
بسم الله الرحمن الرحيم

- **Infertility from Prevention to treatments**

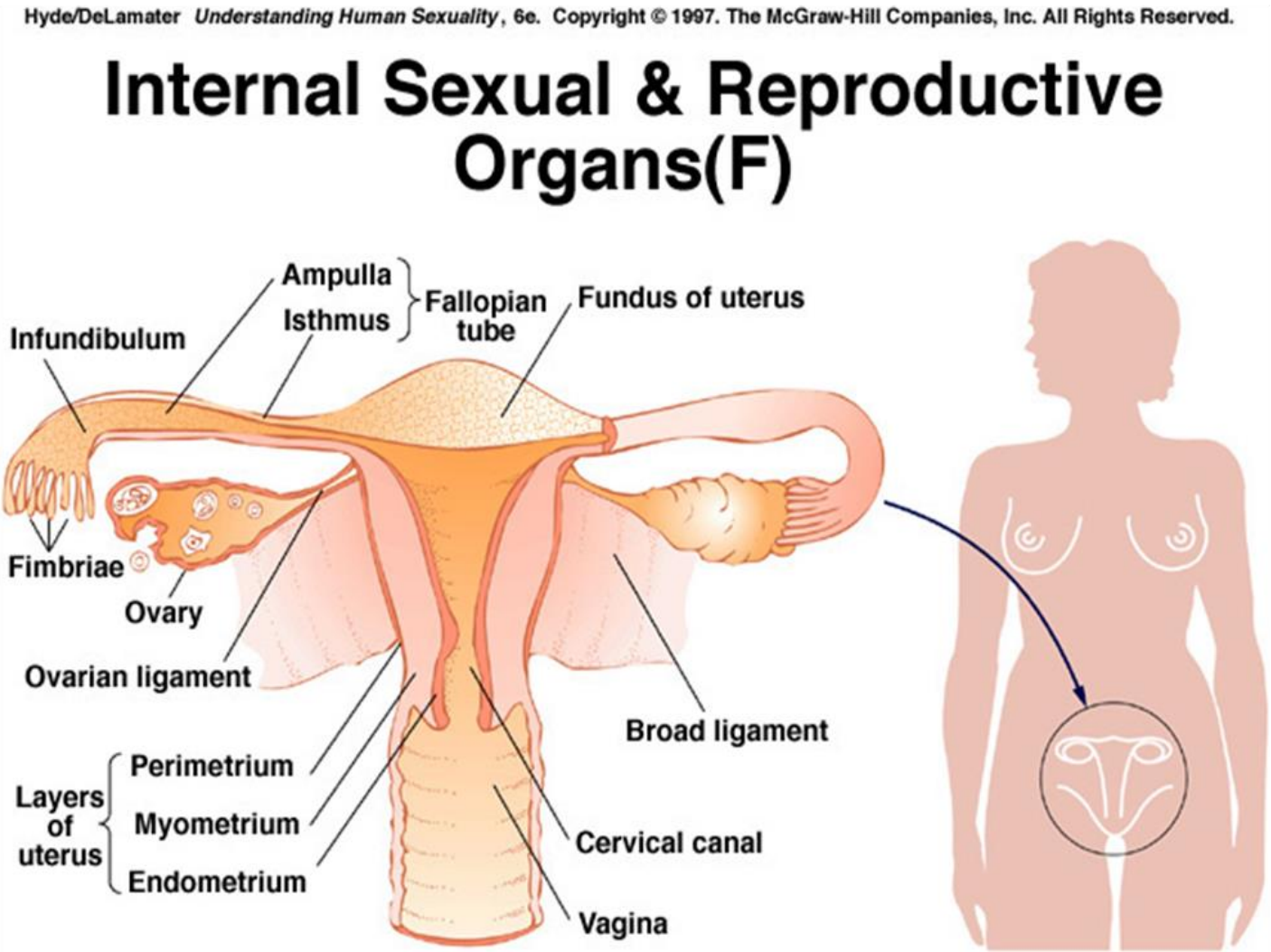
Presented by: Dr Roya Kabodmehri

Overview of Infertility

- Definition: 1 year of well-timed, unprotected intercourse without a pregnancy

- 10-15% of population is infertile (sub fertile)

Female Reproductive Organs



Causes of Female Infertility

- Ovary
- Tubes
- Uterus
- Cervix
- Hormones
- Chromosomes

Causes of Female Infertility - Ovary

- AGE
- Problems with ovulation
- Premature ovarian failure

Ovary - Causes of Anovulation

- Hormone imbalance
- Obesity
- Anorexia
- Significant stress
- Patients display:
  - Irregular menstrual cycles
  - Skipped cycles

Ovary – Premature Ovarian Failure

- Menopause prior to age 40
  - Decreased Estrogen
  - Increased FSH
- Causes
  - Autoimmune
  - Genetic
  - Idiopathic

