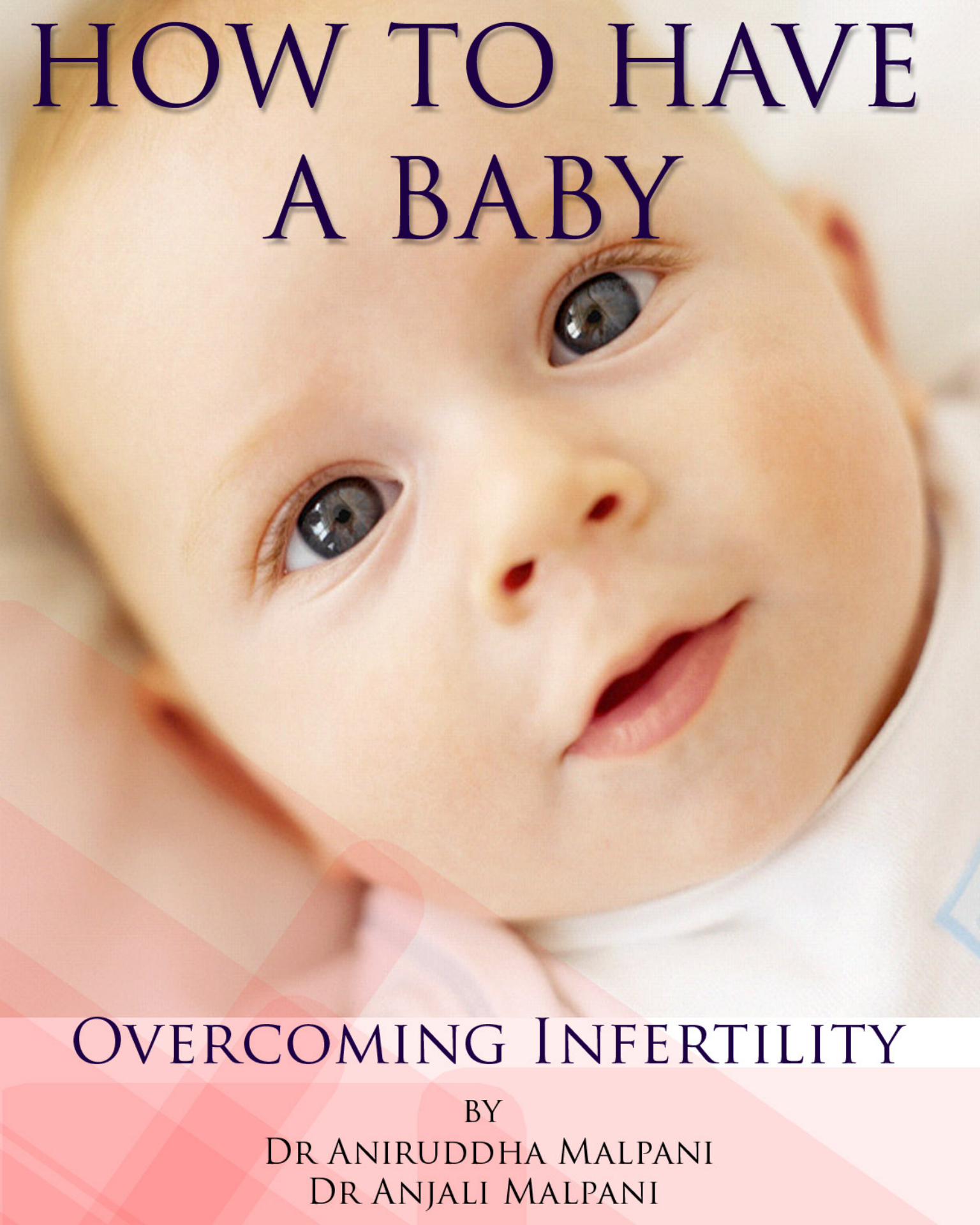


HOW TO HAVE A BABY



OVERCOMING INFERTILITY

BY

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GLOSSARY

PREFACE

Grappling with infertility is a lot like finding yourself trapped in a complex maze . You can't see what's ahead of you so you have no way of keeping your perspective . You wander the same path over and over again - totally lost and bewildered. You are alone with no one to show you the way out.

There are many questions - and few answers. Which are the best doctors ? Which is the most effective treatment ? What options can be utilised so that the way out can be found ?

This book is designed to give infertile couples a complete look at the infertility experience, to help them to negotiate their way through the maze as efficiently as possible. You need to find your own path - and this book will serve as a guide.

Infertility is a problem that affects two people – and their whole family. It brings with it fear, anxiety, anger, guilt, grief - and in the end, hope. It's a problem that reaches deep into your emotional life and invades your emotional relationship. Infertility can steal away all your energy and attention. It can also require a great deal of time and money - and can demand total commitment. It may become your obsession.

Confronting your infertility problem is a process that must be worked through - it takes time and effort. This book will show you that infertility is a difficult condition, but one which you can cope with and resolve.

The most important message of this book is that you must be an active participant in your medical treatment. You are a vital member of your medical team - the more you understand, the better you can participate in the decisions that directly affect your life. Infertility can bring on a feeling of helplessness because you cannot have a baby when you want to. An important way of regaining control is by taking an active part in resolving your infertility by being well-informed.

Why is it so important that you be well-informed ? Unfortunately, many infertile couples have had unhappy experiences, due to lack of information.

1. They may have a problem for which there may be an effective treatment but they may not receive this. Infertility for which there is no effective treatment is devastating, but infertility which is not correctly treated is the real tragedy !

2. They may not have had the correct diagnosis made.

3. Their doctor - no matter how knowledgeable - may not be putting all the pieces together correctly for them.

4. They may be receiving treatment that is actually decreasing their chances of conceiving.

5. There is a certain tolerance level which everyone has - and this limit may be financial, physical or emotional. Sometimes their tolerance may be exceeded before they receive appropriate treatment .

Most importantly, being informed may make a difference in your getting pregnant . It can help you determine if your time, effort and money are being well spent. It may also help you to know when to quit trying . An informed approach will allow you to maintain control of your life, and will help you to realise that everything within your control has been done. And even if you don't get pregnant, you will at least feel satisfied that you fully understand your condition, and that you did your best. That knowledge will be your strength.

This book can be read through from cover to cover - or you may refer to just a specific chapter, pertaining to your specific problem. We have deliberately allowed some repetition, so that chapters can stand on their own.

It is not the goal of this book to teach couples to bypass the medical care they may need . On the contrary, the goal is to educate couples sufficiently so that they can find the right doctor, and as informed patients, participate in their own care.

Our experience has been that the best patients are well-informed patients - patients who take an active part in their treatment, so that they can work with their doctor to develop an effective treatment plan. We hope this book helps to empower infertile patients, so that they can make the right decisions for themselves !

Dr Aniruddha Malpani, MD
Dr Anjali Malpani, MD

Why a new edition for the new millennium?

Reproductive technology has made dramatic advances in recent years – and pregnancy rates achieved with these techniques have improved considerably. This new edition, timed for the new millennium, has information on many exciting new areas, including: intracytoplasmic sperm injection, preimplantation genetic diagnosis, blastocyst transfer, cytoplasmic transfer, assisted hatching, egg freezing, and newer drugs such as the recombinant gonadotropins and GnRH antagonist.

Many changes have occurred in other areas as well, and these have been included in this edition. The internet can help immensely in empowering the infertile couple with information, and we have included a chapter on how infertile couples can use the Net in order to help themselves.

Many women are getting married at an older age, and quite a few are postponing childbearing in order to establish their careers. Infertility specialists are seeing an increasingly large number of older woman who would like to start a family, and we have included a new chapter on the special problems the older woman faces.

We have also included a chapter on alternative medicine, and how couples can make use of this sensibly.

Thanks to the media, many couples have become aware of advances in reproductive technology, which often make headline news. However, unfortunately, in the limited space newspapers and magazines have, they often provide a very distorted version. By focussing only on the success stories, patients often end up having unrealistic expectations of what the technology can offer them. This is why we have included a new chapter on how to critically assess newspaper stories, so that readers don't get carried away.

Unfortunately, infertility treatment has now become a lucrative small-scale industry in many cities – and patients are being exploited. Offering infertility treatment has become very remunerative – and infertility clinics are mushrooming in every town. There is a major danger of overtreatment, which is why it has become even more important for infertile couples to protect themselves – with information and knowledge! We hope this book will help them to protect themselves, so that they can find the best treatment for their problem!

Dr Aniruddha Malpani, MD
Dr Anjali Malpani, MD

CHAPTER I A

Do you have an infertility problem? When to start worrying?

"So, when are you planning to have a baby?" This is the commonest question most newly married couples in India are asked - sometimes even as soon as they have returned from the honeymoon! There is a lot of pressure on couples to have a baby, especially in traditional families, where the wife's role is still seen to be one of perpetuating the family name by producing heirs.

Many couples still naively expect they will get pregnant the very first month they try (the result of watching too many Hindi films, perhaps!) - and are concerned when a pregnancy does not occur. All of us go through a brief interlude of doubt and concern when we do not achieve pregnancy the very first month we try - and we start wondering about our fertility.

What are the chances of a normal fertile couple conceiving in one month ?

Before worrying, remember that in a single menstrual cycle, the chance of a perfectly normal couple achieving a successful pregnancy is only about 25%, even if they have sex every single day. This is called their fecundity which describes their fertility potential. Humans are not very efficient at producing babies!

There are many reasons for this, including the fact that some eggs don't fertilize and that some of the fertilized eggs (embryos) don't grow well in the early developmental stage because of a random genetic error.

Getting pregnant is a game of odds - it's a bit like playing Russian Roulette and it's impossible to predict when an individual couple will get pregnant! However, over a period of a year, the chance of a successful pregnancy is between 80 and 90%, so that 7 out of 8 couples will be pregnant within a year. These are the normal "fertile" couples - and the rest are "labeled" infertile - the medical text book definition of infertility being the inability to conceive even after trying for a year.

What is primary infertility ? What is secondary infertility ?

Couples who have never had a child, are said to have "primary infertility", while those who have become pregnant at least once but are unable to conceive again, are said to have "secondary infertility."

The approach to both types of infertility is very similar. However, patients with secondary infertility have a better prognosis, because they have proven their fertility in the past.

What are the factors which affect the chances of a normal couple getting pregnant in one month ?

The chances of pregnancy for a couple in a given month will depend upon many things, and the most important of these are:

- The age of the woman. At the biologic clock ticks on, the number of eggs and their quality starts decreasing
- Frequency of intercourse. While there is no "normal" frequency for sex, the "optimal" frequency of intercourse if you are trying to get pregnant is about 3 times a week in the fertile period. Simply stated, the more sex the better! Couples who have intercourse less frequently, have a diminished chance of conceiving.
- "Trying time" - that is, how long the couple have been trying to get pregnant. This is an important concept. The longer a couple has been trying to conceive without success, the lesser their chances of getting pregnant without medical help.
- The presence of fertility problems.

What are the factors which affect the chances of an infertile couple getting pregnant in one month ?

What happens when a couple has a fertility problem? The chances of their getting pregnant depends upon a number of variables multiplied together.

Consider a couple where both the husband and wife have a condition that impairs their fertility. For example, the husband's fertility, based on a reduced sperm count is 50 percent of normal values. His wife ovulates only in 50 percent of cycles; and one of her fallopian tubes is blocked. With three relative infertility factors, their chance of conception is 0.5 (sperm count) $\times$ 0.5 (ovulation factor) $\times$ 0.5 (tubal factor) = 0.125 , or 12.5 percent of normal.

Since the chance of conception in normal fertile couples is only 25% in any one cycle, the probability of pregnancy in any given month for this couple without treatment is only 3 percent ($0.125 \times 25 = 0.03125$)! Even if they kept on trying for 5 years, their chance of conceiving on their own would be 60% only.

Thus, infertility problems multiply together and magnify the odds against a couple achieving a pregnancy. This is why it is important to correct or improve each partner's contributing infertility factors as much as possible in order to maximize the chances of conception.

If infertile couples had 300 years in which to breed, most wives would get pregnant without any treatment at all! Of course, time is at a premium, so the odds need to be improved - and this is where medical treatment comes in.

When should you start worrying and seek medical advice?

If you have been having sexual intercourse two or three times a week at about the time of ovulation, without any form of birth control for a year or more and are not pregnant, you meet the definition of being infertile. Pregnancy may still occur spontaneously, but from a statistical point of view, the chances are decreasing and you may now want to start thinking about seeking medical help. There is no "right" time to do so - and if it is causing you anxiety and worry, then you should consult a doctor. Even though you may be embarrassed and feel that you are the only ones in the world with the problem, you are not alone. Many couples experience infertility and many can be helped.

Unfortunately, while infertility is always an important problem, it is usually never an urgent one. This often means that couples keep on putting off going to the doctor. "We'll take care of it next month". Tragically, many find that time flies, and before they realize it, their chances of getting pregnant have started to decline, even before they have had a chance to take treatment properly. Set your priorities, so that you have peace of mind that you tried your best. After all, if you don't take care of your own infertility problem, who will ? Kicking yourself when you are 50 years old for failing to take treatment when you were younger will not help. Remember that everything in life comes back, except for time!

A note of caution.....

There are certain conditions that warrant seeing a doctor sooner:

- Periods at three-week (or less) intervals
- No period for longer than three months
- Irregular periods
- A history of pelvic infection
- Two or more miscarriages
- Women over the age of 35 - time is now at a premium !
- Men who have had prostate infections
- Men whose testes are not felt in the scrotum

CHAPTER I B

Do you have an infertility problem? When to start worrying?

What can you do to improve your own fertility ?

Tips for Infertility Self-help. Before seeking medical help, remember some of the things you can do to enhance your own fertility potential.

Body weight, diet and exercise.

Proper diet and exercise are important for optimal reproductive function and women who are significantly overweight or underweight can have difficulty getting pregnant. Although most of a woman's estrogen is manufactured in her ovaries, 30% is produced in fat cells. Because a normal hormonal balance is essential for the process of conception, it is not surprising that extreme weight levels, either high or low, can contribute to infertility. Body fat levels that are 10% to 15% above normal can contribute to infertility, with an overload of estrogen throwing off the reproductive cycle. Body fat levels 10% to 15% below normal can completely shut down the reproductive process, so that women with eating disorders, such as anorexia nervosa or bulimia, or those who are on very low-calorie or restrictive diets are at risk, especially if their periods are irregular. Female athletes, marathon runners, dancers, and others who exercise very intensely may also find that their menstrual cycle is abnormal and their fertility is impaired.

Stop smoking.

Cigarette smoking has been associated with a decreased sperm count in men. Women who smoke also take longer to conceive.

Stop drinking alcohol.

Alcohol (beer and wine as well as hard liquor) intake in men has been associated with low sperm counts.

Review your medications.

A number of medications, including some of those used to treat ulcer problems and high blood pressure, can influence a man's sperm count. If you are taking any medications, talk with your doctor about whether or not it can affect your fertility. Many medications taken during early pregnancy can affect the fetus. It is important to tell your doctor or pharmacist that you are attempting to become pregnant before taking prescription medications or over the counter medications, such as aspirin, antihistamines, or diet pills.

Stop abusing drugs.

Drugs such as marijuana and anabolic steroids decrease sperm counts. If you have used drugs, discuss this with your doctor. This is confidential information. Both partners should stop using any illicit drugs if they want a healthy baby.

Limit your caffeine (tea, soft drinks and coffee) intake.

Start vitamin supplements.

Taking folic acid regularly helps to reduce the risk of the baby having a birth defect.

How often should you have sex ?

Frequency of intercourse.

The simple rule is - as often as you like; but the more often you have sex, the better your chances. Thus, for couples who have sex only on weekends (often the price they pay for a heavy work schedule) the chance of having sex on the fertile preovulatory day is only one-third that of couples who have sex every other day - which means they may take three times as long to conceive. Many couples complain that they are too stressed out to have frequent sex. Here are some simple measures you can take to increase sexual frequency.

1. Use sexual toys like vibrators or body massagers, to make sex more fun
2. Using a lubricant like liquid paraffin can help to make sex more exciting
3. Playing sex games can help – try taking turns seducing each other!
4. If you find you are too tired to have sex at night after a hard day's work, then why not have sex the first thing in the morning ? This is a great way to start the day, and you can have a quickie when you are taking a shower together !

I tell all my patients – it's much more fun making a baby in your bed room than coming to me! (And think of all the money you'll be saving – it's like being paid to make love to your wife !)

Also remember that you cannot "store up" sperm, which means that there is really no advantage to abstaining from sex if you are trying to conceive. In this case, more is better, and in fact studies have shown that fresh sperm have a better chance of achieving a pregnancy than sperm which have been stored up for many days.

How can you time baby-making sex ?

Timing of intercourse.

Unlike animals, who know when to have sex in order to conceive (because the female is in "heat" or estrus when she ovulates), most couples have no idea when the woman ovulates. The window of opportunity during which a woman can get pregnant every month is called her "fertile phase" – and is about 4-5 days before ovulation occurs. Timing intercourse during the "fertile period" (before ovulation) is important and can be easily learnt . You can use the [free fertility calculator](#) to do so. However, some couples are so anxious about having sex at exactly the right time that they may abstain for a whole week prior to the "ovulatory day " - and often the doctor is the culprit in this over-

rigorous scheduling of sex. This over attention can be counterproductive (because of the anxiety and stress it generates) and is not advisable. As long as the sperm are going in the vagina, it makes no difference which day they go in , so you can have sex daily as well, if you so desire! Just make sure you also have sex during the "fertile days" as well !

Does sexual position matter ?

Position and technique of intercourse.

Pigs are very efficient at conserving semen - the boar literally screws his penis into the cervix of the vagina, obtaining a tight lock prior to ejaculation, to ensure that no semen leaks out. Humans do not have such well-designed mechanisms of technique - and perhaps this is because they are really not necessary. Leakage of semen after intercourse is completely normal. While many women worry that this means that they are not having sex properly or that their body is rejecting the sperm, actually leakage is a good sign – it means that the semen is being correctly deposited in the vagina ! Of course, you can only see what leaks out , and not what goes in ! Most doctors advise a male superior position; and also advise that the woman remain lying down for at least 5 minutes after sex; and not wash or douche afterwards. A number of products used for lubrication during intercourse, such as petroleum jelly , K-Y jelly or vaginal cream, have been shown to kill the sperm . Therefore, these products should be avoided if you are trying to get pregnant . A safe "sperm-friendly" lubricant is liquid paraffin, which is easily available at all large chemists. While it is traditionally consumed orally when used as a laxative, when using it to make a baby you need to apply it liberally locally !

How can the older woman check her fertility potential ?

FSH level

Women who are more than 30 and who wish to postpone childbearing should get their FSH levels checked on Day 3 of their cycle. This is a simple blood test which allows the doctor to check your ovarian reserve (the quantity and quality of the eggs in your ovaries). A high level suggests [poor ovarian reserve](#) and should be a wake-up alarm that your biological clock is ticking away rapidly. It's important that this test should be done in a reliable laboratory.

What about herbal medicines which claim to improve your fertility ?

There are many websites which sell herbs and other potions which claim to improve your fertility. A popular site these days is Ovulex. Take all these claims with a large pinch of salt ! Just because your friend took wild yam and licorice and conceived in the very next cycle does **not** mean that it was the herbs which caused her to get pregnant. Often taking these herbs may cause you to waste time and prevent you from getting the right medical treatment.

How can you balance your career and fertility ?

Balancing a career and fertility

Women pursuing a career often have a hard time balancing their biologic urge to have a baby and the demands of their professional career. Unfortunately, Indian companies still do not give a high priority to family building, and many bosses frown on women employees who are trying to get pregnant, because they are concerned that this will cause them to spend more energy on their family, and detract from their ability to perform their job efficiently. For a minority, putting off getting pregnant means that their fertility declines as they age, and they often regret their earlier decision to postpone childbearing. Professionals often have a harder time coming to terms with their infertility, because this is usually the first time they are forced to confront their own biological frailty and limitations.

Which is the "right time" to plan a baby?

While there can be no simple answer to this question, remember that a woman's fertility is maximal between the ages of 20 and 30. Beyond the age of 30, fertility starts to decline; and this drop is quite sharp after the age of 35; and precipitate after the age of 38. From a purely biologic point of view, nature has designed women's bodies so that they have babies between the ages of 20 and 35. However, the right time to have a baby is a very personal and individual decision, which each couple needs to make for themselves. Public anxiety over infertility is fueled by countless magazines articles warning couples not to wait too long to start a family. We now see many patients who are "pre-infertile" , who assume they'll have trouble conceiving even before difficulties actually arise , just because they are more than 30 years old !

Has the fertility of couples declined in modern times ?

Possibly. The reasons for this include:

1. the increasing age of women at the time of marriage and childbearing
2. the increased incidence of sexually transmitted diseases or STDs which damage the reproductive tract in both men and women
3. decreasing sperm counts in men which is a worldwide phenomenon. An interesting observation made recently, has been that men's sperm counts worldwide have been falling in the last few decades . Whether this is due to environmental pollution; or to the stresses of modern day life remains unclear.

The good news is that there is definitely an increasing awareness about infertility in society today. It is no longer a taboo topic, and couples, supported by their families, are much more willing to seek medical assistance.

Where can I get help ?

The first thing you need to do is become well informed about infertility and your treatment options. This website has over 300 pages of information to help guide you !

Most couples consult their family physician who will refer them to an obstetrician - gynecologist when infertility is a concern. This first visit should include both partners . The physician will usually outline the possible causes of infertility, and provide an evaluation plan. The first step should be to achieve an accurate diagnosis to try to find out why pregnancy isn't occurring. Once a diagnosis has been determined, the couple and physician should talk again about a treatment plan. For difficult problems, referral to an infertility specialist may be suggested.

CHAPTER II A

How Babies are Made – The Basics

Every school child knows that you need eggs and sperm to make a baby. However, we need to examine the basics in greater detail , so let's start by taking a guided tour of the reproductive system.

How does a woman's reproductive system function ?

The Reproductive System of a Woman

The sexual and reproductive organs on the outside of the body are called the external genitals. There are three openings in the genital area. In front is the urethra, from where urine comes out; below this is the opening to the vagina which is called the introitus ; and the third is the anus from where a bowel movement leaves the body.

The outer genital area is called the vulva. The vulva includes the clitoris, the labia majora and the labia minora. The most sensitive part of the genital area is the clitoris. This is a pea shaped organ that's full of nerve endings since its only purpose is to provide sexual pleasure. The clitoris is protected by a hood of skin, and is the equivalent of the man's penis.

The labia majora, or outer lips, surround the opening to the vagina. They are made of fatty tissue that cushions and protects the vaginal opening. Between these outer lips are labia minora, or inner lips. These are sensitive to sexual pleasure. As they are stimulated, they get deeper in color and swell.

The vagina is a muscular tunnel that connects the uterus to the outside of the body. It provides an exit for the menstrual fluid; and an entrance for the semen. Normally flat, like a collapsed balloon, the vagina can stretch to accommodate a tampon, a penis or a baby's head. The walls of the vagina are muscular, smooth and soft. The vagina is a closed space which ends at your cervix.

The uterus, or the womb, is the place where the fertilized egg grows and develops into a baby during pregnancy. The uterus lies deep in the lower abdomen - the pelvis - and is just behind the urinary bladder. It is a hollow organ shaped like a pear and is about the size of the fist. Inside the muscular walls of the uterus is a very rich lining - the endometrium, and it is in this lining that the fertilized egg implants. If pregnancy does not occur, the lining is shed along with blood as the menstrual flow.

The neck of the uterus is called the cervix. It connects the uterus to the vagina and contains special glands called crypts that make mucus which helps to keep bacteria out of the uterus. The cervical mucus also helps sperms to enter the uterus when the egg is ripe.

The two fallopian tubes (also known as oviducts) are attached to the upper part of the uterus on either side and are about 10 cm long. They are about as big as a piece of spaghetti . Each tube forms a narrow passageway that opens like a funnel into the abdominal cavity, near the ovaries. The ends of the fallopian tubes are draped over the two ovaries and they serve as a passageway for the egg to travel from the ovary into the uterus. The tube is lined by millions of tiny hairs called cilia, that beat rhythmically to propel the egg forward. Of course, the tube is not just a pathway - it performs other functions too, including nourishing the egg and the early embryo in its cavity. Also, the sperm fertilizes the egg in one of the fallopian tubes.

The two almond-sized ovaries are perched in the pelvis, one on each side, just within the fallopian tubes' grasp. The ovary serves two functions: the production of eggs and the secretion of hormones. Each month, at the time of ovulation, a mature egg is released by an ovary. This is "picked up " by the fimbria and drawn into the fallopian tubes.

The eggs in the ovary are stored in follicles (from folliculus, meaning sack in Latin). These cellular sacks contain the eggs; as well as granulosa cells and theca cells which nurture the egg , and produce the female hormones. The ovary has about 2 million eggs during fetal life. From that point onwards, the number of eggs progressively decreases, till only about 300,000 eggs are left at the time of birth - a lifetime's stock. During the fertile years fewer than 500 of these eggs will be released into the fallopian tubes - once in each menstrual cycle. Unlike the testis which is continually churning out billions of new sperm, the ovary never produces any new eggs. One of the existing eggs is matured for ovulation each month - and this limited supply runs out at the time of menopause.

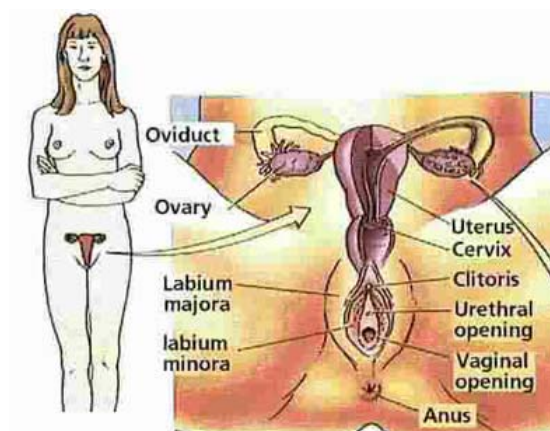


Figure 1. Female external genitalia

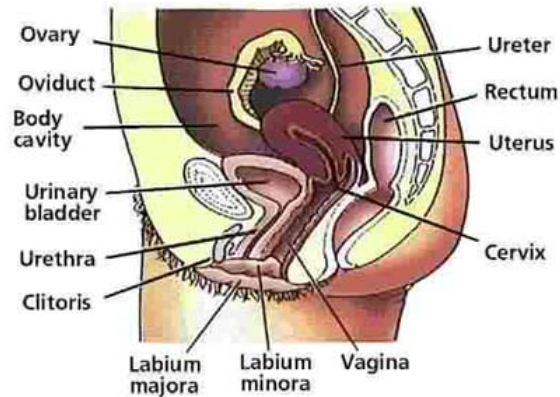


Figure 2. The female reproductive system

Can you explain the menstrual cycle and its role in fertility ?

The Menstrual Cycle

The aspect of the reproductive system that women are most aware of is the menstrual period which they have every month. The menstrual cycle is the time from the beginning of one period to the beginning of the next one. Usually menstrual cycles last about 28- 35 days, though anywhere from 3 to 6 weeks is considered normal .

During the menstrual cycle, the uterus gets ready for pregnancy. Under the influence of the hormones estrogen and progesterone, its lining grows rich and thick to prepare for the fertilized egg. If pregnancy doesn't occur, the uterus must get rid of this lining so that it can grow a new one in the next cycle. The old lining passes out of the uterus through the vagina as the menstrual flow.

The menstrual flow thus consists of:

1. the shed uterine lining
2. blood (this comes from the blood vessels which are torn when the lining is shed)
3. the degenerated unfertilised egg

If the menstrual flow is heavy, there may sometimes be clots in it. Sometimes the uterine lining is shed as large fragments - and these may sometimes looks like bits of pregnancy tissue to some women, who think they are miscarrying.

Many infertile women are obsessed with their menstrual periods, and they worry about every little variation – whether it's too dark, too light, too much or too little. However, remember that the menstrual flow has no connection to your fertility and you should not be too concerned about variations, which are quite common and of little significance.

CHAPTER II B

How Babies are Made – The Basics

How do a woman's hormones control her fertility ?

The Hormones

Reproduction is like an orchestra - and the reproductive organs need to be synchronised to perform at just the right time for them to work properly. It is the fertility hormones which play the conductor's role.

Hormones are chemicals the body makes to carry messages from one part of the body to another . There are two major female hormones - estrogen and progesterone - which are produced by the ovaries.

The cycle of ovarian hormone production has two phases. In the first half called the follicular phase, estrogen plays a dominant role. During this phase the egg matures inside the ovary in its follicle. The egg; the surrounding cells (which nurture the egg and are called granulosa cells and theca cells); and the fluid (called follicular fluid) which accumulates in progressively larger amounts during this phase, is called a follicle. The follicle secretes a large amount of estrogen (produced by the granulosa cells) into the bloodstream, and the estrogen circulates to the uterus where it stimulates the endometrium to thicken.

The second phase of hormone production begins at ovulation, midway through the cycle, when the follicle changes into the corpus luteum. This produces estrogen ; and also large quantities of progesterone throughout the second half of the cycle. Travelling through the bloodstream to the uterus, progesterone complements the work begun by estrogen by stimulating the endometrium to mature and making it possible for a fertilized egg to implant in it. In case pregnancy does not occur, production of estrogen and progesterone falls 10 to 14 days after ovulation as the corpus luteum dies, and the endometrium is shed from the body as the menstrual period.

How is the release of hormones regulated by the body ? This is a complex self-regulating system, which uses negative feedback control loops, much like a thermostat for an oven does. As the temperature increases, the thermostat shuts off the heater to reduce its heat output. When the temperature falls below the thermostat's setting, the thermostat signals the heater to turn up the heat again, thus maintaining the desired temperature. A similar signaling relationship exists between the pituitary gland and the ovaries in women; and the testes in men . For example, as the concentration of gonadotropins in the blood rises, this signals the woman's ovaries to increase hormonal output of estrogen. In turn, when the blood levels of estrogen rise , the pituitary gland slows its release of gonadotropins, thus maintaining the desired equilibrium.

Fig 5. A schematic of the hormonal changes during the menstrual cycle. The interplay of the pituitary and ovarian hormones regulate the changes which occur in the uterine lining.

How does a man's reproductive system work ?

The Reproductive System of a Man

The male reproductive system begins in the scrotum, the sack behind the penis. This contains two testicles, which make men's sex cells, called sperm; and the male sex hormone, called testosterone. The testicles feel solid, but a little spongy, like hard boiled eggs without the shell. They hang from a cord called the spermatic cord. It's normal for one testicle to hang lower than the other; and for one testicle to feel slightly larger than the other.

The testicles make sperm best at a temperature a few degrees cooler than normal body temperature. This is why nature designed a scrotum - so that the testes can hang outside the body to keep them cool.

The testicles start making sperm when a young man reaches puberty. This is in response to the male sex hormone, testosterone, which starts being produced at this time. The testes keep making sperm for the rest of the man's life.

The testes have two components, the seminiferous tubules, where sperms are produced, and the "interstitium" or the tissue in between the tubules, which contain the Leydig cells which produce the male sex hormone, testosterone, which causes the male sexual drive.

Most of the testis is composed of the tightly coiled microscopic seminiferous tubule, which if uncoiled would reach a length of 70 cm. The sperms are produced inside the seminiferous tubule, and these converge and collect into a delta (like the mouth of a river) near the upper part of the testis called the rete testis which then empties through a series of very small ducts out of the testis towards the epididymis. The epididymis is an amazing structure - it is a very long tiny tubule (about 5-6 meters long), which runs back and forth in convolutions and loops to form a tiny compact structure with a head, body and tail that sits like a cap on the top of and behind the testis. The tail of the epididymis then leads to the vas deferens - a thin cord like muscular tube, which is part of the spermatic cord and which ends at the ejaculatory duct in the prostate. Here it is joined by the seminal vesicle ducts and they all open into the prostatic part of the urethra - which in turn leads to the urethra in the penis.

Mature sperm take about 75 days to develop in a process called spermatogenesis which takes place in the seminiferous tubules. The primordial germ cells in the testis, called the spermatogonia, which are "immortal" stem cells, divide repeatedly to form primary spermatocytes. These undergo meiotic (reduction) division to form secondary spermatocytes, which differentiate to form spermatids, which then ultimately mature to form spermatozoa. Sperm production takes place as though it were on an assembly line - with the more mature sperms being passed along toward the center of the tubule from where they swim towards the efferent ducts of the testis towards the epididymis. The spermatogenic cells are supported and nourished by large cells called the Sertoli cell, which help to support sperm maturation. This can be a very "temperamental" assembly line - things often go wrong, causing low sperm counts.

When the sperm leave the testis, they are not yet able to swim on their own. They acquire the capacity to do so in their passage through the epididymis - which is like a swimming school for the sperm. They spend between 2 to 15 days here during which they attain maturity and fertilising potential. Sperm are propelled along this tunnel by frequent contractions of its thin muscular wall. Most of the mature sperm are then stored at the end of the epididymis - where they wait to be rushed through the vas deferens and ejaculated at the time of orgasm.

CHAPTER II C

How Babies are Made – The Basics

What happens during ejaculation ?

During ejaculation, the epididymis and vas deferens muscles contract to propel the sperm into the ejaculatory duct. Here the sperm is joined with the secretions of the seminal vesicles and prostate gland (which contribute the bulk of the seminal fluid) to form the semen. The powerful muscles surrounding the base of the urethra then cause the semen to squirt out of the penis at the time of orgasm. Semen and urine never mix in a healthy male (even though the final passage for both is common) because the bladder sphincter muscle contracts during sexual stimulation, thus closing down the exit from the bladder to the urethra during ejaculation - preventing urine from leaking forward out of the bladder during sex and also preventing semen from accidentally going backward into the bladder.

What about the penis and fertility? Most men equate their fertility potential with their virility - and therefore the size of their penis. However, the size of the penis has little to do either with fertility potential or with sexual ability. (In any case, if you worry that your penis is too small, you're not alone - most men think their penises are too small!)

During ejaculation, about one teaspoon of semen spurts out of the penis. Semen is a milky white color, the consistency of egg white. Sperm account for only about 2 to 3% of semen. Most of it consists of seminal fluid - the secretion of the seminal vesicles and the prostate gland, which provide a vehicle for the sperm into the vagina.

A normal ejaculation contains 200 to 500 million sperm. How can so many sperm fit into only a teaspoon of semen? Simple - sperm are very tiny. If one average ejaculation filled an Olympic size swimming pool, each sperm cell would still be smaller than a goldfish. Sperms are the smallest living cells in the human body - and the egg the largest. Basically, sperms are designed so that they can deliver their contents - the male genetic material - to the egg. This is why they are designed like projectiles - the male DNA is in the chromosomes in the sperm head nucleus, and the tail propels the sperm up towards the egg. Sperm are also very fragile. Men make so many because very few survive the swim through the female reproductive system to fertilize an egg. Perhaps the reason for this is an evolutionary hangover. Female fish deposit eggs on the sea-bed. This is why male fish need to produce millions of sperm which are sprayed into the sea water where millions will be wasted in order to ensure that some reach the eggs.

What happens to the sperms if you don't have sex for many days? Unfortunately, you cannot "store up" sperms. If ejaculation does not occur for many days, the sperms in the reproductive ducts simply die. This is why a sperm count done after many days of abstinence shows a high number of dead or immotile sperms. But just like you cannot store your sperm, you cannot run out of sperm either - masturbation and sex cannot use sperm up. The body keeps making sperm as long as a man has even one normal testicle.

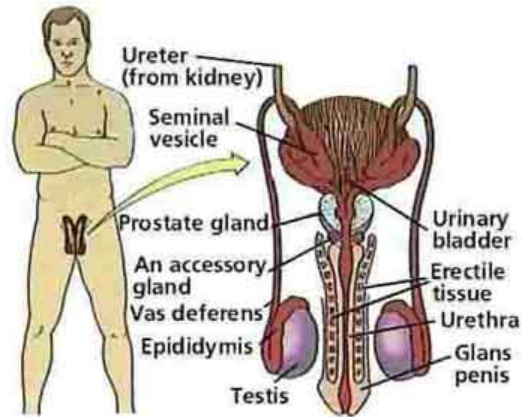


Figure 3. The male reproductive system - front view

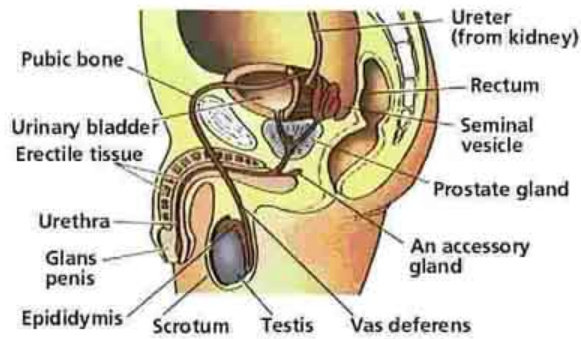


Figure 4. The male reproductive system - side view

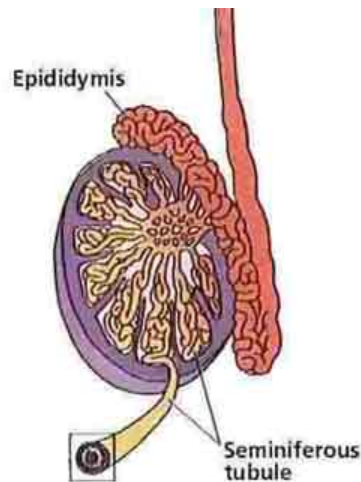
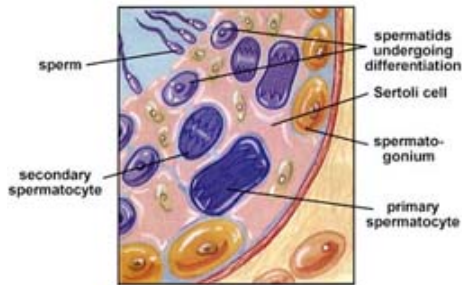


Figure 5. A section through the testis and epididymis



How does testosterone affect male fertility ?

The Role of Testosterone

As already mentioned, the main male sex hormone is testosterone and this is made by the testicles, starting at puberty. Testosterone is produced by specialized cells in the testis called the Leydig cells. These are stimulated to release testosterone in response to the LH signal from the pituitary . LH is luteinizing hormone - the same hormone found in women.

In addition to testosterone, the production and maturation of sperm in the seminiferous tubules of the testis is stimulated by FSH produced by the pituitary gland - and this FSH is identical to that found in women. FSH acts on the Sertoli cells to cause them to secrete androgen-binding protein, which binds testosterone and facilitates its action on sperm production. The Sertoli cells also produce growth factors such as SGF (seminiferous growth factor) which help to regulate spermatogenesis.

Note that there are two separate components in the testis - and that the Leydig cells are outside the seminiferous tubules where the sperms are manufactured. This explains why there is no relation between virility (which depends upon testosterone production) and fertility (which depends upon sperm production).

Testosterone does more than just allow men to make sperm. It also triggers the growth of facial hair, the deepening of men's voices, and the development of a male physique - all the changes which make boys into men. Testosterone is also important in creating desire for sex - it increases libido.

CHAPTER II D

How Babies are Made – The Basics

What happens to the sperm once they enter the woman's vagina ?

The sperm's odyssey in the female reproductive tract

A million million spermatozoa,
All of them alive;
Out of their cataclysm but one poor Noah
Dare hope to survive.

-- Aldous Huxley

When a man and woman have sexual intercourse, the man places his erect penis inside the woman's vagina. Here it releases millions of sperm when ejaculation occurs. Once the sperm have been deposited here they have a long and arduous journey ahead of them, like salmon entering the mouth of a river to swim upstream to spawn.

Some of the sperm swim straight up into the fallopian tubes through the cervix and uterus - and some of them are so fast, that sperms have been found in the tubes in as little as a few minutes after ejaculation. Some sperms die in the acidic vaginal fluid; and some enter the cervical mucus and cervical crypts. They are stored here and can remain alive here for as long as 48 to 72 hours.

During this time, the sperms are released in small numbers and these continue to swim towards the fallopian tubes. This is why you don't need to have sex every day to get pregnant even though the egg remains alive for only 24 hours.

Sperms in the female reproductive tract swim under their own steam - as a result of the whip- like activity of their tail which propels them on. Of the millions of sperms released in an ejaculate, only a few hundred will make the arduous trip upto the egg successfully. Perhaps this is why so many millions of sperms are produced in the first place even though only one is needed to fertilize the egg - because the wastage is so prodigal.

What happens to the egg when conception occurs ?

What about the other partner in this mating dance, the egg ? Remember that a mature egg is released from the ovary (this process is called ovulation) only once during the menstrual cycle. This is the "fertile time", during which a pregnancy can occur.

How does the egg reach the tube ? When ovulation occurs, the mature egg is released from the follicle in the ovary. This process of follicular rupture looks a bit like a small volcano erupting on the ovarian surface. At this time, the tubal fimbria, like tentacles, sweep over the surface of the ovary, and actually "swallow" the egg.

The egg has a shell, called the zona pellucida, which looks like the ring around Saturn. It is surrounded by a cluster of nest cells called the corona cells which serve to nurture the egg. They form the cumulus oophorus which is a sticky gel which protects the egg and also helps the beating of the hair-like cilia of the fallopian tube to propel the egg towards the uterus - like a conveyor-belt. The egg must now wait in the protective confines of the fallopian tube, for a sperm to swim up and reach it. An egg remains alive for about 24 hours, and if fertilization does not occur, it dies.

What happens when the egg and sperm meet ?

The process of fertilization

Of the few hundred sperm which reach the egg, only one will successfully fertilize it. The process of fertilization is truly the primeval mating dance - the fertilization tango - when the mother's chromosomes (in the egg) and the father's chromosomes (in the sperm) fuse together to create a new life - one which is totally different from all others, because of its unique genetic composition. We have now learnt quite a lot about fertilization thanks to in vitro fertilization (IVF) - and it is truly one of Nature's miracles.

During the time the sperm spend in the female reproductive tract, while swimming towards the egg, they acquire the capacity to fertilize it - a process called capacitation. When the sperms reach the corona cells (only a few hundred successfully make the trip, guided by chemicals produced by the egg which serve as guiding beacons to the sperms) they become hyperactivated - they start beating their tails in a frenzy. This is useful because it provides the mechanical energy the sperm head needs to burrow its way through the outer shell of the egg called the zona.

The sperms disperse the cumulus oophorus (and so far it's a team effort) and when they reach the egg, they first bind to the zona. A chemical is released here by the sperms in a process called the acrosomal reaction in which the acrosome (which sits like a cap on the head of the sperm and behaves much like a battering ram) is removed. The acrosomal enzymes dissolve the zona pellucida by making a tiny hole in it, so that one sperm can swim through and reach the surface of the egg. At this time, the egg transforms the zona to an impenetrable barrier, thus preventing other sperm from entering it.

The genetic material of the sperm (the male pronucleus) and the genetic material of the egg (the female pronucleus) then fuse - to form an embryo, which then divides into 2 cells. These cells in turn then continue to divide rapidly, producing a ball of cells - the embryo. The embryo then travels through the fallopian tube (which nurtures it and propels it) into the uterus - a journey which takes about 3 to 5 days. The embryo must then break through its zona (this is called embryo hatching); and then attach itself to the lining of the uterus in a process called implantation - and in 9 months , if all goes well, a baby is born.

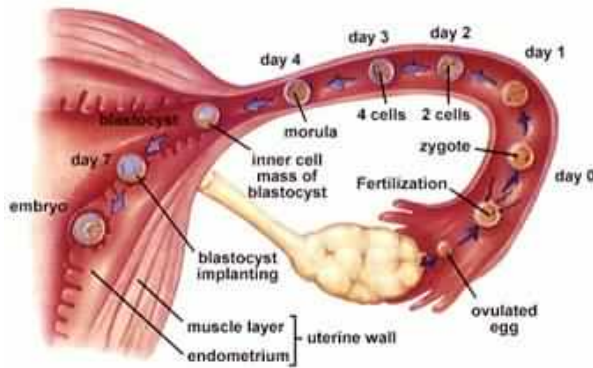


Fig 6. How an egg is fertilised

CHAPTER III

Finding Out What's Wrong – The Basic Medical Tests

What are the basic medical tests needed to assess fertility ?

In order to understand why pregnancy doesn't occur , we need to examine only the four critical areas which are needed to make a baby - eggs, sperm, fallopian tubes, and the uterus. The tests, which often seem endless, will actually fall into examining one of these four areas. In 40% of cases, the problem will be with the male, in 40% with the female, and in 10% both partners will have a problem. In some cases, about 10%, no cause can be identified (unexplained infertility) even after exhaustive testing.

Before starting with tests, the doctor takes a detailed medical history from the couple, and also performs a physical examination for both of them, to determine if this can provide clues as to the cause of the problem. The doctor will need to find out details about your menstrual cycle, as well as your sexual habits and past history of surgery or illness, so you should be prepared to answer these questions. Many clinics give patients a form to fill out, so that they can provide all this information. A physical examination can also provide the doctor with useful information, and he will look specifically for important clinical findings such as abnormal hair growth, excessively oily skin, or the presence of a milky discharge from the breast.

How are these basic infertility tests done ?

However, for most couples, investigations are needed to establish a diagnosis. These specialized tests constitute the infertility workup and they can be completed efficiently in one month . Timing the procedures properly during the menstrual cycle is important and we have found the following strategy useful in our practice.

Remember that the couple must be seen together and the first test which should be done is a semen analysis. Sadly, sometimes the wife will have undergone innumerable tests (sometimes repeatedly !) and the husband's semen analysis (where the problem lies) has not been done even once.

The first day the bleeding starts is called Day 1, and the semen analysis to check the husband's sperm count and motility can be done on Day 3-4 , after requesting him to abstain from ejaculation for at least 3 days . The wife's blood is then tested for measuring the levels of her four key reproductive hormones: prolactin, LH (luteining hormone) , FSH (follicle stimulating hormone) , TSH (thyroid stimulating hormone). Since these levels vary during the menstrual cycle, they should be done between Day 3-5 of the cycle. We then do a hysterosalpingogram (an X-ray of the uterus and tubes) for her after the menstrual bleeding has stopped - between Day 5-7, to confirm her uterus and

tubes are normal. We then see the couple on Day 9 with all these reports and review the results . These three basic tests allow us to check whether the eggs, sperm, uterus and tubes are normal.

Some doctors will perform further testing during the rest of the month, though we rarely do these tests in our own practise . They include: ultrasound scans for ovulation monitoring between Day 11-16 ; and the scan results can be used for timing the PCT (postcoital test) as well, during which time the cervical mucus is assessed also. A serum progesterone level can be measured on Day 21, about 7 days after ovulation , and this provides information about the quality of ovulation. Some doctors will also performed a laparoscopy in the same month (Day 20-25) ; and combine it with an endometrial biopsy , if desired.

With this strategy, time is not wasted, and couples can be reassured that a possible reason for the cause of the infertility , if it exists, will be detected within one month.

Unfortunately, it is very common to find that tests are done piecemeal - or sometimes, not done at all. Often treatment is started before coming to a diagnosis. Conversely, some doctors take so long to do the tests, that patients get fed up - after all, they want treatment!

The workup should not stop when a problem is discovered - it is still important to complete the testing, since it is possible that infertile couples may have multiple problems. Many diseases, such as pelvic inflammatory disease (PID) which can cause the tubes to get blocked, can be "silent", so that the patient may have absolutely no signs or symptoms.

A single test abnormality does not necessarily mean that a problem exists and the test may need to be repeated, to confirm that it is a persistent problem.

Sometimes it can be difficult for patients to come to terms with the fact that there is a major problem which presents a significant hurdle to getting pregnant. The truth can be bitter , but it's far better to face up to it and deal with it, rather than live in a fool's paradise ! With today's advanced reproductive technology, we can always find a solution, no matter what the problem – but remember that unless you can intelligently identify the problem, you cannot find a solution !

It is only after the workup has been completed , that a treatment plan can be formulated - and you will now need to make decisions about treatment options.

CHAPTER IV A

Testing the Man – Semen Analysis

Why should the man be tested first ?

In the past, infertility was blamed wholly and solely on the woman. This may have been to protect the fragile male ego, was because the male psyche equates fertility with virility, and views failure to father a child with shame. Studies today however show that 40% of infertility is because of a medical problem with the man.

The vast majority of men have simply no way of judging their fertility before getting married (unless, of course, they have had a premarital affair and fathered a pregnancy - the ultimate proof of male fertility ! Rarely, however, some men may know they have a fertility problem - for example, a sexual problem of impotence, which prevents consummation of the marriage; or one of hypospadias (in which the urethra is located at the base of the penis and the semen cannot be put in the vagina); or undescended testes (in which both the testes are not in the scrotum).

When testing a couple for infertility, the man must always be tested first. Tests for the woman are far more complicated, invasive and expensive - it is much simpler to find out if the man has a problem.

Where should the semen analysis be done ?

The most important test is an inexpensive one - the semen analysis. The fact that it is so inexpensive can be misleading, because many patients (and doctors !) feel that it must be a very easy test to do if it is so cheap, which is why they get it done at the neighbourhood lab. However, its apparent simplicity can be very misleading, because in reality it requires a lot of skill to perform a semen analysis accurately. However, it is very easy to do this test badly (as it often is by poorly trained technicians in small laboratories) , with the result that the report can be very misleading - leading to confusion and angst for both patient and doctor. This is why it is crucial to go to a reliable andrology laboratory which specialises in sperm testing for your semen analysis, since the reporting is very subjective and depends upon the skill of the technician in the lab.

How do I provide a sample for semen analysis ?

For a semen analysis, a fresh semen sample, not more than half an hour old is needed, after sexual abstinence for at least 2 to 4 days. The man masturbates into a clean, wide mouthed bottle which is then delivered to the laboratory.

Providing a semen sample by masturbation can be very stressful for some men - especially when they know their counts are low; or if they have had problems with masturbation "on demand" for semen analysis in the past. Men who have this problem can and should ask for help. Either their wife can help them to provide a sample - or they can see sexually arousing pictures or use a mechanical vibrator to help them get an erection.

Some men also find it helpful to use liquid paraffin to provide lubrication during masturbation. For some men, using the medicine called Viagra can help them to get an erection, thus providing additional assistance. If the problem still persists, it is possible to collect the ejaculate in a special silicone condom (which is non-toxic to the sperm) during sexual intercourse, and then send this to the laboratory for testing.

The semen sample must be kept at room temperature; and the container must be spotlessly clean. If the sample spills or leaks out, the test is invalid and needs to be repeated. Except for liquid paraffin, no other lubricant should be used during masturbation for semen analysis - many of these can kill the sperms. It is preferable that the sample is produced in the clinic itself - and most infertility centres will have a special private room to allow you to do so - a "masturbatorium".

How does the lab analyse the semen ?

After waiting for about 30 minutes after ejaculation, to allow the semen to liquefy, the doctor will check the semen.

- **The volume of the ejaculate.** While a lot of men feel their semen is "too little or not enough", abnormalities of volume are not very common. They usually reflect a problem with the accessory glands - the seminal vesicles and prostate - which are what produce the seminal fluid. Normal volume is about 2 to 6 ml. A very low volume will cause problems, because too little semen may mean that the sperm find it difficult to reach the cervix. A very high volume surprisingly will also cause problems, because this dilutes the total sperms present, decreasing their concentration.
- **The viscosity.** During ejaculation the semen spurts out as a liquid which gels promptly. This should liquefy again in about 30 minutes to allow the sperm free motility. If it fails to do so, or if it is very thick in consistency even after liquefaction, this suggests a problem - most usually one of infection of the seminal vesicles and prostate.
- **The pH.** Normally the pH of semen is alkaline. An alkaline pH protects the sperms from the acidity of the vaginal fluid. An acidic pH suggests problems with seminal vesicle function - either absence of the seminal vesicles, or an ejaculatory duct obstruction.
- **The presence of a sugar called fructose.** This sugar is produced by the seminal vesicles and provides energy for sperm motility. Its absence suggests a block in the male reproductive tract at the level of the ejaculatory duct.

The most important test is the visual examination of the sample under the microscope.

What do sperm look like ?

Sperm are microscopic creatures which look like tiny tadpoles swimming about at a frantic pace. Each sperm has a head, which contains the genetic material of the father in its nucleus; and a tail which lashes back and forth to propel the sperm along. The mid-piece of the sperm contain mitochondria, or the power house, which provide the energy for sperm motion.

Ask to see the sperm sample for yourself under the microscope - if normal, the sight of all those sperms swimming around can be very reassuring . You are likely to be awestruck by the massive numbers and the frenzy of activity. If the test is abnormal, seeing for yourself gives you a much better idea of what the problem is! A good lab should be willing to show you, and to explain the problem to you.

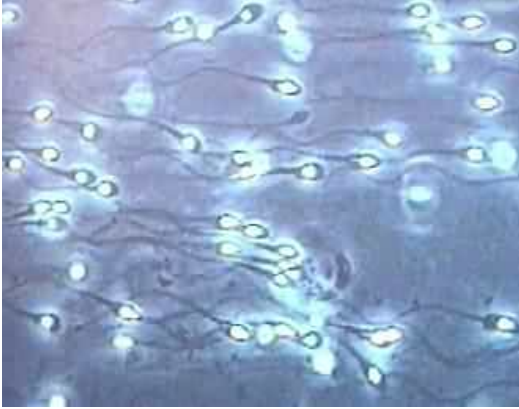


Fig 1. Sperm as seen under a microscope

CHAPTER IV B

Testing the Man – Semen Analysis

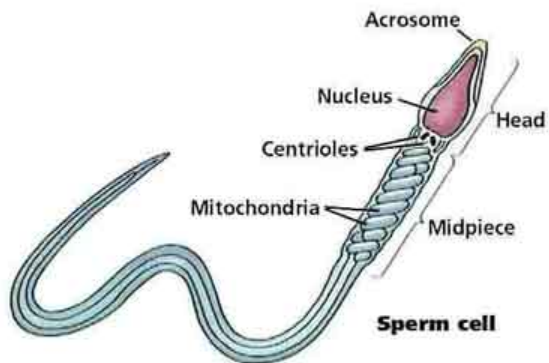


Fig 2. The anatomy of a sperm

What is a normal sperm count ?

If there are enough sperms.

If the sample has less than 20 million sperm per ml, this is considered to be a low sperm count. Less than 10 million is very low. The technical term for this is oligospermia (oligo means few). Some men will have no sperms at all and are said to be azoospermic. This can come as a rude shock because the semen in these patients look absolutely normal - it is only on microscopic examination that the problem is detected.

What is normal sperm motility ?

Whether the sperms are moving well or not (sperm motility).

The quality of the sperm is often more significant than the count. Sperm motility is the ability to move. Sperm are of 2 types - those which swim, and those which don't. Remember that only those sperm which move forward fast are able to swim up to the egg and fertilise it - the others are of little use.

Motility is graded from a to d, according to the World Health Organisation (WHO) Manual criteria, as follows.

Grade a (fast progressive) sperms are those which swim forward fast in a straight line - like guided missiles.

Grade b (slow progressive) sperms swim forward, but either in a curved or crooked line, or slowly (slow linear or non linear motility).

Grade c (nonprogressive) sperms move their tails, but do not move forward (local motility only).

Grade d (immotile) sperms do not move at all.

Sperms of grade c and d are considered poor. If motility is poor (this is called asthenospermia) , this suggests that the testis is producing poor quality sperm and is not functioning properly - and this may mean that even the apparently motile sperm may not be able to fertilise the egg.

This is why we worry when the motility is only 20% (when it should be at least 50% ?) Many men with a low sperm count ask is - " But doctor, I just need a single sperm to fertilise my wife's egg. If my count is 10 million and motility is 20%, this means I have 2 million motile sperm in my ejaculate - why can't I get her pregnant ? " The problem is that the sperm in infertile men with a low sperm count are often not functionally competent - they cannot fertilise the egg. The fact that only 20% of the sperm are motile means that 80% are immotile - and if so many sperm cannot even swim, one worries about the functional ability of the remaining sperm. After all, if 80% of the television sets produced in a factory are defective, no one is going to buy one of the remaining 20% - even if they seem to look normal.

What is normal sperm morphology ?

Whether the sperms are normally shaped or not

- what is called their form or morphology. Ideally, a good sperm should have a regular oval head, with a connecting mid-piece and a long straight tail. If too many sperms are abnormally shaped (this is called teratozoospermia, when the majority of sperm have abnormalities such as round heads; pin heads; very large heads; double heads; absent tails) this may mean the sperm are functionally abnormal and will not be able to fertilise the egg. Many labs use Kruger "strict " criteria (developed in South Africa) for judging sperm normality. Only sperm which are "perfect" are considered to be normal. A normal sample should have at least 15% normal forms (which means even upto 85% abnormal forms is considered to be acceptable !)

Sperm clumping or agglutination.

Under the microscope, this is seen as the sperms sticking together to one another in bunches. This impairs sperm motility and prevents the sperms from swimming upto through the cervix towards the egg.

Putting it all together, one looks for the total number of "good" sperms in the sample - the product of the total count, the progressively motile sperm and the normally shaped sperm. This gives the progressively motile normal sperm count which is a crude index of the fertility potential of the sperm. Thus, for example, if a man has a total count of 40 million sperm per ml; of which 40% are progressively motile; and 60% are normally shaped; then his progressively motile normal sperm count is : $40 \times 0.40 \times 0.60 = 9.6$ million sperm per ml. If the volume of the ejaculate is 3 ml, then the total motile sperm count in the entire sample is $9.6 \times 3 = 28.8$ million sperm.

**What does the presence of pus cells in the semen signify ?
Whether pus cells are present or not.**

While a few white blood cells in the semen is normal, many pus cells suggests the presence of seminal infection. Unfortunately, many labs cannot differentiate between sperm precursor cells (which are normally found in the semen) and pus cells. This often means that men are overtreated with antibiotics for a "sperm infection" which does not really exist !

Some labs use a computer to do the semen analysis. This is called CASA, or computer assisted semen analysis. While it may appear to be more reliable (because the test has been done "objectively" by a computer), there are still many controversies about its real value, since many of the technical details have not been standardised, and vary from lab to lab.

What does a normal semen analysis report mean ?

A normal sperm report is reassuring, and usually does not need to be repeated. If the semen analysis is normal, most doctors will not even need to examine the man, since this is then superfluous. However, remember that just because the sperm count and motility are in the normal range, this does not necessarily mean that the man is "fertile". Even if the sperm display normal motility, this does not always mean that they are capable of "working" and fertilising the egg. The only foolproof way of proving whether the sperm work is by doing IVF (in vitro fertilisation)!

What are the reasons for a poor semen analysis report ?

Poor sperm tests can results from:

- incorrect semen collection technique, if the sample is not collected properly, or if the container is dirty
- too long a time delay between providing the sample and its testing in the laboratory
- too short an interval since the previous ejaculation
- recent systemic illness in the last 3 months (even a flu or a fever can temporarily depress sperm counts)

If the sperm test is abnormal, this will need to be repeated 3-4 times over a period of 3-6 months to confirm whether the abnormality is persistent or not. Don't jump to a conclusion based on just one report - remember that sperm counts do tend to vary on their own! It takes six weeks for the testes to produce new sperm - which is why you need to wait before repeating the test. It also makes sense to repeat it from another laboratory, to ensure that the report is valid.

What if my sperm count is zero (azoospermia) ?

Azoospermia

Some men will find to their dismay that they have a zero sperm count. This is called azoospermia, and comes as a complete shock, as these men have normal libido, can ejaculate normally, and their semen looks normal .

If the report shows your sperm count is zero, please ask the laboratory to re-check it again. It's useful to request the laboratory to check two consecutive semen samples, ejaculated about 1 hour apart (sequential semen analysis). The laboratory should be also requested to centrifuge the sample and check the pellet for sperm precursors. Some men will have occasional sperm in the pellet, which means they are not really azoospermic. This is called cryptozoospermia.

If the report is persistently zero, then the next step is to find out what the reason for the azoospermia is. There are 2 possibilities - obstructive azoospermia; or non-obstructive azoospermia. Men with obstructive azoospermia have normal testes which produce sperm normally, but whose passageway is blocked. This is usually a block at the level of the epididymis, and in these men the semen volume is normal; fructose is present; the pH is alkaline; and no sperm precursor cells are seen on semen analysis. On clinical examination, they typically have normal sized firm testes, but the epididymis is full and turgid.

Some men have obstructive azoospermia because of an absent vas deferens. Their semen volume is low (0.5 ml or less); the pH is acidic and the fructose is negative. The diagnosis can be confirmed by clinical examination, which shows the vas is absent. If the vas can be felt in these men, then the diagnosis is a seminal vesicle obstruction.

Men with non-obstructive azoospermia have a normal passageway, but abnormal testicular function, and their testes do not produce sperm normally. Some of these men may have small testes on clinical examination. The testicular failure may be partial, which means that only a few areas of the testes produce sperm, but this sperm production is not enough for it to be ejaculated. Other men may have complete testicular failure, which means there is no sperm production at all in the entire testes. The only way to differentiate between complete and partial testicular failure is by doing multiple testicular micro-biopsies to sample different areas of the testes and send them for pathological examination.

What if the sperm count is persistently low ? Then other tests may be advised, to try to pinpoint what the problem is; and these are described in the next chapter.

CHAPTER V A

Beyond the Semen Analysis

What additional tests can be done for a man with an abnormal semen analysis report?

For the man with a poor semen sample, additional tests which may be recommended include specialized sperm tests; blood tests; and testis biopsy.

Antisperm Antibodies Test

The role of antisperm antibodies in causing male infertility is controversial, since no one is sure how common or how serious this problem is. However, some men (or their wives) will possess antibodies against the sperm, which immobilize or kill them and prevent them from swimming up towards the egg. The presence of these antibodies can be tested in the blood of both partners, in the cervical mucus, and in the seminal fluid. However, there is little correlation between circulating antibodies (in the blood) and sperm-bound antibodies (in the semen).

There are many methods of performing this test, which can be quite difficult to standardize, as a result of which there is a lot of variability between the result reports of different laboratories. The older methods of testing used agglutination methods on slides and in test tubes.

Perhaps, the best method available today is one such uses immunobeads, which allow determination of the location of the antibodies on the sperm surface. If they are present on the sperm head they can interfere with the sperm's ability to penetrate the egg; if they are present on the tail they can retard sperm motility. Of course, if the test is negative, this is reassuring; the problem really arises when the test is positive! What this signifies and what to do about it are highly vexatious issues in medicine today, and doctors are even more confused about this aspect than the patients.

Semen Culture Test

In the semen culture test, the semen sample is tested for the presence of bacteria, and , if present, their sensitivity to antibiotics is determined. Interpreting this test can also be problematic! It is normal to find some bacterial in normal semen samples - and the question which must be answered is : are these bacteria disease- causing or not?

Tests which assess the sperm's ability " to perform" include the following sperm function tests.

Postcoital Test (PCT)

The postcoital test is the easiest test of sperm function, since it is performed in vivo. It is done when the wife is in the " fertile" period, during which time the cervical mucus is profuse and clear. The gynecologist examines a small sample of the cervical mucus, under the microscope, a few hours after intercourse. (This can be embarrassing and awkward for the patient, but it is not painful at all). Finding 5-10 motile sperm per high

power microscopic field means that the test is normal. A normal test implies normal sperm function and can be very reassuring.

An abnormal test needs to be repeated and, if the problem is persistent, one needs to determine if the defect lies in the sperm or in the mucus, by cross-testing with the husband's sperm, donor sperm, wife's mucus and donor mucus.

Bovine Cervical Mucus Test

The bovine cervical mucus test is another form of testing for the ability of the sperm to penetrate and swim through cervical mucus, with the difference that in this case, the mucus used is that of a cow (since this is commercially available abroad in a test kit.) The sperm are placed in a column of cervical mucus and how far the sperm can swim forward through the column in a given amount of time is checked with the help of a microscope.

Sperm Viability or Sperm Survival Test

This is a simple test, which provides crude (but useful!) information on the functional potential of the sperm. The sperm are washed using the same method which is used for IVF (either a Percoll spin or sperm swim up) and the washed sperm are then kept in a culture medium in the laboratory incubator for 24 hours. After 24 hours, the sperm are checked under the microscope. If the sperm are still swimming actively, this means that they have the ability to "survive" in vitro for this period- and this is reassuring. If, however, none of the sperm are alive after 24 hours, this suggest that they may be functionally incompetent.

Sperm Penetration Assay (SPA, Hamster Assay)

Since the basic function of a sperm is to fertilize an egg, scientists were very excited when they found that normal sperm could penetrate a denuded (zona-free) hamster egg. A zona-free hamster egg is obtained from hamsters egg. A zona-free hamster egg is obtained from hamsters and the covering (the zone) removed by using special chemicals. The egg are then incubated with the sperm in an incubator in the laboratory. After 24 hours, the eggs are checked to ascertain how many sperm have been able to penetrate the egg. The result gives a penetration score, which gives an index of the sperm's fertilizing potential. This is a very delicate technique and is not available in India. In any case, nowadays scientists the world over are quite disenchanted with the test, since the correlation between IVF results (the ability to fertilize human eggs) and the SPA (the ability to penetrate zona-free hamster eggs) is quite poor.

- Testing for acrosomal status
- HOS test - hypo-osmotic swelling test-which tests for the integrity of the sperm membrane
- CASA - computer-assisted sperm analysis
- Hemizona assay
- Electron microscopy of sperm

A test which has recently become very fashionable is the Sperm Chromatin Structure Assay (SCSA) and the sperm DNA Fragmentation assay. These test the integrity of the

DNA in the sperm nucleus, and thus the ability of the sperm to fertilise the egg. While they seem very attractive, the major problem with these tests is that they provide information which is applicable only to groups of patients. Thus, we know that men with a higher degree of DNA fragmentation have a higher chance of being infertile. However, they do not provide any information for the individual patient, which means their utility in clinical practise is very limited.

The aforementioned tests are highly sophisticated and are not easily available. Another drawback is that these tests are often not standardized adequately, so that interpreting their results can be quite difficult. This is why we do not do any of these tests in our own practise, because we feel they do not provide any clinically useful information.

The ultimate sperm function test is IVF, since this directly assesses whether or not the husbands' sperm can fertilize the wife's eggs. The best way to perform this test is to culture some of the eggs with the husband's sperm and the others with donor sperm of proven fertility, at the same time. If the donor sperm can fertilize the eggs, and the husband's sperm fail to do so, then the diagnosis of sperm inability to fertilize the egg is confirmed. However, even this test is not infallible, since it has been shown that about 5% of sperm samples which fail to fertilize an egg in the first IVF attempt, can do so in a second attempt at IVF. In any case, it is obviously not practicable or feasible to use IVF as a test for sperm function in clinical practice.

CHAPTER V B

Beyond the Semen Analysis

What blood tests can be done for infertile men ?

Blood Tests for Men

For most infertile men, the semen analysis is the only test which needs to be done - after all, the only job of a man is to provide sperm to fertilise the egg ! For men with a low sperm count, there is no need to do any other tests, since these do not provide any useful information. However, many doctors still do blood tests for measuring the levels of key reproductive hormones, such as prolactin, FSH, LH and testosterone. These are just a waste of time and money since they provide no useful information and do not alter the treatment plan.

For men with azoospermia (zero sperm count), additional blood tests may be useful . The serum FSH (follicle-stimulating hormone) level test is a useful one for assessing testicular function. If the reason for the azoospermia is testicular failure, then this is reflected in a raised FSH level. This is because, in these patients, the testis also fails to produce a hormone called inhibin (which normally suppresses FSH levels to their normal range). A high FSH level is usually diagnostic of primary testicular failure, a condition in which the seminiferous tubules in the testes do not produce sperm normally, because they are damaged.

This test is done by a radioimmunoassay or chemiluminescent assay, and since it is a sophisticated test, it is best done in a specialized laboratory. Abnormal test results should be repeated and rechecked for confirmation. The other reason for a high FSH level in some men is the consumption of clomiphene (a medicine often prescribed for the empiric treatment of oligospermia). This is why the test should be done only when no medication is being taken. While a high FSH level is diagnostic of testicular failure, a normal FSH level provides no useful information. Thus, men with complete testicular failure may also have normal FSH levels.

While a high FSH level suggests primary testicular failure, it cannot differentiate between partial testicular failure and complete testicular failure. This means that even men with very high FSH levels can have occasional areas of sperm production in their testes, and these testicular sperm can be used for TESA-ICSI (testicular sperm aspiration and intracytoplasmic sperm injection) treatment.

Rarely, the FSH level may be low. A low FSH level is found in patients with hypogonadotropic hypogonadism. Hypogonadotropic hypogonadism is an uncommon (but treatable!) cause of azoospermia. Along with an FSH level test, most doctors also do a LH (luteinizing hormone) level test, which provides mostly the same information.

A testosterone level test provides information on whether or not the testes are producing adequate amounts of the male hormone, namely, testosterone. Most infertile men have normal testosterone levels, because the compartment for testosterone production is

separate from the compartment which produces sperm, and is usually intact in infertile men. A low testosterone level causes a decreased libido and this can be treated by testosterone replacement therapy in the form of tablets or injections. Of course, this therapy will not increase the sperm count.

For men with azoospermia and erectile dysfunction, measuring the prolactin level will help to detect men who have hyperprolactinemia (high prolactin levels). Though this is a rare problem, they can be effectively treated with medical therapy with bromocriptine and the results are very gratifying.

Of what use is an ultrasound exam in evaluating an infertile man ?

Ultrasound

An ultrasound of the testis has become a popular test to perform, but its helpfulness is limited. The size of the testis is better assessed by clinical examination, using an orchidometer (which consists of a string of graduated plastic ovoids on a string, and can be used to assess testicular volume by comparison) ; and while a Doppler ultrasound will often diagnose the presence of a varicocele, this is usually of little clinical significance. The danger of finding a varicocele is that the knee-jerk response is to do surgery to correct it , and this rarely benefits the patient. A transrectal ultrasound (TRUS) can be useful, but only in evaluating selected patients with obstructive azoospermia, when a block at the level of the seminal vesicles is suspected because of ejaculatory duct obstruction, and this test is best ordered by a specialist. Unfortunately, a lot of doctors will order these tests "routinely" for all infertile men, without thinking critically.

Of what use is a testicular biopsy ?

Testicular Biopsy

A testicular biopsy is done in order to find out whether sperm production in the testis is normal or not. This is the "gold standard" for judging testicular function, since here the testicular tissue is being examined directly. How is a testicular biopsy performed? This is a simple surgical procedure, which can be done under a local anaesthetic, in an operation theatre or even in the doctor's clinic, if it is well equipped. The test takes about 5-10 minutes to be carried out; and a biopsy could be taken from just one testis, or from both testes, depending upon the nature of the problem.

The removed bit of tissue is then placed in a special preservative fluid called Bouin's fluid, which is then sent to a pathologist for examination under a microscope after staining.

The biopsy surgery doesn't hurt, because the local anesthetic numbs the tissues. There may be dull ache for a few days after the procedure, but this can be relieved by mild analgesics.

Since testis biopsy is a surgical procedure, most doctors would use it as the last resort when testing the man. If you are advised to have a testis biopsy, ask the doctor how the

result will change your treatment (a question you should ask before being subjected to any medical test, in fact!).

The only group of infertile men who should be offered a testis biopsy are those with azoospermia. Men with oligospermia should not be subjected to a testis biopsy because the biopsy report is always normal in these men (and this is not surprising - after all, since sperm are present in the semen, they are obviously being produced in the testes!)

Formerly, when doctors performed a testis biopsy, they would send only one chunk of tissue for testing. However, today we know that a single biopsy may not be representative of the entire testis. Sperm production is not uniformly distributed throughout the testis, especially in men with testicular failure. This means that in order to get a true picture of sperm production in the testis, the doctor needs to sample at least 4 different areas of the testis, all of which need to be examined. You should also insist that your doctor send the testicular tissue to the pathology laboratory in a special preservative called Bouin's fluid. In the past, a testis biopsy was purely a diagnostic procedure. Today, it is also used to retrieve testicular sperm in order to treat men with severe male factor infertility. These testicular sperm can be used for intracytoplasmic sperm injection (ICSI). Specialised infertility clinics also have the ability to freeze the testicular tissue. This testicular sperm freezing can be very useful, especially in men with small testes, as the biopsy does not need to be repeated again during treatment.

The interpretation

While the biopsy is an easy test to perform, it is difficult to interpret properly, unless done by an expert. The doctor looks for evidence of sperm production in the seminiferous tubules. In some cases, there is no sperm production at all (absent spermatogenesis); or the sperm production is arrested at a particular stage (maturation arrest) This implies testicular failure, which is usually irreversible, and there is no treatment for this malady. If, on the other hand, sperm production in the testes is completely normal, and yet there are no sperm in the ejaculated semen, this clearly means that there is a block in the male reproductive tract. This is the one condition in which a testis biopsy is extremely useful (i.e., in the evaluation of the azoospermic male, to determine if there is a block to sperm transport).

