Introduction

This booklet contains information about a number of different conditions and treatments

that relate to infertility. Not all of the information will be relevant to your particular needs

and circumstances but some will and we hope you find this useful.

This book is not intended to replace the information given to you during consultation or

by staff at your centre but should compliment that received at consultation and other

visits.

More detailed information about specific treatments, for example IVF, will be provided

separately according to your specific needs.

All efforts are made to keep the information contained within this booklet up-to-date and

accurate. However this is a fast moving field and if new information becomes available

which is material to your treatment and that is not provided here it will be issued as supplementary information.

We would welcome your comments about this booklet and any type of information we

provide to enable us to continue to improve our services.

Comments should be sent to

Quality Manager, Asian Reproductive Medicine Centre (ARMC), 3rd Floor, BMT Centre,

Puthiyara, Kozhikode, Kerala, India.

Tel: +91 495 2724101,102

E mail: info@armcivf.com

NB: If you would like this information available in large print, Braille, audiocassette,

video or translated into another language, please contact the centre as above.

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Managing Director, ARMC, Kozhikkode, India.

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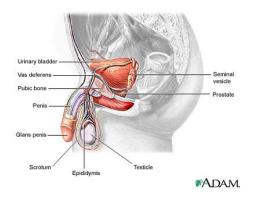
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Reproductive system

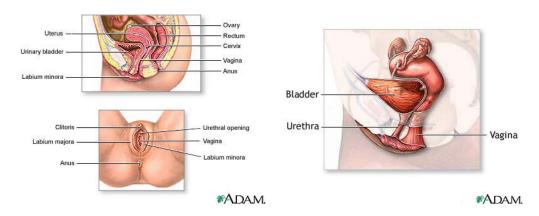
Male Reproductive system

This consists of Testes, Epididymus, Vas, Ejaculatory duct, Seminal vesicles, Prostate gland and Penis. The sperms produced by the cells in the testes will be stored in Epididymus and ejaculated through the urethra during intercourse. A normal erection is required prior to normal ejaculation. The hormone called testosterone also is produced by specific cells in the testes. The vas deferens, spermatic veins and artery and lymphatics together constitute spermatic cord. The abnormal dilatations of these veins are termed as Varicocele.



Female Reproductive system

This consists of External genitalia, Vagina, Cervix, Uterus, Fallopian tubes and Ovaries. Ovaries produce eggs. Fallopian tubes are the two tubular structures on either side of the uterus which carry sperms towards the site of fertilization at its distal part. The finger like projections at the distal end of fallopian tubes is known as fimbria. Uterus has one cavity inside where the fetus grows. The internal lining of the uterine cavity is known as endometrium which sheds out during each menstrual bleeding and then re grows.



Chapter 2

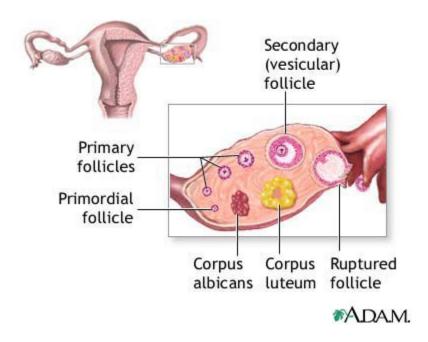
Menstrual Cycle, Fertilization and Pregnancy

Menstrual Cycle:

The normal menstrual cycle is 28days long and it can vary from 21-35 days. Menstrual cycle has different phases

1).Menstrual bleeding - 2-7days. 2) Follicular phase - from the first day of menstrual bleeding to about day12 of the cycle. Egg selection and development of dominant follicle happens. 3) Ovulation - Rupture of the follicle releasing the egg. This happens between $12th - 16^{th}$ days of the cycle. 4) Luteal phase - During this phase endometrium undergoes certain changes to prepare for implantation. This extends from day 16 to 28 of the cycle.