Causes of Female Infertility – Fallopian Tubes

- Infection (chlamydia)
- Endometriosis
- Tubal ligation (female sterilization

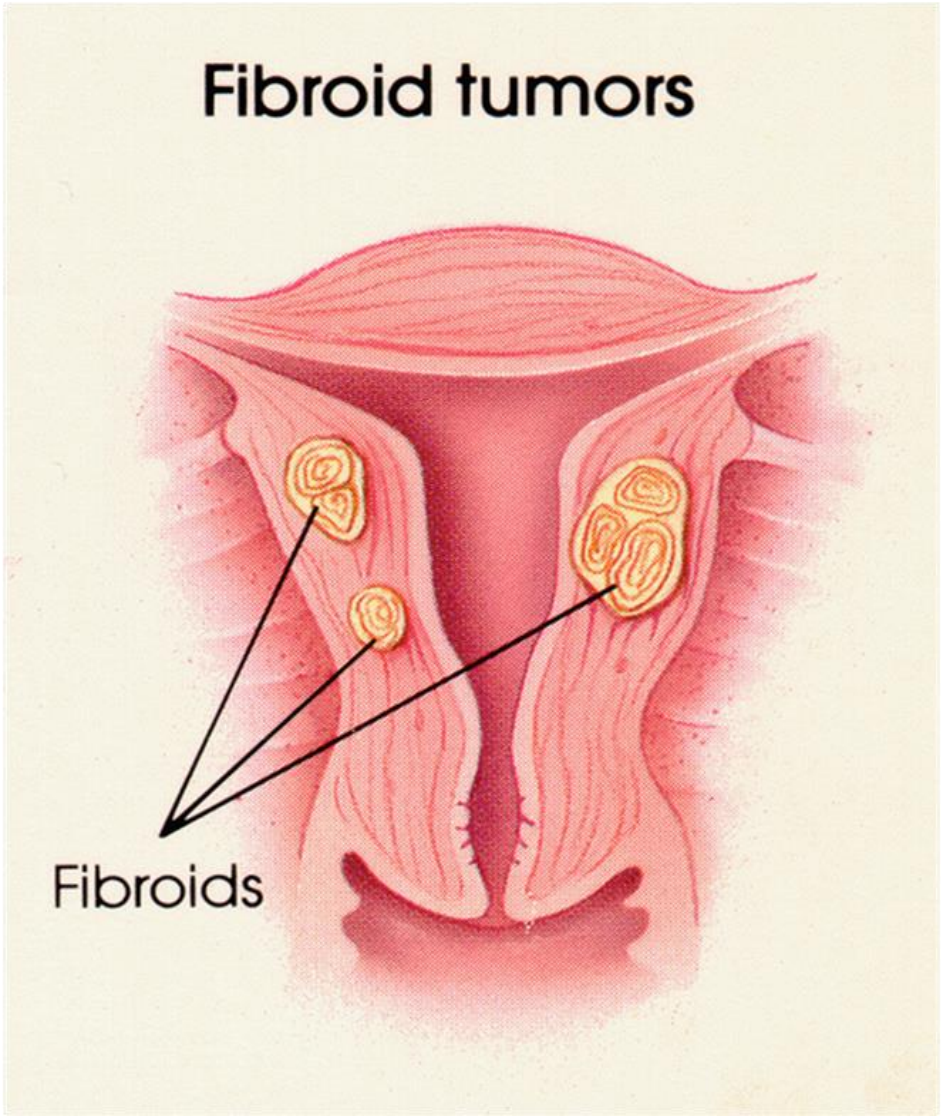
Open Tubes

Blocked Tubes

Female Infertility - Uterus

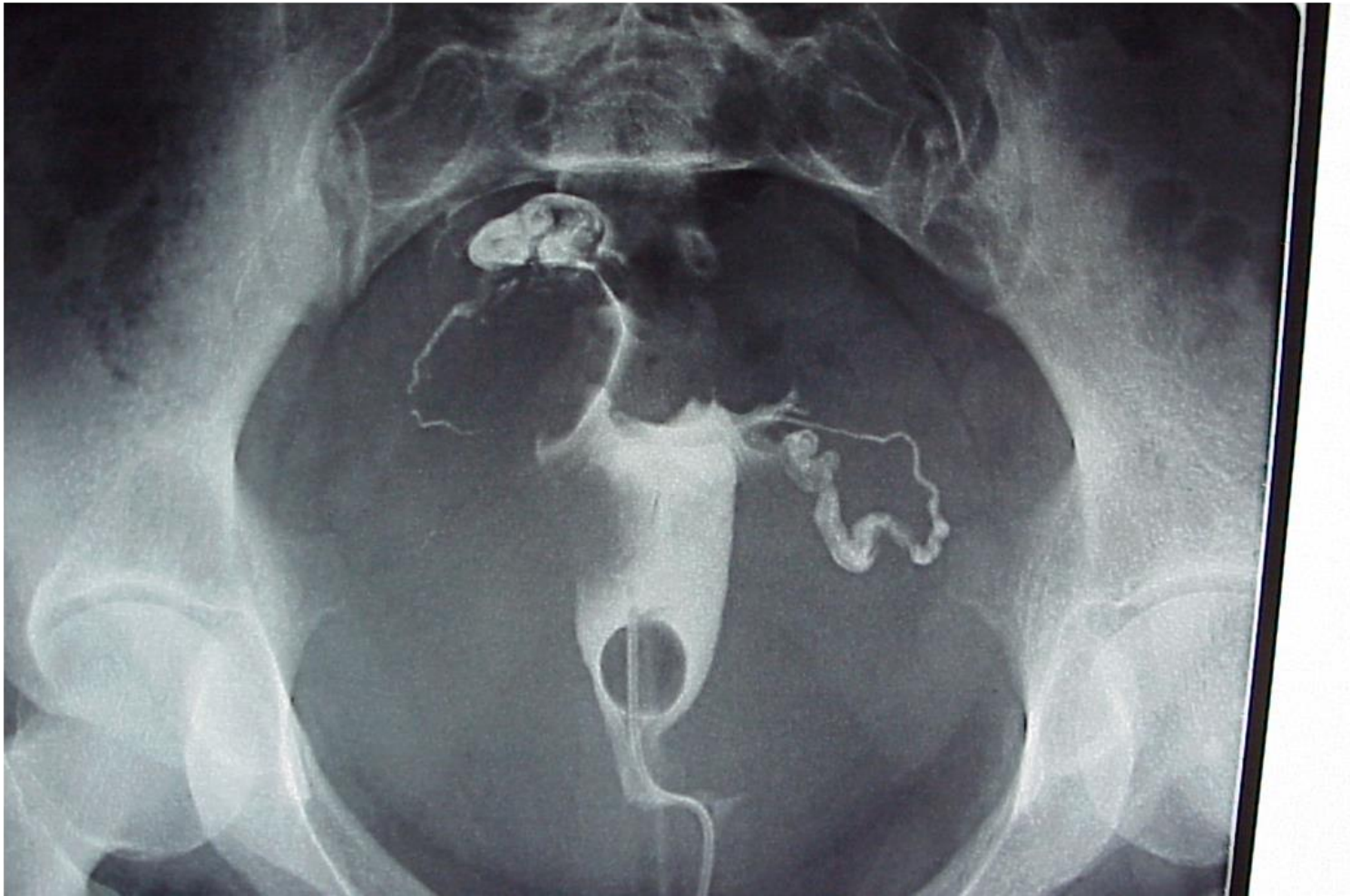
- **Uterus**
  - **Fibroids**
  - **Polyps**
- Mullerian (congenital) defects
  - Absent
  - Bicornuate/Septum