A testis biopsy is often a procedure which is done badly because it is so "minor" so beware! It is preferable that the biopsy be done by a specialist; a poorly done biopsy may make reconstructive surgery on the epididymis more difficult later on, by causing adhesions and fibrosis (scarring). The commonest problem with the biopsy, however, is that the biopsy result is not reported accurately by the pathologist. Interpreting a testis biopsy is difficult and requires special expertise and is not something that the ordinary pathologist does well. You should retrieve and retain your own slides and preserve them carefully. The pathology laboratory can also be instructed to keep the tissue ("blocks") carefully. It is unfortunately common to find that a testis biopsy has to be repeated simply because the first one was done so badly that its results could not be accurately interpreted. It may also be a good idea to get a second specialist's opinion on the testis biopsy slides. Vasography is another surgical test in which a radio- opaque dye is injected into the vas to determine if it is open, and, if blocked, to find out the exact site of the block. This test

requires very delicate surgery and X-ray equipment and is a very infrequently done procedure because it can damage the vas.

For some men with testicular failure, a karyotype (study of the chromosomes) is useful, because it allows one to determine if a chromosomal problem (e.g., Klinefelter's syndrome, 47, XXY, with an extra X Chromosome) is responsible for the azoospermia. Some clinics also offer testing for microdeletions on the Y-chromosome (mYC) a newly discovered cause for testicular failure in about 15% of infertile men. While there is no treatment for this disorder, at least the test result provides an answer to the question of why the testes have failed a question which, unfortunately, medicine today still cannot answer, in the majority of patients.

CHAPTER VI A

Diagnosis and Treatment for Male Infertility -- More Confusion!

The commonest reason for male infertility is a low sperm count, and the commonest reason for this is what doctors called "idiopathic" - which simply means, we do not know ! This is one of the reasons why the diagnosis of male infertility is so frustrating for both patients and doctors - there are few tests available which allow us to pinpoint the cause of the problem. This also means that there is very little in the form of effective therapy which we can offer these men - if we do not know what is wrong, how can we treat it?

However, what about those conditions which we think we do understand? Let's discuss these in detail.

What is a varicocele ?

Varicocele

One of the reasons for a low sperm count according to some doctors is a varicocele. A varicocele is a swollen varicose vein in the scrotum - usually on the left side . The condition occurs because blood pools in the varicose testicular veins (pampiniform plexus) since the valves in the veins are leaky and do not close properly. The reason for infertility associated with a varicocele are unclear. Perhaps the accumulation of blood causes the testes to be hotter and so damage sperm production; or the pooled blood brims over with abnormal hormones which may change the way the testes make sperm. The effect of the varicocele on an individual's sperm count is variable - and this may range from no effect whatsoever, to causing a decreased sperm count. Varicoceles may also have a progressively damaging effect on sperm production, so that the sperm count may decline with time.

How is a varicocele diagnosed?

How is a varicocele diagnosed? The doctor examines the patient in the erect position and feels the spermatic cord - the cord like structure from which the testis hangs. The patient is also asked to cough at this time. A varicocele feels like a "bunch of worms" and on coughing, this gets transiently engorged. Confirmation of this diagnosis is best done by a Doppler test at the same time. The Doppler is a small pen like probe which is applied to the cord. It bounces sound waves off the blood vessels and measures blood flow by magnifying the sound of blood flowing through the veins. This can be recorded. Patients with a varicocele have a reflux of blood during coughing which shows up as a large spike on the tracing. Other tests which are done uncommonly to confirm the diagnosis of a varicocele include: Doppler ultrasound; special X-ray studies called venograms; and thermograms.

What are the areas of controversy about the varicocele? Most doctors are still not sure whether a varicocele causes a low sperm count or not ! It is possible that the varicocele may be an unrelated finding in infertile men - a "red herring" so to speak. Strangely enough, only a quarter of men with varicoceles have a fertility problem. Thus, many men with large varicoceles have excellent sperm counts which is why correlating cause (varicocele) and effect (low sperm count) is difficult.

This means that surgical correction of the varicocele may be of no use in improving the sperm count - after all, if the varicocele is not the cause of the problem, then how will treating it help? In fact, controlled trials comparing varicocele surgery with no therapy in men who have varicoceles and a low sperm count have shown that the pregnancy rate is the same – so that it does not seem to make a difference whether or not the varicocele is treated !

Is surgery for varicocele repair useful ?

Because surgery for varicocele repair is simple and straightforward , many doctors still repair any varicoceles they find in infertile men, following the dictum that it's better to do something, rather than do nothing ! However, keep in mind that varicocele surgery may result in an improvement in sperm count and motility in only about 30% of patients - and it is still not possible for the doctor to predict which patient will be helped. Of course, just improving the sperm count is not enough - and pregnancy rates after varicocele repair alone are in the range of 15%. If a man with a low sperm count gets pregnant after varicocele surgery, he believes (as does his surgeon, who is happy to take the credit !) that the pregnancy was a result of the surgery ! However, randomised controlled studies have shown that varicocele surgery does not improve pregnancy rates in men with low sperm counts. When men with varicoceles and low sperm counts were divided into 2 groups, of which one was subjected to surgery, and the other left untreated, 15% in both groups attained a pregnancy ! One danger of doing a varicocele repair is that when it doesn't help, patients get frustrated, and refuse to pursue more effective options, such as the assisted reproductive techniques. Today, most infertility specialists would advise infertile men with varicoceles to consider going in for IVF or ICSI, rather than for varicocele surgery.

How is a varicocele surgically repaired ?

There are 4 methods available to repair varicoceles - conventional surgery; microsurgery; laparoscopic surgery and radiologic balloon occlusion.

In conventional surgery, a small cut is made in the groin; the spermatic cord is lifted out of the scrotum; and the engorged veins are tied off. This is the commonest method used. The risks include: the risk of the varicocele recurring , which is about 20 %, because some of the smaller veins are not identified and are missed during surgery; the risk of hydrocele formation - a collection of fluid around the testes , because lymph vessels are indirectly tied off too, so that more fluid is accumulated - the risk being about 5 %; and

inadvertent damage to the testicular artery (the blood supply to the testis) - which can actually decrease sperm production !

Microsurgery is a newer method, in which under an operating microscope, the surgeon individually ties off the enlarged veins in the spermatic cord. The testicular artery and lymphatic ducts can be preserved confidently, because the surgery is done under high magnification.

Radiologic balloon occlusion is not very commonly performed. in this minor procedure, a silicone balloon catheter is passed under X-ray guidance to the testicular vein; here the balloon is inflated and left in place permanently, thus blocking the engorged veins and repairing the varicocele.

The "subclinical varicocele": These are tiny varicoceles which cannot be felt by the doctor; but can be detected by Doppler examination. Whether correcting them is helpful or not is still a matter of individual opinion.

Many surgeons will combine varicocele repair with medical therapy to try to increase the sperm count by driving the testis to work harder, but how effective this is still not clear.

In our clinic, we do not believe that diagnosing or treating a varicocele helps improve fertility in men with a low sperm count.

CHAPTER VI B

Diagnosis and Treatment for Male Infertility -- More Confusion!

What is obstructive azoospermia ?

Duct blockage

If the passage (reproductive tract) between the penis and testes is blocked there will be no sperm in the semen - azoospermia. If the reason for the azoospermia is a duct blockage, this is called obstructive azoospermia. Blockages can be caused by infection (gonorrhea, chlamydia, filarisis, or TB); or by surgery done to repair hernias or hydroceles.

What surgery can be done to treat obstructive azoospermia ?

If the passage is blocked, surgical repair can be attempted by performing a long and complicated 2 to 3 hour micro surgery called a vasoepididymal anastomosis (VEA) . This is highly specialised surgery which is best done by an experienced microsurgeon, since the tubes involved are so fine and delicate.

This is technically difficult and intricate surgery because it needs to be done under high magnification . The surgeon tries to bypass the block, so that the sperm can reach the penis .

Surgical results can be poor for the following reasons:

- Technical difficulty, because of the minute size of the tubes; Often patency cannot be restored, and the sperm count remains zero. The anatomic patency rate is about 50 % for most patients (which means that sperm can be found in the semen after surgery).
- These sperm are often poor in quality and are successful in giving rise to a pregnancy in only about 25% of patients, as the sperm that make their way out may not be mature or motile since they have not spent enough time in the epididymis, which functions to mature the sperms in the body.
- Secondary damage to the epididymis and duct system may have occurred because they have been subjected to high pressure for a long time, causing multiple leaks and blocks, making surgery less successful.
- Damage to the functional lining of the epididymis, either as a result of the infection which caused the block or as a result of the high pressure, so that it no longer works effectively and sperms cannot mature here properly.

The best chance of success is with the first surgical attempt - repeat surgery has a dismal success rate and is rarely worthwhile.

One of the uncommon causes of obstructive azoospermia is an ejaculatory duct obstruction. These men have low semen volume, no fructose in the semen; and an acidic semen, because their seminal vesicles are blocked. Sometimes, this is because of an

ejaculatory duct cyst, which can be diagnosed by TRUS (transrectal ultrasound). This can sometimes be treated by a TURED (transurethral resection of the ejaculatory duct) procedure, which is performed by passing an endoscope into the urinary bladder, but the results of surgical repair are often very poor.

What about men with an absent vas (CBAVD, congenital bilateral absence of the vas deferens) ?

Congenital absence of the vas (the sperm-carrying tube)

Men with an absent vas deferens have azoospermia, with a low volume ejaculate; acidic pH; and no fructose in the semen. This is because their seminal vesicles are also absent. The vas deferens is absent from birth, this being a congenital defect, but one which is diagnosed only when they are trying to conceive. Conventional treatment in the past consisted of creating a pouch surgically, into which the epididymis was made to open. This was called a spermatocele and sperms were aspirated from this and used for artificial insemination. However, pregnancy rates were very poor. The technique of PESA with ICSI has revolutionised our approach to these men, and allows many of them to father a pregnancy.

What can a man who has had a vasectomy do if he wants more children ?

Vasectomy

Men often have this operation to render them sterile once they have completed their family. This is safe, easy surgery which involves cutting the vas deferens (the sperm carrying tube) and sewing it shut , so that sperm passage is blocked . These sperms are absorbed into the body so that although ejaculation is normal, there are no sperms in the semen.

If the man changes his mind after a vasectomy, and wants to father another child, microsurgery can rejoin the cut ends so that the sperm can once more pass through into the semen. This reversal surgery is called vasovasostomy or VVA (vasovasal anastomosis) . It is expensive and only a few doctors are adequately trained to perform the operation - and even then success is not guaranteed. The best results are when the reversal process is performed within 5 years after the vasectomy, before antibodies are developed to the sperm . Good surgeons have reported pregnancy rates of as high as 80% using meticulous microsurgical technique.

Do sperm antibodies cause male infertility ?

Immunity problems with sperm

If varicoceles are controversial, immune sperm problems are even more so. However, while the controversy surrounding varicoceles is now quite old, the immune problem is a relatively newer area, which means we have even more questions about this, and even fewer answers !

In one of Nature's quirks , men can develop antibodies to their own sperm; or the wife can develop these against the husband's sperm . What happens is that the body's defense mechanisms destroys its own sperm ; or the wife's hostile cervical mucus does so, as

though the sperm were enemy bacteria or virus. This can happen after problems of inflammation, injury to the testes, surgery, infection, or blockage.

Problems start with making a diagnosis. Antisperm antibodies are suspected when the sperms clump to one another (agglutinate) on a sperm test. A poor postcoital test, which shows all immotile sperms in the mucus is also a tip-off, because one of the reasons for this is cervical mucus hostility because of antibodies.

There are many tests available to detect sperm antibodies. Blood tests for antisperm antibodies can be done for both the wife and husband using ELISA methods. This is an easy test to do but interpreting it is hard - what does a positive test mean? Could it be responsible for infertility? Most doctors don't think so, because they argue that the presence of these antibodies in the blood is of little clinical importance - but the debate goes on ! These older tests are now considered to be obsolete. The newer antibody tests which are more reliable, are done on the sperm itself, using immunobead testing, and these can tell the doctor whether the antibodies are on the sperm head or tail. However, interpreting the significance of a positive result remains a vexed issue!

Treatment is equally confusing - and included testosterone injections in the past in order to suppress sperm production - the rationale being that if there are no sperm there will be no further formation of the battling antibodies ! Corticosteroids have also been used successfully to stop a person from making antibodies, but these drugs can have significant side effects , as a result of which they are not considered standard therapy today.

Today, washing the sperm in the lab to clean away the seminal fluid which contains the antibodies , along with timed intrauterine insemination (IUI) , is the first-line treatment. For other patients, where the antibodies are tightly bound to the sperm head, IVF or ICSI may be needed.

Can hormone imbalance cause male infertility ?

Hormone imbalance

Unlike the woman, hormone imbalances in the man are not a common cause of fertility problems . These problems can stem from organs as far apart as the brain or the testicles, and can show up in blood tests. They can arise because of:

- Head injury
- A tumour in the pituitary gland at the base of your brain
- A tumor in the adrenal gland, above the kidneys.
- Malfunctioning of the pituitary gland
- Cirrhosis of the liver
- Conditions present from birth, such as and Klinefelter's syndrome (47, XXY syndrome)
- A thyroid problem

One problem is that of hyperprolactinaemia (a high prolactin level). This is usually caused by a pituitary malfunction or tumour; and can be detected by a blood test. Patients with hyperprolactinemia often also have decreased libido and may be impotent.

Treatment with bromocryptine to suppress the high prolactin levels is highly successful in achieving pregnancy.

Another problem is that of hypogonadotropic hypogonadism (poor function of the testes because of inadequate stimulation of the testes by the gonadotropic hormones, FSH and LH produced by the pituitary). Most hypogonadotropic patients are hypogonadal - that is, they have low levels of the male hormone, testosterone. This means they have poorly developed secondary sexual characters ; an effeminate appearance; scanty hair; decreased libido , and small flabby testes. This can be confirmed by blood tests which show low levels of FSH and LH. This can be treated by replacement therapy with the gonadotropin hormones - HCG and HMG. These are expensive injections and a fairly long course of treatment is needed for them to work , but they are effective in enhancing sperm production in these men.

How does substance abuse affect male fertility ?

Substance abuse

As Shakespeare said "Alcohol increases the desire but takes away the performance." Not only are alcoholics unable to perform, but their liver function also deteriorates , resulting in excessive levels of the female hormone, estrogen , which has a severe sperm suppressing effect.

Drugs of abuse can also create malformed sperm with poor motility ; they also alter hormonal balance and testicular function ; and cause impotence and erection problems. Tobacco is a potent toxin. It attacks the tail of the sperm so that it is unable to swim to its goal. The testicular artery can go into spasm because it is choked with nicotine. Prolactin levels in smokers tend to be higher so sexual desire disappears in smoke.

CHAPTER VI C

Diagnosis and Treatment for Male Infertility -- More Confusion!

How do undescended testes cause male infertility ?

Undescended testes

Undescended testes are a tragic cause of male infertility, since often it is preventable. Some babies are born with one or both testicles up in their bellies instead of hanging down in the scrotum. Sometimes the condition might correct itself by the time the toddler is around 2 years old. (Don't worry unduly if you find the testes "disappearing occasionally " from the scrotum of a young boy. These are called "retractile " testes, and are very common.) However, if left unattended , the undescended testes tend to get damaged by the heat in the abdominal cavity ; and they can even become cancerous in adult life. The child should be operated before two years of age or else fertility can be lost forever. Treatment with hormonal injections (HCG injections) to cause testicular descent is another alternative.

How does testicular torsion cause male infertility ?

Torsion

If one of the testicles has undergone torsion, (the doctor's word for twisting) , it could be damaged since it is starved of blood.

Signs of torsion are an excruciating pain and swelling of the testicle. Sadly, it is often misdiagnosed as a testes infection, and left untreated. This causes the testis on that side to shrivel up and die (atrophy). The best way to make the diagnosis of torsion is with a Doppler ultrasound ; and emergency surgery is needed right away, to untwist and fix the testis. The other testis must also always be fixed surgically to prevent it from undergoing torsion . Unfortunately, often, sperm antibodies are produced which decrease sperm production in the other testis .

Which infections cause male infertility ?

Infections

The commonest reason for azoospermia in India used to be smallpox - the virus attacks and damages the epididymis, causing ductal obstruction. Tuberculosis also damages the epididymis, causing azoospermia. However, making a specific diagnosis of tuberculous epididymitis can be very difficult, because it is often a silent and indolent disease. Gonorrhea, chlamydia , syphilis and other STDs can also play havoc with the male genital tract; causing irreparable damage to its epithelium (internal lining).

Mumps can also cause orchitis (inflammation of the testis) - especially when it affects young men. This can cause severe damage to the testes, resulting in testicular failure.

What about other genital tract infections? Many doctors will do a semen culture, to look for a treatable cause of infertility, if the semen sample shows many pus cells. If the test is

positive treatment with antibiotics is instituted. Male reproductive tract infections (such as prostatitis) are often chronic, and may require many weeks of antibiotic treatment. It is therefore important to recheck the semen culture after therapy, to ensure that treatment has been adequate. However, the relation between the presence of bacteria in the semen and male infertility is still unclear. Do the bacteria really cause the infertility? Does treating the infection help to improve fertility? More questions than answers, once again !

Which medications can cause male infertility ?

Medication and its effects

Some medications can play havoc with the sperm count or with the sex drive. These include :

Drugs for high blood pressure like reserpine, methyl dopa, guanethidine, and propranolol; nitrofurantoin for urinary infection; corticosteroids; anabolic steroids for muscle building; and anti psychotic drugs.

A rare problem is that of anti cancer drugs and radiation therapy - used to treat young men with Hodgkin's disease, lymphoma, leukemia and testicular tumours. In these men, the chemotherapy and radiation therapy used to treat the disease also wipes out sperm production, rendering them sterile. An option available today is to store the sperms (sperm banking) which can later be used for inseminating the wife to achieve a pregnancy.

Does heat cause male infertility ?

Detrimental effects of heat:

The testicles are in the scrotum because they can't make sperm at body temperature - they need a cooler environment, so they hang outside the body where the temperature is 0.8 degrees centigrade cooler. Tightly encased groins because of jock straps, tight jeans, lungottis, and nylon briefs cause the testicles to be pressed back into the warmth of the body, especially when combined with hot tub baths and saunas. Working in hot sedentary jobs for long periods like foundries, boiler plants and engine rooms, may also cause a lower sperm count as your testicles get too hot.

In the past, doctors used to advise that the testes could be protected from this damage by wearing loose fitting cotton trousers and cotton boxer shorts; and applying a cold ice water soaked towel around the scrotum at least two or three times a day. However, unfortunately, this does not help at all !

Occupational hazards

These affect fertility by upsetting the hormonal balance; and suppressing sperm production.

Dangerous chemicals include: heavy metals, like lead, nickel, mercury; insecticides, petrochemicals, pesticides, benzene, xylene, anaesthetic gases, and X- rays.

What ejaculatory problems can cause male infertility ?

Ejaculation problems

Very often a perfectly fertile man may not be able to ejaculate. Since he can't make love

he can't make babies. Some men can't have an erection (erectile dysfunction, ED or impotence) and some cannot achieve an erection sufficient for intravaginal penetration or ejaculation in the vagina.

An older theory held that 80% of impotency problems, (which are very common) were rooted in psychological inhibition and fears which could respond to sex therapy and counselling. However modern research has lowered this figure and estimates that 50% are due to physical causes ranging from inadequate blood flow to the penis, diabetes, neurologic defects, and hormonal problems.

How does the doctor suspect a physical problem? By asking a simple question - Do you have wet dreams? If men have nocturnal ejaculations (wet dreams) this would suggest that the physical apparatus is sound, and that the problem is psychological.

Testing, includes nocturnal penile tumescence (NPT) testing, which monitors for normal night-time erections; and measuring blood flow through the arteries of the penis (using Doppler methods).

Treatment that may be prescribed includes:

- Viagra (sildenafil citrate), to induce an erection
- Injections of papaverine and prostaglandins, (chemicals which cause blood vessel to dilate) can be self-injected into the penis under medical supervision. These substances increase the blood flow to the penis, thus creating an erection.
- A surgical implant or penile prosthesis to give an artificial erection.
- Microsurgery to plug leaks in the veins of the penis, thus preventing the loss of turgidity of the erect penis.

The sperms can also be collected by masturbation and used for artificial insemination. This has a very high success rate, because there is really no fertility problem as such for these patients.

What is retrograde ejaculation ?

Retrograde ejaculation

This means that the semen goes backwards into the bladder instead of coming out of the penis, so that very little or no semen is ejaculated at the time of orgasm, and the urine looks cloudy after having sex. This occurs when the bladder sphincter muscle does not contract properly during orgasm, as a result of which the semen leaks back from the urethra into the bladder. This could be caused by prostate surgery, a spinal injury, diabetes, high blood pressure medication and congenital problems.

A simple way to diagnose retrograde ejaculation is to examine a man's urine after he ejaculates. If there are sperm in the urine, this confirms the diagnosis.

Self-help includes trying to have sex with a full bladder and while standing up, because this makes the muscle around the opening of the bladder more likely to stay closed.

Some medications like decongestants can also help the sphincter muscle to close. Surgery can also be performed on the opening of the bladder to prevent it from misbehaving, but this is not very successful.

An effective treatment option is to collect the sperm and use it for artificial insemination. After passing urine, the man alkalinizes his urine by drinking sodium bicarbonate; and

then urinates immediately after ejaculation. The recovered sperm in the urine are processed and used for insemination. Pregnancy rates with insemination are usually low because the recovered sperm are often of poor quality, and sometimes IVF needs to be done with these sperm to give a reasonable chance of pregnancy.

What is anejaculation ?

A nejaculation

Some men find that they can get an erection, but they are unable to ejaculate. This is an uncommon problem, and is often not diagnosed correctly, because many doctors don't consider this diagnostic possibility. This is called aspermia, but because it is so uncommon, most of these men are misdiagnosed as having azoospermia! Most of these men can be helped by teaching them to use a vibrator in order to ejaculate. A vibrator is a simple device, and you can buy one from our Online Store. The surface of this vibrates rapidly, and it is used to provide prolonged mechanical stimulation to the penis, until ejaculation occurs. You can read more about this at www.drmlpani.com/anejaculation.htm.

What is electroejaculation ?

Electroejaculation for spinal cord problems

Men with spinal cord problems cannot ejaculate because of neurologic damage. They can now be helped to father a pregnancy with the help of a technique called electroejaculation. A probe is inserted into the man's rectum (under general anesthesia) and electrical stimulation delivered to the prostate in a gradually increasing fashion to induce an ejaculation. The man usually attains an erection and ejaculates in about five minutes. The recovered sperm can then be used for IUI, IVF or ICSI, depending upon their quality (which is usually poor).

Treating the couple

If the man has a low sperm count, since so little can be done with conventional therapy to improve the sperm count, today we usually offer them one of the assisted reproductive technologies. This might seem unfair, since the wife is being treated for what is essentially the husband's problem, but the fact of the matter is that there is very little effective therapy for a low sperm count. Since the fertility of the couple is the sum of the fertility potential of both the partners, a male factor problem can often be treated by treating the wife!

Conclusion

Conventional treatment of male infertility has poor success rates and leaves a lot to be desired. However the availability of assisted reproductive technology in recent times has revolutionised our approach to male infertility, and using techniques such as ICSI, most infertile men can be helped to have their own babies. This is a rapidly developing area, and the spectacular advances which have occurred in recent times are described in the chapters to follow.

CHAPTER VII

The Man with a Low Sperm Count

Why is treatment of a low sperm count so confusing ?

Many infertile men are obsessed about their sperm count - and this seems to become the central concern in their lives. Remember that the real question the man with a fertility problem is asking is not: What is my sperm count or motility or whatever? But - are my sperm capable of working or not? Can I have a baby with my sperm? Since the function of the sperm is to fertilize the egg, the only direct way of answering this question is by actually doing IVF for test fertilization. This is, of course, too expensive and impractical for most people which is why the other sperm function tests have been devised.

The major problem with all these tests, however, is that they are all indirect --- there is no very good correlation between test results, pregnancy rates, and fertilization in vitro for the individual patient. This is why offering a prognosis for the individual patient based on an abnormality in the sperm test result is so difficult, and why we find that different doctors give such widely varying interpretations based on the same sperm report.

This is really not surprising when you consider how abysmal our ignorance in this area is - after all, we do not even know what a "normal" sperm count is! Since you only need one "good" sperm to fertilise an egg, we do not have a simple answer to even this very basic question! While the lower limit of normal is considered to be 10 million progressively motile sperm per ml, remember that this is a statistical average. For example, most doctors have had the experience of a man with a very low sperm count (as little as 2-5 million per ml) fathering a pregnancy on his own, with no treatment. In fact, when sperm counts are done for men who are undergoing a vasectomy for family planning, these men of proven fertility have sperm counts varying anywhere from 2 million to 300 million per ml. This obviously means that there is a significant variation in "fertile" sperm counts, and therefore coming to conclusions is very difficult for the doctor (leave alone the patient!)

In order to make sense of this, you need to understand two important concepts - "trying time" and "fertility potential of the couple". If your sperm count is low, but you have been trying to have a baby for less than 1 year, it still makes sense to keep on trying for about 1 year, since 10% of men with low sperm counts will father a pregnancy in this time. If however, you have already tried for more than 2 years with no success, you need to move on and do something more - the chances of a spontaneous pregnancy are now very low. Remember, that a doctor does not treat just a "low sperm count report" - he treats patients!

What can the man with a low sperm count do ?

So what is the man with a low sperm count to do? Unfortunately, there is no method of increasing the sperm count today! The modern protocol for managing male infertility is based on the man's motile sperm count; and on a simple test, called a sperm survival test.

The sperm are washed, and their recovery assessed; the washed sperm are then kept in culture medium in the incubator for 24 hours and then rechecked. If there are more than 3 million motile sperm per ml, this is reassuring. If, however, none of the sperm is alive after 24 hours, this suggests that they may be functionally incompetent. Treatment depends upon how low the count is. If it is only moderately decreased (total motile sperm count in the ejaculate being 20 million), it makes sense to try to improve the fertility potential of the wife, and the easiest treatment for men with moderately low sperm counts is superovulation plus intrauterine insemination. If after doing this and trying for 4 treatment cycles (the reason 4 is the "magic" number is that most patients who are going to become pregnant with any method will usually do so within 4 cycles) no pregnancy ensues, you need to go on and explore further alternatives, such as IVF or ICSI.

For men with a motile sperm count of more than 5 million in the ejaculate, IVF would be the first treatment offered. This would allow us to document if the sperm can fertilize the eggs or not. If fertilisation is documented, then the patient has a good chance of getting pregnant. However, if the motile sperm count is less than 5 million, or if there is total failure of fertilisation in IVF, then the only treatment available is ICSI (intracytoplasmic sperm injection, pronounced "eeksee") or microinjection. ICSI has revolutionised our approach to the infertile man, and it promises the possibility for every man to have a baby, no matter how low his sperm count.

Why do I have a low sperm count ?

What about the answer to the million dollar question: --- Why do I have a low sperm count? Unfortunately, nine times out of ten, the doctor will not be able to answer that question, and no amount of testing will help us to find out - this is labelled as "idiopathic oligospermia" which is really a wastepaper basket diagnosis for "god only knows!". Modern research has shown that the reason some men have a low sperm count maybe because of a microdeletion on the Y-chromosome. This is an expensive test, which is available only in research laboratories at present, and does explain why we have little effective treatment for this common problem! We do know that a low sperm count is not related to physique, general state of health, diet, sexual appetite or frequency. While not knowing the cause can be very frustrating, medicine still has a lot to study and understand about male infertility, which is a relatively neglected field today.

Is there any connection between a low sperm count and sexual performance ?

The major cause of male infertility usually is a sperm problem. However, do remember that this is no reflection on your libido or sexual prowess. Sometimes men with testicular failure find this difficult to understand (but doctor, I have sex twice a day! How can my sperm count be zero?). The reason for this is that the testis has two compartments. One compartment, the seminiferous tubules, produces sperms. The other compartment, the "interstitium" or the tissue in between the tubules (where the Leydig cells are) produces the male sex hormone, testosterone, which causes the male sexual drive. Now while the tubules can be easily damaged, the Leydig cells are much more resistant to damage, and will continue functioning normally in most patients with testicular failure.

This is why the diagnosis of a low sperm count can be such a blow to one's ego --- it is so totally unexpected, because it is not associated with other symptoms or signs. Men react differently - but common feelings include anger with the wife and the doctor; resentment about having to participate in infertility testing and treatment since they feel having babies is the woman's "job"; loss of self-esteem; and temporary sexual dysfunction such as loss of desire and poor erections. Many men also feel very guilty that because of "their" medical problem, they are depriving their wife the pleasures of experiencing motherhood. Unfortunately, social support for the infertile man is practically non-existent, and he is forced to put up a brave front and show that he doesn't care. Since he is a man, he is not allowed to display his emotions. He is expected to provide a shoulder for his wife to cry on - but he needs to learn to cry alone. However, remember that the urge for fatherhood can be biologically as strong as the urge for motherhood - and we should stop treating infertile men as second class citizens.

CHAPTER VIII A

Microinjection: The Latest Advance in Treating the Infertile Man

The introduction of Microinjection Technology into the in vitro fertilization laboratory has revolutionized our treatment of the infertile man. Intracytoplasmic sperm injection, or ICSI (pronounced "eeksee"), is a new infertility treatment that uses micromanipulation technology for treating male infertility. What ICSI promises is the possibility for every man to father his own baby - no matter what his medical problem!

What is ICSI ?

What exactly is ICSI? As the name suggests, ICSI is a technique in which a single sperm is injected into the centre of the cytoplasm of the egg, in order to achieve fertilization . While this may sound very crude, ICSI allows the IVF laboratory to achieve fertilization with very few sperm. The beauty of the technique is that since the sperm is being injected directly into the egg, all that is needed to achieve fertilization are live sperm - no matter how abnormal these may appear to be. With ICSI the equation "1 egg plus 1 sperm = 1 embryo" becomes possible!

How is ICSI performed ?

The Procedure for ICSI

ICSI is done in a superovulated cycle during which fertility drugs (human menopausal gonadotropin - HMG- injections) are administered to the wife to aid in the production of multiple eggs, which are then removed under vaginal ultrasound guidance as is done for IVF.

In normal circumstances, the egg is surrounded by a cluster of cells known as the cumulus corona cells, and this is called the oocyte cumulus corona complex. These cumulus cells are removed by repeated passage of the oocyte cumulus corona complex through fine pipettes, and by treating them with a chemical called hyaluronidase so that these cells are stripped off. The denuded eggs are examined, and only mature eggs (eggs in metaphase II, which have a polar body) are used for ICSI.

Sperm is collected from the man, usually through masturbation. For men with severe oligospermia, we have found it useful to use sequential ejaculates. Even though the first semen sample may not contain any sperm, we often find motile sperm in the second (or even the third sample, for men with enough stamina !) This maybe because the later samples contain "fresher" sperm. Since these samples contain such few sperm, they need to be processed very carefully, so that all the sperm in the sample are recovered in the culture medium , and can be used for ICSI.

For men with variable sperm counts, which vary from zero to a few thousand, it may be helpful to freeze a sample (which contains sperm) in advance. For patients with azoospermia, sperm harvesting techniques need to be used to retrieve the sperm. For men

with obstructive azoospermia,(because of duct blockage or absence of the vas deferens) , the simplest technique is called PESA (percutaneous epididymal sperm aspiration), in which the sperm is sucked out from the epididymis by puncturing it with a fine needle. Occasionally, one may have to use microsurgery to find epididymal sperm, and this is called MESA (microepididymal sperm aspiration).

How can ICSI be used to treat men with a zero sperm count (azoospermia) ?

For patients with obstructive azoospermia in whom sperm cannot be found in the epididymis, it is always possible to find sperm in the testis. The easiest way to retrieve this is through TESA or testicular sperm aspiration , in which the testicular tissue is sucked out through a fine needle, under local anaesthesia. The testicular tissue is placed in culture media and sent to the lab, where it is processed. The sperm are liberated from within the seminiferous tubules (where they are produced) and are then dissected free from the surrounding testicular tissue.

Using sperm from the epididymis and testis for ICSI in order to treat patients with obstructive azoospermia is logical, and thus conceptually easy to understand. However, surprisingly, it is possible to find sperm even in patients who have testicular failure (nonobstructive azoospermia) - even in those men with very small testes. The reason for this is that defects in sperm production are "patchy"- they do not affect the entire testis uniformly.

This means that even if sperm production is absent in a certain area, there may be other areas in the testis where sperm production would be normal (this could be because the genetic defect that causes abnormal spermatogenesis may be "leaky"). Since such few sperm are needed for ICSI, we can find enough sperm in over 50 per cent of patients with testicular failure , even if their testes are as small as a peanut!

What is TESE (testicular sperm extraction) ICSI ?

However, while finding sperm is quite easy in men with obstructive azoospermia (since their testes are functioning normally), patients with nonobstructive azoospermia (testicular failure) can be very challenging. Often, sperm production in these men is sparse, and multiple sites in the testis may need to be sampled before being able to find sperm. This can be done by performing multiple tiny microbiopsies , and this is called TESE or testicular sperm extraction. (One of our patients suggested that we call this procedure TSEICSI - which stands for testicular sperm extraction with ICSI, and pronounce it as "sexy"!) This can be done through the needle, or as an open procedure performed under direct vision through a tiny skin incision under local anesthesia and sedation.

Finding sperm in the testicular tissue can be a laborious process , depending on the degree of sperm production, and for some men with partial testicular failure, it can take upto 2-3 hours to find the sperm. Also, testicular sperm are technically hard to work with in the laboratory and only some IVF clinics have the requisite expertise. For men with nonobstructive azoospermia, some clinics perform the TESE the day prior to egg retrieval, because they believe culturing the testicular tissue in the incubator for 24 hours

helps the sperm to acquire motility, which makes them easier to work with. In case no sperm are found, either the couple decides to cancel the egg retrieval and abandon the cycle, or to go ahead with using donor sperm for IVF, as a backup option.

In patients in whom surgery needs to be performed in order to recover testicular or epididymal sperm, it is now possible to freeze the excess sperm. These sperm can then be thawed and used in future cycles in needed, thus sparing the patient the need for repeated surgery for sperm retrieval.

CHAPTER VIII B

Microinjection: The Latest Advance in Treating the Infertile Man

How is a single sperm injected into the egg for ICSI in the IVF laboratory ?

Once eggs and sperm have been collected, the actual process of injecting a single sperm into the egg is carried out in a laboratory. The injection is performed on a heating stage, on a specialized inverted microscope (which allows one to magnify details up to 400 times) equipped with Hoffman modulation contrast optics (which enhance "optical contrast", so that the details of the egg can be visualized easily). The precise control that is needed for microinjection is provided by using specialized micromanipulators, which allow one to execute very fine movements.

The eggs and sperm are manipulated using fine glass pipettes, made of thin capillary tubing, which are even finer than a human hair. These are custom made, the holding pipette being designed to hold a single sperm. Live sperm are placed in a drop of viscous polyvinyl pyrrolidone (PVP) solution, which serves to slow down the activity of the sperm. (It is helpful to slow down the sperm, so that they can be picked up more easily by the injecting needle.) A single sperm is then selected and its tail is pinched or broken to immobilize it. This is usually done by crushing the sperm tail by rolling it between the injection pipette and the base of the petri dish. It is essential to immobilize the sperm, so that it cannot move after it has been injected into the egg. A single immobile sperm is then picked up by sucking it into the injection pipette.

The egg is secured in place by applying gentle suction to its shell (the zona) with a holding pipette. The sperm is then injected directly into the centre (cytoplasm) of the egg by moving the injection pipette very precisely with the help of the micromanipulator into the egg, and then blowing the sperm out very gently into the cytoplasm of the egg. In order to do this, it is important to breach the zona of the egg and the outer membrane of the egg. The skill of the embryologist is a critical factor in the success of the ICSI process. After injecting the sperm, the pipette is withdrawn. Remarkably, once the injecting pipette is withdrawn, the egg will close and assume its original shape within 60 seconds. One can visualize ICSI as the sperm being given a "piggyback" ride into the egg, so that what the sperm cannot accomplish on its own, the laboratory does for it! The only requirement for ICSI is that the sperm should be alive, and there should be as many sperm as there are eggs.



Fig 1. A view of the micromanipulator

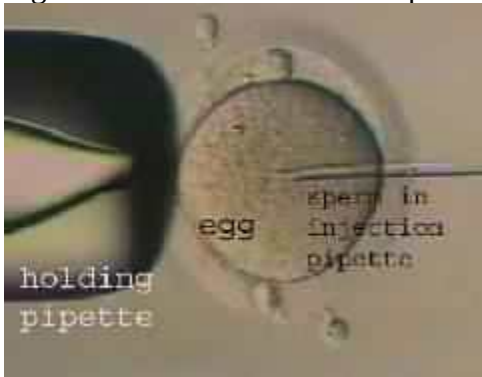


Fig 2. A single sperm is being injected into an egg during an ICSI procedure

Once all the eggs are injected with a single sperm each, they are placed in the CO₂ incubator, and then observed approximately 14 hours later to see if fertilization has taken place. If fertilization has occurred, the 2-4 cell embryos can be transferred into the wife's uterus about 48-72 hours after ICSI, as is done for IVF. Interestingly, embryo implantation rates in these patients are quite high, because the wives are usually young and completely normal.

Fertilization rates in the range of 60-80 per cent have been achieved in experienced hands-which means, of 100 microinjection eggs about 60 form embryos after ICSI. In fact the technology is now reliable enough to virtually guarantee fertilization, if there are sufficient good quality eggs. The pregnancy rate in one ICSI cycle is about 35 percent. Remarkably, the chance of achieving a pregnancy does not depend upon the sperm count or number (since you only need as many sperm as there are eggs!), but rather on the number and quality of eggs retrieved, which, in turn, depend upon the woman's age. The risk of having a baby with a birth defect is not increased with this technique.

ICSI is expensive at present, because of the advanced technology it utilizes. Nevertheless, it is now available in most of India's large cities, and as times goes by, it is hoped that the cost of this procedure will decrease, making it affordable for more patients.

ICSI has now become the preferred method of achieving in vitro fertilisation in our clinic. This reduces the risk of unexpected total fertilisation failure sometimes seen with IVF (research has shown that up to 25% of patients with "unexplained " infertility with an apparently normal semen analysis may have dysfunctional sperm which cannot fertilise eggs in vitro).

What are the risks of doing ICSI ?

The Risk Factor

More than 100,000 babies have been born worldwide after ICSI , and detailed studies have shown that there is no increased risk of birth defects or genetic anomalies , as a result of the technique.

It is possible , however, that some of the male children born as a result of this technique may be infertile as well (for example, if the cause for the testicular failure is a defective genetic locus, such as a microdeletion on the Y chromosome).

What recent advances have taken place in ICSI ?

Recent Advances

For some patients with severe testicular failure, sometimes, it is not possible to find any sperm at all as even in spite of taking multiple testicular biopsies. In such patients pregnancies have been achieved even by injecting round spermatids (immature precursor cells from which the sperm are formed) from the testis into the egg. This is now an area of intense research all over the world, but the results have been disappointing so far. Other labs are trying to develop methods of in vitro spermatogenesis, in order to mature the spermatids in vitro.

For men with no testis at all, the only technologic solution today would be cloning using nuclear transfer technology. This involves inserting the nucleus from an ordinary cell of the man (which contains all his DNA) into his wife's unfertilised egg (the nucleus of which has been removed) and then activating it by electrofusion. While cloning has been performed successfully in many animal species, it has never been used for treating humans so far.

CHAPTER IX A

Ultrasound - Seeing with Sound

How is ultrasound (sonography) used for treating infertility ?

Ultrasound or sonography has helped revolutionize our approach to the infertile patient. Ultrasound machines are a very useful addition to the gynecologist's bag of tricks; and help him to "image" or see structures in the female pelvis. Ultrasound uses high frequency sound waves much like SONAR machines used in ships for detecting submarines underwater. The high frequency sound waves are bounced off the pelvic organs; and the reflected sound waves are received by the probe (transducer) and a computer is used to reconstruct the waves into black and white images on the monitor. Ultrasound machines today are all real-time machines, which give dynamic images.

In the old days, ultrasound for infertility was done through the abdomen. This required you to fill up your bladder (till it was ready to burst !) so that the sound waves could be transmitted into the pelvis. However, the standard ultrasound technique today for infertility is vaginal ultrasound (endovaginal scanning) in which a long, slim, slender probe is inserted into the vagina and used for imaging the pelvic organs. Not only is this much more comfortable for you; it also gives much sharper and clearer pictures, since the probe is much closer to the pelvic structures.

What can you see on ultrasound? The ultrasound gives clear pictures of the uterus; and the ovaries. It allows the doctor to look for fibroids; ovarian cysts; and ectopic pregnancies. It is also excellent for early diagnosis of pregnancies. However, the ultrasound scan is not very good for assessing whether or not the tubes are normal.

How is ultrasound used for follicular scanning to monitor ovulation ?

Ovulation scans allow the doctor to determine accurately when the egg matures; and when you ovulate. This is often the basic procedure for most infertility treatment since the treatment revolves around the wife's ovulation. Daily scans are done to visualize the growing follicle, which looks like a black bubble on the screen. Most women can see the follicle clearly for themselves - and know by the scans when the egg has ruptured. Other useful information which can be determined by these scans is the thickness of the uterine lining - the endometrium. The ripening follicle produces increasing quantities of estrogen, which cause the endometrium to thicken. The doctor can get a good idea of how much estrogen you are producing (and thus the quality of the egg) based on the thickness and brightness of the endometrium on the ultrasound scan.



Fig 1. Ultrasound scan showing multiple follicles



Fig 2. Ultrasound scan of the uterus, showing a normal endometrium, which appears as a triple band in the center of the uterus

What if an ovarian cyst is found on ultrasound scans ?

One of the commonest findings on an ultrasound scan is an ovarian cyst. A cyst is a collection of fluid surrounded by a thin wall (a fluid-filled sac) that develops in the ovary. Typically, ovarian cysts are functional (not disease-related) and disappear on their own. During ovulation, a follicle may grow , but fail to rupture and release an egg. Instead of being reabsorbed, the fluid within the follicle persists and forms a follicular cyst.

The other type of functional cyst is a corpus luteum cyst, which develops when the corpus luteum fills with blood. Functional ovarian cysts usually resolve on their own, and are not to be confused with other pathological conditions involving cystic ovaries, specifically polycystic ovarian disease, endometriotic cysts, or ovarian tumours.

Since an ultrasound picture is just a black and white shadow, the doctor has to be skillful in interpreting what the image means. Simple cysts are thin walled, and appear as a large black bubble. Cysts which contain blood (for example, chocolate cysts found in patients with endometriosis) will have echoes within them, which appear white, and these are described as complex masses on ultrasound. The incidence of follicular cysts is increased in infertile patients taking drugs (such as clomiphene and HMG) for ovulation induction. Functional ovarian cysts usually disappear within 60 days without treatment. However, if the cyst is larger than 6 cm, or persists for longer than 6 weeks, then further testing may be needed.

Who should do the ultrasound scans ?

Who does the scans? Ultrasound scans can be done either by a radiologist; or by the gynecologist or infertility specialist himself. Remember that the eye only sees what the mind knows, so you must go to a good clinic for your scans.

The benefit of having the scans done by the infertility specialist himself is that he can make immediate decisions regarding your treatment based on the scan findings. If the radiologist does the scans, then you have to wait till your doctor has seen the report before knowing what to do next since the radiologist does not make the treatment decisions.

In any case, it is vital that the ultrasound scans be done in the Infertility Clinic itself, so that your waiting can be minimized - and you don't have to run around from the sonographer to the gynecologist. If there are any abnormal findings, it is vital that your gynecologist see the actual ultrasound for himself during the scan. This provides much more information than the printed pictures.

Today, thanks to the magic of telemedicine, many of our patients can email the jpeg images of their ultrasound scans to us, wherever in the world they may be, so we can actually "see " the images and interpret them ourselves.

CHAPTER IX B

Ultrasound - Seeing with Sound

What recent advances have occurred in ultrasound ?

Recent Advances in Ultrasound

Ultrasound technology has made dramatic advances in recent years, and now tests have been described which allow the doctor to use ultrasound to assess tubal patency. Basically, these involve passing a fluid into your tubes through the uterus; and the gynecologist can see the passage of the bubbles into the tubes and out into the abdomen. Since this test (sonosalpingography) can be done in the doctor's clinic itself, and does not involve X-ray radiation, it has advantages - especially for documenting that the tubes are normal. However, the gold standard for tubal testing remains HSG (hysterosalpingography, an X-ray of the uterus and tubes) and laparoscopy today, because it provides us with a "hard copy" image which can be critically examined.

Doppler: The newer ultrasound machines have Doppler attachments which allow the doctor to judge the flow of blood in the blood vessels. Colour Doppler allows the doctor to "see " the blood flow in the pelvic blood vessels, mapped in color on the monitor. While still a research tool, it may provide important information for assessing the infertile patient in the coming years.

Three – dimensional ultrasound. Using sophisticated microprocessors, the newest ultrasound machines allow the doctor to reconstruct the image, so that he gets a three dimensional view. While this provides excellent pictures, the true value of this technique for infertility still has to be evaluated. It can be useful in assessing women with uterine anomalies, because it helps the doctor to differentiate between a septate uterus and a bicornuate uterus.

How can ultrasound guided procedures be used to treat infertility ?

Ultrasound now also offers infertile patients newer treatment options not available before. Modern surgical techniques have progressively become less and less invasive - all to the patient's benefit ! From laparotomy to laparoscopy , and now to ultrasound guided procedures, we are witnessing a change in the gynecologist's armamentarium from the knife to the endoscope to the guided needle !

The benefits to the patient of "minimally invasive surgery" are many and include : reduced costs; reduced hospitalisation ; reduced risk of complications; and better preservation of fertility, with increased chance of conception for the future.

Ultrasound-guided procedures can be used to treat a variety of problems seen in the infertile woman:

1. Egg pickup for IVF - The use of vaginal ultrasound for egg pickup has made egg retrieval a short, simple and inexpensive procedure, which can be performed in a day-care unit, under sedation and local anesthesia . The ovaries are normally present in the pouch of Douglas, and are very accessible transvaginally. Moreover, the presence of adhesions does not interfere with egg collection.
2. Ovarian cyst aspiration. An ovarian cyst is a very common condition in which fluid collects in the ovary. However, cysts which are more than 5 cm in size need to be treated, as they can cause problems (eg twisting and rupture). Normally, surgery had to be done to remove these cysts - and often this damaged the surrounding normal ovary as well. With ultrasound-guidance, we can stick a needle from the vagina into the cyst, and empty the contents (usually clear fluid) by sucking it out. This empties the cyst, which often does not recur.
3. Treatment of ectopic pregnancy . With technological advances (ultrasound and beta-HCG blood tests) the diagnosis of tubal pregnancy can be made very early, usually before rupture. It can be treated by injecting a toxic chemical, methotrexate, into the sac, which causes the tissue to die and then get reabsorbed, without any surgery whatsoever. In more advanced tubal pregnancies, potassium chloride can be injected direct into the heart of the baby in the ectopic gestational sac, thus killing it and preventing it from growing.
4. Ultrasound-guided tubal embryo and gamete transfer for IVF and GIFT techniques. Techniques have been devised to pass a special tube - the Jansen-Anderson catheter set - into the fallopian tubes through the vagina under ultrasound guidance, so as to place the embryos and /or the gametes in the fallopian tube. Since the tube offers a better environment for the gametes and embryos than the uterine cavity, it is believed that this will improve pregnancy rates.
5. Tubal recanalisation for cornual blocks (proximal tubal obstruction). Often cornual blocks are due to the presence of mucus plugs and amorphous debris in the tubal lumen. Ultrasound guided tubal catheterization can effectively treat the blocked tubes in some of these patients.

The scope of ultrasound guided procedures has increased dramatically in the last few years; and with further improvements in technology, we can expect this list to become even longer, and doctors become more versatile with using this technology.

CHAPTER X A

Laparoscopy -- The Kinder Cut

What is laparoscopy ?

Laparoscopy (also called endoscopy or pelviscopy) is a surgical procedure in which a telescope is inserted inside the abdomen through a small cut below the navel, so that the doctor can have a look at the pelvic organs in the infertile woman. A laparoscopy can lead to the diagnosis of many problems which cause infertility including damaged tubes, endometriosis, adhesions and tuberculosis.

When is laparoscopy done?

In the past, a diagnostic laparoscopy was a routine part of the workup in infertile women, in order to complete their evaluation. Generally, the procedure was performed after the basic infertility tests were done, since it is a surgical (invasive) procedure. Today, however, the utility of laparoscopy in treating infertile women is very limited, and we rarely perform laparoscopies in our clinic.

Timing the surgery

Some doctors will time the laparoscopy during the premenstrual phase (the week before the next period is due). They combine the laparoscopy with a dilatation and curettage (D & C) (scraping the inside of the uterine cavity) so that they can also get information on the woman's ovulatory status in the same procedure.

Some doctors try to perform the diagnostic laparoscopy during the post-menstrual phase, when the uterine lining is thin, so that they can combine it with a hysteroscopy at the same time.

What precautions need to be taken before laparoscopic surgery ?

The patient is advised not to eat or drink anything for a specific time before the operation. Some tests may also be done before the procedure, to ensure safety for anesthesia, though for most young healthy women tests are usually not needed. Some doctors may want a HSG (hysterosalpingogram) done before performing a laparoscopy.

The surgery is usually done on a day-care basis. Laparoscopy is done under general anesthesia so that the patient remains asleep during surgery and does not feel any discomfort.

How is the laparoscopy performed ?

The laparoscopic procedure

First of all, the abdomen is cleansed and draped for the procedure. Then an instrument may be placed in the uterus through the vagina. A gas, such as carbon dioxide or nitrous oxide or air is then allowed to flow into the abdomen just below the belly button. This gas creates a space inside by pushing the abdominal wall and the bowel away from the organs in the pelvic area and makes it easier to see the reproductive organs clearly.

The laparoscope, which is a slender tube, like a miniature telescope, is then inserted through a small incision just below the navel. During the laparoscopy a small probe is placed through another incision in order to move the pelvic organs into clear view. A diagnostic laparoscopy is incomplete without a "second puncture" because, without this second probe, it is not possible to visualize all the structures completely.

During the laparoscopy the entire pelvis is carefully scanned and the organs inspected systematically - the uterus; the ovaries; and the lining of the abdomen, called the peritoneum. In addition to looking for diseases affecting these structures, the doctor also looks for adhesions (bands of scar tissue), endometriosis and tubercles. In case abnormalities are found, the doctor can either try to correct them (operative laparoscopy), or take out bits of tissue for histologic examination (biopsy) with a biopsy forceps. A blue dye (methylene blue) is then injected through the uterus and fallopian tubes to check whether the tubes are open. When the surgery is complete, the gas is removed and one or two stitches inserted to close the incisions. Since the incisions are so small, often stitches are not needed and they can be closed with Band-Aids.



Fig 1. A laparoscopy being performed. Note that the view through the laparoscope can be seen on the TV monitor.

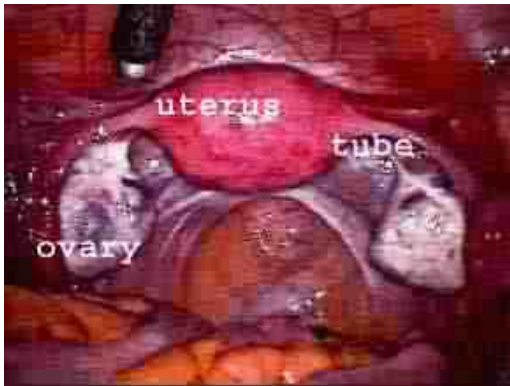


Fig 2. Normal pelvis as seen during a laparoscopy. The uterus is the reddish structure in the center; on either side of which are the pink fallopian tubes. These run towards the ovaries, which are white in colour.

As stated earlier, along with laparoscopy, some doctors carry out a dilatation and curettage (D & C) and send the endometrial curettings for histologic examination to rule out the possibility of hidden tuberculosis, and also to find out if ovulation is taking place. Others will do a diagnostic hysteroscopy at the same time, to ensure that the uterine cavity is normal.

Most doctors today use videolaparoscopy, in which a video camera is connected to the laparoscope, so that what the surgeon sees can be displayed on a TV monitor. This kind of laparoscopy can be very useful for documentation and record-keeping. It is also very helpful for patient education, since the doctors can use the video or CD later on to explain to the patient the exact nature of her problem.

Recent advances in miniaturization have allowed companies to manufacture very tiny laparoscopes. These are as thin as a needle, and are called microlaparoscopes or needlescopes. These allow doctors to perform laparoscopy in the clinic itself, without using anesthesia. However, the quality of the images is still not very good with these tiny scopes.

Dr Brosens from Belgium has also introduced the technique of transvaginal hydrolaparoscopy. This allows the doctor to examine the pelvis by inserting a tiny scope through the vagina, so that no abdominal incision needs to be made. The value of this technique as compared to conventional laparoscopy is still being studied.

What is an operative laparoscopy ?

During operative laparoscopy, many problems which cause infertility can be safely treated through the laparoscope at the same time that the diagnosis is made. When performing operative laparoscopy, additional instruments such as probes, scissors, biopsy forceps, coagulators and suture materials are placed into the abdomen, either through the laparoscope or through two or three additional incisions called "suprapubic punctures", which are made above the pubis.

Some of the disorders that can be corrected with the help of the procedures above include: releasing scar tissue and/or adhesions from around the fallopian tubes and ovaries; opening blocked tubes; and removing ovarian cysts. Endometriosis can also be destroyed by burning it from the back of the uterus, ovaries, or peritoneum during operative laparoscopy. Under certain circumstances, small fibroid tumors can be removed and ectopic pregnancies can be treated.

When performing operative laparoscopy, surgeons may use electrocautery instruments, lasers, and sutures. The choice of the technique used depends on many factors including the surgeon's training, location of the problem, and availability of equipment.

What is a "second-look laparoscopy ? "

Sometimes, a "second-look" laparoscopy may be recommended. This procedure is performed following either operative laparoscopy or major tubal surgery. Second-look laparoscopy can take place within a few days following the initial surgery or many months afterwards. During the procedure, the doctor determines whether adhesions are re-forming or if endometriosis is returning and these conditions can be treated in needed.

After surgery, the patient needs to rest for about 2 to 4 hours in order to recover from the effects of anesthesia. She can usually go home the same day and resume normal work in 2 to 3 days. Sexual activity can be resumed in a week or so, depending upon the doctor's advice.

CHAPTER X B

Laparoscopy -- The Kinder Cut

What can you expect to feel after the laparoscopy ?

After the operation, there may be some discomfort. This may include:

- Mild nausea as a result of the medication or the surgical procedure
- Pain in the neck and shoulder due to the gas inside the abdomen, which irritates the phrenic nerve and causes "referred pain" perceived in the shoulder
- Pain in the areas where the instruments passed through the abdominal wall
- A scratchy throat and hoarse voice if a breathing tube was used during general anesthesia
- Cramps, like menstrual cramps
- Discharge like a menstrual flow for a day or two
- Muscle aches

Most of these minor symptoms will disappear within a day or two after surgery. The abdomen may feel swollen for a few days. Any unusual or peculiar symptoms should be reported at once to the doctor.

To really appreciate the benefits of laparoscopy, one should remember that the alternative is major surgery (laparotomy) which involves a large abdominal incision, a four to six day hospital stay, and four to six weeks of postoperative recovery time.

What are the complications of laparoscopy ?

While the doctors may term laparoscopy as being "minor" surgery, remember that for the patient all surgery is major! The risk of laparoscopy are minimal. But certain conditions increase the possibility of complications. If there has been previous surgery in the abdomen, especially involving the bowel, there is an increased risk. Other conditions that lead to a higher risk of complications are evidence of an infection in the abdomen, a large growth or tumor within the abdomen, and obesity.

Complications among young, healthy women under going laparoscopy are rare and occur only in about three out of 1000 cases. These complications can include injuries to structures in the abdomen such as the bowel, a blood vessel or the bladder. Most often, these injuries occur when the laparoscope is placed through the navel. If such an injury occurs during the procedure, the physician can perform major surgery and correct the damage through a longer abdominal incision. Sometimes, complications may arise after surgery. If bleeding or pain appears excessive or if high fever develops, the doctor should be informed.

How can I be sure my doctor will perform the laparoscopy properly ?

Unfortunately, many gynecologists are not skilled at performing a laparoscopy properly. In order to choose the best doctor for performing your laparoscopy, you need to ask him the following questions.

1. How many laparoscopies have you done?
2. Do you use multiple punctures?
3. Do you use a video for recording the operation?
4. If you find a problem, will you correct it at the same time? Ideally, if the doctor finds a problem during the laparoscopy, he should correct it at the same time, rather than call you again for a second surgical procedure, which only adds to your expense and risk.

A good doctor has a lot of experience in performing laparoscopies; uses multiple punctures, so he can assess the pelvis properly; and always provides documentation (in the form of a video, CD or DVD) so the findings can be reviewed by another doctor.

Which is better - a laparoscopy or a HSG ?

Comparing laparoscopy and HSG.

In our practise, we prefer using an HSG to document tubal patency, because it is much less expensive; is non-surgical; and provides a hard copy record , which all doctors can refer to later on. Some doctors still believe that both the HSG and laparoscopy are complementary procedures, and you may even need both, especially if your tubes are blocked. HSG provides information only about the inside of the tubes and uterine cavity, whereas in laparoscopy, not only can the tubal patency be determined, but two other disorders (endometriosis and tubal adhesions) inside the abdomen which affect tubal function and which do not show up on HSG can also be diagnosed. However, while it is true that a laparoscopy offers the doctor a chance to diagnose and treat these problems at the same time , it is still unsure whether correcting these problems actually helps to improve the patient's fertility !

A common problem which patients face in practice is that many doctors will insist on repeating the laparoscopy. One reason for this is that doctors feel that they need to do the laparoscopy for themselves, because they cannot "trust" another doctor's judgment. This is, of course a major problem for patients, who suffer repeated (and unnecessary) laparoscopies. Having a video record should help to minimize this problem.

What happens if your laparoscopy was normal and the second doctor wants to repeat it anyway? Sometimes doctors have little to offer in the way of effective treatment and since there is nothing else to do, they suggest a repeat laparoscopy to which the hapless patient is forced to agree. If your first laparoscopy did, in fact indicate you had a problem, a second look laparoscopy may be indicated (and this should have been discussed with you after the first laparoscopy) to determine if the problem has been

successfully resolved. Ask the doctor what information he hopes to get by doing the repeat laparoscopy and how this will change your treatment. If you feel the doctor wants to do a laparoscopy for no very good reason, refuse. It's a surgical procedure after all - and it's your body.

Thinking it over

One benefit of laparoscopy is that in addition to allowing the accurate diagnosis of a problem, if it exists, operative laparoscopy can also be done in the same surgery to correct the problem. However, we feel that the routine use of laparoscopy is not called for in treating infertile patients, since a HSG can provide similar information at much less risk and expense. We use the procedure very sparingly in our practise.

What happens after the laparoscopy ?

At the follow-up visit, discuss with the doctor what he found at the time of the laparoscopy and also how to proceed on the basis of the findings. There are three possible courses of action:

1. Normal findings: Such findings are the commonest result and can be very assuring ! These help to confirm the diagnosis of "unexplained infertility".
2. Abnormal findings, such as peritubal adhesions or endometriosis, which could be corrected at the time of laparoscopy itself: Perhaps the doctor may suggest a second look laparoscopy or HSG after some time to document that the problem has, in fact been corrected or else in addition medical treatment may be advised to try to correct a residual problem (e.g. antibiotics for pelvic infection). A quandary may arise when the laparoscopy reveals a finding which may be of no relevance to the problem of infertility. For example during laparoscopy the doctor may detect small fibroids, early endometriosis, or an ovarian cyst. These are common disorders and are often found in fertile women as well. Just making a diagnosis of these disorders does not automatically mean that they need to be corrected: they may be red herrings, which do not affect fertility. In fact, unnecessary surgery to remove these disorders can aggravate your infertility.
3. Abnormal findings: which could not be corrected during the laparoscopy: For treatment of these problems, the doctor may advise IVF (for example, for patients with irreparably damaged fallopian tubes).

CHAPTER XI A

Hysteroscopy

What is hysteroscopy ?

Hysteroscopy, as the name suggests (hystero = uterus; scopy = to see), is a surgical procedure in which a telescope is inserted inside the uterus to examine the uterine lining. This procedure can assist in the diagnosis of various uterine conditions which can cause infertility, such as:

1. submucous (internal) fibroids
2. scarring (adhesions or synechiae)
3. endometrial polyps
4. uterine septa and other congenital malformations

Before performing hysteroscopy, a hysterosalpingogram (an x-ray of the uterus and fallopian tubes) may be performed to provide additional information about the cavity which can be useful during surgery. Many doctors will also do a vaginal ultrasound as a diagnostic aid. Diagnostic hysteroscopy is usually conducted on a day-care basis with either general or local anesthesia and takes about thirty minutes to perform.

How is hysteroscopy performed ?

The first step of hysteroscopy involves cervical dilatation - stretching and opening the canal of the cervix with a series of dilators. Once the dilatation of the cervix is complete, the hysteroscope, a narrow lighted telescope, is passed through the cervix and into the lower end of the uterus. A clear solution (Hyskon or glycine) or carbon dioxide gas is then injected into the uterus through the instrument. This solution or gas expands the uterine cavity, clears blood and mucus away, and enables the surgeon to directly view the internal structure of the uterus.

The doctor systematically examines the lining of the cervical canal; the lining of the uterine cavity; and looks for the internal openings of the fallopian tubes where they enter the uterine cavity - the tubal ostia.

Some doctors may do a curettage (a surgical scraping of the inside of the uterine cavity) after the hysteroscopy and send the endometrial tissue for pathologic examination.

What is operative hysteroscopy ?

The technique of hysteroscopy has also been expanded to include operative hysteroscopy. Operative hysteroscopy can treat many of the abnormalities found during diagnostic hysteroscopy at the time of diagnosis.

The procedure is very similar to diagnostic hysteroscopy except that operating instruments such as scissors, biopsy forceps, electrocautery instruments, and graspers can be placed into the uterine cavity through a channel in the operative hysteroscope. Fibroid tumors, scar tissue (synechiae or adhesions), and polyps can be removed from inside the uterus. Congenital abnormalities, such as a uterine septum, may also be corrected through the hysteroscope.

What is hysteroscopic tubal cannulation ?

A relatively new method for treating proximal tubal obstruction (cornual blocks, where the tubes are blocked at the utero-tubal junction) is that of hysteroscopic tubal cannulation. Many studies have shown that this kind of block is often because of mucus plugs or debris which plug the tubal lining at the uterotubal junction which is as thin as a hair. It is now possible to pass a fine guidewire through the hysteroscope into the tubes, and thus remove the plug or debris and open the tubes - thus restoring normal tubal patency with "minimally invasive surgery"!

Another advance has been the development of the method of fallopscopy - in which a very fine flexible telescope is passed into the tube through the hysteroscope, so as to visualize the interior of the entire tube.

After a hysteroscopy, patients often have cramping similar to that experienced during a menstrual period; and some vaginal staining for several days. Regular activities can be resumed within one or two days after surgery. Sexual intercourse should be avoided for a few days or for as long as bleeding occurs.

What are the complications of hysteroscopy ?

Complications occur rarely during hysteroscopy. In a few cases, infection of the uterus or fallopian tubes can result. Occasionally, a hole may be made through the back of the uterus - a perforation. However, this is usually not a serious problem because the perforation closes on its own. Frequently, when extensive operative hysteroscopy is planned, diagnostic laparoscopy is performed at the same time to allow the surgeon to see the outside as well as the inside of the uterus to try to reduce the risk of accidental uterine perforation. Other possible complications include allergic reactions and bleeding.

CHAPTER XI B

Hysteroscopy

What are uterine(endometrial) polyps ?

Polyps

Endometrial or uterine polyps are soft, fingerlike growths which develop in the lining of the uterus (the endometrium). They develop because of excessive multiplication of the endometrial cells, and are hormonally dependent , so that they increase in size depending upon the estrogen level. They can usually be detected on an ultrasound scan if this is done mid-cycle, when estrogen levels are maximal, but are easily missed if the scan is not done at the right time of the menstrual cycle. Polyps are an uncommon but important cause of infertility, because they can easily be removed during hysteroscopic surgery.



Fig 1. Uterine polyp as seen during hysteroscopy

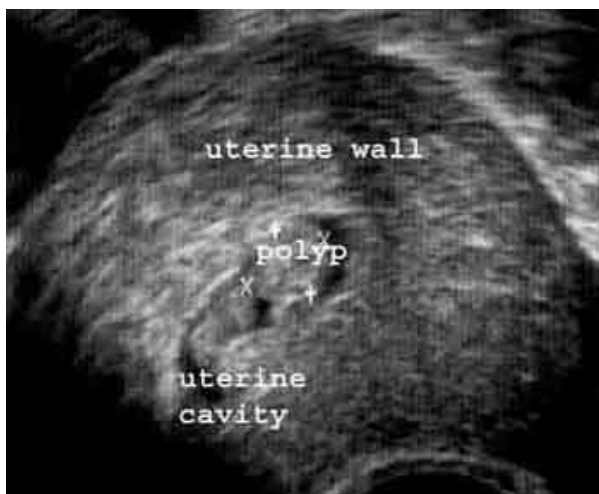


Fig 2. Uterine polyp seen during ultrasound scan after infusion of saline which outlines the polyp in the cavity

How do fibroids (myomas) affect fertility ?

Fibroids

While the commonest problem found in the uterus is a fibroid (myoma or leiomyoma), this is rarely a cause of infertility, and is usually an incidental finding of little importance. Fibroids are common benign smooth muscle tumors which arise in the wall of the uterus, and may be single or multiple. About 25% of all women over the age of 35 have fibroids.

Most fibroids develop in the wall of the uterus (intramural) or protrude outside of the uterine wall (subserous fibroids), and these can usually be left alone, since they do not hinder fertility, and neither do they cause problems during the pregnancy. In fact, unnecessary surgery to remove the fibroid often causes more harm than good. This surgery often creates adhesions, which causes the tubes to get blocked.

However, if the fibroids are very large, they may need surgical removal, and this procedure is called a myomectomy. Some doctors give an injection of a GnRH analog prior to surgery in order to shrink the fibroid and make surgery technically easier. When performed by an expert, it is a safe and effective procedure which can be accomplished with minimal blood loss. However, sometimes because of uncontrollable bleeding the surgeon may be forced to remove the entire uterus (a procedure called a hysterectomy), and this is obviously a disaster for the infertile woman!

The standard technique for removing a fibroid is through open surgery (laparotomy). It is now also possible to remove fibroids through the laparoscope, but laparoscopic myomectomy does not allow for optimal reconstruction of the uterus. Submucous fibroids are an important cause of infertility, because they interfere with implantation of the embryo, by acting as a foreign body. These are best removed by an operative hysteroscopy. While surgery can remove the fibroid, it can recur again, and most doctors advise the patient to try to conceive as soon as possible after surgery.

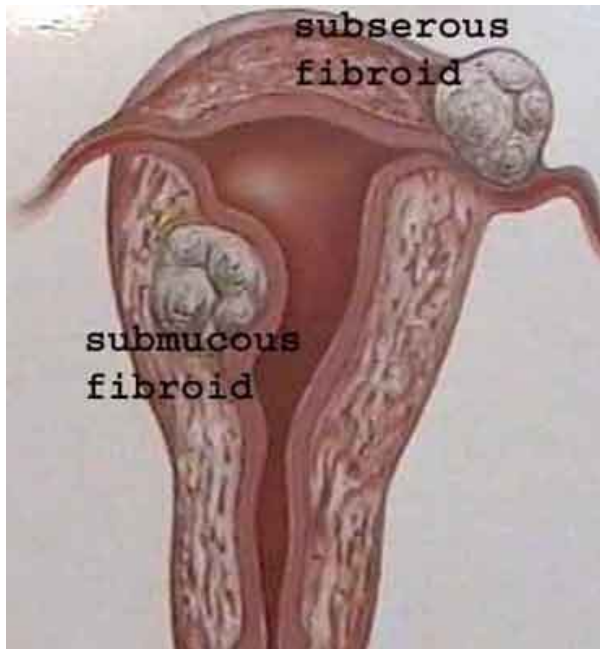


Fig 2. Schematic showing a submucous fibroid; and a subserous fibroid compressing the right fallopian tube

Fibroids may grow larger during the pregnancy, but usually pregnancy and delivery are uneventful. In rare cases, after a myomectomy, uterine rupture may occur during pregnancy or delivery, and this complication may result in severe blood loss, fetal loss and even maternal death.

Because of the potential for catastrophic results, it is recommended that women have cesarean deliveries in the following circumstances: 1) when the myomectomy involved full-thickness incision of the uterine wall or multiple deep uterine incisions or 2) when myomectomy was complicated by infection which may have weakened the uterine wall or 3) when there is doubt regarding the adequacy or extent of the uterine repair.

The uterus was often a neglected organ in the infertility workup, partly because we did not have the tools to study it properly. Hysteroscopy, hysterosalpingography and vaginal ultrasound are all complementary procedures for evaluating the uterine cavity in the infertile woman. The HSG is good for looking for polyps, adhesions and septa which appear as "filling defects" on the X-ray. However, careful radiologic technique is a must. Vaginal ultrasound is excellent for detecting submucosal fibroids or polyps, which can be missed on hysteroscopy and HSG. Of course, the major advantage of hysteroscopy is it offers the chance of treating the problem as well!

What are the new techniques for studying the role of the endometrium in infertility?

We are now also developing newer techniques to study the uterus. One of our major areas of ignorance today is the complex process of embryo implantation. It is obvious that the endometrium has a key role to play in this process, in which the embryo has to appose and attach itself to the maternal endometrium and invade into it. At present, the tools we have to study endometrial function and receptivity are very crude. They include primarily transvaginal ultrasound, to assess the endometrial thickness and texture, but this provides very limited and indirect evidence of endometrial functions. Colour Doppler ultrasound has also been used to assess endometrial blood flow (perfusion), but its utility is limited.

Since embryo-endometrium interaction is a biochemical process, a lot of study has been done on the role of the molecules involved in this process. Recent research has shown that the normal endometrium contains various cell adhesion proteins called integrins, which allow the embryo to interact with it. Studies have shown that the endometrium of some infertile women is deficient in some of these integrins, and this deficiency may be responsible for failure of the embryo to implant successfully. Thus, testing the endometrium for beta integrin can be a useful marker for uterine receptivity. This test involves doing an endometrial biopsy at a specific point in the menstrual cycle, and evaluating this with special staining techniques, but is only available on a research basis so far.

CHAPTER XII A

The Tubal Connection

What are the fallopian tubes ?

The fallopian tubes project out from each side of the body of the uterus and form the passages through which the egg is conducted from the ovary into the uterus. The fallopian tubes are about 10 cms long and the outer end of each tube is funnel shaped, ending in long fringes called fimbriae. The fimbriae catch the mature egg and channel it down into the fallopian tube when released by the ovary .

The tube itself is a muscular highly movable structure capable of highly coordinated movement. The egg and sperm meet in the outer half of the fallopian tube, called the ampulla. Fertilization occurs here, after which the embryo continues down the tube toward the uterus. The uterine end of the tube, called the isthmus, acts like a sphincter, and prevents the embryo from being released into the uterus until just the right time for implantation, which is about 4 to 7 days after ovulation.

The tube is much more complex than a simple pipe, and the lining of the tube is folded and lined with microscopic hair like projections called cilia which push the egg and embryo along the tube. The tubal lining also produces a fluid that nourishes the egg and embryo during their journey in the tube.



Fig 1. Normal tube and ovary, as seen during laparoscopy

How do tubal diseases cause infertility ?

TubalDisease

Tubal abnormalities account for between 25% and 50% of female infertility .Tubal damage usually occurs through pelvic infection , and this is called pelvic inflammatory disease (PID). Often, we cannot find out the cause for the inflammation. However, some of the causes of pelvic infection that can be pinpointed are :

- Sexually transmitted diseases (e.g. Gonorrhea, Chlamydia)
- Infection after childbirth, miscarriage, termination of pregnancy (MTP) or IUD (intrauterine device) insertion
- Post-operative pelvic infection (e.g. perforated appendix, ovarian cysts)
- Severe endometriosis
- Tuberculosis

Besides causing blocked tubes, any pelvic inflammatory disease can also produce bands of scar tissue called adhesions, which can alter the functioning of the fallopian tubes. PID can be a silent disease, and most women with tubal damage because of PID are completely unaware that they have this disease.

Pelvic tuberculosis is a fairly common cause of tubal damage in India. The tuberculosis bacteria reach the tubes from the lungs through the bloodstream and can cause irreparable tubal damage.

How is tubal disease diagnosed ?

Making a Diagnosis of Tubal disease

A number of tests are available to judge whether or not the tubes are open.

The simplest and oldest test for tubal patency is the RT or Rubin's test named after its inventor. In this test, gas is passed under pressure into the tubes through the cervix and uterus - either with a special machine (Rubin's apparatus) or with an ordinary syringe. The doctor then listens with a stethoscope placed on the abdomen to determine if he can hear the sound of gas passing through the fallopian tube. Even though this test is now obsolete, because it is so unreliable, a number of doctors still do it.

Blood tests for chlamydial antibodies: Since an infection with chlamydia is the commonest reason for tubal disease in the West, some doctors test the blood for antibodies against chlamydia . Women who have antibodies against chlamydia have been exposed to this infection in the past, and are considered to be at higher risk for tubal damage.