In the normal menstrual cycle, an egg develops each month within one of the ovaries. The egg develops within a fluid filled 'cyst' called follicle. During ovulation follicle ruptures releasing the egg. The egg is then carried toward into the fallopian tube by fimbria, to meet sperms (hopefully). Out of many sperms, only one sperm will be selected by the egg for fertilization. After fertilization it is known as zygote and then embryo. Embryo is carried towards the uterine cavity by fallopian tube for implantation. If fertilization/implantation does not occur, menstrual bleeding follows.



Causes of Infertility

It can be caused by problems affecting either the female or male or a combination of both. Approximately 25% of patients that attend with infertility problems have more than one problem.

Male causes

Sperm of insufficient quantity or quality to reach the fallopian tube or achieve fertilization.

There are many possible causes of this, but they broadly fall into three categories

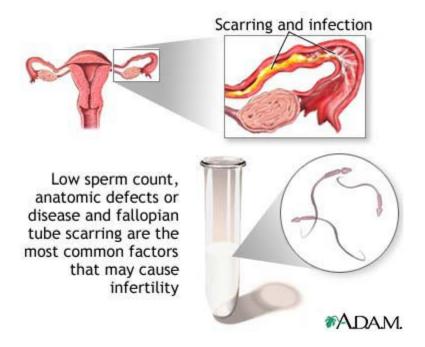
- 1. Complete absence of sperms: No sperm being produced by testes or blockage of vas preventing sperm from appearing in the ejaculate.
- Sperm of reduced number and / or quality: Damage to the sperm forming cells (Infection, Trauma, smoking, alcohol etc.); Antibodies to the sperm; Temperature (occupation, Varicocele), Infection in the male glands(STDs)
- 3. Sexual difficulties: Physical illness (Diabetes, Spinal cord damage etc); Drugs (Anti hypertensive); Psychological.

Female causes:

- 1. Disorders of ovulation Annovulation: Most common reasons are Weight changes, polycystic ovaries, Hormone abnormalities (Hyper prolactinaemia, Thyroid disorders etc), and premature menopause.
- 2. Damage to fallopian tube preventing the egg and sperm coming together Infection, Previous operations etc.
- 3. Endometriosis
- 4. Fibroids
- 5. Anti sperm antibodies
- 6. Congenital abnormalities
- 7. Implantation failure

Unexplained Infertility:

The percentage of couples fall in this category is between 10-20%. In this group, despite careful evaluation, no definite abnormality could be found.



Chapter 4.

Common Investigations in Infertility

Investigations for Male partner

- 1. Semen analysis, Semen Culture and sensitivity, Semen Morphology staining, Semen Fructose
- 2. Blood Hormone assays FSH, LH, TFT, Prolactin, Testosterone etc.
- 3. Testicular biopsy TESA,PESA

- 4. Colour doppler scanning of Scrotum To detect Varicocele
- 5. TRUS- Trans Rectal Ultra Sonography- For ejaculatory duct obstruction

Investigation of Female Partner

- 1. Ultrasonography Transvaginal/Transabdominal. Follicular study
- 2. Sono salpingography
- 3. Hysterosalpingogram
- 4. Laparoscopy
- 5. Hysteroscopy
- 6. Blood Hormones FSH,LH,TFT,Prolactin, DHEAS, AMH
- 7. Antisperm antibodies

Chapter 5

SEMEN ANALYSIS

How to do Semen Analysis?

Semen analysis has a very important role in the evaluation of male infertility. It is a simple diagnostic test in the initial evaluation of an infertile couple.

Things to remember.

- 1. Minimum of 2 to 3days abstinence from sexual activity is required before collecting semen sample for analysis.
- 2. The collection bottle should be clean from dusts, pollutants and chemicals.
- 3. The entire sample should be collected in the collection bottle
- 4. It can be collected by masturbation or while during sexual intercourse
- 5. The collection bottle should be securely closed and delivered to the concerned lab within 60 minutes of collection. It is always better to collect the sample in the designated room provided by the laboratory if available.
- 6. Always perform two consecutive studies if some abnormality is reported.
- 7. Absence of sperms in semen is known as Azoospermia.

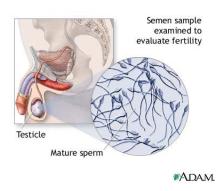
What is a normal semen analysis? (WHO norms)

- 1. Total volume of not less than 2ml
- 2. Total sperm count of not less than 20millions/ml
- 3. Total sperm motility of not less than 50%
- 4. Total normal sperm morphology of not less than 30%

What are the other semen tests?