Female Infertility

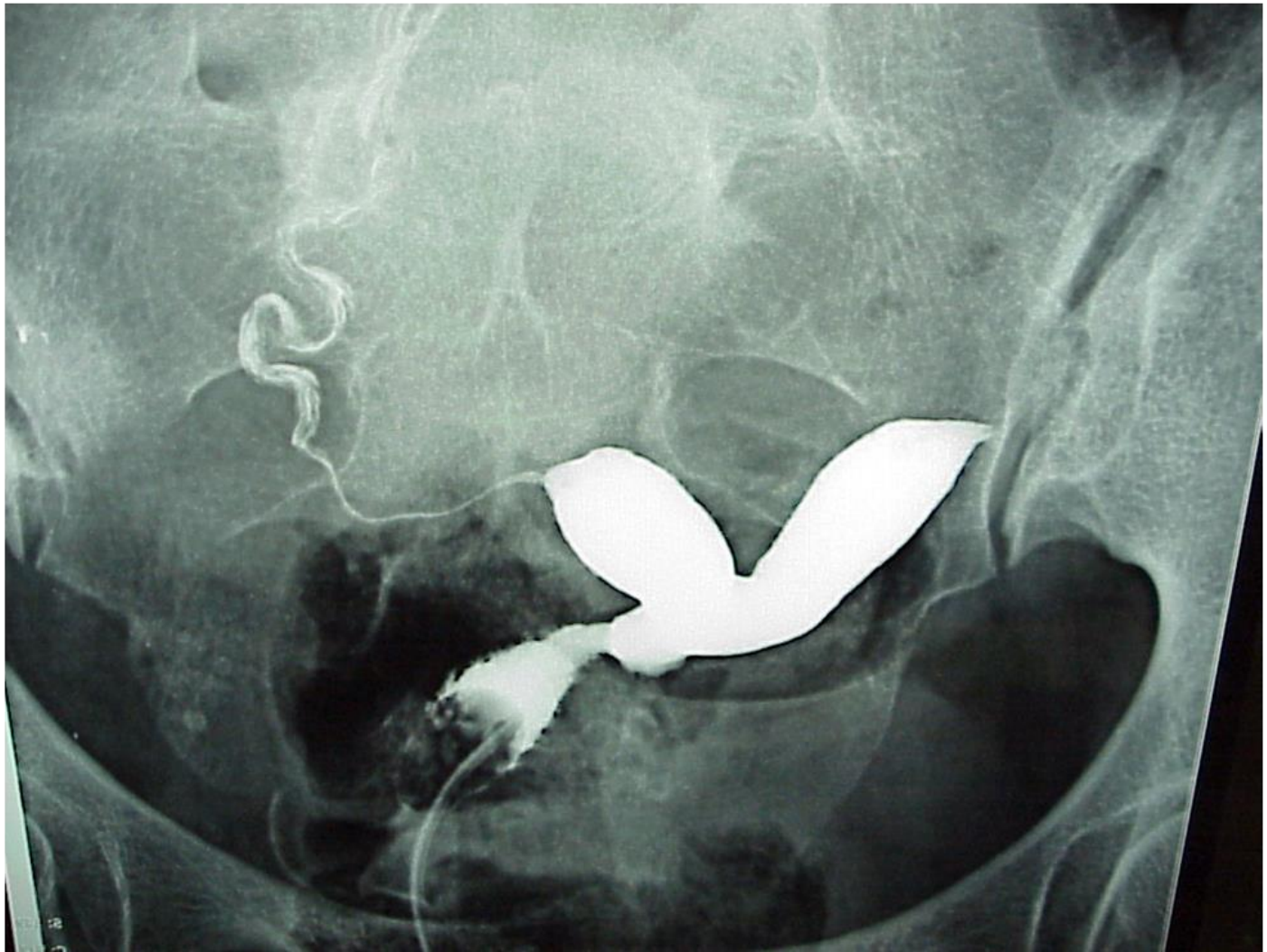


- Uterine muscle tumor
- Benign (>95%)
- 25-30% of women

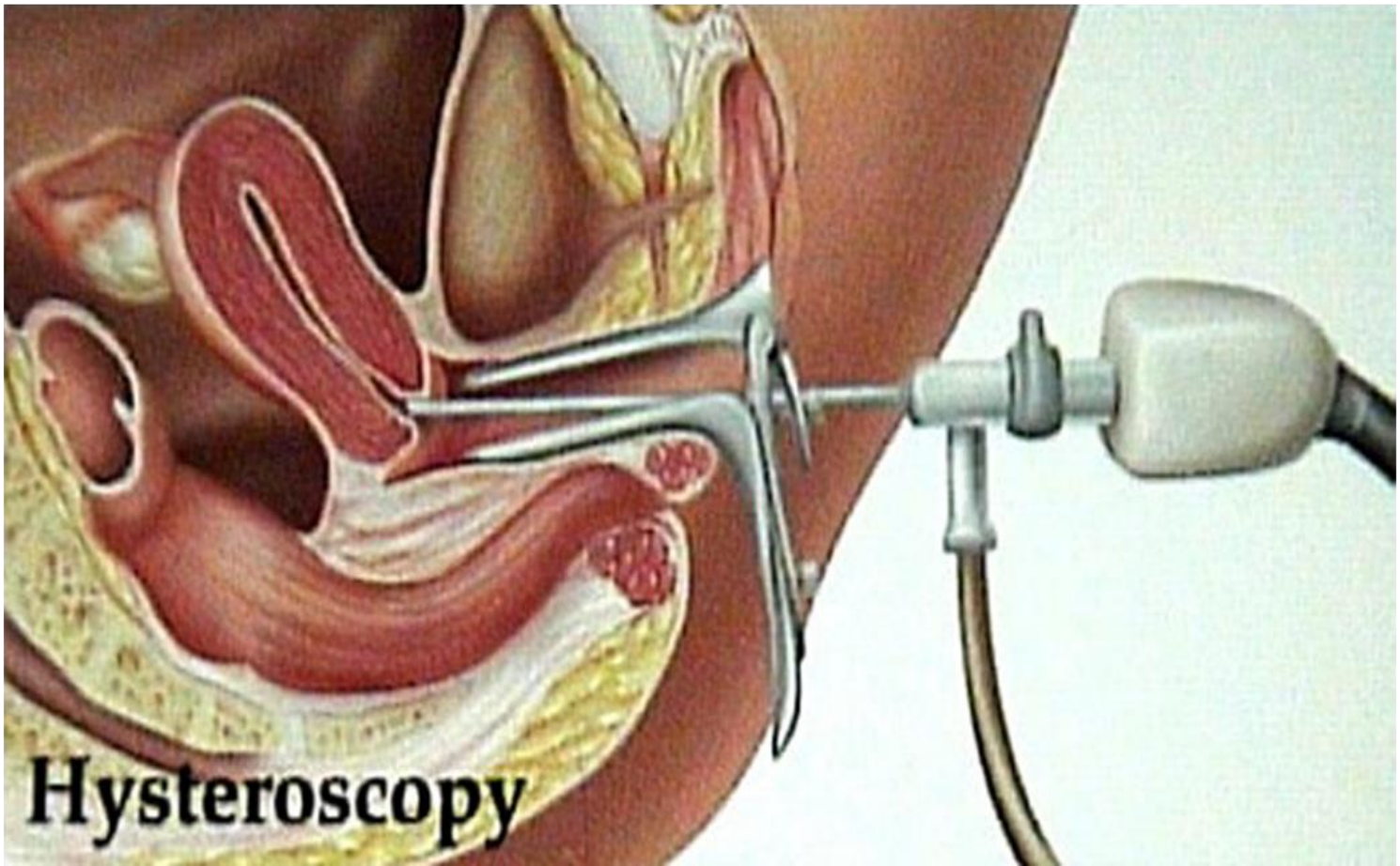
Fibroid Uterus



Mullerian Defect



Treatment with Hysteroscopy



Female Infertility - Cervix

- Cervix
  - Post-surgical
    - Stenosis
    - Mucus changes

Female Infertility - Hormones

- Endocrine abnormality (hormones)
  - Thyroid
  - Prolactin
  - Polycystic ovary syndrome (PCOS)
    - Estrogen, insulin
  - Hypothalamic hypogonadism
    - Stress
    - Exercise (ballet dancer)