Hysterosalpingogram (Uterotubogram) or HSG is a specialized X-ray of the uterus and tubes. An HSG is done after the menstrual flow has just stopped - usually on Day 6 or 7 of the period, at which time the lining of the uterus is thin. It is done in an X-ray Clinic. The patient is advised to take an antibiotic and a pain-killer before the procedure by many doctors. After being positioned on the X-ray table, the doctor places a special instrument into the cervix, called a cervical cannula, which is made of metal. Many doctors now prefer to use a balloon catheter , as this makes the procedure less painful. A radio-opaque dye (a liquid which is opaque to X-rays) is then injected into the uterine cavity. This is done slowly under pressure, and pictures are taken - preferably under an image intensifier. The passage of the dye into the uterine cavity and then into the tubes and from there into the abdomen can be seen; and X-ray pictures taken. These provide a permanent record.

At least 3 films need to be taken to provide a reliable record - including an early film for the uterine cavity; and a delayed film to make sure the spill in the abdomen is free.

A normal HSG defines the inside of the reproductive tract. This appears as a triangle (usually white on a black background) which represents the uterine cavity; and from here the dye enters the tubes which appear as two long thin lines, one on either side of the cavity. When the dye spills into the abdomen from a patent (open) tube, this appears as a smudge in the X-rays.

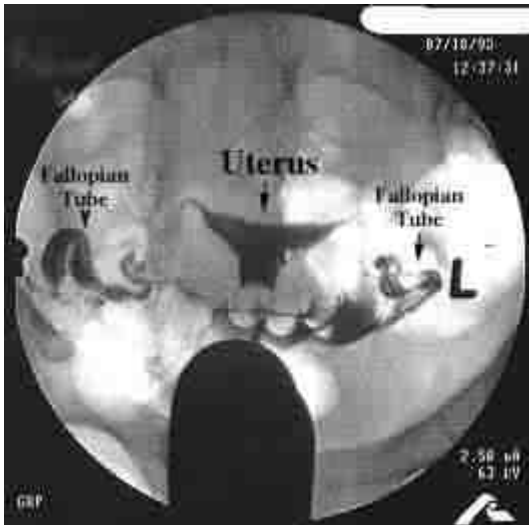


Fig 2. Normal HSG findings (the dye appears black and outlines a normal cavity and fallopian tubes)

An abnormal HSG may show a problem in the uterine cavity - and this appears as a gap or filling defect. However, the commonest problems on HSG appear in the tubes. If the tubes are blocked at the cornual end (at the uterotubal junction), then no dye enters the tubes and they cannot be seen at all. If the block is at the fimbrial end then the tubes fill up; but the dye does not spill out into the abdominal cavity and the end of the tubes are often swollen up.

Sometimes, like any other medical test, the HSG may provide erroneous results. For example, the cornu of the uterus may go into spasm, as a result of which the dye may not enter the tubes at all. This may be interpreted as a tubal block, whereas in reality the tubes are open. Also, if a hydrosalpinx is very thin and if the dye is injected under pressure, the dye may appear to spill into the abdomen through a tear in the wall of the hydrosalpinx - suggesting tubal patency when really the tubes are closed.

While the HSG is usually very reliable for determining whether or not the tubes are open, it provides little information on structures outside the tube which could nevertheless impair tubal function - such as peritubal adhesions. If the spill is "loculated", (i.e. it collects in small puddles), the presence of adhesions can be suspected, but not confirmed.

An HSG can be painful - and when the dye is injected into the uterine cavity, most women will experience a considerable amount of pain. You should be prepared for this - and taking a pain-killer prior to the procedure will help to reduce the pain.

An HSG can be technically difficult for some women (especially if the cervix is too small or too tight) - and it is better if a gynecologist is present at the time of the HSG to assist the radiologist if needed. Many gynecologists will do the HSG themselves.

The major risk of an HSG is that of spreading an unrecognized infection from the cervix up into the tubes. This is uncommon, but in order to reduce the risk, many doctors advise antibiotic coverage during the procedure.

If the HSG shows that the tubes are closed, then it may be advisable to repeat the HSG; and also to do a laparoscopy to confirm this diagnosis.

Laparoscopy. This has already been described, and is the gold standard for making a diagnosis of tubal disease.

What are the limitations of diagnosing tubal disease ?

Limitations of HSG and laparoscopy

The trouble with both HSG and laparoscopy is that they only provide information as to whether or not the tube is open or closed. While a closed tube will never work, they do not provide any information on how well an apparently open tube works. Remember, that just because a tube is patent does not necessarily mean that it works!



Fig 3. Laparoscopy shows a large hydrosalpinx on the right side

Another limitation is that they will rarely provide any information as to why the tubes are blocked. Occasionally, however, this can be suspected by other signs (for example, by seeing the tubercles diagnostic of TB in the abdomen during laparoscopy).

What are the recent innovations for tubal factor diagnosis and treatment ?

Recent innovations in this field include:

Fluoroscopic guided procedures: Using an image intensifier, and techniques borrowed from coronary angioplasty, the radiologists can now insert special catheters under fluoroscopic guidance into each of the tubes. This is called selective salpingography; and

allows much better visualization of each tube. It also allows the radiologist to treat cornual blocks which are due to mucus plugs by tubal cannulation.

Sonosalpingography: Under ultrasound guidance, with Doppler facilities if available, the gynecologist can inject fluid into the tubes through the cervix and see the flow of the fluid into the tubes and abdomen on the ultrasound screen. This is a simple bedside test which a gynecologist can do to judge if the tubes are normal - and can be reassuring if positive.

Tuboscopy: At the time of laparoscopy, the doctor can insert a fine telescope into the fallopian tube through its fimbrial end, to inspect the inner lining of the tube, to judge whether or not it is healthy.

Fallopосcopy is a recent advance, pioneered by Dr Kerin of USA. In this method, a very fine flexible fiberoptic tube is guided through the cervix and uterus into each fallopian tube, thus allowing the doctor to actually visualize the inner lining of the entire length of the fallopian tube - something which was never possible so far. This can provide useful information about the extent of tubal damage, and the possibility for successful repair.

CHAPTER XII B

The Tubal Connection

What is the role of surgery in opening a blocked tube ?

Surgical Treatment

Once the doctor has assessed the damage and pinpointed the location of the blockages he will decide on treatment alternatives and how to proceed. The first choice in the past used to be an attempt at surgery to repair the tubal damage. However, because results with tubal surgery were not very encouraging, many patients with tubal damage are now advised to undergo IVF (in vitro fertilization) as their first treatment option.

In order to select between IVF and tubal surgery, we need to differentiate between intrinsic tubal damage and peritubal damage. If the tubes have been damaged because of a problem outside the fallopian tubes, such as peritubal adhesions or endometriosis, which have caused the tubes to get kinked, then surgery may be useful. However, surgery is not advisable for patients if the tubes have been blocked because of TB; the tubes are very badly damaged; if the tubes are blocked at multiple places; or if the tubes have been blocked because of intrinsic tubal disease.

The likelihood of surgical success (in terms of pregnancy), depends on the severity of the tubal damage. If a previous infectious process has caused scarring of the fallopian tube, the inner delicate lining may have become irreversibly damaged. All operations can result in re-establishing patency in some cases - but the main aim of the surgery is not to just open the tubes, but to achieve pregnancy - and the tubes have to become capable of capturing the egg and transporting it to the uterus for this to happen. Unfortunately, surgery cannot reverse tubal damage once this has occurred.

What if only one tube is blocked? One normal tube is sufficient to allow a pregnancy - and most surgeons would not advise tubal surgery for these patients. Obviously, the chances of pregnancy for such patients is half that of normal women and therefore establishing a pregnancy may take twice as long. The danger of trying to surgically repair a single blocked tube is that adhesions because of the surgery may cause both the tubes to become blocked !

How is tubal microsurgery performed ?

Tubal Microsurgery

Microsurgery entails the use of the following surgical techniques:

- Using a microscope (for adequate magnification)

- Avoiding unnecessary trauma to the tissues
- Employing delicate surgical instruments
- Employing fine suture (stitching) material and ensuring precise suturing
- Handling tissues with great care and respect, to minimize tissue damage
- Ensuring that no bleeding is left unattended and no clots are left behind (because this can lead to the formation of adhesions or scar tissue after the surgery)

The microsurgery operation may take from 1 to 4 hours. Depending on the extent of pelvic damage and is usually done under spinal or general anesthesia. The incision used is usually a "bikini cut" (Pfannensteil incision) The length of stay in hospital is usually 3 to 7 days. Tubal microsurgery can be expensive and may cost up to Rs.40,000. Sometimes a "check or second-look laparoscopy " is performed about one week after surgery to ensure that tubal patency is maintained and to remove any small adhesions that may have started to re-form.

What are the options for treating proximal tubal occlusion ?

Proximal Tubal Damage

The tubal obstruction could be at the uterotubal junction and this is called a cornual block. The conventional surgical repair of cornual blocks involved reimplanting the tube into the uterus - and had dismal success rates. However, with microsurgery, it is possible to see the very fine ends of the tubes under high magnification and to join them together. This has a pregnancy rate of about 50%, since the function of the rest of the tube is basically intact.

Recently, doctors have realized that a number of patients have cornual blocks because of the presence of mucus plugs and debris in the very fine cornual segment of the tubes. Newer nonsurgical methods have now been devised to treat this. These involve the passage of a fine guide wire or a fine balloon into the cornual end of the tube through the uterus. This is called a "balloon tuboplasty" or "cornual recanalisation," and can be done under ultrasound guidance; hysteroscopic guidance; or fluoroscopic (X-ray) guidance. This is a significant advance, since it saves patients the need for major surgery; and also has excellent pregnancy rates.

Salpingolysis

This procedure entails division of adhesions surrounding the tubes. When no other damage is apparent, success rates may be as high as 65%.

Tubal Reanastomosis

These include a variety of procedures which involve removing the damaged portion of the tubes and rejoining the healthy ends of the tube together . Success rates vary according to the area of damage but are usually within the range of 20 - 50%.The chances of success are higher when the defect occurs in the middle section of the tube.

Distal Tubal Damage

If the tubes have been severely damaged and have formed a hydrosalpinx (in which the

fimbriae stick to one another and the tube is closed off) the surgery required is called neosalpingostomy, in which the surgeon opens the hydrosalpinx and creates a new opening for the repaired tube. While this is technically easy, success rates are very poor (about 20%) because the physiologic functioning of the fimbriae rarely returns to normal.

If the damage is less severe (fimbrial agglutination, in which the fimbriae are stuck to one another; or phimosis, in which the tube is narrowed, but open), then surgical repair is more successful, with pregnancy rates being about 50%.

What are the risks of tubal surgery ?

The risk of having an ectopic (tubal) pregnancy is increased following tubal surgery. Fallopian tubes which have been operated on may have a damaged inner lining, and this can impair the movement of the embryo down the tube. This is why, in patients who have had tubal surgery, the diagnosis of a pregnancy should be made as soon as possible (preferably within a few days of missing a menstrual period), to rule out the possibility of an ectopic pregnancy.

The best chance of success is with the first surgical operation; therefore, you need to go to a specialized centre. The chances of success will depend upon the extent of tubal damage and also on the skill of the surgeon. The best chance of achieving a pregnancy is in the first few months after surgery, and most women who are going to get pregnant after tubal surgery will conceive within this time. Some doctors believe that using ovulation induction and / or intrauterine insemination after tubal surgery helps to maximize the chances of a pregnancy.

If the patient has not conceived within one year after the surgery, then follow-up testing in the form of an HSG and / or laparoscopy is advisable, to determine whether the fallopian tubes are still open.

If the first surgery has been unsuccessful, the chance of success as a result of reoperation is very low, and IVF is the only treatment choice for such patients.

In the future, it is possible that tubal transplants may become a reality and that scientists may also develop artificial synthetic tubes to replace damaged ones.

With operative laparoscopy, it is now possible to open damaged tubes through the laparoscope, thus saving the patient major surgery. A hydrosalpinx can be repaired by opening it with a laser or cautery and then keeping it open with sutures: and even the complicated operation of tubal reanastomosis has been performed by experienced surgeons through the laparoscope (using sutures or special adhesive glue). However, the results with this surgery are often poor, because these damaged tubes often do not function properly even after the surgery.



Fig 4. Schematic showing damaged fallopian tubes because of pelvic inflammatory disease (PID). The left tube has formed a hydrosalpinx; and the right is engulfed in peritubal adhesions.



Fig 5. Operative laparoscopy, during which an adhesion is being divided (adhesiolysis)

How can a tubal ligation be reversed ?

Reversal of Sterilization

In women, sterilization for family planning is usually done through an operation called tubal ligation, which is usually carried out through the laparoscope. The aim of the operation is to block the tubes and prevent the sperm and egg from meeting each other.

Why Do Women Ask for Reversal?

The vast majority of people are very happy with sterilization. Nevertheless, there are a few women who are very distressed afterwards and would do almost anything to get things undone. The commonest reason why such women regret sterilization is because their child dies or because they have remarried and wish to bear their new husband's child.

What Can Be Done?

If there is a reasonable amount of tube remaining, even if only on one side, then it may be possible to perform tubal microsurgery to rejoin the tubes. On the whole, the more tube

which has been left undamaged, the better the chances of success. Thus, patients who have had a tubal ligation done through the laparoscope, using Falope rings (silastic bands) or clips, have an excellent chance of achieving a pregnancy after microsurgical reversal of the ligation, because these methods cause minimal tubal damage.

After reviewing the operative notes, a laparoscopy may be advised, so that the exact state of the fallopian tubes can be assessed. If the patient has enough normal tube, tubal microsurgery may be attempted and pregnancy rates can be as high as 75% in favorable cases. Some skilled surgeons can even perform this type of tubal reanastomosis through the laparoscope (using sutures or special adhesive glue). If, unfortunately, the patient has had both tubes completely removed or if the tubes are very badly damaged, then the only chance of success will be with IVF.

Most patients who will conceive after tubal reanastomosis will do so within 1 year. If they do not, then the next step for them would be IVF.

CHAPTER XIII A

Ovulation -- Normal and Abnormal

How does ovulation occur normally ?

Normal ovulation

Normally, one of the ovaries releases a single mature egg every month, and this is called ovulation. Women may notice pain or abdominal discomfort at the time of ovulation and occasionally have some slight vaginal bleeding. The presence of regular periods, premenstrual tension and dysmenorrhoea (period pains) usually indicate that the menstrual cycles are ovulatory.

Eggs are stored in the ovaries in follicles. Follicles exist in two major categories - growing and non-growing (primordial). Eggs in the primordial follicle are in a very immature form. In this state they are not capable of being fertilized by a sperm until they undergo a maturing process which culminates in their release from the ovary at the time of ovulation.

Egg maturation and ovulation is stimulated by two hormones secreted by the pituitary - follicle stimulating hormone (FSH) and luteinizing hormone (LH) . These two hormones must be produced in appropriate amounts throughout the monthly cycle for normal ovulation to occur.

Every month, at the start of the menstrual cycle, in response to the FSH produced by the pituitary gland, about 30-40 primordial follicles start to grow. Of these, only one matures to form a large fluid-filled structure, called a Graafian follicle which contains a mature egg, while the others die (a process called atresia). The mature egg is released from the follicle when the follicle ruptures in response to a surge of LH produced by the pituitary. After ovulation has occurred, the follicle from which the egg has been released forms a cystic structure called the corpus luteum. This is responsible for progesterone production in the second half of the cycle.

You can see an excellent animation (which will open in a new browser window) of the hormonal changes which occur during a normal menstrual cycle at Serono Fertility Lifecycle.

Most women who have regular periods have ovulatory cycles. Women who fail to ovulate or who have abnormal ovulation usually have a disturbance of their menstrual pattern. This may take the form of complete lack of periods (amenorrhoea), irregular or delayed periods (oligomenorrhoea) or occasionally a shortened cycle due to a defect in the second part (luteal phase) of the cycle.

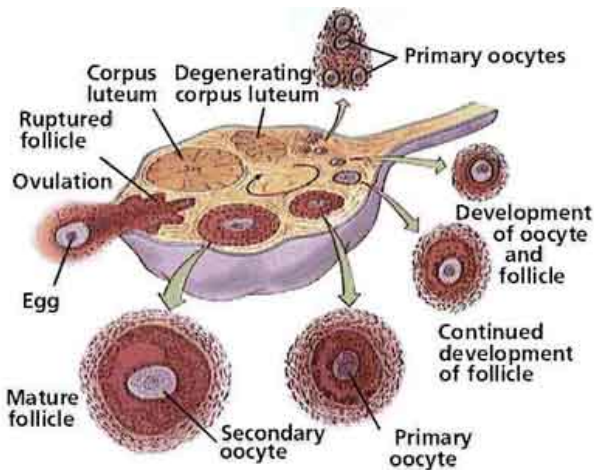


Fig 1. Schematic of the ovarian follicle during its development (clockwise)

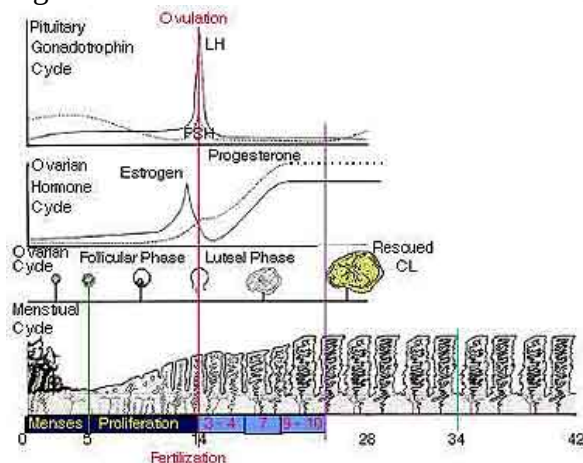


Fig 2. The hormonal changes which occur during a normal ovulatory cycle, if pregnancy occurs. The purple line marks the point when the embryo implants.

How can I find out if I am ovulating ?

Detecting ovulation - when do you ovulate?

Menstrual period timing (Calendar method)

To determine the length of the menstrual cycle, one only needs to note the date of the beginning of the menstrual period (first day of flow) for two consecutive periods, and then count the day from one date to the next. Keeping track of the length of menstrual cycles will help determine the approximate time of ovulation, because the next period begins approximately two weeks from the date of ovulation.

The rough rule to calculate the approximate date of ovulation is : NMP minus 14 days, where NMP is the (expected) date of the next menstrual period. This is because the luteal phase for most women is 14 days long.

Keeping track of the menstrual cycle by charting it can indicate other ovulatory disturbances . For example, if a menstrual cycle that is normally 28 days starts to occur every 35 or 40 days, this may mean that ovulation is disturbed, and an evaluation is needed.

Is BBT charting of any use ?

Basal Body Temperature (BBT) chart

During the luteal phase of the cycle, the corpus luteum produces the hormone progesterone, which elevates the basal body temperature. When the basal body temperature has gone up for several days, one can assume that ovulation has occurred. However, it is important to remember that the BBT chart cannot predict ovulation - it cannot tell you when it is going to occur !

The basal temperature chart can be a useful tool. It allows the patient to determine for herself if she is ovulating as well as the approximate date of ovulation, but only in retrospect. Basal body temperature charts are easy to obtain and the only equipment required is a special BBT thermometer.

General instructions for keeping a basal body temperature chart include the following :

1. The chart starts on the first day of menstrual flow. Enter the date here.
2. Each morning immediately after awakening, and before getting out of bed or doing anything else, the thermometer is placed under the tongue for at least two minutes. This must be done every morning, except during the period.
3. Accurately record the temperature reading on the graph by placing a dot in the proper location. Indicate days of intercourse with a cross.
4. Note any obvious reason for temperature variation such as colds, or fever on the graph above the reading for that day.

The major limitation of the BBT is that it does not tell you in advance when you are going to ovulate - therefore its utility in timing sex during the fertile period is small. Interpreting the BBT chart can be tricky for many patients - rarely do the charts look like those you see in textbooks!

Also, keeping a BBT chart can be very stressful - taking your temperature as the first thing you do when you get up in the morning is not much fun. What is worse is that you start to let the BBT chart dictate your sex life. This is why though the BBT chart used to be a useful method in the past, its utility is limited today - and newer methods are available which are more accurate are available. We advise our patients never to chart their BBTs - we feel they are just a waste of time.

Manufacturers have now incorporated a microprocessor along with the digital thermometer, to create an electronic fertility management device , called The Bioself Fertility Indicator. This makes calculation of the "fertile days" much easier, because it combines and optimises both the basal body temperature and calendar method of ovulation prediction.

What about using fertility software programs ?

Fertility Software Programs

Newer software programs (easily available on the internet) , such as CycleWatch, help you learn about your body's fertility signs by giving you the tools to document and analyze your observations. For women who are comfortable with computers, this is a useful tool to organize your cycle data and analyze your cycles to determine fertile times.

You can also use our free online fertility calculator to determine when you ovulate !

Of what use is an endometrial biopsy ?

Endometrial biopsy

After ovulation, the endometrium is prepared for implantation of the fertilized egg by the progesterone secreted by the corpus luteum. In order to determine if ovulation is occurring normally, an endometrial biopsy used to be done in the past . During this procedure, a small amount of endometrium from inside the uterine cavity is extracted surgically and sent for pathologic examination under a microscope. This is a standard procedure usually done just before the period begins. It can be done in the doctor's office or in an operating theater. No anesthesia or hospitalisation is needed. However, it does cause discomfort during the procedure (about as much as a severe menstrual cramp) and an analgesic can be taken a half-hour prior to the procedure to decrease this discomfort. When examining the endometrial biopsy, the pathologist looks for the influence of the estrogen and progesterone hormones on the endometrial glands. If progesterone has been produced in that cycle, the endometrial glands show secretory changes . In fact, the effect of progesterone on the endometrium is so predictable, that the biopsy can be "dated" - that is, the pathologist can predict on which day the next period will start! If there is a "lag" between the predicted day and the actual day, then this suggest a luteal phase defect, which means that the production of progesterone is deficient. If no progesterone at all has been produced, then the endometrium will be reported as being proliferative (under the influence of only estrogen) - which suggests that the cycles are anovulatory (i.e., ovulation did not occur in that cycle).

Because an endometrial biopsy is painful and provides limited information, few doctors use it anymore.

Of what use is a D&C (curettage) ?

Curettage

A curetting used to the commonest procedure done for infertile patients. In fact, a number of infertile patients will request that a curetting be done for them, since they feel that the curetting will "clean out" the dirt they have in their uterus and allow them to conceive. This is an old wive's tale and is based on " I know someone who got a baby after a curetting".

The correct technical term for curetting is D and C - dilatation and curettage - which means the cervix is stretched (dilated) and the uterine cavity scraped (curetted) to collect the endometrium) . This is an obsolete procedure for an infertile woman, and can actually be harmful. The only use of a D&C is to provide endometrial tissue which can be examined under the microscope to see if the woman is ovulating or not. It has absolutely no fertility-enhancing role whatsoever.

Since this endometrium can be obtained much more easily, safely and cheaply with an endometrial biopsy (in which only a strip of endometrium is removed) there should rarely be any need to do a D&C for an infertile woman. Patients have often have repeated D&Cs - and these can actually damage the cervix and even block the tubes, if infection

occurs after surgery. The only possible role for a D&C today is when tuberculosis of the uterus is suspected.

How does testing for progesterone help ?

Blood test for progesterone

The progesterone level in the blood may be measured to confirm that ovulation has taken place. This test is done on Day 21 of the cycle (about 1 week after the expected date of ovulation) . A normal level is between 10 ng/ml - 20 ng/ml and indicates that the corpus luteum is producing enough progesterone, and is good retrospective evidence that ovulation occurred. A very low level means that the cycle was most probably anovulatory. An intermediate level may suggest a luteal phase defect (in which the corpus luteum does not secrete enough progesterone).

How can I find out when I am ovulating and use this information to track my fertile time ?

While the above tests will tell a women whether or not she ovulates, the following symptoms and tests which can be used in order to determine when you ovulate are of greater importance, since they provide information which can be used to identify the "fertile period" prospectively.

How can I use cervical mucus monitoring to monitor my ovulation ?

Cervical mucus (Billing's method)

By checking your cervical mucus daily, as described in the chapter on the cervical factor, you can determine when you ovulate. Just before ovulation, your cervical mucus is thin, profuse, clear and stretchy, like raw egg whites. After ovulation, the mucus becomes thick, tacky, scanty and sticky. You can learn to appreciate this change in your mucus (by seeing and feeling it) and this allows you to predict when ovulation occurs quite accurately. You can learn the technique for tracking your cervical mucus in the Chapter on The Cervical Factor.

Abdominal pain

Approximately 25 percent of women may experience a pain on one side of the abdomen that is associated with ovulation. This is called mittelschmerz (a German word, which means midcycle pain) and is usually related to the release of an egg from the rupturing follicle. It is a good idea to mark the date when it occurs since this information is helpful in determining when ovulation occurs.

CHAPTER XIII B

Ovulation -- Normal and Abnormal

How is ultrasound used to monitor ovulation ?

The role of ultrasound in monitoring ovulation

The egg develops within a follicle in the ovary. This follicle is a thin-walled structure containing fluid with the egg attached to the wall. Usually, only one follicle develops per month. This follicular growth can be monitored by ultrasound, usually done with a vaginal probe, which projects an image of the ovary onto a screen.

The follicle appears as a circular fluid-filled bubble on the screen, and can be seen when it is about 7 to 8 mm in size. It grows at about 1 to 2 mm per day, and is ready for ovulation when it measures 18 to 25 millimeters in diameter. Following ovulation, the follicle usually disappears from the scan picture completely and this is the best evidence of ovulation.

Often, at the same time, fluid can also be detected in the abdomen behind the uterus - this is the follicular fluid which is released when the follicle ruptures. Defects detectable by ultrasound are follicles that do not grow at all, or do not grow to a big enough size, or occasionally follicles that do not rupture at the appropriate time (luteinised unruptured follicle).

Since ultrasound allows assessment of follicular development, it is especially useful for patients having timed intercourse or having ovulation regulated with fertility drugs. It is usually done on a daily basis, from about the 11th day of the cycle.

Follicle tracking on ultrasound usually takes about 5 minutes to perform. No preparation is needed; except that the bladder must be emptied before the scan. Ask to see the picture of the follicle on the monitor - and you should be able to see the growth of the follicle and its rupture for yourself on the screen.

Older ultrasound machines used abdominal probes . These require that the patient have a full bladder, so that the sound waves can reach the ovary. Not only are they much more uncomfortable for the patient (who has to sit waiting till the bladder is almost bursting) but the quality of the pictures is also much poorer as compared to the vaginal scan.

How do I use ovulation prediction kits (OPK) ?

Commercially available ovulation prediction kits (OPK)

Ovulation prediction test kits (OPK) are available abroad (or in India at a few chemists) over the counter . If you live in India, you can also buy them from our online store.

These kits detect LH which is produced in large quantities shortly before ovulation and can be found in the urine . Once the LH surge has occurred, ovulation usually takes place within 12 to 44 hours. Urine testing is started about two days prior to the expected day of ovulation and continues until the test becomes positive. The urine should be collected at the same time every day - and testing the first morning urine sample is a good idea.

If your menstrual cycles are irregular, testing should be timed according to the earliest and latest possible dates of ovulation. For example, if your cycle ranges between 27 and 34 days, you could possibly ovulate between days 13 and 20. Therefore, testing should

begin on day 11 and continue until ovulation is indicated or through day 20. There is an 80 percent chance of detecting ovulation with five days of testing and a 95 percent chance with ten days of testing. Occasionally, ovulation may not occur in a particular cycle. If the ovulation prediction test has been timed and performed accurately and has not turned positive, you should discontinue testing and begin again with your next menstrual cycle. Persistent failure of the test to turn positive may indicate a problem with regard to ovulation.

Once a test has registered positive, indicating that ovulation is about to take place, it is no longer necessary to continue testing. Remaining tests in a kit may be saved and used in the following menstrual cycle if pregnancy does not occur.

Ovulation prediction kits offer the advantage that they allow you to predict when ovulation will occur - thus maximising the chances that intercourse will be timed at your most fertile period. They can also be done in the privacy of your own home. However, they are expensive; and some of the kits have very tedious and involved testing procedures, so that errors are not uncommon.

A newer device, The ClearPlan Easy™ Fertility Monitor, is a palm-sized, electronic system, that provides information about fertility status by interpreting the levels of two hormones, estrogen and luteinizing hormone, in the urine. You need to test your urine for the presence of these, using dip sticks, and the information is then input into the system, which uses it to calculate your fertile days.

How can I use the new pocket microscopes to track ovulation ?

Salivary ferning

Another way of monitoring ovulation uses a pocket microscope, to check for the phenomenon of "saliva ferning." You need to let your saliva dry on a glass slide, and then examine it under the device, to check for ferning. Prior to ovulation, the saliva shows the presence of crystallisation or ferning when it dries, and this suggests that ovulation will occur soon. Though these devices are now commercially available, their reliability is still unclear.

What blood tests can be used to predict ovulation ?

Blood tests

The growing follicle secretes the hormone estradiol in increasing amounts and its blood level rises rapidly several days prior to ovulation. If ovulation is being induced through fertility drugs, estradiol blood tests may be done on a daily basis in order to determine if the developing follicles are growing properly. Normally, the estradiol blood levels should increase rapidly (as a rule of thumb, they double every 24 hours).

Since the luteinizing hormone (LH) blood level rises rapidly just before ovulation (this is called the LH surge), frequent blood samples for measuring the LH level can also be taken a few days prior to the anticipated time of ovulation in an attempt to predict when the follicle is mature and ready for ovulation.

What happens when ovulation is abnormal ?

Abnormal ovulation

Abnormalities of ovulation may appear in several ways. Menstrual cycles shorter than 21 days or longer than 35 days are often associated with anovulation. In addition, patients may skip menstrual periods for time intervals of three months or more and this is called oligomenorrhea (infrequent periods) . If the periods stop entirely, this is called amenorrhea.

Many hormonal systems work together to produce regular menstrual periods, and the blood levels of the hormones that make up these systems need to be tested in order to determine the reason for the ovulatory disorders.

What are the blood tests which are used to diagnose problems with ovulation ?

The hormone blood tests, which are usually done on the third day of your cycle, include:

The FSH level: The FSH level gives a good idea of the ovarian reserve (ovarian functional capacity) - an index of the number of eggs remaining in the ovaries. A high FSH level suggests that the ovary has either failed or has started to fail. If the FSH level is very high (in the menopausal range) then the diagnosis is ovarian failure. If the level is borderline, then some doctors will do a clomiphene citrate challenge test , which allows for an earlier diagnosis of failing ovaries. Even women with regular menstrual cycles may have poor egg quality, as reflected by an elevated FSH levels. This is called oopause. Ovarian reserve can also be assessed by measuring the levels of the ovarian hormone inhibin in the blood. Low levels of inhibin suggest poor ovarian function. However, this test is still new and is not easily available.

A very low FSH level suggests hypogonadotropic hypogonadism. This seemingly verbose term simply means that the ovary in these patients is not working properly because of inadequate production of FSH by the pituitary gland. However, in most anovulatory patients, the FSH level will be in the normal range, and this can be reassuring.

The LH level: This is the other gonadotropin hormone produced by the pituitary; and provides much the same information the FSH level does. Another useful test is the LH:FSH ratio which is normally 1:1. If, however, the LH level is much higher than the FSH level, this suggests a diagnosis of polycystic ovarian disease.

Thyroxine and TSH. These test for thyroid function. The thyroxine level is high in patients with overactive thyroid glands (hyperthyroidism). In patients with decreased thyroid function (hypothyroidism), the TSH level is increased.

Prolactin: Prolactin is a hormone produced by the pituitary gland that induces lactation or milk formation.. High prolactin levels (hyperprolactinemia) can interfere with ovulation . A milky discharge from the breast nipple , not related to pregnancy or nursing , is called galactorrhea, and this is a telltale symptom of high prolactin levels and needs to be investigated. If the prolactin level is elevated, the doctor will need to recheck it to

confirm it is persistently high. There are many reasons for an elevated prolactin level, including certain drugs as well as stress. In some women, the reason for a high prolactin level can be a small tumour in the pituitary gland. This is called a prolactinoma or microadenoma, and the doctor may advise you have an X-ray of the skull (or even a CT scan or MRI scan) to rule out this possibility. However, most infertile women with hyperprolactinemia can be easily treated with a medicine called bromocriptine, which is a dopamine agonist medication . Another medication which can be used to treat hyperprolactinemia is oral cabergoline, which is usually taken twice a week. Only if the pituitary tumour is very large (microadenoma) is surgical removal needed, and this is very uncommon.

What is ovarian failure ?

Ovarian failure

Ovarian failure is a disease in which the ovaries fail to produce eggs. This disease is uncommon, occurring in only about 10% of women whose periods do not occur at all, a condition called amenorrhea (absence of periods). Ovarian failure may be genetic (for example, in girls with Turner's syndrome, a chromosomal disorder) or may be acquired (for example, following radiation or chemotherapy for cancers; surgery to remove the ovaries for treating ovarian cancer or severe endometriosis; autoimmune ovarian failure; or for unexplained reasons.) Ovarian failure is diagnosed by finding a high FSH level. In such patients it is usually not possible to stimulate ovulation and they have any eggs, and they suffer a premature menopause. The only effective medical treatment for these patients is the use of donor egg IVF . However, in a very small proportion of these patients, ovulation can resume spontaneously.

What are the treatments available for inducing ovulation?

Induction of ovulation

What forms of treatments are available for inducing ovulation?

The most commonly prescribed medicines for induction of ovulation include the following: clomiphene citrate, human menopausal gonadotrophin (HMG) and follicle stimulating hormone (FSH), HCG (human chorionic gonadotropin), bromocriptine, GnRH (gonadotropin releasing hormone) and GnRH analogue.

For women with hypogonadotropic hypogonadism (low FSH and LH levels), the treatment of first choice is HMG. This is effective replacement therapy; and excellent pregnancy rates can be achieved in these women.

For women affected by hyperprolactinemia, the drug of first choice is bromocriptine.

For most other women, the drug of first choice is clomiphene - the "workhorse" of ovulation induction. If this does not work, then HMG is resorted to.

Poor responders to HMG can be treated with GnRH analogues in conjunction with the HMG; or by adding a hormone called the human growth hormone.(HGH).

HCG (human chorionic gonadotropin) is given to trigger off the release of the egg.

In patients with high androgen levels (high blood levels of male hormones), dexamethasone can be used as an adjunct, since this suppresses androgen production.

You can read more about these medicines and how they are used in the Chapter on Understanding Your Medicines.

Often ovulation induction requires an investment of time, money, energy and emotion before a satisfactory response is achieved. After all, every woman is different and there can be no standard "formulae". Careful monitoring of the response to ovulation induction is the key to therapy - and this usually involves daily ultrasound scans and/or blood tests. It is often a tedious process - which may involve "trial and error" to tailor the therapy to the individual patient's ovulatory response. With the treatments available today, however, correcting ovulatory dysfunction is one of the most rewarding and successful of infertility treatments.

CHAPTER XIV A

The Older Woman

How does age affect fertility in the woman ?

Most infertility specialists define an older woman as one who is more than 35 years, but this is an arbitrary number. A woman's fertility does not fall off at a particular age, but starts declining gradually after the age of 30. After 35, the drop is fairly dramatic; and after 38, it's even more so. However, there is no magic number at which fertility disappears and this decline is a progressive irreversible process.

In the past, it was assumed that as the woman got older, her entire reproductive system started failing. However, today we know that the uterus and the fallopian tubes remain relatively unaffected by age; and that the reason for the decline in fertility is the diminished number of eggs left in the ovary. Every girl is born with a finite number of eggs, and their number progressively declines with age. A measure of the remaining number of eggs in the ovary is called the "ovarian reserve"; and as the woman ages, her ovarian reserve gets depleted. The infertility specialist is really not interested in the woman's calendar (or chronological age) , but rather her biological age - or how many eggs are left in her ovaries.

What are the tests for measuring ovarian reserve ?

Various tests have been described , to measure the ovarian reserve, so that we can determine which patients are good candidates for treatment. These tests are based on measuring the level of the FSH level in the blood; and include a basal (day 3) FSH level. A high level suggests poor ovarian reserve; and a very high level is diagnostic of ovarian failure. A test that can provide earlier evidence of declining ovarian function is the clomiphene citrate challenge test (CCCT). This is similar to a " stress test " of the ovary; and involves measuring a basal Day 3 FSH level; and a Day 10 FSH level , after administering 100 mg of clomiphene citrate from Day 5 to Day 9. If the sum of the FSH levels is more than 25, then this suggests poor ovarian function, and predicts that the woman is likely to have a poor ovarian response (she will most probably grow few eggs, of poor quality) when superovulated. Another test which has been recently developed is the measurement of the level of the hormone, inhibin B , in the blood. Low levels of inhibin B (which are produced by " good " follicles) suggests a poor ovarian reserve. However, just because a test result is normal does not mean that the quality or number of the eggs will be good - the final proof of the pudding is always in the eating !

The menopause is easy to define, because it is the point at which the menses cease, and at this time the eggs in the ovaries are finally depleted. However, the quality of eggs starts declining well before the menopause starts. Dr Jansen calls this the "oopause" - the time period before the menopause, during which fertility progressively declines because of deterioration in the quality of the eggs. This can manifest itself in many ways, some of which are extremely subtle, which is why the oopause can be so hard to identify. Initially, these women may present as having recurrent miscarriages, and then as having

"unexplained infertility". While the number of eggs they grow seems fine initially, they do poorly in the IVF lab. Initially they may have unexplained implantation failure of apparently satisfactory embryos; and later, poor quality embryos; and then failure of fertilization.

What is the relationship between infertility and the midlife crisis ?

Infertility and the Midlife Crisis

Many women in their late 30s early 40s have postponed marriage or childbearing to obtain their education, establish themselves in careers, and become financially secure. These aspirations frequently have worked against the decision to have children. The passage of time, however, alters the way many women feel about motherhood by changing their perceptions about themselves as well as about the world around them. Additionally these changes may also have to do with having a new sense of maturity as well as a feeling of accomplishment. Thus, as women-and men-feel more secure about themselves, their feelings and ideas about children and parenthood may also change.

As a couple moves into midlife, they must also begin recognizing and coming to terms with their own mortality. For many, parenthood is a part of successfully completing an important stage in life. As couples begin to see and understand the passage of their own lives, the need to pass along life experiences to new generations enhances the meaning of life.

Men and women in midlife, who have made the decision to have children , may find to their dismay that they are frequently thwarted by the inability to conceive or by recurrent miscarriages. For women, the realities of the biologic clock cannot be overlooked. At this point, many couples are faced with dual crises which can compound their problems - infertility , as well as a midlife crisis - the developmental life changes that normally occur in the middle years. This is why we suggest that women who are more than 30 and who wish to postpone childbearing should get their FSH levels checked on Day 3 of their cycle. This is a simple blood test which allows the doctor to check your ovarian reserve (the quantity and quality of the eggs in your ovaries). A high level suggests poor ovarian reserve and should be a wake-up alarm that your biological clock is ticking away rapidly. It's important that this test should be done in a reliable laboratory.

As women reach menopause, they begin to realize that the option of conceiving and bearing a child is closed to them. Just as the array of other life choices begins to narrow, the loss of this ability to choose to have a child can result in sadness and deep disappointment. The realization of this "missed opportunity" can also lead to self-recrimination and depression.

CHAPTER XIV B

The Older Woman

What are the fertility issues unique to older women ?

This is why the older woman presents a number of unusual personal problems. For one, most women can hear their own biologic clock ticking away loudly, and don't like being reminded about the fact that their age can be a limiting factor in their fertility. Moreover, many of these women are busy executives pursuing a career. They are very used to being successful, and find it difficult to come to terms with their biologic frailty. Because of all the media hype, they expect the assisted reproductive technologies to provide them with a quick answer.

However, few reports emphasise that pregnancy rates in older women, even with IVF, are only half of what they are with younger women - so that typically, a woman who is more than 40 years of age has a less than 10 % chance of having a live birth in an IVF cycle. Older women also find it much more difficult to get social support. Society can be both sexist and ageist, and most people feel it is "unnatural" for an older woman to want to try to get pregnant.

The major problem for the older woman is that time is at a premium ! She simply cannot afford to waste her precious time on ineffective treatments; and it is better for her to move on to IVF sooner rather than later !

Older women present doctors with many challenging problems. For one, they usually respond poorly to ovarian stimulation, and pregnancy rates with treatment are lower. They also have an increased risk of having a miscarriage - and in women over 41 years of age, this risk can be as much as 50% ! Moreover, as a woman ages, she has an increased risk of having medical problems in her pregnancy, because of preexisting medical problems such as diabetes and hypertension.

An especially thorny issue is the increased risk of birth defects because of aging eggs. As eggs get older, they have an increased risk of harbouring chromosomal errors, and this increases the risk of the baby having a chromosomal error, such as trisomy 21 (Down syndrome). Most clinics will offer prenatal diagnosis (such as chorion villus sampling, and amniocentesis) to these women to screen for birth defects during pregnancy - but since some of these procedures increase the risk of a miscarriage, the couple often find themselves on the horns of a dilemma - and it is hard for them to decide whether to do the test or not to.

What is the oldest age at which an infertility specialist should accept a woman for treatment ? Is there a particular age at which a woman should be denied treatment ? If so, then why ? and what should this age be ? and who should decide ? " Menopausal mums" have grabbed much media attention, and have raised a number of controversies - which still remain unresolved.

Much research is going on to try to increase the pregnancy rates after IVF in older women. One high tech option is to screen the embryos for aneuploidy (an abnormality in chromosomal number) using FISH (fluorescent in situ hybridisation) for preimplantation genetic diagnosis, a technique in which embryos are biopsied and their chromosomes

analysed using probes. If only chromosomally normal, healthy embryos are transferred back, then many researchers feel that embryo implantation rates and pregnancy rates will be higher. Another option is assisted zona hatching, using chemicals or a laser, to create an opening in the zona (shell) of the embryo. Scientists feel that this technique can allow the embryo to "hatch" and thus escape from the zone and implant into the uterine lining more easily. Some IVF clinics with advanced facilities, such as ours, now offer these **advanced techniques** on a routine basis.

For older woman with a persistently poor ovarian response, many options have been explored to try to improve the number of eggs produced. This includes using supplemental growth hormone; and the newer recombinant gonadotropins. However, the results of these have been disappointing, and the fact remains that we do not have an effective method of helping poor ovarian responders.

How can donor eggs help the older infertile woman ?

A very effective option for older woman whose own eggs do not grow well is that of using donor eggs or donor embryos. However, this is obviously a very sensitive emotional issue, and each couple needs to make their own decision. While using donor eggs and embryos does dramatically improve pregnancy rates, it is often an option many couples find hard to come to terms with.

It is also becoming increasingly difficult to find suitable egg donors. While egg donation has become commercialised in USA, this has raised a lot of hue and cry, because critics feel that young women are being enticed to "sell their eggs". Finding altruistic egg donors is an uphill task for most women, because they are often very reluctant to ask for help, since this would involve telling others about their problem.

Support groups like NEEDS (National Egg and Embryo Donation Society) in the UK have been very helpful in motivating voluntary egg donors by creating public awareness of the need for healthy young women to donate their eggs. Clinics have also adopted various approaches to help resolve this problem. Some large clinics run successful anonymous egg donation programs; others use known **egg donors** (either paid or unpaid); and others encourage their patients to share their supernumerary eggs (often for a financial consideration) with other patients.

An exciting option for the future may be that of egg banking. A lot of research is being focussed on developing more efficient methods to cryopreserve and store eggs. If this becomes clinically practicable, then it may become possible to freeze a woman's eggs or ovarian tissue when she is young, and store these for her in liquid nitrogen at -196 C, so that she can use her own "young" eggs in the future, whenever she decides to start her family !

CHAPTER XV

Polycystic Ovarian Disease (PCOD)

What is PCOD (polycystic ovarian disease) ?

Patients suffering from polycystic ovarian disease (PCOD) have multiple small cysts in their ovaries (the word poly means many). These cysts occur when the regular changes of a normal menstrual cycle are disrupted. The ovary is enlarged; and produces excessive amounts of androgen and estrogenic hormones. This excess, along with the absence of ovulation, may cause infertility. Other names for PCOD are polycystic ovarian syndrome (PCOS) or the Stein-Leventhal syndrome.

How is PCOD diagnosed ?

Diagnosis

PCOD can be easy to diagnose in some patients. The typical medical history is that of irregular menstrual cycles, which are unpredictable and can be very heavy ; and the need to take hormonal tablets (progestins) to induce a period. Patients suffering from PCOD are often obese and may have hirsutism , (excessive facial and body hair) as a result of the high androgen levels. However, remember that not all patients with PCOD will have all or any of these symptoms.

This diagnosis can be confirmed by vaginal ultrasound, which shows that both the ovaries are enlarged; the bright central stroma is increased ; and there are multiple small cysts in the ovaries. These cysts are usually arranged in the form of a necklace along the periphery of the ovary. (It is important that your doctor be able to differentiate multicystic ovaries from polycystic ovaries.)

Blood tests are also very useful for making the diagnosis. Typically, blood levels of hormones reveal a high LH (luteinising hormone) level; and a normal FSH (follicle stimulating hormone) level (this is called a reversal of the LH : FSH ratio, which is normally 1:1); and elevated levels of androgens (a high dehydroepiandrosterone sulphate (DHEA-S) level) ;

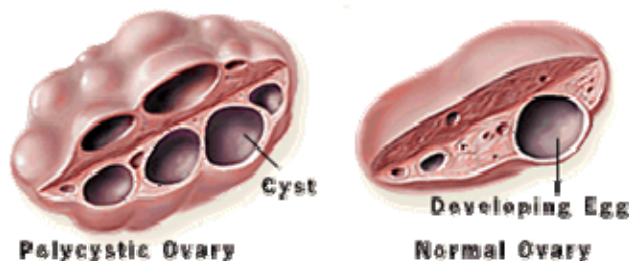


Fig 1. A schematic, comparing a polycystic ovary with a normal ovary.

What is the cause of PCOD ?

We don't really understand what causes PCOD, though we do know that it has a significant hereditary component, and is often transmitted from mother to daughter . We also know that the characteristic polycystic ovary emerges when a state of anovulation

persists for a length of time. Patients with PCO have persistently elevated levels of androgens and estrogens, which set up a vicious cycle. Obesity can aggravate PCOD because fatty tissues are hormonally active and they produce estrogen which disrupts ovulation. Overactive adrenal glands can also produce excess androgens, and these may also contribute to PCOD. These women also have insulin resistance (high levels of insulin in their blood, because their cells do not respond normally to insulin).

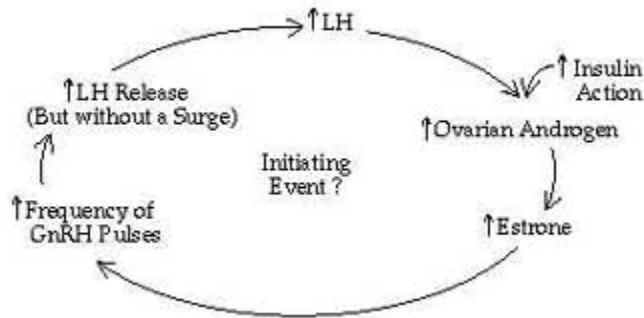


Fig 2. The self-perpetuating vicious cycle of elevated levels of androgens and estrogens in PCOD

What is occult PCOD ?

While some women with PCOD will have all the classic symptoms and signs, many have what we call "occult PCOD". This means that they may be thin, have regular periods, no hirsutism and normal looking ovaries on ultrasound, but still have PCOD. This problem is detected only when these patients are superovulated, at which time they over-respond by producing a large number of follicles.

Interestingly, many of these patients present with recurrent pregnancy loss (recurrent miscarriages), and often their doctor does not make the correct diagnosis for them.

How is PCOD treated ?

Treatment

Treatment of PCOD for the infertile patient will usually focus on inducing ovulation to help them conceive.

Weight loss: For many patients with PCOD, weight loss is an effective treatment - but of course, this is easier said than done! Look for a permanent weight loss plan - and referral to a dietitian or a weight control clinic may be helpful. Crash diets are usually not effective.

Increasing physical activity is an important step in losing weight. Aerobic activities such as walking, jogging or swimming are advised. Try to find a partner to do this with, so that you can help each other to keep going.

How can ovulation be induced in patients with PCOD ?

Ovulation Induction:

The drug of first choice for women with PCOD today is metformin (this medicine is also used for treating patients with diabetes.) Doctors have now learned that many patients with PCOD also have insulin resistance - a condition similar to that found in diabetics, in that they have raised levels of insulin in their blood (hyperinsulinemia) , and their response to insulin is blunted. This is why some patients with PCOD who do not respond to clomiphene are treated with antidiabetic drugs, such as metformin and troglitazone. Studies have shown that these drugs improve their fertility by reversing their endocrine abnormality and improving their ovulatory response.

In the past, the drug of first choice used to be clomiphene; this may be combined with low-doses of dexamethasone, a steroid which suppresses androgen production from the adrenal glands. Just taking clomiphene is not enough , and you need to be monitored (usually with ultrasound scans) to determine if the clomiphene is helping you to ovulate or not. The doctor may have to progressively increase the dose till he finds the right dose for you. If clomiphene does not work, a newer anti-estrogen called letrozole (which is also used for treating women with breast cancer) can be used. Clomiphene resistant PCO women may need ovulation induction with HMG (gonadotropins). Some doctors prefer to use pure FSH for inducing ovulation in PCOD patients because they have abnormally high levels of LH.

Ovulation induction can often be difficult in patients with PCOD , since there is the risk that the patient may over-respond to the drugs, and produce too many follicles, which is why the risk of ovarian hyperstimulation syndrome (OHSS) and multiple pregnancy is often increased in patients with PCOD. The doctor has to find just the right dose of HMG (called the threshold value) in order to induce maturation and release of a single , or only a few follicles , and this can sometimes be very tricky.

Difficult patients may also need a combination of a GnRH analog (to stop the abnormal release of FSH and LH from the pituitary) and HMG to induce ovulation successfully.

How is surgery used to treat patients with PCOD ?

Surgery:

A recent treatment option uses laparoscopy to treat patients with PCOD. During operative laparoscopy, a laser or cautery is used to drill multiple holes through the thickened ovarian capsule. This procedure is called laparoscopic ovarian cauterisation or ovarian drilling or LEOS (laparoscopic electrocauterisation of ovarian stroma) . This should be reserved for women with PCOD who have large ovaries with increased stroma on ultrasound scanning. Destroying the abnormal ovarian tissue helps to restore normal ovarian function and helps to induce ovulation. For young patients with PCO ovaries on ultrasound, if clomiphene fails to achieve a pregnancy in 4 months time, we usually advise laparoscopic surgery as the next treatment option. This is because LEOS helps us to correct the underlying problem; and about 80% of patients will have regular cycles after undergoing this surgery, of which 50% will conceive in a year's time, without having to take further medication or treatment. Having regular cycles without having to take medicines each month can be very reassuring to these patients !

The skill of the surgeon plays a key role in determining the outcome of the surgery . It is important that the surgeon selectively destroy only the stroma, and NOT the cortex. The cortex of the ovary contains the eggs, and if this damaged, then ovarian function is jeopardised, so that the surgery may actually end up causing infertility ! An additional risk of this surgery is that it can induce adhesion formation, if not performed competently.

In the past, doctors used to perform ovarian surgery called wedge resection to help patients with PCOD to ovulate. The removal of the abnormal ovarian tissue in the wedge breaks the vicious cycle of PCOD, helping ovulation to occur . While wedge resection used to be a popular treatment option, the risk of inducing adhesions around the ovary as a result of this surgery has led to the operation being used as a last resort.

For patients who do not respond to the above measures, ovulation induction plus intrauterine insemination is the next step.

How is IVF used for treating patients with PCOD ?

If 3 cycles of IUI have failed, then IVF is the best treatment option for patients with PCOD. However, many IVF clinics have little experience in superovulating these women, and they often mess up their superovulation. Because these women grow so many eggs in response to the HMG injections used for superovulation, and because doctors are very worried about the risk of ovarian hyperstimulation, they often end up triggering egg collection with HCG when the eggs are immature. They consequently get lots of eggs, but since most of these are immature, fertilisation rates and pregnancy rates are very poor.

In our clinic, because we have extensive experience in dealing with women with PCOD (which is much commoner in the Middle East and South India than in the West), we do a much better job at getting these women to grow many mature eggs. Also, because we carefully and meticulously flush each and every follicle at the time of egg collection, the risk of PCOD patients developing ovarian hyperstimulation in our clinic has been virtually zero in the last 8 years.

The good news is that with the currently available treatment options, successful treatment of the infertility is usually possible in the majority of patients with PCOD.

CHAPTER XVI

The Cervical Factor

What is cervical mucus ?

Normal cervical mucus

Cervical mucus is a jelly-like substance produced by tiny glands in the cervix called cervical crypts. It has a protective function and may prevent bacteria from getting into the uterine cavity. The mucus changes predictably and cyclically during the menstrual cycle. During the first half of the cycle before ovulation, when the hormone estrogen is produced in ever increasing amounts, the mucus made by the cervical glands becomes watery and copious. Sperm can penetrate the watery mucus easily, and when intercourse takes place, they swim through it into the uterus.

After ovulation the quality of the mucus changes because the corpus luteum of the ovary now starts to make the hormone progesterone. Mucus produced under the influence of progesterone is thicker, stickier and its quantity is reduced. Sperm cannot swim through this mucus, and it forms a barrier to sperm entry into the uterine cavity.

Even if intercourse occurs at the time the cervical mucus is at its most favourable, only about 1 in every 2000 sperm enter the mucus. The rest of the sperm remain in the vagina, where they die, because of the acidic pH of the vagina. Those sperm that have entered the mucus can survive there for long periods - certainly for several days after intercourse. Once in the cervical mucus, they steadily swim upwards from it into the uterus over a period of 48 to 72 hours. Thus the cervical mucus acts as a sperm reservoir, to be banked on if intercourse does not take place at ovulation. This is why you don't need to have sex everyday in order to conceive! The cervical mucus also acts as a filter - and allows only the best sperm to swim through it into the uterus and up towards the egg present in the fallopian tube.

How can you track your mucus ?

Observing the mucus

Mucus flows from the cervix down the walls of the vagina and can be observed when it reaches the vulva. You can learn to observe the changes in your mucus by becoming aware of the wet, lubricative feeling produced by the mucus, and by observing the mucus itself at the vulva. This is called the Billing (fertility awareness) method, and is very useful in allowing you to determine when you ovulate.

You need to chart what the mucus looks like and feels like daily, from the day your bleeding stops. You will find the mucus present at your vaginal opening - the vulva. Remember, you do not need to feel inside the vagina; this will simply confuse the picture, because the vagina is always moist. It is the vulva which is the mucus (fertility) monitor.

In a typical 28 days menstrual cycle, at the end of bleeding, the sensation you experience is one of dryness and no mucus is seen or felt. In some women, there is some mucus, but it is thick, sticky, and scanty. This is the basic infertile pattern of dryness and lasts for two to three days. Once this is over, you may notice a feeling of moistness at the vulva and the mucus will change in appearance and feel. It becomes thinner, clearer, more profuse and stretchy, like raw egg white. This fertile-type mucus produces a slippery wet lubricative sensation at the vulva. The last day of this fertile-type mucus (that is, the vulva feels lubricative) is called the peak of fertility, because it is the most fertile day of the cycle. You will know it is the last day only in retrospect; and after this, the important thing to realize is that the peak day is not necessarily the day of the highest mucus formation; it is simply the last day that the mucus discharged has fertile characteristics. Ovulation usually occurs with 24 hours of the peak mucus signal. Therefore, these are the best days to have intercourse in order to maximize the chances of conception.



Fig 1. Normal cervix 2. Profuse cervical mucus

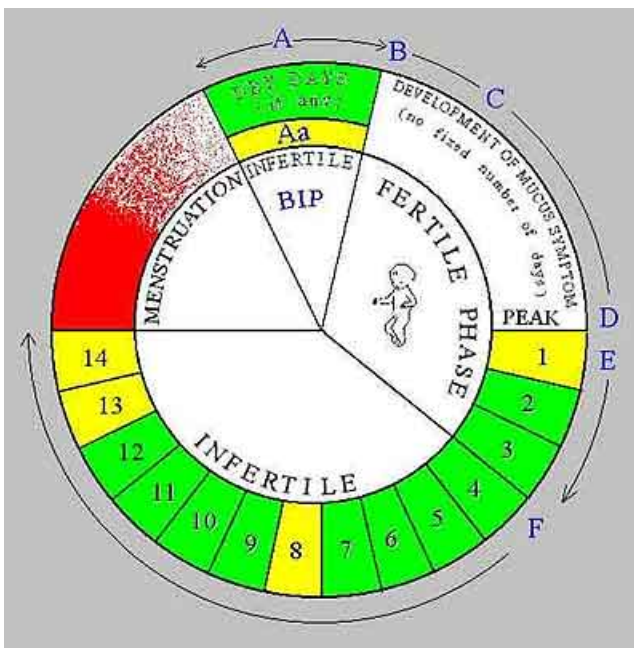


Fig 3. The Billing calendar for charting cervical mucus. The time period marked C is the "fertile period".

How can problems with cervical mucus affect fertility ?

Problems with the cervical mucus

In some women, the cervical mucus may prevent the sperm from moving freely into the uterus. Such a barrier may be because of the following reasons:

- There is not enough of it to allow the sperm to move easily
- The mucus is too thick and sticky
- The mucus is not compatible with the husband's sperm.

How does the doctor test your cervical mucus ?

Tests on the cervical mucus

Problems with cervical mucus usually cause no symptoms. Tests need to be done to assess whether the mucus is normal or not.

The doctor examines the cervix and the cervical mucus daily from about the tenth day of the period. The mouth of the cervix is graded, depending upon how open it is; and the mucus is graded for its amount; its stretchability ("spinnbarkeit") ; and its ability to fern. For the ferning test, a small drop of mucus is placed on a glass slide and allowed to dry. It should crystallize, forming branches which look very like fern leaves. These grades are added to give an Insler mucus score. Healthy cervical mucus is profuse in volume; very stretchable (upto 10 cm in length); and ferns easily.

What is the postcoital test (PCT) ?

The post coital test (PCT) :- This is one of the oldest tests in investigating infertility and has been done for well over 100years. Timing the PCT is critical, and it must be done in the preovulatory period, when the mucus is profuse and clear. The gynaecologist examines a small sample of the cervical mucus under a microscope some hours after sexual intercourse. The mucus is sucked painlessly from the cervical canal during an internal examination. Most doctors feel that the best time to do this is about 6 to 24 hours after sex, but this timing is not critical. The test is said to be positive if many normal live sperm are seen swimming in the mucus sample. The sperm should be swimming in a fairly straight line and reasonably vigorously. A positive PCT is very reassuring and implies that :

1. The husband is likely to be producing enough normal sperm
2. Intercourse results in semen being deposited in the vagina
3. The cervical glands are healthy
4. Sufficient estrogen is being produced before ovulation, suggesting that ovulation is normal
5. There are no antibodies in the mucus hostile to the sperm

What if the PCT is negative (that is, no sperm are seen in the mucus; or they are all dead)? Some of the reasons for a negative test are:

- The PCT was not done at the best time. For example, the PCT may have been done too early or too late in the cycle. Wrong timing is the commonest reason for a negative test and can even cause repeatedly negative tests.
- There was no ovulation the month of the test - perhaps because of the strain or stress of making love to order.
- The sperm count was poor. Obviously, men with persistently low sperm counts, or men with poor motile sperm, may be responsible for a negative PCT.
- There may be an abnormality of the cervix - for example, chronic infection in the cervix may prevent production of adequate mucus; and some women with a scarred cervix may not produce enough mucus. Patients who have had surgery on the cervix (for example, cervical conisation, in which a cone of cervical tissue is removed to treat cervical dysplasia) often have this problem.
- The cervix is producing antibodies to the sperm.
- Medications such as clomiphene, tamoxifen, progesterones and danazol - all drugs used for infertility problems - can interfere with the production of good mucus.

Remember that a negative test is meaningful only if it is repeatedly negative under perfect conditions.

We never do the PCT test in our practise, because we feel it provides very limited information, and does not affect the treatment plan.

What is the in vitro sperm mucus penetration test ?

If the mucus is good but the post-coital test is repeatedly bad, an 'in-vitro' mucus penetration test, or sperm invasion test, can be performed. This is performed simply by putting a drop of freshly removed mucus next to a drop of freshly ejaculated semen on a microscope slide. The interface between the two drops is examined for about a quarter of an hour, and it is then possible to see if the sperm are penetrating the mucus and swimming actively in it. If this does not occur, then it is likely that there is some form of immune response between the sperm and the mucus, and further tests should be conducted to examine this.

Cross-over testing can be performed using the mucus and semen under examination in various combinations with donor mucus and semen. This will show if the problem is with the sperm or the mucus.

Another simple test for antisperm antibodies in the mucus is called the sperm cervical mucus contact test (SCMC for short) where the sperm and mucus are mixed together. If, under the microscope, the sperm are seen to be shaking in a characteristic way, this means that there are anti-bodies present.

How can poor cervical mucus be treated ?

Cervical problems can be corrected depending upon what the cause is. For example, if the reason for the poor mucus is:

- lack of ovulation, then ovulation can be induced
- cervical infection, then this can be treated by cauterising or freezing the abnormal cervical tissue, so that this is destroyed, and is then replaced by healthy cervical glands
- thick or viscous mucus can occasionally be treated by cough medicines (expectorants, which contain guaifensin (Robitussin) in a dose of 1-2 tsp per day, beginning three to four days prior to when you want to conceive.) Just like guaifensin helps to thin the thick phlegm if you have a cough, it also helps to thin the cervical mucus.
- scanty mucus, then mucus production can be enhanced by supplemental low-dose estrogens.

For resistant cervical problems, the easiest solution may be to bypass the cervix entirely, by injecting the sperm direct into the uterus - intrauterine insemination.

Sometimes the problem is one of "cervical hostility " to the sperm - that is there are antisperm antibodies in the mucus that are killing the sperm. For this condition the outlook is now more hopeful:

- Some doctors recommend that the woman avoid contact with sperm for a period of time. This may cause the antibodies to disappear because their production is no longer being stimulated by repeated exposure to the antigen. The couple can have sex, but the husband must wear a condom so that the sperm don't come into contact with the cervix. This course may be recommended for six months, until the antibodies have disappeared. For obvious reasons, this treatment is rarely suggested now a days!
- Some doctors have tried insemination with the husband's semen directly into the uterus - intrauterine insemination. This means bypassing the cervix and therefore the site of the antibodies. This treatment has had limited success in some clinics but there is doubt about its value. This is because if antibodies are being produced, they may be in the tube and the uterine cavity as well.
- Steroids may be given to prevent production of antibodies. To be effective they have to be given in high doses and this may cause serious side effects. However, these treatments are rather experimental and not definitely effective.
- IVF. The presence of antisperm antibodies in the cervix will not interfere with in vitro fertilisation; and this may be a treatment option for difficult patients.

CHAPTER XVII

Hirsutism -- Excess Facial and Body Hair

What is hirsutism ?

Hirsutism is the growth of long, coarse hair on the face and body of women in a pattern similar to that found in men. Besides being cosmetically distressing, hirsutism may also signal the presence of a hormone imbalance or a hormone-producing tumor.

Normal hair growth

Each hair grows from a follicle deep in the skin. As long as these follicles are not completely destroyed, hair will continue to grow even if the shaft, which is the part of the hair that appears above the skin, is plucked or removed.

Adults have two types of hair, vellus and terminal. Vellus hair is soft, fine, colorless, and usually short. In most women, vellus hairs grow on the face, chest, and back and give the impression of "hairless" skin. Terminal hairs are the longer, coarser, darker, and sometimes curly hairs that grows on the scalp, pubic, and armpit areas in both adult men and women. The facial and body hair in men is mostly of the terminal type.

What causes hirsutism?

What causes hirsutism?

Most often, excess facial and body hair is the result of abnormally high levels of androgens or male hormones in the blood. Androgens are present in both men and women, but men have much higher levels. These hormones cause hairs to change from vellus to terminal. Once a vellus hair has been transformed to the coarser terminal hair, it usually does not change back. Androgens also cause terminal hairs to grow faster and thicker. Both the ovaries and the adrenals produce androgens. To some degree, estrogens and progesterone, female hormones, prevent the effect of androgens.

The circumstances described below can lead to high androgen levels, which in turn can cause hirsutism.

Genetics

There are very obvious family and racial differences in hirsutism patients. In some women, the skin is very sensitive to even low levels of androgens and their follicles produce primarily terminal (coarse and dark) hairs. If your mother, grandmother or sister experienced the disorder, then you are at a greater risk of developing it.

Polycystic ovarian syndrome

This is the commonest reason for hirsutism in infertile women. Polycystic ovarian syndrome causes the ovaries to develop many small cysts and to overproduce male hormones. The disorder is often associated with hirsutism, irregular ovulation, menstrual disturbances and obesity.

Ovarian tumors

On rare occasions, androgen-producing ovarian tumors cause hirsutism. When this is the case, hirsutism progresses rapidly; and may even cause virilisation - in which the woman starts developing masculine characteristics, such as a deep voice and an enlarged clitoris.

An ovarian mass may be detected during a pelvic examination. Tests may also need to be done to make sure that tumors are not present when male hormone levels are high.

Adrenal disorders

The adrenal glands, which are located just above each kidney, also produce androgens. The most common disease of the adrenal gland that can result in hirsutism is an inherited disorder called late onset adrenal hyperplasia. Adrenal tumours and other adrenal diseases such as Cushing's disease can also cause overproduction of androgens.

How is the cause of hirsutism diagnosed ?

Determining the cause

When trying to determine the cause of hirsutism, several blood tests need to be done to measure androgen levels. These tests are done by radioimmunoassay in a specialised laboratory - and include levels of: testosterone; androstendione; 17-hydroxyprogesterone; and DHEA-S (dehydroepiandrosterone sulphate). These tongue-twisters are simply the chemical names of androgens produced in the body. Which particular hormone is increased will tip off the doctor as to where the problem lies -whether in the ovaries or in the adrenal glands. A pelvic ultrasound or special x-ray studies may also need to be done to detect ovarian or adrenal tumors. Hormone suppression or stimulation tests which further evaluate the function of the ovaries and adrenal glands may also be required. During these tests, blood is measured for hormone levels both before and after the administration of a specific hormone medication. For example, the ACTH (adrenocorticotrophic hormone) stimulation test is conducted in order to check for the presence of late onset adrenal hyperplasia.

How is hirsutism treated ?

Treatment

Of course, the priority will be to correct the problem of infertility - thus for example, if the problem of hirsutism is due to anovulation due to polycystic ovarian syndrome , the primary goal will be to induce ovulation.

Low doses of steroids called dexamethasone or prednisone may also be prescribed if the adrenal gland is overactive. This medicine is usually taken at bedtime and serves to suppress production of the ACTH hormone which stimulates the adrenal gland.

Hormone treatment may prevent new hairs from developing. However, it usually takes many years for the excess hair to develop, and a significant decrease in the rate of hair growth will not be seen for at least six months of hormone treatment. Once a hormone treatment has proven to be effective, it may be continued indefinitely. However, terminal hairs that are already present will not fall out or disappear with hormonal therapy and must be removed by other means.

Cosmetic therapy

For temporary hair removal, many women with mild hirsutism pluck the unwanted hairs. Waxing, another alternative, is essentially the same as plucking.

Depilating agents are chemicals that dissolve the hair shafts on both facial and body hair and may also be used to remove unwanted hair. These chemicals can cause irritation and facial skin is particularly sensitive.

Shaving is probably the simplest and safest temporary hair removal procedure. Although frequently required, it is virtually painless and seldom has side effects. Contrary to popular belief, shaving does not make hair grow faster. An electric razor produces less skin irritation than a blade.

Electrolysis is the only permanent way to remove unwanted hair. During this procedure, a very fine needle is placed next to the hair shaft into the follicle. A mild electric current is sent through the needle and permanently kills the hair follicle. It is not possible to use this technique to remove hairs from very large areas of the body because each hair must be treated individually. In addition, the technique, although quite effective, is expensive, time consuming, and moderately uncomfortable. If hormonal therapy is being started, it is best to delay electrolysis for at least six months so that the growth of new terminal hairs will be reduced.

The latest cosmetic technique to remove hair uses a laser to kill the hair follicles very precisely, and this is now becoming increasingly popular. Laser depilation is speedy, relatively painless, efficient and possibly permanent. A Ruby Laser produces red light which is highly absorbed by the melanin pigment in the hair and only minimally absorbed in skin. This means that the hair is selectively targeted by the light and hence destroyed without any damage to the skin around the hair follicle.

CHAPTER XVIII

Endometriosis -- The Silent Invader

What is endometriosis ?

Endometriosis ("endo") is a common disorder that affects women of reproductive age. It occurs when normal endometrial tissue (the lining of the uterus) grows outside the uterus. This misplaced tissue may implant itself and grow anywhere within the abdominal cavity. Many specialists feel that severe endometriosis is more likely to be found in infertile women who have delayed pregnancy and for this reason, the condition is sometimes labeled a "career woman's disease".

Endometrial tissue, whether it is inside or outside the uterus, responds to the rise and fall of estrogen and progesterone produced by the ovaries during the reproductive cycle. Under the influence of the hormones, the misplaced tissue swells; and when hormonal levels drop, the tissue may bleed. Unlike the normally situated endometrium, which is shed from the body as menstrual discharge, this blood and tissue has no outlet. It remains to irritate the surrounding tissue.

The disease is highly unpredictable. Some women may have just a few isolated implants that never spread or grow, while in others the disease may spread throughout the pelvis. Endometriosis irritates surrounding tissue and may produce web like growths of scar tissue called adhesions. The scar tissue can bind the pelvic organs and even cover them entirely. Many women who have endometriosis experience few or no symptoms. However, in some women, endometriosis may cause severe menstrual cramps, pain during intercourse, and infertility.

It is a disease which has been called an "enigma wrapped inside a mystery ", and there is a lot about it that we do not understand as yet.

What causes endometriosis?

What causes endometriosis?

Several theories exist as to how endometriosis begins. One possibility is retrograde menstruation, the backward flow of the menstrual discharge through the fallopian tubes into the pelvis. According to this theory, the endometrial cells may implant on the ovaries or elsewhere in the pelvic cavity.

What does endometriosis look like ?

What does it look like?

Early implants look like small, flat dark patches or flecks of blue or black paint ("powder-burns") sprinkled on the pelvic surfaces. The small patches may remain unchanged, become scar tissue or spontaneously disappear over a period of months. Endometriosis may invade the ovary, producing blood filled cysts called endometriomas.

With time, the blood darkens to a deep, reddish brown or tarry color, giving rise to the description "chocolate cyst." These may be smaller than a pea or larger than a grapefruit. In some cases, bands of fibrous tissue called adhesions may bind the uterus, tubes, ovaries, and nearby intestines together. The endometrial tissue may also grow into the walls of the intestine - but although it may invade neighboring tissue, endometriosis is not a cancer.

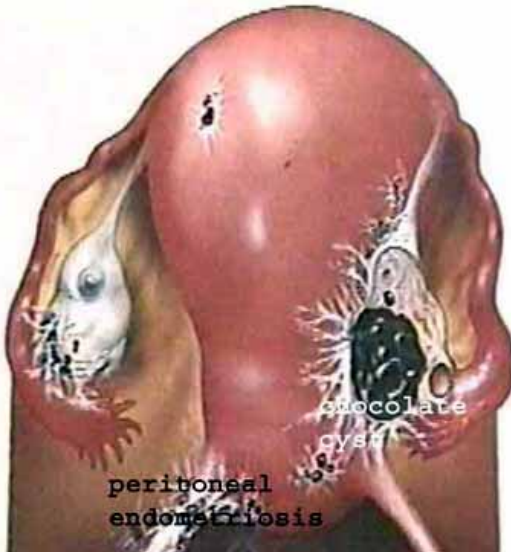


Fig 1. Schematic, showing a chocolate cyst (endometrioma) in the right ovary; and peritubal adhesions because of endometriosis



Fig 2. Laparoscopy, showing minimal endometriosis, in the form of " powder-burn" deposits.



Fig 3 . Laparoscopy, showing a small chocolate cyst in the left ovary. This can be very easy to miss, so a careful multiple puncture laparoscopy is essential to make an accurate diagnosis of endometriosis.

What are the symptoms of endometriosis ?

What are the symptoms?

Progressively increasing dysmenorrhea (periods pains or menstrual cramping) may be a symptom of endometriosis. These are caused by contractions of uterine muscle initiated by prostaglandins released from the endometrial tissue. A puzzling feature of endometriosis is that the degree of pain it causes is not related to the extent of the disease. Some women with extensive disease feel no pain at all. A woman with endometriosis may notice that as the disease progresses her periods become more painful or that the pain begins earlier or lasts longer.

Endometriosis can cause pain during intercourse, a condition known as dyspareunia. The thrusting motion of the penis can produce pain in an ovary bound by scar tissue to the top of the vagina or in a tender nodule of endometriosis. Most women who have endometriosis report no bleeding irregularities. Occasionally, however, the disease is accompanied by vaginal bleeding at irregular intervals; or by premenstrual spotting.

