IVF).

BASIC INVESTIGATIONS BEFORE STARTING IVF TREATMENT

(1) Transvaginal Sonography:

When a patient visits an IVF center for the first time, and thereafter, on second – third day of her menstrual cycle, trans-vaginal sonography is done to detect any uterine or endometrial abnormality and to study the number of eggs (antral follicles) in her ovaries. This Antral Follicle Count (AFC) is a very important tool to detect a female's egg producing capacity. A dosage of hormone injections is also fixed according to her AFC.

(2) Blood Investigations of couple:

Basic blood investigations of a couple, including hormonal assays and various infections' detection tests are carried out. In selected couples we may have to do genetic tests too.

(3) Semen analysis:

Sperm count, motility and quality of sperms in semen is checked in the laboratory. If semen parameters are normal, we freeze this semen sample for future emergency need.

(4) Hysteroscopy:

A hysteroscopy before starting IVF treatment is essential. Hysteroscopy is the best way to check that your womb is healthy and ready to carry a baby. This minor procedure is done pre-menstrually under general anaesthesia. As it is done transvaginally, there are no cuts on your body and you are discharged from hospital within 4-5 hours.

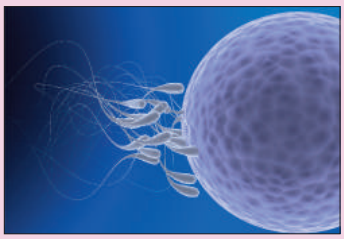
How is hysteroscopy helpful?

- We can see the normalcy of endometrial cavity, where your embryos are going to implant and develop and if any problem is there, we can tackle it by the same procedure, so that it will help us in enhancing your IVF success.
- We can do endometrial scratching procedure in same sitting,which may increase embryo implantation rates in subsequent IVF cycle.
- An endometrial biopsy is taken to detect endometrial infection, specially endometrial tuberculosis. For this biopsy material is sent for TB PCR testing in a laboratory.

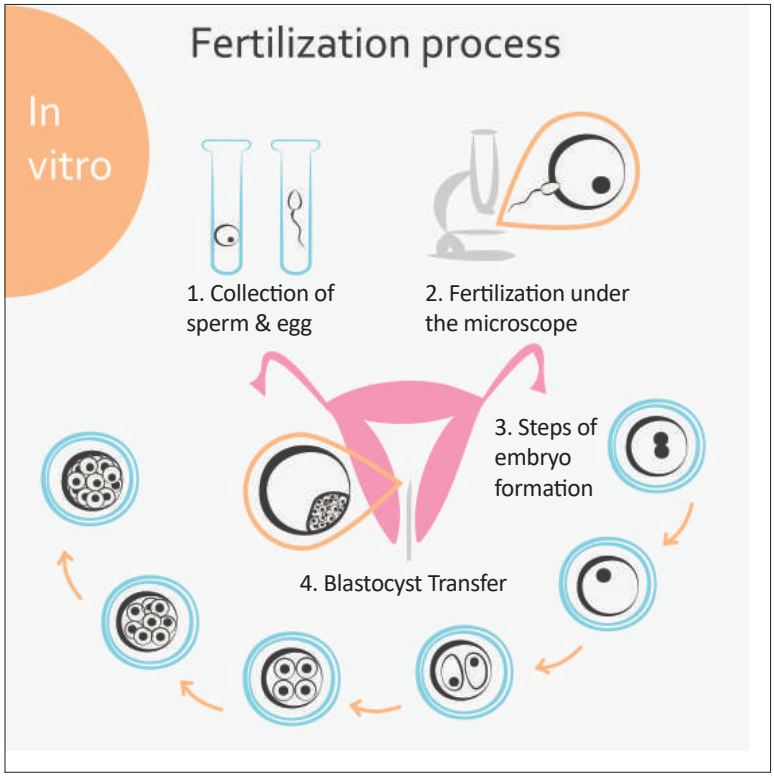
If all these tests are normal, IVF treatment is started from 2nd day of a patient's period.

HOW IS THE ACTUAL IVF PROCESS DONE?

IVF treatment is divided into three major components. (1) stimulation of ovaries by hormonal injections and ovum pick up (2) Fertilization of eggs and sperms in embryology lab (3) embryo transfer in uterus



Test Tube Baby treatment can be commonly described as Fertilizing Female Ovum with Male Sperm outside body and implantation of fertilized Egg (embryo) into uterus for further development. The fertilization of egg and sperm is carried out outside the human body, hence, this entire procedure is known as **In vitro Fertilization (IVF)**. Previously it was done in test-tube, hence was popularly known as Test-tube Baby treatment.



of the patient. Now, we will understand these steps in detail.

(1) Stimulation of ovaries by hormonal injections and ovum pick up

Only a trained gynecologist, who is qualified exclusively for infertility treatment should undertake this task. No ordinary gynaecologist can do this job perfectly. An infertility expert decides whether the couple is fit to undergo the IVF treatment.

The main requirement in this procedure is to produce adequate number of eggs. So we give hormonal injections to patient for 10-11 days from 2nd day of her period and trans-vaginal sonography is done on 5th/6th and 9th/10th day. When eggs achieve satisfactory size, one special injection is given for final maturity of eggs and after 36 hours of that injection, under general anaesthesia, eggs are retrieved under sonography guidance. There is no scar on the body in this entire procedure.

(2) Fertilization of eggs and sperms in embryology lab

Embryologist means an expert in developing embryos in a laboratory environment. An embryologist is the heart of an entire IVF center. As the heart is having a major role in human body, embryologist has a very important role in an IVF clinic. The primary role of the embryologist is to process semen and eggs for IVF procedure,and these sperms and ova (eggs) are placed together in an incubator, where the sperms fertilise the eggs. Sometimes due to less number of sperms or abnormal sperms, the sperms do not enter by themselves into the female egg and fertilise them. In such cases where IVF is likely to fail, a procedure known as ICSI is implemented.

LAB FACILITIES:
In IVF center, IVF laboratory is heart of the centre.The success of IVF also depends on competent embryologist as well as Laboratory equipments and its inner sterilized environment

ICSI (Intracytoplasmic Sperm Injection) is a modern technique In which, using a very powerful microscope, sperms are directly injected into a female's eggs. So fertilisation is ensured and chance of success is more. Using this technique, in cases of severe male infertility also, pregnancy is possible by using the husband's own sperms, thereby avoiding the need of donor sperms.

Majority of IVF centres now do ICSI for all patients undergoing IVF treatment to get maximum fertilisation of embryos.

After ICSI treatment, eggs with injected sperms are kept in a special incubator, where a special sterile environment like a mother's fallopian tube or mother's uterus is created artificially so that the embryos grow properly.

In some events, due to less number of sperms or due to rare availability of sperms, the sperms do not enter themselves into the female egg and fertilise one. In such cases where IVF fails, ICSI is implemented. **ICSI (Intracytoplasmic Sperm Injection)** is a modern treatment option. In this treatment, using a powerful microscope sperms are directly injected into the female egg. So chances of fertilization and success is more.

(3) Embryo transfer in uterus of the patient

When day 3 or day 5 embryos (Blastocysts) are ready, the patient is once again called at the center, and the best quality, 2-3 embryos are placed in her uterus by a minor procedure, called "**Embryo Transfer**", which is done without anesthesia. Thereafter these embryos grow in a normal way in the uterine cavity. As 2-3 embryos are kept into the uterus, chances of twin pregnancy is a little high.

After transfer of embryos into the uterus, the patient is asked to rest for about one to one and half hours and then sent home.

She is given a few supplements and supportive medicines in the form of vaginal tablets or injections. After two weeks she is called for the result of the procedure by a blood test known as B-HCG.

Chapter 03

Male Infertility Workup

Did you know that the cycle of sperm production and maturation takes about 74 days? This means that things you do today can affect your sperm for up to 3 months. Examples are - repeated hot water immersion, high fever, some medications, strenuous exercise, smoking, and alcohol or recreational drug use.

Heat exposure to the testicles has been shown to have a very detrimental effect on sperm production and quality, which is the reason for recommending that men who are trying to initiate a pregnancy avoid hot tubs, long-distance driving or extended bicycle rides.

In natural conception, to conceive a child at least 20 million/ML sperms are required. Out of them, about 50% sperms should have good motility

Contrary to popular belief, storing up your sperm by not ejaculating for long periods of time does not improve your sperm quality. You may gain a slightly higher number of sperm in your ejaculate, but you will likely also have fewer motile (swimming) sperms and a higher concentration of sperms with DNA fragments, dead cells and debris.

WHY DO I NEED TO HAVE AN ANALYSIS?

A semen analysis will tell you how many sperms are being produced, but much more information may be gained, such as:

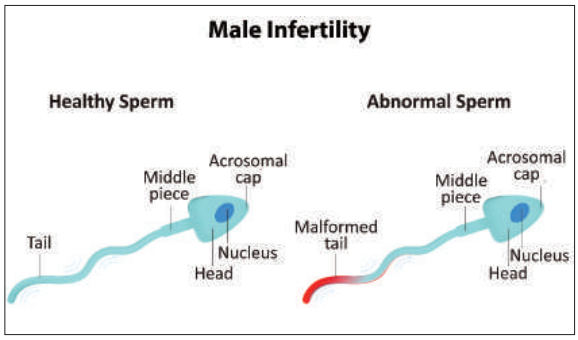
Sperm Count: This tells the number of sperm in the semen sample. A normal sperm count should be more than 20 million sperm/mL. Low sperm count may indicate a problem in the body - giving the doctor a clue that may warrant further testing and treatment.

Volume: How much semen is produced? The normal volume is 2-5 milliliters, which is about a teaspoon to a tablespoon; large variations from this can indicate other medical conditions that may require treatment.

Motility: The percentage of sperm that are swimming (active).

Progression: The quality of forward movement of the motile sperms; sluggish sperm may not be able to navigate the fallopian tubes and reach the egg to fertilise it.

Morphology: The shape of the sperm cells themselves; abnormally shaped sperms have difficulty



in normal fertilization of an egg.

Other Semen Elements: Also present in semen are a number of other cell types, such as white blood cells, immature sperm cells, different types of crystalline formations, bacteria and cellular debris. Some of these can be indicative of prostate infection, and can alert your physician about the need for other treatment.

WHAT DO I NEED TO DO TO PREPARE FOR A SEMEN ANALYSIS?

The most important thing to consider is your abstinence time. This means the length of time since your last ejaculation, which includes not only sexual intercourse, but also masturbation or wet dreams. For a good analysis your abstinence should be no more than 5 days and no less than 2 days. A less than optimal sample can lead to an incorrect diagnosis.

The preferred method of semen collection is masturbation without the use of lubricants. There are not yet any lubricants that have been proven to be non-toxic for sperm cells. Intercourse and withdrawal are also not acceptable, as specimen loss and contamination with vaginal fluids, bacteria and cells often occurs.

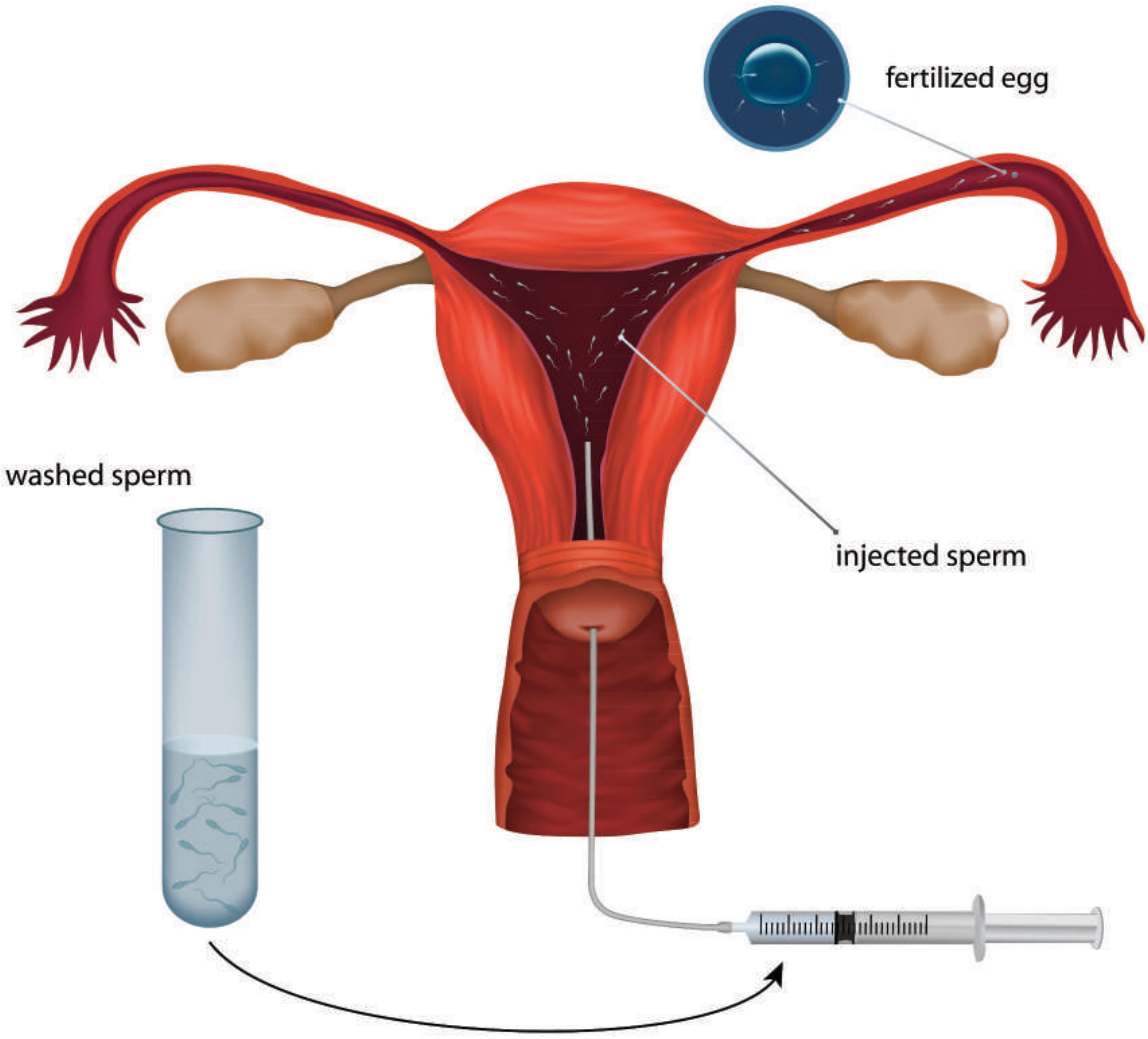
WHAT ABOUT PRIVACY? WILL I BE INTERRUPTED?

Please be assured that we make every effort to decrease your stress level at our facility. Most of the decent fertility clinics will have specially made private rooms- 'Boy's Rooms' for your privacy. Viagra tablets and porn videos are also provided if needed.

If you are producing a sample at home and delivering it to the lab, you should demand a sterile plastic specimen bottle from the centre and keep it near body temperature during transport. Please make sure the bottle is well-tightened; a loose cap can result in sample loss and an inaccurate analysis. Please make sure that your semen sample reaches the clinic within 20-30 minutes.

Chapter 04

Know about Intrauterine Insemination Treatment (IUI)



The most basic artificial reproductive treatment is Intra-Uterine Insemination, which is popularly known as IUI.

DIFFERENCE BETWEEN IVF AND IUI PROCEDURES

IUI and IVF (Test-tube baby treatment) are different procedures.

• **IUI (Intra Uterine Insemination):** In this process, an egg is not fertilised outside human body, but after processing the semen sample in a laboratory, washed semen sample is directly inseminated inside the female uterus using a thin tube and fertilisation of egg and sperm is allowed to occur naturally inside the fallopian tube of the female partner.

• **IVF (Test Tube Baby):** Here female eggs are taken outside the human body and after fertilising them with male sperms in incubators, the embryos are cultured for 3-5 days and then 2-3 healthy embryos made by this process are transferred inside the female uterus for further growth.

IN WHICH INFERTILE PATIENTS IUI IS USEFUL?

(1) Male factors:

• *Low Sperm count and motility:*

Normal sperm count should be more than 20 million/ML. But, if it is around 15-20 Million/ML and motility is less than 20-30%, using IUI technique for 3-4 cycles, pregnancy can be achieved in 35-40 % cases.

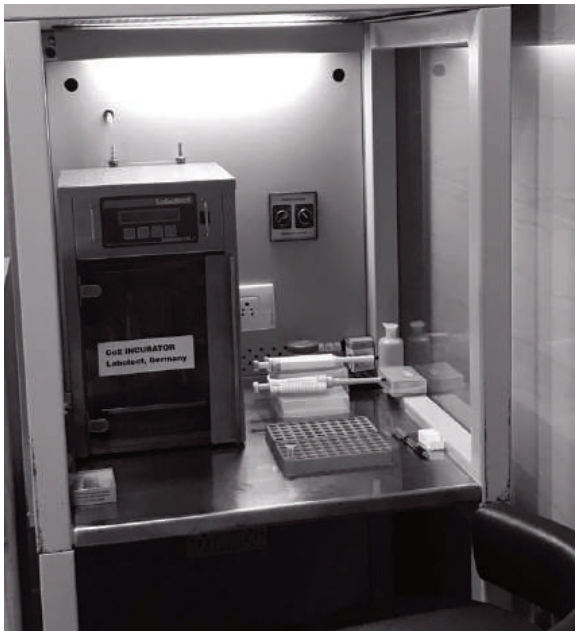
If sperm count is lower than 10 Million/ML, then IVF - ICSI technique is required.

Other factors-

• In some cases, due to physical or psychological problem, the husband is unable to do intercourse, IUI treatment is required .

• If husband is suffering from the cancer of testes, and doctor has advised him to go for chemotherapy or radiotherapy, it will affect the semen report drastically. So before commencing chemotherapy, his semen is collected and frozen, which is used in future for his wife to achieve pregnancy by IUI.

• If male partner lives out of city or in a foreign country and comes home for just a few days, and due to rarely done, timed intercourse, it becomes difficult to get a baby. In such cases, when the husband is in home town, his semen is collected, frozen and stored. So in his absence also, we can treat his wife to make her pregnant with IUI of frozen semen sample during her ovulation days. There are few examples in foreign countries that



such frozen semen was used after the death of the husband by the female to conceive a child.

(2) Female factors:

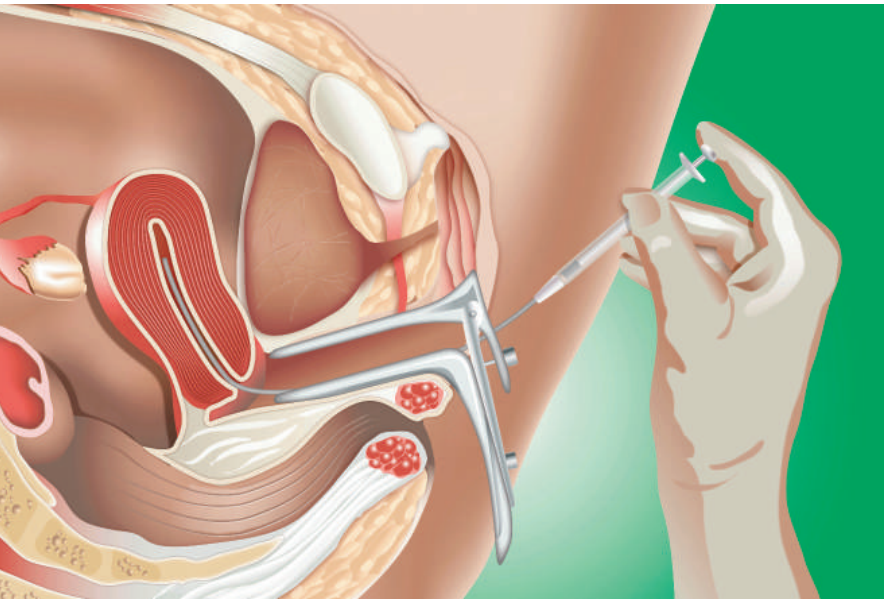
• During intercourse, semen enters into female uterus. But sometimes, the **cervical mucus** is not of good quality to keep male sperms live. Hence, the sperms cannot reach the ovum and thus conception is not possible. In such cases, IUI treatment is helpful, because in IUI technique, male sperms are directly introduced into the female uterus bypassing the cervix, so there is no effect of cervical mucus on them.