Causes of Male Infertility

- Abnormality in sperm production
- Abnormality in sperm function
- Obstruction in the ductal system

Abnormalities of Sperm Production

- Genetic
  - Y chromosome microdeletions
- Damage to testes – anatomical
  - Cryptorchidism
  - Varicocele
- Infection
  - Mumps orchitis

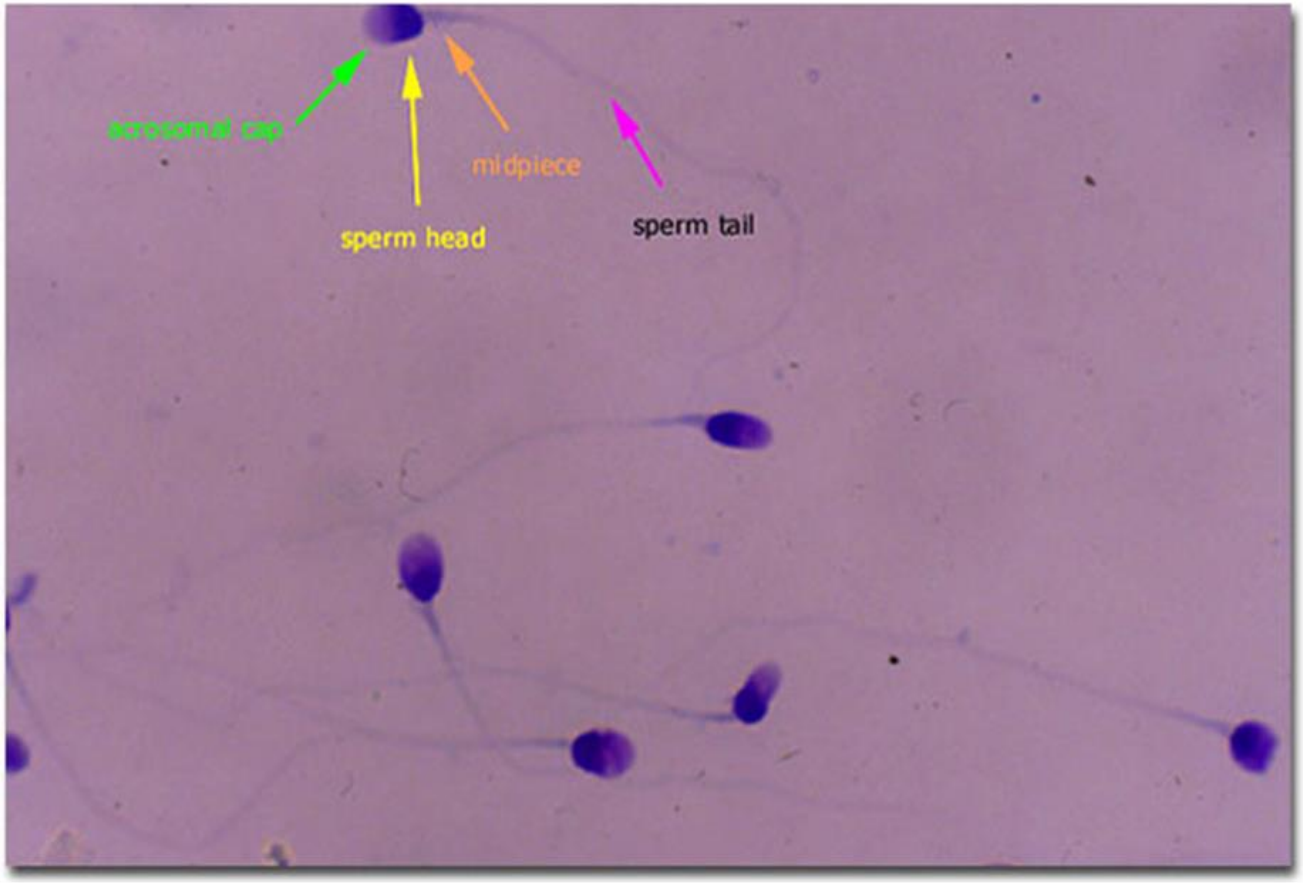
Abnormalities of Sperm Function

- Antisperm antibodies
- Genital tract inflammation
  - prostatitis
- Varicocele
- Failure of acrosome reaction
- Problems with sperm binding/penetration