How does endometriosis cause infertility ?

How does endometriosis cause infertility? The relationship between mild (early) endometriosis and infertility is controversial. The most recent theories regarding the endometriosis-infertility link focus on the fact that endometriosis may lead to a form of mild inflammation within the pelvis. In some women with mild endometriosis, the levels of certain chemicals called cytokines (released in response to inflammation) are increased in the abdominal cavity, and these hormones may have a negative effect on follicle and egg development, egg-sperm binding and fertilization, normal tubal function, and even implantation. Sometimes, the endometriosis may be coincidental and unrelated to the fertility problem. In these patients, other factors may be involved in a couple's infertility, such as poor quality sperm or ovulation disorders- and the endometriosis is a "red herring". Some women who have the condition are able to conceive, while others may be infertile due to endometriosis or a combination of factors.

The disease may hinder conception in various ways - especially when it is severe. Endometriosis may inflame surrounding tissue and spur the growth of scar tissue or adhesions. Bands of scar tissue may bind the ovaries, fallopian tubes, and intestines

together and thus interfere with the release of eggs from the ovaries or the ability of the tube to pick up the egg. Rarely, severe endometriosis may cause the tubes to become blocked. The presence of chocolate cysts in the ovary may also impair ovulation.

How does the doctor diagnosis endometriosis ?

Diagnosis

Endometriosis cannot be diagnosed from symptoms alone. While a physician may suspect the disease if an infertile woman complains of severe menstrual cramps or pain with intercourse, many patients with the condition have no discomfort at all. The diagnosis can be confirmed only by a laparoscopy

Laparoscopy enables the doctor to look inside the pelvis and inspect the reproductive organs to confirm the presence of endometriosis. In fact, since endometriosis is often without symptoms, many doctors advise laparoscopy as part of the diagnostic study for all infertile women.

Looking through the laparoscope the surgeon can see the surface of the uterus, tubes, ovaries, and other pelvic organs. He can visually confirm the presence of the endometriosis and gauge its extent. If desired, a small piece of tissue can be removed for microscopic examination (biopsy). It is easy to miss early endometriosis if the laparoscopy is not performed carefully. The entire ovary should be inspected carefully; and if it is enlarged, it should be punctured to look for "chocolate" cysts.

In most cases, the surgeon will treat the endometriosis during laparoscopy. If so, he makes other small abdominal incisions through which additional instruments are introduced for operative laparoscopy. The surgeon may vaporize the lesions with a laser beam , or destroy them with an electric current called diathermy. Ovarian cysts can be excised (removed) or opened and drained (marsupialised) and their inner lining destroyed.

However, whether treating the endometriosis surgically actually helps to improve fertility is still a very controversial issue. Sometimes, overenthusiastic surgery may actually decrease a patient's fertility, because the doctor ends up removing a lot of normal ovarian tissue along with the wall of the chocolate cyst.



Fig 4. Operative laparoscopy, for removal of a chocolate cyst of the ovary (endometrioma)

Other imaging technologies, such as ultrasound, computerized tomography or magnetic resonance imaging may be used to get more information about the extent of the disease.

However, these procedures are useful only for identifying endometriotic cysts in the ovary.

What medications are used for treating endometriosis ?

Hormone medication

The goal of hormonal treatment is to simulate pregnancy or menopause, two natural conditions known to inhibit the disease. In each case, the normal endometrium is no longer stimulated to grow and regress with each monthly cycle, and menstruation ceases. The growth of misplaced endometrial tissue usually will be suppressed as well. To simulate the hormonal environment of pregnancy, birth control pills are prescribed. To be effective against endometriosis, the pills must be taken continuously without pausing for withdrawal bleeding. This state is sometimes called pseudopregnancy. The hormone derivative danazol is the medication most frequently used to treat endometriosis. During treatment with danazol, estrogen levels are reduced to the low levels characteristic of natural menopause. This state is sometimes called pseudomenopause. Danazol is an expensive medication which is usually prescribed for six months or more. Unfortunately, large endometriotic cysts of the ovary are generally resistant to the drug.

Analogues of GnRH, the gonadotropin releasing hormone, are the newest class of hormones used for endometriosis treatment. Brand names include Lupron and Synarel. These analogues switch off production of FSH and LH from the pituitary, thus inducing a menopausal state. These analogs can be given in the form of special injections called depot preparations, which release small quantities of the drug daily, allowing administration at monthly intervals.

Medical therapy used to be prescribed in the hope that it would cause the endometriosis to shrink sufficiently so that it would no longer interfere with conception after the treatment is stopped. However, since pregnancy cannot occur during the medical therapy of endometriosis, and because the treatment has been shown not to be helpful in improving fertility, medical therapy for endometriosis is no longer advised for infertile patients.

How is surgery used for treating endometriosis ?

Surgery

Treating endometriosis with medicines has definite limitations. Medication usually controls mild or moderate pain and may eliminate small patches of the disease. But large chocolate cysts in the ovary are less likely to respond, and drugs cannot remove scar tissue. This is why surgery may be needed to improve fertility by removing adhesions, lesions, nodules or endometriomas.

As described earlier, laparoscopy can be used as a therapeutic tool. For example, fluid can be drained ; adhesions freed; and patches of endometriosis destroyed using a laser or electrical current. Even large endometriomas can be removed through the laparoscope by a skilled surgeon, so that today most cases can be successfully treated through the laparoscope. Open surgery (laparotomy) is needed only very rarely.

How is IVF used for treating endometriosis ?

IVF

Treatment cannot "cure" endometriosis - but it can control it. If an infertile woman with endometriosis fails to conceive even after surgical treatment, the next option is superovulation with intrauterine insemination, since the fallopian tubes in these patients are usually open. If this fails, then IVF (in vitro fertilization) can be very useful. However, the ovarian response in some of these patients can be poor, especially if they have large chocolate cysts, or have had surgery for these cysts. Fertilisation rates in some patients with endometriosis can be a little lower than for other patients, perhaps because of an intrinsic oocyte abnormality.

Endometriosis is a disease affecting millions of women throughout the world. For many, the condition goes unnoticed. But for others it demands professional attention, especially when fertility is impaired. The best strategy to maximize chances of conception is to select a specialist who is familiar with the latest developments in endometriosis management.

CHAPTER XIV

Ectopic Pregnancy – The Time Bomb in the Tube

What is an ectopic pregnancy ?

An ectopic pregnancy is one which develops outside the uterus. Most ectopics are found in the fallopian tube and these are called tubal pregnancies. However, they can also occur at other pelvic sites and these include: the ovary; the abdomen; and the cervix.

Fertilisation normally occurs in the outer half of the fallopian tube which is called the ampulla. The embryo is then propelled along the fallopian tube, by the coordinated beating of the cilia which line the tube, towards the uterus. An ectopic pregnancy occurs when the embryo gets stuck in the fallopian tube and implants here, instead of moving on to the uterus.

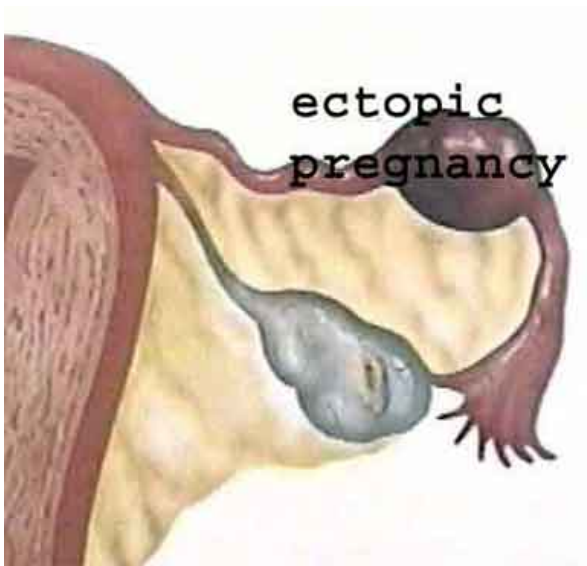


Fig 1. Schematic of unruptured ectopic pregnancy in right fallopian tube

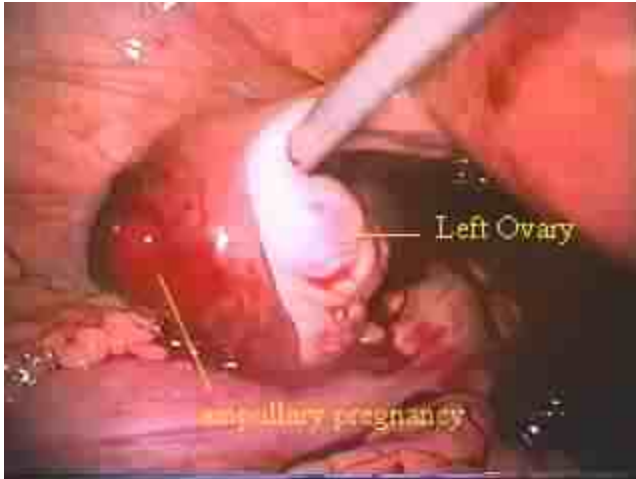


Fig 2. Ruptured ectopic pregnancy in ampulla of left fallopian tube. Observe the blood collected in the pelvis.

Ectopic pregnancy occurs once in every one hundred pregnancies. The commonest cause of a tubal pregnancy is tubal damage, which is most often due to pelvic inflammatory disease. If tubal damage is severe, the tube gets totally blocked, as a result of which the patient is infertile. However, with less severe infection, the tube remains open, but the tubal lining is damaged, as a result of which the cilia can no longer function effectively. Other reasons for tubal damage include: tubal surgery, infection following IUCD insertion; and previous tubal pregnancy.

Infertile patients are at increased risk for ectopic pregnancies, for unclear reasons. Perhaps the cause of their infertility is subtle tubal damage. There is also an increased risk for tubal pregnancy after IVF, since the embryo may sometimes migrate after embryo transfer from the uterine cavity to the fallopian tube. The risk of ectopics after GIFT is greater than with IVF.

How is ectopic pregnancy diagnosed ?

Initially an ectopic pregnancy may appear just as a normal pregnancy - with a missed menstrual period and symptoms such as sore breasts and nausea. However, there is often abnormal vaginal bleeding which may occur at the time of, a little later than, the expected period. Often, this bleeding is mistaken for a period. Pain on the side of the ectopic occurs commonly and may be associated with a feeling of light-headedness. If the tube ruptures, this usually results in severe abdominal pain, fainting and shock. Making the diagnosis on clinical examination is difficult, and the only suspicious finding may be pain on internal examination.

A tubal pregnancy used to be a catastrophe. Diagnosis was usually made only after the tube had ruptured - and emergency surgery was required to stop the bleeding and save the mother's life. Often this meant removing the whole tube, which was often completely damaged. Consequently, the chances of a patient's conceiving after this was markedly reduced.

Today, an ectopic pregnancy can be diagnosed very early using blood tests for HCG ; and vaginal ultrasound. Both these tests need to be done simultaneously in order to interpret them correctly. Beta HCG is a very specific "marker" for pregnancy. This blood test is very sensitive and if negative, virtually excludes any risk of a significant ectopic pregnancy. A positive HCG level confirms that the patient is pregnant, but does not provide information about the site of the pregnancy. A vaginal ultrasound allows the doctor to locate the gestational sac of the early pregnancy. Occasionally, the sac may be seen outside the uterus, making a positive diagnosis of ectopic on sonography. Often, however, the sac cannot be seen clearly in ectopic pregnancies, especially if it is in an early stage. Then, both the scan and HCG levels need to be studied. In a normal intrauterine pregnancy, the doctor should be able to see a gestational sac in the uterine cavity on vaginal ultrasound, if the HCG level is more than 2000 mIU/ml (this is called the discriminatory zone). However, if the level is more than 2000 mIU/ml and the doctor cannot see a gestational sac , this means that the diagnosis is an ectopic pregnancy.

Another blood test which can be helpful is a serum progesterone level, which is low (less than 15 ng/ml) in patients with ectopic pregnancies, as compared to normal pregnancies.

Sometimes, differentiating between an ectopic pregnancy and an early miscarriage can be difficult. In these cases, if a curettage shows that there is no pregnancy tissue in the uterus (as tested by histopathologic examination) then an ectopic is suspected. The diagnosis can be confirmed by laparoscopy, if needed, which shows that the pregnancy is in the tubes, where it appears as a dark bluish bulge.

How is ectopic pregnancy treated ?

The major benefit of early diagnosis is that with early treatment it is possible to save the tube, thus preserving fertility and increasing the chances of a normal pregnancy in the future. If the ectopic is very early and the HCG levels low, one can choose to simply wait and watch. Often, the HCG levels will fall, meaning that the pregnancy is being reabsorbed by the body on its own and no treatment is needed. Medical treatment is also possible. This involves the use of the anti-cancer drug, methotrexate, which acts on the rapidly dividing cells of the tubal pregnancy and kills them, thus preventing the pregnancy from growing further. After giving an intramuscular injection of methotrexate, the beta HCG levels need to be monitored regularly, to ensure they are falling, till they decline to zero. This confirms that the pregnancy has been successfully destroyed. If the diagnosis is made early, methotrexate treatment of ectopic pregnancies is very successful.

Ultrasound - guided treatment is also useful for treating tubal pregnancies which have not ruptured. This involves the injection of the toxic chemical, potassium chloride , into the fetus in the tube under ultrasound - guidance. This kills the pregnancy tissue, allowing the body to reabsorb it.

Surgical treatment for early tubal pregnancies can be done through the laparoscope as well; with salpingotomy, the pregnancy can be selectively removed and the tube saved.

If the tube has ruptured, and blood has collected in the abdomen, then emergency surgery is needed. In these cases the tube is often so badly damaged, that it has to be removed entirely. When this occurs, a couple not only mourns the loss of a pregnancy, but also the possible loss or reduction in their fertility. This sense of loss is accompanied by the discomfort and anxiety of having had an emergency operation.

How does an ectopic pregnancy affect future fertility ?

What about the chances of getting pregnant after an ectopic pregnancy? Because tubal disease usually damages both sides, the chances of being infertile are increased. Also, the risk of a repeat ectopic pregnancy are increased even if the other tube seems normal. However, about 60% of women who have had a tubal pregnancy the first time will have a normal pregnancy the next time without further treatment. Early testing during pregnancy to rule out a repeat ectopic is essential!

If pregnancy does not occur within about a year of trying, then treatment is needed. Treatment options for fertility will depend upon what surgery was done for the ectopic pregnancy; and what the condition of the other tube is. Often, a second look laparoscopy is needed, to assess tubal status. Options may include: ovulation induction; tubal surgery; laparoscopic surgery; and often IVF.

Having had an unsuccessful outcome the first time makes getting pregnant very stressful - especially if the tubal pregnancy ended in a rupture. However, with the right treatment, chances of having a baby are quite good - after all, the fact an ectopic pregnancy occurred means that the eggs and sperms are good!

CHAPTER XX

Unexplained Infertility : Causes and Overcoming it.

What is unexplained infertility ?

Unexplained infertility simply means we do not know why the couple is infertile - it is a confession of medical ignorance. Patients with unexplained infertility fall into two groups. One is the group who really have no infertility problem whatsoever, but are just plain "unlucky". The other is the group which do have a reason for their infertility - but the reason is so subtle, that with present-day medical technology, we cannot find it.

Infertility may be said to be 'unexplained' if the woman is ovulating regularly, has open fallopian tubes with no adhesions or endometriosis ; if the man has normal sperm production; and the postcoital test is positive. Intercourse must take place frequently, particularly around the time of ovulation, and the couple must have been trying to conceive for at least one year.

Using these criteria, about 10% of all infertile couples have unexplained infertility. However, the percentage of couples classified as having unexplained infertility will depend upon the thoroughness of testing; and the sophistication of medical technology.

How is unexplained infertility diagnosed ?

The diagnosis is one of exclusion - that is, one which is made only after all the tests have been performed and their results found to be normal. This is why, the frequency of this diagnosis will depend upon how many tests are done by the clinic - the fewer the tests, the more frequent this diagnosis.

What are the causes of unexplained infertility ?

Possible causes of unexplained infertility

1. **Tubal Abnormalities:** It is possible that there may be a subtle defect in the mechanism by which the fimbria "pick up" the egg at ovulation; or the cilia in the tube may not function properly.
2. **Abnormal eggs:** It would appear that a very small number of cases of unexplained infertility are due to the persistent production of abnormal eggs. These may have a deformed structure or chromosomal abnormalities.
3. **Trapped eggs:** In some cases it would appear that eggs are produced, and mature correctly within the follicle which then goes on to become a corpus luteum without however first bursting to release the egg. The egg is therefore effectively 'trapped' inside the unbroken corpus luteum - called a luteinized unruptured follicle (LUF) syndrome.
4. **Luteal phase abnormalities:** The luteal phase is the part of the cycle that follows after the egg has been released from the ovary. It may be inadequate in one way -

and this is called a luteal phase defect.

The corpus luteum produces the hormone called progesterone. Progesterone is essential for preparing the endometrium to receive the fertilized egg. Several things can go wrong with progesterone production: the rise in output can be too slow, the level can be too low, or the length of time over which it is produced can be too short. Another possibility is a defective endometrium that does not respond properly to the progesterone.

Luteal phase defects can be investigated either by a properly timed endometrial biopsy; or by monitoring the progesterone output by taking a number of blood samples on different days after ovulation and measuring the progesterone level in them.

5. **Immunological factors:** The immune system can react against the man's sperm, and kill them, immobilize them or make them stick together. Women can also develop an immune reaction to the coating of their own eggs, which can prevent sperm from attaching to them.
6. **Infections:** Certain infections have been shown to be responsible for some cases of unexplained infertility. For example, mycoplasma or chlamydia may be present in numbers that are not enough to show up in a clinical examination, but which nevertheless cause infertility. This is why some doctors use empiric therapy with antibiotics.
7. **Inability of sperm to penetrate eggs:** Some men have a completely normal sperm count, but their sperm cannot fertilise the egg. The only way to make this diagnosis is by IVF; if donor sperm can fertilize the eggs; but the husband's sperm fail to do so, then the diagnosis is confirmed.
8. **Uterine factor:** Some women have an abnormal endometrium (uterine lining) which does not allow the embryo to implant . This is a subtle finding, which is often missed. It can be diagnosed by doing serial vaginal ultrasound scans, to assess the thickness and texture of the endometrium. In some infertile women, the endometrium remains persistently thin. This may be because of inadequate uterine blood flow, or poor estrogen receptors in the endometrial cells. This can be a difficult problem to treat, and therapy is usually empirical (either low-dose aspirin or high doses of estrogen).
9. **Psychological factors:** Studies on infertile groups of men and women have produced contradictory findings about the importance of psychological factors in causing infertility. Emotional disturbances undoubtedly appear to have some significance. This is only reasonable if you realise that the whole hormonal cycle, with its delicate adjustments, is controlled from the brain. This is an area which needs further investigation.

Has anything been missed?

Previous tests should be carefully reviewed to ensure that the diagnosis is in fact "unexplained" - and that no test has been omitted or missed. It may sometimes be necessary to repeat certain investigations. Thus, for example, if a previous Laparoscopy has been done by a single puncture and been reported as normal, it may be necessary to repeat the Laparoscopy with a double puncture, to look for early endometriosis.

How is unexplained infertility treated ?

How can unexplained infertility be treated?

Remember, you still have a fairly good chance of getting pregnant on your own without needing any treatment at all! If no abnormality is found, your chance of getting pregnant without treatment within 3 years is about 1 in 3. Taking treatment helps to increase the chances of your conceiving - and also makes it likelier that you will get pregnant sooner. The treatment of luteal phase defects is as controversial as their diagnosis. They can be treated by using clomiphene which may help by augmenting the secretion of FSH and thus improving the quality of the follicle (and therefore the corpus luteum which develops from it). Direct treatment with progesterone can also help luteal phase abnormalities. The progesterone can be given either as injections or vaginal suppositories.

Many patients are worried that if we are not able to find the cause of the infertility, we will not be able to treat them. Fortunately, this is not true - today, our technology for treating infertility is far superior than our technology for making a diagnosis ! In any case, most infertile couples are not really interested in a diagnosis of what the problem is - they are much more interested in finding the solution to their problem - getting a baby ! Today, with assisted reproductive technology, the chance of treatment being successful is very good. Intrauterine insemination with superovulation is the simplest approach, and it helps because it increases the chances of the egg and sperm meeting; but some patients may also need IVF or ZIFT . IVF can be helpful, because it provides information about the sperm's fertilizing ability, and also allows the doctor to perform in the lab what is not happening in the bedroom (whatever the reason for this) ; ZIFT on the other hand, has a higher pregnancy rate, and is very useful in these patients, since they have normal fallopian tubes.

CHAPTER XXI

Secondary Infertility -- Caught Between Fertile And Infertile Worlds

For most people, infertility conjures up the image of a couple without a child. But what about the couple who has borne a child, and now wants to extend their family but find they are unable to do so?

What is secondary infertility ?

Secondary infertility, is the inability to conceive after one or more successful pregnancies. The medical causes are similar to those of primary infertility, and include sperm problems, tubal factors, endometriosis, and ovulation difficulties. However, there are differences. For one thing, the couple is older, which is why time is at a premium!

Moreover, there are emotional aspects that are unique. The couple experiencing secondary infertility often finds it difficult to gain understanding or sympathy from family, friends and relatives. Since they have one child, most people assume that the couple will have no problem having another. Even other infertile couples offer little sympathy! Patients with primary infertility often resent couples who have a baby, and believe their own pain would disappear if only they too could bear one child. A common remark is, "You have one child, you should be grateful for that." These couples are caught between two worlds, fertile and infertile - and are excluded from both!

Guilt and frustration are common emotional responses. The frustration is borne out of surprise because the couple didn't think it would be difficult to conceive a second time (unless they had difficulty in getting pregnant the first time as well). However, just because they have got pregnant once doesn't make them immune to all the illnesses which can cause infertility - and tubes can get blocked and sperm counts drop as time goes by!

Secondarily infertile couples who had an elective abortion done for the first pregnancy and cannot conceive a second time around have a very hard time coping with their feelings of guilt. They often feel they are being punished for their sin of rejecting the child when they had it.

Couples with a child at home may also feel guilty. This arises because they catch themselves feeling that their one child isn't good enough for them; and also for their inability to provide their child with a sibling.

The child of a secondarily infertile couple may also bring unwitting pressure on his parents by asking when he 'll have a baby brother or sister. This is especially difficult when the child is being asked by his friends why he doesn't have a baby brother or sister and then begs his parents for a baby.

Parents may become very overprotective, fearing that something may happen to the one child they do have. They may also push pin all their hopes on their one child, and may push him to be a high achiever.

Many couples with secondary subfertility choose never to take medical treatment; often, this is because they are unsure about whether they do have a problem - and they keep on trying, hoping to hit the jackpot once again (after all, if they could do it once, why can't they do it again?)

What are the chances of a couple with secondary subfertility conceiving with medical treatment? While this would depend on the individual's problem, their chances are really about the same as a couple with primary subfertility. While they have the benefit of having "proven" their fertility once, they usually have the handicap of an increased age against them.

If the couple chooses to seek medical intervention, they also must decide what to tell their child about medical procedures. The presence of a child at home can make coping with the demands of infertility treatment much more difficult!

The financial burden of taking treatment can also add to the emotional burden of the couple and they may wonder if they shouldn't be spending the money on the child they already have rather than pursuing the hope of expanding their family.

Adoption can be a choice for some of these couples - but it's often more complicated because they worry about the possibility of "favoritism" ; and may also feel that it is unfair to their biological child to bring an adopted child into the family.

Coming to terms with secondary infertility is no easier than coming to terms with primary infertility - and it's important that the family of the secondarily infertile couple share their feelings together and maintain a positive attitude.

CHAPTER XXII

Empty Arms -- The Lonely Trauma of Miscarriage

How are abortions classified medically ?

An extended definition of infertility includes women who conceive but cannot carry a pregnancy to term - women who have repeated miscarriages. The technical term for this is recurrent pregnancy loss. This is one of the most frustrating problems in reproductive medicine today, because we still do not understand it well. Patients with repeated miscarriages have hundreds of questions - and we still do not have the answers ! The medical term for a miscarriage is an abortion. Most miscarriages start with vaginal bleeding which is initially slight and painless. This is called a threatened abortion, because the pregnancy is threatened by the bleeding. This bleeding is from the mother, and is not fetal blood. About half the time this stops spontaneously and results in no harm to the pregnancy. At this stage, the most useful test is an ultrasound scan (usually done with a vaginal probe). If a fetal heartbeat can be seen, this means that there is a 95 % chance that the pregnancy will proceed normally. On the other hand, if the ultrasound scan shows that the fetus has not developed properly ("blighted ovum " or anembryonic pregnancy when no fetus can be seen; or a missed abortion or intrauterine fetal death when the fetus is seen but the heart is not beating, then nothing can be done to save the pregnancy.

In such cases, the bleeding progresses, and the uterus starts contracting. This is felt as painful cramps, and the mouth of the uterus (the cervix) opens. This is called an inevitable abortion (because it cannot be stopped). If some of the pregnancy has already been pushed out by the contractions, this is called an incomplete abortion.

In patients with a blighted ovum, missed abortion, inevitable or incomplete abortion, the treatment is a uterine curettage (D&C) - a short surgical procedure which is performed to empty the uterus and remove the pregnant tissue.

Abortions which occur in the first twelve weeks of pregnancy are called first trimester abortions. Those which occur between the 13th to 20th weeks are called second trimester abortions.

How often do abortions occur ?

The magnitude of the problem

Perhaps 20-30% of all women spot, bleed or suffer cramps during their first twelve weeks of pregnancy, and about 10% miscarry. This figure may be an underestimate, because there are a number of women who miscarry unknowingly, thinking that their period was late or heavy. It is very common for women to have one miscarriage during the first twelve weeks of their pregnancy . The commonest reason for a first trimester miscarriage is a genetic defect in the embryo. This is actually Nature's defense mechanism, to prevent the birth of a baby with a birth defect. The genetic error is a random event which happens by chance , and occurs because a genetically abnormal egg or sperm gets

fertilised. This is not a sign that they have a health problem, because most of them will probably have a healthy baby the next time they get pregnant without any treatment. This is why most doctors will not do any testing for couples who have had a single first trimester miscarriage - the testing is usually not cost effective, and rarely provides any useful information.

If however, a patient has had two or more miscarriages consecutively, this is called repeated or habitual abortion. Now although the risk of miscarrying again does increase, this risk is still quite small, and increases from the 15% risk a normal woman has to 35% - which still means there is a 65% chance that they will not have a miscarriage again.

What are some of the myths about abortions ?

Most women who miscarry do so only once. Their risk for miscarrying again is not increased and is the same as that of a normal woman's - about 15%

Women who are over thirty five are no more liable to miscarry

Travelling, lifting weights and sex does not threaten a healthy pregnancy. As the old saying goes, " You cannot shake a good apple off a tree."

If you've had a previous miscarriage, it is very normal to be frightened and worried during your next pregnancy. It is important to understand that exercise, working and intercourse do not increase the risk of pregnancy loss. Likewise, staying at home and resting in bed probably do not prevent miscarriage.

What are the causes of repeated abortions ?

Causes

Repeated miscarriages can happen because of any of the following:

- Chromosomal abnormalities
- Hormone imbalance
- Physical Illness
- Polycystic Ovary Syndrome
- Immune problems
- Antiphospholipid antibodies
- Problems in the uterus
- Life style of the woman

Let's discuss these in detail.

How do chromosomal abnormalities cause miscarriages ?

Chromosomal Abnormalities

At least 60% of spontaneous miscarriages occur because of a chromosomal abnormality at conception. This means that a genetically (chromosomally) defective sperm or ovum gives rise to a genetically abnormal fetus. The miscarriage is Nature's defense mechanism, which aborts a defective fetus, rather than giving birth to a defective baby.

Since most of these genetic defects are chance occurrences, the risk of it being repeated again in the next pregnancy is very small.

In order to establish the diagnosis of a genetic cause for repeated pregnancy loss, a karyotype (study of the chromosomes) of the fetal tissue (if available) may be done. It is expensive, and often the cells fail to grow in culture, so that the study may not be possible. Moreover, since little can be done even if a defect is detected, it has little impact on patient management. However, it does provide an explanation for some patients with recurrent pregnancy loss.

In about 5 % of couples, a chromosome abnormality found in one of the parents explains recurrent miscarriage. This is detected by doing a chromosomal study on the parent's blood. The commonest problem is a structural defect (break or loss of a piece of the chromosome, called a deletion; a rearrangement of a bit of a chromosome, called a translocation) .

If the karyotype is normal, then the patient can be reassured that the miscarriages were a chance genetic event, and they can feel comfortable continuing with their efforts to have a baby. However, if the karyotypes are abnormal, this is a permanent situation, which indicates an increased risk of miscarriage. Genetic counselling should be sought to discuss the degree of risk. Depending upon the individual problem, this risk may be anywhere from 25% to 100%. Since chromosomal rearrangement at conception (when the sperm fertilises the egg) is a random event, there is little which can be done to treat this. Options may include: continuing to try to conceive a baby naturally; adoption; donor eggs (if you have the genetic problem) or donor sperms (if the husband has the genetic problem).

How do hormonal imbalances cause miscarriages ?

Hormone Imbalance

Patients may miscarry because they have a luteal phase defect - that is, the amount of progesterone hormone produced after the egg is released is reduced. Progesterone is the hormone which supports the pregnancy. It helps implantation of the embryo in the uterus and if this is deficient, there can be a problem with the embryo lodging itself in the uterine lining.

A luteal phase defect is suspected if the menstrual cycles are short - especially if the luteal phase (the time of the menstrual cycle between ovulation and the next menstruation) is shorter than 12 days.

This diagnosis can be confirmed by a blood test (a serum progesterone level done one week after ovulation is low) and an endometrial biopsy (which will show that the endometrium is "out of phase").

The doctor can help provide luteal support by prescribing progesterone during the last two weeks of the menstrual cycle after ovulation. If the woman is already pregnant, treatment may be with vaginal suppositories of natural progesterone for the first twelve weeks of the pregnancy; or progesterone injections intramuscularly. However, this treatment is controversial.

Which illnesses can cause repeated abortions ?

Illnesses

Health problems that can cause repeated miscarriages are:

- Uncontrolled thyroid disease, especially hypothyroidism
- Severe heart, liver or kidney disease
- Systemic lupus erythematosus an illness in which the woman produces antibodies against her own body tissues.

What about TORCH Infections? Certain infections called TORCH (which stands for Toxoplasmosis, Rubella, Cytomegalovirus and Herpes) , may be a cause for a single miscarriage, but are NOT a cause for repeated miscarriages. While a number of specialists will do these tests, and even start treatment based on the results, these tests are not worthwhile for patients who undergo habitual abortion. They just waste a lot of the patient's time and money.

A positive TORCH test simply means the patient has positive antibody levels against that particular infection. Thus, a positive Toxo IgG test means that the patient has anti-toxoplasmosis antibodies which protect her against a repeat toxoplasmosis infection. This means a positive test is actually a good sign and suggests that the patient is protected against that infection because she has been exposed to that infection in the past. Unfortunately, many doctors do not know how to interpret these results and scare the patient into thinking that the positive test result means she has an active infection which can cause her to miscarry again. In fact, some doctors will even attempt to "treat" the "infection" ! This wastes time and causes needless distress. If your doctor asks you do a TORCH test after a miscarriage, you should refuse and find a better doctor !

Although infections of the uterine cavity (for example, due to mycoplasma) are frequently thought to be a cause of recurrent pregnancy loss, substantial proof of this is lacking. Studies have in fact failed to indicate a greater incidence of infection in women with a history of miscarriage when compared to normal fertile women.

How does PCOD cause repeated miscarriages ?

Polycystic Ovary Syndrome

Exciting research done recently by Dr Howard Jacobs at the Middlesex Hospital, London, shows that polycystic ovary syndrome can also be a cause of recurrent miscarriages. In PCOS, the ovaries produce a large amount of the LH hormone. PCOS patients also have insulin resistance, and the high LH levels and high insulin levels have a detrimental effect on the egg, so that at the time of ovulation, the egg which is released is overripe and unhealthy. If such an egg is fertilised, the embryo is also likely to be unhealthy, and is consequently rejected by the body after 6-8 weeks as a miscarriage. Treating the abnormal insulin resistance in PCOD patients who have had repeated miscarriages with metformin helps many of them to have healthy babies . The interesting point of these studies is that it tells us that we should also be focussing on what is happening at the time of fertilisation - and not just what goes on after the pregnancy. Problems with the eggs and sperms at the time of fertilisation will manifest themselves as a miscarriage later on, but these are often neglected by the doctor.

How do immune problems cause repeated abortions ?

Immunity problems

The immune system plays an important protective role in maintaining health throughout life, by defending against infection. It "rejects" the foreign invaders (bacteria, viruses) which are recognised by the body as being "outsiders". It is now becoming evident that inappropriate activation of the mother's immune system may cause early first trimester miscarriages.

Current theory suggests that during a normal pregnancy, the fetus, which carries the father's foreign genes (and is therefore immunologically foreign to the mother) can nevertheless survive in the mother's uterus because of a special protection from the mother's immune system - the uterus is a "privileged" site. This is why it is not "rejected" like other foreign tissues (such as kidney transplants) are. This means that in the normal course of events, the fertilised egg somehow stimulates a protective maternal immune response which allows implantation and growth. For certain couples, this protective response does not occur, and the maternal immune system rejects the father's foreign material in the fetus, resulting in miscarriage. Tests are available to check for this, but these are still in the experimental stage. Treatment is in the research phase too, and includes sensitising the mother to the father's genes, by injecting his blood cells into her skin, the theory being that exposure to the foreign cells will stimulate her immune system to provide the normal protective immune response when she gets pregnant.

How do antiphospholipid antibodies cause repeated abortions ?

Antiphospholipid antibodies

Some women produce antibodies against the circulating substances that cause blood clotting. These are called lupus anticoagulant or anticardiolipin or antiphospholipid antibodies. They severely inhibit fetal development (by blocking off the blood supply to the fetus by causing clots in the maternal-fetal circulation) and cause miscarriages. Their presence can be detected by a blood test. Treatment is possible, either with low doses of aspirin (which decreases the clot formation); or with a steroid (prednisone) which suppresses the mother's abnormal immune system.

How do uterine problems cause repeated abortions ?

Problems in the Uterus

Miscarriages because of uterine problems usually occur after the twelfth week. These could be because of :

- A congenital abnormality of the uterus, which the woman is born with, but which does not cause any problems, until she gets pregnant . The common types of uterine anomalies include: a septate uterus (in which a wall divides the uterine cavity); a unicornuate uterus, in which the uterus has only one horn , because only one half has developed properly; and a bicornuate uterus, in which the uterus has two halves or horns, because the two did not fuse normally during their development in utero). This abnormal uterus cannot grow normally to hold and

- retain the pregnancy and this is consequently expelled. In women with a septate uterus, if the embryo implants on the abnormal tissue of the septum, the pregnancy may miscarry because the septum cannot support a pregnancy.
- Fibroids, which are growths of smooth muscle tissue inside the uterus. While most fibroids will not mar a pregnancy, if the fibroid is very close to the lining of the uterus (submucous fibroid), it will interfere with the implantation of the embryo in the uterus, and will cause its expulsion.
 - Intrauterine adhesions (Ashermann's syndrome). These are uncommon, and are fibrous bands of scar tissue in the uterus, which interfere with implantation of the embryo. They may be formed after a uterine curettage (after an abortion) and can be diagnosed by hysteroscopy or hysterosalpingography. They can be removed by hysteroscopic surgery, allowing uneventful pregnancies in the future.
 - Incompetent os, in which the cervix (mouth of the womb) is weakened. When the growing fetus presses on it, the weakened cervix opens, leading to expulsion of the growing foetus. This condition may be congenital; or because of a cervical tear or injury during previous pregnancy or miscarriage; or could be a result of over enthusiastic surgical dilatation of the cervix during previous surgery. The insertion of a cervical stitch, called the Shirodkar stitch after the Indian doctor who discovered this condition and invented the surgical operation to correct it, can be very effective. The cervical stitch is a simple surgical operation, usually done after 12 weeks of pregnancy after an ultrasound shows that the baby is healthy; and it helps by strengthening the weakened cervix. The stitch is removed two weeks before the baby is due, or when labor starts, whichever is first.

Diagnosis of these anatomic defects can be made by hysteroscopy or hysterosalpingography. An ultrasound examination can suggest a problem exists, but usually cannot provide a definitive diagnosis. Newer imaging techniques such as 3-D ultrasound or MRI scanning can also provide useful diagnostic information.

Can lifestyle factors cause repeated abortions ?

Lifestyle

If patients are regularly exposed to toxic fumes and chemicals (example, workers in chemical factories; or nurses and anesthetists in operating rooms) these could damage the developing fetus (which is very sensitive to poisons) and cause a miscarriage. Recent studies show that even men exposed to environmental toxins can cause their partner to miscarry a fetus (presumably because their sperms are damaged by the toxins). Smokers, alcoholics and drug abusers also have an increased incidence of miscarriages.

What about the emotional aspects of dealing with repeated abortions ?

The emotional aspects

Human society still tends to dismiss miscarriage complacently; it is a subject which is rarely discussed. A foetus for most people is a non-person and a miscarriage is a non-event. But, to the would be parents, the developing fetus is a baby with an identity, especially if you have seen it on the ultrasound screen and heard its heart throbbing with

a Doppler. When the child is lost, it is a bereavement and your sense of loss, tinged with pain, anger, isolation and depression, can be profound - especially when it follows a long period of infertility.

After a miscarriage, it is normal to experience a period of grief. Find support from each other; and from others who have had a similar experience. Healing does happen in time. Focus on getting through the grieving rather than on the suffering.

What should you know about planning your next pregnancy after you have had an abortion ?

Your next pregnancy

After a miscarriage, making the decision to go in for another pregnancy is difficult.

Collect as much information as possible to try to find out the possible causes of the loss and whether they might influence a future pregnancy.

If you have had 2 or more miscarriages, then tests are usually done to try to find a cause.

These include the following:

- Hysterosalpingogram or hysteroscopy to make sure there are no defects in your uterus (womb)
- Blood tests, such as serum progesterone, to rule out a luteal phase defect
- Blood tests for antiphospholipid antibodies (lupus anticoagulant)
- The VDRL (Venereal Diseases Research Laboratory) blood test, for sexually transmitted diseases
- Karyotype, for you and your husband, to rule out chromosomal abnormalities.

The doctor may also want to send the aborted tissue for chromosomal study, to find out if the fetus was chromosomally normal or not.

Often many doctors will do what is called a "TORCH" test - but this is a waste of money for most patients, since it provides little useful information.

When to start the testing depends upon you. While few doctors would do anything after one miscarriage (since your chance of having a healthy pregnancy even without tests and treatment is better than 85%), most would start a workup after two miscarriages. Often, nothing is found, and this can be very frustrating to the doctor and patient. But do remember that medical technology has its limitations, and we still do not know a lot about the early embryo and its development.

What are the treatment options for women who have had repeated abortions ?

What about treatment? Sometimes it is possible to treat the underlying problem - for example, by taking a cervical stitch to treat an incompetent os; or removing a uterine septum by hysteroscopic surgery.

In our experience, we have found that many women with recurrent pregnancy loss have occult PCOD (polycystic ovarian disease) , which is usually not diagnosed correctly. We have found that the following empiric treatment, based on experience, helps treat many women who have experienced recurrent early pregnancy losses: Metformin, 1500 mg

daily; folic acid, 5 mg daily; and low dose aspirin, 50 mg daily. When they conceive, we continue all the above; and also add 600 mg vaginal progesterone suppositories daily till 20 weeks.

Often the only option for many women is to try again. Remember, even if you have had 3 or more miscarriages, your chance of carrying the next baby to term is still more than 50 % - even with no specific treatment, and just tender loving care!

Deciding when to start the next pregnancy is a decision only you can make. It takes a lot of courage and both of you need to be ready.

Your next pregnancy probably won't be as joyful as you would like. Insist that your pregnancy be monitored carefully. Whenever the slightest problem occurs, you'll feel vulnerable and terrified - but don't panic.

Everyone will make suggestions about what you should do to make your pregnancy successful. This can be annoying - but remember they are doing it because they care! The easiest way to handle this is to listen, and then do what you and your doctor feel is best for you.

Your child birth experience can be bittersweet - memories surface about your loss, especially if you are at the same hospital. You probably will need to do some grieving in addition to celebrating the new life.

The experience of miscarriage will also affect your parenting. Bonding with your child may also be delayed because you feel the need to protect yourself from more sorrow - so you wait till you are certain that all is safe and sure with your baby. Moments of panic will occur when the baby is ill or too quiet or with someone else. You are also likely to treat your children as "extra special" - and be less objective than other parents.

What are the chances of having a healthy baby after repeated abortions ?

If you've experienced recurrent miscarriage, you may feel hopeless and confused regarding a positive pregnancy outcome. Remember that miscarriage is not an uncommon event. Your testing will focus on trying to find out the known causes of recurrent miscarriage. But knowledge of this problem is still limited, and no obvious cause is detected in upto 50% of couples with repeated pregnancy loss. This can be very frustrating - both to the patient and the doctor. The encouraging news is that the spontaneous cure rate is very high; and successful treatment is available for treating certain uterine and endocrine causes. So even if your evaluation does not reveal a treatable cause and you do not undergo treatment, your chance of achieving a healthy pregnancy despite having had several miscarriages in the past is still better than 50% - and the only "treatment " you need is tender loving care !

CHAPTER XXIII

Understanding Your Medicines

What medicines are used for treating infertility ?

You must be aware of what medicines you are taking and why. It's easy for doctors to prescribe medicines - but it's your responsibility to be well-informed about your medicines, so you know what to expect.

Medicines used in infertility treatments include:

1. Bromocriptine (Proctinal, B-crip, Parlodel)
2. Clomiphene (Clomid, Fertyl, Ovofar, Serophene)
3. Danazol (Ladogal, Danazol)
4. H.M.G. (Menogon, , Repronex, Menopur, Nugon,)
5. F.S.H. (Gonal-F, Recagon, Follistim)
6. H.C.G. (Pregnyl, Profasi, Ovidrel)
7. GnRH analogues (Buserelin, Synarel, Lupron, Lucrin)
8. GnRH antagonists (Cetrorelix, Antagon)
9. Metformin (Glyciphage, Glucophage)

How is bromocriptine used for treating infertility ?

Bromocriptine

This is a drug which is used specifically to treat women with hyperprolactinemia - a condition in women fail to ovulate because the pituitary is producing too much of the hormone called prolactin. Hyperprolactinemia is the cause of menstrual disturbance in about 10% of anovulatory women. Bromocriptine lowers prolactin levels to normal (the normal range in most laboratories being less than 20 ng/ml) and allows the ovary to get back to normal.

Side effects: The drug often causes nausea and dizziness during the first few days of treatment but the chances of these symptoms occurring can be reduced by starting the drug at a very low dose and gradually building up to a maintenance dose of 2 or 3 tablets daily.

Dose: A 2.5 mg tablet is available ; and the starting dose is usually 2.5 mg to 5 mg daily - taken at bedtime. After starting bromocriptine, prolactin levels can be tested (after at least one week of medication) to confirm that they have been brought down to normal. If the levels are still elevated, the dose will need to be increased. Once normal prolactin levels have been achieved (and some women need as much as 4 to 6 tablets a day to achieve this) this is then the maintenance dose. Once your prolactin blood level is within the normal range, your periods should become more regular and you should start ovulating

normally again. Remember that bromocriptine only suppresses an elevated prolactin level while you are taking it – it does not "cure" the problem. This is why the tablets must be taken daily until a pregnancy occurs, after which they should be stopped. This is expensive medication - and some pharmaceutical companies may provide it at reduced rates if your doctor requests them to do so on your behalf.

Some women cannot tolerate bromocriptine. For these women, an alternative option is cabergoline, which is as effective in reducing high prolactin levels, and has fewer side effects.

How is danazol used for treating infertility ?

Danazol

This is a synthetic hormone, prescribed as one type of treatment for endometriosis. It acts by suppressing the brain's production of follicle stimulating hormones and hence suppresses ovarian function. This is similar to an artificial menopause and results in the shrinking of not only the endometrium in the uterus (and hence no periods); but also hopefully the misplaced patches of endometrium outside the uterus found in patients with endometriosis, causing them to disappear.

Side Effects: Hot flushes, weight gain, acne, hirsutism (hairiness). These side effects are quite troublesome, and some women have to discontinue the drug because of these. Usually, while taking the danazol, your periods will stop completely - pseudomenopause.

Dose: The standard dose used to be 800 mg daily (4 tablets of 200 mg each). However, the side-effects at this dose are considerable, and many doctors have reported good results with doses as low as 200 mg daily. The usual course of treatment is 6-9 months and the extent of the improvement in endometriosis is then reviewed. While danazol is useful for suppressing the lesions of endometriosis, it is not useful for treating endometriosis in infertile women. While taking the danazol, ovulation is suppressed, and because all it achieves is temporary suppression of the lesions, once you stop the danazol, the endometriosis recurs. This is why it is usually not advised for treating infertile women with endometriosis anymore, because it has not been shown to be helpful in improving pregnancy rates.

How are steroids used for treating infertility ?

Steroids - Dexamethasone, is often used as an adjunct to ovulation induction treatment, especially in patients with hirsutism who have high levels of androgens. It helps by suppressing the production of androgens by the adrenal glands. The dose is usually a 0.5 mg tablet, taken daily at bedtime. Side-effects at such a low dose are unusual. Some IVF clinics also use steroids after embryo transfer, because they believe this helps to improve pregnancy rates by inducing immune suppression and enhancing embryo implantation rates.

How is clomiphene (clomid) used for treating infertility ?

Clomiphene

Clomiphene is the drug of first choice for inducing ovulation - growing eggs. It is cheap, effective, easily available and well tolerated. It is also used for superovulating normal women to help them grow more eggs. Clomiphene is an antiestrogen and it acts by "fooling " the pituitary into believing that estrogen levels in the body are low as a result of which the pituitary starts producing more FSH and LH - the gonadotropin hormones which in turn leads to stimulation of the ovaries. Only women who produce estrogen will respond to clomiphene; and some doctors will test for this by seeing if they bleed in response to progestins - a progestin challenge test.

The starting dose is one tablet (50 mg.) a day for five consecutive days. The first tablet can be taken on day 2, 3, 4 or 5 of the cycle - this is usually decided by your doctor and depends on the length of your menstrual cycle. It is not enough to just take clomiphene - it is equally important to monitor the response as well. This is best done by serial daily vaginal ultrasound scans. The ovulation induced by clomiphene occurs about 5 to 7 days after the course of tablets is completed - that is, day 12-16 of your cycle. If ovulation fails to occur, the dose can be increased for subsequent cycles, till upto 200 mg per day. Often human chorionic gonadotrophin (HCG) is given to trigger ovulation to mimic the woman's natural LH surge. Ultrasound and blood oestrogen levels may be used to determine the best day to administer HCG. If ovulation does not occur - the patient becomes a candidate for HMG or FSH (see below). Usually blood testing of progesterone levels (done 7 days after ovulation) accompanies clomiphene treatment to help identify the correct dosage needed. Clomiphene induces ovulation in approximately 70% of appropriately selected patients and has a 30-40% pregnancy rate.

Clomiphene increases a woman's risk of twin pregnancy by approximately 10%. However, the risk of having more than two babies is 1 %. Occasionally ovarian cysts occur following clomiphene administration. These usually disappear when the drug is stopped.

Side effects can include hot flushes and mood swings early in the cycle,; and depression, nausea and breast tenderness later in the cycle. Severe headaches or visual problems, though rare, are indications to stop the medication.

As clomiphene works as an "antioestrogen" it can have an adverse effect on : 1. the cervical mucus making it thicker than usual; and 2. the endometrium (uterine lining), causing it to become thin. It is therefore important to check on sperm/mucus survival with a post coital or post insemination test; as well as check the endometrial thickness on ultrasound scans. If the cervical mucus is poor or the endometrial lining is thin, a change of medication may be advised. Alternatively, low-dose estrogens may be added to your treatment.

An alternative option for clomiphene is the newer anti-estrogen, letrozole. This drug is also used for treating women with breast cancer, and is as effective as clomiphene in

inducing ovulation, with the advantage that it does not cause the endometrial lining to become thin.

Long term effects: As the drug is only given for 5 days early in the cycle it does not have any long term effect on future ovulations or on hormone levels; or on pregnancy. Some doctors were worried that the prolonged use of clomiphene would increase the risk of the patient developing ovarian cancer. However, extensive research has shown that this worry is unfounded.

Misuse of clomiphene: Clomiphene is an easy drug to misuse because it is cheap and easy to prescribe. It is common to find patients who have been taking clomiphene for months on end, with no result. Clomiphene should not be taken, unless adequate monitoring is also performed simultaneously. It should also not be prescribed for more than 4 months. If it hasn't worked by then, you should move on to the next stage of treatment. Clomiphene is also commonly misused as "empiric " treatment - as a treatment to "enhance fertility" when the doctor cannot offer anything else.

How are gonadotropin injections used for treating infertility ?

Gonadotropins

Gonadotropin treatment is "big-gun " therapy, and is usually reserved for difficult anovulatory problems. The two gonadotropin hormones, Follicle Stimulating Hormone (FSH) and Luteinizing Hormone (LH) are produced in the pituitary and their secretion is controlled by a third hormone, Gonadotropin Releasing Hormone (GnRH), released by the hypothalamus. At the start of a new cycle, the hypothalamus begins to release GnRH. GnRH then acts on the pituitary gland to release FSH and LH. These two hormones stimulate the ovary, causing follicles to develop (as the name suggests, this is the primary action of the FSH - to stimulate follicular growth). When it is time for ovulation, a sudden burst of LH is released from the pituitary (the LH surge) which causes the egg to be released from the mature follicle in the ovary.

This is a very finely tuned system, designed by Nature to ensure the release of a single mature egg every month. This involves orchestrating a symphony of messages from the ovary, the pituitary and hypothalamus. The messages are transmitted by hormones - which are chemical messengers in the blood stream. When the egg is ripe, the mature follicle releases an ever increasing amount of estrogen, which is produced by the granulosa cells which line the follicle. This estrogen produced by the dominant follicle progressively increases in quantity as the egg matures, until a surge of estrogen is released into the blood (the estrogen surge). This high level of estrogen stimulates the pituitary to release a large amount of LH hormone - the LH surge. This LH in turn acts on the mature follicle, causing it to rupture to release the mature egg. Thus it is the mature egg which signals the brain that it is ready for release, and triggers off its own ovulation!

How does Nature ensure that only one egg is released every cycle? About 30-40 follicles will start growing in response to the FSH produced by the pituitary. However, of these follicles, only one is destined to grow (become dominant) and rupture to release its

mature egg. The others will die - a process called atresia. The dominant follicle releases increasing amounts of estrogen as it grows bigger. This estrogen in turn decreases the production of FSH by the pituitary (in a negative feedback control loop), so that without high levels of FSH, the smaller follicles no longer have a stimulus to grow; and they gradually die. The dominant follicle by now has become so big, that it can grow by itself, and doesn't need the additional FSH stimulation.

What are HMG injections and how are they used in infertility treatment ?

HMG (Human Menopausal Gonadotropins, Menotropins)

When the pituitary doesn't release FSH and LH or releases them in an improper balance, HMG (Human Menopausal Gonadotropin) substitutes for them and acts directly on the ovaries to stimulate the development of the follicle. HMG is a natural product containing both human FSH and LH, 75 or 150 international units of each per ampule. Brand names include Menogon, Repronex and Menopur. This material is extracted from the urine of post menopausal women, carefully purified and then freeze dried in sterile glass ampules where it is sealed until use.

Recently, biotechnology (using recombinant DNA) has been used to produce synthetic FSH. Chinese Hamster ovary cells have been genetically engineered , so that they are capable of quickly producing, or "expressing", commercial quantities of FSH in bioreactors . Brand names include: Follistim and Gonal-F. This is an exciting advance, and means that companies can now manufacture large quantities of pure hormone, without risk of contamination. However, these products have been priced exorbitantly, which makes them unaffordable for many patients. While they are as good as the conventional urinary gonadotropins, they are no better – and may actually be less cost-effective, because they are so expensive. Hopefully, increasing competition may mean that these hormones will be inexpensively available in the future. However, this is likely to take a few years more.

Dose: Most women need to take daily injections of HMG over a period of several days each month. The exact number of days will be determined by your physician through monitoring your response to the injections. HMG therapy usually begins on day 3 to day 5 of the menstrual cycle. If you are not menstruating, the injections may be started at any time. Every patient is different in her response to HMG and even the same patient may not respond in the same way from cycle to cycle. Therefore, the dosage of HMG required to produce maturation of the follicle must be individualized for each patient. This is the key to success with these injections. It is recommended that the lowest possible dose consistent with good results be used. HMG cannot be taken orally because it is a protein and would be digested in the stomach. It is given by intramuscular injections into the buttocks, or the thighs.

Side effects: Many women worry that if they take HMG, this will cause them to "run out of eggs" because the HMG stimulates the maturation of a large number of eggs. However, remember that every month, 30-40 eggs start to mature. In the natural cycle,

only one matures, while the rest die. HMG helps to rescue the eggs which would otherwise have died, so it does not cause you to lose or waste your precious eggs !

Along with its intended benefits, HMG is a potent drug with the potential to cause side effects. The most common side effect with HMG relate to overstimulation of the ovary and every effort is made to avoid this by monitoring the response to HMG carefully. Mild to moderate uncomplicated ovarian enlargement, sometimes accompanied by abdominal distension and/or abdominal pain occurs in about 20% of those treated with HMG and HCG. This generally is reversed without treatment within 2 to 3 weeks.

A potentially serious side-effect of HMG is the ovarian hyperstimulation syndrome (OHSS) which is characterized by enlargement of the ovary and an accumulation of fluid in the abdomen. This fluid can also accumulate around the lungs and may cause breathing difficulties. If the ovary ruptures, blood can accumulate in the abdominal cavity, as well. The fluid imbalance can also affect blood clotting and, in rare cases could be life threatening. Fortunately, the hyperstimulation syndrome is not common, occurring in about 1 - 3% of patients. Treatment consists of bed rest and careful monitoring of fluid levels.

Another risk with HMG therapy is when it is too successful at producing eggs - thus resulting in mutiple pregnancies, with the risks associated with these. Of the pregnancies following therapy with HMG most (80%) will be single births. The multiple gestation rate is approximately 20%, the majority of which have been twins. About 5% of the total pregnancies result in three or more conceptuses. Despite careful monitoring, multiple gestations can not be altogether avoided.

Other adverse reactions that have been reported with HMG therapy are mild and include allergic sensitivity, pain, rash, swelling at the injection site. Many women are worried that the HMG will cause them to put on weight. However, remember that the HMG is a "natural" hormone. It does not affect your caloric balance, and does not cause you to become fat ! However, many women do restrict their physical activity when taking infertility treatment. This restriction causes them to burn fewer calories, and this may lead to weight gain which they then attribute mistakenly to the HMG injections. HMG may cause fluid retention, but this is temporary, and HMG injections have no long-term side-effects.

How is HMG therapy monitored ?

Monitoring HMG therapy

Monitoring of patients receiving HMG therapy is essential for dosage adjustment and prevention of side effects. Each woman's response is different and the dose given needs to be adjusted carefully. The two most commonly used techniques are serum estrogen levels and ultrasound. Estrogen levels in the blood help the doctor to determine how well the ovaries there is a greater chance of multiple births and the decision may be made to avoid the ovulatory injection of HCG.

Studies show that about 75% of women taking HMG will ovulate. It is estimated that 20% to 42% of patients receiving HMG will become pregnant, as long as the fallopian tubes are open and the sperm count is adequate.

Intercourse is advised daily or every other day beginning on the day prior to the administration of HCG. Your doctor may want to advise you further on this point. Some doctors will perform an intrauterine insemination on the day of ovulation to increase the chances of a pregnancy.

HMG has to be imported into India, and is very expensive. It is therefore best used by infertility specialists only. The commonest use of HMG today is in IVF treatment where it is used to stimulate several eggs to grow (superovulation).

How are FSH injections used for treating infertility ?

FSH (Follicle Stimulating Hormone)

This represents a more recent purified form of HMG which contains mostly FSH and negligible amounts of LH. The indications for use, administration and ovarian response are almost identical to HMG. However, as FSH contains almost no LH, it has a theoretical advantage for women with PCO (polycystic ovarian syndrome) who characteristically have an elevated LH level. However, it is also more expensive than HMG.

How are HCG injections used for treating infertility ?

HCG (Human Chorionic Gonadotropin)

HCG is produced by the placenta during pregnancy. Because it is very similar biologically to LH it is used to trigger ovulation by mimicking the natural LH surge at mid cycle. It can be used in combination with Clomid and also HMG/FSH to induce ovulation. It is isolated and purified from the urine of pregnant women. It is available in ampoules as a sterile white powder containing 5000 IU or 10000 IU. This powder is dissolved in a diluent and administered by IM injection. Ovulation occurs 36 hours after the HCG trigger shot. Recently, HCG has also been manufactured using recombinant DNA technology, and this is available under the brand name, Ovidrel.

How is GnRH used for treating infertility ?

Synthetic GnRH

Synthetic GnRH stimulates the pituitary gland to secrete LH and FSH. It is used to induce ovulation in selected women with hypothalamic dysfunction. The hormone has to be given in a manner which mimics the natural secretion of LHRH, i.e. in "pulses" approximately 90 minutes apart. This is given by means of a small pump placed under the skin of the arm or abdomen. This treatment is now given instead of HMG at certain specialist centres. It has the advantage over HMG that it produces an ovulation cycle which is similar to the natural cycle and multiple ovulation is very unusual.

How are GnRH analogs used for treating infertility ?

GnRH Analogues

These drugs may be used for the treatment of endometriosis and fibroids. They work by initially stimulating, then switching off (down-regulating) the pituitary gland, and are administered intranasally or by injection. They thus induce a "menopausal" state, allowing the endometriosis and fibroids to shrink, since there is no further production of estrogens. Brand names include Buserelin, Lupron and Lucrin.

GnRH analogs are most commonly used today as adjunctive therapy in order to enhance induction of ovulation with HMG, especially for IVF (in vitro fertilisation) treatment. Your own gonadotropins (FSH and LH) produced by your pituitary are turned off by the GnRH analogues (this is called pituitary downregulation) , so that your physician has a clean slate to work with when administering exogenous gonadotropins to induce superovulation.

How are GnRH antagonists used for treating infertility ?

GnRH antagonists

Currently, most in-vitro fertilization (IVF) centres use pituitary down-regulation with gonadotrophin-releasing hormone (GnRH) agonists to prevent premature luteinization. However, this requires at least 7–14 days of GnRH agonist pretreatment. A more rational approach would be to use the newer GnRH antagonists, which cause an immediate blockage of the GnRH receptors on the pituitary gland. Brand names include Anatgon and Cetroride. Thus , treatment with the antagonist can be limited to only those 2-3 days when high oestradiol levels may induce an LH surge. However, clinical experience with GnRH antagonists in IVF treatment thus far has shown mixed results, with no evidence that they are any better than the traditional GnRH analogues.

Growth Hormone

Some women will respond very poorly to HMG injections. They grow few or no follicles, inspite of being given large doses. In some of these "poor responders" synthetic growth hormone (HGH, human growth hormone) has been used to try to enhance the response of the ovary to the HMG. However, the response to this very expensive drug has been quite disappointing, and it is no longer used.

How is metformin used for treating infertility ?

Metformin

The drug of first choice for women with PCOD today is metformin (this medicine is also used for treating patients with diabetes.) Doctors have now learned that many patients with PCOD also have insulin resistance – a condition similar to that found in diabetics, in that they have raised levels of insulin in their blood (hyperinsulinemia) , and their response to insulin is blunted. This is why some patients with PCOD who do not respond

to clomiphene are treated with antidiabetic drugs, such as metformin and troglitazone. Studies have shown that these drugs improve their fertility by reversing their endocrine abnormality and improving their ovulatory response.

What medicines are useful for treating male infertility ?

Medicines Used In Male Infertility Treatments

HMG and HCG

These are useful in stimulating sperm production in men with hypogonadotropic hypogonadism (men with low FSH and LH levels, because of hypothalamic or pituitary malfunction), but this is a rare condition.

Treatment often takes many months to restore the sperm quality to fertile levels. Combination treatment is required, with HCG stimulating testosterone production; and FSH stimulating sperm production. Initially, the man takes HCG injections thrice a week for about 6 months. This normally causes the size of the testes to increase and the testosterone to reach normal levels. HMG injections are then added. These can be mixed with the HCG and are also given thrice a week. Once sperm production has been achieved, the HMG can be stopped; and HCG treatment continued alone. While sperm counts achieved are usually low (less than 10 million per ml), a successful pregnancy can be achieved in 50 % of correctly diagnosed patients.

Unfortunately, these expensive injections are often misused as "empiric" therapy in men with low sperm counts - with expectedly disappointing results.

Bromocryptine

As in the female, this is used to lower unusually elevated levels of prolactin.

Testosterone

This is given to suppress sperm production in the hope that when medication is stopped (usually after 5-6 months), then the sperm production will "rebound " to higher levels than originally (testosterone rebound). This form of treatment is now seldom used as it may further impair fertility and is hazardous. Testosterone is also be used for the treatment of impotence or diminished libido when blood testosterone levels are low. Testosterone is available as an oily injection and is given intramuscularly, usually once a week. Oral preparations are also available now, but these are more expensive and may not be as effective.

Clomiphene

This is the most commonly prescribed medicine for infertile men. Its use is largely empirical and very controversial as the results are not predictable. This is usually prescribed as a 25 mg tablet, to be taken once a day, for 25 days per month, for a course of 3 to 6 months. It acts by increasing the levels of FSH and LH, which stimulate the

testes to produce testosterone and sperm. The group of men who seem to benefit the most from clomiphene have low sperm counts, with low or low-normal gonadotropin levels. However, while clomiphene may increase sperm counts in selected men, it hasn't been proven effective in increasing pregnancy rates.

Antibiotics

Just as in the female, antibiotics can resolve a chronic infection in the reproductive tract in the male. Often no specific organism is isolated but improvement in the numbers of normal sperm as well as the reduction in white cells in semen can be seen in some men following several weeks of antibiotics.

Vitamins

No supportive evidence that they work but sometimes they are worth a try.

Ayurvedic treatment and other magic potions

Everyone seems to have a "magic potion" to cure low sperm counts - the trouble is that no one has ever proven that anything works! Take all claims with a liberal pinch of salt.

Why is medical treatment of low sperm counts ineffective ?

The problem with the medical treatment of a low sperm count is that for most people it simply doesn't work. After all, if the reason for a low sperm count is a microdeletion on the Y-chromosome, then how can medication help ? The very fact that there are so many ways of "treating" a low sperm count itself suggests that there is no effective method available. This is the sad state of affairs today and much needs to be learnt about the causes of poor production of sperm before we can find effective methods of treating it.

However, patients want treatment, so there is pressure on the doctor to prescribe, even if he knows the therapy may not be helpful . When most patients go to a doctor, they expect that the doctor will prescribe a medicine and treat their problem. Since most people still believe there is a "pill for every ill", they expect that the doctor will give them a medicine (or an injection) which will increase their sperm count. No patient ever wants to hear the truth that there is really no effective treatment available today for increasing the sperm count.

Since most doctors know this, they are pressurised into prescribing medicines for these patients, because they do not want the patient to be unhappy with them. They are worried that if they do not fulfill the patient's expectation of a prescription, the patient will desert them, and go elsewhere, which is why they often do not tell the patient the complete truth. The doctor also remembers the occasional anecdotal successes (who come back for followup , while the others desert the doctor and are lost to followup) is why patients with low sperm counts are put on every treatment imaginable - with little rational basis - Vitamin E, Vitamin C, high-protein diets, Proxeed, hoemeopathic pills and ayurvedic churans. However, the very fact that there are hundreds of medicines itself proves that there is no medicine which works !

Many doctors justify their prescriptions by saying - " Anyway it can't hurt - and in any case, what else can we do? " However, this attitude can be positively harmful. It wastes time, during which the wife gets older, and her fertility potential decreases. Patients are unhappy when there is no improvement in the sperm count and lose confidence in doctors. It also stops the patient from exploring effective modes of alternative therapy - such as IVF and ICSI . Today empiric therapy should be criticised unless it is used as a short term therapeutic trial with a defined end-point.

A word of warning. Medical treatment for male infertility does not have a high success rate and has unpleasant side effects, so don't take it unless your doctor explains his rationale. The treatment is best considered "experimental" and can be tried as a therapeutic trial. Make sure, however, that semen is examined for improvement after three months and then decide whether you want to press on regardless.

It is worth emphasising how small the list for male infertility treatment is - especially as compared to female treatment. This simply reflects our ignorance about male infertility - we know very little about what causes it, and our knowledge about how to treat it is even more pitiable!

CHAPTER XXIV

Intrauterine Insemination (IUI)

What is intrauterine insemination (IUI) ?

Sometimes nature needs help to start a pregnancy - and the doctor can do this by giving the sperm a piggy back ride through a fine tube into the body. This procedure is called intrauterine insemination (IUI) or artificial insemination with husband's sperm (AIH) - and effectively, the doctor is giving nature a helping hand by increasing the chances of the egg and sperm meeting.

When is IUI used for treating infertility ?

IUI is useful when:

1. The woman has a cervical mucus problem - for example, it maybe scanty or maybe hostile to the sperm. With an intrauterine insemination (IUI) the sperm bypass her cervix and enter the uterine cavity directly.
2. The man has antibodies to his own sperm. The " good" sperm which have not been affected by the antibodies are separated in the laboratory and used for IUI.
3. If the man cannot ejaculate into his partner's vagina. This is usually because of psychologic problems such as impotence (inability to get and maintain an erection) and vaginismus (an involuntary spasm of the vaginal muscles so that vaginal penetration is not possible); or anatomic problems of the penis, such as uncorrected hypospadias; or if he is paraplegic.
4. The man suffers from retrograde ejaculation in which the semen goes backward into the bladder instead of coming out of the penis.
5. For unexplained infertility, since the technique of IUI increases the chances of the eggs and sperm meeting.
6. If the husband is away from the wife for long stretches of time (for example, husbands who work on ships or work abroad), his sperm can be frozen and stored in a sperm bank and used to inseminate his wife even in his absence.

How is artificial insemination performed ?

Methods for performing AIH

There are various methods of doing AIH (artificial insemination by husband). The crudest and simplest technique involves simply injecting the entire semen sample into the vagina by a syringe. You can also perform artificial insemination in your own bedroom. This is called self-insemination. However, this is a waste of time if used for treating an infertility problem - after all, why go to a doctor to do something which you can do for yourself at home? Remember, a syringe is no better than a penis ! It is only useful if the

reason for doing AIH is the inability of the husband to ejaculate in the vagina. However, a number of doctors still use it as they do not offer anything better.

A refinement of this technique is that of using a spilt ejaculate. The first squirt of semen which gushes forth during ejaculation is richest in sperm. This is because the sperm "surf" on the wave of the seminal fluid which carries them forward to the outside world. The man masturbates into a 2-part container, so that this first part goes into one container, while the rest goes into another. This is not as difficult as it sounds, and gets easier with practice! The first bottle is saved and the contents used for artificial insemination. This method is suitable for a small proportion of cases (for example, for the uncommon problem of a large volume of semen, which "dilutes " the sperm; or where laboratory facilities for sperm processing are not available).

How is IUI performed ?

Intrauterine insemination (IUI)

In this method, the sperms are removed from the seminal fluid by processing the semen in the laboratory and they are then injected directly into the uterine cavity. It is not advisable to inject the semen direct into the uterus, as the semen contains chemicals (prostaglandins) and pus cells which can cause severe cramping; and even tubal infection.

How is the IUI timed ?

Timing

Timing the IUI is very important - it must be done during the "fertile period" when the egg is in the fallopian tube. Pinpointing the time of ovulation accurately using either vaginal ultrasound or ovulation test kits is crucial. A good clinic should provide this as a 7-day week service, since there is a 1 in 7 chance that ovulation will occur on a Sunday - eggs don't take a holiday! It is important to superovulate the wife at the same time (with clomid or HMG injections) , so that she produces more than one egg. Superovulation increases her fertility potential as well, thus increasing the chances of conception by improving the chances of the eggs and sperm meeting.

The IUI is done either when ovulation is imminent or just after. The husband masturbates into a clean jar - preferably in the laboratory or clinic itself, and after at least three days of sexual abstinence to get optimal sperm counts. Some men may have considerable difficulty producing a semen sample at the appropriate time, because of the tremendous stress they are under, and the " pressure to perform". For these men, using a previously stored frozen sample can be helpful. Viagra (sildenafil citrate) can also be used to help them to get an erection, as can using a vibrator.

The best sperm are separated from the rest of the seminal fluid, by special laboratory processing techniques. This separation takes about 1 to 2 hours. The actual insemination procedure is simple and takes only a few minutes to perform. It is not painful, though it can be uncomfortable. The wife lies on an examining table, and a speculum is placed in the vagina. The doctor puts the sperm through a thin plastic tube (catheter) through the cervix into the uterus. There may be a bit of uterine cramping at this time; and some

discomfort for about 12 to 24 hours. Some patients may experience a little vaginal discharge after the procedure, and they are worried that all the sperm are leaking out of the uterus. However, this discharge is just the cervical mucus - the sperms cannot "fall out" of the uterine cavity.

No special bed rest is required after the IUI. Some doctors may repeat the insemination after 24 hours. We usually encourage our patients to have intercourse on the night of the IUI, and for 2-3 days after this as well, to maximize the chances of the sperm and egg meeting.

How are the sperm processed in the laboratory for IUI ?

Sperm processing:

Sperm processing allows the doctor to concentrate the actively motile sperms into a small volume of culture fluid. Sperm do not remain alive in the culture medium for very long unless maintained at the right conditions - hence a prompt insemination after sperm processing is important. This is why processing should preferably be done in the clinic itself, so that time is not wasted in transporting the sperm after the wash.

Laboratory Techniques:

There are different methods of processing the sperm, and all of these require special laboratory expertise.

1. The simplest method is that of washing the semen with a culture medium (by centrifuging it and collecting the pellet) but this is a poor technique and is not recommended.
2. The swim-up method uses a layering technique, in which a special culture medium is placed above the semen in a test-tube. The good quality sperm will swim up into the culture medium; and after 45 to 60 minutes, this medium (with the motile sperms) is removed and injected into the uterine cavity.
3. The more sophisticated methods today use a density gradient column. This method allows one to separate the good quality sperm from the immotile sperm, the pus cells and the seminal plasma, because these are lighter than the motile sperms. It provides the best recovery of motile sperms and is the standard technique in use today, especially for poor quality sperm samples.

What recent advances have occurred in IUI treatment ?

Recent advances

Of late, doctors have tried adding various chemicals to the washed sperm to try to improve their motility, so as to increase the chances of their reaching their goal. These chemicals include caffeine and pentoxifylline and they may be helpful in some patients. During IUI, sperms are injected into the uterine cavity in the hope that they will then swim up from here into the fallopian tubes where they can fertilize the egg. But then, why not inject the sperms direct into the fallopian tubes where the eggs is present? This feat was technically difficult to accomplish in the past, because the tubes are so thin. Today, with specially designed catheters (Jansen-Anderson catheter sets), it is possible to do this in the doctor's clinic. Thus, the processed sperm can be injected directly into the tubes

under ultrasound guidance, without anesthesia or surgery! This is an intratubal insemination - also known as a SIFT - (sperm intrafallopian transfer). However, pregnancy rates are no better with this method than with IUI, which is why it is rarely performed today.

Psychological

Issues

Men may feel a loss of self-esteem because they feel that they need a doctor's help to do what a "normal man" should have been able to do by himself. They also feel guilty about having to subject their wife to the pain and intrusion of insemination. Women may feel anger towards their husbands for having the fertility problem. The insemination may also make patients feel that someone has "intruded" into their sex life and this may affect their intimacy.

What is the success rate of IUI treatment?

Success Rates of IUI

The success rate of IUI depends upon several factors. First of all the cause of the infertility problem is important. For example, men with normal sperm counts who are unable to have intercourse have a much higher chance of success than patients who are undergoing IUI for poor sperm counts. In addition, female factors play an important role. If the female is more than 35, the chance of a successful pregnancy is significantly decreased. Generally, the chance of conceiving in one cycle is about 10-15%; and the cumulative conception rate is about 50% over 4 treatment cycles. (Remember, Nature's efficiency for producing a baby in one month is about 15 to 25 %). However, if IUI is going to work for a couple, it usually does so within 4 treatment cycles. If a pregnancy has not resulted by this time, the chances of IUI working for you are very remote. You have reached the point of diminishing returns, and should stop persisting with IUI and explore the option of IVF .

What are the risks of IUI treatment ?

Risks of IUI

The major risk of IUI today is that of multiple pregnancy. Since the patient is being superovulated, more than one egg may get fertilized, resulting in twins or even triplets or quadruplets. Because the doctor cannot precisely control how many follicles will grow or rupture, the risk of a multiple pregnancy is actually even more after IUI rather than IVF . In fact, most of the infamous cases of high-order multiple births (such as sextuplets and octuplets) have occurred after IUI. If you grow too many follicles, you may choose to cancel the cycle. Some clinics can also offer you the option of saving the cycle by converting it to IVF. This can be a cost-effective option, since it allows you to make good use of the eggs you have grown.