• When woman is having **ovulation problem** due to hormonal imbalance (eg PCOS), superovulation with ovulation induction medicine or hormonal injections and IUI gives satisfactory results in many cases.

• Female age is a significant factor as far as success with IUI is concerened. Intrauterine insemination is less useful for women over 40 years. IUI has also been shown to have a reduced success rate in younger women with a significantly elevated day 3 FSH level or low AMH level or other reasons of significantly reduced ovarian reserve.

• In cases with **mild endometriosis**. (Please refer to chapter on endometriosis for details).

• **Unexplained Infertility:** When all reports of husband and wife are normal and inspite of all basic treatment, if couple is not achieving parenthood, this condition is known as unexplained infertility. Some patients may get success with 3-4 cycles of IUI.



HOW IS INSEMINATION PERFORMED?

The woman is given medications for proper development of 1-4 eggs and insemination is timed to coincide with ovulation (egg release from the ovary). We predict ovulation day by serial follicular study with trans-vaginal sonography from 11th to 16th day of period.

A semen sample is either collected at home or in the clinic by masturbation, after 2-5 days of abstinence from ejaculation.

The semen is 'washed' in the laboratory (procedure is called sperm processing or sperm washing). Sperms are separated from the bad components of the semen and concentrated in a small volume. Various media and techniques can be used for the washing and separation. Sperm processing takes about 30-60 minutes.

A speculum is placed in the vagina and the cervical area is gently cleaned.

The washed specimen of highly motile sperm is placed higher in the uterine cavity using a sterile, flexible catheter.

There should be little or no discomfort during the procedure. So no need to get worried for this procedure. Most clinics advise the patient to remain lying down for a few minutes after the procedure, although it has not been shown to improve success. There is no need to take additional rest at hospital or home after this procedure.

DONOR SEMEN

When a donor's semen is used for conception, it is known as IUID.

If semen report is very poor and the couple cannot afford cost of IVF-ICSI treatment or husband is having a genetic problem, which can be transmitted to the offspring, then we advise IUI treatment with donor semen.

HOW MANY INSEMINATIONS TO TRY BEFORE DOING IVF?

- The short answer is to move on to IVF after 3-4 failed IUIs.
- If the female is aged 40 or above or ovarian reserve is low, consider IVF earlier.
- In vitro fertilization has a significantly higher success rate as compared to IUI.

IUI is not recommended for the following patients:

- Women who have severe disease of the fallopian tubes or blocked fallopian tubes.
- Women with a history of pelvic infections.
- Women with moderate to severe endometriosis.
- Elderly women/women with low AMH level or poor ovarian reserve.
- Low sperm count-less then 10 million/ml.

A couple who are undergoing IUI treatment must keep in mind that after taking IUI treatment for 3 to 4 times, if no result is achieved, then the treatment must be changed.

SUCCESS RATES FOR IUI

Success rates with IUI depends on patient's age and the reasons for her infertility.

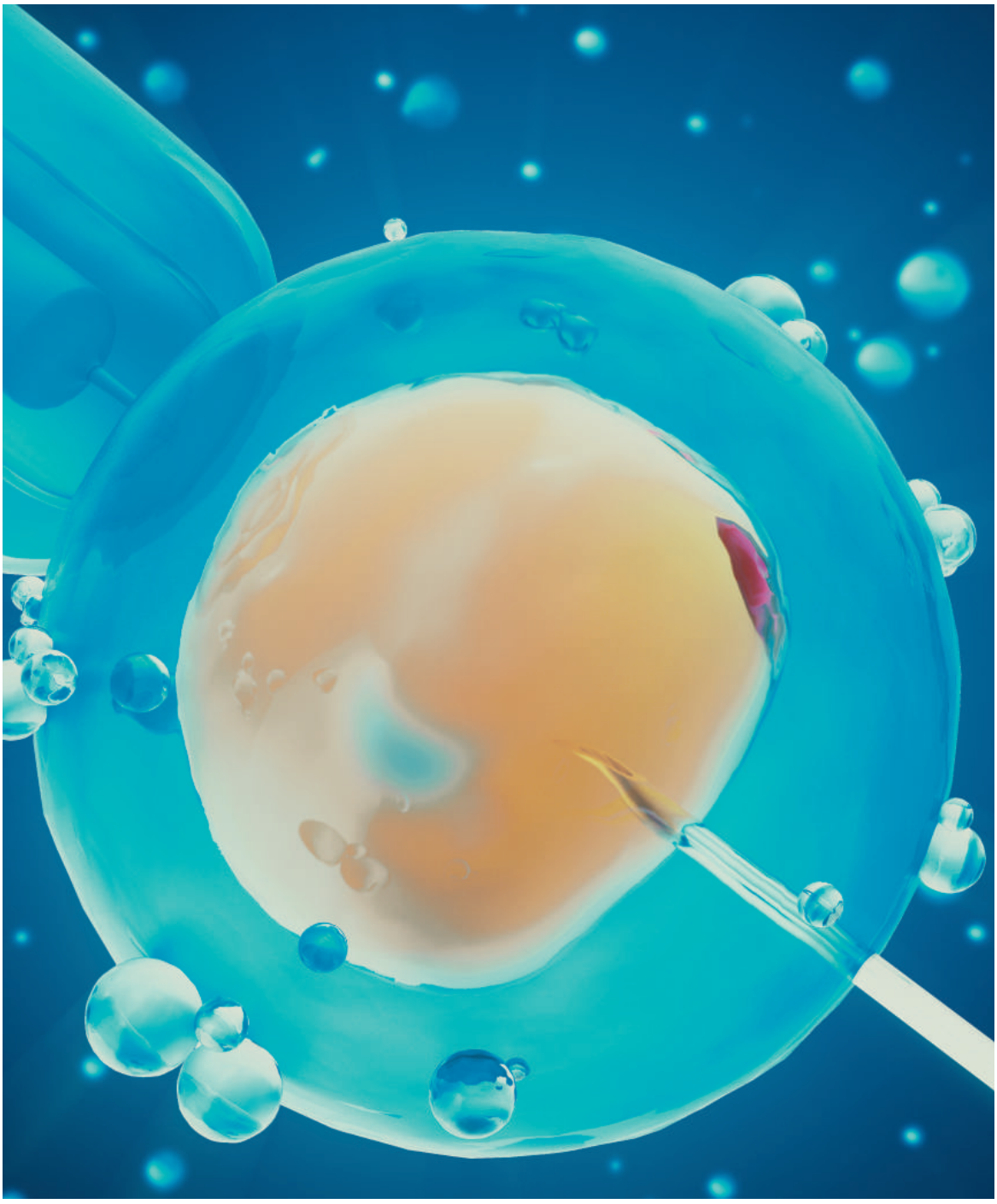
If a couple is having unexplained infertility, in which the female's age is under 35, if they are trying for 2 years, and if husband's semen report is normal - we would generally expect about:

- 10% chance per month of getting pregnant and having a baby with ovulation induction by tab Clomiphene or Letrozoland artificial insemination for up to 3 cycles (lower success after 3 attempts).
- 15% chance per month of getting pregnant and having a baby with injectable HMG/FSH medication and IUI for up to 3 cycles.
- 65% chance of conceiving and having a baby with 1 IVF cycle (success rates vary between clinics).

Chapter 05

Severe Male Factor Infertility & It's Treatment

ICSI, PESA, TESE



When the reason for infertility lies with the male partner, it is referred to as male infertility. Male infertility factors contribute to approximately 30-40% of all infertility cases, and it alone accounts for approximately one-third of all infertility cases. A variety of sperm problems can account for male infertility. Sperm can be completely absent in the ejaculate **(azoospermia)** or present in low concentrations **(oligospermia)**. They may have poor motility **(asthenospermia)** or an increased percentage of abnormal shapes and forms **(teratospermia)**. There may also be abnormalities in the series of steps required for fertilization, such as sperm binding to and penetrating the egg.
In this chapter, we will learn about the most effective treatments available for severe male infertility-defined as:
• Sperm concentrations-less than 10-15 million per milliliter
• Sperm motility-less than 35%
• Semen sample with very poor sperm morphology

HOW IS MALE INFERTILITY DIAGNOSED?

• Physical examination of the penis, scrotum and prostate
• Semen analysis to determine the number and quality of sperm
• Blood test to check for infections or hormone problems and for genetic testing (Hormone levels are just as important in male fertility as they are in female fertility)
• Making a culture of fluid from the penis to check for infections, if required
• Sperm function tests-DNA fragmentation tests

HOW IS MALE FERTILITY IMPROVED?

Conventional Treatment options:

• Taking medications to help increase sperm production
• Taking antibiotics to heal an infection
• Taking hormones to improve hormone imbalance
• Avoiding taking long hot showers, using hot tubs or saunas
• Wearing looser underwear such as boxer shorts versus jockey shorts

INTRACYTOPLASMIC SPERM INJECTION (ICSI)

Intra cytoplasmic sperm injection (ICSI) is a laboratory procedure developed to help infertile couples undergoing in vitro fertilization (IVF) due to severe male factor infertility.
ICSI involves the insertion of a single sperm directly into the cytoplasm of a mature egg (oocyte) using a microinjection pipette (glass needle).
ICSI can facilitate fertilization by sperm that will not bind to or penetrate an egg. It can also be used to treat men with extremely low number of sperms. However, ICSI is generally unsuccessful when used to treat fertilization failures that are primarily due to poor egg quality.

Indications for ICSI

• Very low numbers of motile sperm with normal appearance.
• Problems with sperm binding to and penetrating the egg.
• Anti-sperm Antibodies (immune or protective proteins which attack and destroy sperm) of sufficient quality to prevent fertilization.
• Prior or repeated fertilization failure with standard IVF.

WHAT CAUSES MALE INFERTILITY?

Male infertility usually occurs due to inadequate number or motility of sperms or abnormal sperms or problems with ejaculation.
Sperm abnormalities may be caused by one or more of the following:
• Inflammation/Infection of the testicles
• Swollen veins in the scrotum (varicocele)
• Undescended testes (at birth, in normal circumstances, testes should come down in scrotum from original position in abdomen)
• Sometimes, the semen sample looks normal but under the microscope, it is revealed that there are no sperms present. This can be the result of a blockage of the ducts that carry the sperm from the testes to the penis and is called **obstructive azoospermia**. Causes can be pre-existing genetic condition, injury to the groin area, blockage caused from a previous infection, hernia repairs etc.
• In more rare cases, a man may not be able to produce a sample because he cannot ejaculate outside the penis. This can be caused by a medical problem called **retrograde ejaculation**, in which the semen is discharged backwards into the urinary bladder, rather than forwards.

Other Reasons for a low sperm count or lack of sperms include:

Use of alcohol, tobacco or other drugs, severe mumps infection after puberty, hormonal disorder, exposure to poisonous chemicals, exposure to radiation, wearing restrictive or tight underwear, history of sexually transmitted diseases, urinary tract infections, use of certain types of medications.

dard IVF methods.

• Frozen sperm collected prior to cancer treatment that may be limited in number and quality.

• Absence of sperms, secondary to blockage or abnormality of the ejaculatory ducts that allow sperm to move from the testes. In this situation, sperm are obtained from the epididymis by a procedure called microsurgical epididymal sperm aspiration **(MESA)**.

• Absence of sperm in the ejaculate, but presence of sperm in the testes. Sperm can be obtained by testicular biopsy or Testicular Sperm Aspiration **(TESA)**.

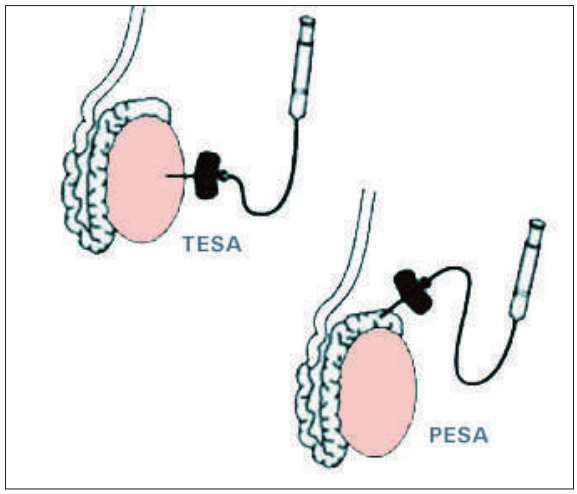
With ICSI, egg fertilization rates of 60% and cleavage rates of 80% or more of fertilized eggs are expected. Other factors such as poor egg quality and maternal age may cause these percentages to drop. Very severe male factor can also be responsible for lower fertilization, poor embryo growth, and a lower pregnancy rate.

Recently IVF with ICSI has been shown to be successful even if men with non-obstructive azoospermia, i.e. a problem with the testicles producing sperms. Most patients with non-obstructive azoospermia have very low production of sperms by the testicles. In more than 50% of men with non-obstructive azoospermia and with no sperm in their ejaculate, enough sperms are found with an extensive testicular biopsy to perform ICSI. Even in patients whose routine diagnostic testicular biopsy did not reveal sperms, a thorough search of testicular tissue often reveals enough sperms for ICSI.

Fertilization and pregnancy rates with ICSI from sperms of men with non-obstructive azoospermia may be lower than in patients with obstructive azoospermia. As we discussed above, many men with non-obstructive azoospermia probably have some genetic etiology for this. It may be that azoospermia could be passed on to male offspring from IVF with ICSI.

ICSI as a procedure does not increase chances of genetic abnormality in the offspring

There does appear to be a slight increase in the chance of having a child with a genetic or chromosomal abnormality in ICSI pregnancies. These are likely related to the genetic characteristics of the infertile man rather than to the ICSI procedure itself. Therefore when a couple is using ICSI for a severe male factor, there may be a greater risk of an abnormality than in a couple using ICSI



for a mild male factor. Men who have sperm counts of less than 5 million per ml., should consider having chromosome testing (karyotype) and Y chromosome microdeletion test done for themselves, since they may have 5-10% chances of having abnormal chromosomes. There does not appear to be any increase in birth defects in ICSI offspring.

ICSI is a technique that has been a major breakthrough for the treatment of male infertility. It is now very exciting that even men with azoospermia, whether it is obstructive and non-obstructive have the option of IVF with ICSI to have his own biological offspring. In the past, donor insemination, adoption, or life without a child were their only options.

RETRIEVING SPERM BY PESA, TESE OR TESTICULAR BIOPSY

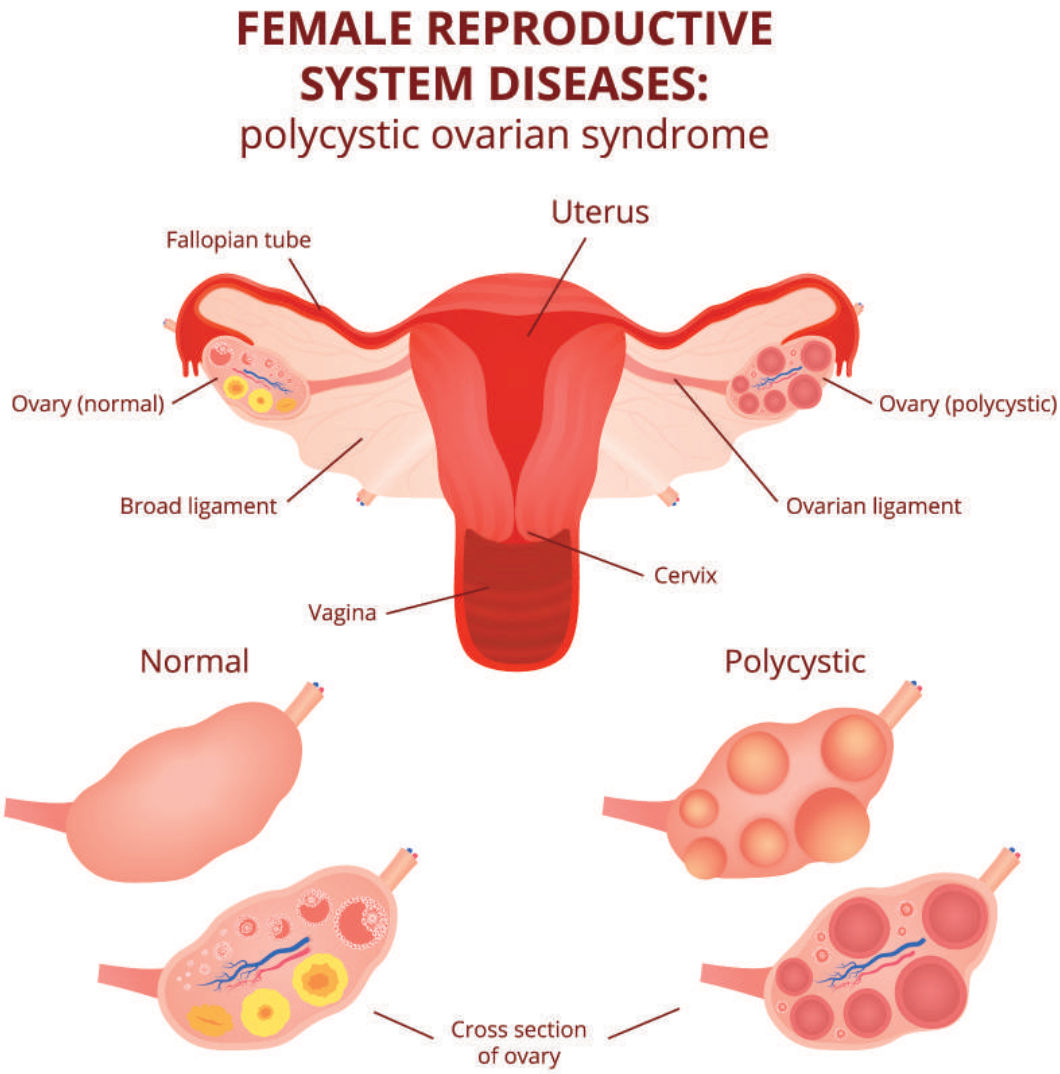
Whatever the cause, an inability to produce a sperm during the routine semen analysis is no cause for panic. There are usually healthy sperms in the testes in most of the cases, we just have to get them. We have several procedures that can recover the sperm so it can be used for fertilization. One such procedure is called **Percutaneous Epididimal Sperm Aspiration or Testicular Sperm Extraction (PESA and TESE)**. In this procedure, a needle is inserted into the testicle and fluid or tissue is withdrawn. The fluid is then inspected under a microscope and healthy sperm are extracted from it. Epididymal sperm can even be frozen for future use so that the man does not have to go through a sperm retrieval each time.

If PESA or TESE is unsuccessful in retrieving sperm, a second option may be to do a **Testicular Biopsy**. In this procedure, a tiny cut is made on the testes to remove a small sample of tissue from the testes. The tissue is then inspected under a microscope and any healthy sperm found are extracted from it.

These procedures sound painful, but they are done under local or general anesthesia and shouldn't be uncomfortable for the patient. Most patients return to work the following day.

Chapter 06

Menstrual Irregularities, Anovulation & Polycystic Ovarian Syndrome (PCOS)



Do irregular periods mean you have Polycystic Ovarian Syndrome (PCOS)? The truth is that there are many causes of irregular periods but PCOS is the most common cause. About 7% of the overall population, about 25% of young fertile women and over 50% of women with irregular periods have PCOS.

If your menstrual periods are not monthly and there is a gap of more than 5 weeks between periods, you may have PCOS. Many women with

PCOS also have some hormonal problems of androgen excess (alteration in level of male hormones in blood) which may cause excess hair growth on upper lip, chin, breasts and abdomen. It may also cause pimples. Most of these symptoms will start in the teenage years. Specific blood tests can help identify elevated male hormones (androgens) in women.

About 2/3 of women with PCOS will be overweight, although 1/3 of women with PCOS are normal weight. These thin women with PCOS are often surprised to find out they have PCOS, as many believe that only overweight women have PCOS.