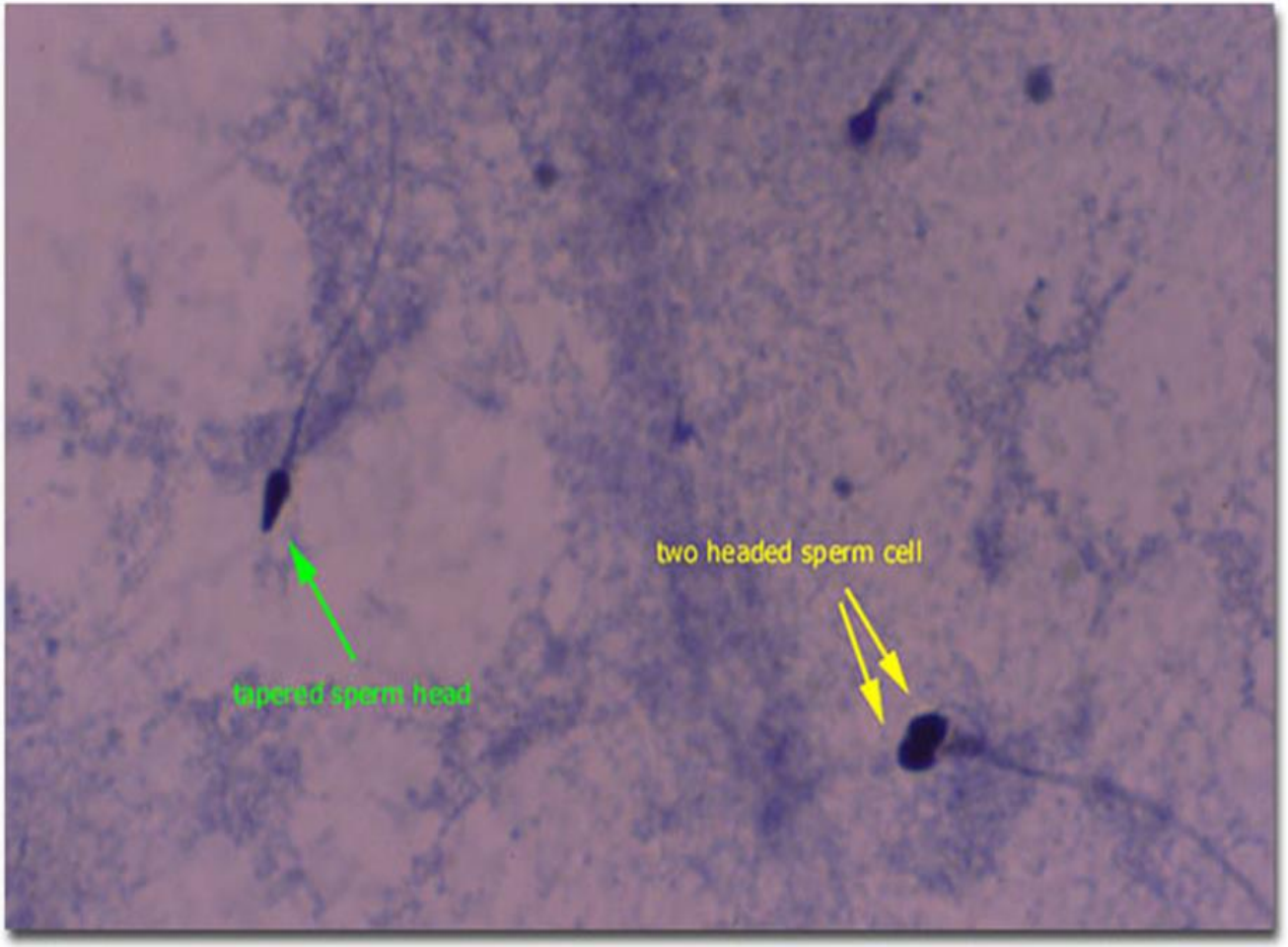
Obstructions in Ductal System

- Vasectomy
- Congenital bilateral absence of the vas deferens
- Epididymis/ejaculatory ducts
  - Congenital or acquired