In poorly equipped clinics, there is also a risk of developing an infection after the IUI, if appropriate sterile precautions are not taken. This can tragically actually cause infertility ! While many gynecologists today offer IUI treatment, many of them are not specialized enough to provide a comprehensive service. This often means that patients need to run around from the gynecologist to the ultrasound scan center to the lab . Not only is this

very time consuming and frustrating, it often means that the care becomes fragmented because of poor coordination. Try to find a clinic which offers all the services under one roof.

The other major risk of IUI is that many gynecologists repeat it again and again, because they do not have anything better to offer. Rather than referring the patient for IVF, they keep on subjecting the patient to repeated cycles of IUI (sometimes as many as 12 cycles !). Patients ultimately get fed up and frustrated, and lose confidence in doctors and themselves, as a result of which they deprive themselves of IVF technology. Often, patients will change doctors, but the new gynecologist will repeat the same IUI treatment, even though the patient has already done many IUI cycles in another clinic.

The other common problem is that many gynecologists persist in doing IUI when the man has a low sperm count (oligospermia). Their rationale is that we will concentrate the good sperm and inject them in the uterus. This is doomed to fail. Unfortunately, IUI is not a good treatment for oligospermia , because the problem is not just a low sperm count, but functionally incompetent sperm ! ICSI is a much better option for these couples !

How much does IUI treatment cost ?

The Cost Factor

The cost of performing IUI varies from clinic to clinic, but is about Rs 3000 to Rs 8000 for the entire treatment cycle. Of course, if gonadotropin injections are used for superovulation, the treatment then becomes much more expensive - and can be as much as Rs 20000 for one month's treatment.

IUI is a simple, inexpensive, effective form of therapy, and can usually be tried first, before going on to more expensive and invasive options. However, it can be very stressful and close cooperation between the husband and wife (and the doctor) is essential!

CHAPTER XXV A

Test Tube Babies - IVF & GIFT

The birth of Louise Brown through in vitro fertilization (IVF) in 1978 was a major milestone in infertility treatment. It dramatically changed the treatment options for infertile couples, and techniques for assisted reproduction have evolved rapidly since then. In a short span of 20 years, IVF has become the cornerstone of reproductive medicine, and IVF clinics today routinely perform techniques which were thought to belong to the realm of science fiction a generation ago !

What are the assisted reproductive technologies (ARTs) ?

This chapter will help you understand assisted reproductive technologies (ART) such as IVF and Gamete Intra-fallopian Transfer (GIFT) that are now standard medical treatments for infertility. A few years ago, these techniques were used as methods of last resort, when everything else which had been tried had failed. Today, specialists will often resort to these techniques first, since they offer such excellent results, rather than waste the patient's time and money with the traditional ineffective options. Today, thanks to IVF technology, there is practically no infertile couple who cannot be offered treatment. However, as with all technology, you need to understand exactly how it works, and when it should be used.

IVF

IVF is the basic assisted reproduction technique , in which fertilization (Fertilisation Video) occurs in vitro (literally, in glass) . The man's sperm and the woman's egg are combined in a laboratory dish, and after fertilization, the resulting embryo is then transferred to the woman's uterus. The five basic steps in an IVF treatment cycle are superovulation (stimulating the development of more than one egg in a cycle), egg retrieval, fertilization (Fertilisation Video) , embryo culture, and embryo transfer. IVF is a treatment option for couples with various types of infertility, since it allows the doctor to perform in the laboratory what is not happening in the bedroom - we no longer have to leave everything up to chance! Initially, IVF was only used when the woman had blocked, damaged, or absent fallopian tubes (tubal factor infertility). Today, IVF is used to circumvent infertility caused by practically any problem, including endometriosis; immunological problems; unexplained infertility; and male factor infertility. It is a final common pathway, since it allows the doctor to bypass nature's hurdles, and overcome its inefficiency, so that we can give Nature a helping hand !

What tests need to be done prior to doing IVF treatment ?

Tests prior to IVF

In order to perform IVF, only 3 things are required - eggs, sperms and a uterus, and before starting the IVF cycle, the doctor will check these.

First, a sperm survival test is carried out . This is a "trial" sperm wash, using exactly the same method as will be actually used in IVF, to assess whether an adequate numbers of

sperms can be recovered in order to do IVF. This test will also help the laboratory to decide which method of sperm processing should be used during IVF.

A blood FSH level will provide an idea of the "ovarian reserve", and provide information on whether or not the woman will produce enough eggs after superovulation . For older women, some clinics do a clomiphene citrate challenge test . If the level is very high, this suggests early ovarian failure , and it may be a better idea to consider donor eggs.

Many clinics may do a hysteroscopy, in order to assess that the uterine cavity is totally normal. They may also do a "dummy" embryo transfer to make sure there are no technical problems with this procedure. Some clinics also do a cervical swab test, to rule out the presence of infection in the cervix.

If a woman has blocked fallopian tubes with large hydrosalpinges, some clinics will remove these prior to the IVF cycle, because they feel that the presence of a hydrosalpinx decreases pregnancy rates after IVF.

For men who have difficulty in producing a semen sample " on demand", the clinic may also freeze and store the sample prior to treatment, as a backup. This can help to prevent the tragedy of having to abort an entire treatment cycle because the man could not produce a semen sample when needed.

Blood tests which may be done include tests for immunity to rubella ; and tests for Hepatitis B, and AIDS. Most doctors will also advise patients to start taking folic acid, as part of prepregnancy care, as this helps to reduce the risk of certain birth defects.

Patients who stand a very poor chance of success with IVF include the following :

- Older women, whose ovaries are failing. However, there is no upper age limit at which IVF should not be done,- and in fact, for older women, it might represent their only chance of success. It's not really the age of the woman which is the limiting factor - it's the quality of her eggs.
- Men whose sperm count is very low. Most clinics will consider doing IVF only for men with at least 3 million motile sperm in the ejaculate. If the sperm counts are lower than this, then ICSI (or microinjection) is a better option.
- Women with a damaged uterus (for example, because of healed tuberculosis) because the chance of successful implantation of the embryo in the uterus becomes very poor.
- It is also not advisable to go in for IVF treatment without trying simpler treatment options first. IVF is a complex procedure involving considerable personal and financial commitment, so other treatments are usually recommended first.

What are the 5 basic steps of an IVF treatment cycle ?

These are:

1. Superovulation
2. Egg retrieval
3. Fertilisation
4. Embryo culture
5. Embryo transfer

The Basic Steps of IVF

How is superovulation performed ?

Superovulation or Ovulation Enhancement

During superovulation , drugs are used to induce the patient's ovaries to grow several mature eggs rather than the single egg that normally develops each month. This is done because the chances for pregnancy are better if more than one egg is fertilized and transferred to the uterus in a treatment cycle. Depending on the program and the patient, drug type and dosage varies. Most often, the drugs are given over a period of nine to twelve days. Drugs currently in use include : Human Menopausal Gonadotropin (HMG) , Follicle Stimulating Hormone (FSH) , Human Chorionic Gonadotropin (HCG) and gonadotropin releasing hormone (GnRH) analog .

Today, most IVF programs use GnRH analogs (such as Lupron or Buserelin) in combination with gonadotropins during ovulation enhancement. Treatment with the analogs prevents the release of FSH and LH from the pituitary gland during treatment ("pituitary downregulation") and thereby prevents premature ovulation. This therefore gives the doctor much more control over the superovulation phase, because we can then grow eggs to suit our convenience, as we have taken over control of the cycle. Patients are often confused as to why we need to suppress the pituitary hormones when we are trying to grow lots of eggs. Remember that the GnRH analogs suppress the pituitary, and have no direct effect on the ovary, so that they do not suppress egg production. GnRH analogs can be used either in the form of a long protocol (when they are started from Day 21 of the previous cycle) ; or as a short protocol (when they are started from Day 1 of the cycle). Another option is to use the newer GnRH antagonists (such as Antagon or Cetroride), which can selectively suppress the LH surge, and it is hoped that these may provide better control. However, the pregnancy rates with these are no better.

How is superovulation monitored ?

An ultrasound scan is done on Day 3, to confirm that there are no cysts in the ovary, and that downregulation has been achieved. A blood test for estradiol can also be done, to ensure that the ovaries are quiescent and downregulated, and the result should be less than 50 pg/ml. The HMG injections for superovulation are then started from Day 3. The dose of HMG used needs to be individualized for each patient., and depends upon the antral follicle count and ovarian morphology. Our standard dose is 225 IU daily for patients less than 35; 300 IU daily for patients more than 35; 450 IU daily for poor responders; and 150 IU daily for patients with PCOD.

Timing is crucial in an IVF treatment cycle, in order that the doctor recover mature eggs. To monitor egg production, the ovaries are scanned frequently with vaginal ultrasound, usually on a daily or alternate day basis from Day 10 onwards. Blood samples are also drawn in some clinics, to measure the serum levels of estrogen , and sometimes luteinizing hormone (LH). While some clinics do this on a daily basis, we feel this is very unkind to the patient, who often ends up feeling like a pincushion ! For most patients, the ultrasound scan provides enough information, and it is very rarely that we need to do

blood tests for our patients - we try to be kind ! The dose of the HMG is adjusted, depending upon the ovarian response.

By interpreting the results of the ultrasound, we can determine the best time to harvest or remove the eggs. Follicles usually grow at a rate of 1-2 mm/day, and a mature follicle has a diameter of about 16-20 mm in size . Thus, if a patient has about 10 follicles on ultrasound, of which the largest is more than 18 mm, we know that the follicles are mature and the eggs are ready for retrieval. The endometrium should also be examined carefully on the vaginal scan, and this should be thick (more than 7 mm, and have a triple texture). Some clinics also measure the blood estradiol level, to provide additional information, and each mature follicle produces about 200-300 pg/ml of estrogen . When the follicles are mature, we prescribe an injection of human chorionic gonadotropin (HCG) to trigger ovulation. The use of HCG allows us to control when ovulation will take place - and this is 36 to 39 hours after the HCG injection. This precise control allows the IVF team to be prepared to harvest eggs just before that time. The HCG simulates the woman's natural LH surge, which normally triggers ovulation.

This is what a typical IVF treatment protocol in our clinic looks like. Treatment starts from Day 1 (the day the bleeding starts) of the cycle. At this time, we downregulate by starting Inj Buserelin

(Suprefact, GnRH analog mfr by Hoechst), 0.5 ml sc daily . On Day 3, we do an ultrasound scan to confirm there is no ovarian cyst, after which we start superovulation with 3 ampoules (225 IU) of HMG (Menogon) daily. The dose of HMG will depend upon the ovarian morphology and the antral follicle count.

We do the next scan on Day 10, after which we do scans every alternate day, to monitor follicular growth.

This is what the daily schedule would look like.

Day 1. Inj Buserelin, 0.5 ml sc. (Downregulation starts)

Day 2. Inj Buserelin, 0.5 ml sc.

Day 3. Inj Buserelin, 0.5 ml sc. Vaginal ultrasound scan to confirm there is no ovarian cyst. If there is no cyst, we can commence superovulation. If there is a cyst larger than 30 mm, we can aspirate it and continue with treatment.

Day 4 Inj Buserelin, 0.5 ml sc. Inj Menogon (75 IU), 3 amp IM. Superovulation starts.

Day 5 Inj Buserelin, 0.5 ml sc. Inj Menogon (75 IU), 3 amp IM

Day 6 Inj Buserelin, 0.5 ml sc. Inj Menogon (75 IU), 3 amp IM

Day 7 Inj Buserelin, 0.5 ml sc. Inj Menogon (75 IU), 3 amp IM

Day 8 Inj Buserelin, 0.5 ml sc. Inj Menogon (75 IU), 3 amp IM

Day 9 Inj Buserelin, 0.5 ml sc. Inj Menogon (75 IU), 3 amp IM

Day 10. Inj Buserelin, 0.5 ml sc. Inj Menogon (75 IU), 3 amp IM.

Vaginal ultrasound scan to monitor follicular growth

The Buserelin and Menogon injections will continue on a daily basis; and scans will be performed every alternate day, until the follicles are mature. This is usually Day 14- Day 16 for most patients. At this time, an HCG injection will be given, and eggs retrieved 36 hours after this.

With older forms of superovulation regimes using clomiphene and HMG, the treatment cycle was cancelled in roughly one quarter of the IVF cycles. One of the reasons for this was that some of these women had a premature , spontaneously occurring LH surge with resulting premature spontaneous ovulation . When this happened, the follicles ruptured prior to egg collection, and the eggs were lost in the pelvic cavity, as a result of which they could not be retrieved. While spontaneous LH surges are very rare with the use of GnRH analogs, we still need to cancel cycles in about 10 % of patients.

When may an IVF cycle be cancelled ?

The commonest reason for canceling a cycle today is a poor ovarian response. If patients grow less than three follicles, and if the estradiol level is low, the chances of a pregnancy are poor, and patients may decide to abandon the cycle. The problem of a poor ovarian response is commoner in older women and in women with elevated FSH levels, and these can be difficult patients to treat ! Patients who have a poor ovarian response during IVF treatment are often very upset, because this is not something they (especially if they are young) are mentally prepared for. Most young women expect to grow a lot of eggs, and are shattered when they don't do so. However, remember that this is not the end of the road - it simply means that the superovulation regime will need to be modified for the next treatment cycle. The doctor may need to increase the dose of HMG in order to grow more follicles, and this is often helpful for young women.

The other reason to cancel a cycle is when patients grow too many follicles ! These are usually patients with PCOD; and if there are more than 25 follicles, or if the level of the estradiol is more than 6000 pg/ml, many clinics will cancel the cycle, because the risk of ovarian hyperstimulation syndrome (OHSS) is very high. An alternative option is to go ahead with egg collection, and freeze all the embryos. This allows the doctor to salvage the cycle; and if the embryos are not transferred, the risk of OHSS is reduced. The frozen embryos can then be transferred later, giving the patient a good chance of achieving a pregnancy.

In our clinic, however, we do not need to cancel these cycles. This is because we use a special technique during egg collection with a double lumen needle, which allows us to remove all the granulosa cells from each follicle at the time of egg retrieval, by flushing each follicle meticulously. Since these cells are the ones responsible for producing the chemicals which cause OHSS, by removing them we reduce the risk of our patients getting OHSS dramatically !

CHAPTER XXV B

Test Tube Babies - IVF & GIFT

How is egg retrieval performed ?

Egg Retrieval

Egg collection is accomplished today by ultrasound-guided aspiration (www.drmalpani.com/videos/ultrasound-guided-egg-retrieval.wmv). This is a minor surgical procedure , that can be done even under intravenous sedation. We prefer doing it under general anesthesia in our clinic , because we feel this is safer, kinder for our patients, and allows us to collect more eggs. The ultrasound probe is inserted through the vagina. The probe emits high-frequency sound waves which are translated into images of the pelvic organs and displayed on a monitor , so that the mature follicles can be seen as black bubbles on the screen. The doctor guides a needle through the vagina into each mature follicle. The follicular fluid containing the egg is then sucked out through the needle into a test tube, and all the follicles are aspirated, one by one. This is a very precise procedure, which requires considerable skill, and takes about 10-40 minutes to perform, depending upon the number of eggs. On an average , we retrieve about 4-16 eggs for each patient. If there are few eggs, we flush each follicle, to ensure that each egg is retrieved.

The older method of performing egg retrieval involved a laparoscopy, and the eggs and follicular fluid were aspirated under direct vision. However, this method is rarely used today, because the vaginal-ultrasound guided method is much quicker, easier and safer.

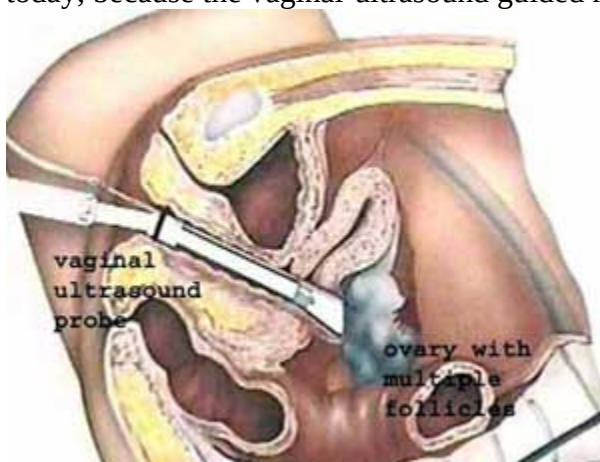


Fig 1. Schematic of egg collection under vaginal ultrasound guidance. If you click on the picture, you can watch a video of an actual egg retrieval procedure done in our clinic

How are the eggs inseminated in the IVF laboratory ?

Insemination and Fertilization

The aspirated follicular fluid is then immediately carried into the laboratory (which is adjoining the operation theater) where it is examined by the embryologist under a stereozoom microscope, in order to identify the egg. Each egg is surrounded by sticky cumulus cells, and is called an oocyte-cumulus complex. These are washed in medium, graded for their maturity and then transferred into the CO2 incubator. The maturity of an egg determines when the sperm will be added to it (insemination). Insemination can be done immediately upon harvest, but is usually done after 2-6 hours.



Fig 1. Checking the eggs under the stereozoom microscope in the IVF lab. If you click on the picture, you can watch a video of an actual egg retrieval procedure done in our IVF laboratory



Fig 2. Mature oocyte cumulus complex, as seen under a stereozoom microscope in the IVF lab, during egg retrieval. The egg is in the center, surrounded by the cumulus cells.

On the day the eggs are harvested (this is called Day 0) , the husband provides a semen sample. The sperm are separated from the seminal plasma in a process known as washing the sperm, and these washed sperm are used to inseminate the eggs. Some men may have considerable difficulty producing a semen sample at the appropriate time, because of the tremendous stress they are under, and the " pressure to perform". For these men, using a previously stored frozen sample can be helpful. Viagra (sildenafil citrate) can also be used to help them to get an erection, as can using a vibrator.

A defined number of sperm (usually 100,000 sperm/ ml) is placed with each egg in a separate dish containing IVF culture medium. The dishes are placed in a CO₂ incubator with a controlled temperature that is the same as the woman's body - 37 C. The conditions in the incubator and the culture medium are designed to mimic the conditions in the fallopian tube, so that the embryos can grow happily in vitro. The culture medium , which has to be very pure, contains various ingredients such as protein, salts, buffer and antibiotics which allow optimal growth of the embryo - think of it as "chicken soup for the embryo " !



Fig 3. A view of the incubator - the heart of an IVF lab.

How is fertilisation checked in the IVF lab ?

About 18 hours after insemination (this is called Day 1) , the embryologist checks to see how many eggs have fertilized. This is called a pronuclear check, and normally fertilized embryos at this time are single cell , with 2 pronuclei. Each pronucleus appears as a clear bubble within the embryo, and the male pronucleus represents the genetic contribution of the husband , while the female pronucleus represents the contribution of the wife. When these fuse, a new life, with a unique genetic composition is formed. Abnormally fertilized embryos (for example, those with three pronuclei), or those which have failed to fertilise, are discarded, or used for research.



Fig 4. A normal 2-PN embryo on Day 1 (about 18 hours after egg retrieval) . This is a good quality embryo, because the two pronuclei (the clear bubbles in the center) are touching each other; and the pronucleoli they contain are aligned properly. If you click on the picture, you can watch a video of how the sperm fertilise the egg as seen under the microscope in our IVF laboratory

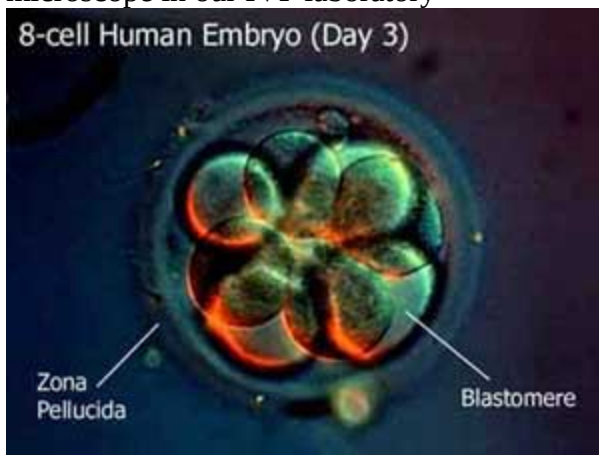


Fig 5. A beautiful 8-cell embryo on Day 3 (about 72 hours after egg retrieval) . This is a Grade A embryo, with regular, equally sized, clear blastomeres; and no fragments
There is quite a lot of suspense and anxiety till you find out from the lab how many embryos have fertilized. This is a biologic variable which we still cannot control. Sometimes, even though the eggs and sperm may look excellent , there may be a total failure of fertilization. This can be a major blow, because it means that there are no embryos to transfer. Poor fertilization rates may be because of : poor lab conditions; a sperm problem, or an egg problem. If only one patient has poor fertilization on a particular day, in a good lab, then it's usually the sperm which are held to be responsible .

How are embryos cultured in the IVF lab ?

The normally fertilized embryos are left in culture, where they continue to divide, and their quality graded after another 24 hours. Good quality embryos divide rapidly; and healthy embryos have 2-4 cells, of equal size, with clear cytoplasm and few fragments on Day 2 (about 48 hours after egg retrieval) . The IVF lab is the heart of the IVF clinic today, and an IVF clinic is only as good as its lab ! Unfortunately, most patients have no idea of what happens in the lab, and they rarely get a chance to talk with the embryologist, the skilled biologist who works in the IVF lab. The embryologist is the unsung hero of IVF treatment who does all the important work behind the scenes. The dramatic improvements in pregnancy rates with IVF today are because of the important contributions embryologists have made to finding the best ways of growing and culturing embryos in vitro.

Many patients are worried that their eggs, sperms or embryos may get mixed up with someone else's. While this can happen, the probability of it happening in a well-run laboratory is very low, because good labs have quality control mechanisms to prevent such mixups from occurring.

After 48 - 72 hours, when embryos usually consist of two to eight cells each, they are ready to be placed into the woman's uterus. This procedure is known as embryo transfer.

CHAPTER XXV C

Test Tube Babies - IVF & GIFT

How is embryo transfer performed ?

Embryo Transfer

Embryo transfer is most often done on an outpatient basis. No anesthesia is used, although some women may wish to have a mild sedative. The patient lies on a table or bed, usually with her feet in stirrups.. Using a vaginal speculum, the doctor exposes the cervix. One or more embryos suspended in a drop of culture medium are drawn into a transfer catheter, a long, thin sterile tube with a syringe on one end. Gently, the doctor guides the tip of the loaded catheter through the cervix and deposits the fluid containing the embryos into the uterine cavity. The procedure should be done with great care and usually takes between 10 and 20 minutes. Some doctors perform the transfer under ultrasound guidance, to ensure proper placement of the embryos in the uterine cavity. Most doctors advise a few hours of bed rest after the transfer.

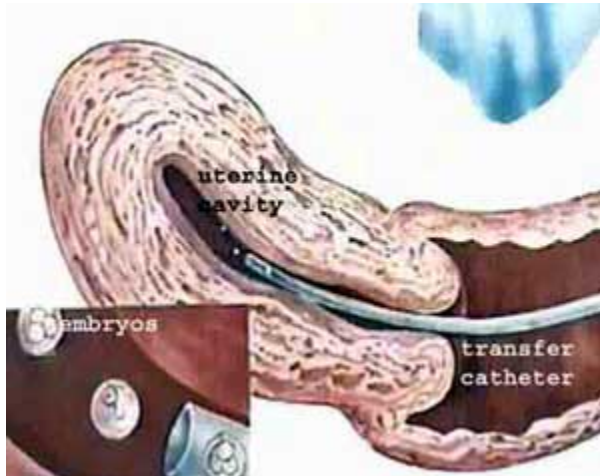


Fig 5. Schematic of the embryo transfer procedure

Most clinics today transfer 2-3 good quality embryos on Day 2 or Day 3. Embryos are graded according to their appearance and rate of cell-division and good quality embryos are those which have 4-8 cells, of equal size, with clear cytoplasm, and with few fragments. These are called Grade A embryos. Embryos with more fragments are assigned a lower grade, and they usually have a lower chance of implanting . However, the babies which result from these embryos are completely normal, if they do implant successfully. You should ask the doctor to show you your embryos under the microscope. Some times, only embryos of poor quality are available for transfer. While the chance of getting pregnant when only poor quality embryos are transferred, you can be reassured that if a pregnancy results, the children will be normal !

How many embryos to transfer is one of the most difficult decisions facing an IVF patient today. The more the embryos transferred, the greater the chances of getting pregnant. Since the purpose of an IVF cycle is to achieve a pregnancy, then why not transfer as many as possible? However, the price you pay for transferring more embryos is that the risk of a multiple pregnancy increases as well.

In some countries, such as the UK, doctors are allowed to replace a maximum of only 2 embryos, to reduce the risk of high-order multiple births. Some clinics in Scandinavia have now started transferring only one embryo (this is called SET or single embryo transfer) in young women, in order to reduce the risk of a multiple pregnancy. In USA and India, there are no laws, and some clinics will transfer 4 embryos for young patients, and upto 6 for older women - and this number is quite arbitrary.

Doctors have tried to develop an embryo score (based on the number of embryos and embryo quality) in order to predict the chances of a pregnancy after embryo transfer, but this is still not precise. I always tell patients that if IVF technology was perfect, and if every embryo became a baby, we would transfer only one embryo, and I wouldn't need to discuss this with them. Since the technology is still not perfect, and we still cannot predict which embryo will become a baby, there is no easy answer as to how many embryos to transfer. This is why many clinics will allow patients to decide for themselves. This is always a difficult decision, and you need to carefully weigh the pros and cons before making up your mind. There is no right or wrong number - and you need to take the path of least regret.

Transferring more embryos increases the chances of getting pregnant, and also increases the risk of a multiple pregnancy. However, a high-order pregnancy is a complication for which the doctor can perform a selective fetal reduction, in order to reduce this to twins. Not getting pregnant may be a worse outcome for some patients! If embryo freezing facilities are available, then supernumerary embryos can be stored, and this needs to be factored in as well.

What happens after the embryo transfer ? The terrible 2ww - 2 week wait !

The embryo transfer completes the medical treatment in the IVF cycle and most clinics provide "luteal phase support" after the transfer , usually with estrogen tablets and progesterone suppositories, to increase the chances of implantation. However, this period is often the hardest part of an IVF cycle for the patient, because of the agony and suspense of waiting to find out if a pregnancy has occurred. This can be determined by a blood test , which measures the level of the hormone, HCG (human chorionic gonadotropin) only 10 to 14 days after the transfer. For many patients, these 14 days are often the longest days of their life !

A positive beta HCG level (of more than 10 mIU/ml) means you are pregnant, and the doctor will then monitor your pregnancy to confirm it is healthy; intrauterine; and to check how many embryos have implanted.

It is normal to blame yourself for something you may or may not have done during this time if you do not conceive. Therefore, try not to do anything for which you will blame yourself if you do not get pregnant. In general the following guidelines are offered:

- No tub baths or swimming for 48 hours after replacement
- No douching or tampons
- No intercourse or orgasms until the fetal heartbeat is seen on ultrasound, or the pregnancy test is negative
- Do not undertake excessive physical activity such as jogging, aerobics, or tennis
- No heavy lifting

- You may return to "work" after 24 hours of bed rest (getting up for bathroom and meals only) and one to two days of light activity.

It's safe to travel 2-3 days after the transfer.

If you are unsure whether or not to do something, take the "path of least regret". Ask yourself - if I don't get pregnant, will I blame myself for doing this ? And if the answer is yes, don't do it !

You may have some vaginal spotting or bleeding prior to your blood test. However, you must have the blood test done, even if you think your period has started. There are no symptoms or signs which will be able to tell you whether or not you are pregnant.

Many doctors used to advise "strict bed rest" after an embryo transfer. However, remember that your physical activity does not affect your chances of getting pregnant. Resting when you are well can be very emotionally taxing, and we encourage patients to lead as normal a life as possible. Many patients are worried that if they cough or sneeze , the embryo will "fall out". However, remember that this is physically impossible, and that if the embryo is going to implant, it will, no matter how much you exert physically. Remember that God has designed the human body with enough sense, that coughing and sneezing will not cause the embryos to "fall out". The uterine cavity is a "potential space", and once the embryos are placed here, they appose to the uterine wall and are not affect by gravitational forces. I remind patients that it's fine for them to do whatever normal couples would do after having sex - after all, how does it matter to the embryo that it arrives in the uterine cavity in the normal course of events, after the couple had sex, or after spending 2 days in the IVF laboratory and then being transferred into the cavity with a catheter ?

Thus, there are numerous stages to every IVF treatment cycle, each of which must be reached and completed before moving on to the next stage:

- more than one should egg develop
- eggs should mature
- ovulation should not occur before the eggs can be collected
- eggs must be retrieved during the "pick-up"
- sperm must fertilize at least one egg
- fertilized eggs must divide and grow healthily,... and all this so that...
- the embryos might get implanted in the uterus

Think of it as a series of hurdles, all of which have to be cleared , in order to win the race !

Why doesn't every embryo become a baby?

The enigma of embryo implantation - why doesn't every embryo become a baby?

While modern technology is very good at making embryos in the laboratory, we still cannot control the implantation process. We do not know which embryo will become a baby - and this can be very frustrating, for both patients and doctors ! Many patients who do not get pregnant after an embryo transfer start believing that their bodies are defective, and that they have "rejected" the embryo. They feel that if they failed to become pregnant even after the doctor transferred 3-4 good quality embryos, that they are flawed.

However, you need to remember that embryo implantation is a very complex process, which consists of a series of phases in which the embryo has to appose and attach itself to the maternal endometrium and invade into it.

First, the embryo has to undergo further development, till it reaches the blastocyst stage, when it hatches from its shell, known as the zona. The hatched blastocyst then needs to implant in the endometrium, and the three phases of implantation are known as apposition, adhesion and invasion, and occur during the period of time known as the implantation window. Apposition, or orientation of the embryo (which is at the blastocyst stage at this time) within the cavity of the uterus, starts when the cavity has become minimal due to the suction of endometrial fluid by pynopods (small protrusions found on the surface membrane of the cells lining the uterus). Adhesion of the blastocyst is a progressive phenomenon that ties the embryo to the endometrium and is the primary event initiating invasion. Many molecules, such as cytokines, growth factors and cell adhesion proteins called integrins play an important role in this complex process during which the blastocyst and maternal endometrium must undergo an exquisite dialogue. Invasion is a self-controlled proteolytic process that allows the embryonic trophoblast to penetrate deep into the maternal decidua and to invade the endometrial spiral arteries by producing chemicals called proteinases. How implantation is regulated and brought about remains an enigma, but we need to remember that the implantation process is surprisingly inefficient in humans - Nature is not always very competent! After IVF, it's only about 10%, which means that only 10% of embryos implant successfully to become a baby.

The responsibility for this low efficiency has to be shared between the embryo as well as a defective embryo-endometrium dialogue. We still cannot successfully predict which patient will get pregnant after embryo transfer . We now know that one of the major reasons for failure of the embryo to implant is a genetically abnormal embryo. Basic research on implantation is of great interest today, because embryonic implantation is the major factor limiting in allowing pregnancy after ART, but we still need to learn a lot about this "black hole" in our knowledge, before we can learn to control it !

Many patients blame themselves when they don't get pregnant after an embryo transfer. They feel that the fact that the embryo did not implant means either that their body is defective; or that it "rejected" the embryo; or that they did not rest enough. However, please do remember that embryo implantation is a complex process, which you cannot influence by your diet or physical activity - so there is no need for you to blame yourself if the embryos do not implant.

How can you maximise your chances of success after IVF ?

Maximizing Chances For Success

Women:

- Avoid all unnecessary medications other than paracetamol (Tylenol) . If you are taking other prescription medications check with us prior to beginning your treatment cycle.
- No smoking or alcohol use. Studies show both can result in lower pregnancy rates and a greater risk of miscarriage. Why put yourself through this if you are not doing everything YOU can to insure your success.
- No more than two caffeinated beverages per day.

- Avoid change in diet or weight loss or fad diets during IVF cycle. A healthy well balanced diet works best.
- Refrain from intercourse following embryo replacement until the pregnancy test is done .
- Normal exercise may continue unless enlargement of your ovaries produces discomfort.
- Avoid hot tubs or saunas.

Men:

- Fever greater than 100.4 C one to two months prior to IVF treatment may adversely effect sperm quality. Be sure to let us know. If you are sick, please take your temperature and report any febrile illnesses.
- Sitting in hot tubs and saunas is not recommended. Please refrain from this for at least three months prior to treatment.
- Drugs, alcohol, and cigarette smoking should be avoided for three months prior to treatment and at all times during the ongoing IVF treatment cycle to get the best results.
- Abstain from intercourse for at least three days, but not more than seven days prior to collection of semen for egg collection and during treatment.

How much does IVF cost ?

The Cost of IVF

The cost of a single IVF treatment cycle varies widely from approximately Rs 70,000 to more than Rs 120,000 depending on the program and the items included in the fee. It is important to get an itemized listing from the selected program of what costs are included in the treatment cycle. Try to find your "total" medical cost - how much you will have to spend out of your own pocket for the entire treatment. Many clinics do not include the cost of certain procedures (such as ultrasound scans) and these can then add up to quite a bit ! Other expenses to be aware of include time missed from work and travel and lodging expenses. The number of treatment cycles needed to achieve pregnancy will, of course, determine the final cost.

A reduction in cost may be obtained by using "Natural Cycle IVF." This procedure does not employ ovulation enhancement; therefore the additional expense on the injections used for superovulation is eliminated. However, only one mature egg is usually obtained, and the pregnancy rate per cycle is therefore less for this method. A newer technique called "in vitro maturation" allows doctors to collect many immature eggs, and then mature them in the laboratory.

CHAPTER XXV D

Test Tube Babies - IVF & GIFT

What is embryo freezing ?

Embryo Freezing

Since most IVF programs superovulate patients to grow many eggs, there are often many embryos. Since the risk of multiple pregnancies increases with the number of embryos transferred (and in fact the law in the UK prohibits the transfer of more than 2 embryos to reduce this risk), many patients are left with "spare" or supernumerary embryos. These can be discarded; or used for research.

It is now also possible to freeze these embryos and store them in liquid nitrogen. These stored embryos can then be used later for the same patient - so that she can have another embryo transfer cycle done without having to go through superovulation and egg collection all over again. Moreover, since this embryo transfer is done in a "natural" cycle (when she is not taking any hormone injections) some doctors believe the receptivity of the uterus to the embryos is better. For women with irregular menstrual cycles, frozen embryo transfer can also be done in a " simulated natural cycle", in which the endometrium is primed to maximize its receptivity to the embryos by using exogenous estrogens and progesterone.

Since pregnancy rates with good-quality frozen-thawed embryos are as good as with fresh embryos, we encourage all our patients to freeze and store their supernumerary embryos, rather than discard them. Freezing is very cost-effective, since transferring frozen-thawed embryos is much less expensive than starting a new cycle, so that it serves as a useful "insurance policy" in case pregnancy does not occur. However, since it is worthwhile freezing only good quality embryos, the option of freezing is a "bonus" which is available to only about 30% of all IVF patients.

About half of all embryos frozen survive the freezing -thaw process. It is reassuring to know that the risk of defects is not increased as a result of freezing. These frozen embryos can be stored for as long as is needed - even for many years. When they are in liquid nitrogen, at a temperature of -196 C, they are in a state of suspended animation, and all metabolic activity at this low temperature stops, so that a frozen embryo is like Sleeping Beauty !

Once stored, embryos can be used by the couple during a later treatment cycle, donated to another couple or removed from storage. These options should only be undertaken after considerable discussion and written consent from the parties concerned.



Fig 6. The Programmable embryo freezer. You can see the liquid nitrogen vapours clearly.

Egg freezing

While we still cannot freeze unfertilised human oocytes efficiently, a new technique called vitrification (which uses ultra-rapid cooling together with an increased concentration of cryoprotectants) may allow us to offer this option to our patients, in the future, allowing the facility of egg storage and egg banking.

What happens if the IVF cycle fails ?

Analysing a failed IVF cycle
If you don't get pregnant after your IVF attempt, you are likely to be very disappointed and disheartened. However, remember that this is not the end of the road - it's just the beginning ! At the end of the IVF cycle, you need to sit down with your doctor and analyse what you learnt from it. Was the ovarian response good ? Was the endometrium receptive ? Did fertilisation occur ? Was the embryo transfer easy and atraumatic ? Why didn't pregnancy occur (the million dollar question, though this is usually a question we still cannot answer !) Can you repeat the same treatment, or do you need to make changes before going in for your next attempt ? When can you go in for your next IVF cycle ? And even if you do not get pregnant, at least the fact that you attempted IVF should give you peace of mind that you tried your best , using the latest technology medical science has to offer.

What about your next IVF cycle ?

The second time around - the next IVF cycle

Most doctors would advise you to wait for a month before starting a new cycle. While it is medically possible to do the next cycle immediately, most patients need a break to marshall their emotional strength before starting again. Your doctor may need to modify your treatment, depending upon an assessment of your previous cycle. For example, if the ovarian response was poor, the doctor may advise you to increase the dose of drugs used for superovulation. If fertilisation did not occur, you may need to go in for microinjection (ICSI). If the quality of the embryos was poor, you may be advised to consider a ZIFT (

ZIFT Video) rather than IVF. ZIFT will also be advised if the embryo transfer was difficult and traumatic, as this allows us to bypass the cervix and transfer the embryos directly into the fallopian tubes. However, if the cycle was satisfactory, the doctor will often advise you to repeat exactly the same treatment again - and all that it may take to achieve your IVF success is time, patience, and another attempt.

Interestingly, we often find that couples going through a second IVF cycle are much more relaxed and in control. This may be because they are aware of all the medical and procedural minutiae, and are better prepared for these; and also because they have had a chance to establish a personal relationship with the medical team. Also, since they have already faced failure the first time around, many of them are much better able to cope with the stress of IVF, since they are prepared for the worst. With today's IVF technology, we can confidently reassure any patient that we can help them to get pregnant, provided they have inexhaustible resources of time, money and energy !

CHAPTER XXV E

Test Tube Babies - IVF & GIFT

What is GIFT (gamete intrafallopian transfer) ?

GIFT

GIFT stands for gamete intrafallopian transfer and this used to be a popular alternative to IVF in the past. A gamete is a male or female sex cell - a sperm, or an egg. During GIFT, sperm and eggs are mixed and injected into one or both fallopian tubes. After the gametes have been transferred, fertilization can take place in the fallopian tube as it does in natural, unassisted reproduction. Once fertilized, the embryo travels to the uterus by natural processes.

As in IVF, a GIFT treatment cycle begins with ovulation enhancement which is followed by egg harvest, usually by means of laparoscopy. But the similarity to IVF ends here. In IVF, an embryo is transferred. In GIFT, gametes are transferred.

Only patients with at least one normal, healthy fallopian tube are candidates for GIFT. These include women who have unexplained infertility or mild endometriosis and couples whose infertility results from male, cervical, or immunological factors. Some doctors recommend that couples with male factor infertility proceed with GIFT only if it has been proven that the man's sperm can fertilize the woman's egg either by in vitro fertilization or by past pregnancies.

What are the basic steps of GIFT ?

The Basic Steps of GIFT
The basic steps of GIFT are superovulation , egg harvest, insemination, and gamete transfer. The eggs are usually harvested during laparoscopy. During this same laparoscopy procedure, which takes about an hour , eggs are mixed with sperm and the gametes are transferred.

Insemination

The harvested eggs are examined under the microscope and graded for maturity. The selected eggs are placed in individual dishes and combined with sperm (insemination). The sperm are prepared in advance in the same manner as for IVF. Some doctors prefer to allow the dishes to sit for about 10 minutes before the transfer, since during this period the sperm adhere to the zona pellucida of each egg. Many programs load eggs and sperm individually into a catheter and inject them into one or both of the fallopian tubes.

Gamete Transfer

The sperm egg mixture is loaded into a specially designed catheter . This is then directed into the fallopian tube(s) through their fimbrial opening while looking through the laparoscopy. Up to four eggs and sperm may be injected into one or both tubes. Gametes will be transferred only if the fallopian tubes appear healthy. If the surgeon determines

that the tubes are unhealthy, IVF should be attempted instead. For this reason, GIFT should be undertaken only at facilities that have the capability to do IVF.

Pregnancy Rate

Specialists generally agree that pregnancy rates are higher for GIFT than for IVF- in fact, GIFT is about twice as successful as IVF. In part, this may be due to the type of patient accepted into GIFT programs. It may also be because the in vivo tubal environment is more "physiologic " for the gametes and embryo than the in vitro environment.

The advantages of this technique are :

- the fallopian tube acts as the laboratory
- the embryo will reach the uterus at a later stage in its development, as with normal conception.
- the procedure is considered morally acceptable to some religious groups which object to IVF, as conception occurs within the human body.
- the endometrium will also be more receptive to the embryo because of the greater time the embryo takes to reach the uterus.

How do GIFT and IVF compare ?

GIFT & IVF Compared

There are several differences between GIFT and IVF. The most important one is that GIFT requires at least one healthy fallopian tube, whereas IVF is appropriate treatment for women with tubal disease or even no fallopian tubes at all. At present, GIFT requires laparoscopy for transfer, while an IVF treatment cycle can be completed without laparoscopy. This is one of the reasons many IVF clinics no longer offer GIFT , even though it offers a higher pregnancy rate - because they do not have easy access to an operation theatre. Ideally, you should opt for treatment in a clinic which offers all the procedures, so that the doctor can select the one which is best for you, depending upon your individual circumstances.

In the case of GIFT, fertilization occurs unobserved inside the body. With IVF, fertilization takes place in a laboratory dish and can be confirmed visually with a microscope. Visual confirmation of fertilization is especially important in cases of male factor or unexplained infertility. To obtain visual confirmation and still have the greater chance of pregnancy afforded by GIFT, one of the variations of GIFT described later (ZIFT, PROST or TET) may be used, to give the patient the benefit of combining the advantages of both the procedures.

Vaginal GIFT

A major disadvantage with conventional GIFT is that a surgical procedure - laparoscopy - is needed to transfer the eggs and sperm into the fallopian tube. Recently, a non-surgical method has been described by Dr. Jansen and Anderson from Sydney IVF, Australia, in which the gametes can be transferred into the fallopian tubes through the vagina and cervix under ultrasound guidance. This requires a special set of catheters which allow the doctor to enter the uterine ends of the fallopian tubes through the cervix. Once the catheters have been accurately positioned - and ultrasound can help in this - the gametes are injected into the tubes. Since this does not involve surgery, the benefits to the patient

are obvious - less expense, no hospitalization, no scar and no anesthesia. However, the technique does require much more technical expertise and is still being investigated more thoroughly. Also, the pregnancy rates with the method are less than with conventional laparoscopic GIFT.

What is ZIFT ?

Variations of GIFT

Variations of GIFT include procedures with names like ZIFT, PROST, TET - an alphabetic potpourri !

ZIFT, zygote intrafallopian transfer, is also called PROST, which stands for pronuclear stage transfer. When a sperm penetrates an egg, the sperm introduces its nuclear material into the egg. Approximately 14 hours after penetration, two distinct pronuclei, one from the sperm and one from the egg, are visible under the microscope. Pronuclei are taken as indicators that fertilization has occurred. A zygote is a fertilized egg before cell division begins. For ZIFT, eggs are removed by transvaginal aspiration and fertilized in a laboratory dish. The next day, when the fertilized eggs have reached the pronuclear stage, the embryos are transferred to the fallopian tubes during laparoscopy.

Approximately 24 hours after a fertilized egg reaches the pronuclear stage, it divides for the first time and becomes a two cell embryo. This cell division is called cleavage. It is at this stage or later that TET, tubal embryo transfer, may be attempted. The fertilized and dividing egg (early cleavage stage embryo) is transferred to the fallopian tube during laparoscopy.

PROST, ZIFT, and TET differ from GIFT in that fertilization takes place in a laboratory dish instead of the fallopian tube. Moreover, they differ from IVF in that the fertilized egg is transferred to the fallopian tube instead of to the uterus. They offer the best of both IVF and GIFT - documentation of fertilization in vitro; and higher pregnancy rates because of tubal transfer. However, the cost of ZIFT, PROST, or TET is usually greater than IVF or GIFT

CHAPTER XXV F

Test Tube Babies - IVF & GIFT

How can you make sense of IVF success rates ?

Success Rates - Making Sense of the Figures
The most important question most patients have about IVF and GIFT is : What are my chances of getting pregnant ?

This is a difficult question to answer, since there are so many variables involved. Chances of success depend upon:

- the wife's age - chances decline with increasing age - precipitously so over the age of 40
- the reason for the IVF / GIFT - chances of pregnancy decline when IVF is done for male factor infertility
- the quality of the IVF Clinic and its services
- the number of embryos /eggs transferred
- the superovulation regime used

Of course, there are some variables about which nothing can be done - such as the wife's age. But other variables can be controlled to try to maximize chances of a pregnancy ! The good news is that with improving IVF technology, pregnancy rates with IVF have increased dramatically.

Pregnancy rates are related directly to how many embryos are transferred. For example, when 3 good quality embryos are transferred, the chance of pregnancy is about 40% in that cycle. The number of embryos transferred needs also to be balanced against the risk of multiple pregnancy, which naturally increases with more embryos.

With this in mind, the Fertility society of Australia recommends that no more than 3 embryos be transferred during any treatment cycle. Studies done the world over show that the average pregnancy rate per cycle for IVF is about 30 % for most patients; and about 30% for GIFT.

How can a patient interpret this figure ? For example, let us consider a 30 year old patient with irreparable tubal damage who goes through one IVF cycle. She can look at the pregnancy rate figure of 30 %. in two ways . A success rate of 30 % means there is an 70 % chance she will not get pregnant. On the other hand, if she takes no treatment, her chance of getting pregnant is zero . The IVF cycle has increased this to 30 % - no one can do any better than this today !

Of course, for the couple who gets a baby, it's a 100% baby - and for the one who fails, it's 0% - so for the individual patient, it's really not a question of statistics ! Each IVF treatment cycle is a bit like taking a gamble - and you need to hope for the best and prepare for the worst !

IVF and GIFT treatment should not be considered to be a single shot affair. Patients should plan (mentally at least !) to go through at least 3 to 4 cycles to give themselves a

fair chance of getting pregnant. With 4 treatment cycles, the chance of getting pregnant (the cumulative conception rate) is about 70 %. What this means, is that even though the chance of getting pregnant in a single cycle may never be more than 40%, over 4 cycles, the chances increase to 70% because the success rate is cumulative.

Thus, let us assume the pregnancy rate for IVF at a clinic is 30%. If 10 patients start an IVF cycle, 3 will get pregnant, leaving 7 patients. If these 7 do another IVF cycle, another 30% (2.1 patients - so let's say another 2) will conceive. If the remaining 5 do another cycle, 1 more will get pregnant; and at the end of the 4th cycle, 1 more will conceive; so that of the 10 patients who started, 7 will have got pregnant in 4 attempts. This is because the chances of getting pregnant in the next IVF cycle do not decrease just because a pregnancy has not occurred in the previous cycle - so the best bet would be to keep on trying.

Theoretically, we could reassure every couple taking IVF treatment that they would get pregnant - provided they were willing to go through as many cycles as were required, till they hit the jackpot ! Of course, one has to set a limit somewhere, and the decision when to stop is something which only the couple can make for themselves . After more than 6 failed IVF cycles, the chance for a pregnancy with IVF does decline.

What games do some IVF clinics play with their pregnancy rates ?

Games IVF Clinics Play with Pregnancy Rates

Of course, some clinics have much better pregnancy rates - and others much worse.

Nevertheless, many clinics will quote inflated rates - and this can mislead patients !

Unfortunately, in India there is no central registry or monitoring of IVF clinics, so that you pretty much have to trust what the doctor tells you. In many countries in the West, the law mandates that IVF clinics provide their pregnancy rates to a central authority - thus ensuring that IVF clinics maintain high standards and quality control. This is very helpful for patients.

Different programmes define success in various ways. To most couples, success is a baby, not a pregnancy - so that what needs to be determined is the "take home baby rate" . Some clinics quote pregnancy rates when describing their success rates - and these can be considerably higher than the live birth rate , depending upon how a pregnancy is defined. Thus, some programs define pregnancy when the pregnancy test is positive; others define pregnancy as a fetus seen on ultrasound.

So called biochemical pregnancies are also fairly common after IVF. These are pregnancies confirmed by blood and urine tests but in which the embryo does not develop beyond the earliest stage. No gestational sac and no fetus is seen on ultrasound examination. Counting biochemical pregnancies will, of course, inflate the pregnancy rate.

Other ways of juggling with pregnancy rates include: accepting only patients who have a good chance of getting pregnant, or selectively reporting pregnancy rates achieved in younger women (and excluding other patients from data analysis).

Most good programs today express their pregnancy rate as the number of babies born per treatment cycle, and this is the figure you should be looking at.

Newer procedures

IVF technology is improving by leaps and bounds and many exciting advances have taken place recently. Many of these are now available in India, and these include the following.

What is assisted hatching ?

Assisted Hatching

One of the major problems with IVF today is the low pregnancy rate after successful embryo transfer. The reason why such few embryos implant successfully (only 1 of 10 embryos will become a baby) is one of the things we really do not understand today. Dr. Cohen from New York believes this is because the surrounding shell of the embryo (called the zona pellucida) hardens when it is cultured in the laboratory. They therefore use "embryo surgery" called zona drilling or assisted hatching to "soften" the shell of the embryo, and they believe this helps to increase pregnancy rates by improving implantation rates, since embryo hatching (Laser Hatching Video) is facilitated. This can be done using an acid (acid Tyrode's) or with a laser.



Fig 8. Assisted hatching. The embryo is held securely, and a carefully controlled stream of acid is blown through a fine pipette in order to drill a hole in the zona (shell). If you click on the picture, you can watch a video of how we do a laser-assisted embryo hatch in our clinic

Embryo surgery has also been used for embryo biopsy, for preimplantation genetic diagnosis, in which single cells are removed from the developing embryo, to make sure the embryos are healthy and have no genetic disease. This is described in more detail in Chapter 26.

Embryo multiplication, by removing some of the cells from the embryo and allowing them to divide, can allow doctors to "multiply" the number of embryos formed in vitro. The new embryos can then be coated with a new shell (zona) and then transferred into the uterus. This could help to increase the chances of pregnancy in women who can produce only a small number of embryos.

Other scientists feel that the reason for the poor implantation is the poor quality of the embryo cultured in vitro. They have therefore tried to improve embryo quality in the laboratory by trying to provide it with more natural ("physiological") culture conditions. This is done by a method called co-culture in which the embryo is cultured along with "feeder cells" in the culture dish . These cells provide the embryo with the extra

nourishment they need for better growth. Better pregnancy rates are claimed with co-cultured embryos as compared to embryos grown under traditional IVF conditions.

Cytoplasmic transfer

Some patients going through IVF grow lots of eggs, but persistently form poor embryos which fail to implant. In some of them, this may be because they have a problem in their cytoplasm (the area within the shell of the egg that lies outside of the nucleus) - either in their mitochondria or the cell-division apparatus . Dr Cohen hypothesised that it should be possible to correct this problem by replacing just the cytoplasm of the egg, instead of the whole egg, thus keeping the mother's own genetic contribution (the DNA contained in the nucleus) to the baby intact. This high-tech method is called cytoplasmic transfer, and uses cytoplasm donated from the healthy eggs of another woman.

What is blastocyst transfer ?

Blastocyst transfer

The formulation of new laboratory culture media - the liquid in which the embryo is grown in vitro - has made it possible to "grow" embryos in vitro beyond the typical 2 to 3 day state of development , till they become blastocysts. A blastocyst is the final stage of the embryo's development before it hatches out of its shell (zona pellucida) and implants in the uterine wall.

Initial studies suggest that transfer of the embryo on day 5, at the blastocyst stage, may yield higher pregnancy rates. There may be two possible reasons for this. Firstly, transfer of the blastocyst to the uterus may be more physiologically appropriate , since this mimics nature more closely, so that the implantation rate may be higher. Also, waiting till the blastocyst stage allows the doctor to select the "best " embryos, since unhealthy embryos are likely to die (arrest) before they reach this stage.

Blastocyst transfer also significantly reduces the possibility of potentially dangerous high-order multiple births, such as triplets. Higher implantation rates allows doctors to transfer fewer blastocysts - perhaps only one - reducing or avoiding multiple births and their associated problems. Supernumerary blastocysts can also be successfully cryopreserved with resulting pregnancies after thawing.

While blastocyst transfer is a very promising advance for patients who grow lots of eggs (good ovarian responders), its utility for the difficult patient - the poor ovarian responder - is still debatable. This is because if there are few eggs, there is a very real risk that none of them may develop to the blastocyst stage. All of them may "arrest", so that there are no embryos available for transfer. Every patient needs to balance these risks and benefits , depending upon the clinic's experience and success rate.

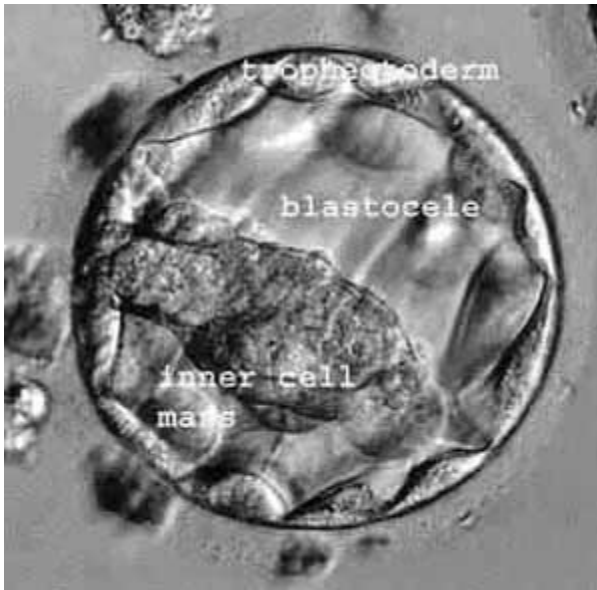


Fig 5. A beautiful blastocyst on Day 5.

How can we simplify IVF ?

Simplifying IVF

Some people might ask whether all this is relevant to Indian conditions. While these technologic refinements are very exciting, IVF clinics in India should also focus on simplifying IVF technology - so that it can be made more affordable for the average Indian couple. Advances which have occurred which have helped to simplify IVF and make it more easily available include the following.

Intravaginal culture: This is a technique for IVF , which provides the same rate of fertilization which conventional IVF does, at a fraction of the cost. In this method, which was first described by Dr. Ranoux of France in 1984, the eggs and sperm are placed in a sterile vial which is then sealed and placed in the woman's vagina. Thus, the woman acts like her own incubator, since she keeps her eggs and embryos at body temperature. Since expensive laboratory equipment is not needed, this is much cheaper - and as effective as conventional IVF !

Natural cycle IVF: Natural cycle IVF is much less expensive because it does away with the high expense of gonadotropin injections used for superovulation. In this method, the single egg which the woman grows in her unstimulated ovulatory cycle is used for IVF. While the pregnancy rate is lower, the expense (and the stress of IVF) is much less ! Interestingly, "gentler" IVF is becoming increasingly popular in the West as well. Many doctors are very critical of the large amounts of hormones which are being used in traditional IVF in order to produce large quantities of eggs. Gentler ovarian stimulation (using only clomiphene or smaller doses of HMG) has also become popular once again, since it reduces the risks of complications, such as ovarian hyperstimulation and multiple pregnancy.

Transport IVF: Transport IVF is a recent innovation pioneered in the Netherlands; and by Dr. Kingsland of UK. In this, the egg retrieval is performed by the gynecologist in his own clinic or hospital; and the eggs (in the follicular fluid) are then transported to a central IVF laboratory by the husband in a portable incubator . Insemination, fertilization

and embryo transfer take place in the central laboratory. This method allows gynecologists to take an active part in their patients' treatment; ensures high quality, since all laboratory procedures are performed in a central laboratory; and also minimizes patient inconvenience (since superovulation and egg retrieval are done by the local gynecologist, the number of visits the patient has to make to the IVF Center are minimized.)

CHAPTER XXV G

Test Tube Babies - IVF & GIFT

What about using donor sperm, donor eggs and donor embryos in an IVF cycle ?

Donor Sperms, Donor Eggs and Donor Embryos

Couples with no sperm or eggs can undergo IVF and GIFT with the use of donor sperm or eggs.

For IVF, cryopreserved donor sperm are processed in the same way as fresh sperm. In some cases of female infertility, fertilization may be attempted first with the husband's sperm, and if this fails, donor sperm may be used in a second attempt. Alternatively, if several eggs are aspirated, some may be inseminated with the partner's sperm and some with donor sperm.

Donor eggs can be used in GIFT or IVF for women who have no eggs (ovarian failure) but who do have a healthy uterus. For GIFT, the woman must also have at least one functional fallopian tube. In GIFT, the donor's eggs are mixed with sperm from the husband. This mixture is injected into the patient's fallopian tubes, while hormone supplements prepare the uterus and aid in the initiation of pregnancy. For IVF, an embryo resulting from the fertilization of a donor egg and the husband's sperm is placed inside the patient's uterus.

A couple may also choose to use donor eggs if the woman has a genetic disease that could be passed on to a child. Donor eggs can also be used in some cases of long standing infertility when other procedures have failed - for example, women with many previous unsuccessful IVF cycles. The use of egg donation is now becoming increasingly commoner , as older women are seeking infertility treatment. Since the chance of a pregnancy in the older woman depends directly upon the quality of her eggs , many older women opt to use donor eggs from younger women - which increases their pregnancy rates dramatically. This also creates headline news, for example, when a menopausal woman has given birth with donor eggs. In rare cases, when both the man and woman are infertile, donor sperm and donor eggs have been used together.

Unfortunately, it is still not possible to freeze and store eggs on a routine basis - they are too fragile ! This is why fresh eggs need to be used for donor egg treatments. These may come either from another infertile patient; or a volunteer egg donor; or a friend or relative, who offers to donate eggs.

Egg donation for IVF or GIFT requires the egg donor to undergo ovulation induction and ovum aspiration. The donation of eggs carries more risk and inconvenience to the donor than does the donation of sperm.

The use of donor eggs requires that the cycles of the donor and the recipient be closely synchronized. This requires treatment of the recipient, so that her endometrium is primed and is receptive to the embryos at the time of transfer. For amenorrheic women with ovarian failure, this can be achieved by treating them with exogenous estrogens and progesterone. Other women who are cycling need to be downregulated with GnRH analogs before starting treatment with exogenous estrogens.

In the future, it is possible in the future that scientists will discover ways to collect and store immature eggs. This may make " egg banks " a reality , and considerably simplify the technique of egg donation .

Couples with both a sperm and an egg problem can also use donor embryos. Since embryos can be stored, some infertile couples going through an IVF cycle, who have chosen to freeze their supernumerary embryos for themselves, are willing to donate their surplus frozen embryos to other infertile couples when they get pregnant. Since donor eggs are still so hard to come by, many couples may choose to resort to using donor embryos, since these are much more easily available. You can think of donor embryo treatment as very similar to adopting a baby - with the difference that you are carrying the pregnancy and giving birth to the baby !

Some couples are worried that if they use donor eggs or donor embryos, their body will "reject " them, because these are genetically foreign. However, remember that all embryos are genetically foreign to the mother, because half the genetic material comes from the father ! The uterus is an "immunologically privileged" site, and donor embryos have as good a chance of implanting as normal embryos.

CHAPTER XXV H

Test Tube Babies - IVF & GIFT

What are the risks and complications of IVF ?

Risks and Complications of IVF and GIFT

Many couples are still worried that babies born after IVF are abnormal or weak. You need to remember that in one sense there is nothing "artificial" about these babies - they aren't synthetic babies which are being manufactured in the laboratory ! Remember that IVF is a form of assisted reproductive technology, where technology is being used to assist Nature to accomplish what it has failed to do for the infertile couple ! Over a hundred thousand babies have now been born after IVF treatment, and the risk for birth defects is not increased after IVF treatment.

What is OHSS (ovarian hyperstimulation syndrome) ?

The most worrisome complication of IVF is that of ovarian hyperstimulation syndrome (OHSS), because of superovulation. The cause of "hyperstimulation syndrome" is that superovulated ovaries contain many follicles which are loaded with estrogen. After ovulation, a huge amount of estrogen-rich fluid is poured directly out of the enlarged and fragile ovaries into the abdominal cavity. This fluid also contains chemicals like kallikrein-kinin and VEGF(vascular endothelial growth factor), which then coat the lining of the abdominal cavity (called the peritoneum) and cause it to become very permeable (leaky) .

Fluid (serum) literally pours out of your bloodstream into the peritoneal cavity because of the "leakiness" of the abdominal cavity's lining. The ovaries balloon in size, your abdomen swells, you get lightheaded with relatively low blood pressure, and you may get dizzy because of the decreased blood volume. Many women will have mild degrees of hyperstimulation syndrome with a little bit of lower abdominal swelling, discomfort, and dizziness. This does not require hospitalization, just bed rest at home. It is only the rare, severe cases that require hospitalization.

The occasional patient today who develops severe hyperstimulation must go into the hospital, have intravenous fluids for several days, and wait for her ovaries to reduce in size and for her body to readjust. Some patients may even need to be admitted into an intensive care unit for monitoring and observation, since this can be life-threatening. At one time this was a very dangerous condition only because it was not fully understood.

We now know that by putting a small "paracentesis" catheter into the abdomen and draining all of this fluid, the patient is made much more comfortable, she can breathe more easily, and by getting rid of this estrogen irritation, fluid leakage into the abdomen slows down dramatically. Thus, even in the very rare cases of severe hyperstimulation syndrome, knowledgeable treatment makes the likelihood of any dangerous outcome very remote.

In our clinic, we prevent OHSS by carefully aspirating each and every follicle at the time of egg retrieval , and flushing it repeatedly with a double-lumen needle, until it collapses completely. By removing the follicular cells which are responsible for producing VEGF and causing OHSS, we have been able to prevent OHSS very successfully in our clinic by using this novel technique.

Interestingly, the worst cases of hyperstimulation syndrome occur when a woman becomes pregnant. This is because her placenta is making HCG and stimulating the ovaries to continue to pour out large amounts of estrogen-rich fluid. So although it is a very unpleasant side effect to endure, hyperstimulation syndrome often means good news.

If you grow too many follicles (more than 25) , or if your estradiol level is very high, the doctor may be forced to cancel the IVF cycle, because of the high risk you run of developing ovarian hyperstimulation syndrome. In some clinics, doctors can salvage this cycle by collecting all the eggs and freezing all the embryos. Since the embryos are not transferred, the risk of hyperstimulation is reduced; and the frozen embryos can then be transferred in a future cycle.

Complications can also occur during the egg harvest procedure. The removal of eggs through an aspirating needle entails a slight risk of bleeding, infection, and damage to the bowel, bladder, or a blood vessel.

What about the risk of a multiple pregnancy after IVF ?

In all techniques of assisted reproductive technology, the chance of multiple pregnancy is increased when more than one embryo or egg is transferred. Although some would consider having twins to be a happy result, there are many problems associated with multiple pregnancy, and problems become progressively more severe and common with triplets and each additional fetus thereafter. Women carrying a multiple pregnancy may need to spend weeks or even months in bed or in the hospital. There may be enormous bills for the prolonged and intensive care for premature babies. There is also a greater risk of late miscarriages or premature delivery in multiple pregnancies.

A recent treatment option for women with multiple pregnancies is that of selective fetal reduction, in which one or more of the fetuses is selectively destroyed (usually by injecting the toxic chemical, potassium chloride , into its heart under ultrasound guidance). In most cases, the killed fetus is then reabsorbed by the body - and the other fetuses continue to grow. Of course, the risk of all the fetuses being lost because of a miscarriage (as a result of inadvertent trauma during the procedure) is also present, and is about 10% in experienced hands.

There is approximately a five percent chance of an ectopic pregnancy with IVF and GIFT. This is not because of the procedure, but rather because women going through IVF already have damaged tubes, which predisposes them to having an ectopic.

IVF is physically demanding - and stressful ! The effects of blood tests, anesthetic and operation are tough on your body. Hormone stimulation causes lethargy and fatigue, not withstanding the sometimes extensive travelling required each day. Some people find treatment conflicts with their employment or other commitments.

A final risk is not physical, but psychological. The major risk for most patients is that even after spending all the time, money and energy required for a treatment cycle, they will not get pregnant. Couples undergoing IVF and GIFT have described the experience as an emotional roller coaster. The treatments are lengthy, involved, and costly. These procedures often create high expectations but are more likely to fail than to succeed in a given cycle. The unsuccessful couples will feel frustrated in their quest for pregnancy. It is common to feel angry, isolated, and resentful toward both the spouse and the medical team. At times, this feeling of frustration leads to depression and feelings of low self-esteem. The support of friends and family members is very important at this time.

What about the dangers of overtreatment and undertreatment ?

The danger of overtreatment and undertreatment

IVF techniques have now become well established, and most towns in India have one or more IVF clinics today. This is all for the best, because infertile couples no longer need to travel long distances for IVF treatment. However, because offering IVF has become a fashionable trend, there are now too many IVF clinics in competition with each other. Many of these clinics are poorly equipped, and the staff inadequately trained, with the results that pregnancy rates are poor. Many clinics have started, and then closed down in a few months, without being able to achieve even a single pregnancy - dashing many patient's hopes in the process. Unfortunately, this often means that all IVF clinics start getting a bad reputation. In order to protect yourself, it's a good idea to ask the clinic staff to actually show you the embryos under the microscope. Most good clinics do this routinely, and some even offer video records. Not only is this reassuring for the patient, it also helps them to "bond" with the embryos !

Another danger of too many IVF clinics is the risk of overtreatment. In order to remain profitable, many clinics now offer IVF to infertile couples as a treatment of first choice (rather than reserving it for patients who truly need it). While this does help them to keep their financial bottomline healthy and to increase their pregnancy rates (since many of these patients are young couples, who never needed IVF in the first place !) , it is an inappropriate use of limited medical resources. IVF treatment should be reserved only for patients who really need it. Paradoxically, while rich patients end up getting IVF even when they don't need it, poor patients are often deprived of this treatment even though they need it, because of the expense involved. Unfortunately, the Government still does not consider that providing infertility treatment should be a part of its family planning program. Hopefully, this will change in the future, and providing infertility services will be seen to be a part of comprehensive reproductive care services. This will provide many more infertile couples access to assisted reproductive technology.

How can you support each other during your IVF cycle ?

Supporting each other

You may not be able to comfort each other enough at times of disappointment, especially when you are both upset. If you don't have a family or a friend who can provide support (without pressure), then the positive and sensitive assistance offered by a support group may be very suitable, either in the short term or longer. Yet other people may seek the more specialized assistance of a counselor, who is either attached to the clinic or based in the community.

Going through an IVF cycle can be very stressful, and you need to be prepared for the ups and downs. Many clinics have found that optimistic and well-prepared patients do have better pregnancy rates, and counselling and emotional support can be very helpful in improving your chances of getting pregnant !

Every time you start a cycle, you have to hope for the best and be prepared for the worst. It literally is like gambling - and hoping that you hit the jackpot ! Many patients find the first cycle the most stressful - and find it much easier to do a second cycle, because they are more in control and understand much better what they are going through.

If you judge the outcome of an IVF cycle only on the basis of whether or not you get pregnant, then with the limitations of today's technology, you are more likely to be disappointed than otherwise. However, do remember that each cycle also provides you with valuable information, such as whether the sperm fertilise the egg or not, so that you can plan your future course of treatment. Going through an IVF cycle can also give you peace of mind that you tried your best !

How can you select the best IVF clinic for yourself ?

Selecting an IVF/GIFT Programme

There are now over 300 IVF clinics in India, so how do you go about selecting the best ? This can be difficult and confusing, but remember that when selecting an IVF program, information is crucial. Important points for consideration include the qualifications and experience of personnel, types of patients being treated, support services available, cost, convenience, and rate of successful pregnancies. Older programs have established live birth rates based on years of experience. Although new programs won't have as much experience and may still be determining their live birth rates, their personnel may be equally qualified.

The range of services offered by an IVF program should be carefully considered. Not all programs are equipped to provide all services, such as tubal transfer, ZIFT ([ZIFT Video](#)) , sperm donors , ICSI and cryopreservation of embryos. It is best to select a full-service clinic, which offers all the possible treatment options, so that the one which is best for you can be used.

The above considerations and answers to the following questions, which may be asked of the program, will help you make an informed decision when choosing an IVF/GIFT program.

What questions should you ask when selecting an IVF clinic ?

Cost and Convenience

1. How much does the entire procedure cost, including drugs per treatment cycle?
2. Do we pay in advance? How much?
3. What are the modes of payment?
4. How much do we pay if my treatment cycle is cancelled before egg recovery? Before embryo replacement?
5. What are the costs for embryo freezing, storage, and transfer?
6. How will the treatment schedule affect our commitments at work?
7. If I must have lodging, is there a low cost place for me to stay? Do you help arrange this?
8. If I do not get pregnant, when do I make my next appointment for further evaluation and counseling ?

Details About the Program

1. How many doctors will be involved in my treatment?
2. To what degree can my own doctor participate in my treatment?
3. What types of counselling and support services are available?
4. Whom do I call day or night if I have a problem?
5. Do you freeze embryos (cryopreservation)?
6. Is donor sperm available in your program? Donor eggs?
7. Do you have an age limit?

Success of the Program

1. When did this program perform its first IVF procedure? First GIFT procedure?
2. How many babies have been born from this program's IVF efforts? GIFT efforts?
3. In the past two years, how many treatment cycle have been initiated for IVF? For GIFT?
4. How many deliveries were twins or other multiple births?

If you are going through an IVF cycle, you will find the following tracking chart very useful in monitoring your treatment.

CHAPTER XXVI

PGD - Preimplantation Genetic Diagnosis The Newest ART

What is PGD (preimplantation genetic diagnosis) ?

PGD, or preimplantation genetic diagnosis, is a new technique, which marries the recent spectacular advances in molecular genetics and assisted reproductive technology. Preimplantation genetic diagnosis enables physicians to identify genetic diseases in the embryo, prior to implantation, before the pregnancy is established.

PGD was first developed for patients who were at risk of having children with serious genetic disorders, which often discouraged them having their own biological children. These couples are often faced with attempting a type of "Russian Roulette" to have children, many times having to confront the difficult decision to terminate an affected pregnancy.

Consider a woman known to be carrying an X-linked disease with a 50% risk of an affected male in each pregnancy. In addition, her daughters have a 50% risk of being carriers, but are unlikely to be clinically affected. She may not wish to become pregnant if she has to make decisions about an affected child in a viable pregnancy. However, she would become pregnant if she knew she had conceived a daughter, and with preimplantation diagnosis this possibility becomes a reality. PGD thus eliminates the need for possible pregnancy termination after prenatal diagnosis of a genetically-affected fetus.

Research has shown that it is possible at three days after fertilisation to remove one or two cells from an 8-10 celled embryo without detriment to its further development. Embryos were sexed on the basis of the presence or absence of a DNA fragment specific for the Y chromosome; in 1990 two sets of twin girls were born to five couples at risk of passing on an X linked disorder. Subsequently, a number of babies have been born after the preimplantation genetics has ruled out diagnosis of cystic fibrosis, Tay Sachs disease, Lesch Nyhan syndrome, Duchenne muscular dystrophy and for diseases carried on the X chromosome.

Sexing the embryo to avoid X linked disease remains the commonest reason for preimplantation diagnosis, now optimally carried out by the molecular cyto genetic technique of FISH (fluorescent in situ hybridisation) with DNA probes derived from the X and Y chromosomes.

How is PGD done ?

Techniques

How is PGD done? After IVF, on the 3rd day, the 8-cell embryo is biopsied. to obtain blastomeres (single cells) for molecular diagnosis. An embryo biopsy is done using micromanipulators under the visual control provided by an inverted tissue culture microscope. The embryo is held in position using a holding pipette, while a glass needle is used to drill a hole through the zona pellucida (the shell or the outer layer of the embryo) using a laser or acid Tyrode's. A single cell is then removed by gentle suction. The cell (called a blastomere) is then available for genetic diagnosis.

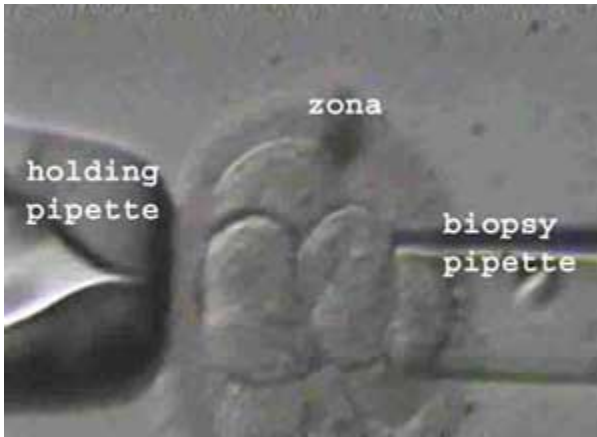


Fig 1. Embryo biopsy, with a single blastomere being sucked out from the 8-cell embryo. This will be sent for analysis.