Also many women with PCOS have some degree of insulin resistance, that is, elevated insulin with normal glucose levels, pre-diabetes or true diabetes. This needs to be tested by very specific blood tests in all women with PCOS.

Most women with PCOS have ovaries with many follicles or small cysts, not all women with PCOS have polycystic ovaries. In ultrasonography test, PCOS ovaries will look enlarged, with multiple small follicles located in periphery of the ovary-typical of "Pearl Necklace appearance".

Other causes of irregular menses:

Of course, other diseases can cause irregular or infrequent periods and simple blood tests can identify these causes. Three common causes are hypothyroidism, elevated prolactin levels and pregnancy.

WHAT CAUSES PCOS?

While the exact cause of PCOS is unknown, doctors believe that hormonal imbalances, specially pituitary gland hormones LH and FSH, overproduction of the hormone androgen and genetics play a role. Women are more likely to develop PCOS, if their mother or sister also has the condition.

SYMPTOMS OF PCOS

Symptoms of PCOS typically start soon after a woman begins to menstruate for the first time. The type and severity of symptoms varies from person to person. The most common characteristic of PCOS is irregular, mostly delayed menstrual periods.

Other symptoms may include:

- Acne
- Weight gain
- Hirsutism (inappropriate hair growth)
- Infertility
- Miscarriages

Because in some cases, PCOS is marked by an increase in male sex hormones, this condition may cause women to develop certain masculine characteristics, such as excess hair on the face, chest, stomach, thumbs or toes.

Many women with PCOS are more likely to develop other concurrent health problems, such as diabetes, hypertension, and high cholesterol in later life. These are linked to the weight gain typical in women with PCOS.

TREATMENT

There is no permenant cure yet, but there are many ways you can decrease or eliminate PCOS symptoms and feel better. Your doctor may offer different medicines that can treat symptoms such as irregular periods, acne, excess hair, and elevated blood sugar. Fertility treatments are available to help women get pregnant.

Why weigh reduction is important?

Losing as little as 5% excess weight can help women ovulate more regularly, sometimes this helps in treating their infertility and lessen other PCOS symptoms. The ideal way to do this is through diet and exercise.

You may feel that it is difficult to lose excess weight and keep it off, but it is important to continue the effort. Your efforts help reduce the risk for developing serious health complications that can impact women with PCOS much sooner than women without PCOS. The biggest health concerns are diabetes, heart disease, and stroke because PCOS is linked to having high blood pressure, pre-diabetes, and high cholesterol. Weight reduction diet and exercises are explained in next chapter of this book.

PCOS INFERTILITY TREATMENT

Main reason for infertility in PCO patient is delayed ovulation or no ovulation, and due to this, menstruation cycle gets disturbed, delayed and sometimes excessive. So to treat PCO related infertility, main aim is to regularize ovulation, which in normal cases occurs between 12^{th} to 16^{th} day of menses.

Following drugs are helpful in inducing ovulation in time:

1.Clomiphene Citrate/Letrozole:

Usually any of these drugs are given alone or in combination with gonadotropins (hormones) injections, from $2/3^{rd}$ day of menses and ovulation is monitored by transvaginal sonography from $10^{th}/11^{th}$ day of menses for 4-5 days. When de-

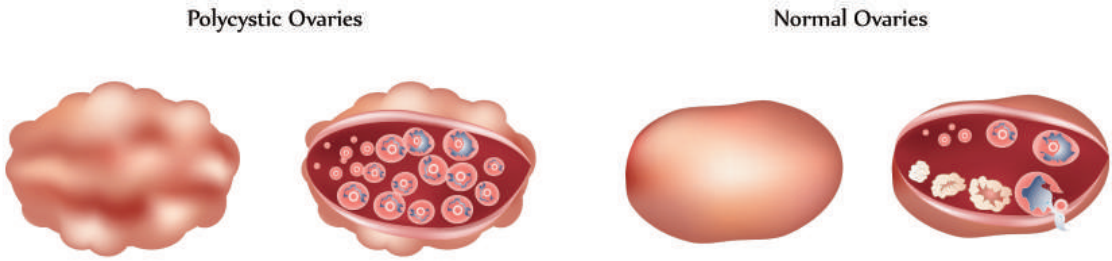
sired size of egg/2-3 eggs are achieved, ovulation triggering injection - HCG is given and patient is advised to do intercourse after 24 hours or planned IUI is done after 36 hours depending upon her duration of infertility, previous failed cycles or other associated infertility factors.
If pregnancy is not achieved, sometimes drug dose requires increment.

2.Gonadotropins:
Gonadotropins are naturally occurring hormones that stimulate your ovaries to release one or more eggs. This medication may help you ovulate if you are not ovulating regularly. Women with PCOS who do not respond to clomiphene or letrozole treatment may benefit from fertility drug treatment with gonadotropins.
When ovulation is induced with gonadotropins, most of the time IUI is done in that cycle, as it increases the chance of getting pregnant than natural intercourse.

3.Other supplementations:
Metformin:
To reduce high insulin levels and stabilize your hormones, your doctor may prescribe a medication called metformin. After taking metformin in conjunction with ovulation induction medicine or hormones your ovulation cycles may become more regular and may help in proper ovulation.
N-Acetylcysteine and Myo-Inositol:
They are the natural supplements, which have shown some promises for treatment of infertility caused by PCOS in form of improving ovulation.
Other medicines:
Sometimes medicines to treat hyperprolactenemia or thyroid problems are required in patients with irregular periods/scanty or excessive periods.

4. Laparoscopic Ovarian drilling:
It is a minor surgical treatment that can trigger ovulation in women who have polycystic ovary syndrome (PCOS). Electrocautery is used to do multiple tiny punctures in peripheral follicles to drain excess fluid.
This surgery is not advised in all patients, but it can be an option for women who are still not ovulating after losing weight and after trying fertility medicines or she is responding to ovulation induction medicine, but not getting results. In this case laparoscopic ovarian drilling is done along with diagnostic laparoscopy and hysteroscopy procedure, which is done to look for tubal patency and interior of uterine cavity.
What To Expect After Surgery?
If you have a laparoscopy procedure, you will likely go home the same day and can do your normal activities within 24 hours. Your return to normal life will depend on how quickly you recover from surgery, which may take only 4-5 days.
How Well It Works?
For women who do not respond to treatment


Thinning hair
Hair on
lip/chin/neck
Acne
Depression
Hair on back
Hair on chest
Excess weight
around waist
Missed periods,
ovarian cysts &
infertility
Dark discoloured
skin & spots
Signs & Symptoms
of PCOS



with medicines such as clomiphene or gonadotropin injections, about 30-40% of them may start responding to ovulation induction medicine and may be able to become pregnant after they have ovarian drilling surgery.
The major side effects are rare and mainly operative procedure related, but rarely there are chances of reduction in ovarian reserve, if PCO drilling is done vigorously, using cautery in extensive amount.

5. Intrauterine Insemination (IUI) and IVF:

Depending on the initial testing, a fertility specialist may recommend a patient to start with timed intercourse or intrauterine insemination (IUI) with medications to induce ovulation and that can be scheduled around the development of the follicle(s) determined by serial sonography monitoring, provided that the fallopian tubes are open and the sperm counts are normal. The typical success rates with IUI are about 10 to 15 % per cycle; a woman's individual success rate with IUI is largely impacted by her age.
If after 3-4 failed attempts with IUI, or if the patient is presenting with other factors, such as blocked fallopian tubes, or sometimes in cases where hyper stimulation of ovaries occur due to ovulation induction therapy, she may require IVF treatment.

OVARIAN HYPERSTIMULATION SYNDROME (OHSS)

PCOS and use of fertility treatments to stimulate ovaries can increase the risk for OHSS. It affects about 10% of women who undergo traditional IVF, but now with the use of newer antagonist protocols for stimulation and with better freezing techniques, chances of ovarian hyperstimulation are very less.
Ovarian hyperstimulation syndrome (OHSS) causes swelling of the ovaries with leaking of fluid within the body. When it occurs, OHSS is usually temporary and resolves within 1-2 weeks. Mild symptoms include bloating, discomfort/pain in abdomen, nausea, vomiting, constipation and weight gain. Severe cases of OHSS occur rarely and can lead to hospitalization due to serious symptoms and complications including severe pain, swelling in the abdomen, breathing problems, decreased urination, increaed tendency to clotting of blood etc.
Ultrasound to keep check on the ovaries and collection of fluid in abdomen and blood tests to check on hormone levels are used to monitor for OHSS risk.

Prevention of OHSS

To prevent or lessen the development of OHSS, infertility expert may make changes to the dosage of your fertility drugs. This may mean delaying the use of a hormone treatment or not using it. In some cases, a drug called Cabergoline may be recommended to prevent OHSS.
Another strategy is to freeze embryos and delay embryo transfer in IVF until OHSS symptoms have resolved, which we follow in almost all PCO cases undergoing IVF. This has almost made most of the IVF clinics 'OHSS Free' while optimising success rates of IVF treatment.

Chapter 07

Obesity and Infertility

Obesity is a known risk factor for ovulation problems, but it also contributes to infertility in women who ovulate normally. Research shows that excess weight can reduce your chances of becoming pregnant. Obesity has a number of adverse effects on a woman or man's fertility.

WHAT IS OBESITY?

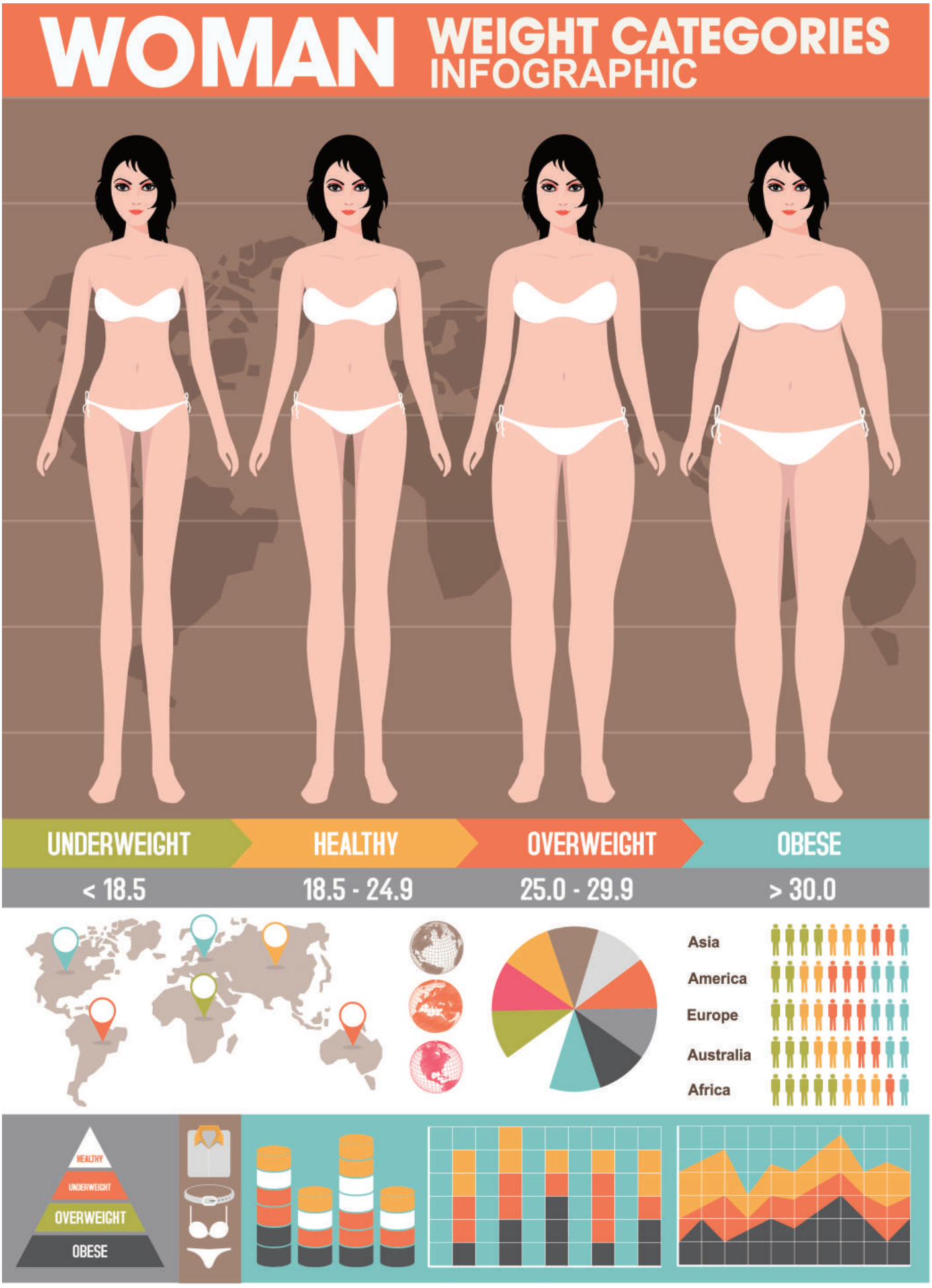
Obesity is defined as excess adipose tissue (fat). There are several different methods for determining excess adipose (fat) tissue; the most common being the Body Mass Index (BMI) .

BMI is calculated by dividing a person's body weight in kilograms by their height in meters squared.

The BMI cutoffs are:

Below 18.5	Underweight
18.5-24.9	Normal weight
24.5-29.9	Overweight
30 and greater	Obese
40 and greater	Morbid or extreme obesity

If BMI is above 30, capacity of conception in female decreases . According to one research,a woman with a BMI of 35 was found to be 26% less likely to achieve a spontaneous pregnancy


WOMAN
WEIGHT CATEGORIES
INFOGRAPHIC
UNDERWEIGHT
HEALTHY
OVERWEIGHT
OBESE
< 18.5
18.5 - 24.9
25.0 - 29.9
> 30.0
Asia
America
Europe
Australia
Africa
HEALTHY
UNDERWEIGHT
OVERWEIGHT
OBESE

than women who were normal weight or overweight but not obese. A woman with a BMI of 40 or more was 43% less likely to get pregnant.

HOW OBESITY AFFECTS FERTILITY?

1. Obesity affects your hormones

When your body mass index goes past the overweight category (BMI of 25–29.9) into the obese category (BMI of 30 and above), hormonal changes may occur in your body. When your levels of natural hormones change, your chances of conception decrease.

2. Obesity leads to insulin resistance

The hormonal imbalance that comes with obesity often leads to insulin resistance. That is a major risk factor on the road to diabetes - but it also affects your fertility and can create abnormal menstrual cycles. Insulin resistance can lead to anovulation, in which your body does not produce eggs properly.

3. Obesity affects natural and assisted pregnancies

Obesity makes it more challenging to become pregnant, no matter whether you're using natural means or by reproductive technologies such as in vitro fertilization (IVF). It also increases your risk for a miscarriage. This issue may be caused by the hormonal issues or because of your body is producing poor quality eggs.

4. Obesity decreases your partner's fertility, too

Although much of the focus on obesity and infertility is on women, it absolutely affects men too. For men, obesity leads to a drop in testosterone hormone level which can lead to infertility. On top of that, erectile dysfunction occurs at a higher rate among obese men.

Most of the time obesity is associated with hormonal disturbances in infertile women, in the form of Polycystic ovaries associated with anovulation, other pitutary or thyroid gland dysfunction or it can be due to genetic problems or problems related to unhealthy life style and eating habits.

HOW TO COPE WITH THIS PROBLEM?

When you visit a doctor, in the first visit, doctor will advise you to reduce your weight. And you start dieting, and exercise immediately, but this will not give any magical result in a short time. Sometimes because of crash dieting also there are severe hormonal disturbances leading to anovulation, worsening your infertility problem. Sometimes, weight is reduced, but it will not help your infertility problem.

To keep your ovary fit, add healthy food in your diet:

• Eat fresh food (Please avoid re-cooked food).

• Eat fruits and vegetables raw. (By making soups or juices of vegetables and fruits, the nutrients of vegetables and fruits are destroyed).

• Do not decrease carbohydrates in your food. But eat the same without any process. Use wheat, juwar or bajra by making roti, thepla, bhakri etc. In place of polished rice, use red rice (Brown Rice), so the content of fiber is high in your food.

• Protein is required for maintenance of all hormones in ovary. So, increase protein level in your diet. Pulses, eggs, fish, paneer are rich sources of protein.

• Wherever fat is used, use the ones containing essential fatty acids like Omega-3, and Omega-6. These are available from groundnut oil, sesame oil, olive oil, dry fruits mainly from almonds and walnut.

• Walnut gives you Alfa Lipoic Acid, which works like insulin which also helps to reduce fat.

• Micro-nutrients like selenium, zinc, and chromium increases effectiveness of insulin, which are easily available from green vegetables, fish, eggs, full grains, and cereals. Zinc and Chromium effectively improve pimples and wrinkles over the skin.

• Vitamin B12 is available from Fresh Curd, Paneer, Sprouted Beans and fermented food items like dosa, idli, dhokla etc.

• In problems like PCO, requirement of calcium in-

creases. Have more calcium content in your diet. Food like chocolate, cakes, sweets, processed food, aerated drinks reduce calcium and chromium in the body. This effectively reduces insulin production and increases fats. So please avoid such items in your diet.

• You may take tablets of Vitamin A, E, D, and B12 and Calcium in your diet supplement.

EXERCISE

Regular exercise is a key for regular menstrual cycle. And regular menstrual cycle means regular ovulation and increase in chances of pregnancies. It is necessary that to reduce your weight, exercise is equally important as your diet. Over enthusiastics do excess exercises, but it is not necessary. Regularity in exercise is important.

• 30 - 40 minutes aerobic exercise per day for 3 to 5 days in the form of walking, jogging, cycling, swimming, dancing will also help you to keep your goals.

• To balance your weight, at least twice a week practice muscle strengthening exercises. This is done with dumbbells, or using various machines in a gym.

• You can do yoga at least 10 to 15 minutes per day, which will include muscle stretching in your exercise schedule. Meditation may also be included into your workout plans.

• To reduce your weight, contact a dietician and gym/yoga trainers, who will guide you to appropriate exercise and proper food.

Exercise boosts up functions of almost all the body parts including ovaries. It will enhance insulin, which will control your sugar levels. This helps you in balancing sugar levels in your blood, which will improve your ovulation. While trying to reduce your weight, it is important that you have proper sleep and a stress-free mind also.

Chapter 08

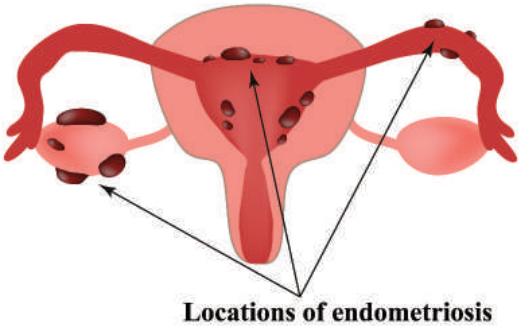
Endometriosis & Chocolate Cyst

Endometriosis is a common, benign disease. In endometriosis, cells those normally grow inside the uterus as uterine lining (Endometrium) are found outside of the uterus. The cause of Endometriosis, which occurs typically in menstruating women, is unclear. Endometriosis may be found in up to 5-10% of all women during their reproductive life.

What causes the pain in endometriosis?

The misplaced endometrial tissue still responds to a woman's monthly cycle - the tissue builds up, breaks down, and bleeds under the control of the

Endometriosis



Locations of endometriosis

1 in 10 women of reproductive age (15-49 years) is sick with endometriosis

176 million women today suffer from endometriosis

ovarian hormones. But unlike the tissue and fluids within the uterus, which are expelled during menstruation, the tissue from Endometriosis has no place to go. The result can be inflammation and scar tissue formation around this collection of menstrual blood of the endometrial implants.

SYMPTOMS OF ENDOMETRIOSIS

The symptoms of Endometriosis most commonly include pain, infertility and abnormal menstrual bleeding. Severe pain in lower abdomen and back (dysmenorrhoea), which occurs during the menstrual cycle, can vary in intensity and duration.