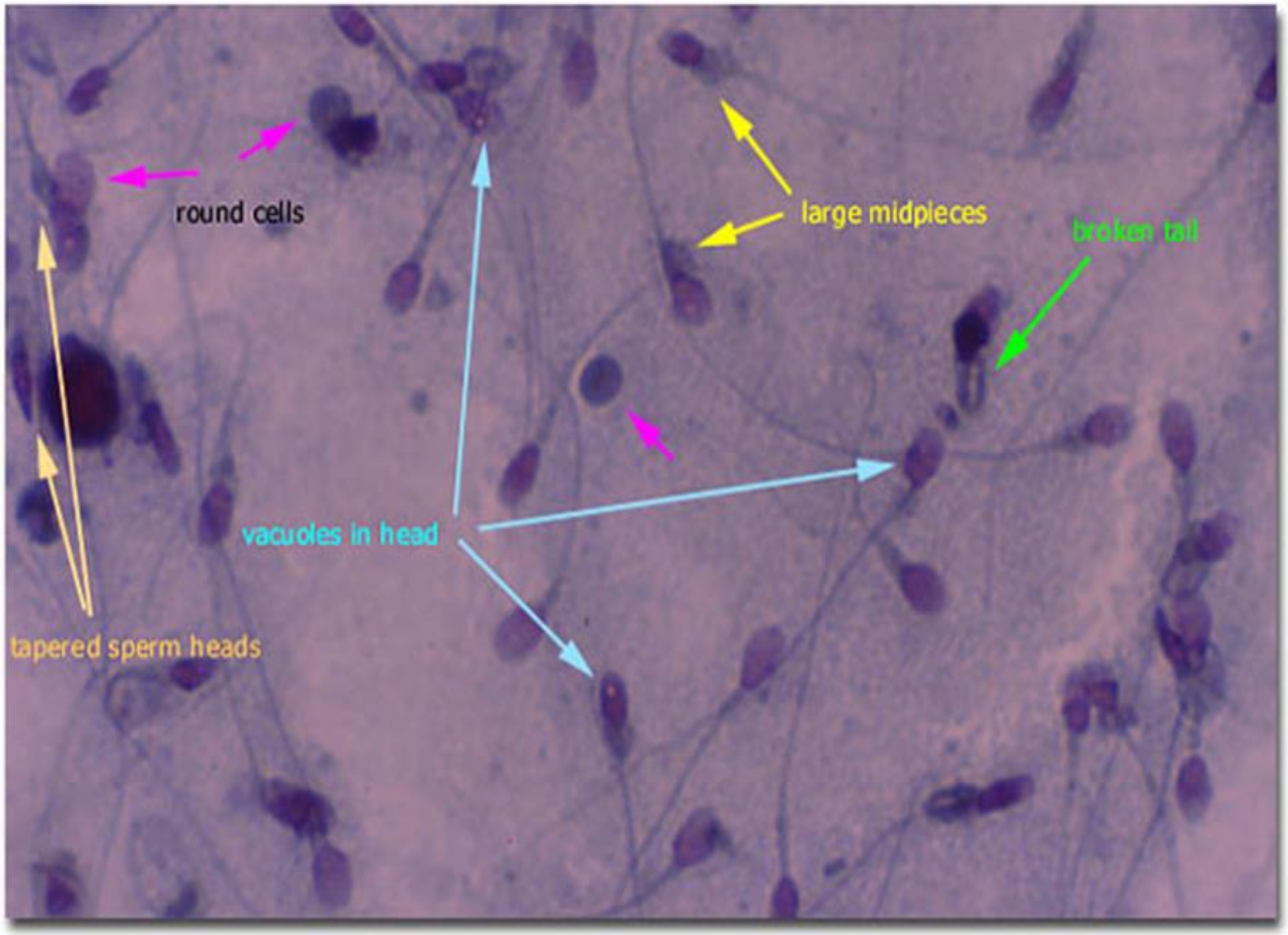
Normal Sperm Morphology



Abnormal Morphology



Abnormal Morphology



Male Infertility - Lifestyle

- Tobacco
- Marijuana
- Alcohol
- Cocaine
- Steroids (can be permanent)
- Heat
- Exercise