1. Semen culture and sensitivity test: To identify the semen infection and to decide about the most sensitive antibiotic.

- 2. Sperm morphology staining For detailed study of sperm morphological abnormalities.
- 3. Semen fructose estimation to identify the outflow tract obstructions.





Follicular Study

What is a follicular study?

Ultrasonographic study of development of follicle in ovary along with endometrial development.

What is purpose of a follicular study?

To confirm that a follicle is developing at the correct time in the cycle and is releasing the egg, in other words to confirm ovulation.

Why is follicular study carried out on?

- 1. To confirm ovulation
- 2. Monitoring of ovulation induction
- 3. To help the timing of Intra uterine insemination

How is follicular study carried out?

This is usually carried out by ultrasound examination using a vaginal probe. A probe is inserted into the vagina. The procedure is carried out with empty bladder. It also helps the clinician to see the uterus and endometrium.

How many scans are needed?

Two, three or four times depending on the follicular development.



Chapter 7:

Hystero salpingo graphy (HSG)

It is radiographic visualization of the uterine cavity by injecting a radio opaque dye into the uterine cavity. It is a mildly painful procedure done under aseptic precautions. An HSG done under C-ARM control is the latest trend, so that a cine picture of the dye flowing through the uterine cavity and fallopian tube can be documented for future reference.

Chapter 8

Laparoscopy and Hysteroscopy

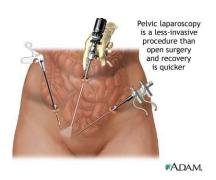
Laparoscopy:

It is visualization of interior of abdominal cavity through a telescope (5mm/10mm), inserted through a small 'key hole' incision made below umbilicus. The procedure will be done under anaesthesia and the abdomen will be distended with CO2 for better visualization. Additional 'Key Hole' incisions will be made depending on the requirement to deal intra abdominal pathology.

Indications are to treat Polycystic ovary (PCO), endometriosis, removal of fibroids, removal of ovarian cystectomy, to correct tubal blocks, Adhesiolysis, to treat ectopic pregnancy and tubal recanalisation

Hysteroscopy:

Hysteroscopy is the visualization of the interior of the uterine cavity by using an endoscope inserted through the cervical canal under anaesthesia. Uterine cavity will be distended with saline or Glycine depending on the type of procedure. It is indicated in conditions- Tubal cannulations, Intrauterine septum resection, resection of sub mucous fibroids, release of intrauterine adhesions, removal of foreign bodies (eg:retained Cu-T) etc.



Chapter 9:

Common Diseases in Infertility

Male:

Varicocele:

Varicocele is the abnormal dilatation of testicular veins around the testes. It causes decrease in sperm count and motility. It can be confirmed by colour Doppler scanning. Surgical treatment of Varicocele is known as TVL-Testicular vein ligation. It helps to improve sperm quality in 30% individuals.

Azoospermia

Azoospermia is the absence of sperms in the semen. It has to be confirmed twice. If it is due to obstruction of vas or ejaculatory duct, the sperms can be retrieved from testes or Epididymus by TESA or PESA and can be used for ICSI. If it is due to testicular failure, the only option will be to use donor programmes or adoption. Testicular failure can be due to Mumps, congenital or late correction or non correction of undescended testes.

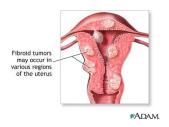
Female:

Endometriosis:

Endometriosis is the abnormal presence of endometrium in sites other than uterine cavity. Common sites are ovaries, peritoneal cavity and myometrium. It presents as severe dysmenorrhoea, ovarian cysts, infertility and chronic pelvic pain. The laparoscopic correction is the ideal initial line of treatment and if not successful in achieving pregnancy IVF-ICSI will be the alternate option

Polycystic ovarian disease – PCO/PCOD.