Analysis of genetic material (DNA) from a single cell is performed either using a technique called FISH (fluorescent in situ hybridisation) or PCR (polymerase chain reaction) . FISH utilises fluorescent probes, which are specific for a given chromosome, and therefore allows one to screen embryos for chromosomal normality. PCR allows one to amplify (multiply) a selected DNA sequence of interest, so that it can be analysed. After the analysis on the single cell, the embryos are kept in culture and allowed to further divide. Once the appropriate molecular diagnosis is made, unaffected embryos can be transferred back into the uterus in the IVF cycle.

PGD is now also being used in order to increase pregnancy rates for older infertile women. One of the reasons older women have a poorer pregnancy rate is because their embryos are often chromosomally abnormal, because of the fact they have older eggs (which may have genetic defects). PGD allows the doctor to select only the chromosomally normal embryos, so that only these can be transferred back into the uterus, resulting in a higher pregnancy rate.

What are the controversies regarding the use of PGD ?

PGD for sex selection - right or wrong

While PGD represents the cutting edge of reproductive technology, and gives us an idea of what may be possible for the future, it also raises a number of worries and concerns, especially in India, where people are worried that it may be used for sex-selection.

PGD is emotionally a very touchy area, because not only are we dealing with human embryos - the very start of new life, but we are studying their basic blueprint - their genes - the stuff of which humanity is made. Obviously, this is likely to cause people to take very strong views on what is right and what is wrong - so that they start thinking with their hearts rather than their heads ! Many people confuse PGD with genetic engineering. A familiar refrain is we shouldn't be doing any of this because scientists are becoming too big for their boots - they are trying to play God by tinkering with the genes , and it is far better that they leave this entire field well alone, since we will never be able to understand any of it - it is beyond human wisdom. This is a common knee-jerk reaction, which precludes further rational debate.

The other view point is - Why not ? If man can improve on Nature, then why should he not try? After all, building a house is simply man's way of improving on nature - and if we can improve man himself, then why not? Seen in this light, then studying the molecular genetics of the human embryo would be the ultimate goal of all medicine. In the past, doctors used to treat adults. In the beginning of the 20th century, we started treating children, and the field of pediatrics was born. We can now treat the fetus - and the future patient of the 21st century will be the embryo - this is a logical progression!

If we allow people to choose when to have babies; how many to have; and even to terminate pregnancies if they inadvertently get pregnant, then why not allow them to select the sex of their child, if it is possible?

We should allow patients freedom to choose for themselves - medical technology should empower them with choices they can make for themselves! A common criticism against PGD for sex selection is that it will cause an unbalanced sex ratio. In reality, PGD will allow couples to balance the sex ratio in their families, rather than unbalance it! For example, take a couple with a baby girl, who want to have a second baby. If they leave things upto chance, half of them will have a second baby girl - causing unbalanced intrafamily sex ratios ! PGD will allow them to make sure that they have a balanced sex ratio in their family, if they so desire. Seen in this light, PGD is perhaps the ultimate form of family planning there is!

CHAPTER XXVII

Using Donor Sperm

What is donor insemination (TID) ?

THERAPEUTIC INSEMINATION BY DONOR [TID] means using the sperm (Sperm Video) from an anonymous donor to achieve a pregnancy, and is a treatment option if the man is infertile. While TID is a well established method for treating male infertility, it can be very difficult for the couple to accept. With the newer options for treating male infertility, such as microinjection, the need for TID has declined. However, these new techniques can be very expensive, and because they are out of the reach of many couples, TID is still a viable option.

What are the psychological issues raised by donor insemination treatment ?

Getting set for TID

Before a couple choose TID as a treatment, they must remember the taxing ethical, emotional and psychological repercussions it has for both of them. The husband may feel threatened, isolated, inferior, insecure and jealous. He may wonder whether he will be able to play father to " another man's child ". In fact, with the advent of microinjection, coming to terms with TID has become even more difficult, since many men are forced to resort to TID rather than use microinjection with their own sperm (Sperm Video) , purely for financial reasons.

The woman may be resentful that she has to undergo treatment and turmoil for something that is not actually her "fault". She may also worry about bearing the baby of a total stranger ; and will often have no support as this is something which she may not be able to share with anyone - even her own mother.

Couples undergoing TID often undergo psychologic reactions which can be difficult to cope with. The sense of isolation is even more than with other forms of infertility, since most couples do not tell anyone they are undergoing AID - so that they miss the social support and sympathy which other infertile patients receive. The stress can be tremendous because the sperms of another man are being inseminated into the wife, and both partners experience many conflicting emotions. The involvement of a completely unknown third party as a sperm donor can make coping with the pregnancy especially difficult . Fantasies and nightmares may occur about the unknown donor - and there are

also concerns as to whether the child will be normal and what the child will look like . Many men also experience sexual impotency at this time, but this is only temporary. Now is the time to talk, for togetherness. Air out all your apprehensions with honesty and maturity. Discuss how you will make sure that you will both be equal partners in parenthood. She will have to reassure her husband with tact, gentleness and humour of her commitment to him. Love, patience and understanding are very important - this is a time when the couple needs each other the most. Seek counselling from your gynaecologist or fertility expert. Discuss other choices too. Don't rush into adopting a sperm (Sperm Video) - explore the alternative options as well!

Who are the sperm donors ?

Who are the donors?

The donors are healthy men between 20 to 40, from a sound background, and usually graduates. Those who are healthy, with no family history of illness are requested to provide a sperm sample for testing. This semen is analyzed, and accepted only if it has superior qualities: a count over 100 million per millimetre; and motility of 70% to 80%. Blood is checked to make sure they are negative for AIDS, Hepatitis and STDs.

How is the sperm frozen and stored in a sperm bank ?

After liquefaction, the semen sample is mixed with an equal quantity of the cryoprotectant medium (a chemical which prevents the sperm from being damaged even at very low temperatures) and is loaded into plastic straws. These are uniquely coded and sealed; and then placed in steel tubs of liquid nitrogen where they are frozen to - 196 degree Celsius. One day later, one straw is removed and thawed to see how the sperms survived the cold (cryosurvival). Only samples which contain at least 25 to 40 million motile sperm are accepted.

The sperms are then kept in cold storage for 6 months, which is how long it takes for the HIV virus (which causes AIDS) to become detectable in a person's blood after infection. This is called the quarantine period. The donor's blood is then retested for HIV, hepatitis and STDs, and the infected donors weeded out.



Fig 1. Sperm being frozen in liquid nitrogen

Donors are paid a little more than conveyance costs - they are usually philanthropic men who have experienced fatherhood and want to make another couple happy. They are not

allowed to produce more than 10 babies and the doctors generally scatter the offspring so that there is no risk of half siblings unwittingly marrying each other.

What about using a known sperm donor ?

Known Donors

Sometimes couples wish to use a friend or relative as donor. However, there are many dangers in doing so. Over time, the donor's psychological make-up as well as the relationship with the donor may change. This could create social and legal problems. Furthermore, you will become dependent upon the donor's discretion to keep the insemination a secret. This is why using a known donor is not usually a good idea - however tempting this may seem.

How is donor insemination treatment performed ?

The Treatment Process

The couple signs a consent form for TID after appropriate counselling. The doctor will need to ensure that at least one of the woman's fallopian tubes is open - and may advise a hysterosalpingogram or laparoscopy to confirm this.

The woman may be treated with fertility drugs to ensure ovulation. Daily vaginal ultrasound scans are done from the 11th day of the cycle to view the evolution of the egg and discover exactly when the maturing follicle bursts.

For frozen sperm, a straw of the appropriate donor (who best matches the husband's physical traits) is picked out and rechecked under the microscope to see that the sperm are actively motile. The doctor matches the donor and the husband for height, build, hair colour, skin colour, eye colour, Rh factor and blood group.

Under sterile conditions, the donor sperm is injected through a plastic catheter into the cervix. The patient rests for about ten minutes and that's that. The husband is encouraged to be present at the time of the insemination - this is one way that both the partners can be close during the process; and some clinics will even allow the husband to do the actual insemination himself, so he feels more "involved". There is no reason not to make love shortly after TID if this is what the couple wants to do.

After each insemination there is then a two weeks waiting period to find out if it's been successful. It's an emotional roller coaster - anticipation, insemination, menstruation, desperation, and then, hopefully - elation.

Success statistics mimic nature. They are 10% in a 25 year old woman in one cycle; so that over six treatment cycles the chance of a pregnancy is about 60% in a 25 year old - and only about 20% in a 38 year old. It takes nature time to make babies, and patience is needed. The chances of success are highest if the female partner is young, has no fertility problem and the husband has no sperm. Irregular menstrual cycles; or a history of endometriosis or tubal infection decreases the chance of pregnancy. Interestingly, pregnancy rates with TID are lower in women whose husbands have a low sperm count, as compared to those whose husbands have no sperms at all. The reason for this is not entirely clear.

Once you get pregnant, your pregnancy is like a normal pregnancy - with the same risks of miscarriage and birth defects as any other. If you change your obstetrician, you do not

even need to tell your new doctor that you have conceived by TID. He will never know; and the name on the birth certificate will be yours and your husband's. With TID strict confidentiality is maintained, and the identities of the patients and donors are kept secret. Historically, parents have kept TID a secret from the child and from friends and relatives. Unlike adoption, TID is not obvious to those who know the infertile couple. It is entirely up to the parents to tell the child the circumstances of his or her birth and most Indian doctors advice against it . However, there is always the burden of secrecy which the parents have to bear for the rest of their life.

Why is it safer to use frozen sperm samples for donor insemination ?

The Donor Semen Sample - Fresh or Frozen?

Traditionally, gynecologists have used fresh semen samples (ejaculated recently} for TID. However, using fresh semen samples for TID can be hazardous to the patient's health. It is best to use frozen cryopreserved, tested samples from a sperm bank for TID. It used to be felt that pregnancy rates with frozen samples were poor as compared to fresh samples. However, recent studies have shown that if the frozen samples contain a sufficient number of motile sperm, pregnancy rates with fresh and frozen samples are comparable.

Common problems

- to tell or not to tell friends and family
- the need to explain to employers and co-workers the need to arrive late, leave early, take time off - without being able to give a reason why to deal with an erratic ovulation cycle caused by anxiety
- to keep your sexual relationship on an even keel
- to work out a plan when one partner wants TID and the other does not

Disadvantages of fresh semen

- There are no records of the donors and no information as to his medical and family history.
- It's impossible to match the physical traits of the donor and the husband.
- Using known donors can lead to rocky legal , emotional and ego problems.
- The quality of the sample is always suspect, but beggars can't be choosers.
- It could be difficult to produce a donor at the critical time and occasionally a treatment cycle has to run dry.
- The spectre of transmission of AIDS looms large since fresh semen cannot be tested for AIDS

Advantages of frozen sperm

- No risk of STD and AIDS as the samples are quarantined for three months and the donors are retested
- Around the clock availability; no scheduling bottle neck.
- High quality product since it is tested before and after freezing

- Rh negative donors can be used for Rh negative women
- Physical traits of husband and donor can be matched

What is sperm banking ?

Sperm banking

While the major application of sperm banking today is for donor insemination, sperm banking is also useful in a number of other areas as well. Thus, we can store and freeze husband's sperm samples for treating the wife, and this is very useful in the following circumstances.

- When the husband has situational erectile dysfunction, so that he cannot produce a semen sample by masturbation at the appropriate time of an IUI or IVF cycle, storing a sample is very useful . This frozen sample can be used as a backup, in case the man cannot produce a sample at the required time. However, in many cases, because the man knows that a frozen sample is available , this helps to take the pressure off, so that many of them can produce a fresh sample with little difficulty!
- When the husband is away (working overseas or traveling), his frozen sample can be used to treat his wife.
- For men with very variable sperm counts, it can be helpful to store the "good samples", so that these can be used. Unfortunately, pooling many frozen samples together does not help to increase the sperm quality.
- For men with cancers, sperm freezing offers them a chance of conserving their reproductive potential.

CHAPTER XXVIII

Surrogacy : Surrogate Mother & Parenting

What is surrogacy ?

The word surrogate means substitute or replacement - and a surrogate mother is one who lends her uterus to another couple so that they can have a baby. In the West, where fewer and fewer babies are offered for adoption, surrogacy is gaining popularity, despite controversial legal and ethical hassles.

Who needs surrogacy treatment ?

Which women need surrogates? The commonest reason is a woman who has no uterus. This may be absent from birth (Mullerian agenesis); or may have been removed surgically (hysterectomy for life-saving reasons, such as excessive bleeding during a caesarean). Other women who may wish to explore surrogacy include those who have had multiple miscarriages; or who have failed repeated IVF attempts for unexplained reasons.

Women who agree to become surrogates may do so for compassionate reasons. These include a sister, mother or close friend of the couple . They may also do so for financial remuneration - and this could be a woman, with or without children, known or unknown to the couple , who rents her womb for a fee.

There are two main kinds of surrogacy:

- The surrogate mother provides the egg. In this case, the surrogate is inseminated artificially by the husband's sperm. In this case, the infertile woman has no genetic relationship to the baby.
- More commonly, the infertile woman provides the egg, which is then either transferred to the surrogate mother by GIFT along with her husband's sperm; or fertilised in vitro by IVF with her husband's sperm and an embryo transfer performed to the surrogate's uterus, which then acts as an incubator for the next nine months.

Certain guidelines have been laid down to try to minimise misuse of the surrogacy technique; and a surrogate motherhood contract needs to be drawn up, which should specify that the child will become the legitimate adopted child of the infertile couple , the intended parents. This needs to be signed by the couple, the surrogate, and her husband.

The legal waters of surrogate motherhood will continue to be murky, and there are no laws or guidelines in India as yet. This is why the element of trust between the couple and the surrogate mother is so important.

It is vital that the surrogate and the couple consider the future of the child. The receiving mother should ideally be present at the birth and care for the baby in hospital. She can even be prepared for breast feeding (induced lactation) by hormone treatment.

What are the complex issues raised by surrogacy ?

Surrogacy has spawned a host of legal and emotional issues to which there are no "right" answers. Like:

- What will you do if the surrogate insists on keeping the child?
- How much should you pay the surrogate?
- If she gets ill as a result of the pregnancy who will pay the medical costs?
- Is it possible to put the receiving mother's name as mother on the birth certificate?
- Will you tell the child about the surrogacy?
- Will surrogates undertake pregnancy for profit?
- What happens if the child is handicapped and is unwanted by the couple and the surrogate mother ?
- What happens if the surrogate dies during child birth ?

Many people are worried about the possibility of the surrogacy technique being misused. They feel it may allow the exploitation of poor women who may be used as "mother machines" to bear babies - much like the wet nurses of yesteryear.

Surrogacy has received quite a lot of bad press recently - especially when the contract goes sour and there is a dispute over the baby between the commissioning parents and the surrogate mother - this make headline news. The Courts then need to have the wisdom of Solomon to assign the rights of the "genetic" mother; the "birth" mother; and the "social or rearing" mother.

Nevertheless, we must remember that surrogacy does offer one method of achieving parenthood to a few couples who could never have a baby by any other means.

The road to surrogacy is a rocky one and requires much thought. It is perhaps the most complex and difficult way to achieve parenthood.

CHAPTER XXIX

When Enough is Enough - The Decision to End Treatment

When should you consider stopping infertility treatment ?

One of the most difficult aspects of infertility treatment may be examining the question of when to stop medical therapy. You may find yourselves asking, " When should we stop? When will we know that we have done all that we can?"

Only you can tell when you have had enough - you need to make the final decision for yourself. Everybody has a different limit - but it needs courage to recognise when you have reached it. Some couples start planning for alternatives early on in medical treatment and when they reach their limits, they are prepared to try something else. Others may keep going to a point which pushes them beyond their final limits - and sometimes even further !

There are several reasons why infertile couples have trouble stopping treatment. First, there always seems to be a new medical option bringing hopeful opportunities , and patient's hopes are kept alive by new developments. The pace of change in this field has been very rapid, so that was just a possibility a few years ago quickly becomes a standard treatment that is being offered to a lot of people today. When it seems all the medical possibilities have been exhausted, researchers come up with a new solution, offering another chance to people who dream of bearing children. How can you pass up a new treatment when you've been willing to try everything else?

Some couples also seem to get "hooked" onto treatment, and are willing to give up everything to pursue their dream of a baby - they live on hope. Many couples cling to the fantasy that "one more try" would have resulted in a healthy pregnancy.

Another reason is that some physicians may not recommend ending treatment. Physicians are generally optimistic that treatment will eventually work and this biases their ability to provide advice about ending treatment appropriately (to say nothing of their financial motives).

Some couples also feel guilty about stopping treatment even when they have had enough, because they feel they have let their doctor down by not getting pregnant - especially when the doctor has tried so hard! Many couples have lived a lifetime with the notion that if they try hard enough, they will succeed, so that the decision to end treatment seems like "giving up" or a lack of ability to persevere and beat the odds.

How will you recognise when you have had enough? Watch out for some of these factors:

- Do you feel emotionally and physically tired all the time?
- Do you feel sad or depressed much more than you used to?
- Are you finding it harder to be optimistic about your next treatment?
- Do you glumly anticipate a treatment's failure in order to fend off disappointment?
- Are you finding it harder to follow the doctor's instructions?
- Has your relationship with your spouse started to deteriorate even further? Are you fighting a lot more?
- Do you find yourself wondering why in the world you are doing all this?

There are positive reasons to consider ending treatment too - you don't have to wait till you are a wreck before making this decision!

- Are you beginning to focus more on the child, but not your genetic contribution to the child?
- Does the idea of stopping seem like a relief to a lot of your troubles?
- Are you directing attention to other areas of your life - and enjoying it?
- Do you feel proud of how hard you tried, and don't feel the need to do any more?
- Is your curiosity about alternatives increasing?

If you're considering ending treatment, you and your partner will probably find that one of you is ready to stop before the other reaches that point. Remember, it's perfectly natural for people to move at different paces, especially through a process as complex and challenging as infertility and its treatment.

How does one decide to stop infertility treatment ?

Facing the Decision

If you do find yourself faced with the decision to end fertility treatment, but you're not sure how to go about finalizing it, there are several steps that may help you determine what's best for you. Consider establishing a time frame. It sometimes helps to make a schedule for yourself, even if you decide to modify it later. You could decide, for example, that you will try for another year, or until your next birthday.

Another step that might be helpful is to take a brief "vacation" from treatment. Depending on your feelings after a break, you may realize that you're not ready to stop or - or that now is the time to end treatment.

Infertility, with its endless tests and treatments, has probably meant that so far your life has been put on "hold". But, through grieving and resolving your grief, you can move on again. Remember, you need to finish mourning for the loss of your child before making this decision. Grieving is letting go - letting go of unfulfilled dreams and replacing them with a comfortable reality, to allow resolution.

Talk to others who have decided to move on. This is especially helpful if you are having difficulty deciding what to do next. Ask others how they made the decision and how they

feel about it now. Additionally, professional counseling can be very helpful in assisting you with decision making.

Finally, accept and expect that your infertility will remain a part of you. The decision to stop treatment brings resolution and closure, but it may not necessarily remove the ache of infertility. However, once you do accept your decision, you may find that your disappointment gradually disappears.

CHAPTER XXX

Child Infant Adoption & Myths on Adoption :

Adoption - Yours by Choice

When should you consider adoption ?

You don't have to be superhuman, superkind, superloving or perfect to be able to adopt a child - you just have to be ready. Being ready only happens when you've had time to get used to the idea - and if you are infertile, it is never too early to consider adoption. You can begin gathering information from adoption agencies even though you may not be fully committed. It is always a wise strategy to investigate alternatives in case pregnancy does not occur - after all, statistically, the overall chance of pregnancy for an infertile couple undergoing treatment is only about 50 to 70 percent after one or more years of trying.

Also, because many agencies do not accept people over a certain age as adoptive candidates, especially for infants, it is important to collect information so that you don't discover later that you are too old to fulfill a particular agency's requirements.

To couples just beginning to consider adoption the central concern is: can we love an adopted child as our own? Other doubts include:

- What kind of children are available for adoption? Aren't they all misfits or discards?
- Won't adopted children grow up maladjusted?
- What will our families say and do? Will they love a child we adopt?
- Won't the child go off to find its birth parents once it grows up anyway?
- Why do we have to go through so much agony to build a family? Infertility was one struggle and now adoption with its waiting list is a whole new one.
- What will society say? Will our child be accepted by friends and neighbours?

As you find yourself more ready to accept adoption as an alternative, these questions often lose their importance. Some of them disappear when you finish grieving for your biological child - the child that never was - and resolve this grief by allowing healing. Through grief, you learn to focus less on the process of obtaining children and more on the children themselves. A couple must, together and separately, come to terms with their loss - to learn to say good-bye, before they are ready to consider adoption. The other doubts disappear after you talk with adoption agencies; adoptive parents and their families; read books about adoption; and learn how adoption is accomplished. The question then is no longer "Can we do this?" but becomes "How do we do this?"

You will learn that in many ways families with adopted children are the same as any other families. You'll express love, have disputes and make compromises in your daily lives. Your child will be your child, no matter how you came to have him.

Adoptive parenting may be your second choice but it's just as good as biological parenting. It is different - don't try to compare them, one isn't better than the other. However, you will have to deal with several issues that occur only in adoptive families. Prepare yourself to discuss adoption with your child - and to truthfully deal with the myths and misconceptions that many people have about adoption. You may also find that you and your child will often be faced with questions and ignorant comments which assume that adoption is a second-best alternative for all involved.

Adoption cannot solve the problems associated with infertility - it is not a cure for the physical aspects of infertility and neither does it cure the emotional pain. But adoption will provide you with the challenges and rewards of loving and being loved by a child.

Most adoptions are closed adoption in which the biological parents and adoptive parents do not come in contact with one another. The adoptive parents have only fragmentary, if any, information on the birth parents. Furthermore, adoption agencies make every effort to keep the adoption records closed and unavailable to everyone, including the adoptive parents, the birth parents and the adopted child. Most agencies believe that the clear separation of the adoptive parents from the birth parents is necessary for the adoptive family to be "normal".

What is involved in the adoption process?

What is involved in the adoption process? Many people naively believe that adoption simply consists of walking into an agency and walking away with a baby. Of course, it's much more complex than this. It involves considerable paperwork; asking questions; solving problems; researching; spending money ; and going through emotional ups and downs. It takes time and work but remember that those who want to adopt will always succeed. These procedures have been designed for your benefit so don't be lured into taking "shortcuts" - these can hurt you in the long run. After all, adoption is not just a means of finding babies for infertile couples, but a way of finding the right family for a particular child.

Each adoption agency has different requirements so you may find that even though you are turned down at one agency, another will readily accept your application.

Most agencies suggest that:

- The age between the adoptive parents and the child be less than 40 years.
- The couple should have been married for at least five years to attest to the stability of the relationship.
- The couple should have a regular source of income.
- Neither of the partners should have a major illness which may reduce your life-span.

The professional who will be guiding you through this process is a medical social worker, who is fully qualified and trained. Find an agency where you are comfortable with the social worker assigned to you.

You should learn about the requirements for adoption; and the average waiting time for placement. You'll need to decide upon many factors including the child's age and sex -

and there may be certain limitations on your choice. Costs vary widely, and you should enquire how much it will be.

Once an agency accepts your application, detailed interviews, both separately and jointly, are conducted. Agencies may ask you to supply references from relatives, employers and friends. Furthermore, an adoption worker will come to your home and evaluate your suitability as parents - the home study. At some point after the home study period, a child is identified who is or who might be available for adoption. You'll then have to decide whether or not to accept the child - it's finally your choice. If you choose to adopt, there is a supervisory period once the child arrives in your home, and this may range from a few weeks to several years. After a specified period, your child is legally adopted by an adoption decree.

When is adoption not the right answer ?

When Adoption is not the answer

Infertile couples are often under tremendous pressure to adopt - friends may tire of your problem and question why you don't adopt if you want a baby so badly; and others who have already adopted may enthusiastically recommend the option to you. But you should never try to force yourself to be comfortable with adoption if the idea is disturbing - this is not a time for selflessness. There are no set guidelines to determine who should or should not adopt. Remember, adoption does not mean trying to find a baby now to take care of you in your old age; neither is it a method to try to use to keep your marriage together. Signs suggesting indecision could include denial of your disappointment about infertility; persistent fantasies about what life might have been with biological children; and the desire to keep the adoption a secret. Prospective parents may also have fears that an adoptive child may not measure up to family standards. If you have any doubts, it may be a good idea to temporarily postpone your adoption plans and discuss your anxieties before proceeding further.

What are some of the myths about adoption ?

Myths about Adoption

Myth: If an adoptive family really loves the child and does a good job of parenting, then an adopted child will not be curious about his or her birth parents.

Fact: Children are often curious about those who play major roles in their lives. Most, if not all, adoptive children will want to know about their biological roots.

Myth: Adopted children are better off not knowing they are adopted.

Fact: Adoptees almost always find out that they are adopted. They then discover that their family has been dishonest with them. Adopted children may build better self-esteem when they have a clearer picture of personal birth origins.

Myth: Once the process of adoption is over, it is the same as having a biological child.

Fact: There are real differences in birth and adoptive families. The adoptive child will have different questions about adoption at each stage of development.

Myth: Adoptive parents make better parents because they want a child so badly.

Fact: The degree of desire for a child does not necessarily make for better parenting.

Myth: An adoptive child belongs to his new family forever and owes them something more than ordinary offspring.

Fact: An adoptee child offers neither more nor less to his parents than a birth child.

Myth: Once a couple has decided to adopt, it is more likely they will become pregnant on their own.

Fact: It is neither more nor less likely that a couple who has adopted will achieve pregnancy.

Myth: Once adoption has taken place, the pain of infertility will cease.

Fact: The pain of infertility often lingers after the family has been established by adoption. Although happy with their adoptive families, couples may still want to pursue having a biological child. Adoption is not a cure for infertility, but it can be a cure for childlessness.

Myth: Prospective parents should adopt only after all possibilities of having a biological child have been exhausted.

Fact: Because of rapid developments in infertility management, there is no longer a clear stopping point for possible infertility therapies. It is helpful for prospective parents to look into alternative means for starting a family early in their infertility work-up - remember, taking infertility treatment and considering adoption are not mutually exclusive choices ! Just because you are taking treatment does not mean that you are not "committed to adoption"; and just because you are considering adoption does not mean that you are decreasing the chances of the infertility treatment as a result of your "negative attitude". Often, couples pursuing infertility treatment may actually begin to see how an adopted child could be a good choice for them.

Myth: It is extremely difficult to adopt.

Fact: Although the adoption process can be tedious, adoption is possible for most couples.

Myth: Since India has an overpopulation problem, with so many unwanted children, adoption is a "better" choice for the infertile couple than taking treatment.

Fact: You cannot force someone to adopt a child, and adoption is not the best solution for all infertile couples. They need to be able to make their own choice. While adoption is a reasonable solution for some infertile couples, this is a choice which they have to make for themselves.

A good book to read to find out more information about adoption is Nilima Mehta's **Ours By Choice**, which is available from the Family Service Center, Eucharistic Congress Bldg III, 5 Convent Street, Bombay 400 039.

CHAPTER XXXI

Child free living - Life without children

What is childfree living ?

Choosing not to have children at all is an option which you can select - to live childfree. Remember, childfree living is a choice you can make - choosing not to have children isn't the same as having childlessness thrust upon you.

You may find that coming to terms with your childlessness gives you the ability to take control of your own life again. Infertility often means living in a state of suspended animation - waiting and waiting forever through tests and treatments for a baby. If you choose to live childfree, you can get on with living again. Plans can be made to explore the endless possibilities of career, travel, recreation, hobbies and togetherness as a couple when previously all the uncertainty made this impossible. When you are chasing the dream of a baby, it is easy to forget that life has the potential for many other dreams and fulfillments.

It is crucial, however, for both partners, should they choose the childfree alternative, to feel they can happily fill their lives with work and other interests. If the husband has a successful career but the wife has little to replace the parenting function, unhappy consequences are likely.

One of the biggest fears people express when considering a childfree life is that they will regret this decision in their older years and end up being lonely and miserable. In India, children are often a form of social security for old age. However, remember that children are not an insurance policy against loneliness in old age - they can also create problems for their parents! People also worry that when they die, they will have nothing to leave behind. The truth is that children are not the only ones who remember you, nor are they the only means of establishing everlasting memory.

How can you adapt to the decision to live childfree ?

Remember, there can be real advantages to life without children: more personal freedom, more time to spend on your own interests, and more emotional energy to invest in your emotional relationships. Start enjoying your time with your spouse more - remember the early heady days of your marriage before you were striving for a child? Try to recapture those magic moments again.

A new lifestyle may be difficult to think about and many people advise that you try to do many things that interest you to give yourself a chance to spend some of your pent-up needs - the need to be needed and the need to do something. It's a matter of balance. The answer to wanting one thing exclusively is to be involved in many things - to spread

yourself around. Taking a holiday to mark the end of treatment and the beginning of a new lifestyle can be very helpful and allows time to relax and assess the situation.

Acceptance or resolution of infertility doesn't mean putting all desire to have children into the past and forgetting about it. Infertility, your experiences and thoughts will always be a part of you and will be remembered with mixed emotions, including sadness, regret and frustration, over the years. Acceptance is more an acknowledgement that your hopes weren't to be and that you have to make some readjustments. It is not something you can do suddenly. You gradually come to this point, maybe over the course of your infertility tests and treatments or maybe only when treatment has finished.

The way in which people cope with childlessness will depend on many factors, but remember that:

- There is no "right" way of coping with childlessness. Each person's way of coping will depend on their own experiences and emotions and has to suit that individual.
- You have to give yourself time.
- There will be times when it is easier to manage than at others, and your level of coping will fluctuate. There are bound to be moments of doubt and questioning - what if...?
- Denying that it is hurting doesn't help. The more you express your feelings in words, tears, writing down your thoughts or whatever, the easier it will seem.
- You may feel angry because the thought of childlessness might be so hard to contemplate. This might be directed toward your partner, yourself, your doctor. Recognise that this is a start to acknowledging your feelings.
- Try not to apportion blame - there is no one to blame
- Others have survived this crises and gone on to lead happy and contented lives.

Even as you get older, you may still find that other people treat you as "odd " or different" because you have no children. You have to accept this - and learn that you need not conform to others' norms to lead a happy life.

Creating a new identity without children is an important part of asserting control over your infertility. This involves trying to think beyond children and deciding what you want for yourself. The only effective way to cope with childlessness is to build up your self-esteem which may have been battered by the experience of infertility. Creating a new identity does not mean abandoning your reasons for wanting a child. Just as those reasons shaped your infertility experience, so they affect the form that your resolution takes. For example, you may choose to spend time with a children's organisation as a volunteer.

Taking an interest in other people's children on a regular basis may also be helpful. When you were a child, remember how you longed to see that special auntie or uncle? Enjoy the children around you - use your energies for a child that exists. Another useful outlet for the longing to nurture is to keep pets. A lovable and furry pet such as a dog or cat are most popular, because they can give love back, but infertile couples report pleasure in almost anything alive - from fish to flowers to gardens.

The passage of time heals - but it can't be hurried. Time brings a sense of perspective or the "larger view of life" for those who have had tunnel vision focused on infertility for a number of years.

Soul searching can be helpful - and try answering these questions together - honestly.

- Why do you want a child?
- Why would you not want to have a child?
- Think of the time before you tried for a baby. What made you happy? What did you do with your time? What did you look forward to?
- What are your other dreams and ambitions besides having a child?

Remember, that the value of, and reward from, a firm resolution are what you make of it. If you select a child-free life, and then treat it as a second-rate existence, that's exactly what it will become. But if you invest it with all your interests, pleasures, energies and talents, this lifestyle can be creative fun, delightful and filled with accomplishment. Such a lifestyle may not be for everybody, but it may be just right for you!

CHAPTER XXXII

Infertility Stress & Support, Coping with Infertility :

Stress And Infertility

What is the relationship between stress and infertility ?

Stress has become a buzzword today. It is one of the most over used words in our vocabulary - and one of the most poorly understood ones as well. Stress is defined as any event that a person perceives as threatening, and in order to protect itself, the body responds to stressors with a classic "fight or flight" response, which nature designed to allow survival. In response to stress, the hypothalamus produces a hormone called corticotropin releasing factor (CRF) which activates the hypothalamic-pituitary-adrenal (HPA) system, causing it to release neurotransmitters (chemical messengers) called catecholamines, as well as cortisol, the primary stress hormone.

The relationship between stress and infertility is still poorly understood today. While there is little doubt that infertility causes considerable stress, the question whether stress can cause infertility, and whether stress reduction can enhance pregnancy rates in infertile couples, is still very controversial.

Can stress cause infertility?

Can Stress Cause Infertility?

Historically, infertility, particularly "functional" infertility, was attributed to abnormal psychological functioning on the part of one or both members of the couple. Preliminary works in the 1940s and 1950s considered "psychogenic infertility" as the major cause of failure to conceive in as many as 50% of cases. As recently as the late 1960s, it was commonly believed that reproductive failure was the result of psychological and emotional factors. Psychogenic infertility was supposed to occur because of unconscious anxiety about sexual feelings, ambivalence toward motherhood, unresolved Oedipal conflict, or conflicts of gender identity. Fortunately, advances in reproductive endocrinology and medical technology as well as in psychological research have de-emphasized the significance of psychopathology as the basis of infertility, and modern research shows that there is little evidence to support a role for personality factors or conflicts as a cause of infertility. This perspective unburdens the couple by relieving them of the additional guilt of thinking that it is their mental stress that may be responsible for their infertility.

Biologically, since the hypothalamus regulates both stress responses as well as the sex hormones, it's easy to see how stress could cause infertility in some women. Excessive stress may even lead to complete suppression of the menstrual cycle, and this is often seen in female marathon runners, who develop "runner's amenorrhea". In less severe cases, it could cause anovulation or irregular menstrual cycles. When activated by stress,

the pituitary gland also produces increased amounts of prolactin, and elevated levels of prolactin could cause irregular ovulation. Since the female reproductive tract contains catecholamine receptors catecholamines produced in response to stress may potentially affect fertility, for example, by interfering with the transport of gametes through the Fallopian tube or by altering uterine blood flow.

However, more complex mechanisms may be at play, and researchers still don't completely understand how stress interacts with the reproductive system. This is a story which is still unfolding, and during the last 20 years, the new field of psychoneuroimmunology has emerged, which focuses on how your mind can affect your body. Research has shown that the brain produces special molecules called neuropeptides, in response to emotions, and these peptides can interact with every cell of the body, including those of the immune system. In this view, the mind and the body are not only connected, but inseparable, so that it is hardly surprising that stress can have a negative influence on fertility.

Stress can reduce sperm counts as well. Thus, testicular biopsies obtained from prisoners awaiting execution, who were obviously under extreme stress, revealed complete spermatogenetic arrest in all cases. Researchers have also showed significantly lower semen volume and sperm concentration in a group of chronically stressed marmoset monkey, and these changes were attributed to lower concentrations of LH and testosterone (which were reduced in the stressed group). However, how relevant these research findings are in clinical practise is still to be determined.

In addition to these direct effects, stress can also suppress libido, cause erectile dysfunction, and result in a reduction in the frequency of intercourse, which in turn could also reduce fertility. Also, many women start overeating in response to the stress of infertility. The increased fat cells then disrupt the hormonal balance, making a bad situation even worse.

While studies have shown that infertile couples do show psychologic dysfunction and even psychiatric abnormalities (such as depression or anxiety), this is actually a chicken and egg problem, and in reality the response of the infertile couple is a perfectly "normal" response to their abnormal situation, which is designed to help them to cope with the difficult circumstances they find themselves in. However, many people start blaming the couple, and many couples themselves start believing that it is the stress which they are under which is causing them to be infertile.

Victim blaming is popular - especially where fertility and women are concerned, and instead of providing them with support, couples receive completely gratuitous and unwanted advise. Ironically, victim blaming has become more prevalent today because of the fashionable "holistic health" belief about the influence of the mind on the body, which holds that even patients with cancer can cure themselves by the power of positive thinking. Many IVF couples too may subscribe to the belief that success is practically guaranteed if the patient remain optimistic and relaxed. Thus, if the attempt fails, it was because the patient was "too tense" or " too stressed out".

This myth has been perpetuated by anecdotes of friends or relatives who have conceived while on holiday, and stories of couples conceiving after many years of infertility after they have adopted a baby are a part of today's "urban myths".

Stress and infertility often have a circular relationship, and they can aggravate each other, setting up a vicious cycle. Infertile couples, who are under stress because of their

infertility, start blaming themselves for their infertility. This increases their stress levels and further aggravates the problem! As one mind-body expert has said, "Stress causes illness causes more stress which causes more illness."

How does infertility cause stress ?

Infertility Causing Stress

Research has shown that women undergoing treatment for infertility have a similar, and often higher, level of "stress" as women dealing with life-threatening illnesses such as cancer and heart disease. Infertile couples experience chronic (long-term) stress each month, first hoping that they will conceive and then dealing with the disappointment if they do not.

It is helpful to differentiate between external stress and internal stress; as well as stressors you can control and those which you cannot. Internal stress arises when you are not able to achieve the goals you set yourself while external stress is created by relatives, friends, and work pressures. Some stressors you can do nothing about - for example, the frustration you feel when your period starts. However, there are many others which you can control. As an example, many patients get upset when they are forced to wait in the doctor's clinic. Waiting can be stressful, so do carry a book to read - while you cannot control the stressor, you can modify your response to it, and this helps to decrease your distress.

Why is infertility stressful ?

Why Infertility is Stressful

When diagnosed with infertility, many couples feel helpless and no longer in control of their bodies or their life plan. Infertility can be a major crisis because the important life goal of parenthood is threatened. Most couples are accustomed to planning their lives and experience has shown them that if they work hard at something, they can achieve it. With infertility, this may not be the case!

However, not all stress faced by infertile couples is emotional or psychological - infertility treatment can be physically stressful as well! Blood tests; injections; hysterosalpingograms, inseminations and surgery can be painful, awkward, and embarrassing.

There is considerable financial stress too and this is especially acute for poor patients. Infertility treatment is expensive, and this represents a major hurdle. Many patients drop out of treatment because they cannot afford it, and this can be very hard to come to terms with, especially when they know they could have got pregnant, if only they could have afforded the treatment.

Some of the hormonal medications you may need to take can also cause mood swings and emotional upsets, making it harder for you to cope with the stress.

Don't forget the impact of being stressed on your personal relations. Being stressed out can add to marital distress and disrupt sexual intimacy as well, making a bad situation even worse. It can also alienate you from your friends, cutting off sources of support. Also, if you are always irritable, tense, and angry, it's going to be hard to build a rapport

with your doctor or his clinic staff. You may get a reputation as being a "difficult" patient, and this may make it harder for you to get good medical care. There are certain times which are especially stressful:

- Having to time sex when trying at home
- Waiting for the menses. The suspense can be killing each month - and is even worse when the period is delayed for any reason
- Having to answer questions from family-members and friends. Many of these questions are insensitive and hurtful.
- Having to juggle infertility treatment with work pressures
- Making a decision to see the doctor
- Deciding which medical treatment to take
- Waiting for results -Is the sperm count normal? have the eggs fertilized?

Many of these stresses are amplified considerably during IVF treatment. Many couples start IVF focused anxiously on one primary concern: failure of the procedure. To compound this anxiety, couples are aware that they have little control over the final outcome - and this helplessness can make the situation even worse.

The inconvenience of daily injections and blood tests, the perception of low success rates, the wait for results, and financial pressures only add to the travails. Often, IVF is their last hope after many years of trying, and they feel that their entire future rides on the outcome of the cycle.

While it is true that couples cannot control the outcome, they can be helped to control their responses to the various phases of the process and to the overall outcome.

It has been suggested that patients who are better able to cope with stress have higher pregnancy rates, although there have been relatively few studies in this area. Interestingly, we find that patients coming for the second IVF treatment cycle are much more relaxed and in control, so that they are less "stressed out".

What can you do to reduce your stress ?

What are Some Methods for Reducing Stress?

Perhaps the best general approach for treating stress can be found in the Serenity Prayer by Reinhold Niebuhr, "God, Grant me the serenity to accept the things I cannot change, the courage to change the things I can change, and the wisdom to know the difference." Remember that no single method is uniformly successful: a combination of approaches is generally most effective. Also, what works for one person does not necessarily work for someone else.

There are a number of very useful books which deal with stress management techniques in great detail. A special bonus is that these tools will help you cope with stress for the rest of your life as well! Some of these tools, which you need to learn how to use, so that you can deal better with the ups and downs of your infertility include: imagery, visualization, hypnosis, auto-suggestion, meditation, positive thinking, progressive muscular relaxation, deep breathing, biofeedback, and massage.

CHAPTER XXXIII

Infertility Help & Support from Stress, Coping with Infertility :

The Emotional Crisis of Infertility

Sir William Osler, a famous physician, once said that human beings have two basic desires - to get and to beget. To have your own family is a universal dream . This dream can become a nightmare for the infertile couple and learning that you have an infertility problem can cause painful and difficult emotions. Infertility is like a chronic illness that uses up a large amount of a couples' resources - emotional and financial - and involves the expenditure of a considerable amount of time, money, physical and emotional energy.

What are the emotional responses to infertility ?

Everyone's response to infertility is different depending on individual situations, emotional strengths, coping methods and personality. You will be confronted with the emotional impact of infertility before, during, and after treatment. It is better to prepare yourself for these difficult periods, so that with emotional support and mental preparation, you can successfully reduce the potential pain of infertility.

Discovering that you have an infertility problem

Although you may have friends who have experienced infertility and you're aware that it is a common disorder, the news is almost always unexpected. As you examine the issues surrounding infertility, you may find yourself experiencing some uncomfortable emotions. Some of the most common ones are:

Shock: In most cases, infertility is not diagnosed until after one year of unsuccessfully trying to conceive. Because of this, you may suspect that you have a problem before finding out for sure. For many couples, infertility is very difficult to accept. Most couples initially respond with feelings of shock and disbelief. After planning for years to have a child "one day", you may feel that your life's plan has been put on hold. These feelings generally only last a short while and are not emotionally harmful when you recognize and address them.

Denial: Another part of the emotional process is often denial. You and your partner may find yourselves saying "it can't be happening to us," and rather than confronting infertility, you may choose to deny the problem. However, this phase serves an important purpose and allows you to adjust to an overwhelming situation at your own pace as you work at resolving your infertility. Denial is only unhealthy if it lasts for a prolonged period and prevents you from accepting the reality of infertility.

Fantasizing: For some women, denial also leads to fantasizing - and they dream of what life would be like with a child. They feel that all their problems would be solved if they got pregnant . They lose touch with reality and everytime they start treatment, they think they are going to conceive . They find it difficult to cope when it fails.

Guilt: Guilt is an unfortunate but common response to infertility. In an attempt to determine why you are infertile, you may wonder if past behavior caused the problem. Some individuals may feel that they are being punished for past sexual activities or an elective abortion. Often infertile partners may feel that they are depriving fertile partners of the opportunity to have children. The inability to produce a baby may also make you feel you have let your family down because you have not been able to fulfill what is expected of you - especially so if you (or your husband) are the only son or daughter of your parents. In large joint families, this stress can be stifling - and fertile daughters-in-law are given special privileges from which infertile women are excluded.

Bargaining: This is a common response - especially if you believe in God. You promise to fast ; offer penance ; offer money; and to be good for the rest of your life if He gives you a pregnancy. Many infertile patients have visited an endless number of temples and "holy men" - and done "yagnas" and "tapasya" - in order to conceive, often at considerable expense.

Blame: You may blame one another for your inability to conceive, especially when only one member is infertile. Also, you may respond differently to the emotional aspects of infertility. For example, one of you may find that the other is less concerned about having a child. As a result of these differences, one partner may grow resentful because the other is not experiencing the same emotions on an equal level.

Sadness and Depression: The number of losses associated with infertility makes depression a very common response. In addition to the loss of a baby, infertility represents the loss of fulfilling a dream and the loss of a relationship that you might have had with a child. What you are mourning for is the absence of experience - and this type of sadness can be especially hard to deal with. You and your partner may have even more difficulty dealing with these losses because friends and family often underestimate the emotional impact of infertility - and you have no one to talk to . The nature of infertility is such that you may never know definitely whether you are able to conceive or what is causing the problem. Your grief therefore has nothing to focus on - and there is the continual hope that "this will be the time" which can leave your emotions painfully suspended, creating a continual "hoping against hope" attitude. When someone dies, the death brings family and friends together to grieve the loss - and this helps in healing . In contrast, infertility is a very private form of grief - you grieve alone without social support because the loss is hidden.

Hopelessness: Hopelessness is related to depression and usually results from the up and down cycle of emotions produced by infertility and its treatment. Most likely, you'll feel hopeful during mid-cycle when you've been treated and are looking to success. But if the cycle is unsuccessful, hopelessness can occur, and you may feel that you'll never become pregnant. Starting over again each month can make dealing with infertility especially tough. After the disappointment of several unsuccessful cycles, you may find it difficult to maintain a positive attitude. You may think that it gets easier with time - but it never does - and every time it fails, old wounds (which you hoped had healed) open again. After all, every time you start a treatment (especially when it is a new type of therapy

you have never tried before; or treatment with a new doctor), you always do it with the hope that "this" time it's going to work for you. If you didn't have this hope, no matter how small, no one would ever start treatment at all!

Loss of Control: You and your partner have probably planned your lives so that you'll begin a family at the most favorable time. Many of us think everything is possible if we work hard enough - and not being able to have a baby is often the first time you experience failure against forces at work which are beyond your control, no matter how hard you try. You may have practiced birth control for years and waited until your careers were established before trying to have a baby. Discovering that you are infertile removes these feelings of control over your own life. During treatment, you may find yourself putting other parts of your lives on hold. This might include postponing moving to a new home, continuing your education, changing jobs, or establishing new relationships. The more you give up, the less in control you're likely to feel. Each treatment cycle can become a roller coaster of emotions with its ups and downs - the hopes of success and the frustration of failure.

Anger: Anger arises from having to confront a great deal of stress and many losses, including the loss of control. It is not unusual to resent pregnant women, and friends and family who do not seem to understand the emotional tension associated with infertility. Often the anger is directed towards doctors - and this is one of the reasons why so many infertile patients change doctors so frequently.

Isolation: Feeling alone is a common experience among infertile couples and coping even more difficult. Most people cannot comprehend and complex feelings associated with infertility. Insensitive remarks, such as "relax and you'll get pregnant," or "after you adopt you'll have a child of your own," are not based on fact and can cause a great deal of pain. It is not unusual for relationships to change if friends and family are unable to understand and empathize with your feelings. Let your friends know that what you need is not their advice, but their support.

Infertility is an experience that continually fluctuates in intensity and direction, so that at different times you may have different needs and experience different emotions. There are no set "stages" in this experience, and, while, at one time, your emotions can be mystifying and frighteningly intense, at another time, you may simply feel numb. There may be moments when the fact of being infertile dictates every facet of your life. The way you learn to deal with the experience of infertility will also be different at different times. One day a particular strategy may help you a lot, but later on you may find it useless. At times you may find that the pain you experience is very destructive, but at others you may find it a useful motivating force in your life. It is important to acknowledge that emotional responses to infertility vary greatly, as do different people's methods of coping with them. Each person has to find his or her own way of coping with the infertility situation, and sometimes might need help to accomplish this.

CHAPTER XXXIV

Infertility Stress & Support : Coping with Infertility

How can you cope with the stress of infertility ?

Even though the stress of infertility is often unavoidable, there are many steps that you can take to decrease the pain. First of all, both of you must recognize that you'll have different feelings and different reactions at different times. If you expect your partner to behave in a certain way, you may create additional stress. Together, you should become informed about infertility and its treatment. Learn to focus on those factors which are within your control (for example,, stopping smoking) than those over which you have no control (for example, your age). As you examine the treatment options and emotional stages, you can identify in advance the times that you will have difficulty. Then, as a couple, you can plan to make them easier. Talk about your feelings concerning infertility and its treatment. Determine if your expectations of one another are realistic, and accept differences of opinion that your partner may have.

How can you share your feelings about infertility ?

Sharing Your Feelings

Sharing your feelings is essential when dealing with the emotional aspect of infertility. At times, valued friendships are especially important, but friends and family may not understand what infertility means, and they will sometimes make insensitive remarks. As a result, feelings of isolation may increase, and this could lead to depression and loneliness.

Although it is true that many people do not understand infertility, it is important to remember that others don't know what you're going through unless you tell them. If friends make discouraging comments, try not to close them out. You may want to attempt to let them know how you feel and how they can help. Some of the following tips may be helpful.

- Don't assume that everyone understands your needs and what you're thinking.
- Don't always put on a brave front. Friends and family may think that you are not distressed and don't need emotional support.
- Try to identify your feelings and share them. Putting your thoughts down on paper is often a helpful exercise.
- Offer friends and family reading material concerning infertility. Articles or books with quotes from individuals who are infertile are especially beneficial.
- Become aware of your own anger directed towards your body, your partner, and your friends. It is important to recognize its effect on you and your ability to communicate with others.

- Examine your expectations of yourself and try to understand that infertility can lead to feelings of helplessness and loss of control.
- Examine your expectations of others. You will be disappointed if you expect others to always be there for you.
- Accept your own feelings and acknowledge that there may be a time when it is okay for you to avoid certain emotionally painful situations.

How can you cope with your infertility in your daily life ?

Coping with infertility in everyday living

Undergoing treatment can "eat up" into your entire day - waiting to talk to the doctor, waiting to take your injections, waiting to do scans, waiting for blood test reports - it's endless and all you do is wait! The treatment seems to take all day - and you don't seem to have time to be able to do anything else. You need to take control of your time. While some waiting is unavoidable, a lot can be minimised. Can your husband learn to give you the injections so that you don't have to come into the clinic for them? Can you get the blood tests reports on the phone? Also, learn to make good use of the waiting time - you can read more about your problem ; and also talk to other patients in the clinic - this often become the place for an informal "support group" meeting!

The waiting to get pregnant also makes you put the rest of your life on "hold" you find you cannot make plans for the future because you do not know what lies ahead. Should you plan to go on a holiday next month - what if you get pregnant? Should your husband accept the new job, even if it means a transfer to another city and you will have to find a new doctor? This can be frustrating - not only are you not getting pregnant, but you also cannot get on with the rest of your life! You need to try to separate infertility from other important aspects of your life - and remember that you are a worthy person irrespective of your fertility. Women often have a harder time, because they have been taught that their life revolves around their family - which has yet to be started! Often getting a job is helpful, because it keeps you occupied and bolsters your self-esteem by confirming what you know - that you can accomplish useful things with your life irrespective of your fertility.

How can you cope with your friends and relatives ?

Talking to relatives and friends can be difficult when they ask awkward and thoughtless questions about infertility. Some typically painful questions include:

- So when are you going to start a family? You two aren't getting any younger!
- When are you going to stop concentrating on your career and start on a family?
- Well, I guess we'll never be grandparents.
- Oh, I have just the opposite problem - I get pregnant so easily.
- I wish you'd take one of my kids - they drive me crazy!
- I hear they're having tremendous success with test-tube babies. Why don't you try it?
- You can always adopt.
- Any good news yet?

Questions and comments from others can be turned into opportunities for you to explain your situation more fully to close friends; or you can discourage further discussion. Be firm and pleasant - and don't let yourself be put on the defensive. After all, just because a question is asked does not mean it deserves an answer, so with a smile, you can let them know that it's none of their business without being rude yourself.

Think about how you will respond to these questions - and plan ways in which you can successfully manage the conversation. There are emotional barriers between the fertile world at large and infertile couples - and you need to work to overcome this!

Dr Epstein has described activities which you can use to help yourself at <http://www.mindspring.com/~yepstein/activ.htm>. Check this out - it's a very valuable DIY resource !

What times can be especially difficult ?

Times that may be especially difficult

Social gatherings such as weddings where the conversation focuses on pregnancy and children can be difficult to cope with. You'll also inevitably have friends who become pregnant during your infertility treatment. The news that infertile friends have conceived with treatment can be bitter-sweet - you are happy for them, and know that this also means there is hope for you; but you feel it's unfair that you are not the one pregnant, and sometimes despair whether you will ever be able to have baby. Furthermore, holidays and birthdays may bring added stress by reminding you that time is passing by without children.

Time becomes the enemy - whether it is the incessant ticking of the biologic clock, or the endlessness of waiting for the next menstrual period. The few days before your next period is due can be hell for both of you. The suspense is killing - and you await every day with bated breath to see if the period has started. Each twinge of pain or drop of discharge is monitored carefully - and if the period is delayed, hopes start rising. Then, when the menstrual flow starts, all the castles in the air come crashing down, and you are inconsolable. You sometimes wonder - is it worth beginning all over again?

Coping with treatment is difficult too - especially when you know that for most treatments, it is impossible to predict what the outcome is going to be. Also, with nature's imperfection and today's technology, the chance of your not getting pregnant in any cycle will always be more than the chance of your conceiving. Often the key to success may be to repeat the treatment several times but this can be pure torture! You need to be realistic about your chances of conceiving - this level headedness can help to buffer the disappointments and tribulations of failure. Some women feel that they must maintain a "positive" attitude, no matter what and put up a brave front to the world - but pretending to be hopeful when you are broken inside increases your burden.

How can you regain control ?

Regaining Control

In order to decrease your feelings of helplessness and to regain control of your emotions, there are several things you can do. First of all, take the time to learn about your

infertility. By doing this, you will feel more in control at your doctor's office and you'll be better able to understand the tests and procedures that you're undergoing. Read about infertility treatment, and discuss your ideas and opinions with your physician. It's also important to talk with all of your health care providers. For example, your nurses may be able to help you with troublesome emotions as well as medical questions, or a technician could explain test procedures and results.

You need to make an "action plan" outlining possible courses of action as regards your medical treatment. For each treatment cycle, hope for the best and prepare for the worst. If you get pregnant, that's fine; but you should know what to do next if you do not so that you are not shattered when it doesn't work. Many couples refuse to think about the possibility of failure and plan treatment on an ad-hoc single cycle basis. This is unrealistic and you are only fooling yourself. Being realistic allows you to cope with the ups and downs of treatment - and you need to have a time perspective which includes 4 to 6 treatment cycles, so as to give yourself a reasonable chance of success.

During treatment, you need to set your own limits. Sometimes, treatment becomes a merry-go-round, which never stops and you find that you just can't get off. Some patients get "hooked" onto treatment and never give up - at great pain and expense to themselves. Decide when you will stop treatment and which treatments you will try. This is a decision only you can make and it should satisfy you that you have done all that you want to - so that you do not have any residual feelings of regret later! If medical therapy becomes too stressful, consider taking a break. When necessary, make it a point to remind friends and family that these are your decisions and that you know what's best for you.

Little things that you do for yourself can make a big difference in how you handle your infertility. Write down positive things you have done or good things that have happened, and read them often. Plan a special evening, and share your thoughts and feelings with your partner. You and your partner may want to join a support group so that you can meet people who are experiencing infertility. It is also important to become more informed about infertility, so that you can share this information with friends and family who do not seem to understand the stress and pressure surrounding this disorder.

Many patients find religious support at this time is very helpful - and a deep belief and abiding faith in God can help you immensely in tiding over this crisis in your life. Others use meditation to help themselves.

How does infertility affect your marriage ?

How Infertility Affects Couples

Infertility is a medical problem that involves two people - and both of you remain involved even if only one person needs medical treatment. Attend medical appointments together if possible - it is very lonely and frightening sitting alone in the doctor's office, and the support you give by your presence is very helpful. Sometimes the partner who is undergoing all the tests and treatment (usually the woman!) may feel resentful and angry at all the poking and prodding. Blow off your feelings - but not at your partner - rage at fate instead. Chances are your spouse would do anything to take this burden from you. If you are the partner who is not being treated, you may feel strangely guilty that you are getting off "free". You may also be upset and blame your partner for the infertility problems - but being upset and giving needless blame are two different things. Some

husbands are very upset about all the procedures that their wives have to undergo - and often cannot bear to see the pain they have to go through.

Men and women generally respond to infertility differently. Generally, while men are concerned about infertility, it may be less crucial to their self-esteem and identity. Also, handling the emotional impact of infertility may be more difficult for them because they are not used to voicing and sharing these types of concerns - they are taught to bottle up their feelings. On the other hand, women frequently accept the label of infertile as a key aspect of themselves and who they are. In Indian society, the pressure to conceive is directed towards the woman, and it is often she who has to bear the brunt of its impact. It is common among infertile couples for the woman to be the much more verbal and emotional partner. This often leads to the wife thinking and talking incessantly about infertility, and her whole world now revolves around how to have a baby. She talks (or complains or screams or cries) about it and wishes her husband could feel the intensity of her pain. He tries to be supportive, but never seems to be able to do or say the right thing, so he gets "put off and shut off" and refuses to talk about it - exacerbating the tension even more. In order to help keep infertility from becoming an all-consuming event and to break this vicious cycle of one-sided conversation in which no productive communication occurs, the "20-minute rule" recommended by Merle Bombardieri of Resolve, is very useful. You need to set aside a period of time each evening to talk about infertility. Use a timer to limit each person to 20 minutes and let one speak and then the other. The person not speaking needs to listen intently.

This technique is useful in achieving the following outcomes:

- The wife will talk less about infertility and will present her feelings more succinctly.
- The husband is more willing to listen because he is assured of an end point.
- The wife feels she has an interested listener and is supported.
- The rest of the evening may be spent in more pleasant pursuits.
- You may both feel relieved to see the other feeling better.
- In all likelihood, as the wife feels she has less need to talk about infertility, the husband will begin to be more expressive - so that the wife no longer needs to "grieve for two".

Communication in your relationship may change as you and your partner deal with infertility and its treatment. Sometimes, you may keep emotions to yourselves as you try to protect one another from painful feelings. This may create especially difficult feelings such as anger, blame, and guilt, and you may find that there is even more pressure in your relationship. You have the right to feel differently about infertility treatments and choices - after all, even though you are a couple, you are still individuals with your own separate identities. Individual responses depend on personality, coping mechanisms, who has the fertility problem, and your relationship with your partner. You may feel hopeful and optimistic, while your partner feels hopeless and despondent - and you may find that you are balancing on opposite sides of an emotional seesaw. You can agree to disagree - but keep your heads and fight fairly, and honestly.

Acknowledge the fact that infertility does put a lot of stress on the marriage. In fact, it is not uncommon for some marriages to break down because of the pressure which

infertility subjects them to. However, if you have the maturity to deal with this crisis in your life together, you will find that learning to cope with infertility allows you and your partner to grow and become closer as you share your feelings throughout this difficult time - and your marriage will become much stronger than most marriages because you have weathered a difficult time together successfully.

A sense of humour will help you cope much better with the stresses of infertility. I recommend that all my patients watch the film,

This is based on a true life story. Not only is it very funny, it will also help you cope better with your spouse !

What is the relationship between stress and infertility ?

Stress and Infertility

Most infertile couples are under considerable stress. Personal, social, family, financial. Hardly surprising - when you want to get something and you cannot, this is a perfectly normal and natural response. Thus, it's obvious that infertility causes stress.

However, what about the converse - can stress cause infertility?

Stress is ubiquitous, and- and in today's world, stress is something we are all exposed to. It has now become fashionable to blame the "stress of modern life" for all ills - including infertility, and many elders feel that it is the stress which the modern generation is exposed to, which is responsible for the increase in the incidence of infertility. Stress can cause disruption of the body's equilibrium, and excessive stress can interfere with ovulation, so that women may not produce eggs. While this is a biologic explanation for how stress can cause infertility, it is unfortunately become all too common to blame stress for everything. Often a form of victim-blaming - "You are too stressed out to get pregnant. Just relax and go for a holiday, and you'll get pregnant".

However, while stress can decrease fertility, it is obviously too simplistic to blame the couple for being stressed out. Thus, if a woman has blocked tubes, then this is going to cause her stress - and it's obvious that in this case it's the blocked tubes causing the stress, rather than the stress causing the tubes to get blocked! However, for some couples, specially those with unexplained infertility, this relationship can be a complex chicken and egg problem.

It is useful to develop constructive ways of coping with the stress of infertility. Many programs have focused on the mind-body relationship for the infertile couple, and have reported gratifying successes. While this is useful as a sole mode of treatment; it is perhaps even more useful in teaching couples to cope with the stress of taking treatment.

We too encourage our patients to be optimistic - to hope for the best, while preparing for the worst. However, since many patients blame themselves when they do not get pregnant, the backlash of this is that then the wife does not conceive, the husband often blames her further by saying she was too stressed out, which is why she didn't conceive. This is simply adding insult to injury, and is very unfair!

When should you seek professional help to cope with your stress ?

When Professional Help May be Necessary

If you remain depressed, rather than having "ups and downs" that seem to be related to

your treatment, you may need to seek professional therapy. Counseling can help you honestly examine your feelings, determine your priorities, and improve your coping skills.

There are several signs that indicate serious depression. If you find yourself constantly feeling sad, desperate, worthless, or inadequate, professional counseling may help you better understand your situation. Other signs that indicate a need for professional counseling are lack of motivation, withdrawal from social activities, feeling overly sensitive, vulnerable, or guilty, and having suicidal thoughts.

In addition to the emotional signs of depression, there are several biological and physical signs that you should look for. For example, if you're having difficulty falling asleep or staying asleep or if you find yourself waking up early and being unable to go back to sleep, this could signal depression. Other signs are excessive increase in or loss of appetite, loss of sexual desire, and fatigue.

You might also want to seek help if you and your partner are unable to communicate with each other about your infertility and its treatment, and if you're having difficulty coping with extreme anger or resentment.

It is important to select a therapist who has experience in infertility treatment and the difficulties and emotions that go along with it. Remember, you are choosing the therapist. It is acceptable to interview a number of professionals in order to select someone who is familiar with your situation and who makes you feel comfortable.

Dr. Domar has pioneered the development of specialized Mind-Body programs which are specifically designed for infertile couples. These teach couples useful tools, such as yoga and meditation, to help them to elicit the relaxation response which improves their physical and emotional responses to stress; and also behavioral strategies to enhance coping skills. The goals of these programs are to increase sense of control and well-being; and develop skills to ease the infertility treatment process, and has been shown to help many patients.

CHAPTER XXXV

Infertility Pregnancy and Sexuality

How does infertility affect your sexuality ?

Infertility brings about many changes in a couple's relationship. It may bond you closer together in unspoken sadness and hope - and allow mutual support and understanding which leads to a sharing never before experienced. Or it may bring out feelings of resentment, of guilt, and of despair. As the initial months of investigations turn into frustrating years it is not surprising that sex quickly loses many of its associations with pleasure and becomes instead an activity with a purpose.

Failure to conceive certainly destroys self esteem, self worth and sexuality. All these negative feelings are reflected in the bedroom, which is, after all, where all the 'problems' started.

The psychological effect of a diagnosis of infertility on sexuality has largely to do with the self image. Fertility is one very basic expression of sexuality. The man with six sons in many cultures has more status than a man who has borne none - he is considered to be more potent, more virile.

The emotional response to a diagnosis of infertility is a grief reaction. It involves many losses: those of potential children and the family planned and dreamed about, genetic continuity, the experience of conception, pregnancy and birth, the gift of grandchildren to one's own parents, the central meaning of one's life plan and marriage, and the procreative potential in sexual relations. It is common for a woman to feel "less of a woman" and a man "less of a man", at least for a time, when faced with infertility. Many men describe feeling a "dud", "sexual failure" and many other expressions relating to feeling emasculated.

Women, too, often feel their sexuality threatened when faced with the possibility of not becoming pregnant. Women are probably more powerfully socialised into the expectation that they will reproduce than are men. When this is thwarted, there is often the feeling of having failed as a "proper woman", as shown in this statement:

"I saw the blood (of the menstrual period) today. I feel weak and tearful. All the strength I'd thought I'd acquired just seems to have drained away. The discomfort serves as a reminder of my failure. For many women menstruation is a sign of femininity and potential for motherhood. All it signifies to me is my failure".

And another comment about sexual attractiveness:

"I have always been told I was pretty. I like the way I look, and I feel confident in social situations. After my pelvic surgery, the doctor told me he had never seen a worse mess of

adhesions in his life. He said it looked like a little kid had been let loose with a pot of glue and stuck everything all together. I am ugly on the inside and pretty on the outside. I would gladly have the reverse if it would make me a baby."

Which are the times when sexuality is particularly affected ?

There are significant periods which impinge on feelings about sexuality of the couple faced with infertility. These are:

1. Trying to get pregnant
2. Investigation and diagnosis
3. Treatment
4. Menopause

1. Trying to get pregnant

The usual advice for a couple trying to start a family is to have unprotected sexual intercourse for at least twelve months before having fertility investigations. This waiting period can be nerve-racking ! Doubts about one's fertility almost always result in a heightened awareness of signs of fertility that surround us. Pregnant friends, noisy children in markets, media coverage of new reproductive technologies, hints from eager parents wanting grandchildren - all these can begin to erode the sexual self-confidence of the couple wishing to have children. Inevitably, sexual intercourse is timed for the fertile time of the woman's cycle. Spontaneity goes out the window as the sexual life of a couple comes to be associated month after month with procreating and the failure to conceive. Men often come to feel like a stud bull, and women may feel it is pointless to engage in sexual activity when it is unlikely to result in pregnancy.

2. Investigation and diagnosis

Those not faced with infertility would be staggered by the number, complexity, and invasiveness of medical procedures that a couple with a fertility problem go through in their search for an answer to why pregnancy is not occurring. As one patient put it - " It's like donating your body to science while you're still alive!"

A basic procedure is the Basal Body Temperature Chart. Although useful from a medical point of view, it is also the surrendering of some very personal information about oneself, as shown by this quote:

"There is no inner recess of me left unexplored, unprobed, unmolested. It occurs to me when I have sex, what used to be beautiful and very private is now degraded and very public. I bring my chart to the doctor like a child bringing a report card. Tell me, did I pass ? Did I ovulate ? Did I have sex at all the right times as you instructed me?"

The Temperature chart becomes a way of ruling one's life - and ruining one's sex life. It is also a public declaration of making love. With the desire for a child becoming increasingly frustrated, life can become an endless maze of temperature changes,

ovulation calculations, timing of sex and the disappointing signs of one's menstrual onset. Anxiety, depression and fighting over sex can often be traced to this source. "Ordinarily my husband was the instigator of sex. During my fertile time, I felt I had to seduce him. What quite often happened was that we'd end up fighting instead of making love."

"It was pretty hard to feel an urge to make love when your wife is expecting a command performance."

It is not just the physical charting but the mental charting (which may continue indefinitely) that is a source of stress, even if the partner is not aware of what is happening.

"One of the things that freaked me out about charting my temperature was the accompanying need for the X's. I guess that is what brought home to me that we had stopped making love as frequently as we had used to."

"The ultimate moment for me was when I found myself 'cheating' on the charts. I put in a few more X's here and there to make things look good...then I said to myself, " Good heavens - has it come to this ?"

"At first it was quite exciting - I felt as if I was actually doing something. We would both look at the chart and go for, say, six X's in a row - in fact our frequency of intercourse increased I'm sure. By now we've gone through the stage of 'saving up sperm' and have hit the stage of almost total abstinence. I put in an occasional X so that the nurse doesn't get the impression that there's something wrong with our marriage."

Providing a sample for semen analysis can also be stressful:

"I looked around desperately for something to turn me on - there was nothing - not even soap. After 15 minutes I gave up - literally sore as hell."

Most men feel their masculinity is 'on the line' when having this done, sometimes to the extent of being unable to produce the specimen. It is not uncommon for the man to become impotent for a short time while he is undergoing such procedures.

"The first time it happened I thought - here it is - middle age. I'll never get it up again."

While post-coital tests are painless and physically unobtrusive, many find them very difficult because they intrude so much on your relationship. There's the need to comply with a specific time, the rush to the surgery or clinic to keep the appointment, the embarrassment and real fear of 'failure' if all does not proceed as had been 'instructed'.

"They told us to make love first thing in the morning and then come in. Well, what if you don't feel like it ? We're dreadful in the morning. We put the alarm on at 6 o'clock and we had the kettle on to make coffee...making love was the last thing we felt like doing...he hated it and I hated making him do it."

The power play dynamics in the doctor-patient relationship takes on a new dimension when fertility is being investigated. Couples are desperate to find an answer to their difficulties and hence are compliant and rarely let the clinician know they are under stress ("not coping"). They must expose the most intimate aspects of their lives - their sexual relationship and their desire to have children.

"There's a coyness about the way doctors handle sex. It's as if infertility has nothing to do with sex, yet it's everything to do with it. I never know whether I want them to assume that I don't have problems, or whether I want them to ask me if I do have any difficulties."

3. Treatment

A couple's decision to commence a treatment programme, such as IVF or Donor Insemination signifies hope and excitement that they can overcome infertility and produce children like everyone else. However, like the investigative period, it again signals a further, if not more intense, invasion of their sexuality and sexual relationship.

Once accepted on to an IVF programme, most women are confronted at each attempt with the barriers to becoming pregnant, to become mothers, and thereby expressing a major aspect of "femaleness". The low pregnancy rate - about 35% per treatment cycle - means most will leave the programme with a reconfirmed sense of failure, at least for a short time, and certainly if they have had little emotional support.

The use of donor sperm to cause a pregnancy, as in a donor insemination programme where the male partner is infertile, brings home to the man his inability to reproduce. Some of the feelings of inadequacy may have been worked through during the period following diagnosis, but it is not uncommon for these feelings to be rearoused when the programme actually begins. At most infertility clinics, the men are encouraged to be present while their wives are being inseminated. Some even do the insemination themselves (a painless and simple medical procedure). This encourages bonding between the couple at this time, and especially gives value to the participation of the husband in the act of the conception of their child.

During IVF treatment, after the embryo transfer, most doctors will advise patients not to have intercourse. However, this does not mean that you cannot have sex! Sex does not always mean putting a penis in the vagina - and you can use your imagination to give each other sexual pleasure in other ways - for example, by mutual masturbation.

With nearly all forms of infertility treatment, rarely is the infertility cured, and clearly not where donor egg or sperm is used. For example, women with blocked fallopian tubes who become pregnant on an IVF programme, still face further IVF attempts if they wish to become pregnant again. A feeling of defectiveness may remain despite pregnancy and a live birth.

4. Menopause

Menopause is a time when all women are confronted by their sexual identity, simply because the physical signs of being a woman are changing forever. It is a difficult time of adjustment for many women, and for those with infertility it means saying goodbye, yet again, to motherhood.

It is useful to ventilate feelings of frustration, anger, and feeling "taken over", as your sexuality gets trampled upon throughout the course of investigation and treatment. This will restore a sense of personal worth. Remember that it is normal, expected and almost inevitable that your sex life will take a beating for a time.

It is useful at this stage to join a support group or talk to a counsellor - who can help you to separate sex from reproduction - perhaps by throwing away the BBT chart for a while, or taking a break in the middle of a treatment programme to have a romantic holiday.

CHAPTER XXXVI

Infertile Couples : Problems, Help & Support Groups

Support Groups - Self-Help is the Best Help

Infertility causes great personal suffering and distress. Most of this is hidden from the public gaze, and this is why it is still not talked about openly. The reasons for the lack of public support for the infertile couple include: the dismal ignorance about the causes of infertility and its treatment; and the failure of infertile couples to make their problems (and the solutions to them) known to the public, because of their low self-esteem and reluctance to talk about their problems, thus making this a vicious cycle.

Infertile couples are socially isolated and emotionally very vulnerable. They need a place where they can get together and talk to people in the same boat as themselves, to help them tide over this crisis in their life. After all, if infertile patients will not look after their own interests, then who will?

Infertility Friends is India's first support group for infertile couples. This is a non-profit registered charitable trust for infertile couples, where they can get together and discuss their problems. In order to facilitate this process, the Patient Education Library has over 30 videos, 50 books and 100 brochures on infertility, which help patients to learn more about their problems.

Its mission is to provide compassionate and informed help to people experiencing the crisis of infertility ; and to increase visibility about infertility issues by public education. Its goals include: providing indepth, reliable medical information which encourages people to make informed decisions on options and treatment; encouraging patient self-education resulting in a stronger doctor-patient relationship; and offering emotional support services to reduce anxiety and help restore feelings of control, self-worth and optimism.

How does a support group help infertile couples ?

How does a support group help ? No one understands infertility as well as someone who has been there. However, finding another couple experiencing the same problem can be difficult. Infertile people simply have no way of finding one another without help - and this is where support groups can help. Contact with other infertile couples is one of the best ways to break through the isolation and despair of the infertility experience. You realise that "you are not alone" . By joining a support group you learn that there are others who can understand the devastation of a failed cycle or the jealousy of a friend's pregnancy. The craziness of scheduled sex, the exhaustion of endless medical treatments and the agony of family gatherings are all well known in a support group.

The best help is self-help; and an additional bonus many people find is that by helping other infertile couples in their time of need, they learn to help themselves ! Being able to ventilate your feelings and to get emotional support can be a healing experience.

The internet has also become a very valuable source of emotional support, and you'll find many online communities of infertile couples, who network with each other, and provide much needed support and practical information. These cyberspace support groups allow you to communicate with dozens of other infertile couples from all over the world ! The Internet provides a safe cloak of anonymity, so you never need to reveal your identity. A good example of such a support group, which uses bulletin boards to allow couples to "talk" to each other is at <http://www.fertilethoughts.net/>. You can post your message online, read about other's problems - and offer advise as well !