In some patients pain may occur at the time of sexual intercourse or passing stools or while urinating. Some patients, even with severe Endometriosis, may not experience any pain or discomfort.

The accurate diagnosis of Endometriosis is important regardless of pain severity. Even mild cases of Endometriosis may affect fertility due to scarring, altering the pelvic environment with an increased number of white blood cells or inflammatory chemicals and possibly alter the local pelvic immune system.

HOW ENDOMETRIOSIS MAY AFFECT FERTILITY?

Endometriosis has been found to be present in up to 20-25% of infertile women. Infertility associated with endometriosis has been attributed to:

1. Distorted anatomy of the tubes and ovaries
2. Interference with oocyte (egg) development or release
3. Altered Fertilization and/or early embryo development
4. Altered or reduce receptivity of the Endometrium

DIAGNOSIS

While vaginal or ultrasound examination may suggest endometriosis in form of presence of chocolate cyst of ovary, the only definite way to diagnose the disease is with direct inspection through Laparoscopic procedure.

TREATMENT OF ENDOMETRIOSIS

1) Surgery

Endometriotic spots which are present in lower abdomen are burnt by a procedure known as "laparoscopic fulguration". If a the patient is diagnosed having ovarian chocolate cysts in laparoscopy, the chocolate material is drained and cyst wall is removed from the ovary. This surgery is known as "Cyst Excision", in which ovary is preserved. Endometriotic adhesions can also be excised with this key-hole surgery.

Chocolate cyst leads to reduction in ovarian reserve. Chocolate cyst can recur and multiple surgeries on the same ovary can lead to faster depletion

of the egg reserve and make infertility treatment more difficult. So once you are diagnosed with having chocolate cyst of more than 3 cms, do not delay the active treatment of infertility.

In some patients, because of severe endometriotic involvement of bladder or rectum, severe pain occurs while urinating or passing stool. These cases also require laparoscopic intervention by expert laparoscopist.

(2) Injections or medicines:

In some cases, after doing laparoscopy, some patches may be difficult to remove completely. In such cases, hormonal injections like Luprolide or Decapeptyl can be given to suppress secretion of hormones FSH and LH. By this procedure, remaining endometriosis also dries up. But as the effect of these medicines gets reduced over time, endometriosis gets active again. So medical management is not a good option to treat infertility related to endometriosis.

Thus, there is no permanent cure of endometriosis. Even after taking treatment, there is no guarantee that this will not recur.

WHAT ARE THE TREATMENT OPTIONS FOR INFERTILITY ASSOCIATED WITH ENDOMETRIOSIS:

As stated above, even after taking proper treatment of endometriosis or chocolate cyst, it may recur, leading to infertility. After treatment of mild endometriosis, there are maximum chances of conceiving a baby within next 6 to 12 months. After taking endometriosis treatment for moderate to severe cases, immediate consultation with infertility specialist should be done to start active treatment of your infertility in form of Intra-Uterine Insemination (IUI) or In-Vitro Fertilisation (IVF).

Chapter 09

Infertility Treatment for Blocked Fallopian Tubes

About 20 percent of females coming to an infertility center are found to have problems in fallopian tubes.

FUNCTION OF FALLOPIAN TUBE

The sperm fertilizes an ovum (which is released from the ovary) in the fallopian tube before it reaches the uterus. This fertile egg (embryo) arrives at the uterus and establishes itself in uterine linings, known as endometrium. So, in the process of conception an important role is played by fallopian tubes. It is very necessary that all the functions of fallopian tubes like integrity of its inner wall, free movement of its fine hair like structures, known as "Cilia", which help eggs to move towards uterus, and open pathway from ovary to uterus etc. should be in order.

HOW TO DIAGNOSE PROBLEMS OF FALLOPIAN TUBES?

(1) Transvaginal sonography:

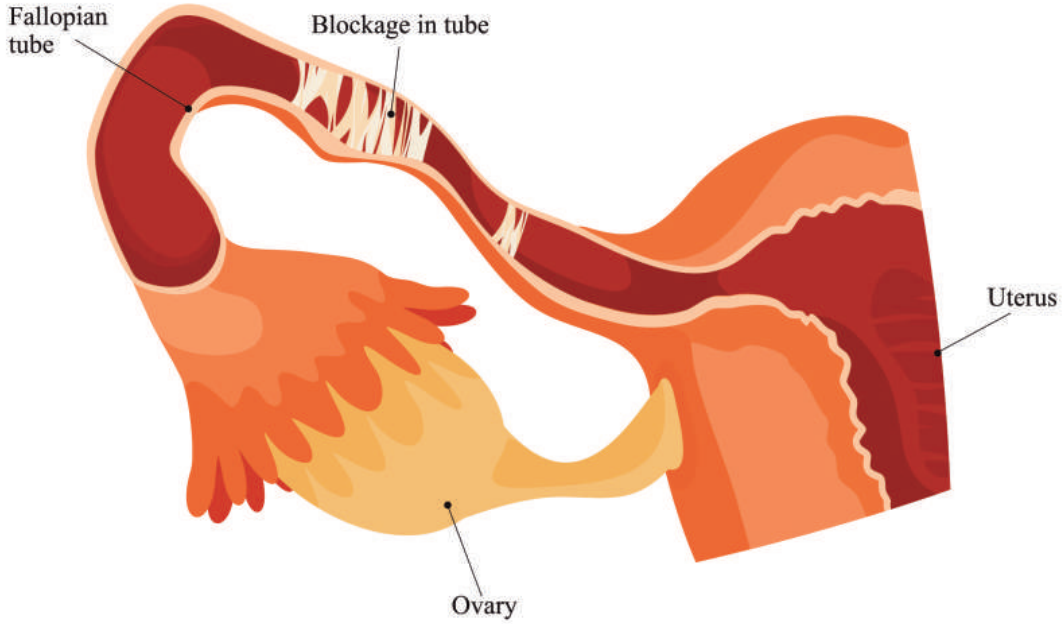
This will help in diagnosis of hydrosalpinx (collection of infected fluid in fallopian tubes due to tubal blockage) or pyosalpinx (collection of pus in fallopian tubes).

(2) Hysterosalpinography (HSG)

Normally this test is carried out within first 5 days after completion of the menstrual cycle. This is carried out at the Radiology Clinic. Using radio opaque dye, x-ray of uterus is taken, to observe where this dye is flowing from uterus towards ovary via fallopian tube. If the dye flows without any kind of difficulty in passing from fallopian tube, it suggests that the tube is fully open and without any obstacle. But where there is an obstacle in the tube, the dye gets blocked here. By doing this test, one can identify, if there is any defect in the fallopian tubes and the uterus.

This is very important test but there are few **disadvantages** of this test.

FALLOPIAN TUBE OBSTRUCTION



• Unpleasant and Painful procedure (as done without anaesthesia)
• The procedure involves exposure to radiation (low doses) and contrast media (which might cause an allergic reaction). HSG is contraindicated in women with known adverse reaction to contrast media.
• Limited information on uterine wall, which might make it difficult to differentiate between bicornuate uterus and septate uterus .
• No information on fallopian tube structure or anatomical relationship between tubes and ovaries
• False negative results due to technical difficulties.

In some cases, by doing this test, some minor blockages are removed by the procedure itself, so the chances of conception increase.

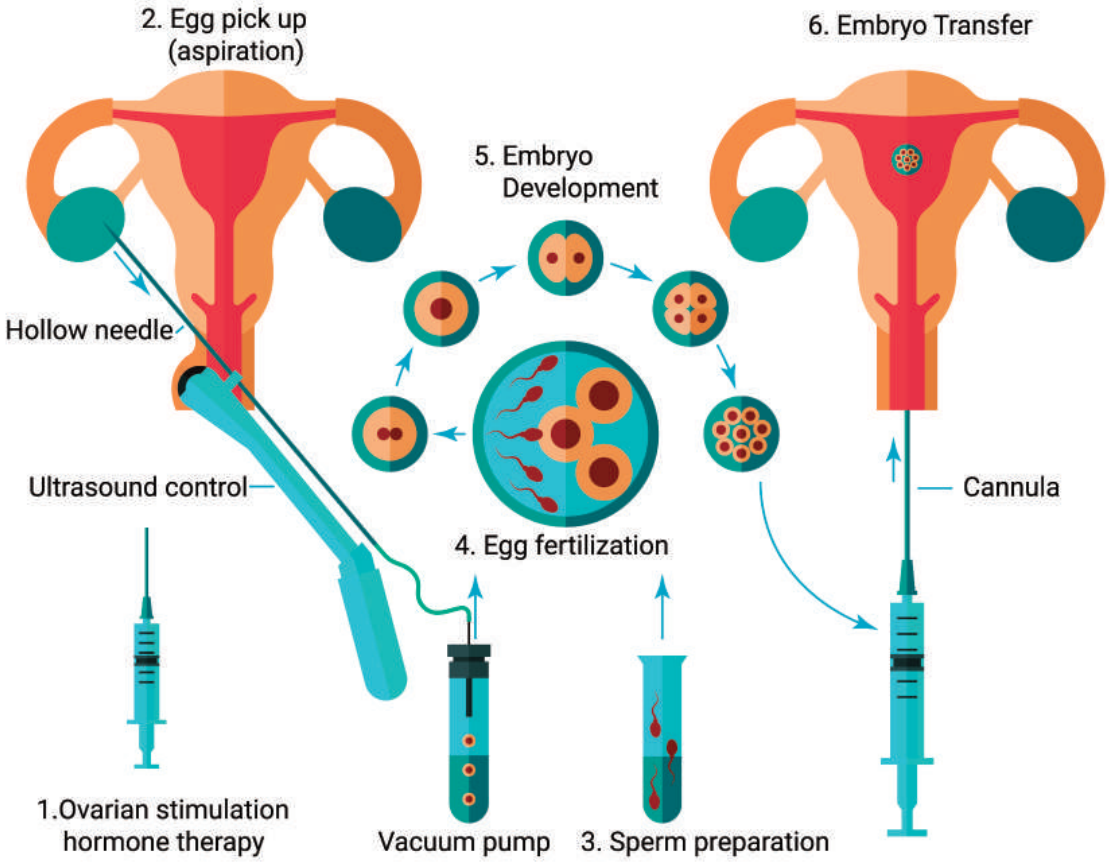
In some cases, the patient may have some side effects of dye used. Hence, this test is only to be carried out with expert doctor's presence. This is a much cheaper test, but now a days, it is done in selected patients only due to its limitations.

(3) Diagnostic Laproscopy:

In this test, a telescope like instrument is introduced within the abdominal cavity, and on the outer side of it, there is a video camera and this can also be monitored on a TV monitor in a magnified view. This is known as **video laparoscopy**. In this case, a small puncture is made near the naval area, from where a telescope is inserted and outer aspect of uterus, fallopian tubes, and ovaries are observed directly. To check for patency of fallopian tubes, blue coloured dye called methelene blue dye is injected inside the uterus and we can see dye coming out from fallopian tubes (if tubes are normal) by this procedure. Using this procedure, the other end of fallopian tube and its relationship with ovary also can be seen clearly.

By other type of telescope, which is insereted through cervix the inner walls of uterus can also be checked and treatment also can be carried out simultaneously, if there is a problem in uterine cavity. This kind of endoscopy is known as **Hysteroscopy**.

The laparoscopy procedure is a blessing to infertile couple. But the equipment is costly, and it requires special training. The patient has to get admited for one day in the hospital. Though it is a



In Vitro Fertilization

minor procedure, it needs to be done under general anaesthesia to make patient comfortable during and after procedure. So after doing all basic investigations and if no result is achieved, then only this test is advised.

The main advantage of this procedure is that, if any treatable problem is found during procedure, treatment is also possible at the same time.

TREATMENT OF BLOCKED FALLOPIAN TUBE:

(1) Surgery

In some cases, this defect is since birth while in majority of cases, it developes afterwards. Mainly this is due to an infection in the uterus and surrounding structures. One of the important reasons in our country for this is Genital Tuberculosis. In some cases after abortion (termination of unwanted pregnancy or miscarriages), specially when done after 10-12 weeks, tubal blockage occurs due to infection.

In very few cases, blocked fallopian tubes can be corrected by tubal microsurgery. If the tube is stuck somewhere, it can be released (adhesiolysis). But in every case, we do not get success, and microsurgery requires some special training. The operation is costly, and sometimes, even when tubes are opened after the operation, there are chances of partial blockage, leading to pregnancy in the fallopian tube itself, known as “Ectopic Pregnancy” which, if undiagnosed and untreated can be dangerous for the patient.

If hydrosalpinx is found with tubal blockage, the tube is de-linked from the uterus by laparoscopic hydrosalpinx clipping procedure to increase IVF success-rates in subsequent IVF cycle.

(2) Assisted Reproductive Technique:

In common language, this is popularly known as Test-Tube Baby. In this technique, the eggs are fertilized with sperms outside the female body, in a special embryology laboratory, the fertilized egg (embryo) is transferred into the uterus. This procedure bypasses function of fallopian tubes. So, if fallopian tubes are blocked, by using this technology, the chances of conception are far more than surgery to open the blocked fallopian tube. When IVF technology was invented, it was used mainly for patients with blocked fallopian tubes, but now this treatment is offered to patients with all other reasons of infertility too.

Chapter 10

Fertility Treatments For Advanced Age

More than 20 percent of couples have difficulty in conceiving a child. The recent tendency to delay childbearing in order to pursue a career has led more women in their late 30s and early 40s to attempt conception for the first time. Higher education, careers, misinformation or lack of information regarding technological advancements, financial constraints, improper guidance and many more reasons contribute to couples not having children at the "proper age" as per our Indian scenario. Studies have demonstrated that almost 70% of women over the age of 40 will experience infertility. Because fertility in women decreases with advancing age, prompt evaluation and aggressive treatment are critical in infertile women over the age of 40.

FERTILITY AND AGE

There is a consistent decline in fecundity (the chance to conceive in any given month) with increasing age. The average 25 year old woman, who is trying to conceive may have a 25% per month chance for pregnancy, if all fertility factors are optimal. Compare this with the 5% per month chance for conception that the average 40 year old woman has. This age associated decline in fertility (and increase in miscarriages) is largely due to abnormalities in the egg itself. High rates of abnormal chromosomes distribution are a major factor that can explain a lower rate of successful pregnancies in older women.

When reviewing treatments for infertility, one must consider success ultimately, in terms of a baby being born. In addition to decreasing fecundity, older women experience an increasing incidence of miscarriages. Women over age 40 have approximately a one in three chance of having a miscarriage in any given pregnancy. In addition at age 40, one in sixty live births are genetically ab-

normal.
With this in mind, it seems reasonable to promptly evaluate women over 35, who are concerned about fertility. Due to increased incidence of genetic abnormalities, women over age 40 should be counseled about prenatal genetic testing such as chorionic villus sampling, nuchal translucency screening, amniocentesis or double/Triple marker testing.

PATIENT EVALUATION

The usual trial period of one year of attempting conception prior to an infertility evaluation may not be appropriate for women who are above 35 years of age. A basic infertility evaluation is indicated for any couple who have been attempting conception for six months if the woman is approaching the age of 35.
Laboratory and other tests should include:

• A semen analysis for the patient's partner.
• Evaluation of ovarian reserve (Antral follicle count-AFC) by transvaginal sonography of ovariesand AMH on 2nd day of period.
If above all reports are normal, and patient wants to continue with the routine treatment, diagnostic laparoscopy to rule out tubal patency and hysteroscopy to see for normalcy of endometrium is a must .
The basic evaluation should be performed over a period of one month in women approaching 40 years of age, rather than spreading it over a number of cycles. Any abnormalities that are uncovered in the basic evaluation should be corrected promptly.

OVARIAN RESERVE

To predict an individual woman's fertility rate, in addition to her age, both clinical and laboratory methods are available to evaluate ovarian reserve. The best tests are direct measures of the ovary, such as the Antral Follicle Count (AFC) and Anti-mullerian Hormone (AMH) level; indirect measures, such as clinical history and levels of pituitary hormones, are common tools for prediction of ovarian reserve.

AFC: Antral follicles are the smaller follicles, (between 2 and 10 mm), seen in the ovary, with transvaginal sonography that are lost as a woman ages. In younger women, the AFC is 10-20, declining by 5% per year through age 37, and then accelerating to a loss of 10% per year thereafter.
AMH: Anti-mullerian hormone (AMH) is a blood test that directly measures ovarian reserve.It is produced directly by early stage ovarian follicles. High levels (over 2.0) are favorable, while low levels (less than 2.0) indicate decreased ovarian reserve. AMH may be the best measure of the menopausal transition and ovarian age. It may also be useful in predicting the effects of chemotherapy on ovatrian functions and in determining the treatment of PCOS too.
AMH seems a superior predictor of ovarian response compared to other markers, including age, and day 3 FSH and estradiol. It offers similar predictive value compared to AFC. AMH can be drawn at any time in the menstrual cycle, and is not affected by hormonal therapy, including oral contraceptives.
The ultimate test of ovarian reserve is response to treatment and whether a pregnancy results from that treatment.
Risk factors for early loss of ovarian reserve include smoking, family history of early menopause, shortening menstrual cycle interval and previous ovarian surgery.

TREATMENT

If the evaluation is normal, or if abnormalities have been corrected and the patient still does not conceive in a short period of time, aggressive therapy is indicated.
Treatment options for age-related infertility include controlled ovarian hyperstimulation with in-

trauterine insemination (COH-IUI), IVF and egg donation.

1) Controlled ovarian hyperstimulation with intrauterine insemination (COH-IUI)

COH-IUI increases the chance to conceive in any given cycle. They cannot improve egg/embryo quality. COH-IUI involves taking fertility medication to increase the number of mature eggs released in a given cycle and the placement of washed sperm into the uterine cavity at the time of ovulation. This treatment has limited success in women over forty and older, with delivery rates of less than 5% per cycle. We do not advise the use of ovulation induction medicine Clomiphene in women over 40 years of age due to its limited effectiveness.

2) IVF

For couples with tubal disease, endometriosis, or sperm abnormalities, as well as couples with unexplained infertility who want to accelerate their chance for pregnancy, IVF is an appropriate procedure. Pregnancy rates with IVF are higher than from COH-IUI, but do decline significantly with increasing age.

Treatment strategies with IVF for older women include

- More aggressive stimulation protocols,
- Assisted hatching of embryos,
- Replacing more embryos at the time of embryo transfer
- Preimplantation genetic diagnosis (PGD) may help to decrease the rate of miscarriages in this group of older patients by excluding the transfer of genetically abnormal embryos.
- Blastocyst embryo transfer (allowing embryos to develop longer outside the body before replacement) has also proven more successful in older women, who have more than 4 good quality day 3 embryos.

Egg Donation

Egg donation has become an accepted and successful technique to achieve pregnancy in older women. Studies show that a pregnancy rate of over 60% per cycle can be expected in patients, who are aged 40 and older. This treatment is the only treatment available to improve egg/embryo quality in older women.