It is one of the most common diseases in females causing infertility. It is a life style disorder resulting in obesity, abnormal hair growth, irregular menstrual cycles and infertility. The treatment modalities range from, weight reduction, ovulation induction, metformin, laparoscopy and IUI. If all modalities fail IVF will be the natural option.





Infertility treatments

Male:

- 1. Drugs
- 2. Varicocele surgery
- 3. IUI
- 4. ICSI

Females

- 1. Ovulation Induction
- 2. Treatment of infections
- 3. Laparoscopy and Hysteroscopy
- 4. IUI
- 5. IVF and ICSI

Chapter11

Intrauterine Insemination

Intrauterine insemination or IUI is the artificial insertion of sperm directly into the uterine cavity. The sperm is always processed before insemination. This treatment is usually coupled with ovulation induction.

The purpose of this treatment is

- 1. To improve the woman's fertility by enhancing her ovulation by increasing the number of eggs which are produced more than would have been the case naturally.
- 2. To time when the eggs are ripe by scanning the ovaries
- 3. To prepare the sperm by special preparation techniques

4. To inseminate the sperm directly into the uterine cavity at a precisely determined time to ensure the sperm is as close to the egg at the time it is released, and to by-pass any possible hostile effects of the cervical mucus on the sperm.

Treatment involves the following stages

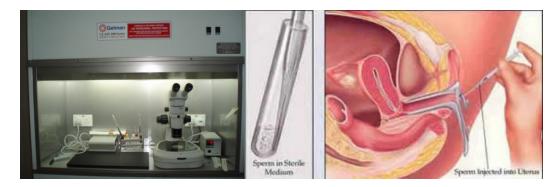
- 1. Ovulation induction
- 2. Ovulation monitoring follicular study
- 3. HCG injection
- 4. Sperm processing
- 5. Insemination
- 6. Luteal support with progesterone.

Success rate:

The chances of a pregnancy resulting are between 7-10% per treatment cycle. The chances will vary according to the individual circumstances of the couple.

How many treatment cycles?

For the treatment of unexplained infertility 3 cycles of treatment are normally carried out and then the situation reviewed. Subsequent advice will depend on a number of factors like the female age and the period of infertility. Normally IVF will be recommended after three failed IUI treatments.



Chapter 12

In Vitro Fertilization (IVF)

In Vitro Fertilization or IVF is the fertilization outside the human body of the egg by the sperm and replacement of the fertilized egg back inside the cavity of the uterus.

IVF may be necessary for a number of different conditions

- Blockage/damage of fallopian tubes
- 2. Endometriosis
- 3. Unexplained infertility

- 4. Male factor infertility
- 5. Ovulation problems that are difficult to treat by conventional methods
- 6. Combination of infertility factors

IVF cannot be carried out in

- 1. Absence of uterus or diseases of uterus preventing implantation
- 2. Ovarian failure
- 3. Contraindications for the procedure Previous pelvic abscess or major bowel surgery in pelvic area
- 4. Major medical contra indications for pregnancy

Upper age limit

Generally IVF may not be very successful after the female partner age of 40yrs.

Success rate

It depends on various factors ranging from female partner's age to the indication for IVF. A good general rule is that a couple embarking upon IVF has a 1 in 5 chance having a live birth with each attempt. The particular circumstances that affect your chance of successful treatment will be discussed with you and the most up to date results will be provided to you.

Steps of IVF treatment

- 1. Preliminary evaluation
- 2. Menstrual cycle Day 2 hormone assays and male partner evaluation
- 3. Injectable hormones- t produce multiple eggs
- 4. Ovulation induction monitoring by ultrasound scanning and blood hormone studies
- 5. Egg retrieval from the ovaries This will be done under general anaesthesia as a day care procedure. Patient will be discharged on the same day
- 6. Fertilization of the egg by sperm in the IVF laboratory
- 7. Embryo transfer on Day2/3/5
- 8. Luteal support with progesterone
- 9. Follow up after 2 weeks for pregnancy test

Complications

- 1. Ovarian hyper stimulation
- 2. Multiple pregnancy
- 3. Pelvic infection
- 4. Ectopic pregnancy

IVF – A team work

IVF treatment to be successful involves a large number of professionals with different expertise who together form the Multidisciplinary Team. During the course of your treatment you will be seen by different members of this team at different stages. Your day to day contact will be with the nursing team. The majority of who have experiences with infertility practitioners who can answer most of your concerns. The medical team will undertake the removal of eggs and replacement of embryos. The embryology team will perform IVF laboratory and ICSI works.