Unfortunately, misconceptions about support groups prevent many people from making use of this valuable help.

Some are concerned that joining might cause them to dwell even more on the infertility. But the reality is that infertility can pervade every aspect of your life and obsession with getting pregnant will occur whether or not you join a group. Trying to shut out painful feelings will only make them worse.

Others may feel that infertility is too private or personal or traumatic to share with a group of strangers. You may also believe that you should be able to handle this on your own. In truth, infertility is too traumatic not to share with others, and there is nothing wrong or weak about reaching out for help. A support group simply provides a safe, warm supportive environment - you need never say a word if you don't want to.

Another reason for not joining a group is concern that it promotes a feeling of futility. The perception may be that a group is only for those who have hit bottom or are without hope. This is far from the truth - and in fact, many support group members have ended up with successful pregnancies thanks to the information they obtained from the support group's library.

It's easy to believe that nothing except a successful pregnancy will make any difference in coping with infertility - but that's not true. Joining a support group may be just what you need to find crucial information or to deal with the devastating feelings that accompany being infertile. Joining may be frightening - but it's well worth the risk. You do not have to struggle alone.

Addresses

INFERTILITY FRIENDS,
59, Bombay Samachar Marg,
Fort, Mumbai - 400 023.

Voice Mail : 9721834

Email : malpani@vsnl.com

Website: <http://www.infertilityfriends.org/>

Additional useful sources of information include:

Resolve, Inc
1310 Broadway
Somerville, MA 02144-1731. USA.
www.resolve.org

The American Society for Reproductive Medicine
2140 11th Avenue South, Suite 200
Birmingham, AL 35205-2800. USA.
www.asrm.org

Infertility Federation of Australasia
PO Box 426
Erindale Centre
Wanniassa ACT 2903. Australia.
CHILD - The National Infertility Support Network
Charter House, 3 St Leonards Road
Bexhill on Sea, East Sussex, TN40 1JA. UK.
www.child.org

ISSUE
114 Lichfield Street
Walsall, West Midlands WS1 1SZ. UK.
www.issue.co.uk

CHAPTER XXXVII

Miths and Misconceptions

What are some of the myths and misconceptions about infertility ?

Myth: Painful periods cause infertility.

Fact: Painful periods do not affect fertility. In fact, for most patients, regular painful periods usually signal ovulatory cycles. However, progressively worsening pain during periods (especially when this is accompanied by pain during sex) may mean you have endometriosis.

Myth: Infrequent periods cause infertility.

Fact: As long as the periods are regular, this means ovulation is occurring. Some normal women have menstrual cycle lengths of as long as 40 days. Of course, since they have fewer cycles every year, the number of times they are "fertile" in a year is decreased. Also, they need to monitor their fertile period more closely, since this is delayed (as compared to women with a 30 day cycle).

Myth: Blood group "incompatibility" between husband and wife can cause infertility.

Fact: There is no relation between blood groups and fertility.

Myth: The reason I'm not getting pregnant is because most of the sperm leaks out of the vagina after intercourse.

Fact: Loss of seminal fluid after intercourse is perfectly normal, and most women notice some discharge immediately after sex. Many infertile couples imagine that this is the cause of their problem. If your husband had his climax inside you, then you can be sure that no matter how much fluid you lose afterwards, enough sperm will reach the cervical mucus. This discharge is not a cause of infertility.

Myth: If you work at it and want it enough, you'll get pregnant.

Fact: Unlike many other parts of your lives, infertility may be beyond your control. While newer methods of treatment have improved most couples' chances of having a baby, some problems are still unsolvable.

Myth: Just pray and have faith.

Fact: Believing in God can help you to maintain a positive outlook - but sheer will and blind faith won't overcome a physical problem like blocked tubes or absent sperms.

Myth: A man can judge his fertility by the thickness and volume of his semen.

Fact: Semen consists mainly of seminal fluid, secreted by these seminal vesicles and the prostate. The volume and consistency of the semen is not related to its fertility potential,

which depends upon the sperm count. This can only be assessed by microscopic examination.

Myth: Infertility is hereditary.

Fact: If your mother , grandmother or sister have had difficulty becoming pregnant, this does not necessarily mean you will have the same problem ! Most infertility problems are not hereditary, and you need a complete evaluation.

Myth: A retroverted ("tipped") uterus causes infertility because the semen cannot swim into the cervix.

Fact: About one in five women will have a retroverted uterus. If the uterus is freely mobile, this is normal, and is not a cause of infertility. This is not an indication for surgery !

Myth: We should be having intercourse every day to achieve pregnancy.

Fact: Sperm remain alive and active in woman's cervical mucus for 48-72 hours following sexual intercourse; therefore, it isn't necessary to plan your lovemaking on a rigid schedule. Although having sexual intercourse near the time of ovulation is important, no single day is critical. So, don't be concerned if intercourse is not possible or practical on the day of ovulation.

Myth: A woman ovulates from the left ovary one month and the right ovary the next month.

Fact: Only one ovary actually ovulates each month. However, the pattern may not be regular from side to side.

Myth: Pillows under the hips during and after intercourse enhance fertility.

Fact: Sperm are already swimming in cervical mucus as sexual intercourse is completed and will continue to travel up the cervix to the fallopian tube for the next 48 to 72 hours. The position of the hips really doesn't matter.

Myth: If you just relax, you'll get pregnant.

Fact: If pregnancy has not occurred after a year, chances are there is a medical condition causing infertility. There is no evidence that stress causes infertility. Remember, all infertile patients are under stress - it's not the stress which causes infertility, it's the infertility which causes the stress !

Myth: Periods that occur less than or greater than 28-day intervals are irregular.

Fact: A woman's period will often vary from month to month. As long as a woman can count on a period at a regular interval every month, this is normal.

Myth: I've never had symptoms of a pelvic infection, so I can't have blocked tubes.

Fact: Many pelvic infections have no symptoms at all, but can cause damage, sometimes irreversible, to tubes.

Myth: My gynecologist has done an internal examination and said I am normal; therefore I should have no problem getting pregnant.

Fact: A routine gynecological examination does not provide information about possible problems which can cause infertility.

Myth: If a woman takes fertility drugs, she'll have a multiple birth.

Fact: Although fertility drugs do increase the chance of having a multiple pregnancy (because they stimulate the ovaries to produce several eggs) the majority of women taking them have singleton births.

Myth: A man's sperm count will be the same each time it is examined.

Fact: A man's sperm count will vary. Sperm number and motility can be affected by time between ejaculations, illness, and medications.

Myth: I have no problems having sex. Since I am virile, my sperm count must be normal.

Fact: There is no correlation between male fertility and virility. Men with totally normal sex drives may have no sperms at all.

Myth: All physicians are equally interested in the treatment of infertility.

Fact: Not all physicians or even all infertility centers have similar interests. It is important for you to ask your physician about the available treatment he/she can offer you and what are the pregnancy results following such treatment in his/her practice.

Myth: Infertility treatment should not be offered in India, because there are too many babies in this country already . Why exacerbate the population problem by producing more ?

Fact: The right to have children is a fundamental right of every human being and a very basic biologic urge. Just because a neighbour has too many children should not deprive the infertile couple of their right to have their own.

Myth: Azoospermia (no sperms) is a result of excessive masturbation in childhood.

Fact: Masturbation is a normal activity which most boys and men indulge in. It does not affect the sperm count. You cannot "run" out of sperms, because these are constantly being produced in the testes.

Myth: It must be the couple's fault if they are infertile.

Fact: Infertility carries a major social stigma - and this "victim-blaming" is very common, partly because most people know so little about their own fertility.

Myth: Infertility is not a medical illness and treatment should not be covered by insurance.

Fact: Infertility is a medical problem, which is often amenable to medical treatment. Insurance should cover the treatment costs.

Myth: IVF is too expensive for India to be able to afford.

Fact: IVF and related technologies are undoubtedly expensive - but then, so is heart

surgery. Yet, no one objects when over Rs 1 lakh are spent to try to salvage the heart of a 70 year old man (whose life expectancy in any case is only about 5 years and is not extended by the surgery). Why then should medical technology not be used to help couples in their thirties (with their whole lives ahead of them) have their own baby ? In fact, IVF is a much more cost-effective use of medical resources than a number of other accepted surgical procedures (such as joint replacement surgery or kidney transplants).

CHAPTER XXXVIII

Helping Hands - How Friends and Relatives Can Help

How can friends and relatives help infertile couples ?

This chapter is to help friends and family members to understand the needs of an infertile couple better. Sometimes it's difficult to know what to say to a couple who are confronted by an infertility problem because it's such a private matter, that you'd rather not intrude. And, sometimes, it seems as if no matter what you do or say, it's the wrong thing.

Here are a few suggestions which may help you provide the support they need.

1. Be ready to listen. Infertile couples have a lot on their mind and need someone to talk to - help them get things off their chest.
2. Don't offer advice unless you are very well informed . You may not be sure what their specific medical problem is - and in any case, if they need medical advice, they can get it from their doctor.
3. Be sensitive and don't joke about infertility. Remember, infertile couples are hypersensitive about many things - try to put yourself in their shoes.
4. Be patient. Infertile couples are on an emotional roller-coaster and often their moods and actions are unpredictable. Don't get hurt when they seem to be preoccupied with their problems - they are not rejecting you when they want to be alone.
5. Be realistic and supportive of their decisions. Once they've reached a difficult decision, support them, no matter what your personal feelings may be. After all, this is their decision , so don't say things like " I'd never consider doing that !"
6. Don't criticise their doctor or treatment choices. This only serves to aggravate their stress.
7. Understand that individuals and couples respond to infertility differently. Accept them for what they are, as they are, when they are.
8. Above all, be there when they need you and show them that you care.

There is rarely a quick or simple answer to infertility problems. Assessment and treatment procedures usually take considerable time. You can help by not forcing the issue with questions such as "When are you going to have a baby ?" They may not know if they can have a child, much less when it will be. You can help by allowing them to decide if and when they want to talk about it.

Each couple's experience of infertility is very real for them and cannot be compared with others as being more or less serious. The wish to have a baby, and the fear that it might

not be possible, is of paramount importance. You can help by not comparing them with other people you may know about. Refrain from telling stories about other infertile couples - they are rarely helpful.

It is not helpful or medically sound to offer advice such as "relax", "take a holiday", etc. You can help by not giving misguided, albeit well intended, advice, and by helping to break down the myths that surround fertility difficulties.

Some people consider infertility to be a private concern. Yet others find comfort in being able to share it with close friends and family members. It is normal for people to feel sad, angry or depressed at times. You can help by respecting their need for privacy - or, by offering support if there is a need to talk about it. Be prepared to accept the expression of feelings such as anger, sadness and depression.

Those experiencing infertility often feel inadequate because they have no control over their reproductive system. You can provide support by recognising and helping them to see the strengths, qualities and achievements in other areas of their lives.

Some people experience fertility problems after having one child. This is devastating and frustrating for those who feel their families are incomplete. You can offer support by understanding what this means to them. Avoid comments such as "You're lucky to have a child at all!".

Your encouragement, understanding and support for your infertile friend or relative can help to guide them on their long road to resolving their infertility. This support is crucial to their emotional healing.

CHAPTER XXXIX

Rights of the Infertile Couple - and What Society Needs to Do About Them

How can the community support infertile couples ?

The right to have a baby is something most of us take for granted , and we often lose sight of the fact that 1 in 10 married couples will not be able to have the child they want. Infertility is a very common problem , and if you stop to think about it, you will realize that you know at least one person who is infertile amongst your own group of friends or relatives. However, it remains one of those taboo topics which no one wants to talk about, even though it interferes with one of the most fundamental and highly valued human activities - building a family.

Millions of infertile couples in Indian cities today face many obstacles in their attempts to build a much-wanted family, and one of the most frustrating is the lack of insurance coverage for medical treatment. What this means is that while infertility specialists in India can provide even the most advanced reproductive techniques to solve extremely complex infertility problems, at a level of sophistication which is comparable with that in the West (and at a fraction of the price) most couples cannot avail of these techniques because these are not covered by their insurance policy. So near - and yet so far , would sum up the situation for most couples! The financial burden that some of the treatments may place on couples can be large, and adding this on to the emotional and physical consequences of experiencing infertility can literally be the last straw which breaks the camel's back. The strong desire to build a family gives many the strength to face these obstacles, but infertile couples also need additional support from their employers and insurance companies!

While most diseases and medical conditions are covered by insurance, the disease of infertility is often singled out for exclusion, and such discrimination is unfair! Thus, to add further insult to injury, infertile couples not only face the emotional pain associated with not being able to have a child, but also face obstacles put in front of them by their health insurance and employers for reimbursement of the medical expenses they incur on their treatment!

Unfortunately, insurance companies in India still do not provide health insurance coverage for infertility. This is a very archaic attitude, but because the insurance industry in India is still a monopoly, this situation is unlikely to change, until the field gets privatised, or Indian companies fall in line with their Western counterparts.

Insurance companies have traditionally denied claims for infertility on one of the following flimsy pretexts:

1. Infertility is not an illness
2. Treatment of infertility is not medically necessary
3. Treatment of infertility is experimental
4. Infertility treatment is too costly for a country like India to offer

However, it has now been well established that infertility is an illness, which is caused by various medical causes which result in the abnormal functioning of the reproductive systems (such as blocked fallopian tubes or a low sperm count); and that these can be successfully treated in most cases. Medically necessary is usually defined by insurance policies as medically appropriate for treatment of an illness under professionally recognized standards of health care - and treatments such as GIFT, IVF, and ZIFT are now universally acknowledged to be standard medical treatments, which are no longer experimental. While certain infertility treatments can be costly, most are quite inexpensive, and only about 5% of all infertile couples will need expensive treatments like IVF. Moreover, if expensive medical procedures like bypass surgery can be covered, then why should treatment for an abnormally functioning reproductive system be excluded?

Why this discrimination against infertile couples in India? Ironically, this is because of the high premium Indians have always placed on the family unit! The major role of the woman in Indian society was seen to be to have children to propagate the family name. Therefore, if a woman could not have children, she was singled out, ridiculed, ostracised and stigmatised! In fact, given the value Indians have placed on having children, infertile couples should actually receive even more tender loving care from others - and be helped in their quest to complete their family! However, because of centuries of misconceptions and myths regarding infertility (for example, "a barren woman has been cursed by God , and being punished for the sins of a prior life"), it will take a long time for social attitudes in India to change! Infertile couples are an easy and soft target for everyone - ranging from:

- friends ("life is incomplete without a baby!")
- in-laws ("when will I become a grandmother?")
- relatives ("what do they want to earn money for - they do not have any children to leave it to!")
- neighbours ("they may have a lot of money, but what's the use, they don't have any children")
- acquaintances ("no good news yet? Go see this doctor my sister-in-law's cousin went to - he's the best!")
- co-workers ("you don't have any kids, so can you stay on a little longer to finish this job - I need to go back to take care of my children!")
- right to servants (" the reason she shouts so much is because she doesn't have any children - serves her right!")

(Gentle reader, if you recognise yourself here, please suffer a pang of guilt, and promise to improve your behaviour the next time round!)

Many otherwise enlightened people take the attitude that infertility treatment is elective - and even compare it to cosmetic surgery! However, infertility is a serious medical condition - it is both a disease and a life crisis! Others pontificate that these couples should just adopt a baby, rather than take treatment. While adoption is an excellent method of building a family for some couples, it is not acceptable to everyone- and forcing couples to do so when they don't want to is very unfair.

A major problem is that infertile couples in India are too ashamed to stand up for their own rights - with the result that they often suffer in silence! However, infertility exacts a high toll! Not only do many marriages break up, many women are abused for being infertile as well. Also, infertile employees, because of the emotional stress they are under, are often not as productive in the workplace as they could have been if their problem was successfully resolved.

Fortunately, this discriminatory attitude is now being challenged by advocates for infertile couples - at least in the US! The pathbreaking Americans with Disabilities Act (ADA), provides protection against discrimination for Americans with a disability - a disability being defined as "a physical or mental impairment that substantially limits one or more major life activities." The US Supreme Court has clearly ruled that reproduction is a major life activity.

Since infertility is a physical impairment that substantially limits the ability to reproduce, this means that if an individual experiences discrimination because of his or her infertility, a claim can be made that this is illegal under the ADA. Thus, a police woman employed by the city of Chicago sued the city recently because it did not provide infertility insurance coverage. The Court ruled that infertility is a disability under the ADA, and today the city of Chicago covers the cost of infertility treatment incurred by all its employees!

Many employers in India are not still aware of the issues and concerns facing those with infertility. Employers need to be more understanding of the special needs of those of their employees who are infertile, and be willing to make workplace accommodations for those undergoing infertility treatments - for example, allowing the employee to change her work schedule or to take some time off. Employers, insurance companies, and legislators in India also need to take steps to recognize that reproduction is a major life activity - and that infertile couples need all the help we can give them!

Unfortunately, most infertile couples in India do not feel comfortable speaking publicly about this very private struggle, even though they represent all racial, religious, socio-economic and ethnic groups, as well as both sexes. Infertility Friends, India's first support group for infertile couples, plans to actively lobby for recognition of infertility as a medical problem by insurance companies to enable members to benefit from Mediclaim and other medical insurance facilities.

We all need to remember that infertile couples are our neighbors, co-workers, friends and relatives - and they just want to experience the joy of raising a family - an experience that so many of us take for granted!

CHAPTER XL

Alternative Medicine & Infertility : Exploring Your Treatment Options

There is no doubt that modern medicine inspires awe. IVF laboratories and sophisticated ultrasound scanning machines appear very impressive and reassuring when you are infertile. However, paradoxically, even though the effectiveness of reproductive technology has improved dramatically, more infertile patients than ever before have become dissatisfied with their medical care today. This situation has resulted in a move towards 'alternative' medicine, which has become increasingly popular all over the world. Even in the United States of America (the bastion of high-tech scientific medicine), more than 20 per cent of infertile couples have consulted an alternative medicine practitioner, mainly because they were unhappy with modern medical care.

Why are some couples unhappy with modern infertility treatment ?

There are many reasons for this unhappiness with modern medicine. Patients increasingly feel that medicine has become too commercial and that doctors are too busy to spend time with them. They are unhappy with the impersonal nature of modern medicine, especially when the doctor spends more time looking at their lab reports and ultrasound scans, rather than with them. While it is true that patients need technology, they also need tender, loving care; after all, doctors need to look after not only their medical problems, but also their emotional needs!

What can alternative medicine offer infertile couples ?

Alternative medicine, on the other hand, offers a markedly different perspective. Rather than focussing on the infertility in isolation, alternative medicine treats the patient as a whole; hence the popular term, holistic medicine. Doctors practicing alternative medicine sit down and talk to the patient; they touch and feel him and ask many questions. And such attention feels good, in refreshing contrast to the modern doctor who rarely has even 15 minutes to spend with the patient. (Often, tender loving care and personal attention are all that alternative medicine practitioners have to offer, but they offer it very well indeed!) There is no doubt of the efficacy of the placebo effect, and even the simple act of touching the patient, can have a therapeutic effect. Also, alternative medicine doctors are very good at reassuring patients, as contrasted with the coldly scientific approach of western medicine.

Many patients (usually those with unexplained infertility or with ovulatory disorders) do conceive when they use alternative medicine. However, the practice of alternative medicine in India today leaves a lot to be desired. For one, such medicine does not have a universally accepted scientific basis; hence, it is difficult to rigorously analyze its claims. Since there is no need for formal publication or peer review in alternative systems of medicine, there is little scientific documentation available about their efficacy or side-

effects, so that it becomes difficult to confirm claims or dispute them. Consequently, one has to blindly trust the doctor.

Authoritative journals or texts are difficult to find; and most publications use little scientific rigour, being based mostly on anecdotal case reports, with little documentation or proof. Moreover, since there is no official monitoring of the practitioners of alternative medicine, anyone can make tall claims and get away with them! Also, since there are few formal training requirements, anyone can practice alternative medicine, with minimal skills or qualifications. Unfortunately, unscrupulous practitioners have mushroomed, who are out to make a quick buck, and malpractices and quackery flourish, which is why most infertility specialists distrust alternative medicine practitioners today.

How can you protect yourself from quacks ?

How can you protect yourself from quacks ? Remember that quackery is not an all-or-nothing phenomenon. Some products can be useful for some purposes, but worthless for others. For example, while certain ayurvedic herbs can be very useful, often the mass-manufactured ayurvedic medicines available in chemists' shops are completely useless, because they do not contain what they are supposed to! While there is no doubt that homoeopathic medicines can be helpful, the concept of a standard homoeopathic remedy for common illnesses such as headaches and colds flouts a basic homoeopathic principle, which states that remedies need to be tailor made for a particular person and only a skilled homoeopathic physician can identify the required medicines properly.

Unproven methods are not necessarily quackery. Those consistent with scientific concepts may be considered to be experimental, but legitimate practitioners do not go around promoting unproven procedures in the marketplace. Instead, they engage in responsible, properly designed research studies to prove or disprove their claims.

Quackery can harm individuals in many ways. First, is the loss of a tremendous amount of money which patients invest in pursuing this treatment, and many unscrupulous practitioners can bleed patients and their relatives dry - a little at a time. Also, many of the quack therapies can cause direct harm. It is a common misconception that 'natural medicines' have no harmful side-effects - but anything which can have an effect, by definition, also has the potential to cause harmful effects (after all, the desired effects of a medicine are what we call its therapeutic action and undesirable effects are labeled 'side-effects!'). The indirect harm they cause can also be enormous: for example, patients may pursue 'alternative medicine' for treating their infertility and may deprive themselves of the opportunity of getting effective state-of-the-art medical treatment.

Quackery flourishes even in the USA where people are much more sophisticated, and the US Food and Drug Administration (FDA) provides effective policing. Therefore, it is hardly surprising that in India this menace is rampant, and there are far more quacks than regular medical practitioners. Faith healing, for example, is an integral part of Indian traditions, especially in villages where educated priests take advantage of people's ignorance and blind faith.

How can you save yourself from being quacked? Here are some useful pointers by Dr. Stephen Barrett from his Quackwatch Web site (at <http://www.quackwatch.com/>.)

1. Forget about 'secret cures'. True scientists share their knowledge as part of the process of scientific development. Quacks often keep their methods secret to

- prevent others from decisively demonstrating that they don't work. No one who actually discovered a cure for infertility would have reason to keep it secret. If a method really works, the discoverer would gain enormous fame, fortune and personal satisfaction by sharing the discovery with others.
2. Remember that quackery often garbs itself in a cloak of pseudo-scientific respectability and its promoters often use scientific terms and quote (or misquote) from scientific references. Be equally wary of pseudo-medical jargon. Instead of offering to treat your infertility, some quacks will promise to 'detoxify' your body, 'balance' its chemistry, release its 'nerve energy' or 'bring it in harmony with nature'. The use of concepts that are impossible to measure or quantify enables success to be claimed even though nothing has actually been accomplished.
 3. Ignore any practitioner who says that infertility is caused by faulty nutrition or can be remedied by taking supplements. Although some diseases are related to diet, most are not. Moreover, in most cases where diet actually is a factor in a person's health problem, the solution is not to take vitamins but to alter the diet.
 4. Be wary of catchy anecdotes and testimonials. If someone claims to have conceived after using an unorthodox remedy, there is often a rational explanation. Some patients with long-standing unexplained infertility do get pregnant on their own - and they may erroneously give credit to the treatment. Some testimonials, of course, are complete fabrications!
 5. Don't let desperation cloud your judgement! It is true that infertile couples are very susceptible to being quacked, but if you feel that your doctor isn't doing enough to help you, don't stray from scientific health care in a desperate attempt to find a solution. Instead, discuss your feelings with your doctor and consider a consultation with a recognized expert.

The best way you can protect yourself from being taken for a ride, is to make sure you are well informed about your infertility. The 'take-home message' is simple: if it sounds too good to be true, it probably isn't!

Unfortunately, because of widespread quackery in the field of alternative medicine, most infertility specialists today have a poor opinion of what alternative medicine can offer their patients. This often means that doctors end up throwing the baby out with the bath water! There are many areas for which Western medicine today has little to offer the patient. Examples include: medical treatment for a low sperm count, or treatment for a thin endometrial lining. It is possible that alternative medical systems may have effective techniques for treating these conditions - and if we research these, and show that they are effective, we may be able to make significant progress in our ability to help infertile couples.

How can you use alternative medicine intelligently ?

Amongst the various options available, acupuncture has become quite popular, and the theory behind this is that it can re-balance the bioenergy of the body that runs in the Meridian pathways, and this helps to improve tissue function. The "scientific" explanation is that it changes levels of neurotransmitters, the chemicals that nerve cells use to communicate. Herbalists may recommend ginseng as a "tonic" for men and women ; and a combination of false unicorn root (helonias) and vitex tinctures for

women. This realm of herbal practice is probably for experts only, as we still do not know all the side effects of these herbs. In general, it's best to take as little medication as possible when you are trying to get pregnant. Nutritionist therapists suggest using supplements which contain arginine, beta carotene, zinc, and Vitamin C and Vitamin E. Aromatherapists may give a clary sage oil massage which is said to improve estrogen levels; and rosemary, tea tree, lavender and other anti-infective oils for an abdominal massage.

An important area to consider is the mind/body connection. There are now clinics in the USA that claim to have good pregnancy results with meditation, yoga, relaxation and visualization techniques. Again, solid documentation of these results is lacking, but you may want to try these out.

For options like ayurveda and homeopathy, it is important that you go to a reliable practitioner, because these are complex sciences, and you need expert guidance to achieve the best results. We feel that diverse modalities such as massage, Reiki, yoga, ayurveda, acupressure, acupuncture, hypnosis, homeopathy, naturopathy and many others can work in conjunction with each other as part of a unified team rather than in competition.

We need to learn to combine the best of both worlds - high technology with high touch - and this is called integrative medicine, as pioneered by Dr Andrew Weil of the USA. Integrative medicine neither rejects conventional medicine nor embraces alternative medicine uncritically - just because most alternative medicine systems are 'natural' does not automatically make them better! The most important requirement is that you need to find a good doctor, no matter what system of medicine you choose to follow.

It is equally important that you understand the limits and the rationale of the system, so that you are not taken for a ride. Thus, if you have blocked tubes, remember that it is very unlikely that herbal medicine will help you open them. Also, do remember that infertility is a heterogeneous problem - and some modes of therapy may be better for treating certain problems, rather than others! A good doctor will be able to guide you, so that you are aware of the strengths and limitations of each approach.

As a patient, you should feel free to explore all possible options - remember that they are not competitive, and should be seen to be complementary to each other - after all, the goal for all of them is to help you to have a baby! Thus, if you find that Reiki helps you, you can combine Reiki treatment with IVF if you so desire! There is no harm in going to an alternative medicine doctor - but do let your infertility specialist know what other treatments you are taking. The combined knowledge of both old and new healing modalities is ultimately superior than a single-model approach - and you can learn to combine the best of both worlds!

CHAPTER XLI

Making Decisions about Treatment

How can you be sure you are making the right decisions about your treatment ?

Discovering that you have a fertility problem can be a difficult process. In addition to the emotional stress you now find yourselves faced with making endless decisions about treatment. The word "decide" comes from a Latin root meaning "to cut away from." Thus decision making, by its very nature, involves loss, giving up one or more options while grasping another. Not deciding maintains the illusion that you can have it both ways - that there is no loss, no risk. Unfortunately, most infertile couples have not learnt to make their own decisions - and not making decisions is one sense the worst possible decision of all! You cannot allow your doctor to make treatment decisions for you either - this can be disastrous as well.

How can you identify your fertility goals ?

Identifying Your Goals

Most likely, your original goal was to have your own biological child. However, because of your fertility problem, you may be forced to examine your deepest feelings about family, children, and parenting. You could find that you have to re-evaluate your initial plans in order to get the family that you want.

As you work to identify your goals and examine your options, you'll discover that essentially, there are four choices as regards treatment. Depending on the cause and treatability of your infertility, you may need to choose one of the following options:

- To pursue having a biological child with infertility evaluation and treatment
- To try to have a child biologically related to only one parent, either through donor insemination or egg donation
- To adopt a biologically unrelated child
- To decide to remain childless

You may want to rate each of the four options as "desirable," "acceptable," or "unacceptable" at the beginning of your evaluation and periodically re-evaluate these choices.

For some infertile couples, trying to have a biological child and childlessness (child-free living) are the only options. For , the switch from having a biologically related child to adopting or having a child biologically related to only one parent may be easier than having no children at all.

Many couples lose track of the fact that their main goal is to be parents, even if they can't be biological parents. Therefore, they may pursue infertility treatment for several years

and find themselves above the age limit to adopt an infant through an agency. Furthermore, since a woman's fertility decreases after the age of 35, this also decreases the chances of successful treatment. You and your physician should try to take these possible consequences into account when evaluating and choosing your options.

If you are relatively young, there may be a good chance that you will achieve pregnancy without expensive procedures. Therefore you may not wish to explore these as yet. If you are older and have less chances of conceiving, a more aggressive approach might be called for, since time is at a premium.

The decision making process is different for each couple and depends on individual situations and personalities. For example, some couples may opt for expensive high-tech treatments, while others in the same situation will wait to see if they can become pregnant without treatment.

What kinds of infertility treatment are Available?

What Kinds of Treatment are Available?

Once you've discussed your infertility with your physician, you'll find that there are a number of treatments available. These include:

- Medication that may be prescribed for either partner to improve fertility
- Surgery to correct an impediment
- In vitro fertilization (IVF) or gamete intrafallopian transfer (GIFT) for patients who require assisted reproductive technologies
- Donor insemination, if male infertility is the problem
- Egg donation, if the woman cannot produce eggs
- Embryo adoption
- Surrogate parenting, if the woman has no uterus
- Adoption

What questions should you ask your infertility doctor ?

Questions You Should Ask Your Doctor

Your doctor may be able to make recommendations about treatment - but there are a number of questions that you should always ask your physician so that you can make the best decision. Unlike other medical questions, infertility recommendations are not always clear. You need to evaluate whether and how well each treatment option will help you reach your goals. Then you'll have to determine which options you will pursue. The following questions may help you build a foundation of medical information to assist you in your decision making process.

- How much will this treatment improve our chances of pregnancy?
- How much risk is involved and what kind of risk is it?
- How long will we have to undergo this treatment in order to give it a reasonable chance to work?
- Will undertaking this treatment eliminate other options?
- How much will the treatment cost?

- Are there other options if this treatment fails?

Your physician can help you determine how much time, physical discomfort, risk, and money will be required for a particular treatment option. You will have to decide how much money you are willing to spend, and how much emotional stress you can take.

You need to design your own fertility treatment plan. Not only will this help you maintain control over your life as you proceed with treatment, it will also help to ensure you get good quality medical care.

What are the issues which will affect your final decision ?

Issues Affecting Your Choice

Issues which affect your choice include:

Medical Factors:

- Diagnosis (or lack of one)
- Quality and availability of medical care
- Success rate of treatment
- Level of technology required

Personal Factors:

- Age
- Time commitment needed for treatment
- Personal feelings - physical and emotional
- Partner's feelings
- Job and career
- Financial resources
- Ethical and religious concerns
- Family and friends
- Other obligations and commitments
- Willingness to change life-style Aggressive or low-key approach to resolution

Each of us has a different personal decision-making style. It is for you to choose which one of the following best fits your own personal style for making medical decisions:

- I prefer to make the final selection of my treatment after seriously considering my doctor's opinion.
- I prefer that my doctor make the final decision with regard to which treatment should be resorted to, after seriously considering my opinion.
- I prefer to make the final selection about which treatment I will receive on my own.
- I prefer to leave all decisions regarding my treatment to my doctor.

It is important to understand that there are no right or wrong styles, and that your style may change as you proceed through diagnosis and treatment. It is imperative that you find a doctor who respects and understands your personal decision-making style.

Just as there are no right or wrong styles, remember that there are no right or wrong decisions about your treatment, and as your options change with time, you may also change your priorities. Counselling may be helpful in setting your priorities - especially if you and your partner disagree on the course of action. As your options change with time, you may also change your priorities. Try to be as realistic and open-minded as possible. While the final outcome will always remain unknown at the time of making decisions, if you take the time and the trouble to make your own decisions, at least you will have the satisfaction of knowing that you tried your best!

In order to make infertility treatments less stressful, you'll need to place time limits on them. Doing this may help you define your goals more clearly. Many couples are willing to accept only two to three years of therapy, because continuing treatment for long periods of time may cause excessive stress.

It is important that you do not lose sight of your relationship with your spouse. Make sure that each of you understands how the other feels about each stage of treatment. Throughout treatment, both of you may encounter times of ambivalence about having children. This is a normal reaction, and you should remember to have realistic expectations of one another.

If reasonable goals are maintained and difficulties and limitations are kept in mind, stress can be minimized. If this is not the case, then a break from treatment, change in plans, or counseling for stress and marital issues may be good idea.

What tools can you use to make better decisions about your options ?

Sometimes, recording information on a worksheet can be helpful. Here is a sample worksheet for making medical decisions about treatment:

	Option 1	Option 2	Option 3	Option 4
Benefits				
Success				
Risks				
Costs				
Time				

Decision (in the rank of choice)

You may want to take each of the options your doctor has suggested, gather the information you need, and go over the options in terms of :

- Time
- Physical and emotional risks
- Cost
- Chances of success, with and without treatment

Also keep in mind how much money and time is needed, what is available and how much you are willing to invest. As you go through this decision-making process, you will probably find that your answers change with time.

If you do not conceive after pursuing your initial plan of treatment for a set period of time, you may need to re-evaluate your goals and options. You may find that you want to discontinue medical intervention, or you may want to seek a different kind of treatment. Keep in mind that it is not at all unusual for partners to have differing views and feelings about infertility and its treatment . Open communication can help both of you to make the best decision.

How can you prepare yourself ?

Facing Treatment

An early step in the entire process is to try and prepare yourself . Ask yourself if it is worth the risk of pursuing treatment without a guarantee of success. Anticipating difficult situations and emotions may help you deal with them more easily.

Your doctor can provide you with information and can refer you to further sources. You can take steps to prepare yourself for what could be a long and frustrating process. But you may also find that as you and your partner work through the stages of infertility treatment, your relationship grows stronger.

Your physician, support groups, other couples who have made similar decisions, and counselors can also provide support and guidance. Above all, remember that with patience, a positive attitude, and the appropriate treatment, most infertile couples can eventually become parents.

CHAPTER XLII

How to Find the Best Doctor

How do you go about finding the right infertility doctor ?

In a perfect world, you'd have the perfect doctor, who treats you as an intelligent couple, has plenty of time, infinite wisdom, low fees, is totally honest yet compassionate, has a conveniently located clinic and understands your emotional as well as medical problems. While you may never find such a doctor, you need to keep your picture of your ideal doctor in your mind when you are looking for the physician of your choice.

You can find a doctor through:

- Professional referral. Ask any doctor you know for suggestions.
- Friends, other infertile patients, and infertility support groups.
- The yellow pages can also serve as a useful source of possible names if you need to make a comprehensive list.

You can phone the doctors on your list. Although it may appear unorthodox, "telephone shopping" can provide you with a lot of useful information about an individual doctors practice, including details of clinic timings, fees, qualifications, hospital attachments, special interests. After all, if you are willing to research which travel agent will give you the best deal on a holiday trip, then isn't it worthwhile researching into whose hands you are going to put your life in? You can learn a good deal about the doctor and his practice, even before you actually meet him, by merely telephoning and asking the right questions.

While it is true that many mediocre doctors flaunt posh clinics, the setting in which the doctor functions can reveal a lot about him. Is the clinic located in a decent building? Is public access easy? Has the doctor bothered to provide the basic amenities you need (e.g., drinking water, comfortable seating)? What kind of reading material is kept in the waiting area? (Old and torn magazines should qualify as a negative mark . Patient educational literature and current issues of health magazines indicate that the doctor respects your waiting time and wants to use it to educate you). Are the office staff member helpful? How do they answer the telephone? How do they treat other patients? you can learn a lot about a doctor and his practice from the personality of his employees: remember that efficient, caring physicians tend to hire competent, friendly personnel!

What criteria can you use to assess your doctor ?

While selecting a suitable doctor can be difficult, try to find answers to the following questions.

- Credentials - training and qualifications
- Skill and experience

- Accessibility (locations; clinic timings)
- Affordability (fees)
- Professionalism
- Does he prepare for your appointment?
- Explain records and test results?
- Keeps appointments and values your time?
- Manage an efficient clinic?
- Review your status and progress periodically?

Personality and style:

- Does he talk to you? Take time to listen to what you have to say?
- Does he show empathy and compassion?

A good infertility doctor will usually:

- involve both husband and wife in consultations, discussions and planning
- offer recommendations and choices. Since there are no "right" answers, he should allow you to choose your own course of action.
- tailor testing and treatment to your emotional needs and budget
- have time to answer questions and offer support
- chalk out a treatment plan for you, with a discussion of rationale, alternatives, costs, time limits and expected success rates.

Many patients are still not very sophisticated when it comes to selecting their doctor . Most Indians follow a herd mentality, and believe that a busy doctor must be the best - after all, if so many patients go to him, he must be good. However, remember that you need to be more critical when making such a crucial decision - after all, you have to trust that your doctor's skills will provide you with the best treatment for your infertility . There is little point in going to a doctor who is so busy that he has no time to talk to you, or who cannot even remember your name!

Most gynecologists can provide basic infertility workup and testing - but you may prefer to look for a specialised infertility clinic which will provide all the services you need under one roof, especially if you have a complex problem. Many gynecologists are not really geared up to providing the care which an infertile couple needs, and it's not much fun sitting in a room with pregnant women who have come for their obstetric care, if you are infertile.

What are the risks of going to a general gynecologist for your infertility treatment ?

The risks of going to a general gynecologist for treatment are:

1. They may not have the expertise or specialised knowledge to treat your problem, since they may not be aware of recent advances in this field.

2. They may not have access to the specialised tools needed to treat you, with the result that you may have to run around from the doctor to the lab to the ultrasound clinic for your treatment.
3. They may not have a special interest in treating infertility, so that you may end up getting "second class" treatment.
4. A common mistake many gynecologists make is that they keep on repeating the same treatment again and again - wasting valuable time and money in the process.

We often find that by the time patients come to us, they are so fed up and frustrated, since they have wasted so much time and money on repeating ineffective treatments, that they have lost confidence in doctors - and in themselves as well! Don't let this happen to you! While going to an infertility specialist can help you to ensure you are on the right track, this does entail the risk of "overtreatment" as well. Unfortunately, many infertility clinics are happy to do IVF for all infertile patients who come to them, whether or not they really need this!

Which is the best way of getting a second opinion ?

Getting a second opinion

Get a second opinion - this can never hurt and is always helpful. If you find two experts saying the same thing then you know you are on the right track! If on the other hand, they disagree, don't get upset - there are few black and white areas in infertility, and doctors often have different ways of treating a particular problem. Ask questions of both of them and then choose the method which appeals to you - it's finally your decision!

What if you don't understand what the doctor is saying and are getting confused? This is not your fault . If you do not understand anything the doctor says - ask questions! If you still do not understand the fault is his - he is not explaining in terms which you can follow. Find another doctor!

Remember that you need to ask questions to get answers - your doctor cannot read your mind! But also remember that your doctor does not have all the answers - after all, medicine is still an imperfect science, and your doctor is not a fortune-teller. If he does not know the answer, he should tell you this as well.

What can you expect during your first consultation with an infertility doctor ?

How do we do a consultation in our practise? We first ask the couple why they think they have not been able to conceive, and how they expect us to be able to help them . The answers give us a good idea of how much the couple understands about their problem. It's often heartbreaking when we see couples who have been through 3 IVF cycles, and don't even know how many eggs they grew or how many embryos were transferred each time - or even why the IVF was done in the first place.

During a consultation, we first explain, using models, how babies are made. We then review the medical records, and explain to the patient what we feel their medical problem

is. We then explain to them what the treatment options are, and tell them to think about these and then make up their mind. In our clinic, we do not charge for a repeat consultation, in order to encourage patients to ask questions, and to give them time to make up their own mind. We take pride in the fact that our patients have a good understanding of their medical problem, and realistic expectations of how we can help them!

Remember that the purpose of a consultation is to get information. If you do your homework before going, you will be able to make better use of your doctor's time, since you can focus on the issues which are important to you. You then need to go home and process this information, so you can decide what to do. It's very difficult to think straight when you are sitting in front of the doctor, so it's usually a good idea to give yourself enough time to apply your mind and assimilate the information, before making a decision.

There is usually no urgency, since infertility treatment is never an emergency. Beware of a doctor who wants you to decide on the spot - it's hard to do so under pressure, and you may end up making a decision in haste, which you may then repent at leisure. In order to encourage patients to think for themselves, we request them to come back a second time a few days after the consultation. We do not charge for this repeat consultation, and we find this policy allows our patients to ask their questions and decide for themselves!

When should you change your doctor ?

As an infertile patient, you are very liable to being exploited - and quacks in this field abound! Suspect your doctor's credentials when:

- He promises too much.
- He says things like - "that's my secret."
- He doesn't explain clearly what he is doing during treatment.
- He advises too many tests and surgical procedures repeatedly.

When to change doctors

Because infertility is often a long drawn-out process, anger is a natural result - and often this is transferred to your doctor. However, constantly changing doctors or doctor-shopping can be counterproductive! If the quality of care you are receiving is good, be cautious about changing doctors - a doctor who knows you and your infertility well can be of significant help to you.

Changing doctors is never easy, because, over a period of time you do build up a personal relationship with your doctor. However, you should consider changing doctors if you feel that:

- the doctor is incompetent (i.e., he has ignored obvious symptoms, missed a diagnosis, prescribed the wrong drug, or can't get to the bottom of your problem)

- the doctor does not communicate with you effectively (i.e., his explanations are not in lay person's language or no time is given to you to ask questions and bring up related problems)
- the doctor does not pay attention to your needs and concern
- you have lost confidence in the doctor's skill and ability
- you find the doctor is too inconsiderate (i.e., he makes you wait a long time for an appointment, he fails to return your phone calls, he does not provide clinic time during evening or weekend hours)
- your doctor is too expensive.

A common problem patients face is that when they go to a new doctor, he insists on repeating all the tests all over again. While this can be frustrating and expensive, it can be helpful as well, because it allows the doctor to reassess your problem with a fresh perspective. Please ask your doctor to explain why he needs to repeat the tests, and how this will help in your treatment. If tests have already been done, but are more than a year old, or if they have been done from an unreliable lab, you may need to repeat some of these again.

It is all too common to find that infertility clinics do not provide complete medical treatment details to their patients. They often do this in order to make sure that the patient remains with them, and does not go to another doctor. This is very unfair - remember that your medical records are your property, and you are entitled to a copy of them.

You may find that your new doctor criticises the treatment your previous doctor provided. Remember that doctors do have big egos, and they are often intensely competitive and critical of each other. This can upset you, because you may start feeling that you were given substandard medical care. As long as you have a clear understanding of what was done to you and why, you should ignore this criticism - don't let it disturb you. Anyone can be wise with hindsight - and do remember that all doctors will try to do their best to help you to get pregnant!

Many doctors will repeat exactly the same treatment the previous doctor has administered - often because they have nothing better to offer! However, remember that even though you have changed your doctor, you have remained the same - and the purpose of changing doctors should be to allow you to progress further with your treatment.

How should you select an IVF clinic ?

Choosing an infertility clinic

Many couples ask us whether they should travel abroad for treatment. Fortunately, the quality of medical care available in leading IVF clinics in India today is easily on par with the world's best clinics, since they use exactly the same equipment, and the same techniques. In fact, IVF treatment in India is an excellent bargain by international standards, since you are getting exactly the same quality of treatment you would get anywhere else in the world - at a fraction of the cost. This is why so many IVF clinics in India routinely treat infertile couples from overseas.

How does the quality of care in the smaller towns in India compare with that available in the metropolises? Do you always have to travel to a clinic in a large city for treatment? Since there are no standards or regulations (IVF clinics in India today do not need to meet any quality control criteria) you need to be an educated shopper! While the quality of care can be quite good in smaller towns, most of the reputed clinics are in the larger cities. These bigger programs are usually better, because they are busier, and more experienced, and busy IVF programs (which perform more than 150 treatment cycles per year) have been shown to have higher pregnancy rates. However, very busy clinics may not be able to provide you with the personalized care you need, and some can be quite uncaring, so that they make you feel that you are just a cog in a machine. For simpler treatment such as IUI, it is best to look for a good clinic in your own town. However, for advanced treatments, you may be better off going to an established clinic. While traveling can add to your stress and expense, many infertile couples actually prefer not having to take treatment in the city which they live, as they would like to protect their privacy.

Why do you need to be an active participant in your infertility treatment ?

The need for active participation

Remember, you are in charge of your own medical care! Medicine, as both a science and art, often requires choices and there are no "right" answers - you need to make your own decisions. After all, it's your body and your life!

You have a vital interest in treatment decisions and outcomes but lack the medical knowledge and skill to decide alone. The concept of a team - the medical caregivers (doctors, nurses, specialists) and you (the couple), working together, allows each to contribute to a successful outcome and offers you a sense of control over your infertility care.

Your role on the medical team is multifaceted - you need to wear many hats when you are an infertile patient!

Medical Information Researcher: The more knowledgeable you are about your problem and its treatment, the better are your chances of getting pregnant. Educate yourself - you need to become an informed participant in your infertility care in order to ask the right questions and to participate in making decisions about your treatment. After all, what's the point of being intelligent if you cannot use your intelligence to help solve your own problems? You will also need to be able to critically assess press and media reports about " new breakthroughs in infertility treatment" ; and whether these are relevant to your problem or not. An Infertility Support Group Reference Library can be very helpful. A friend who is a doctor can also help in separating the wheat from the chaff. While you do not need to become a doctor, you do need to become an expert on your own problem! You cannot afford to leave everything up to God - or up to the doctor!

Medical Team Manager: Remember - you are the one in charge! You will have to locate, choose, evaluate and sometimes fire members of the medical team. Treatment

Decision Maker: Although your doctor may be better equipped technically to select treatments, the ultimate decision rests with you. Each new treatment phase requires new decisions - allow yourself time to choose and be comfortable before starting a new treatment.

Treatment Monitor: You are the "expert" on what is normal for you - so record and report reactions. Combining medical and patient information helps to improve the odds for successful treatment.

Medical Record Keeper: You must keep all your records - this can be very helpful if you need to change doctors or get a second opinion. File all records in reverse chronologic order and also prepare a one-page summary sheet of what you've been through.

Financial Manager: Infertility treatment can be very expensive - and sometimes it seems to be an endless drain on your financial resources. You must be aware of the costs involved - and you need to decide if you can afford these.

Communicator: Because infertility involves such personal matters as reproduction and sexuality, people sometimes find it embarrassing to discuss their concerns. It is important that you be open and honest with your doctor. Ask questions, listen to the answers and take notes. It often helps to write down your questions before your appointment, so you do not forget important concerns in the stress of the consultation. Remember, the only stupid question is the one you don't ask - so don't hesitate to ask!

What are your rights as a patient ?

Your Rights

1. You have the right to be treated in a humane manner with care, consideration and dignity.
2. You should be given a clear, concise explanation in non medical terms of your problem by your doctor.
3. You should be given a clear, concise explanation of any treatment or investigation including whether such treatment is of an experimental nature.
4. You have the right to have your partner with you in the consulting room.
5. You are entitled to refuse an examination, a particular treatment, or an operation.
6. You have the right to ask for a second opinion. Ask the specialist you are seeing or ask your general practitioner to refer you to another specialist.
7. You have the right to see your medical records.

What are your responsibilities as a patient ?

Your Responsibilities

1. Be assertive - ask, demand, tell, confront, book, change, refuse, persist, understand, question. You don't need to be aggressive - remember, the doctor is on your side!
2. Be well informed - join a self help group. Read the available literature about your particular problem.
3. Keep your own record of all tests, results, and treatments.
4. Make a list of questions before your doctor's appointment - and write down the answers. If you wish to tape the interview, ask the doctor's permission.
5. Book a long appointment if you feel you need more time with the doctor.
6. Inform the doctor or his receptionist if you are unable to attend a consultation.
7. Take your partner with you to the doctor - it can be mutually supportive
8. Defer any treatment you are unsure about .
9. Do not have unreasonable expectations about your doctor. Understand that he may be tired, rushed or sick at times.
10. If you cannot communicate with your doctor, it is in your interests to find someone you can talk to.
11. If you are dissatisfied with your treatment, try to discuss this with the doctor.
12. If you have unexplained infertility and all investigations and treatments have been tried, you may like to return to your doctor every two years to check on new developments in infertility treatment that may help you.

What emotional support can you expect from your doctor ?

Emotional Care

When confronted by infertility, you need more than just medical care - and a good doctor will help to provide you with emotional support as well. Unfortunately, doctors often end up amplifying the stress infertile patients find themselves having to cope with.

Many doctors make patients wait long hours, for no good reason; and others are often insensitive to their emotional needs. Others may be quite thoughtless, and instead of trying to provide special attention to the needs of infertile couples, make them wait with pregnant mothers in the clinic.

A good clinic, on the other hand, can help to alleviate your stress, by recognizing it; teaching patients that this is normal; and showing them how to cope with it. A good doctor will be able to establish a relationship with the couple, based on understanding and respect, to help them maintain and rebuild their self-esteem.

What questions should you ask your doctor ?

Questions to Ask Your Doctor

- Do you have experience in fertility treatment? When do you consult with an infertility specialist?
- Will you refer me to an obstetrician when I get pregnant or will you deliver the baby?
- Will you send me to any other physicians or laboratories for treatments or tests?
- Will you treat my spouse? If not, who will?
- Do you arrange for adoptions?
- Do you document surgeries with photographs or videotapes so I can see your findings for myself or provide them to other doctors?
- Which hospital(s) do you use?

Questions to ask About Tests, Surgery, and Treatments

- What kind of procedure is it?
- What will the procedure tell you?
- What results do you expect?
- How long will it take?
- What will it cost? Does insurance cover it?
- Will it hurt? How will it make me feel afterward?
- Can you do it in your office? As a hospital outpatient?
- Will I be incapacitated? For how long? Will I miss work?
- Will my spouse be involved? How? Will he/she miss work?
- Will it interfere with our sex life? How?

Questions to ask About Medications

- How long will I take it?
- What will it cost? Does insurance cover it?
- Will it hurt or have side effects?
- Do I take it at home or at your office?

CHAPTER XLIII

How to Make the Most of Your Doctor

Remember that just finding a good doctor is not enough. For an infertile couple, the doctor-patient relationship is the ultimate one-to-one relationship, in which you confide fully in your doctor and trust him to help you to conceive. You need to form a partnership with your doctor, so that you can make the most of his skills and abilities.

How can you improve your relationship with your doctor ?

In order to foster and nurture the relationship with your doctor treat it with great care and respect. Don't forget to say 'thank you' to your doctor - after all, he gets fed up of attending to droves of patients with complaints all day long , and would be delighted to hear a patient appreciate his efforts! This simple expression of gratitude by you would make the doctor remember you as a person and treat you as a special patient; getting VIP attention from him helps improve your medical care a good deal! As in a marriage, the doctor-patient relationship depends on good communication and trust built up over time. It is definitely worth spending time and taking trouble to maintain such a beneficial relationship.

Remember that the doctor's staff plays a key role, and you need to learn how the clinic functions. It's very helpful to build up a rapport with the staff (the receptionist, a nurse or an assistant), which can prove very useful when you need to talk to the doctor on a priority basis. The simple rule is that if you treat the staff well, you will be treated well too! A small 'thank-you' gift for the staff can help ensure that you get personalized attention. It's useful to learn which days are the busiest and what times are the best to consult the doctor. You should also find out what steps to take if there is an emergency, or when the clinic is closed.

What do you need to do before you go to your doctor ?

Your visits to the doctor can be expensive, despite being very short. Many doctors have perfected the technique of flying into the examination room, shooting off questions, and rattling off advice. And, before you know it, you're shoved out of the door, worrying about those crucial matters you forgot to ask and the directions you forgot to write down. So, what's the solution? Is there really a secret to getting your money's worth from a doctor's visit? Yes, there is, and it's a simple one: Do your 'homework' thoroughly before visiting the doctor! In order to make the best use of your doctor's time, you need to 'prepare' for your visit, very much like you prepare for an examination. Time spent in getting organized before you go to the doctor can help immensely! A well-organized patient not only makes efficient use of the doctor's time but he is also likely to get better medical care, as he can help the doctor to make an accurate diagnoses. A conscientious patient makes sure that he has all the records with him as well as the vital questions to which he needs answers (preferably, in writing). Patients who value the doctor's time will

do their best to get answers to their queries by tapping external sources such as books, libraries and the Internet, before going to the doctor's clinic. This procedure will allow them and their doctor to focus on what is important to them, so that they can make the best use of the limited 'quality time' that they have with the doctor.

Your doctor is definitely not a mind-reader; you must tell him everything you know, think, and feel about your problem if you want an accurate diagnosis and the best treatment plan. (There is no need to be shy or embarrassed about sensitive subjects such as sexual problems or sexually transmitted diseases as far as your doctor is concerned. Rest assured that doctors have 'seen it all' and 'heard it all'. They're not there to pass moral or ethical judgement on your conduct.)

Do not hesitate to share your thoughts with your doctor. If you think what he is recommending does not make sense, say so, and specify your reasons. If you're worried, do express your anxieties and find out how you can get more information and support to dispel them. If you sit on your chair and listen meekly, your doctor will either assume that you are uninterested in a full explanation --- or that you are too stupid to understand! Remember: the more you ask, the more you will be told!

Do keep in mind that doctors are also human, and they may also be burdened by their own problems. On certain days they may seem rude or curt; on such days, give them a little leeway and a lot of understanding!

Since it is your head on the block, so to say, you are entitled to raise all relevant questions and seek satisfactory answers to them. If you cannot understand your doctor's explanations, ask him to repeat everything in simpler language. Ask him to show you illustrations; also, ask for written material that explains the medical issues in greater detail, so that you can study this later at leisure.

How should you talk to your doctor ?

The following terms can be very helpful when you talk to your doctor:

- Please tell me more about that.
- What does that mean in simple English?
- Could you explain that to me again?
- Could you write that down for me?
- Where can I find more information about this subject?
- You seem rushed. When can I call you to talk about this in more detail?

Try to schedule your next visit at the end of the consultation. If the succeeding question-answer session is something which can be managed on the telephone, then try to do so. You could save both time and money by avoiding an unnecessary visit to the doctor's clinic.

What should you do when you need to phone your doctor ?

However, you need to learn to make intelligent use of the phone to get appropriate help from the doctor. The following routine may help you to help the doctor give you the care you need over the telephone:

- Keep a pen and paper ready so that you can write down the relevant instructions.
- Make sure all your medical records are at hand, so that you can answer questions about your medical problem intelligently and accurately.
- Identify yourself properly, giving your full name as well as your diagnosis (try not to tax your doctor's memory!).
- Ask if you can take a few minutes of the doctor's time now, or whether you should call back again - this is common courtesy!
- Report specific symptoms. For example, rather than just saying, 'I don't feel well, or I've got the flu,' which can be interpreted in different ways, be prepared to describe your symptoms precisely; for instance, fever, sore throat, cough, and/or bodyache.
- When you don't know what you need (for example, you may not be sure how serious the illness is, i.e., if you require a visit to the clinic), tell the staff you're uncertain and request that you speak to a nurse or the doctor's assistant over the phone. Don't be hesitant; if you're feeling concerned or anxious, let the clinic staff know.
- Don't insist on talking only to the doctor every time you call. For example, if you just need to make an appointment, or merely clarify a doubt, the nursing staff or receptionist may be able to help you. To put it differently: respect your doctor's time!
- Don't misuse the phone by trying to wangle a free consultation. Not only is this act unfair to the doctor, but also such a consultation is likely to be very unreliable!

Today, many physicians make themselves, an assistant or other staff member available to their patients over the phone. Pre-visit questions and routine follow-up on the phone can save you - and your doctor - both time and money. Before making a call, you need to certain relevant information in advance:

- When is the best time to call?
- What is the doctor's rule for returning calls?
- Whom should you speak with (e.g., assistant, nurse) if the doctor can't come to the phone?
- What is the phone number for making emergency calls or for calls when the office is closed?
- Whom can you call if your doctor is out of town?

Making effective use of the telephone can help to save both you and your doctor considerable time, effort and money! learn to use this instrument wisely and well.

Many doctors today are happy to answer your queries by email - and this can be very helpful if your doctor is in a different city. Please find out from your doctor what his policy about email queries is !

What tools can you use to make the most of your doctor's visit ?

It's a good idea to carry written checklists with you during every visit. You may have a wide range of questions you would like to ask the doctor, but as a result of the stress generated by the consultation you often forget most of them. Such a situation is very frustrating, and you kick yourself when you get home. To prevent such an adverse outcome, it is prudent to, write down all the questions you need to ask, in order of priority. It is also helpful to write down the doctor's answers. Studies have shown that patients forget about 50 per cent of what the doctor tells them during a visit! Writing down the doctor's answers will prevent such a 'disaster'! Moreover, your doctor also stands to benefit because you need not pester him with your queries all over again!

Try to make sure you go for your consultation as a couple. The presence of your spouse can help reduce your anxiety, give you courage to ask the relevant questions, and also ensure that you have someone to interpret the doctor's statements. As mentioned earlier, do not hesitate to ask questions (and more questions); never mind how many other patients are waiting outside the doctor's clinic, or how stupid the questions may seem to you. When you are with the doctor, his only focus of interest should be you, and it's his job to provide answers. Remember, the only stupid question is the one you didn't ask. Be courteous but assertive while asking questions and obtaining information, but don't turn aggressive or antagonistic. Listen carefully to what your doctor says, and in case of doubt and ambiguity, do not leave till these have been dispelled. Remember, the word doctor is derived from the Latin root docere, which means 'to teach'. Therefore, look for a doctor who is willing to share his knowledge with you!

The most common complaint patients have is that they are made to wait for ages before the doctor sees them! It is only because patients put up with such a situation that doctors get away with this unpardonable behavior. After all, no doctor would remain very busy if all his patients decide to refuse to wait for him! Some patients seem to believe that the longer they have to wait outside the doctor's clinic, the better he must be, since he has so many patients clamoring for his attention. This is simply not true! No matter how hard-pressed a doctor may be, he can always space out his appointments, so that you never have to wait for more than an hour to see him.

In order to ensure that you don't lose your patience while waiting in the clinic, it would be a prudent idea to carry a paperback novel or a Walkman. Nowadays, many doctors keep patient educational leaflets and brochures in their clinics. You could read them in order to use your time constructively! Some clinics are also 'blessed with TV sets, so that patients do not get totally fed up.

While an occasional delay is unavoidable (since a medical emergency could require your doctor's immediate attention), if you are made to wait for an eternity each time,

something is seriously wrong with the doctor's attitude towards patients. For any inordinate delay, the clinic staff should be courteous enough to provide an explanation, and, if needed, an alternative appointment. As an example of efficient patient management, if a doctor at the famous Mayo Clinic in the USA makes you wait for more than 30 minutes without an explanation, you can complain to the hospital manager who will rectify matters.

Make sure you carry photocopies of all your medical records and tests. You can give them to the doctor for his files, if needed. You should have a clear understanding of your medical records so that you can explain the details to another doctor if needed.

Try to do your best to become an ideal patient, and learn to take an active interest in your medical care - it's a simple fact of life that infertile patients who know how to make the most of their doctor get better medical care!

CHAPTER XLIV

Male & Female Infertility & IVF Information

Let The Reader Beware - Making Sense Of Medical Stories In The News

Most infertile couples are aware of the dramatic advances reproductive technology has made in the recent past, and many of them rely on the media (TV, radio, newspapers, magazines) to remain updated with the latest news about infertility treatments.

What are the problems with newspaper reports on infertility treatment ?

However, many news stories about infertility treatment are often misleading and incorrect, and there are many reasons for this. Remember that news, by its very definition, implies something new and unusual. The media is often guilty of oversimplifying or exaggerating results, and headline writers may focus on an angle that gives a distorted impression, which often means that facts are sacrificed at the altar of readability or circulation figures. Since space is limited, many reporters do not provide a balanced perspective, and often focus only on the success stories, so that pictures of doctors and couples holding newborns are very common. While these do provide excellent photo-opportunities, the sad stories of the many failures never sees light of day.

Newspaper articles usually paint a very rosy picture - but these often lead patients to have false hopes and unrealistic expectations. Many reasons can be attributed to the somewhat shoddy standard of reporting in the lay press with respect to infertility. Editors crave for stuff which is 'new' and doctors and hospitals are only too happy to tout their latest gadgets and gizmos. Reporters are often not specialised enough to understand the medical technical background. Often, they do not do their homework properly, which results in misreporting, which is, unfortunately, a common occurrence in India.

The outcome is that patients are often confused and are not sure how the latest advances in reproductive technology apply to them, so that they often rush to their doctor's clinics with the cutting in hand ! The report often raises false hopes and gives them unrealistic expectations. As a result, the media loses credibility, so that they often end up performing a disservice to patients and their doctors. Because the public is eager, for any scrap of medical news, the media often reports individual studies out of context, as if each study could stand alone. However, single studies rarely yield a simple 'yes' or 'no' answer to a medical question. One ought to realise that scientific discovery is a process that often takes years to unfold, and an individual medical report or isolated success story means little. Remember, that new does not always mean better ! For example, many doctors

have started using lasers in the IVF laboratory. However, whether these actually help to increase pregnancy rates is still unproven. Nevertheless, patients get carried away easily by the glamour of this "new technologic advance", and are happy to pay more for the use of the laser, even though it may not help them increase their chances of conceiving. This is why some cynics have suggested that the term LASERS should stand for "Latest Advanced Source for Extra Remuneration for Surgeons" !

How can you intelligently read newspaper reports about infertility ?

What can you do to separate the wheat from the chaff?

First of all, identify the source of the story. Does the information come from a reputed publication (such as The Lancet) or a leading medical professional organisation (such as the American Heart Association)? Second, look beyond the statistics. When reports hurl at you statistics like 'a 50 per cent pregnancy rate ', take a closer look at the exact numbers. Many of us get 'turned off' by numbers, but this attitude can prove dangerous: you need to ask yourself what the numbers really mean and how they apply to you? Benjamin Disraeli once remarked that there are three kinds of lies: lies, damned lies and statistics. Remember that statistical methods are simply tools, and they can produce blatantly wrong conclusions unless sensibly used. How many patients were treated ? How were they selected ? Have these results been consistent ? Have these results been confirmed in other studies and other centers ?

One important safeguard against imperfect or flawed scientific reporting is peer review; i.e., scientists scrutinize each other's work in advance. Almost all well-respected scientific journals rely on peer review to select papers for publication. Any study that has not undergone peer review should be regarded with the utmost scepticism. For example, one should be wary of findings announced at a press conference that are not accompanied by publication in a journal or by a presentation at a scientific forum. Many doctors and clinics will send out press releases to get media attention, in order to attract more patients, even though the information they provide to the press may not be reliable or trustworthy.

What can you do to protect yourself from the inappropriate use of technology in your infertility treatment ?

Inappropriate use of technology

While it is true that reproductive technology does represent one of modern medicine's success stories, the wide range of technological advances in reproductive medicine can leave many infertile patients feeling completely confused. How is a patient to make sense of which technology may be useful for his particular problem? New technology can be dazzling, and undoubtedly, when reproductive technology is used properly, it can help many infertile couples to have a baby. However, technology can be a two-edged sword; and we need to remember that every rose has its thorns! For example, growth hormone was introduced as an adjuvant for superovulation in the early 1990s with great hopes and expectations, and leading doctors announced at many conferences that growth hormone helped to improve pregnancy rates dramatically. Unfortunately, these claims were found

to be unfounded, and no one uses growth hormone anymore. However, many patients ended up wasting large sums of money.

What can you do to protect yourself ? Remember that fashions come and go in medicine as well, and many doctors are happy to jump onto the latest bandwagon, so that they can present papers at conferences and give lectures, to show that they are the leaders in the field. When you read a report of a new advance, it's usually a good idea to let the froth and the hype to settle down before accepting it. If it is in fact a real advance, it will be replicated in many centers all over the world - remember that the best way to assess the true value of a treatment is to see whether it can withstand the test of time !

You need to be aware of the following inappropriate uses of technology in reproductive medicine today, so that no one uses you as a guinea pig .

1. Excessive use of technology, even when it is not required. A prime example of this 'folly' is routine ultrasound scanning to "time " intercourse. While no one will dispute the fact that ultrasound scanning can provide extremely useful information on ovulation, to use this simply to time intercourse only adds to the infertile couple's stress !
2. Use of technology which is not suitable for a particular patient. An example of this would be advising IVF (in vitro fertilization) for all infertile patients, just because the equipment and expertise are available and because the procedure is technically feasible. However, for most infertile patients there are many simpler treatment options available, which should be fully explored before considering IVF.
3. Misuse of technology by unqualified doctors. A common example is the use of lasers or endoscopic equipment for complicated surgery. Just attending a two-day workshop and acquiring a certificate do not make a doctor sufficiently expert in using this technology; a number of mishaps have been reported because of operator inexperience.

There are many reasons for the inappropriate use of medical technology. For instance:

1. The major factor, of course, is money or the need to generate income. Doctors need to justify the purchase of expensive incubators and micromanipulators, and as hospitals have become profit-oriented organizations, doctors are becoming increasingly answerable to the management regarding the profitability of their services. Nowadays, once a piece of equipment has been purchased, it needs to be 'utilised' to make it 'cost-effective'. Woe betide the doctor who does not generate enough money through the latest gadgets! He may find that his contract is not renewed!
2. The glamour and the dazzle of the latest medical gizmos tend to lure most doctors, and this can be as tempting as wanting to drive the latest model car! One gains prestige by being the first to adopt the latest technique; or by being the only one in the world/country/city to possess the latest and newest 'toy'.

3. The pressure from manufacturers to buy the 'latest and newest'. 'New and improved' versions prove attractive, not only to toothpaste consumers, but also to doctors, and the medical industry (both equipment manufacturers and pharmaceuticals) has developed powerful tactics and techniques to induce doctors to prescribe and use their newest products. The companies involved can afford to spend large amount of money on advertising, and they use this capability very effectively to maximize their profits.

The most crucial question is: how can you intelligently apply what you have read to your treatment? Make sure you are well-informed, so that you can critically assess the reported advance, and judge its relevance (as it relates to your problem) for yourself. Make it a point to ask your doctor as well ! Your own doctor can help you make sense of the technology, and put it in the right perspective.

CHAPTER XLV

The Infertile Patient's Guide to the Internet

Most infertile patients are hungry for information - and "Look it up on the Internet" is fast becoming the standard prescription for any infertile couple. Medical journals, text books, encyclopedias, research papers, and huge medical databases once available only to doctors are now just a mouse click away. Savvy patients can even learn about a breakthrough before their doctor does, and the internet has given birth to a new group of informed, empowered patients who want to make medical decisions in partnership with their doctors, instead of just blindly following the doctor's advice.

While everyone knows that there's a wealth of medical information on infertility on the Net, why are most patients in India still so reluctant to make use of this? For one, most Indians have become very used to passively following their doctor's advice. Questions are not encouraged in India - either in the classroom when we are students, or in the doctor's clinic when we become patients. Also, medical jargon can be intimidating, because it is unfamiliar (since many words are derived from the classic languages such as Greek and Latin) and is therefore difficult to follow - so most of us would rather not take the trouble of researching our problem independently.

Many people still prefer to leave everything up to their doctor - after all, that's what you pay him for, isn't it - why confuse yourself with alternatives and options (the "doctor as a highly paid technician" approach). Another problem is that there are still very few sites about infertility in India (most websites are US in origin) with the result that a lot of the information on the Net is irrelevant to Indians.

How can you use the internet intelligently to get the right treatment?

So how can you use the internet intelligently to find out more about your medical problem? Let me start with a warning - it is unwise to try to diagnose yourself - don't try to play doctor! Please seek a qualified medical opinion from your own doctor, who can see you, conduct tests if necessary, and diagnose you properly. Once you have a diagnosis, your search for information on the Net can become focussed and productive.

Search

Engines

Searching for information on the Net is very similar to looking up a book. You turn to the index to look for a particular topic, and on the Net you can use one of the many search engines available, such as <http://www.google.com/>, <http://www.hotbot.com/>, <http://www.altavista.com/>. The trouble is that these engines are unintelligent, so that a search usually retrieves thousands of websites - the majority of which are completely irrelevant to your query - and it's hard to separate the wheat from the chaff. Search engines are most useful when you are looking for information on a rare problem, or very specific information only. Be sure to try several different search engines when looking for information since each one can have different listings included in their data base. You also need to double check your spellings - an error can mean you may not retrieve any useful information at all! Try to be as precise as possible in order to retrieve relevant information only. Thus, looking for "laparoscopic surgery for treatment of endometriosis" will give you more useful results than just looking for "endometriosis".

It's easy to get lost in the flood of garbage which a standard search produces, which is why many infertile couples often despair of ever being able to find anything useful or understandable on the Net. In order to make their life easier, experts have put together evaluated **subject gateways or medical search engines**, to make directed searching for relevant information easier. As their name implies these search services provide the user with a gateway to medical resources on the Internet. However, rather than provide a comprehensive (but unranked or unsorted) listing of Internet sites, only those that meet a defined quality threshold are included. The websites are also ranked, according to their quality and usefulness, as determined by these experts. These gateways are produced by medical libraries, doctors and other organizations, and are useful to both new Internet users - who may be unsure where to begin - and experienced surfers who are frustrated with ploughing through the inevitable volume of irrelevant dross when using any of the more general search tools. Examples of such gateways for patients include: <http://www.healthatoz.com/>, <http://www.achoo.com/>, and <http://www.medhelp.org/>.

If you are a novice, it can be helpful to have a friendly doctor (or medical student) or a librarian to guide you with your first few searches, to teach you how to search efficiently. A cybercafe is a good place to learn how to surf! If you want a comprehensive search of the Internet you must be prepared to search multiple gateways and search engines - the much sought after 'one-stop information medical source' has yet to appear. Remember that there's a lot more on the Net than just tons of textual information on thousands of websites -you can admire anatomy in three dimensions thanks to virtual reality, and even watch video clips of laparoscopic surgery online! However, mining the Net for information need not be a one-dimensional affair - the real charm of the Net lies in its interactivity, so that you can get a response to your queries!

How can you get a second opinion on the internet ?

Online Doctors and Chat Sessions

There are many infertility specialists on the internet who will respond to medical questions - free! The premier site on the web for this service for infertile patients is at www.drimalpani.com/malpaniform.htm, where the authors of this book, Dr Malpani, answer queries sent by email. These responses are meant to educate the questioner and the public and cannot be a method of rendering personal medical care. All the questions and answers are archived (what are called FAQs or frequently asked questions), so that everyone can search, view, and benefit from the information. INCIID Interactive Infertility Forums at <http://www.inciid.org/interact.html> allows access to many medical forums (where you can get answers to queries from medical experts); support forums (where you can interact with other infertile couples); and frequent online chat sessions on various topics.

Email, Newsgroups, Listservs and Mailing Lists

Newsgroups, which are also called Internet Discussion Groups, function like electronic world wide bulletin boards. In a newsgroup you can post or view messages or reply to someone else's. There are many newsgroups for infertile couples, including: alt.infertility, alt.infertility.primary, alt.infertility.secondary, alt.adoption and misc.health.infertility.

You can use Deja News (<http://www.dejanews.com/>) to find the one of interest to you. LISTSERVS, also called mailing lists, are a way of communicating with others via email on various topics of interest. You'll find there's a support group in cyberspace for just about any medical problem, ranging from miscarriage to endometriosis, and instead of being limited to a few local patients, you can communicate with dozens of people going through the same things you are. The Internet also provides a safe cloak of anonymity, so you never need to reveal your identity. There are now many online communities of infertile couples, who network with each other, and provide much needed emotional support and practical information. A good example of such a support group, which uses bulletin boards to allow couples to "talk" to each other is at <http://www.fertilethoughts.net/>. You can post your message online, read about other's problems - and offer advice as well!

If you have been able to identify an expert on your problem, it is also possible to send him an email directly, and he may then reply to you. You can find email addresses of doctors through a little bit of lateral thinking. For example, many leading infertility clinics have websites which list the names, addresses and emails of their faculty members. Also, many authors of medical journal articles (which you can find on the Medline database) now include their email addresses along with their institutional address.

If you want to find out information which is on the cutting- edge of research, or read articles which have appeared in medical journals, then you need to search the Medline database. This MEDLINE database (maintained by the National Library of Medicine in Bethesda, Maryland, USA at <http://igm.nlm.nih.gov/>) is the best way of retrieving medical information today. This database has over 10 million references, and indexes all articles published in reputed medical journals from all over the world. It's quite easy to learn to do a Medline search- and there is plenty of online help available as well! Once you've found the information, how do you evaluate it ? This is still the most difficult part of searching for medical information, and unfortunately many patients become misinformed thanks to the Net. The problem, of course, is anyone can publish on the net - and it's not easy to make out whether the information being presented is credible or not! A good website should be accurate, useful, credible, readable, up-to-date and have useful links to other sites - but the most important guideline is to find the source of the information!

What are some of the other useful websites for infertile patients ?