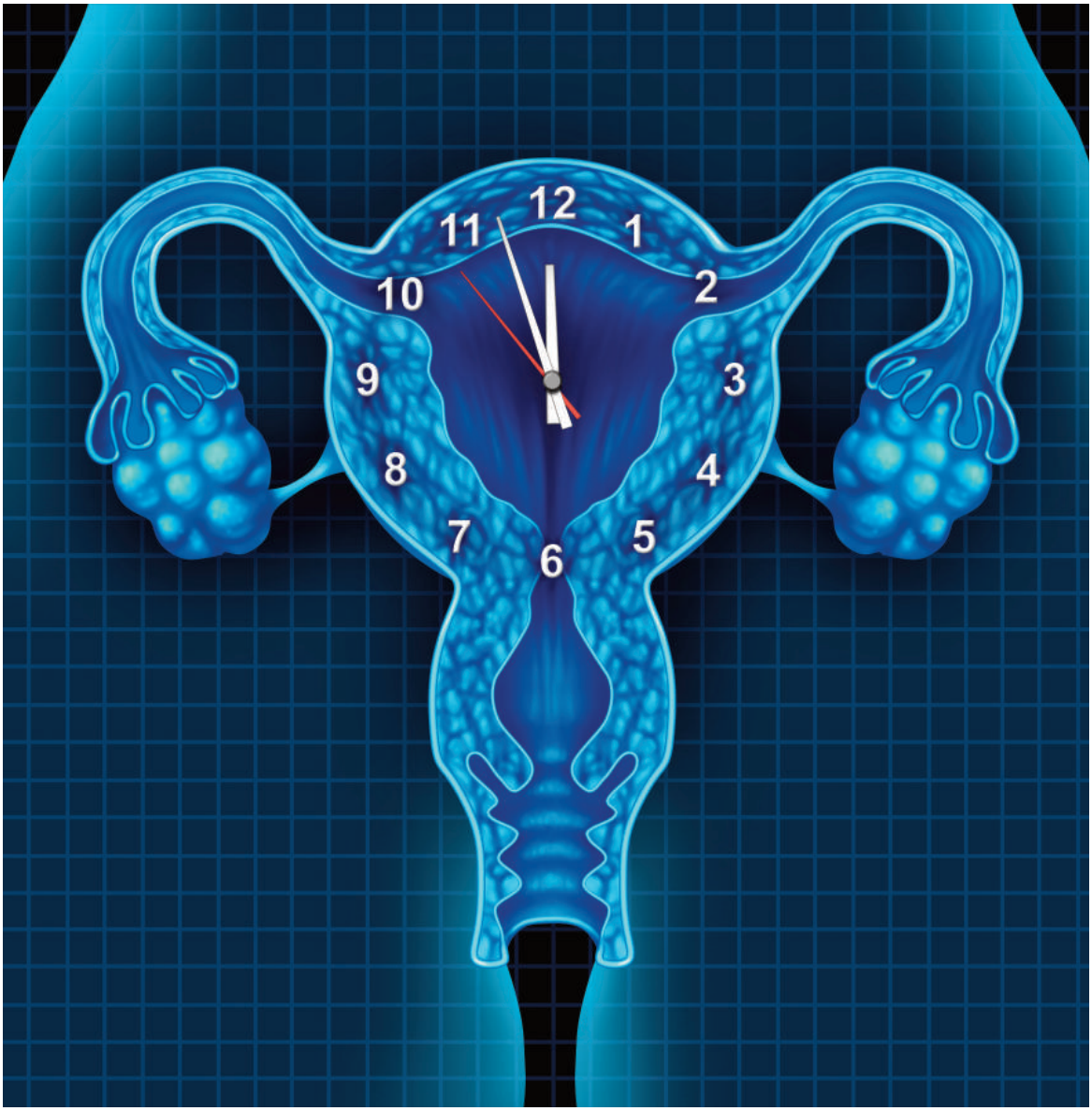
Egg donation involves preparing the patient's uterus with estrogen and progesterone to create an optimal uterus for implantation. An egg donor undergoes hormonal stimulation to produce multiple eggs. The eggs are retrieved with a minor surgical procedure of egg retrival and fertilized with the patient's husband's sperms.

So, positive things with this treatment are, firstly, the sperm is obtained from the patient's husband, and therefore the child is genetically his and secondly, since the pregnancy develops inside the patient herself, she has control over such factors as nutrition, smoking, and drinking during the pregnancy - control she would not have in the case of surrogacy or adoption.

Finally, the woman experiences the positive feelings of pregnancy and delivery and is able to breast-feed her baby. Thus, Egg Donation may be the best medical option for women over the age of 40, who have repeatedly failed other fertility therapies, as well as for women with an elevated FSH and low AMH level.

RECOMMENDATIONS

- One approach to therapy for the infertile woman aged 40 and over who has a normal evaluation, good AFC and normal AMH is to first try one or two cycles of COH-IUI. This may give the patient a small chance of conceiving and also al-



lows the physician to evaluate ovarian response for a future IVF cycle. In addition, it helps the patient to get used to the idea of an aggressive, "high-tech" approach. For the patient who desires the highest chance for pregnancy with her own eggs, IVF is a more successful treatment.

• If the patient does not conceive with COH-IUI. IVF is a next possible step. If her ovarian response is suboptimal, her embryo quality is very poor, or she does not conceive with 1-2 IVF cycles using her own eggs, egg donation should be considered.

• For a patient with an AMH level of less than 1.0, or a day 3 FSH greater than 14 should be offered egg donation as the best medical option.

DRAWBACKS IN IVF TREATMENTS IN OLDER WOMEN

1) Children born to 40 + women with her own eggs, are not always but more prone to genetic disorders such as Down's syndrome. Genetic abnormalities may also lead to unsuccessful IVF cycles and miscarriages following IVF.

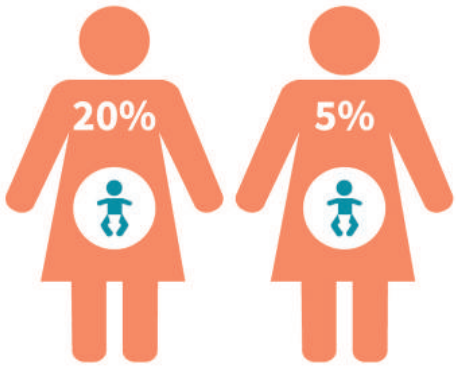
2) With the advanced age, the egg shells start thickening, hence making fertilization and implantation of embryos difficult (Thick Zona).

3) Ageing moms to be have more chances of developing pregnancy induced Hypertension and gestational Diabetes during their IVF conceived pregnancies. But regular checkups, proper antenatal care by expert obstetricians and medications can take care of all these problems and these women can reach up to full term pregnancies safely and deliver a healthy baby.

Recently a news report showed that an Indian woman aged 70 underwent IVF through donor gametes and gave birth to a healthy child… such news gives renewed hope to many women wanting to experience child birth. Though debate is still going on, whether a woman should really bear children at that age and whether it is morally right or not, but with advanced technology, nothing is impossible.

UNDERSTANDING FERTILITY

WOMEN CONCEIVING VIA IVF ARE 30-35% MORE LIKELY TO HAVE MULTIPLE BIRTHS



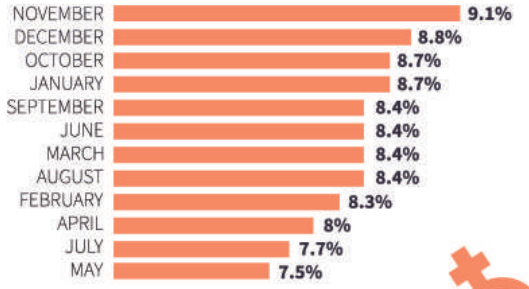
>30 YEARS <40 YEARS

HOW MUCH CHANCE DO WOMEN HAVE TO HAVE PREGNANT EACH MONTH?

5 MILLION BABIES
HAVE BEEN BORN USING IVF
SINCE THE WORLD'S FIRST IN 1978

600%
RISE IN WOMEN 40+
SEEKING IVF SINCE 1978

WHEN MOST BABIES ARE CONCIEVED?



WHAT IS INFERTILITY

<35 UNABLE TO CONCEIVE IN 1 YEAR OF TRYING

>35 UNABLE TO CONCEIVE IN 6 MONTHS OF TRYING

90 000 000
THE NUMBER OF COUPLES AROUND THE WORLD EXPERIENCING FERTILITY PROBLEMS

FERTILITY TIPS

- LOSE WEIGHT
- QUIT SMOKING
- EXERSIZE
- EAT HEALTHY
- RUN LABS

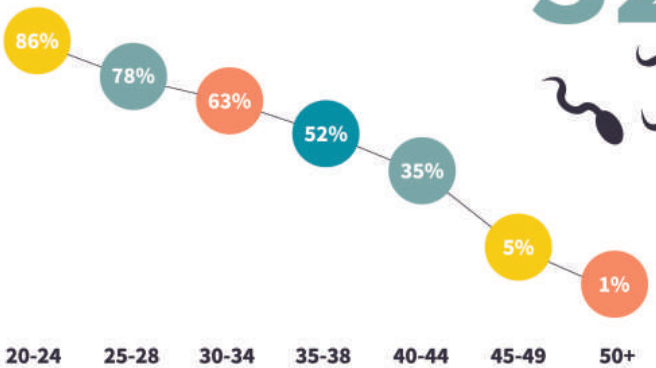
3 OF 7 WOMEN NEED 3 IVF PROCEDURES TO GET PREGNANT

THE AVERAGE SPERM COUNT FOR A MAN IN HIS 30'S HAS DECREASED BY

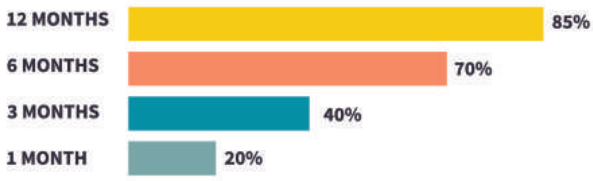
32%

AVERAGE AGE FOR THE FIRST CHILD

FERTILITY BY AGE



TIME TO CONCEIVE



Chapter 11

IVF Treatment With Donor Eggs

WHEN TO CONSIDER?

Prior to the development of in vitro fertilization (IVF), no options were available for women with premature ovarian failure or diminished ovarian reserve or genetically transmittable diseases to achieve motherhood. But, now the latest artificial reproductive technology using donor eggs is a wonderful treatment option for older women and women with ovarian failure, and those with diseased ovaries or genes to make their dreams of motherhood real.

WHO ARE THE APPROPRIATE CANDIDATES FOR DONOR EGG IVF?

• ***Premature Ovarian Failure (POF):***
The primary indication for egg donation was originally for women with premature ovarian failure (POF), defined as menopause occurring before the age of 40 years.
POF affects approximately 1% of the female population; in effect, this condition indicates depletion of a woman's own eggs and cessation of ovarian function at a young age.

• ***Women over 40***
In recent years, the major indication for egg donation at most IVF centers has been for women with

diminished ovarian reserve but with intact ovarian function. It has long been known that, women over 40 years old have reduced fertility in general, and a poorer chance for success after IVF.

• ***Other potential candidates for egg donation include:***

Women who have previously failed multiple IVF attempts, particularly when poor egg quality is suspected, and women carrying transmittable genetic abnormalities, which could affect their offspring (this latter indication has declined with the development and use of pre-implantation genetic diagnosis, or PGD).

TESTING OF THE PATIENT (EGG RECIPIENT)

Women considering using egg donation should undergo a medical evaluation including a complete history and physical examination, to assure that their health would not be significantly jeopardized by pregnancy. It is also important to seek and correct any abnormalities, which could otherwise compromise the success of IVF with donor eggs. Such testing should generally include a transvaginal sonography and hysteroscopy to assess normality of the uterine cavity and uterine linings and a semen analysis to rule out a coexisting male factor.

If the recipient has RH-negative blood type, some precautions are needed in chosing egg donor with specific blood group.

A uterine sounding (trial transfer) may be performed to determine the uterine depth and how easily an embryo transfer catheter can be passed through the cervix.

TESTING OF AN EGG DONOR

A thorough evaluation or screening of each potential egg donor is of critical importance, whether the donor is known to a recipient (e.g., a sister or a friend) or is anonymous. This screening should serve to protect all parties involved (the donor, the recipient and the resulting offspring).

Briefly, the donor should generally be younger than 35 years old, with laboratory evidence of normal ovarian reserve and no indication of impaired fertility. She must undergo testing for sexually transmitted infectious diseases (eg, hepatitis, HIV, HCV) and specific blood tests to prevent certain genetic diseases in offspring (eg, sickle cell disease, thalassemia).

PREPARATION OF THE RECIPIENT

Effective synchronization of the recipient's uterine lining maturation (endometrial thickness) with the growth of the donor's follicles and eggs and the resulting embryos are keys to the success of egg donation. Recipients require treatment with estrogen and progesterone supplements to align their cycle with those of the egg donors. Intact ovarian functions of menstruating recipients are often pre-suppressed with a medication such as Leuprolide prior to the initiation of estrogen. Recipient usually takes oral estrogen or transdermal patches from 2nd day of menses for two weeks, typically on a dosage designed to mimic the natural cycle. Recipient takes vaginal progesterone capsules or cream or injections daily, starting the day of the donor's egg retrieval or in case of frozen cycle, as soon as her endometrial thickness achieves desired changes in sonography. The embryo transfer is done three to five days later. Following the transfer of one or more embryos, the recipient continues treatment with both estrogen and progesterone until her pregnancy test, which is on 14th day of embryo transfer. If pregnancy test on 14th day shows positive results, pregnancy is supported with estrogen and progesterone till the 12th week of pregnancy.

RISKS TO THE RECIPIENT

As the recipient does not undergo ovarian stimulation or egg retrieval, she is not exposed to the potential risks of these procedures (e.g., ovarian hyperstimulation syndrome). The age of the recipient, even if over 40, does not affect pregnancy rates. It is important that the number of embryos transferred be limited, generally to no more than two or three embryos for a day 3 transfer or two embryos if transferred on day 5, at the blastocyst stage to avoid risk associated with multiple pregnancy in older patients.

Other theoretical risks to the recipient include transmission of infectious diseases such as HIV; it is unknown whether eggs can transmit the AIDS virus, and, to date, no cases of HIV transmission through egg donation have been reported. Nevertheless, meticulous screening of potential egg donors is critical.

FACTS YOU SHOULD KNOW…

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Chapter 12

Repeated Miscarriages

Around one percent of all women experience recurrent miscarriages. Doctors define this as - *Loss of consecutive two or more 1st trimester or early 2nd trimester pregnancies.*

Having one miscarriage can be very much disturbing for the couple, but having one after another is often a very traumatic experience. Any future pregnancies will be full of hope but also tinged with a high level of anxiety. Investigations to find out possible reasons for recurrent miscarriage is advisable after the third recurrent miscarriage, but if a patient's age is more than 30 years, she is advised to go for investigations to find out the reason of her repeated miscarriages. Unfortunately, even after all investigations, it's not always possible for doctors to identify the cause for recurrent miscarriage. However, most couples who have had recurrent miscarriages have a good chance of having a baby in the future.

CAUSES OF RECURRENT MISCARRIAGE

1. Hormonal: In some cases an imbalance in reproductive hormones can lead to conditions such as polycystic ovaries, in which due to high levels of LH (luteinising hormone) and testosterone, chances of miscarriages are more. Many times Thyroid dysfunction can be the cause of RPL.

Diagnosis: Short luteal phase duration, PCOS diagnosis by sonography, Prolactin and TSH (thyroid stimulating hormone) measurement, anti thyroid antibodies.

Treatment: Supplementation of vaginal or injectable progesterone, or correction of egg production by ovulation induction drugs; correction of other hormonal or medical problems as indicated.

2. Blood clotting disorders (auto immune diseases): Some blood clotting disorders, such as systemic lupus erythematosus and antiphospholipid syndrome can cause 'hypercoagulation status of blood' and recurrent miscarriages, which affect the flow of blood to the placenta and may cause clots that prevent placenta from functioning properly, depriving the baby of essential oxygen and nutrients, which may lead to miscarriage.

Diagnosis: ACA (anticardiolipin antibody), Lupus Anticoagulant test.

Treatment: Low dose Heparin therapy, Folate Supplementation, Low-Dose Aspirin (ASA) steroids etc. No Proven established value of IVIG (Intraveous Immunoglobulin), WBC immunizations or other Immunologic treatments.

3. Genetic: In a small number of cases, one partner may repeatedly pass on an abnormal chromosome, causing recurrent miscarriage. Studies using preimplantation genetic sceening (PGS) in women with RPL have shown that more than 50% of embryos were found to have aneuploidy (an abnormality of chromosome).

Diagnosis: Parental Karyotypes (a blood test) which detects chromosomal problems in both partners.

Treatment: Preimplantation genetic diagnosis (PGD) using IVF technology or IVF using donor sperm or donor egg depending upon involved gamete.

4.Uterine problems: An abnormally shaped uterus or thick wall splitting the uterine cavity (Septate uterus) or intra-uterine adhesions can increase your risk of recurrent miscarriages and premature birth.

Diagnosis: Hysteroscopy or hysterosalpingogram (HSG)

Treatment: Hysteroscopic resection (removal) of abnormal septum, polyps or fibroids, Hysteroscopic adhesiolysis of intrauterine adhesions and in severe non-treatable problems, use of a gestational carrier (surrogate) to carry a future pregnancy.

5.Cervical weakness: With this problem, repeated abortions occur in late 1st trimester or early 2nd trimester.

Treatment: Cervical encircalage (Os tightening procedure) in next pregnancy, before 20 weeks.

6. Male Factor:

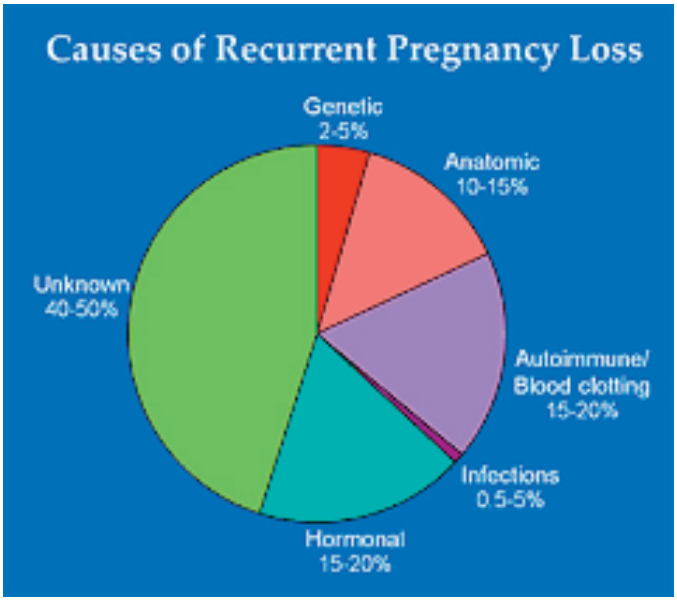
Recent evidence suggests that abnormal sperm DNA may affect embryo quality and increase the miscarriage rate.

Diagnosis: Karyotype (genetic blood test) which detects chromosomal abnormalities, Sperm DNA fragmentation tests.

Treatment: No definitive treatment has been proven, anti-oxidants may be of some value, PGD of embryos, donor sperm.

7. Diminished Ovarian Reserve:

As a woman ages, so do her eggs. So eggs quality and quantity decline with age and so the embryos produced by these eggs have more chances of genetic abnormalities and the chances of a spontaneous abortion in the first 3 months of pregnancy increases.



Diagnosis: Day 2 Antral follicles count by transvaginal sonography and blood AMH level.

Treatment: Tab DHEAS (may or may not be be of proven benefit), IVF with own or donor eggs is the best option.

ENVIRONMENTAL INFLUENCES

Though environmental causes may not lead to repeated miscarriages, they may increase chances of abortions.

Smoking and alcohol increase miscarriage rates. Low Body Weight and obesity has been shown to increase miscarriage rates. Coffee in moderation (<3 cups/day) does not increase miscarriage rates. If the mother smokes or consumes alcohol excessively, there are many chances of miscarriage.

Diagnosis work up:

1. Blood reports: Hormonal levels, blood tests to rule out certain infections and immunology workup by anti phospholipid antibody tests.
2. Chromosomal study of male and female.
3. Chromosomal study of abortus in selected cases.
4. Hysterosalpinography or hysteroscopy to study of size and shape of uterus.

WHAT ARE YOUR CHANCES OF HAVING A HEALTHY BABY?

If your miscarriages are unexplained, then you have a good chance of having a successful pregnancy in the future. You'll be looked after very carefully and given extra support and scans from the beginning of your pregnancy by your expert

obstetrician.

This close tender loving care (TLC), itself can increase your chances of a successful pregnancy. About three quarters of women who have unexplained recurrent losses have a healthy baby eventually with the right support and care.

If you or your partner have a chromosome problem that's causing the miscarriages, it is hard to say what your chances of having a healthy baby are, if you just keep trying. Some problems are not passed on every time you conceive. For further councelling you'll be referred to a genetic specialist.

Many conditions that cause recurrent miscarriages are treatable. Your gynaecologist is the best person, whom you can about your chances of success. The overall chances of a pregnancy are good, even without treatment a woman has a 60-80% chance of conceiving and carrying full-term pregnancy.