Chapter 13

ICSI- Intra Cytoplasmic Sperm Injection

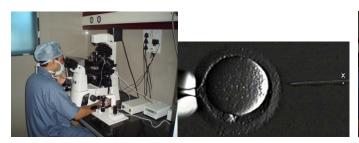
The couple undergoing ICSI goes through exactly the same process as they would in IVF. The key difference is that in IVF the sperm and egg are mixed together in a test tube, where as in ICSI, a single sperm is injected into the substance of the egg.

Conditions which require ICSI.

- 1. Severe male factor infertility Very low sperm count, motility or high percentage of abnormal sperms
- 2. Azoospermia with sperms present only in testes or Epididymus
- 3. Previous failed IVF

Success rate

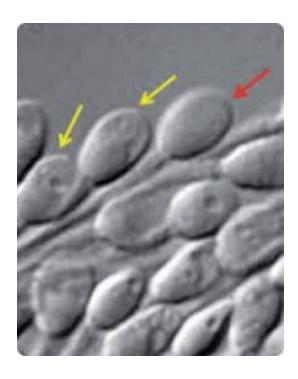
We expect 25% to 40% of embryo transfers to result in clinical pregnancy.





IMSI - Intra-cytoplasmic Morphologically Selected Sperm Injection

IMSI takes ICSI to the next level. ICSI involves us injecting sperm directly into your egg, before we transfer it into your womb. During IMSI, we use a very high power microscope to magnify the sperm around 7000 times. The equipment is more complex and expensive when compared to ICSI This allows us to see in great detail how the <u>sperm</u> looks and to select the best <u>sperm</u> for the ICSI procedure. IMSI is a very new development and is showing promise for a specific group of patients. If we feel you are going to benefit from IMSI we'll discuss this with you. Once the best sperm has been selected the IMSI procedure is carried out in exactly the same way as ICSI.



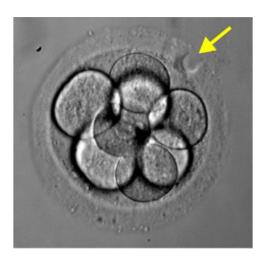
IMSI is available at ARMC IVF. ARMC is the only centre, which you offer IMSI treatment with no additional cost. The first IMSI baby of Malabar region was born out of the treatment at ARMC IVF Calicut in the year 2012. If you would like more information, please contact us.

Chapter 15

Laser Assisted Hatching (LAH)

The advent of the laser has allowed the development of precision techniques to manipulate embryos for enhanced fertility. Laser-assisted hatching can turn around a history of failure for embryos to implant themselves in the uterine wall.

Assisted hatching is used to help the embryo hatch from its protective outer shell, the zona pellucida, and promote implantation in the uterine wall after embryo transfer. Laser-assisted hatching (LAH) with the LYKOS® or ZILOS-tk® uses a highly focused infrared laser beam to remove the zona pellucida in very precise increments. Prior to the clinical availability of the lasers, only mechanical or chemical methods could be used for assisted hatching of human embryos in clinical settings. Laser-assisted hatching requires less handling of the embryo than these other assisted hatching methods. Also, laser-assisted hatching is faster than the other methods and, therefore, the embryo spends less time outside the incubator.



Indications for LAH

- Women over 37 years old
- Women with an elevated baseline level of FSH (follicular stimulating hormone)
- Women with poor prognosis embryos, including conditions such as a thick zona pellucida, slow cell division rate, or high cell fragmentation
- Women who have failed 1 or more IVF cycles
- · Women using frozen/thawed embryos, which may have hardened zona pellucida

Chapter 16

Cryopreservation of Eggs, Sperm and Embryos

Our lab is equipped with the latest technology for cryopreservation and storage, and we were the first clinics to establish an Egg Freezing Program for the general public in North Kerala. By freezing eggs, sperm and embryos in appropriate cases, we can help simplify and lower the cost of future IVF cycles. We have the expert embryology team well experienced in the latest technology in gamete or embryo freezing ie Vitrification.