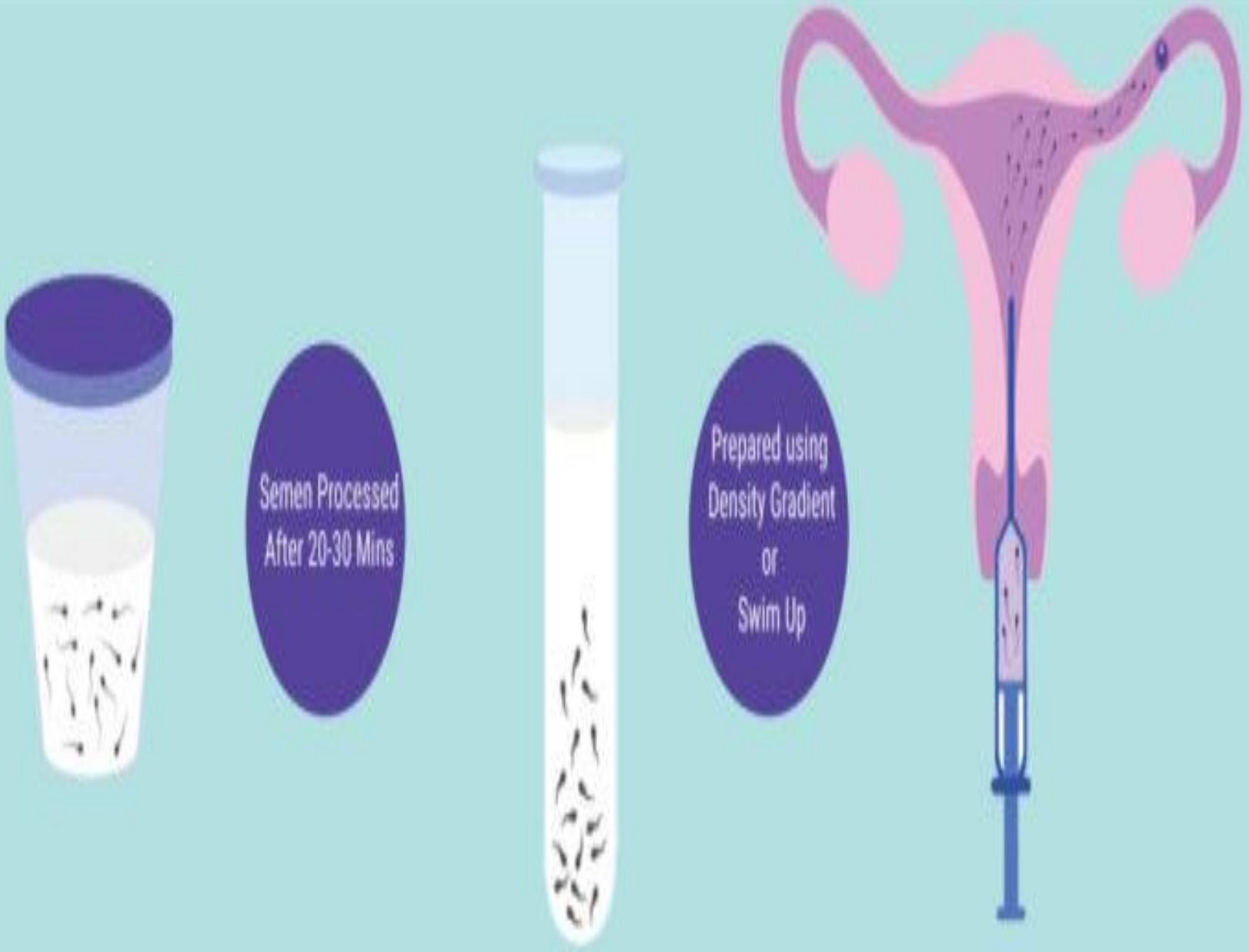
Infertility Treatments

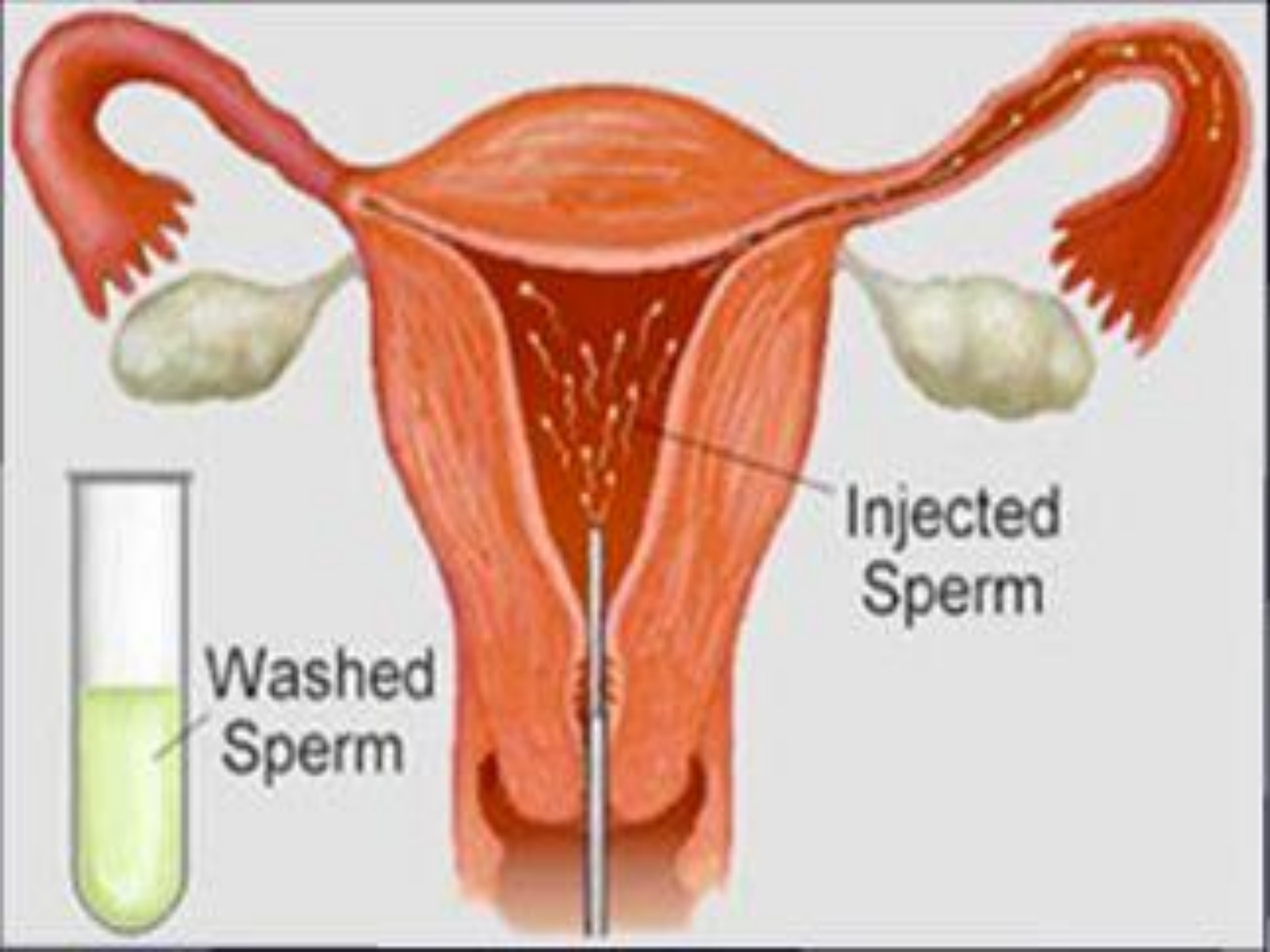
- Improve Timing of Intercourse
- Intrauterine insemination (IUI)
  - Clomiphene citrate + IUI
  - FSH + IUI
- In Vitro Fertilization (IVF)
  - "Standard" IVF
  - Egg donation + IVF
  - Egg Freezing + IVF

Indications for IUI

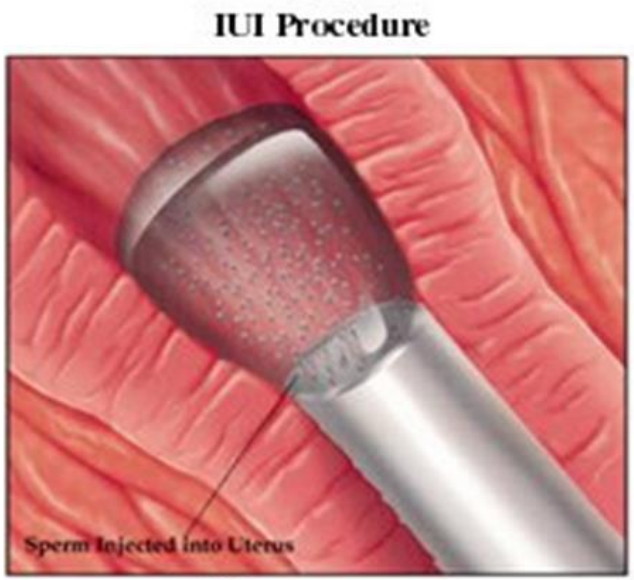
- Unexplained infertility
- Mild endometriosis
- Mild male factor infertility
- Disability (physical or psychological) preventing vaginal sexual intercourse
- Conditions that require specific consideration in relation to methods of conception (such as after sperm washing in a couple where the male is HIV positive)
- Fertility preservation
- As part of donor insemination
- IUI in stimulated cycles may be considered while waiting for IVF, or when in women with patent tubes IVF is not affordable.

1. NICE Guidelines – 2012. 2. Human Reproduction Update, Vol.15, No.3 pp. 265–277, 2009. IUI – The ESHRE Capri Workshop Group