RECURRENT ABORTIONS AND IVF TREATMENT

• Infertility experts may recommend preimplantation genetic screening (PGS) with in vitro fertilization (IVF) treatment. This allows the medical team to screen all available embryos for any genetic abnormalities and to select cytogenetically normal embryoes, which are transferred in the uterus to avoid bad news again.

• Some times repeated miscarriages are because of chromosomal abnormality in one of the partners, then IVF with donor eggs or sperms is the best solution.

• If the cause of RPL is severe auto-immune disese or abnormality in shape of the uterus, then a couple can have a baby with help of surrogacy treatment.

Chapter 13

Surrogacy Treatment

MOTHERHOOD CAN ALSO BE GIFTED

Surrogacy means something different to each person it touches. For intended parents, it is the chance to finally complete their family and realize their dream of parenthood. For surrogates, it is the chance of a lifetime to give the incredible gift of life to another family who needs it and of course a great financial security for themselves. For both parties, surrogacy is an extraordinary journey and a deeply rewarding experience.

WHAT IS GESTATIONAL SURROGACY?

Gestational surrogacy is an ART procedure, wherein eggs from the intended mother are fertilised with the intended father's/donor's sperm or donor eggs are fertilized with intended father's sperms and then these embryos are placed in the uterus of the other woman, who carries the baby to term and delivers it. In this case, the biological mother (genetic mother) is still the woman whose eggs are used, while the surrogate is called the birth mother.

FOR WHOM IS SURROGACY A BOON?

Couples opt for surrogacy when traditional means of conceiving a child have failed, including in-vitro fertilisation, or it is dangerous or life-threating for the woman to get pregnant and give birth.

WHAT SHOULD BE KEPT IN MIND WHILE SELECTING A SURROGATE?

- The surrogate mother is healthy and ideally between 21 and 40 years old (preferably she should be less than 35 years).
- Other than general fitness levels such as blood pressure, sugar levels, thyroid, etc., one should check for the the mental health of the surrogate.
- It is also advisable that the surrogate should

have given birth to at least one healthy baby before opting for surrogacy.

• Any of your close friend or relative can also become a surrogate, if she fulfills the above criteria.

BEFORE STARTING SURROGACY TREATMENT, KNOW THE PROCESS INVOLVED

• After a mutual satisfactory selection has been made, initial medical evaluation including both physical and psychological screenings of surrogate is done.

• Evaluation of the surrogate mother's uterus by transvaginal sonography and if needed, by hysteroscopy is done

• Blood work to screen for infectious disease, including HIV, Hepatitis, HCV and other necessary blood tests of surrogate mother are done.

• Legal contracts are signed, which clearly mention that the fertilized eggs (embryos) will be transplanted into surrogate mother's womb and she will have to take responsibility to carry biological parents baby/babies till delivery as a surrogate mother. All expenses right from conceiving pregnancy to delivery will be paid by the intended parent. Even if a baby is born with congenital abnormality or is still born, the surrogate mother will not be responsible and the couple will have to share all responsibilities.

Even in untoward situations like severe life-threatening complications related to pregnancy or delivery, it will be the couple's responsibility to help surrogate and her family financially up to a certain amount. Most of the centres get health insurance of surrogate.

• Next phase is the IVF process, which begins on a timeline convenient for both the carrier and the intended parent.

Every surrogacy is different, and each surrogate may walk away from her experience with different benefits and rewards. However, each surrogacy is life-changing, and there is something to be gained from every journey.

INDICATIONS OF SURROGACY

The following medical conditions usually necessitate surrogacy:

• Malformation of uterus or severe infection (eg endometrial tuberculosis) or endometrial adhesions leading to thin endometrium, which is not corrected by any medicine or operative procedures.

• Absence or removal of womb by hysterectomy

• Recurring miscarriages

• Repeated failure of IVF

• Other serious medical conditions that make impossibe for a woman to carry pregnancy, such as severe heart disease,liver diseases or bleeding disorders or certain auto-immune diseases.

A gestational carrier is a woman who carries a pregnancy for another woman. This alternative is available for parents who are unable to bear their own children.

Before discussing pros of surrogacy for surrogate mothers, let's know cons (though fewer than pros) related to surrogacy.

The cons of surrogacy may include:

1. A lengthy and medically invasive process for the surrogate mother.
2. Anxiety on the part of everyone involved.
3. Monetary costs for the intended parents. The average cost of surrogacy can be very high.
4. Guilt on the part of the surrogate mother for giving up her baby.

WHAT ARE THE BENEFITS OF SURROGACY FOR THE WOMEN WHO HELP THEM ACHIEVE THIS GOAL?

Here are some of the main ways surrogacy can benefit these amazing women, mostly from poor, weaker socio-economic class of society and their families:

• Surrogates enjoy a deep sense of personal satisfaction and pride knowing they have helped another family in such an incredible and life-altering

way.

• Women who choose surrogacy are able to share their pregnancy journey with the intended parents and develop a strong bond throughout the process. Many surrogates develop lasting relationships with the families they help create.

• Surrogates involve their family members, friends, and other supportive people in the process and are able to set a wonderful example of selflessness and generosity for those around them.

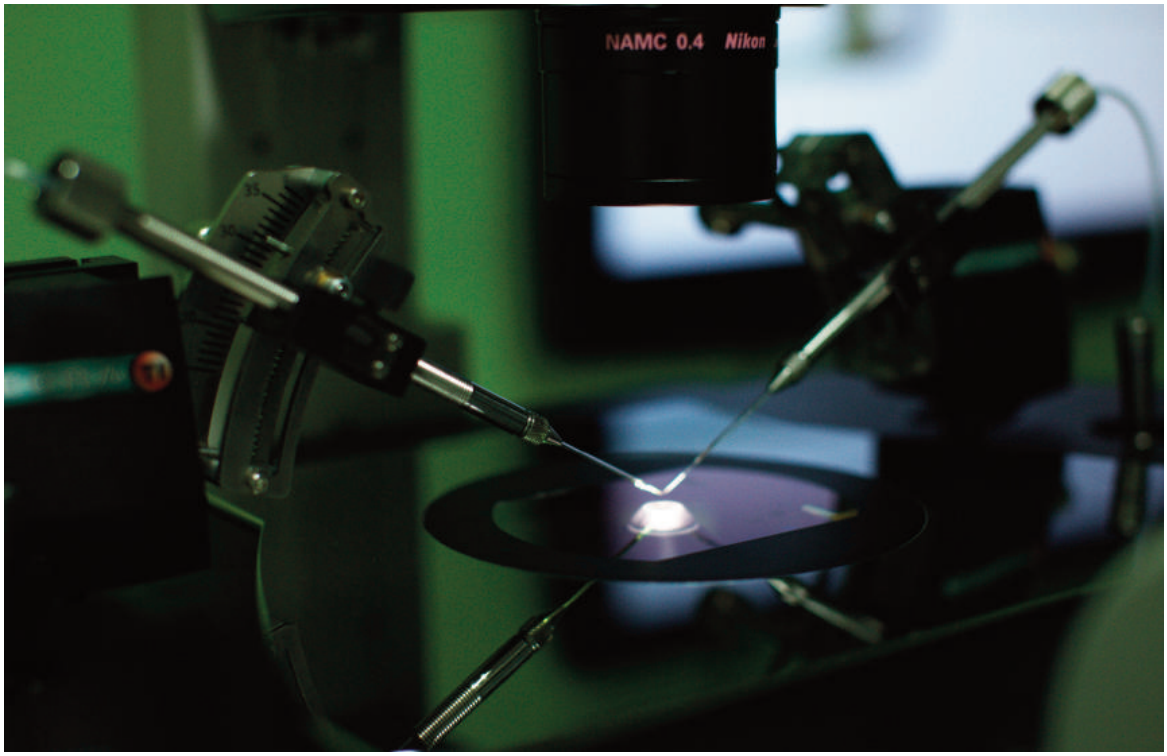
• All of the surrogate's expenses are paid for and reimbursed throughout the pregnancy, and she will enjoy a variety of services throughout the process, including best the best of healthcare.

• Main advantage to our Indian surrogate is that, she receives a huge compensation that can be applied to her financial goals, such as money to get a new house or expenses for school /college education for her own children or for costly medical treatment of a diseased family member.

The ultimate reward… The women who choose surrogacy agree that seeing a completed family at the end of their journey is the ultimate reward that makes it all worthwhile… Yes, motherhood can be gifted!

Chapter 14

Recent Advances That Make In Vitro Fertilization More Successful Than Ever...



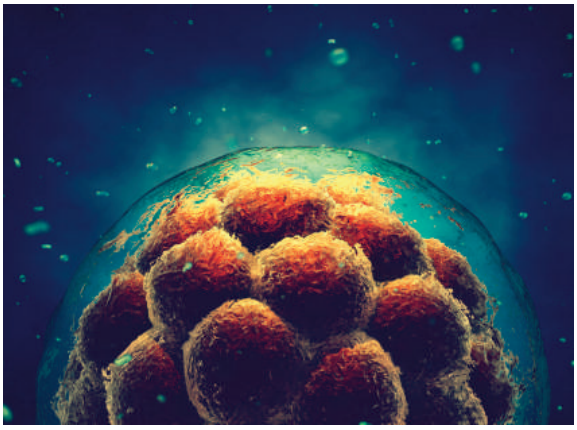
We could make a baby in the laboratory (Test-tube baby) after the revolutionary invention by a few great researchers. IVF (Test Tube Baby) was the ultimate treatment for many infertile females with blocked fallopian tubes to make their almost impossible dreams real. After getting extraordinary success with this technology, to overcome other difficult problems related to childlessness, scientists tried to develop something new out of it and so next the steps were ICSI and TESA for severe male infertility and surrogacy treatment for those unlucky patients, who were having absent uterus due to congenital or acquired conditions. And this is not the end of innovative ideas and inventions made by the experts in this field. The journey of latest inventions in the field of IVF is still continuing.

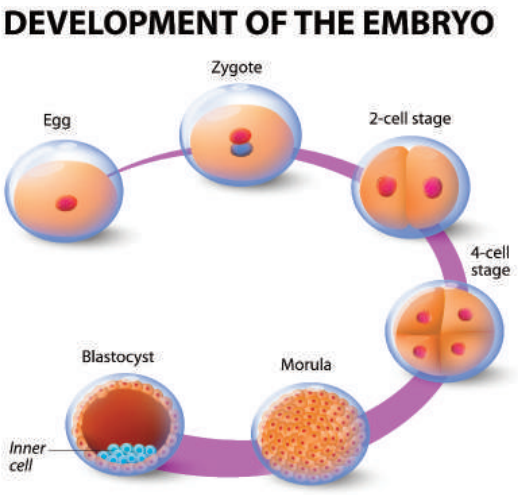
Whatever success we are achieving through these modern artificial reproductive technologies, we are yet to discover reasons for implantation failure (Implantation is a process of embryos to get attached with uterine endometrial linings for further development as a baby in the uterus) and thereby IVF treatment failure, which we get in 35-40% of patients.

Even after offering the best efforts from our side, we don't achieve 100% success. And to overcome such problems related to IVF failures, new technologies are continuously developing.

1. BLASTOCYST EMBRYO TRANSFER

Traditionally, in an IVF cycle embryos were transferred to the uterus on second or third day of development. We are aware that day three embryo transfers are too early when compared to what





happens in naturally conceived pregnancies. In a naturally conceived pregnancy, the embryo reaches the uterus on day four or five because it grows and divides in the fallopian tube for several days after fertilization.

A blastocyst is an embryo that has developed in culture in the IVF laboratory for at least five days after egg retrieval, the stage when in natural cycle also, implantation takes place in uterus. A healthy blastocyst should hatch from its shell (zona pellucida) by the end of six days or earlier and is then ready to begin to implant within the lining of the uterus.

There are now abundant evidences that transferring blastocyst embryos into the uterus five or six days after egg retrieval, results in higher implantation rates per embryo transferred compared to a day three embryo transfer. It is believed that the improved implantation rates following a blastocyst transfer are due to selection of the "best" embryos.

Why Blastocysts are better than Day 3 embryos?

• Allowing embryos to develop an additional two days in the laboratory gives us more discriminatory power to select the embryos with the highest developmental potential.

• Replacing the embryos five to six days after fertilization allows the embryos to arrive in the uterus at a more physiological time (with natural conception- the embryo does not implant until about six days after fertilization).

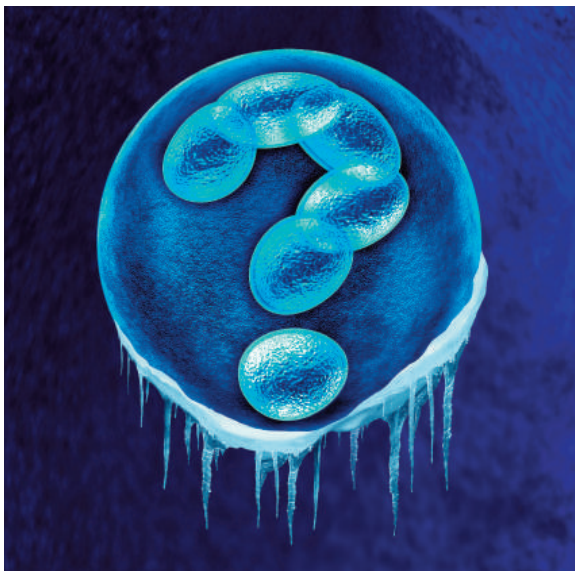
Blastocyst transfer may be of particular benefit for patients who develop many good quality embryos and want to limit their risk of a multiple pregnancy by transferring fewer embryos with higher potential for implantation. Blastocyst Embryo transfer is performed either on day 5 or 6 following egg retrieval.

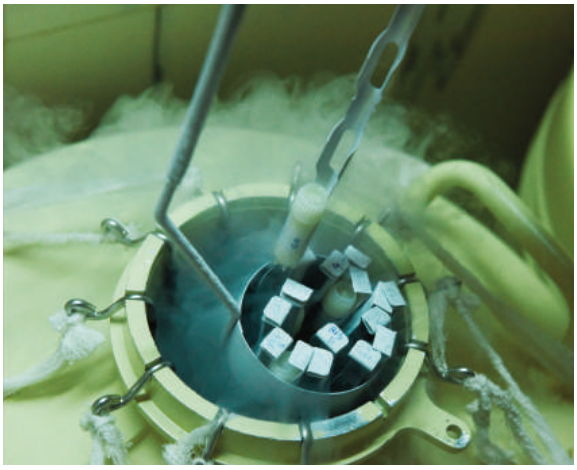
A possible risk with attempting a blastocyst transfer is that in very few cases, none of the embryos may develop to the blastocyst stage (an average of 35-40 % of fertilized eggs develop to the blastocyst stage); therefore, there would be no embryos to transfer. It is generally felt that, if no embryos develop to the blastocyst stage in the laboratory then they would most likely not have become a pregnancy if they were replaced into the uterus at an earlier time.

Most of the IVF centres do Blastocyst transfers only in those patients having more than 5 or more 8 cell good quality embryos on the third day after egg retrieval. Patients should not expect that a large number of blastocysts (or any) may be available for freezing for future treatment.

2. EMBRYO FREEZING BY VITRIFICATION TECHNIQUE

A frozen embryo transfer (FET) is a cycle in which the frozen embryos from a previous fresh IVF or donor egg cycle are thawed and then transferred back into the woman's uterus.





There is much confusion about the ability of frozen embryos to produce pregnancy. Frozen embryo transfer success has improved dramatically over the last several years. In the past, chances for pregnancy with frozen embryos using "slow freezing" method, seemed to be lower than the transfer of fresh embryos. More recent data however, suggests that this is no longer true.
In recent years, the success with frozen embryo transfers (FET) has increased substantially using the latest freezing technique of "vitrification", making it an increasingly popular option to consider before moving to another fresh in vitro fertilization (IVF) cycle. With frozen embryo transfers, you can extend the chance of pregnancy per egg retrieval - ultimately saving you time and money, if you happen to need multiple cycles to achieve pregnancy.
Frozen embryos remain viable for an infinite amount of time after the initial freeze. You may choose to do an FET cycle following an unsuccessful fresh IVF cycle, or after a successful fresh IVF cycle if you're ready to expand your family in future.
The success rates of an FET cycles are comparable to fresh IVF cycles and sometimes result in a higher success rate because of the opportunity to optimize the lining of the endometrium before implantation. Both fresh and frozen cycles have the same primary indicator for success: the maternal age at the time of embryo freezing.
Many patients wait several years between the initially freeze of their embryos and attempting a subsequent FET cycle. Any patient, no matter the amount of time between embryo freezing and thawing, can expect nearly the same potential for success as they experienced with the fresh IVF cycle, from which the frozen embryos came from.

Benefits of Vitrification

• *Lower cost*

As in this cycle we don't have to stimulate patients by hormones and we don't have to do any procedures, cycle cost is reduced to almost half of the fresh cycle.

• *Less Medication and pain*

Instead of hormonal injections, patients use estrogen and progesterone to prepare the endometrial lining of their uterus for implantation of embryos after the embryo transfer. Since the stimulation phase was done in a prior cycle, there is also no egg retrieval requiring anesthesia.

• *Less Stress*

Frozen cycles are often less stressful than fresh cycles because factors like stimulation response, egg development, and embryo growth were considered during the fresh cycle.

• Prevention of ovarian hyperstimulation symptoms in PCO patients, who produce more eggs in fresh cycles.

3. ASSISTED EMBRYO HATCHING USING A LASER

Laser-assisted embryo hatching is a technology which helps embryos to attach to the womb of the mother. This is especially useful in patients with a history of repeated IVF failures. Pregnancy cannot occur unless the embryo hatches. Assisted hatching is used to help the embryo

hatch from its protective outer shell (the zona pellucida), and promotes implantation in the uterine wall after embryo transfer.

What is laser hatching?

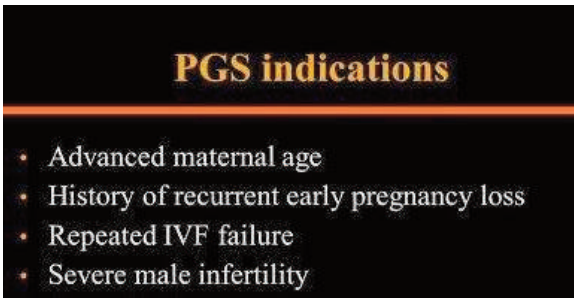
• The laser has allowed the precision to manipulate the embryos to enhance fertility.

• Assisted hatching is a technique where a gap is made in the shell or "zona" of the embryo prior to the embryo transfer.
• The idea is that this small slit in the shell of the embryo improves its ability to hatch out of the shell after it forms a blastocyst

Who will benefit from Assisted Laser Hatching?
1) Advanced maternal age (>37 years old).
2) Patients with elevated Day 3 follicle stimulating hormone (FSH) or low AMH.
3) Patients who require a high dose of gonadotropins due to poor ovarian response.
4) Thick and/or abnormal egg shell.
5) Poor quality/slow developing embryos.
6) Embryos exhibiting excessive fragmentation.
7) Patient with 2 or more previous failed IVF cycles.
8) In Frozen-thaw cycles which may have hardened shell (zona) of embryo.

Pregnancy rates
Pregnancy rates for in vitro fertilization procedures with assisted hatching have been shown in some published studies to be higher than for IVF without hatching.
It is possible to damage embryos with hatching and lower the pregnancy rates. Therefore, it is essential that if assisted hatching is done, it must be expertly performed by properly trained embryologists.