Useful websites for infertile patients include the following: Fertilethoughts at <http://www.fertilethoughts.net/> is a comprehensive site, which has information on infertility, adoption and surrogacy. You can also post your own story online in the Personal Histories section- and read about other patient's experiences as well! There are many bulletin boards and chat rooms as well, so you can network with other couples. <http://infertility.about.com/>, is an excellent starting point, for infertile couples who would like to explore the internet. It provides reviews of selected valuable sites, thus offering you a guided tour of the net so that you don't get lost! FertilityCoach at

<http://www.fertilitycoach.com/> offers very useful coping techniques for infertile couples, and shows them how coaching can be used to help themselves through this difficult time in their life. The International Council on Infertility Information Dissemination at <http://www.inciid.org/> is rich with valuable information; <http://www.ferti.net/>, provides an international directory of infertility clinics; <http://www.ivf.com/> has a lot of practical information for infertile patients; while the Resolve website at <http://www.resolve.org/> has excellent information on advocacy for infertile couples.

Remember that you can also use the internet to order products to enhance your chances of conceiving. This is especially helpful, because of many of these products are still not available in India. Thus, you can order fertility testers and ovulation monitoring kits from <http://www.conceivingconcepts.com/>, books on infertility from <http://www.amazon.com/>, and even software to help you to chart, analyze and predict your fertility cycles from <http://www.cyclewatch.com/>!

It is important to think about how much information you need from the Net to make yourself comfortable with your diagnosis and treatment options. Some people need as much information as they can possibly gather, while others find less information, or information with a specific focus, is best for them.

A warning - do not accept the contents of any single website as definitive. It is in the nature of medical research that many studies contain errors, many conclusions are false, and many reports flawed. This is why you need your doctor's help to make sense of your information search, because he can best explain to you how the information you have unearthed applies to you as an individual. You need to form a partnership with your doctor - but it should be a partnership of well-informed equals, for which you need to do your homework first! Remember that the information you retrieve on the Net is simply a tool to help you to get better medical care - it should help to improve the communication between you and your doctor - not replace it!

CHAPTER XLVI

The Social & Ethical Issues - Right or Wrong?

What are some of the ethical issues surrounding the new reproductive technologies ?

The new reproductive technologies have spawned new ethical concerns. These are controversial subjects, which have attracted wide media attention and public debate. However, the law and public opinion all over the world have lagged behind the advances in artificial conception which have created a "brave new world" of possibilities of giving birth, never before considered possible - using a mix and match combination of sperms, eggs and uteri. In fact, today we have the technology to be able to help any couple to get pregnant - no matter what their medical problem may be ! However, whether or not they should adopt these options is a decision each couple needs to make for themselves !

Artificial conception raises the possibilities of myriad problems - legal or otherwise, which may need resolution by legislation or national guidelines. These relate to :

- The question of embryo research and the time limits to be placed on it
- Basic questions such as - when does life begin ? and what are the rights of an embryo ? remain unanswered.
- Guidelines on semen banking
- The child's right to access to information about his/her genetic background and mode of conception
- The legality of surrogacy
- The registration and monitoring of IVF clinics to ensure that infertile couples are not exploited.

How do the different religions look upon infertility treatment ?

Theologians the world over differ sharply on the subject. For example, to the Catholic Church, adoption is acceptable; as are the use of fertility drugs. GIFT procedures are allowed when the sperms and eggs of the couple are placed in the woman's own Fallopian tubes. However, surrogacy; artificial insemination by husband or donor; and IVF are not allowed, because procreation without sexual union is considered unnatural, and the Church has been quite vocal about its criticism.

In Judaism, donor insemination is forbidden and a child is considered to be the offspring of the biological father. Artificial insemination using husband's sperm and IVF are accepted when there is need to heal the illness of infertility.

Islam does not permit the use of donor sperm.

Most individuals have their personal beliefs regarding the "rightness " or otherwise of many of these techniques. Many people believe that embryos should not be used for

research because they have the potential to become human beings - and in fact, embryo research is banned in Germany by law.

Other feel that to restrict research is unfair to infertile couples, who should be allowed to make their own choices.

There will always be two views of looking at the technology of assisted conception. At one end of the spectrum, will be people who feel that this technology allows couples to manipulate Nature to produce children and will object to it. At the other end will be people who believe that this technology is a triumph of man's ingenuity which can be used to overcome Nature's constraints. It will never be possible to reconcile these viewpoints - since these are based on deeply held personal beliefs (and not facts) - and we will have to learn to live with this moral dichotomy. At least this explains the heated debates about when life begins ! Since it may never be possible to have a consensus on this issue, this decision should not be left to moralists, or philosophers - or the government, or the doctors. Instead, the decision should be left to each individual couple, who provide the reproductive apparatus to create the baby.

Remember, there are no "right" or "wrong" answers - you must follow your own conscience.

CHAPTER XLVII

Cost of Infertility Treatment & IVF Treatment.

How Much Does Treatment Cost?

How much does infertility treatment cost ?

The Economics of Infertility Treatment

Being infertile can be very expensive! Tests and treatment cost considerable money, and since there is no definite endpoint, budgeting for medical expenses can be very difficult.

The availability of modern assisted reproductive techniques, such as IVF, have made treatment even more expensive - since so much expertise and technology is needed for these procedures. This means that there really is no upper limit to how much you can spend in your pursuit of a baby!

You need to control your finances - and it is unfortunately only too common to find patients who are so desperate to have a baby, that they have begged and borrowed, and even sold their lands, possessions and belongings, so that they could continue trying to have a baby.

Of course, for infertile couples, a baby is priceless, but you cannot afford to waste money. You may need to shop around to get a realistic estimate of how much treatment costs. Charges vary widely - and don't automatically assume that the more expensive a clinic, the better it is.

You need to consider the cost-effectiveness of each treatment option. While it is true that an IVF cycle is four times as expensive as an IUI cycle, the chance of a pregnancy is also four times as great! A common mistake patients who are not very well off often make is that they repeat the treatment of IUI repeatedly, because they feel that they cannot afford IVF. However, in the long run, they often end up spending even more! You need to have a plan of action, and to stick to it, rather than to keep on trying the same treatment over and over again, just because it is less expensive!

When considering expenses, you need to consider not only the money you will be spending, but the time and energy you need to invest as well! All of us have finite resources - and you need to invest them carefully!

Ironically, infertile patients who are rich are subject to the risk of overtreatment. Just because they can afford it, doctors advise them to go in for an IVF cycle, while simpler treatments such as IUI could also have helped them to get pregnant.

It is important to get a breakdown of the expenses for all procedures - preferably in writing. For example, for surgery, find out what is included in the quoted figure - does this include just the surgeon's fees ? the assistant's ? anesthesia? theatre charges ? hospitalisation ? followup visits ? Often what is excluded can add up to a pretty penny! This is especially true for IVF treatment, where "hidden expenses" can lead to your spending much more than you had bargained for.

Patients are often reluctant to talk about money and expenses with doctors - but remember, it's your hard-earned money you are spending. You can't afford to shy away from this topic. Doctors are also sometimes vague about money matters - and this makes getting specific figures so much more important.

You need to calculate what your total expenses will be, not just the medical costs. Remember to include travelling costs; lodging and boarding if you are from out-of-town; and the cost of time taken off work.

Do insurance companies cover infertility treatment ?

Unfortunately, most insurance companies in India will not reimburse you for the medical expenses for treating infertility - they still take the old-fashioned view that infertility is not a medical problem! A number of couples are also reluctant to claim for medical expenses for treatment, since they do not wish to disclose to anyone else that they are infertile. Also, Government medical facilities rarely provide quality care for infertility, since this is not a primary concern for them. Until these attitudes change, a number of patients will be deprived of infertility care, because of financial constraints - and this is a shame!

Infertile couples in USA have used the courts to get their medical bills paid. In 1998, the city of Chicago agreed to cover infertility treatments for its employees after a female police officer sued the city for violating the Americans with Disabilities Act. The officer said her infertility was a disability because it impaired a "major life activity." In 13 states in the USA, insurers are required by law to offer some form of infertility coverage. Hopefully, infertile couples and their advocates will be able to successfully lobby for similar changes in India as well.

However, patients have devised ingenious methods to overcome these financial hurdles. For example, young women who can grow lots of eggs and who need IVF but cannot afford to pay for this, have agreed to "share" their eggs. Older women, who need donor eggs and are well-off, can then pay for the entire IVF cycle, and the two can share the eggs, giving both of them a chance to get pregnant. Egg sharing allows the doctor to match financial and reproductive resources, and is beneficial for both donor and recipient. You can also get coverage for some of your medical treatments (such as laparoscopy) by requesting your doctor to say that the surgery was done for treating pelvic pain (which means your expense will be reimbursed by the insurance company) rather than for treating infertility.

Approximate costs for procedures, tests and treatments is summarized in this chart. These figures are for the year 2000 in the city of Bombay, and are only meant to be representative - do remember there can be considerable variation! These are "all-inclusive" medical expenses.

Note:

1 US dollar = Rs 40.00

1 UK pound = Rs 80.00

Compared to the UK and USA, IVF treatment is much less expensive in India, and the quality is as good. This is because doctors charge much less - so that by international

standards, IVF in India is very cost-effective, and quite a few patients do fly down to India for treatment (and have money left over, even after paying for air-fare!) In fact, reproductive tourism has become very popular; and about half the patients we see in our clinic come to us from the US and UK.

Medical tourists can be demanding patients ! They have often lost faith in their own medical system; and many of them are doctors and nurses who make their own medical decisions. They are challenging to treat and I enjoy doing so, because they are well-informed and capable of thinking out of the box - it does take guts to travel to India for medical treatment !

I just did an interview for BBC, and one of the first questions I was asked is - "Why do patients come to your clinic from all over the world ?"

In the beginning, I think the major reason was the fact that our prices were much more competitive than what clinics in the USA and UK charge. However, our major USP is no longer our labour arbitrage . I think what sets us apart is the fact that we are a "focussed factory" (a concept described by Michael Porter and Regina Herzlinger). We run a lean and mean unit , which does IVF and only IVF ! Because we do so many cycles, we are very good at it; and because we do nothing else, we have to be very good at it !

Initial consultation Rs 500 to 1000 (US \$ 20)
Semen Analysis Rs 200 to 500 (US \$ 10)
Hysterosalpingogram Rs 500 to 2000 (US \$ 40)
Hormonal blood assays (FSH, LH, prolactin, estrogen, progesterone) - Rs 200-400 for each test
Testicular biopsy Rs 2000 to 10000 (US \$ 200)
Endometrial biopsy Rs 500 to 2000
Diagnostic Laparoscopy Rs 10000 to 40000 (US \$ 1000)
Operative Laparoscopy Rs 25000 to 50000 (US \$ 1200)
Major surgery (microsurgery for tubal repair) Rs 40000 to 65000 (US \$ 1000)
IUI (insemination) Rs 3000 to 15000
TID (Therapeutic insemination by donor), per cycle Rs 8000 to 20000
HMG treatment cycle (for superovulation) Rs 8000 to 20000 (US \$ 400)
GIFT Rs 50000 to 120000 (US \$ 3500)
IVF Rs 50000 to 120000 (US \$ 3000)
Embryo freezing Rs 20000-40000
Microinjection (ICSI) Rs 80000 - Rs 150000 (US \$ 3500)
Preimplantation genetic diagnosis Rs 150000 - 200000 (US \$ 5000)

CHAPTER XLVIII

HCG Level Pregnancy, HCG Blood Test & Calculator

Pregnant - At Last!

For most infertile patients, getting pregnant is the ultimate dream which keeps them going through tests, treatments and surgery. What happens when the dream finally comes true?

How do you find out if you are pregnant ?

Making the Diagnosis of Pregnancy

How do you find out if you are pregnant ? For most treatments, doctors will wait till you miss your period before starting pregnancy testing. You should ask your doctor when you should schedule a pregnancy test every time you take treatment - after all, you never know when it's going to work! A reasonable choice would be to conduct the test 16 to 18 days after ovulation. For IVF and GIFT cycles, in some clinics, testing may start as early as 10 to 12 days after the embryo transfer or GIFT.

When the pregnancy test is positive, the first response is often one of disbelief since it's hard to believe you are finally pregnant, especially if you have been trying for many years. Some patients get emotional - it's over! The time and effort and money has paid off! Infertility is a memory! But you soon realize that it's not all over. What you want is not a pregnancy but a baby! There are still uncertainties, and things can still go wrong, which is why careful monitoring is essential.

A pregnancy should be documented as early as possible. This is important, because appropriate care and precautions can then be taken at an early stage. The most sensitive pregnancy test is a blood test for the presence of beta HCG (beta human chorionic gonadotropin). The HCG is produced by the embryo, and as the embryo's signal to the mother that pregnancy has occurred.

What is the beta HCG test for pregnancy ?

HCG can be measured in the blood by RIA (radioimmunoassay) or ELISA (enzyme immunoassay) testing; and positive levels (more than 10 mIU/ml) in the blood can be detected as early as 2 days before the period is missed. In the old days, the only way of determining the presence of HCG was by testing the urine, i. e, by using urine pregnancy test kits. Modern urine pregnancy kits (using monoclonal antibody technology) are now quite sensitive and can detect a pregnancy as early as 1 to 2 days after missing a period (at a blood HCG level of about 50 to 100 mIU/ml). The benefit of urine pregnancy test kits is that they are less expensive; and testing can be done at home by the patient herself.

However, instructions need to be followed carefully, and errors in interpreting the test results are not uncommon. These errors could occur if the urine is too dilute; or if the test is not done properly; or if there is a urinary tract infection exists.

The major advantage of blood tests is the fact that they measure the actual level of the HCG in the blood - and this factor can be very helpful in managing pregnancy problems, if they occur. As the embryo grows rapidly, HCG levels normally double every 2 to 3 days. Thus, one reliable sign of a healthy pregnancy is the fact that the HCG levels are increasing rapidly, and often doctors may need to do 2 HCG levels 3 days apart in order to determine the viability of the pregnancy. A rising HCG level is reassuring.

Problems with HCG testing can occur if you have earlier been given HCG (human chorionic gonadotropin) injections for inducing ovulation. Normally, this exogenous HCG is excreted by the body in 10 days; but sometimes it can linger on. This is why, if the HCG level is very low, the test may need to be repeated, to confirm that the level is increasing.

What are "biochemical pregnancies" ?

What are "biochemical pregnancies" ? These are pregnancies in which the HCG test is positive after the period has been missed; the levels increase, but are still low; and no pregnancy is ever documented on ultrasound. Biochemical pregnancies are often seen after IVF and GIFT. While they are not clinical pregnancies, they are of useful prognostic information, because they may mean that your chance of getting pregnant in a future cycle are good.

One drawback with the HCG test is that a positive HCG simply means a pregnancy is present in the body - it does not provide any information about the location of this pregnancy, which may be tubal or ectopic.

During the very early pregnancy, HCG levels are the only way of monitoring the pregnancy. HCG levels which do not increase as rapidly as they should may mean that there is a problem with the pregnancy - the embryo may miscarry because it is unhealthy; or the pregnancy could be an ectopic pregnancy. Differentiating between the two conditions is obviously important, and this is where vaginal ultrasound plays a key role.

How is ultrasound used for monitoring pregnancy ?

With vaginal ultrasound, it is possible to detect a pregnancy as early as 2 to 4 days after a missed period. An early pregnancy is observed as a pregnancy sac or gestational sac in the uterine cavity. The uterine lining is thick and bright white; and the sac (also called a gestational sac) in the uterine cavity. The uterine lining is thick and bright white, and the sac appears as a black bubble in this lining. The sac should grow (at the rate of about 1 mm per day) and, if it does so, this is reassuring. The sac represents only the placental tissue - the embryo is so tiny at this stage, that it cannot be seen on ultrasound. At 6 weeks of pregnancy, an echo can be seen within the sac; this is the embryo. This grows rapidly, so that on scans done by 8 weeks, one should be able to see a beating fetal heart as well. This is very good evidence of a healthy fetus and the chances of a problem occurring in pregnancy after this point are small.

Ultrasound is useful because it provides information about the number of pregnancies (multiple pregnancies are not uncommon after infertility treatment and should be looked for!) ; as well as their location. If the sac is not seen in the uterine cavity, then a tube (

ectopic) pregnancy should be suspected. The ultrasound provides information which is complementary to that of the HCG level. Often both need to be done simultaneously and interpreted together.

What precautions do you need to take once you get pregnant ?

What about do's and don'ts during pregnancy ? What precautions should you take to minimise your risks ? Unfortunately, there is little anyone can do today which is of much use. During pregnancy, most doctors may put you on supplemental progesterone injections (to help support the endometrium); and perhaps multivitamins; and low-dose aspirin. All this treatment is empiric - there is no proof that it works! Also, many patients will put themselves on bed-rest to prevent disturbing the pregnancy and the value of this is doubtful as well. If the pregnancy is going to have a problem, no matter what you do, it will. And if it is going to be uneventful, then you don't really need medical attention in any case. The trouble is we do not know which pregnancy is going to have problems and which one is not! Any bleeding, no matter how slight, should be taken seriously - and usually calls for hospitalisation.

How do you cope if you miscarry after your infertility treatment ?

Unfortunately, it is a fact of life that 10 to 20% of all pregnancies will end in a miscarriage - and the risk of an infertile woman's miscarrying is even higher. This is because they are often older; their medical problems which caused the infertility can also cause miscarriage; and sometimes the infertility treatment also increases this risk. Of course, some of the increased risk is only apparent, because the testing is so intensive and thorough.

Unfortunately, no treatment exists for preventing early miscarriages - and all the doctor (and patient) can do is wait and watch. This can be shattering! Nevertheless, the fact that you have got pregnant provides hope for the future.

If the pregnancy miscarries, then a curettage is needed. This tissue must be sent for histopathologic examination, to provide documentation of the pregnancy. This also helps to rule out an ectopic pregnancy.

Coping with miscarriage after infertility can be hell! When you finally get pregnant after so many years of trying, you feel it is cruel on God's part to then snatch it away. In fact, perhaps the only trauma worse than not being able to conceive, is to lose a pregnancy after trying so hard. Remember that nature is not perfect and neither is medical care. The most painstaking attention to detail cannot stop the unexpected from happening and no amount of obsession with detail will guarantee a perfect outcome.

If you miscarry, you are going to blame yourself - that it was something you did (or did not do) which caused the miscarriage. However, remember that 70% of miscarriages are because of a chromosomal abnormality at conception - something over which you have no control.

We will never know the reason why they occur. This is why most doctors would not investigate you after just one miscarriage, since the chance of finding something significantly abnormal is so small - and your chance of having a healthy pregnancy the

next time is better than 85%. Most would reassure you - and the best option would be to try again (even though this can be emotionally very taxing!). If you've had a previous miscarriage, it is very normal to be frightened and worried - and starting infertility treatment again can be very difficult. You have to start from scratch all over again - and you wonder if and when you will again get pregnant. The lurking fear of losing the pregnancy once more, if you do conceive again, could torment you as well.

How can you make the most of your precious pregnancy ?

Coping with pregnancy after infertility treatment can be difficult even if the pregnancy is going well. So much time, energy, love and money have been invested in the pregnancy, that you don't want to take the slightest chance that something will go wrong. The anxiety can be overpowering - and even the minor aches and pains of pregnancy can send you rushing to the doctor for reassurance that all is well.

Your pregnancy will be monitored carefully, and this may involve frequent visits to the doctor; as well as repeated ultrasound scans. You will be very vulnerable and terrified, and will be bombarded by suggestions from well-meaning friends and relatives as to what to do, and also what not to do.

If you are more than 35 years of age, your doctor may advise you have a chorion biopsy or amniocentesis to screen for genetic defects in the newborn, such as Down's syndrome. Also, if you have multiple pregnancies, frequent hospitalisation and bed-rest may be needed.

Yours is a "premium pregnancy", and will be treated as such even though your risk for complications is no more than any other woman's. However, since the pregnancy is so precious, the hazard is greater than for someone who has no trouble conceiving, which is why an "at risk" approach to managing your pregnancy is appropriate. This is why the chance of your requiring a cesarean section for birth are greatly increased, because neither you nor your doctor will want to take the slightest "chance" of something going wrong.

What about after the delivery ? Is this when the joy and happiness you have been anticipating for so long and happiness you have been anticipating for so long begin? Maybe! Certainly life is never the same when the child you have been looking forward to for so long finally arrives, especially if you have twins! Babies are demanding and not everyone can adjust easily to the new situation. If couples are older then it may be harder for them to cope with the changes, especially after spending years of being together without the company of children.

Is parenting different after infertility treatment ?

The infertile woman who becomes pregnant expects perfection in every aspect of motherhood, because that's the stuff dreams are made of. However, when the reality of pregnancy, delivery and parenting actually takes hold, you may even feel disappointed, because real life is often harsher and unkind than you had imagined. For example, you may have a hard time coping with 2 a.m. feedings and you may even start to resent your having to get up to take care of your newborn. This can make you feel guilty for not appreciating what you have-your child, for which you worked so hard! Don't worry, this feeling is normal and will pass.

Your parenting also is going to be influenced by your experience of infertility, because your child is extra special and it is natural for you to want to dote on him or her. This can be wonderful for your child because he or she will always know how much he or she was wanted and how much he or she is loved - but watch out for the emotional traps of being overprotective and unintentionally spoiling the child.

CHAPTER XLVIX

Infertility Causes, Treatment & Prevention

How can you prevent infertility ?

Often preventing infertility is much easier and better than treating it! What can you do to reduce the risk of being infertile ?

The biggest preventable danger to fertility is due to uncontrolled sexually transmitted diseases (STDs) such as syphilis, gonorrhea and chlamydia. These can cause irreparable damage to the reproductive tract in both men and women. STDs can be prevented by:

- being informed and aware of the risks they pose.
- not engaging in promiscuous sexual activity. Abstinence or monogamy is safest!
- using condoms if there is more than one sexual partner.
- testing for STD if you are at risk
- early and thorough treatment for STDs. This includes: careful followup; testing for cure; and screening of sexual partners.

Often, couples will want to postpone childbearing after marriage. Contraception can also pose a hazard to future fertility, if not selected carefully.

- IUDs should not be used in women who are at risk for STDs because they increase the risk of pelvic inflammation; and it may be a good idea not to use IUDs in women who have never conceived.
- Oral contraceptives usually have no direct effect on fertility at all. However, women who have irregular anovulatory cycles before taking the pill will find that their irregular cycles return once they stop the pill and they may need treatment for this.
- The use of depot contraceptives (such as Norplant) can interfere with the resumption of ovulation, causing infertility.
- Sterilisation (tubal ligation and vasectomy) as a method of family planning should be offered only to patients who are sure they have completed their families; have received adequate counselling; and whose children have grown up.

Women who are more than 30 and who wish to postpone childbearing should get their FSH levels checked on Day 3 of their cycle. This is a simple blood test which allows the doctor to check your ovarian reserve (the quantity and quality of the eggs in your ovaries). A high level suggests poor ovarian reserve and should be a wake-up alarm that your biological clock is ticking away rapidly. It's important that this test should be done in a reliable laboratory.

An important preventable cause of testicular damage in men is uncorrected undescended testes. Undescended testes should be surgically treated at an early age to prevent damage - preferably before the age of 2 years. This requires educating mothers of young boys; and doctors as well.

It may also be a good idea to immunise boys against mumps in childhood, thus preventing the ravage which mumps can cause to the testes in later life.

Drugs - including alcohol, cocaine and marijuana - are all poisons. They can reduce sex drive; damage sperm production; and interfere with ovulation - and sometimes this damage is irreparable. Smoking tobacco also affects reproductive function - by depleting egg production; increasing the risk of PID; and lowering sperm counts. Often, the adverse effect is temporary, so that when these are stopped, the harmful effects on reproductive function are likely to be reversed. However, since abstinence is easier than moderation, the best option is not to smoke, drink or use drugs!

Occupational hazards can also decrease sperm counts. Many toxic drugs - including radiation, radioactive materials, anesthetic gases, and industrial chemicals such as lead, the pesticide DBCP and the pharmaceutical solvent ethylene oxide can reduce fertility by impairing sperm production. Intense exposure to heat in the workplace (for example, long-distance truck drivers exposed to engine heat; and men working in furnaces or in bakeries) can cause long-term and even permanent impairment of sperm production. You should be aware of these hazards and may need to control your exposure if fertility is a concern.

Wearing loose cotton underwear and trousers is advisable - tight clothes increase testicular temperature and may harm sperm production.

X-rays can be harmful to gonads. If X-rays are needed, the scrotum should be covered with a lead shield.

Unnecessary surgery can also cause harm to fertility. For example, appendectomy for chronic abdominal pain in young women can create pelvic adhesions which damage the tubes. It is also important to educate doctors and patients about the necessity (or the non-necessity!) of certain operations in young women. Procedures like ovarian cystectomy to remove small ovarian cysts; myomectomy to remove small fibroids; and D&Cs may actually cause more harm than do good. If surgical procedures are needed, then these should be performed meticulously, preferably using microsurgical techniques. Minimally invasive surgery (laparoscopic surgery and ultrasound guided procedures) offers an alternative to conventional surgery in these patients, where conserving fertility is a major concern.

For some young men with cancers (such as Hodgkin's lymphoma or testicular cancers), the therapy for the cancer (chemotherapy and radiation) can destroy sperm production and render them sterile. For these men, sperm preservation (by freezing in a sperm bank) is an option to maintain their fertility.

Some young couples use abortions as a method of family planning when they inadvertently get pregnant - either very soon after marriage - or even before. These unwanted pregnancies are then removed by medical termination of pregnancy - MTP. A MTP is usually a safe and easy surgical procedure but it can have complications. One of

these is infertility because of blocked tubes following an infection after the surgery. Contraception should be easily available for couples - and they should be taught how to use it effectively.

It is also important to prevent unnecessary damage to the cervix in women. Regular PAP smears to screen for early cervical precancerous disease allows conservative treatment of these lesions when they are found, thus preserving the function of the cervix. Unnecessary surgical treatment of benign cervical lesions such as erosions should also be avoided.

Young women who are obsessed with their fitness can paradoxically impair their own fertility. Excessive dieting ; together with too much exercise in order to maintain a thin figure can actually cause irregular menstrual cycles and stop ovulation. This is especially common in women athletes, swimmers, gymnasts and dancers; and women with anorexia nervosa. Simply regaining body weight can reverse their infertility.

Obesity can also interfere with ovarian function. Excessive fat disrupts normal hormonal production, causing abnormal ovulation. Reducing body weight down to normal can correct the problem.

Another problem which has become more prevalent recently is the advanced age at which women are opting to have babies. Because of socio-economic pressures, women prefer to complete their education and pursue their careers before starting a family. This sometimes means that childbearing is postponed till women are in their late twenties or early thirties - and for some women at least, the biological clock has ticked on too far as a result of this delay. In addition to the natural decline in fertility with increasing age, the longer a woman puts off pregnancy, the more she risks having her fertility threatened for various other reasons - such as endometriosis and STDs. While postponing childbearing can be an economic necessity for some couples, the best time to have a baby from a biological point of view is when the woman is in her early twenties.

CHAPTER L

The Infertile Patient's Prayer and Infertility "Defined"

What is the infertile patient's prayer ?

Lord, Give me Strength...

To keep my cool when another period starts

To keep my chin up when a co-worker announces her pregnancy

To have a good relationship with my friend in spite of her ability to conceive easily and not be jealous of her

To endure my sister-in-law's comments about toilet training

To keep from crying when I see children begging on the roads

To forgive my doctor when he keeps me waiting for 2 hours for a consultation - and then can't remember my name

To make the right decision about treatment

To maintain a good relationship with my husband in spite of all this.

It's helpful to remember the *Serenity Prayer* by Reinhold Niebuhr. "God, Grant me the serenity to accept the things I cannot change, the courage to change the things I can change, and the wisdom to know the difference."

Infertility Is...

Watching your husband playing with your friend's baby and wishing you could give him one of his own

Telling nurses to please take blood from your right arm because the veins in your left arm are all gone because of all the IVs you've had

Avoiding people you haven't seen for a long time because you don't want to hear the question, "Do you have any kids yet?"

Feeling very left out when your friends start comparing their pregnancy or childbirth experiences

Feeling like the whole town is pregnant except for you

Getting tired of people always expecting you to do things because " You don't have any kids to worry about "

Waking up in the middle of the night and wishing you could hear your baby crying

Wishing you could give your parents grandchildren

Wanting to fall apart if one other person says, "Why don't you adopt ?" Easy, right?

Sometimes avoiding friends who are pregnant or with newborns because you just can't handle the situation at that moment

CHAPTER LI

Low Cost & Affordable IVF.

Making IVF affordable

How can we make IVF more affordable ?

IVF and related assisted reproductive technologies (ART) offer great hope to infertile couples the world over. Because these techniques are so expensive, however, they are out of the reach of the vast majority of couples - and especially of those in the developing world. This is because IVF programmes are too technology-intensive at present - and anything which is complicated is bound to be expensive.

A high-tech approach is especially counterproductive in the developing world, where doctors usually blindly duplicate what foreign IVF programmes do. They imitate the Western ideal that is so tempting with its sophisticated equipment - 'never mind the cost'. If this approach were successful, then there would be little to criticize, but it can never be practical because the infrastructure to support such sophisticated services is simply not available in the developing world. Thus, for example, it is easy to buy an imported CO₂ incubator or a reverse-osmosis water-preparation system - but with just no maintenance and after-sales services to keep them functioning properly the result is that these systems often become white elephants.

IVF has developed in two different directions today. One is the high-tech approach, which includes such glamorous techniques such as microinjection, pre-implantation genetic diagnosis, and embryo co-cultures. These 'second generation IVF procedures' are very expensive and labour-intensive, however; they are applicable to few patients; and while worthwhile in advanced IVF laboratories in the West, are not relevant in the developing world, where the basic goal of an IVF clinic service to infertile patients.

The other direction in which IVF is evolving is towards simplification. While it is true that these 'simplified IVF techniques' do not as yet offer as good a pregnancy rate as conventional IVF, they are much more relevant in the developing world. What have these simplifications been?

What is natural cycle IVF ?

Natural cycles

A major expense of the IVF cycle is the cost of the gonadotropin injections used to induce superovulation. Superovulation using GnRH (gonadotropin - releasing hormone) analogs and hMG (human menopausal gonadotropin) has now become the norm for most clinics, since stimulated cycles produce more eggs and therefore more embryos and a higher pregnancy rate. Not only, however, does superovulation carry the risk of ovarian

hyperstimulation carry the risk of ovarian hyperstimulation (a condition in which the ovaries become very enlarged because of the multiple follicles, which can be potentially life-threatening), but also the risk of multiple pregnancies and the related problem of what to do with the unwanted eggs and embryos. A number of clinics are therefore now returning to the 'natural' unstimulated cycle for IVF - which is much less expensive!

The major problem with this protocol was the need for frequent blood or urine tests for LH (luteinising hormone) to determine egg maturity; and the need to be ready to do egg pickups at all hours of the day or night. However, newer protocols using the natural cycle allow ovulation to be induced with hCG (human chorionic gonadotropin), which in turn allows one to minimize LH monitoring, and also to time egg pickup to be during the day. IVF is now turning full circle - remember, the ovum of the first test - tube baby was in fact recovered in a 'natural' cycle.

What is transport IVF ?

Transport IVF

A good IVF programme needs laboratory services of a high standard to ensure that the eggs, sperm, and embryos are maintained in an optimal environment in vitro, and this has been the major stumbling block for most IVF programmes. The major limiting factor with providing IVF services has been the availability of IVF laboratory expertise. The method of transport IVF offers a very attractive solution to this problem. Basically, this means that egg pickups are performed in peripheral clinics and hospitals; and the husband transports the follicular fluid (with the eggs) to the central IVF laboratory using a specially designed incubator which runs off the car battery. All IVF laboratory procedures, and later the embryo transfer, are carried out in the central laboratory.

This method allows gynecologists to take an active part in their patients' treatment, ensure high quality, since all laboratory procedures are performed in a central IVF laboratory, and also allows one IVF laboratory to obtain the necessary experience and expertise that is so important for maintaining high pregnancy rates.

Commercial culture media

Making IVF culture medium in which the eggs and embryos are nourished in vitro is a major problem. Not only is very expensive equipment needed to produce this medium, but scrupulous quality control and testing is needed to ensure that each batch can maintain embryo growth. With the recent commercial availability of quality-controlled and tested culture medium - for example from Medicult and Scandinavian IVF, IVF programmes no longer need to make their own culture medium, as this can now be bought 'off the shelf'. This has helped to minimize one of the variables which used to reduce pregnancy rates for IVF programmes - toxic culture medium.

What is intravaginal culture ?

Vaginal incubation

Incubating the eggs and embryos in vitro requires expensive CO₂ incubators, which must maintain just the right environment for the embryos for long periods of time. The method of intravaginal culture (IVC), however, allows one to provide IVF services without using a CO₂ incubator and is an extremely attractive alternative. Basically, in IVC the eggs and sperm are placed in culture medium in a sterile vial which is hermetically sealed and then placed in the woman's vagina where it is held in place with a vaginal diaphragm. This means that the woman acts like her own IVF incubator and keeps her embryos at the right temperature -- 37° C . This method requires less handling of eggs and embryos and provides a fertilization rate comparable to that of conventional IVF - at much less expense.

Encapsulated gametes

Another innovation in this field has been the concept of encapsulated gamete intrauterine transfer in which the eggs and sperm are transferred into the uterine cavity after placing them in a biodegradable semipermeable matrix. The capsule acts functionally like a temporary incubator chamber which prevents the egg from being damaged as a result of direct contact with the endometrium. After fertilization has occurred in the cavity, the capsule dissolves and releases the embryos for implantation. If this technique lives up to its promise, then many more centres will be able to provide assisted conception services to their patients.

GIFT

While the standard technique for women with blocked tubes has been IVF, the method of GIFT (gamete intrafallopian transfer) developed by Asch is the method of choice for women with non-tubal infertility. In this method the eggs and sperm (gametes) are transferred directly into the fallopian tubes (which is where they 'belong'). Pregnancy rates with GIFT are higher than IVF because the human fallopian tube provides a more physiological milieu for the gametes. GIFT also requires less laboratory expertise than IVF since gamete handling in vitro is minimized. A major limitation with GIFT was the need to perform a laparoscopy in order to transfer the gametes into the tubes. However, Jansen has now developed special catheter sets that allow the gametes to be introduced into the tubes under ultrasound guidance - thus making 'vaginal GIFT' a non-surgical procedure and reducing its expense.

How can we simplify IVF ?

Keep it simple!

In developing countries, IVF clinics need to try to keep IVF as simple and cheap as possible. They should be willing to accept lower pregnancy rates per attempt, but since patients will be able to afford many more attempts, the cumulative conception rate will be quite good. If the cost-effectiveness of treatment is considered (the number of 'take-home babies' per dollar spent) then the cost-effectiveness is likely to be comparable to the best in the world. While it may be true that patients may take longer to get pregnant, they

spend much less money in the long run. Most importantly, this approach will make IVF services available to couples who could never have even dreamed of making a single attempt because of the expense involved.

Simplified protocols are also much more 'patient-friendly'. Since conventional IVF is so expensive, going through the process is very stressful for patients. The monitoring is very intensive and disrupting. Since so much money is at stake, patients are very apprehensive of the outcome, and are distressed if the cycle fails.

Moreover, since the treatment cycle is so expensive, few patients can afford to repeat it - so most have to drop out without succeeding in getting pregnant. If on the other hand, treatment was simplified and inexpensive, patients could be counselled to view each attempt much as an insemination cycle is viewed today - something to be repeated as needed, till the goal is reached. This is a much more realistic option for most patients - and one more of them. This would reduce stress and anxiety considerably, and make treatment much more manageable for the patient.

CHAPTER LII

Why are women scared of IVF?

Why are patients so scared of IVF ?

Since everyone knows that IVF is the most effective way of treating infertility, why are so many infertile couples still so wary of going in for IVF?

Some couples worry that a test tube baby is "weak" or abnormal (and others still believe that the child is grown in a test tube for 9 months and then handed over to the parents!). Fortunately, with increasing awareness, many couples now know that there is nothing "artificial" about a test tube baby. IVF is simply one of the assisted reproductive techniques, which merely allows the doctor to perform in the lab what is not occurring naturally in the bedroom. Multiple studies, done over many years, have come to the reassuring conclusion that the risk of birth defects is not increased after IVF. However, the lack of knowledge about the facts behind IVF is still a problem in smaller towns in India.

In many Indian families, decisions about what treatment to take are still taken by elders, rather than the couple themselves. Many older relatives still think of IVF as "unnatural or abnormal, and are therefore "against it".

A major concern many women have is about the adverse effects of the hormonal injections which they need to take for IVF. We need to remember that these hormones are "natural hormones" - the same hormones which the body produces normally. Some worry that the hormones will cause them to become fat, but it's important to realize that they have no long-term effects, once they get metabolized by the body. while others are concerned that the injections will cause them to "run out of eggs" as a result of which their fertility will decline even faster, or they may become menopausal sooner. Another worry was the fear that the injections would increase the risk of ovarian cancer, but fortunately, many studies have proven that this was unfounded.

A major mind-block is the fear that if IVF fails, then they will have no further treatment option left to explore. Patients know that IVF is the treatment of "final resort" - and many prefer keeping it "in reserve". The unexpressed fear is - if it fails, what next ?

For some, just the fact that the doctor advises IVF itself is a major blow - this forces them to confront the fact that they have a "serious" problem which needs advanced treatment. Many infertile couples still continue to delude themselves that they have a "minor" problem which is "easy to solve" - and does not require "big-gun" therapy.

For others, just the fact that IVF is available helps to reassure them that there is additional treatment they can fall back on - and they prefer keeping it as a "reserve" option.

For a majority of couples, the major limiting factor is the expense. IVF is still extremely expensive, and beyond the reach of most average couples. Once insurance companies start covering medical expenses for infertility, hopefully, this will no longer be a major hurdle. IVF programs which offer money back (risk sharing programs) in case of failure are another innovative approach to helping patients to cope with the financial burden of IVF.

For others, the stress involved in going through an IVF cycle is a major deterrent.

While they have learnt to live with the ups and downs of a normal menstrual cycle, they feel they will not be able to cope with the anxiety and uncertainty associated with an IVF cycle - especially since so much rides on the outcome. The fact that neither they nor their doctors can completely influence the outcome also puts them off.

However, there are major dangers associated with putting off IVF. As with everything else, there is a "right time" for everything, including IVF!

If patients wait too long, their chances of getting pregnant decline as they age - and this decline can be very precipitate after the age of 38. Others get so fed up and frustrated with simpler treatments such as IUI, that they lose confidence in themselves and in their doctors, so that they are no longer willing to attempt IVF. Many will run out of money pursuing cheaper but ineffective treatments.

A practise common to many gynecologists is to repeat IUI (intrauterine insemination) cycles ad infinitum. Most studies have shown that pregnancy rates for any treatment drop after 4 treatment cycles; so that if a treatment has not worked in 4 cycles, the patient should move on to the next step (which is often IVF). However, most gynecologists who do not offer IVF, but do offer IUI, prefer "holding on" to their patients, and rather than referring them for IVF, keep on trying IUI again and again. Often, patients get fed up and frustrated, and lose confidence in both themselves and well as doctors, so that even though there may be effective treatment options available for them, they no longer want to pursue them!

Often, IVF, even though it is more expensive, may be a more cost-effective option!

Do your homework and plan your own course of action, tailored to your own conditions.

While the outcome of IVF is not in your hands, at least making the attempt will give you peace of mind that you tried your best!

CHAPTER LIII

INFERTILITY RECORD SHEET

How can you keep a record of your infertility treatment ?

This form can be useful to summarise and record your infertility history; and is very useful when you need to seek a second opinion.

Date _____

Name _____

Partner Name _____

SOCIAL HISTORY

How long have you been married? _____

How long have you been trying to get pregnant? _____

How long have you been trying to get pregnant with a doctor's help? _____

Was it a General Gynecologist or an Infertility Specialist? _____

About how many times a month do you have intercourse? _____

Does either partner smoke? _____

How much? _____

Does either partner use recreational drugs? _____

Which ones? _____

FEMALE HISTORY

Age _____ Birthdate _____ Height _____ Weight _____

Menstrual periods occur every _____ days. Are they regular? _____

For how many days do you bleed? _____ Do you have endometriosis? _____

Have you ever had pelvic inflammatory disease (PID)?

What pelvic surgeries have you had?

What were the findings?

Number of pregnancies with this partner ____

Number of pregnancies with a previous partner ____

Number of miscarriages ____

Number of abortions ____

Number of tubal pregnancies ____

Number of live births ____

Medical problems and current medications of female partner:

MALE HISTORY

Age ____ Birthdate ____

Number of pregnancies with a previous partner ____

Do you have problems with erection or ejaculation?

Sperm count: ____ million per ml.

Motility ____ %

Male medical problems and current medications

MEDICAL HISTORY

Have you had:

Test	Yes/No	Date	Result
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Hysterosalpingogram

Laparoscopy

Hysteroscopy

Other

Treatment	Yes/No	How many	Date	Any success?
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Ultrasound monitoring

Clomiphene stimulation
with intercourse

Clomiphene stimulation
with insemination

Injectable HMG stimulation
with intercourse

Inseminations without
any stimulation

Injectable HMG stimulation with insemination

In vitro fertilization (IVF)

ICSI

Give details of IVF / ICSI results, if applicable.

Stimulation protocol used

Follicles grown

Eggs retrieved

Embryos transferred

Embryos frozen

OTHER

Are there other pertinent test results, procedures or problems that have been identified?

CHAPTER LIV

DIY - Self Insemination

What is self insemination ?

DIY (do-it-yourself) or self-insemination, is a method in which the woman (or her partner) inserts semen into the vagina herself, without medical intervention. This is a useful technique for couples with sexual dysfunction (e.g. inability to consummate the marriage because of impotence or vaginismus); when the husband cannot perform sexual intercourse for any reason on the fertile days; or for single women or lesbians .

It's surprisingly easy to learn to do, but because most women know so little about their own anatomy, most are very uncomfortable even attempting to try it. This guide should help you with the basics, but the only way to learn is by doing it. You can also ask your doctor for help and she may be able to guide you in the beginning. Some couples may get turned off by the idea, because it is so "clinical", with a little bit of imagination, and your husband's cooperation, you can make it fun!

How is self insemination done ?

So what do you need? Very little, really.

The most important ingredient is a freshly ejaculated semen sample. Ask your husband to ejaculate in a clean glass or plastic container. Make sure this is wide-mouthed, so it's easier for him to aim accurately - you don't want any of it to spill out! Sometimes getting a sample can be difficult, and you may need to seduce your husband! Using a vibrator, or liquid paraffin as a lubricant, can help enormously. You can also use frozen semen samples from a sperm bank, after allowing them to thaw at room temperature.

After the semen sample has liquefied (this takes about 30 minutes), you are now ready to perform the procedure. Ask your husband to put on disposable gloves and then suck up the semen sample into a 10-ml plastic disposable syringe (without a needle). Our patients find it more convenient to use a disposable plastic pasteur pipette, but this may be difficult to find. You can even use a turkey baster, which has become a legendary symbol in the lesbian community, but the small amount of semen does not require such a large instrument.

The semen now needs to be squirted into your vagina, and this is the tricky part. You need to lie on a bed, with your knees and thighs bent, and your knees wide apart, so that your husband can see your vulva clearly. He then guides the tip of the syringe into your vagina (he can do this just by feel, by inserting the left index finger into your vagina, and using this to guide the syringe, which is in his right hand). He can put the syringe in as deep as he wants - don't worry - it won't get lost. He then plunges the barrel, depositing the semen into the vagina.

You may find it easier to lie on the edge of the bed, so that your hips protrude over the edge. Putting a pillow under your hips can make it easier for your husband to perform the insemination. You can remain lying on your back for about ten minutes, after which you can resume normal activity. Some of the semen will leak out, and this is normal.

While using a speculum is not essential, it can help, because it makes it easier to inject the semen at the mouth of the uterus (the cervix). You can use a disposable plastic speculum, and when you insert the speculum, make sure the blades are closed. You can slide it in upwards, or else sideways, turning it when it has been pushed all the way into your vagina. When the handles are above your pubic bone, squeeze them together, which will open your vaginal walls. You will hear a click when the speculum is locked open. If your husband holds a torch, he'll be able to see your cervix, which is round and pink with an opening (the os) in the middle. The mucus may appear as a clear bubble, or a thread like raw egg white. You can use a mirror to see what's going on for yourself, if you so desire! After the insemination, make sure that you release the handles and collapse the blades before removing it from your vagina.

Some women use a cup or cap for self-insemination. Rubber cervical caps are designed for contraception (hence the name "cap") but they can be used for insemination. There is also a cervical cup especially designed for insemination, which is slightly larger and more shallow, the name "cup" indicating that it serves as a semen receptacle. You simply squat down, check the position of your cervix, and insert the cap containing the semen in that direction, holding it upright at all times. Check all around the top of your vagina to make sure that you didn't miss your cervix. The cup can be removed after several hours. Take care to break the suction by hooking a finger over the edge of it before trying to pull it out.

Timing the procedure is extremely important, because you need to inseminate during your "fertile period". Fortunately, it's quite easy to determine when you ovulate, and you can either monitor your cervical mucus, or use an ovulation prediction kit.

You can assemble your own self-insemination kit and this should contain:

- Ovulation prediction test kits (to help you to time the procedure)
- Semen container (wide-mouthed plastic jar)
- Lubricant (liquid paraffin) to help your husband, if needed
- Disposable 10 ml plastic syringe (without needle)
- Disposable paper/rubber gloves

Options:

- Cervical cap
- Plastic speculum
- Torch
- Mirror

If you prefer, you can order a ready-made kit from <http://www.drmlpani.com/store.html>!

CHAPTER LV

Male & Female Infertility laboratory tests - normal ranges and how to interpret them

What is a normal semen analysis report ?

The most important test for assessing male fertility is the semen analysis.

Semen Analysis

Parameter Results /Normal Values

Colour Gray Coagulate? Yes

Liquefy ? Yes

If yes, time in minutes < 30

Volume (ml) 2 to 6 pH 7.5 to 8.0

Sperm concentration 20-200 (million per ml)

Grade of sperm motility Grade a,b (forward progressive)

% motility > 50%

Motile sperm count > 10 million per ml

White blood cells < 1 million/ml

Agglutination nil Morphology > 30 % normal forms

Interpreting the semen analysis reports can be tricky, and you need to remember that values can fluctuate considerably. Read the chapter on Interpreting the Semen Analysis from our book, How to Have a Baby. For some men with azoospermia (zero sperm count), your doctor may need to measure the levels of the following reproductive hormones, in order to make a diagnosis of hypogonadotropic hypogonadism.

What are the normal hormone values for men ?

Normal Hormone Values for men

Testosterone 300 - 1100 ng/dl

Prolactin 7 - 18 ng/ml

Luteinising Hormone (LH) 2 - 18 mIU/ml

Follicle Stimulating

Hormone (FSH): 2 - 18 mIU/ml

Estradiol (Day 3): < 50 pg/ml

What are the normal hormone values for women ?

Normal Hormone Values for women

The most important tests for women are blood tests for measuring the key reproductive hormones. We usually measure 4 key reproductive hormones - FSH (follicle stimulating hormone) ; LH (luteinising hormone) , prolactin; and TSH (thyroid stimulating hormone) on Day 3 of the cycle as part of the basic infertility workup.

Phase of Cycle

Hormone Follicular Day of LH Surge Mid-luteal

Follicle Stimulating < 10 mIU/ml > 15 mIU/ml -
Hormone (FSH)

Luteinising Hormone

(LH) < 7 mIU/ml > 15 mIU/ml -

Prolactin < 25 ng/ml

Thyroid Stimulating Hormone 0.4 - 3.8 uIU/ml
(TSH)

Values can vary from lab to lab, so please check what the normal range is in your lab. Interpreting the results correctly is very important, so please ask your doctor for help !

The FSH level measures your ovarian reserve (ovarian function). A high level (of more than 10 mIU/ml) suggests poor ovarian function.

Very low levels of FSH and LH suggest you have hypogonadotropic hypogonadism.

Normally, the level of LH and FSH is roughly the same. A high LH with a normal FSH level (a reversed LH:FSH ratio of more than 2:1) suggests PCOD (polycystic ovarian disease).

The TSH is an excellent test for screening for hypothyroidism (low thyroid function).

A high level of prolactin is called hyperprolactinemia; and needs to be treated.

The 2 key hormones produced by your ovary are estradiol and progesterone.

Phase of Cycle

Hormone Follicular Day of LH Surge Mid-luteal

Estradiol (E2) < 50 pg/ml (Day 3) > 100 pg/ml

Progesterone < 1.5 ng/ml > 15 ng/ml

The Day 3 estradiol level should be less than 50 pg/ml. A high Day 3 estradiol level suggests poor ovarian reserve. The estradiol level rises in the follicular phase as the

follicle matures, and is very useful for measuring follicular activity. A mature follicles produces more than 200-300 pg/ml of estradiol; and serial E2 levels are often measured for monitoring superovulation in IUI and IVF treatment cycles.

The progesterone level should be more than 15 ng/ml about 7 days after ovulation. This suggests that the corpus luteum is functioning normally. A low Day 21 progesterone levels suggests the cycles was anovulatory (no egg was produced).

If the TSH level is abnormal, the doctor will need to measure the levels of your thyroid hormones (T3 and T4).

Free T3 (Triiodothyronine) 1.4 - 4.4 pg/ml
Free T4 (Thyroxine) 0.8 - 2.0 ng/dl

If you are hirsute (have excessive body hair), then some doctors will measure the levels of the following male hormones (called androgens).

Total Testosterone 6.0 - 86 ng/dl
Free Testosterone 0.7 - 3.6 pg/ml
DHEAS 35 - 430 ug/dl
(Dehydroepiandrosterone sulphate)
Androstenedione 0.7 - 3.1 ng/ml

What are normal beta HCG levels during pregnancy?

beta HCG levels

When you get pregnant, the doctor will monitor the health of your pregnancy by measuring your beta HCG (also known as beta) levels. A pregnancy should be documented as early as possible. [This is important, because appropriate care and precautions can then be taken at an early stage. The most sensitive, accurate and reliable pregnancy test is a blood test for the presence of beta HCG (human chorionic gonadotropin), often just called "beta". The HCG is produced by the embryo, and is the embryo's signal to the mother that pregnancy has occurred. Beta HCG levels vary according to the gestational age. In a non-pregnant woman, they are less than 10 mIU/ml. They are typically about 100 mIU/ml 14 days after ovulation in a healthy singleton pregnancy. They should double every 48- 72 hours in a healthy pregnancy. The levels are higher in a multiple pregnancy; and if the levels don't double as expected, this suggests that the pregnancy is unhealthy. Possibilities include a non-viable intrauterine pregnancy which will miscarry; or an ectopic pregnancy. If the beta HCG level is more than 1000 mIU/ml, and the doctor cannot see a pregnancy sac in the uterine cavity on vaginal ultrasound scan, then it's possible you have an ectopic pregnancy.

Beta HCG levels can be measured in the blood by RIA (radioimmunoassay) , CLIA (chemiluminescent assay) and DELFIA (fluorescent immunoassay) testing; and positive

levels (more than 10 mIU/ml) in the blood can be detected as early as 2 days before the period is missed. In the old days, the only way of determining the presence of HCG was by testing the urine, i. e, by using urine pregnancy test kits. Modern urine pregnancy kits (using monoclonal antibody technology) are now quite sensitive and can detect a pregnancy as early as 1 to 2 days after missing a period (at a blood HCG level of about 50 to 100 mIU/ml). The benefit of urine pregnancy test kits is that they are less expensive; and testing can be done at home by the patient herself. However, instructions need to be followed carefully, and errors in interpreting the test results are not uncommon. These errors could occur if the urine is too dilute; or if the test is not done properly; or if there is a urinary tract infection exists.

The major advantage of blood tests is the fact that they measure the actual level of the HCG in the blood - and this factor can be very helpful in managing pregnancy problems, if they occur. Most clinics start testing beta HCG levels about 14 - 16 days after egg collection; and repeat the test every 48-72 hours. As the embryo grows rapidly, HCG levels normally double every 2 to 3 days. Thus, one reliable sign of a healthy pregnancy is the fact that the HCG levels are increasing rapidly, and often doctors will measure serial beta HCG levels 3 days apart in order to determine the viability of the pregnancy. A rising HCG level is reassuring. Typically, in a healthy singleton pregnancy, the beta HCG level is about 100 mIU/ml about 16 days after ovulation, though this level can vary considerably. The levels are higher in multiple pregnancies; and lower in non-viable pregnancies and ectopic pregnancies.

Problems with HCG testing can occur if you have earlier been given HCG (human chorionic gonadotropin) injections for inducing ovulation. Normally, this exogenous HCG is excreted by the body in 10 days; but sometimes it can linger on. This is why, if the HCG level is very low, the test may need to be repeated, to confirm that the level is increasing.

What are "biochemical pregnancies" ? These are pregnancies in which the HCG test is positive after the period has been missed; the levels increase, but are still low; and no pregnancy is ever documented on ultrasound. Biochemical pregnancies are often seen after IVF and GIFT. While they are not clinical pregnancies, they are of useful prognostic information, because they may mean that your chance of getting pregnant in a future cycle are good.

One drawback with the HCG test is that a positive HCG simply means a pregnancy is present in the body - it does not provide any information about the location of this pregnancy, which may be tubal or ectopic.

During the very early pregnancy, HCG levels are the only way of monitoring the pregnancy. HCG levels which do not increase as rapidly as they should may mean that there is a problem with the pregnancy - the embryo may miscarry because it is unhealthy; or the pregnancy could be an ectopic pregnancy. Differentiating between the two conditions is obviously important, and this is where vaginal ultrasound plays a key role.

Glossary

Abortion: the medical term for miscarriage. The various types include:

- **Complete abortion:** A miscarriage in which all of the products of conception have been expelled and the cervix is closed.
- **Habitual abortion:** A miscarriage occurring on two or more separate occasions.
- **Incomplete abortion:** A miscarriage in which only a portion of the products of conception have been expelled. This usually requires dilatation and curettage.
- **Induced abortion:** An intentional termination of pregnancy.
- **Inevitable abortion:** A miscarriage that cannot be halted.
- **Missed abortion:** A miscarriage in which a dead fetus and other products of conception remain in the uterus for four or more weeks.
- **Selective abortion:** A term often used to refer to intentional termination of one or more gestational sacs within the uterus, usually in the case of a multiple pregnancy (triplets or more).
- **Spontaneous abortion:** A miscarriage or the unintended termination of a pregnancy before the twentieth week.
- **Therapeutic abortion:** An intentional termination of pregnancy for the purpose of preserving the life of the mother.
- **Threatened abortion:** symptoms such as vaginal bleedings, with or without pain, which may end with a miscarriage or with continuation of a normal pregnancy.

Adhesion: An abnormal attachment of adjacent tissues by bands, scars or masses of fibrous tissue.

Adrenal Glands: Two glands near the kidneys that produce hormones, including some male sex hormones - the adrenal androgens.

Agglutination of Sperm: Sticking together of sperm.

Amenorrhea: The absence of menstruation.

Ampulla: The outer half of the fallopian tube, where fertilisation occurs. It opens into the abdominal cavity through the tubal ostium, which is lined by the fimbria.

Androgens: Male sex hormones. Testosterone is one example.

Andrology: The science of diseases peculiar to the male sex, particularly infertility, and sexual dysfunction.

Anomaly: A malformation or abnormality in any part of the body.

Anovulation: Total absence of ovulation. Note: This is not necessarily the same as "amenorrhea." Menses may still occur with anovulation.

Anovulatory Bleeding: The type of menstruation often associated with failure to ovulate. May be scanty and of short duration ; or abnormally heavy and irregular .

Antibody: A protective protein produced in the body that fights or otherwise interacts with a foreign substance in the body.

Artificial Insemination by Donor (AID): The injection of donor semen into a woman's reproductive tract for the purpose of conception.

Artificial Insemination by Husband (AIH): The injection of husband's semen into the wife's reproductive tract for the purpose of conception.

Aspermia: The absence of semen . This is not the same as azoospermia.

Asthenospermia: A condition in which the sperm do not move (swim) at all or move more slowly than normal.

Azoospermia: The absence of sperm in the ejaculate.

Basal Body Temperature (BBT): The temperature of the woman, taken either orally or rectally, upon waking in the morning before any activity. Used to help determine ovulation.

Bicornuate Uterus: A congenital malformation of the uterus in which it appears to have two "horns " (cornu).

Capacitation: The process by which sperm are altered (usually during their passage through the female reproductive tract) that gives them the capacity to penetrate and fertilize the ovum.

Cervix: The lower section of the uterus which protrudes into the vagina

Child-Free Living: A resolution to infertility in which the couple opts for a life-style without parenting, either temporarily or permanently.

Chlamydia: A sexually transmitted disease that may cause impaired fertility .

Chromosomes: Rod-shaped bodies in a cell's nucleus which carry the genes that convey hereditary characteristics. Made up of DNA.

Cilia: Microscopic hair-like projections from the surface of a cell capable of beating in a coordinated fashion.

Clitoris: The small erectile sex organ of the female, located in front of the vagina and similar to the penis of the male.

Clomiphene Citrate: A synthetic drug used to stimulate the hypothalamus and pituitary gland to increase FSH and LH production. It is usually used to treat ovulatory failure due to hypothalamic pituitary dysfunction.

Coitus: Sexual intercourse.

Conception: The fertilization of a woman's egg by a man's sperm resulting in a new life.

Congenital: A characteristic or defect present at birth. It is acquired during pregnancy but is not necessarily hereditary.

Corpus Luteum: The special gland that forms in the ovary at the site of the released egg. This gland produces the hormone progesterone during the second half of the normal menstrual cycle.

Cryobank: A place where tissues (i.e., sperm, oocytes, embryos) are stored in the frozen state.

Cryopreservation (Freezing): A procedure used to preserve (by freezing) and store embryos or gametes (sperm, oocytes).

Cryptorchidism: Undescended testicles.

Dilatation and Curettage (D & C): Dilatation of the cervix to allow scraping of the uterine lining with an instrument (curette). This is also a means to induce abortion in the first trimester of pregnancy.

Dysgenesis: Faulty formation of any organ.

Dysmenorrhea: Painful menstruation.

Dyspareunia: Painful intercourse for either the woman or the man.

Ectopic Pregnancy: A pregnancy in which the fertilized egg implants anywhere but in the uterine cavity (usually in the fallopian tube, the ovary or the abdominal cavity).

Egg (Oocyte) Donation: Surgical removal of an egg from one woman for transfer into the fallopian tube or uterus of another woman.

Ejaculation: The male orgasm during which approximately two to five milliliters of semen (seminal fluid and sperm) are ejected from the penis.

Embryo: The term used to describe the early stages of fetal growth, from conception to the eighth week of pregnancy.

Embryo Transfer: The introduction of an embryo into a woman's uterus after in vitro (or in vivo) fertilization.

Endocrine System: The system of glands including the pituitary, thyroid, adrenals, testicles or ovaries.

Endocrinologist: A doctor who specializes in diseases of the endocrine glands.

Endometrial Biopsy: The extraction of a small sample of tissue from the uterus for examination. Usually done to show evidence of ovulation .

Endometriosis: The presence of endometrial tissue (the normal uterine lining) in abnormal locations such as the tubes, ovaries and peritoneal cavity, often causing painful menstruation and infertility.

Endometrium: The mucous membrane lining the uterus.

Endosalpinx: The tissue lining in the fallopian tube.

Epididymis: An elongated organ in the male lying above and behind the testicles. It contains a highly convoluted canal, four to six meters in length, where, after production, sperm are stored, nourished and ripened for a period of several months.

Erection: The enlarged, rigid state of the penis when sexually aroused.

Estradiol (E2): A hormone released by developing follicles in the ovary. Plasma estradiol levels are used to help determine progressive growth of the follicle during ovulation induction.

Estrogen: A class of female hormones, produced mainly by the ovaries from the onset of puberty until menopause which are also responsible for the development of secondary sexual characteristics in women

Fallopian Tubes: A pair of narrow tubes that carry the ovum (egg) from the ovary to the body of the uterus.

Fertilization: The penetration of the egg by the sperm and fusion of genetic materials to result in the development of an embryo.

Fetal Death: The term often used to include both miscarriage and still-birth.

Fetus: The developing baby from the ninth week of pregnancy until the moment of the birth.

Fibroid Tumor (Leiomyoma): A benign tumor of fibrous tissue that may occur in the uterine wall. May be totally without symptoms or may cause abnormal menstrual patterns or infertility.

Fimbriae: The fringed and flaring outer ends of the fallopian tubes which capture the egg after it released from the ovary.

Follicle: The structure in the ovary that has nurtured the ripening egg and from which the egg is released.

Follicle Stimulating Hormone (FSH): A hormone produced in the anterior pituitary that stimulates the ovary to ripen a follicle for ovulation.

Follicular Phase: The first half of the menstrual cycle when follicle development takes place in the ovary.

Frigidity: The inability to become sexually aroused. Not a known cause of infertility.

Gamete: The male or female reproductive cells- the sperm or the ovum (egg).

Gamete Intra-Fallopian Transfer (GIFT): Procedure in which the sperms and eggs are transferred by laparoscopy into the fallopian tubes where fertilization may then take place.

Genes: Substances that convey hereditary characteristics, consisting primarily of DNA and proteins and occurring at specific points on the chromosomes.

Genetic: Pertaining to hereditary characteristics.

Genetic Abnormality: A disorder arising from an anomaly in the chromosomal structure which may or may not be hereditary.

Genetic Counseling: Advice and information provided, usually by a team of experts, on the detection and risk of recurrence of genetic disorders.

Gestation: The period of fetal development in the uterus from conception to birth, usually considered to be 40 weeks in humans.

Gland: Hormone-producing organ.

GnRH (Gonadotropin Releasing Hormone; LHRH): A hormone released from the hypothalamus that controls the synthesis and release of pituitary hormones FSH and LH.

Gonadotropin: A hormone capable of stimulating the gonads to produce hormones and / or gametes .

Gonads: The glands that make the gametes (the testicles in the male and the ovaries in the female).

Gynecologist: A doctor who specializes in the diseases of the female reproductive system.

Hamster Test (Sperm Penetration Assay), used to determine the ability of a man's sperm to penetrate a hamster egg. Thought to provide evidence of the sperm's fertilising ability.

Hemorrhage: Excessive bleeding.

Hereditary: Transmitted from one's ancestors by way of the genes within the chromosomes of the fertilizing sperm and egg.

Hirsutism: The presence of excessive body and facial hair, especially in women.

Hormone: A chemical, produced by an endocrine gland, which circulates in the blood and has widespread action throughout the body.

Human Chorionic Gonadotropin (HCG): A hormone secreted by the placenta during pregnancy that prolongs the life of the corpus luteum.

Human Menopausal Gonadotropin (HMG): A natural product containing both human FSH and LH. These hormones are extracted from the urine of postmenopausal women.

Hydrocele: A swelling in the scrotum containing fluid.

Hydrosalpinx: A large fluid-filled, club-shaped fallopian tube closed at the fimbriated end . It is a cause of infertility.

Hydrotubation: Lavage or "flushing" of the fallopian tubes with a sterile solution which sometimes contains medication such as antibiotics, enzymes, or steroids.

Hypogonadism: Inadequate gonadal function as manifested by deficiencies in sperm production in males or egg production in females and/or the secretion of gonadal hormones (estrogens and androgens, respectively).

Hypospadias: A malformation of the penis in which the urethral opening is found on the underside rather than at the tip of the penis.

Hypothalamus: A part of the base of the brain that controls the release of hormones from the pituitary.

Hysterosalpingogram: An X-ray study in which a contrast dye is injected into the uterus to show the delineation of the body of the uterus and the patency of the fallopian tubes. Also called a tubogram or uterotubogram.

Idiopathic (Unknown or Unexplained): The term used when no reason can be found to explain the cause of a medical condition.

Immunological Response: The production of antibodies in the woman or man .

Implantation: The embedding of the fertilized egg in the endometrium of the uterus.

Impotence: The inability of the male to achieve or maintain an erection for intercourse due to physical or emotional problems

Incompetent Cervix: A weakened cervix that is incapable of holding the fetus within the uterus for the full nine months. Can be a cause of late miscarriage .

Infertility: The inability of a couple to achieve a pregnancy after one year of regular unprotected sexual intercourse , or the inability of the woman to carry a pregnancy to live birth.

Interstitial Cells: The cells between the seminiferous tubules of the testicles that produce the male hormone testosterone. Also called Leydig cells.

In Vitro (literally, in glass) Fertilization (IVF): A procedure in which a egg is removed from a ripe follicle and fertilized by a sperm cell outside the human body. Also called "test tube baby" and "test tube fertilization."

In Vivo Fertilization: The fertilization of an egg by a sperm within the woman's body.

Kallman's Syndrome: Hypogonadism with anosmia (loss of the sense of smell). Uncommon cause of male infertility.

Karyotype: A study of the chromosomes of the tissue. Used for genetic studies.

Klinefelter's Syndrome: A congenital abnormality of the male wherein he receives an XXY chromosomal complement instead of XY. These men are infertile.

Labia: Folds of skin on either side of the entrance of the vagina.

Laparoscopy: The direct visualization of the ovaries and the exterior of the fallopian tubes and uterus by means of inserting a surgical telescope through a small incision below the naval.

Laparotomy: Abdominal surgery.

Leydig Cells: See interstitial cells.

LHRH: Luteinizing hormone releasing hormone (see GnRH).

Libido: Sexual desire.

Luteal Phase: The days of the menstrual cycle following ovulation and ending with menses during which progesterone is produced by the corpus luteum

Luteal Phase Defect: A shortened luteal phase or one with inadequate progesterone production.

Luteinized Unruptured Follicle Syndrome (LUF): A condition in which the egg is not released during ovulation; the follicle does not rupture and the egg is trapped.

Luteinizing Hormone (LH): A hormone secreted by the pituitary gland. Secretion of LH increases in the middle of the cycle to induce release of the egg.

Menarche: The onset of menstruation in girls.

Menopause: The cessation of menstruation due to aging or failure of the ovaries. Most commonly occurs between the ages of 40 and 50.

Menotropins (Human Menopausal Gonadotropin or HMG): Injections which containing FSH and LH. They are produced by extraction from the urine of menopausal women.

Menstruation: The shedding of the uterine lining by cyclic bleeding that normally occurs about once a month in the mature female.

Miscarriage: A spontaneous abortion of a fetus up to the age of viability.

Mittelschmerz: German for "middle pain," referring to the pain during ovulation that some women experience.

Morphology of sperm: The study of the shape of sperm cells. This evaluation is part of a semen analysis.

Motility of Sperm: The ability of the sperm to move about.

Mumps Orchitis: Inflammation of the testicle caused by mumps virus. Can lead to sterility if infection with the virus occurs after puberty.

Myomectomy: Surgical removal of a fibroid tumor (myoma) in the uterine muscular wall.

Necrostermia: A condition in which sperm are produced and found in the semen but they are dead. These sperm cannot fertilize eggs.

Nidation: The implantation of the fertilized egg in the endometrium of the uterus.

Obstetrician: A doctor who specializes in pregnancy and childbirth.

Oligo-Ovulation: Infrequent ovulation, usually less than six ovulatory cycles per year.

Oligospermia: An abnormally low number of sperm in the ejaculate of the male.

Oocyte: The egg.

Oocyte Retrieval: A surgical procedure to collect the eggs contained within the ovarian follicles.

Orchitis: An inflammation of the testes.

Ovarian Failure: The inability of the ovary to respond to any gonadotropic hormone stimulation, usually due to the absence of oocytes.

Ovaries: The sexual gland of the female which produces the hormones estrogen and progesterone, and in which the ova are developed.

Oviduct: Fallopian tube.

Ovulation: The discharge of a mature egg, usually at about the midpoint of the menstrual cycle.

Ovulation Induction: The use of hormone therapy (clomiphene citrate, HMG,HCG) to stimulate development and release.

Ovum: The egg (reproductive) cell produced in the ovaries each month. (The plural of ovum is ova.)

Pelvic Inflammatory Disease (PID): Inflammatory disease of the pelvis, often caused by infection.

Penis: The male organ of intercourse.

Pituitary: A gland located at the base of the human brain that secretes a number of important hormones related to normal growth and development and fertility.

Polycystic Ovarian Syndrome (PCO): Development of multiple cysts in the ovaries due to arrested follicular growth resulting in an imbalance in the amount of LH and FSH released .

Polyp: A nodule or small growth found frequently on mucous membranes, such as in the cervix or the uterus.

Postcoital Test (Huhner Test): A diagnostic test for infertility in which vaginal and cervical secretions are obtained following intercourse and then analyzed under a microscope.

Progesterone: A hormone secreted by the corpus luteum of the ovary after ovulation has occurred. Also produced by the placenta during pregnancy.

Prostate: A gland in the male that surrounds the first portion of the urethra near the bladder. It secretes an alkaline liquid that neutralizes acid in the urethra and stimulates motility of the sperm.

Pyospermia: A condition in which the presence of white cells in the semen indicates possible infection.

Retrograde Ejaculation: Discharge of semen backward into the bladder rather than forward through the penis.

Retroverted Uterus: uterus that is bent backward.

Rubin Test: Obsolete test in which a gas such as carbon dioxide is blown into the uterus under pressure to test if the fallopian tubes are open.

Salpingitis: Inflammation of the fallopian tubes.

Salpingolysis: Surgery to clear the fallopian tubes of adhesions.

Salpingoplasty: Surgery to correct blocked fallopian tubes.

Scrotum: The bag of skin and thin muscle that holds the testicles.

Secondary Infertility: The inability to conceive or carry a pregnancy after having successfully conceived and carried one or more pregnancies.

Semen: The sperm and seminal secretions ejaculated during orgasm.

Semen Analysis: The study of a fresh ejaculate under the microscope.

Seminal Vesicle: A pair of pouch-like glands above the prostate in the male that produce a thick, alkaline secretion that is passed in the semen during ejaculation.

Seminiferous Tubules: The long tubes in the testicles in which sperm are formed.

Septum: An abnormality in organ structure present since birth in which a wall is present where one should not exist.

Sperm (Spermatozoa): The male reproductive cell, that has measurable characteristics such as:

Motility: Refers to percent of sperm demonstrating any type of movement.

Count (or Density): Refers to the number of sperm present.

Morphology: Refers to form or shape of the sperm.

Viability: Refers to whether or not the sperm are alive.

Sperm Bank: Place in which sperm (from donor or from husband) is stored frozen for future use in artificial insemination.

Sperm Washing: A technique that separates the sperm from the seminal fluid.

Spermatogenesis: The production of sperm within the seminiferous tubules.

Spinnbarkeit: The stretchability of cervical mucus.

Split Ejaculate: A method of collecting a semen specimen so that the first half of the ejaculate is caught in one container and the rest in a second container. The first half usually contains the majority of the sperm.

Surrogate mother: A woman who gestates an embryo and then turns over the child to the infertile couple, who may be its genetic parents.

Testicles: The male sexual glands of which there are two. Contained in the scrotum, they produce the male hormone testosterone and produce the male reproductive cells, the sperm.

Testicular Biopsy: Surgical excision of testicular tissue to determine the ability of the testes to produce normal sperm

Testicular Failure: Occurs when the testes fail to produce sperm.

Testosterone: The most potent male sex hormone, produced in the testicles.

Test-Tube Baby: A child born through in vitro fertilization.

Thyroid Gland: A gland located at the front base of the neck which secretes the hormone thyroid which is necessary for normal fertility.

Tuboplasty: Surgical repair of fallopian tubes.

Turner's Syndrome (Ovarian Dysgenesis): A congenital abnormality of the female wherein she receives an XO instead of an XX genetic sex complement. Women with this condition are sterile.

Ultrasound (Sonography): A imaging technique for visualizing the growth of ovarian follicles during infertility therapy .

Unexplained Fertility: See idiopathic infertility.

Urethra: The tube that carries urine from the bladder to the outside. In men it also carries semen from the prostate to the point of ejaculation during intercourse.

Urologist: A doctor who specializes in diseases of the urinary tract in men and women, and the genital organs in men.

Uterotubogram: See hysterosalpingogram.

Uterus: The hollow, muscular organ in the woman that holds and nourishes the fetus until the time of birth.

Vagina: The birth canal opening in the woman extending from the vulva to the cervix of the uterus.

Vaginismus: A spasm of the muscles around the opening of the vagina, making penetration during sexual intercourse either impossible or very painful.

Varicocele: A varicose vein of the testicles, sometimes a cause of male infertility.

Vas Deferens: A pair of thick-walled tubes about 45cm long in the male that lead from the epididymis to the ejaculatory duct in the prostate.

Vasectomy: Surgery to excise part vas deferens to sterilize a man.

Vasogram: X-ray of the sperm ducts.

Venereal Disease (VD): Any infection pertaining to or transmitted by sexual intercourse. Also known as STD or sexually transmitted disease - most commonly gonorrhea , syphilis and chlamydia.

Viscosity: Thickness of the semen.

Vulva: The external genitalia of the female.

Zygote: An embryo in early development stage.

Zygote Intra-Fallopian Transfer (ZIFT) Transfer of a zygote into a fallopian tube (usually done by laparoscopy)