Cryopreservation of Eggs

Egg freezing benefits two main groups of women. The first are those who are diagnosed with a medical condition whereby the necessary treatments for cure may render them sterile or unable to produce viable eggs. The second is women who are delaying their childbearing for personal reasons, meaning saving eggs now for pregnancy chances at a later time. It is best to have eggs that are frozen when they are of the best quality possible. For instance, eggs frozen at the age of 35 are more usable than fresh oocytes produced at 43 years of age.

As egg freezing technology improves, it may also be used by patients who are undergoing in vitro fertilization (IVF) treatment. Women who produce many excess eggs may eventually be able to elect to freeze their eggs unfertilized, rather than freezing fertilized embryos.

Cryopreservation of Sperm

Our onsite services are available for the short-term storage of sperm specimens as long as the female partner remains our patient. We offer cryopreservation of sperm for men with poor sperm counts who may need a back-up sample stored, those who wish to store a sample before beginning cancer treatment and in cases where the man may be out-of-town at the time of egg retrieval. If long-term storage of your sperm specimen or donor sperm is required, we can help you access quality services, though we do not have an onsite sperm bank.

Cryopreservation of Embryos

Embryo cryopreservation is used most often to store good-quality excess embryos resulting from an IVF-ICSI treatment cycle. Embryos are created after an in vitro fertilization cycle where eggs are retrieved and then placed with sperm. The resultant embryos are then vitrified before being placed in liquid nitrogen for storage.

Chapter 17

Special Procedures

Blastocyst Transfer

This transfer of Day 5 embryos. Blastocyst is the term given to an embryo which has grown normally for 5-6days after fertilization and normally has about 100+ cells.

Surgical extraction of sperm – TESE or PESA

This involves a small operation on the testes to retrieve sperm from either the Epididymus or testes. It is carried out either with local or short general anaesthesia.

Chapter 18

Fertility Counselling

Having a child is a major life event for any individual couple. When this is proving difficult to achieve, and requires medical intervention, it can feel like a major life crisis. The emotional 'ups and downs' experienced by those trying for a baby and undergoing treatments are well recognized within the field of infertility.

For this reason the opportunity for counseling is included as a part of the centre's overall care, and is in accordance with the ICMR guidelines.

Counselling will be helpful for the couples in the following ways.

- 1. To make sense of how the couples are feeling
- 2. Explore and clarify the thoughts and concerns
- 3. Understand the reactions and ways of coping
- 4. Identify choices and make decisions
- 5. Plan their future with or without children
- 6. To Come to terms with treatment not being successful, available or possible at all

The 'roller coaster ride' of investigations, diagnosis, treatment and results can put strain on relationships. This can affect communication and sexual relationships to varying degrees, at varying times. Counselling can help to address these problems. Counselling respects confidentiality, individuality and a person's responsibility to make his/her own decisions.

Chapter 19

Information and Support

The team at ARMC aims to provide the best possible care for every patient. This includes attending to psychological well being as well as to physical needs. Support is provided by all clinic staff to manage not only the practicalities but also the outcomes of treatment – both positive and negative. The clinic staffs are also there to provide information and support to address the implications of treatment particularly those relating to IVF/ICSI procedures.

Chapter 20

Our facilities

Full Infertility evaluation

Fertility Counselling

Hormone assays

Andrology clinic and lab

Ovulation Induction

Follicular study

3D/4D Scanning

Colour Doppler Scanning

Intra Uterine Insemination

In Vitro Fertilization (IVF)

Intra Cytoplasmic Sperm Injection (ICSI)

IMSI

Laser Assisted Hatching

Sperm and Embryo Freezing

Contact Info - ARMC IVF, World wide locations

Kozhikode(Calicut)

(address)

Thrissur

(address)

Mangalore

(address)

Palakkad

(Address)

Kannur

(Address)

Dubai

(Address)

Doha

(Address)

Toll Free No

Email ID:

Team