(4) PRE-IMPLANTATION GENETIC SCREENING/DIAGNOSIS



The most important advance in IVF over the past several years involves embryo biopsy and genetic analysis, which help address the challenge of embryos that look good in the lab, but turn out to be chromosomally abnormal. Having too many or too few chromosomes than normal increases miscarriage rates and the likelihood of problems like Down Syndrome.
Traditionally, fertility experts chose the embryos to place in a woman's uterus according to a grading system based on their appearance. But even top-rated embryos can turn out to have chromosomal abnormalities. Using this new techniques, we now safely biopsy a few cells from each embryo with help of **laser**, send them to genetic laboratory for genetic screening, and freeze all embryos while waiting for results.
What we learn, allows us to select only chromosomally normal embryoes for transfer, rather than relying on their appearance alone. This reduces the risk of miscarriages by about half.
In addition, couples at risk of having a baby with a genetic disease, such as Tay-Sachs, Cystic Fibrosis, or Sickle Cell Anemia, may undergo IVF to have their embryos genetically diagnosed and substantially reduce the odds of transmitting the disease to their children.
We are having detailed information on PGS (pre-implantation genetic screening) and PGD (pre-implantation genetic diagnosis) in next chapter.

5. ENDOMETRIAL RECEPTIVITY ANALYSIS (ERA) FOR RECURRENT IMPLANTATION FAILURE

The ERA test sheds light on a little known cause of implantation failure - the failure of the embryo to attach (or implant) to the endometrial linning of the uterus.
For those who suffer repeated implantation failures after frozen IVF transfers, the ERA test offers a new hope. The Endometrial Receptivity Assay is an advanced, personalized, genetic diagnostic method, developed by fertility experts in Spain, that evaluates a woman's endometrial receptivity from a molecular point of view.

How it is done?
In this test, endometrial biosy is taken by a minor office procedure, on the elected day of previous cycle, in which endometrium is prepared by estrogen and progesterone treatment. This biopsy material taken from the endometrial tissue is sent for molecular diagnosis to analyze the expression levels of 236 genes related to the status of endometrial receptivity using RNA sequencing. Following the analysis, a specific computational predictor classifies, the endometrium as 'Receptive' or 'Non-Receptive' and calculates the most receptive days for implantation and according to the result, frozen embryo transfer day with maximum implantation potential is selected for next cycle.

How it works?

In a natural cycle, the endometrium is receptive to the implantation of embryos between days 19 and 21 of the menstrual cycle, or five to seven days after ovulation. If the endometrium is not receptive during this time frame, the embryo may be 'out of sync' with the uterine lining and transferred at the wrong time during IVF. The ERA test improves the chances of success for patients by determining the right time to transfer a frozen embryo based on the individual patient's uterine wall receptivity.

Chapter 15

Advanced Genetic Testing in Assisted Reproductive Technology

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One of the primary reason for a low rate of pregnancy in females with advanced maternal age who adopt assisted reproductive technique is high incidence of numerical chromosomal abnormality in embryos. It is mainly for this reason that most of the embryos do not develop fully and therefore contribute to failed pregnancy events. With time a wide range of tests have eventually developed in the domain of assisted reproductive technology all of which singularly aim in improving the rate of pregnancy and birth of a normal child in infertile couples. For them who run the risk of having a child with harmful genetic condition that might have remained in any or both the parents in subdued form, pre-implantation genetic diagnosis or PGD is a viable and useful option.

WHAT IS PGD (PRE-IMPLANTATION GENETIC DIAGNOSIS)?

PGD involves use of in-vitro fertilization (IVF) technology to retrieve eggs from a patient's ovaries and fertilizing each of them with sperms but in a laboratory away from the human body. After days of incubation these embryos are carefully tested for common and harmful genetic defects (PGD) and thereafter the normal ones are used for implantation.

One of the most important advantages of PGD is avoiding termination of pregnancy due to the fetus being affected with serious conditions since

they are pre checked using advanced genetic techniques. Examples of disease screened through PGD process are beta thalassaemia, sickle cell anaemia, and cystic fibrosis.

WHAT IS PGS (PRE-IMPLANTATION GENETIC SCREENING)?

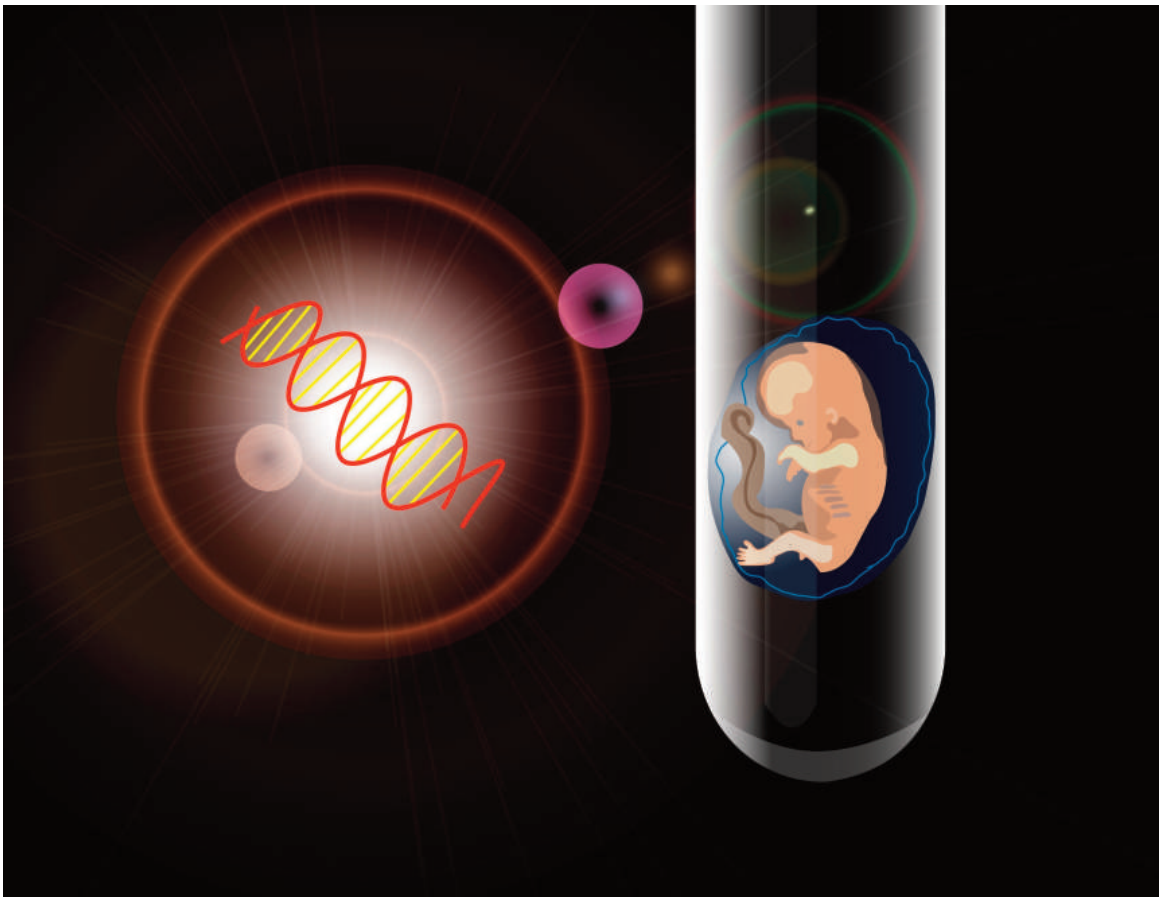
Preimplantation genetic screening or PGS on the other hand is an approach to identify genetically healthy embryos with special regard to the correct number of chromosomes. This method has the potential to increase the probability of a healthy pregnancy virtually across all age groups. Examples of diseases screened by PGS include Down syndrome (Trisomy 21), Edward syndrome (Trisomy 18) and Patau syndrome (Trisomy 13).

In reality, all pregnancies run the risk of harboring defect or abnormality in the chromosomes. In fact, half of the human fertilizations are believed to carry the wrong number of chromosomes in them thus leading to miscarriages. However, this risk increases dramatically with age. Men produce millions of sperms inside their body on a daily basis but women are born with all their eggs within them which are either to be used or naturally destroyed. Hence female eggs '*age*' unlike sperms and hence lose their potency to make healthy babies with age. As a women ages, so do her eggs. This is the main reason why a woman's age is highly critical and an important parameter to consider for getting pregnant.

HOW IT IS DONE?

For both PGS as well as PGD, eggs are collected from a woman and fertilized during an IVF cycle. Following this, a single or few cells of the embryos which are now growing in the laboratory incubator is/are removed with help of laser and subjected to further analysis. In case of PGS, the correct number of chromosomes within these cells are studied using sophisticated technologies such as microarray or next generation sequencing and the normal embryo(s) with desired chromosome numbers are transferred to the uterus to achieve a pregnancy.

On the other hand, in case of PGD, the precise genetic defect that is known in prior as well as confirmed in parents or siblings are directly tested in the cells isolated from the embryos and the one that shows absence of this defect is identified for



implantation.

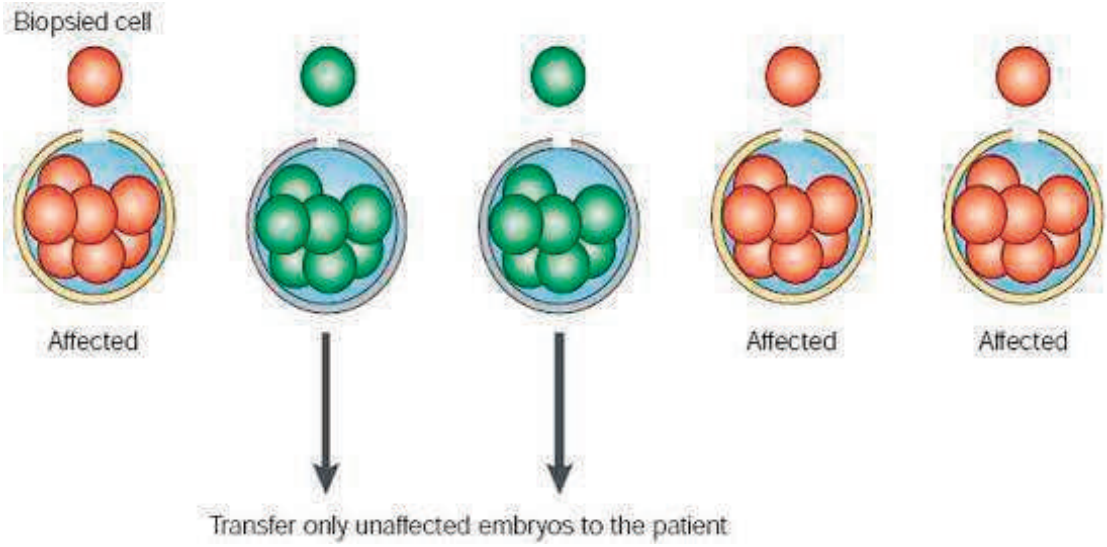
In PGS all chromosomes are screened for their proper number and structure while in PGD precise and known defects are checked to decide selection of embryos for implantation.

DIFFERENT TECHNIQUES FOR PRE-IMPLANTATION GENETIC TESTING

Rapid screening of embryos for PGS is made possible due to the fast evolving technology in the area of medical genetics. Presently, four different technology platforms are employed to screen for defective chromosomes in embryos. These are,

- Next Generation Sequencing (NGS),
- Array Comparative Genomic Hybridization (aCGH)
- Single nucleotide polymorphism microarrays (SNP)
- Quantitative real time polymerase chain reaction (qPCR)

NGS and microarray being the most popular ones. Assisted Reproductive Technology has proved itself to be a boon to couples suffering from infertility and hence cannot conceive by simpler treatments. With recent developments in science and technology the birth rates through assisted reproductive technology is gradually matching that of natural conception and there is a convincing check in emergence of genetic malformations. In this scenario, the supportive role of advanced genetic testing such as PGS and PGD is undisputed and acknowledged to be of immense significance in contributing to the overall success of assisted reproductive technology.



Chapter 16

Repeated IVF Failures WHY ME?

Motherhood is a blissful experience no matter the challenges every woman has to go through. And this is the reason, IVF (in-vitro fertilization) has become a boon for most infertile couples. But in some cases, there are repeated IVF failures. Instead of losing hope, knowing about the causes of it beforehand goes a long way.

Here is an equation that we can use to illustrate the implantation process:
Embryo quality + receptivity of uterine lining = chance for implantation and pregnancy

• ***What is repeated implantation failure?***
When there is no positive result after at least two IVF treatment cycles with transfer of either 3-4 fresh or thawed good quality embryos in a good cleavage stage (6 or 8 cells) or 1-3 blastocysts.

• ***Why do you have repeated implantation failure?***
Often, it is not easy to find reasons to explain. It can be suspected that, failed implantation may be due to a problem with the endometrium or due to the embryo or due to a lack of co-ordination between these two, although everything appears good until transfer.

• ***Role of embryos in implantation***
We know that many human embryos will arrest (die) before day 5. Unfortunately, embryonic arrest also occurs after day 5. Some of the embryos, those we transfer that " *look good*" will die after

we put them in the uterus. It is usually a weakness in the embryo that leads to failed implantation. The cause sometimes is in the sperm or the uterus too.
Percentage of implanting embryos is greatly dependent on female age.
We see about 50% implant under age 35.
We see about 12% implant at age 41-42

• ***Causes of repeated implantation failure***

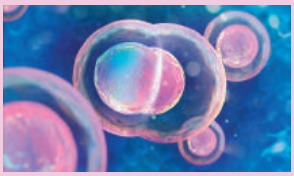
- Embryology: Good embryo development up until cleavage stage but failure at blastocyst level
- IVF treatment with own eggs at advanced age
- Difficult embryo hatching
- Difficult embryo transfer
- Anatomical problems with the uterus
- Endometrial receptivity problem
- Systemic maternal medical problems
- Genetic factors of (one of) the prospective parents

However, in many cases we cannot explain the reason for repeated implantation failure.

WHAT CAN BE DONE TO OVERCOME THIS PROBLEM?

This depends on the suspected underlying reason for failed implantation. Following are few treatment options ,which may help to overcome this problem.

WHAT IS EMBRYO HATCHING?



Hatching is the embryo 'coming out of its skin' so that it can attach itself to the lining of the womb. Normally speaking - the zonapellucida (outer cover) around the embryo is weakened and dissolved by digestive enzymes produced by the lining of the womb after ovulation. Sometimes this does not happen (efficiently) or the skin is too hard, which means it does not dissolve. In assisted hatching we help the embryo to attach by making a hole in the skin with a special laser.

• ***Laser Assisted Hatching***

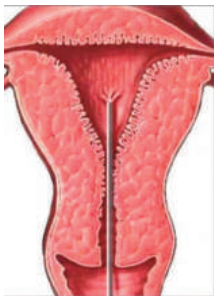
Application of 'assisted hatching', whereby the protective shell around the embryo (the zona pellucida) is thinned out at one spot with a special laser to facilitate hatching and therefore implantation of the embryo in the endometrium.

• ***Blastocyst culture*** can be performed to see whether your embryos have the capacities and qualities to survive until day 5 of embryonic development.

• ***Hysteroscopy*** to rule out anatomical problems at uterine level.

* We can do ***endometrial biopsy*** to check for any endometrial infections like tuberculosis.If we find an infection, we treat it first before starting next IVF cycle.

* ***Endometrial scratching*** can be performed



separately or along with hysteroscopy preferably in the last week of previous cycle in an attempt to augment endometrial receptivity as studies show that chances of implantation increase in cycles following endometrial scratching, as it is thought that endometrial scratching may trigger a '*repair reaction*' in the uterine lining, and that this new lining may be more receptive to an embryo implanting, therefore increasing the chance of pregnancy.

• ***Laparoscopy***

It is done to treat hydrosalpinx (swollen infected tube) by its removal (salpingectomy) or de-linking from uterine cavity (Hydrosalpinx clipping) as it is believed to be important cause of implantation failure as toxins in the hydrosalpinx fluid could have a negative influence on the embryos and it also reduces implantation potential by altering the receptivity of the uterine lining

• ***Frozen Embryo Transfer***

This is done because endometrial receptivity may be sub-optimal in a super ovulation cycle, because of all the hormones which have been injected. Because the thrust of super-ovulation is to focus on growing good quality eggs, sometimes we may not be able to optimize endometrial receptivity at the time at which the eggs are ready for retrieval. Once we have frozen oocytes/embryos, we can then focus all our energies in the next cycle on improving endometrial receptivity. This approach allows us to maximize the chances of implantation, because we are transferring good quality embryos into an optimally prepared endometrium.

• ***Endometrial Receptivity Analysis-ERA***

(Monitoring the receptivity of the lining)

In this treatment, we perform a genetic analysis

Egg cell or ovum sticking to the uterus

of biopsy taken from your endometrium, prepared by estrogen and progesterone hormones in previous treatment cycle to detect the best time of receptivity of your endometrium and embryo transfer in the treatment cycle. This is referred to as ERA Testing (Endometrial Receptivity Analysis).

• ***Pre-implantation Genetic Screening/Diagnosis (PGS/PGD)***

In cases of extreme implantation failure, if you are having normal genes in karyotyping report and your embryos are of good morphological quality, PGS can be offered. This is preimplantation screening of the embryos in the blastocyst phase. This screening checks whether the embryos are genetically normal or not as in most of the cases of recurrent IVF Failure and Repeated Miscarriages, numerical anomalies in genes are major causes.

* If it concerns a genetic abnormality in one of the parents, PGD can be offered, i.e. the genetic diagnosis of the embryos before one is transferred.

• ***Treatment for systemic diseases***

Empirical associations of medications - such as heparineor aspirin (to stop clotting) and short-term use of corticosteroid are avoided as much as possible due to lack of evidences. In specific situations they can be discussed. They can be offered to patients with systemic Auto- immune diseases like Anti phospholipid antibody syndrome etc.

• ***Egg Donation***

As a second last resort and only in extreme cases, despite a good embryo morphology, oocyte donation can be an option to help RIF patients conceive.

• ***Surrogacy***

This will be the last option. Here to increase chance of implantation, embryos are transferred to womb of other woman, who may be known to you or she can be a professional surrogate. This is particularly indicated in patients with poor endometrial lining, even after all possible medical and surgical treatments offered to improve it and in patients who are mentally and physically drained after repeated IVF failures for more than 4-5 times. Though there are cases in which we have given successful results in patients own wombs with 10 or more IVF failures.

So, as we discussed above, many advanced technologies are available to overcome the painful situation of repeated IVF Failures. With proper selection and implementation of these latest technologies, doctor and patient both will get the desired result, which will bring a ray of hope in the life of an infertile couple suffering from recurrent implantation failures.

Chapter 17

Emotions Behind Infertility & It's Treatment

First comes love, then comes marriage… we all know what comes next, right? But, what happens when it is not so easy to conceive?

Every infertile woman, who has struggled to become pregnant, knows that infertility can be a stressful, and sometimes demoralizing experience. The longer it goes on, the more intensive are the medical interventions and because of more physical, psychological, and financial stress, the experience of getting parenthood becomes worse for an individual or a couple, if they don't get the desired results.

Before the era of IVF (In Vitro Fertilization), these infertile couples would never have had a chance to enjoy all the stages of pregnancy, delivery, motherhood and parenting. The scenario now of fertility management by IVF is that every childless couple could get a chance to conceive by various methods available to treat their childlessness.

HOW FERTILITY TREATMENTS TAKE A TOLL ON MENTAL HEALTH?

Here are some of the problematic situations which may drive you crazy and disturb you mentally:

• Are you experiencing repeated IVF failures?

You might encounter multiple failures in IVF treatment cycles or can have miscarriages or premature delivery after conceiving by IVF and then don't get a baby in your hand.

• How do you feel about using donor sperms, or eggs or donated embryos or surrogate treatment to

achieve parenthood?
• Should the donor be a friend or a stranger?
• Should you screen your embryos for abnormalities by using pre-implantation genetic screening procedure?
• Should you reduce chances of high-order multiple pregnancy?
• What should you do with your leftover embryos? Will you pay an annual storage fee, donate them to another couple or for research, or have them destroyed?
• How do you feel about freezing your eggs/embryos for future use?
• Will your religious beliefs affect these decisions?
Not only does a woman's mental health and sense of self worth suffer, but often marriages can similarly be negatively impacted by repeated inability to conceive.

HERE ARE COMMON QUESTIONS SURROUNDING THE ROLE OF MENTAL HEALTH IN FERTILITY.

• Is it my fault? The self-blame game of infertility
No, it is not your fault. Nor is it your partner's fault. Up to 15% of couples experience difficulty with conception, and this often heralds an intensely difficult, stressful time for a couple. On an average, women are often more negatively impacted emotionally and physically by infertility than men, though men can and often do similarly have a sense of failure and inadequacy.

• Are infertility and mental health issues connected?
Infertility is associated with and often causes many different emotional and behavioral changes. The most common include,
anger, depression, anxiety, marital problems, sexual dysfunction, social isolation, sense of loss, decreased self-esteem.
Depression and anxiety are relatively common results of infertility; up to over 50% of couples presenting for infertility treatment suffer from symptoms of depression, and roughly 25% begin infertility treatment with active symptoms of anxiety.

• Does mood impact fertility?
We now clearly see that inability to conceive may lead to disturbed mental health. But, is the opposite true? Do depression and anxiety negatively impact fertility?
There is significant debate on this topic, but overall research indicates that poor mood can impair a couple's chance of conception. Stress, anxiety and depression may modify physiological functioning, including altering levels of various hormones associated with ovulation and eventual conception such as cortisol, luteinizing hormone, and prolactin. Women with elevated biomarkers for stress, specifically cortisol and alpha amylase, and those with a history of depressive symptoms have twice the risk of infertility as compared to women without mood symptoms.

• How to improve mood in the face of infertility?
If you are experiencing symptoms of depression and/or anxiety while trying to conceive, the first thing to do is to prioritize your mental and physical health.

• Please don't be alone
You require the warmth and company of your friends and relatives - your own people, and well wishers. As a couple, you can keep yourself engaged in social life, sports, art, music, cultural events which will pull you out of your nagging negative thoughts.

• Psychotherapy and anti-depressant medicine
Addressing symptoms of depression and anxiety through various modes of psychotherapy can often improve your mental state during infertility treatment and thus increase the likelihood of a successful conception and pregnancy. If required, some anti depressant medicines are also used to keep your mind cheerful and calm.

• Online support
Those patients who are net savvy, online support exists in abundance for women struggling with conception; there are blogs, chat rooms, email lists, newsletters, and social media-based forums. As with anywhere else online, it is important to be cautious with providing too much personal information and to remember that your story may not be the same as someone else's, so always check with your doctor rather than believing what you read.

• Healthy life choices do help
In addition to addressing mood symptoms online and/or with a professional, women can also improve their chance of fertility by making healthy life choices.
• Eating a well-balanced, healthy diet full of fruits and vegetables.
• Exercising regularly.
• Trying alternative methods such as acupuncture, meditation and massage (these therapies

are not going to do any magic as far as your treatment result is concerned, but all these can relax your body and mind when you are passing through those '*stressful*' days.

• Avoiding tobacco and alcohol (This is particularly for our overseas patients).

Take care of yourself. Try to be in company of your partner. Rely on support from family and friends and consider, prioritize and nurture your emotional health during this difficult time. Almost any good habit that can enhance your physical health and well-being will likely improve the likelihood of successful conception and pregnancy.

Chapter 18

Common Infertility and IVF Myths You Should Stop Believing

Infertility and IVF (In Vitro Fertilization) or test tube baby treatment are not without their fair share of myths. Many people view IVF treatment as an expensive treatment that only movie stars and business people can afford. Some even firmly believe that IVF treatments result always in twins and triplets. Some people think that for IVF treatment, only donor gametes (eggs or sperms) are used. Let us discuss a few common myths and actual scientific facts related to infertility and IVF treatment.

Myth 1: "Infertility means you can't have a child"

Fact: Infertility means that you are unable to have a child naturally after a year of trying. With the proper treatment, many people go on to have children. A young woman can conceive naturally with even one working fallopian tube, if she is ovulating properly and the male partner has normal sperm in his ejaculate. Here the success rate may be lower than you would hope for, but it is not still zero. If you are struggling with infertility, you undoubtedly have many questions of your own - and maybe a few misconceptions also. Schedule an appointment with a fertility specialist and find out where you stand. Thanks to modern medicine, many infertile couples become parents - and that is no myth.

Myth: "Wait a year before seeing a doctor."

Fact: Regardless of whether you want to start or grow your family today or several years later, it's never too early to start talking to your doctor about your fertility. Particularly if you and your partner are aged 35 or older, if you have frequently irregular periods or ovulatory problem, such as polycystic ovary syndrome (PCOS), if you have had surgery or

other conditions that might alter your fertility, or if the male partner has reason to believe he may have a low sperm count, it's best to talk with your doctor immediately about your options.

Myth: "There is no hurry to get pregnant! Look at all the women in the news having babies well into their 40's and even 50's!"

Fact: The vast majority of women who become pregnant after their 43rd birthday have used another women's egg or even adopted an embryo to achieve conception. In addition, there are significant health risks to both the baby and the mother when she is of advanced reproductive age. These facts indicate that a woman should seek consultation from her gynecologist or a reproductive specialist as early as possible.

Myth: Infertility is exclusively a woman's problem

Fact: This is untrue. It surprises most people to learn that infertility is a female problem in 35% of the cases, a male problem in 35% of the cases, a combined problem of the couple in 20% of cases, and unexplained in 10% of cases. It is essential, that both the man and the woman be evaluated during an infertility work-up.

Myth: IVF is the only solution for all infertility problems.

Fact: False, IVF is one of the treatment options for infertility. There are other basic options like ovulation induction (OI) with hormonal medications or injections and Intra Uterine Insemination (IUI), which are used as initial treatments and majority of patients conceive with these basic treatments. IVF straight away is needed only in cases of bilateral blocked fallopian tubes, severe degree of endometriosis, elderly/menopausal patients or severe male infertility.

Myth: IVF is only for affluent people - Only rich people can afford IVF treatment.

Fact: False. Though it is expensive, the cost of IVF has not increased massively over the years. Moreover doing the same primary teatment repeatedly without success becomes ultimately even more expensive than IVF. If a patient's financial condition is very poor, sometimes the IVF centre and doctor also consider and offer treatment at an affordable price to poor patients and some centers even offer payment options by installments in collaboration with finance companies.

Myth: IVF is limited to a younger population only.

Fact: False, IVF technology can be used even in older (post-menopausal group) ladies using donor eggs from younger females.

Myth: IVF is successful in all cases. (You have 100% guarantee, that you will get a baby)

Fact: False, IVF is successful in up to 60-65% of cases in one attempt. With more attempts, most couples achieve pregnancy. Success depends on a number of other factors like age of the female, cause of infertility, expertise of the centre, formation of healthy uterine endometrial linings and proper hormonal levels, etc.

Myth: In IVF treatment, donor gametes (donor eggs or sperms) are used in all cases

Fact: Absolutely wrong.

On the contrary, in severe male infertility, where sperm count is as low as 1 million/ml or even zero, we have latest treatment & sperm retrieval technologies like PESA and TESE. This allows us to use husband's own sperms. In the past, in these type of patients, we had to use donor sperms. Now they can become a father of their own babies. In females, we can predict ovarian reserve of our patients and if declining ovarian reserve is detected timely in young patients, she can be guided to undergo IVF cycle with her own eggs as early as possible, before her ovaries stop making eggs. Thus she will get a baby from her own eggs.

Myth: IVF requires admission in the hospital.

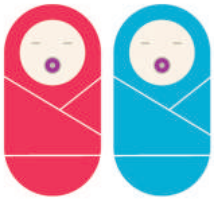
Fact: False, it does not require overnight admission. It is, by and large, an out-patient treatment. Only the egg-collection procedure (ovum pick up) requires a stay of 2-3 hours .

Even after embryo transfer, you can go home after

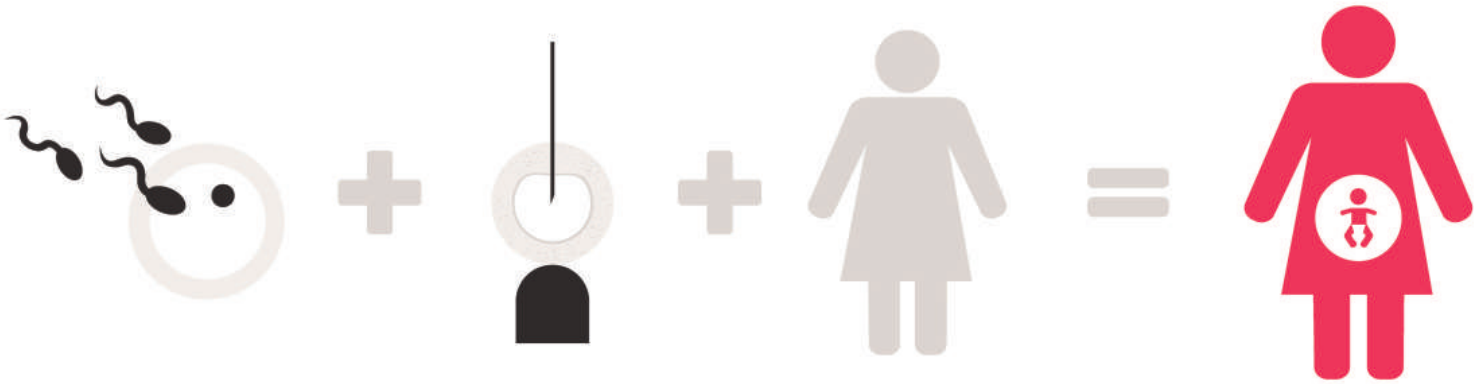
600%
RISE IN WOMEN 40+ SEEKING IVF SINCE 1978

5 MILLION BABIES
HAVE BEEN BORN USING IVF SINCE THE WORLD'S FIRST IN 1978

37% WOMEN UNDER 35
WILL GET PREGNANT AFTER FIRST IVF

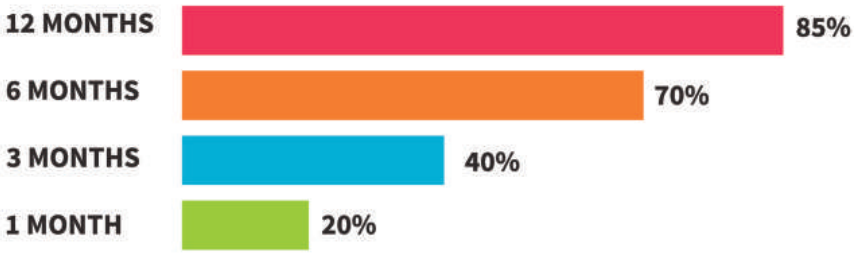


Women Conceiving Via IVF are 30-35% More Likely to have Multiple Births

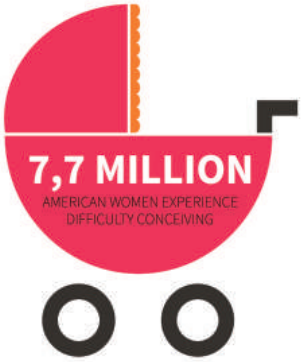


1 OF 6 FAMILIES
STRUGGLE WITH INFERTILITY

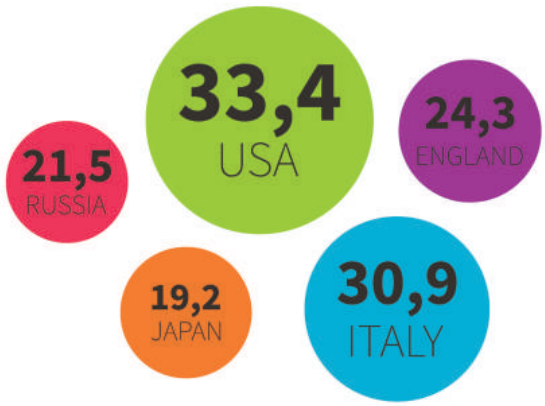
TIME TO CONCEIVE



TOP 5 FACTORS TO CHOOSE FERTILITY CLINIC



AVERAGE AGE FOR THE FIRST CHILD



taking rest for 1-2 hours at hospital.

Myth: IVF always result in multiple pregnancies like twins or triplets.

Fact: Not true, the chances of multiple pregnancies can be reduced by reducing the number of embryos transferred. As 2-3 embryos are transferred to increase the success-rates, of course, chances of twin pregnancy are 30-35%. Only 5-10% of successful patients may have triplet pregnancies.

When ever you are having multiple pregnancy, an expert sonographer or obstetrician can perform *"foetal reduction"* procedure to reduce number of baby/babies in your womb if you wish.

Myth: IVF-ICSI babies have a significantly high risk of birth defects and malformations.

Fact: Not true.There have now been many thousands of babies born with IVF and ICSI. So far, there are no facts or studies which suggest that there is any clear increased risk for birth defects in IVF as compared to conventional insemination. Most studies have shown that the risk of birth defects after ICSI is the same as for babies conceived through IVF without ICSI, and for those conceived naturally.

Male infertility, itself is known to be associated (though in very few cases) with chromosomal and other genetic anomalies. There is known to be an increase in gross chromosomal abnormalities such as balanced translocations in men with very low sperm counts. Also, about 5% of men with very low sperm counts have small areas of missing DNA on their Y chromosomes. So not IVF - ICSI procedure, but the reason of slightly higher risk of genetic/birth defect is due to underlying cause of severe male infertility.

Myth: Complete bed rest is required after embryo transfer.

Fact: There's no need to put your life on pause after the embryo transfer. This idea is an absolute myth. Actually, the scientific fact is that, women who are on bed rest for 24 hours following a transfer have a lower success rate compared with those who returned to their usual routine.

Myth: Special diets can boost your chances of getting pregnant.

Fact: There is no evidence that any specific diet (be it not eating papaya, pineapple or dates or eating any particular food) will increase your chances of success. All of our experts recommend a healthy, balanced diet full of whole grains, proteins, fruits and vegetables to maximize your health and the health of the baby you are trying to conceive through IVF. There is no single food, however, which will make you conceive.

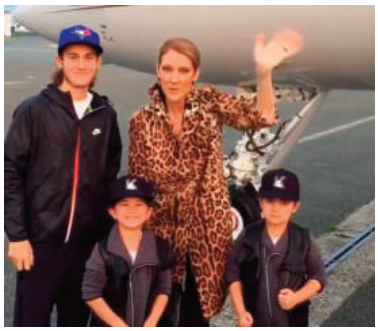
Myth: IVF is dangerous.

Fact: No, it is not dangerous. In fact, it is a safe treatment. In the past only 1-2% of patients were becoming unwell because of severe ovarian hyper-stimulation syndrome (OHSS). Now, with the use of latest hormonal stimulation protocols and expertise in embryo freezing, most of the IVF centres are OHSS-FREE.

Celebrities & their IVF Kids

Millions of couples struggle with infertility and the famous people below are no exception. Each one of these entertainment superstars have had trouble conceiving naturally and resorted to undergoing IVF treatment or artificial insemination. Because of their high profile careers and a stigma about artificial pregnancies, celebs often keep their problems with fertility, miscarriages, and IVF treatments a secret. In recent years, however, more and more entertainers are opening up about using various types of treatments and procedures to get pregnant.

CELINE DION



After six in vitro fertilization attempts, Celine Dion and her husband Rene Angélil gave birth to their son René-Charles in 2000. A decade later, the couple once again used IVF to conceive their twin boys Eddy and Nelson, born in 2010.

NICOLE KIDMAN

Nicole Kidman went through various IVF and fertility treatments before the 2008 birth of her and Keith Urban's daughter Sunday Rose. The couple's second child Faith Margaret was born in 2010 via a gestational surrogate.

MARIAH CAREY

The chart-topping singer, who had previously suffered a miscarriage, underwent IVF treatments to get pregnant. In 2011, Carey and her husband Nick Cannon welcomed their twins Moroccan and Monroe, which she famously nicknamed "Dem Babies."

BROOKE SHIELDS

Brooke Shields reportedly underwent seven IVF treatments before giving birth to hers and Chris Henchy's daughter Rowan Francis in May 2003. The couple was able to naturally conceive their second daughter, Grier Hammon, three years later.

FARAH KHAN AND SHIRISH KUNDER

Bollywood's ace choreographer and director Farah Khan got married to Shirish Kunder in her 40s. The couple tried two years for a baby. Finally, she decided to go through with IVF. Farah gave birth to triplets, on February 11, 2008. She has even suggested this procedure to many other women who were not able to conceive naturally. According to her: "When the choice is to either go childless or IVF, there is no room for doubts. I was 43 when I had my kids and my biological clock had stopped ticking long time ago."

AAMIR KHAN AND KIRAN RAO

Aamir Khan, who had two children from his previous marriage, opted for IVF procedure with his second wife, Kiran Rao. The couple was blessed with Azad on December 5, 2011. Aamir was very open about this procedure and has recommended other couples to opt for it, too.

On the birth of child, Aamir said"

"This baby is especially dear to us because he was born to us after a long wait and some difficulty. We were advised to have a baby through IVF surrogacy, and we feel very grateful to the Almighty that all has gone well."

SHAHRUKH AND GAURI KHAN

Clearing the air over all the rumours surrounding the new entrant in Mannat, King Khan and his wife, Gauri are the recent additions to this list. Much after the birth of their two kids (Aryan and Suhana), the couple also opted for IVF surrogacy, and have now brought home their third child. Shah Rukh Khan says:

"Amidst all the noise that has been going around, the sweetest is the one made by our newborn baby, AbRam. He was born prematurely by several months, but has finally come home".

SOHAIL AND SEEMA KHAN

Sohail Khan and Seema decided to have a second baby, ten years after the birth of their first son, Nirvaan. They, too, decided to consider IVF surrogacy as an option to have their second child. Their second child, Yohan, was born in June, 2011. This much-in love couple had got married in 1998.

KARAN JOHAR

Other than Bollywood Khans, Karan Johar was recently blessed by twins from surrogacy. An overwhelmed Karan said "I am ecstatic to share with you all the two most wonderful additions to my life, my children and lifelines; Roohi and Yash. I feel enormously blessed to be a parent to these pieces of my heart who were welcomed into this world with the help of the marvels of medical science." A single father Karan plans to raise his kids with the help of his mother.

DIANA HAYDEN

The ex-Miss India/World went for fertility preservation 8 years ago. She recently delivered a healthy baby girl using her own frozen eggs.

TUSSHAR KAPOOR

Tusshar Kapoor became father to a baby boy. The actor – who is unmarried – fathered the new born through surrogacy using IVF. An elated Tusshar has named the baby Laksshya. It was director Prakash Jha who inspired Tusshar to take this step. "Last year, I went to Tirupati temple. I happened to meet director Prakash Jha. We were in the same flight. He told me about this procedure (IVF) and how one could be a single parent using the same. I felt inspired and decided to go in for the same."

Courtesy: IVF India

Motherhood:
All love
begins and
ends there.

Robert Browning

" I believe that all infertile couples will benefit from reading this very well-written and comprehensive book. This book answers all the questions infertile patients normally have and this knowledge will help them increase their chances of having a baby."
-Dr Jatin Shah

" Dr. Rupal Shah has made great efforts to make a difficult subject with the latest medical information, simple to understand for the average reader... We are sure that anyone who wants to know about infertility and its solutions will find this book extremely useful"
-Dr Mitsu P. Doshi
-Dr Praful B. Doshi

Dr Rupal N. Shah

M.D (OBGYN), Diploma in Reproductive Medicine (Kiel), Germany

Dr. Rupal N. Shah is a renowned obstetrician, gynaecologist & IVF specialist of Surat.
She is the medical director of a boutique multispeciality women's health care centre of excellence "Rupal Hospital For Women" which was the pioneer of fertility care and treatment in South Gujarat since 50 years. 20,000 babies delivered by her in 23 years professional career,
Her unique experience centre "VAMA" is exclusively run "By all women consultants team – for women". A place that offers comprehensive care to women of all age groups from teenage to menopause and beyond.
She is a creator of Happy Families through Blossom IVF Centre.
Adding smiles to lives of thousands of infertile couples across the world by making dreams of parenthood real.
She has been Invited as a faculty at various academic conferences and workshops across the globe.
Her natural flair for educating patients in form of writing makes her write and edit various health awareness books and articles in various media platforms to bring awareness related to women's health problems.
She has been felicitated for her valuable contribution and exemplary work in the field of women's Healthcare for many prestigious national and state level awards.

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