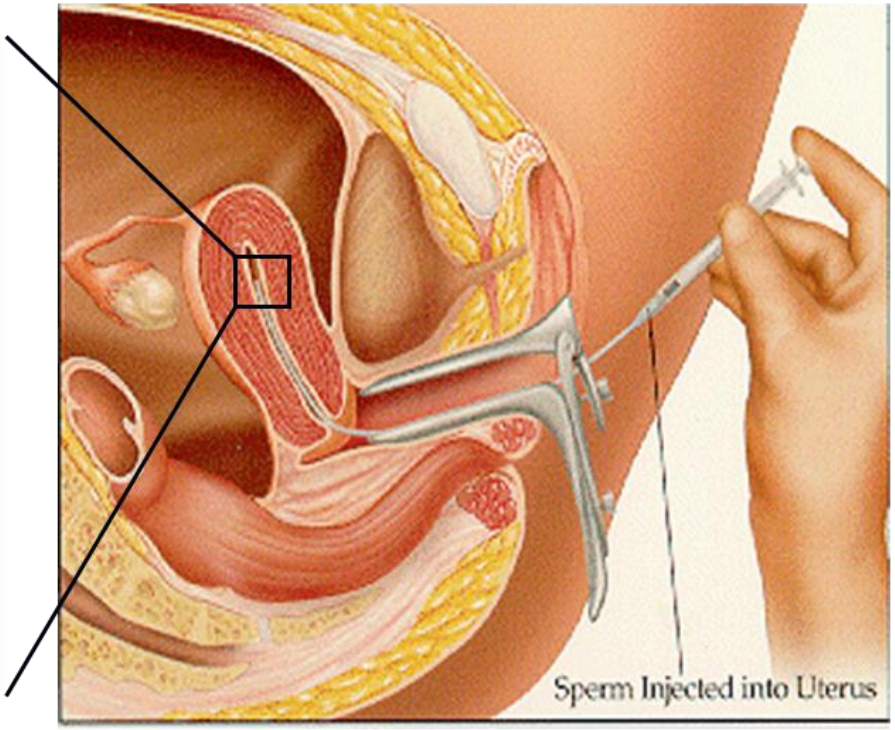

Semen Processed
After 20-30 Mins
Prepared using
Density Gradient
or
Swim Up
Semen Collection
Semen Processing
Insemination


Injected
Sperm
Washed
Sperm

Intrauterine Insemination (IUI)



Through the process of IUI, sperm are placed high in the female reproductive tract to enhance the chance of successful fertilization.



Goal is to Maximize the Chance of Fertilization

- Increase Number of Eggs
- Position Sperm Closer to Eggs

What are contraindications to IUI

- Blocked tubes, major tube pathology
- Genital tract infection in either wife or husband
- Severe abnormality in semen parameters (low count < 5 million in pre-wash sample, asthenospermia, severe teratospermia)
- Genetic reason for above poor semen parameters
- Wife's age advanced
- Multiple aetiologies/co-existing factors for infertility
- Multiple, previous failures of IUI.

Why In Vitro Fertilization?

- Infertility
- DNA Testing
  - Genetic Disorders
  - Gender Selection
- Non-Traditional Life Styles

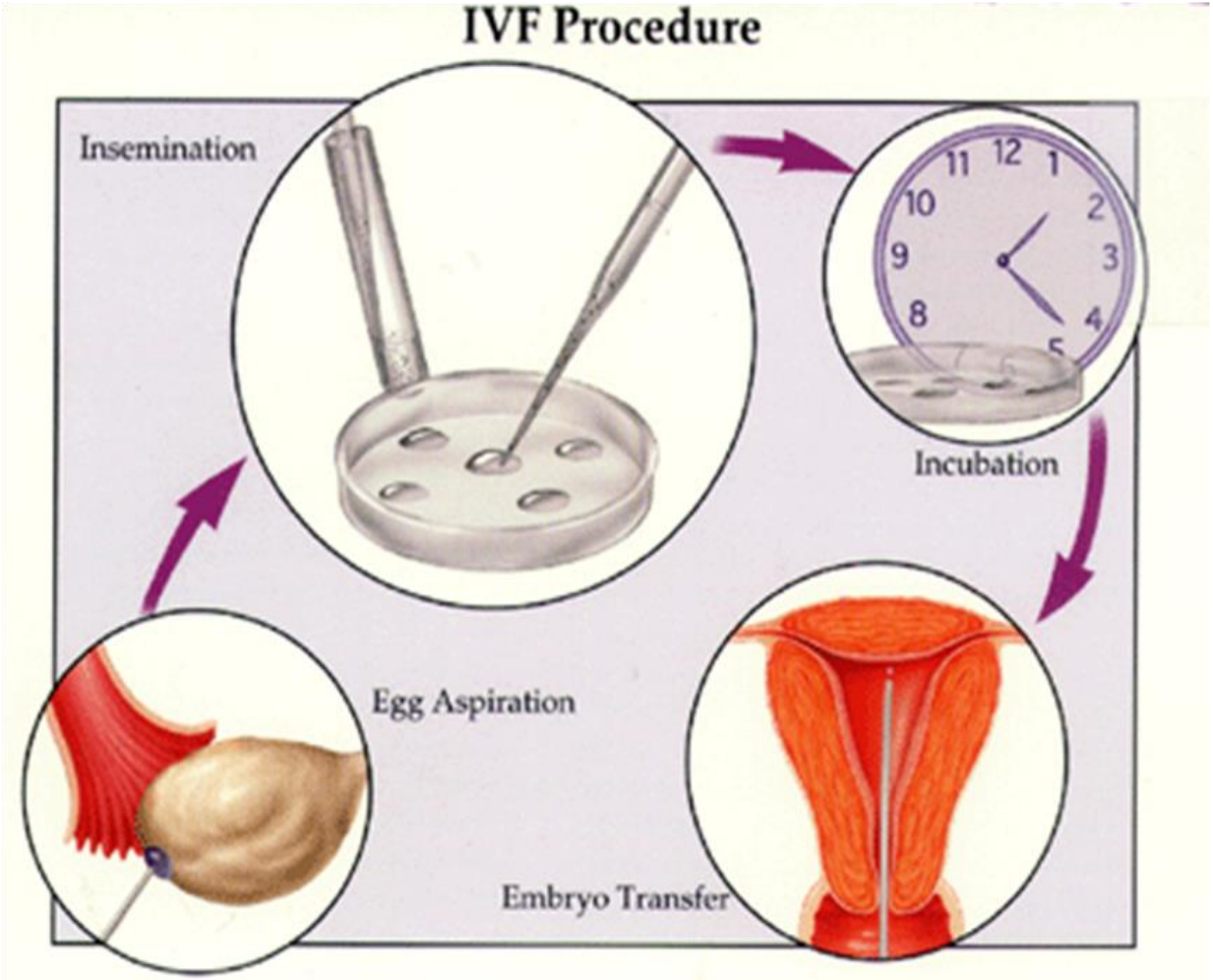
Who Needs IVF?

- Failed other treatments
- Tubal damage
- Significant male factor
- Absent uterus
- Carriers of genetic diseases
- Gender selection
- Cancer patients

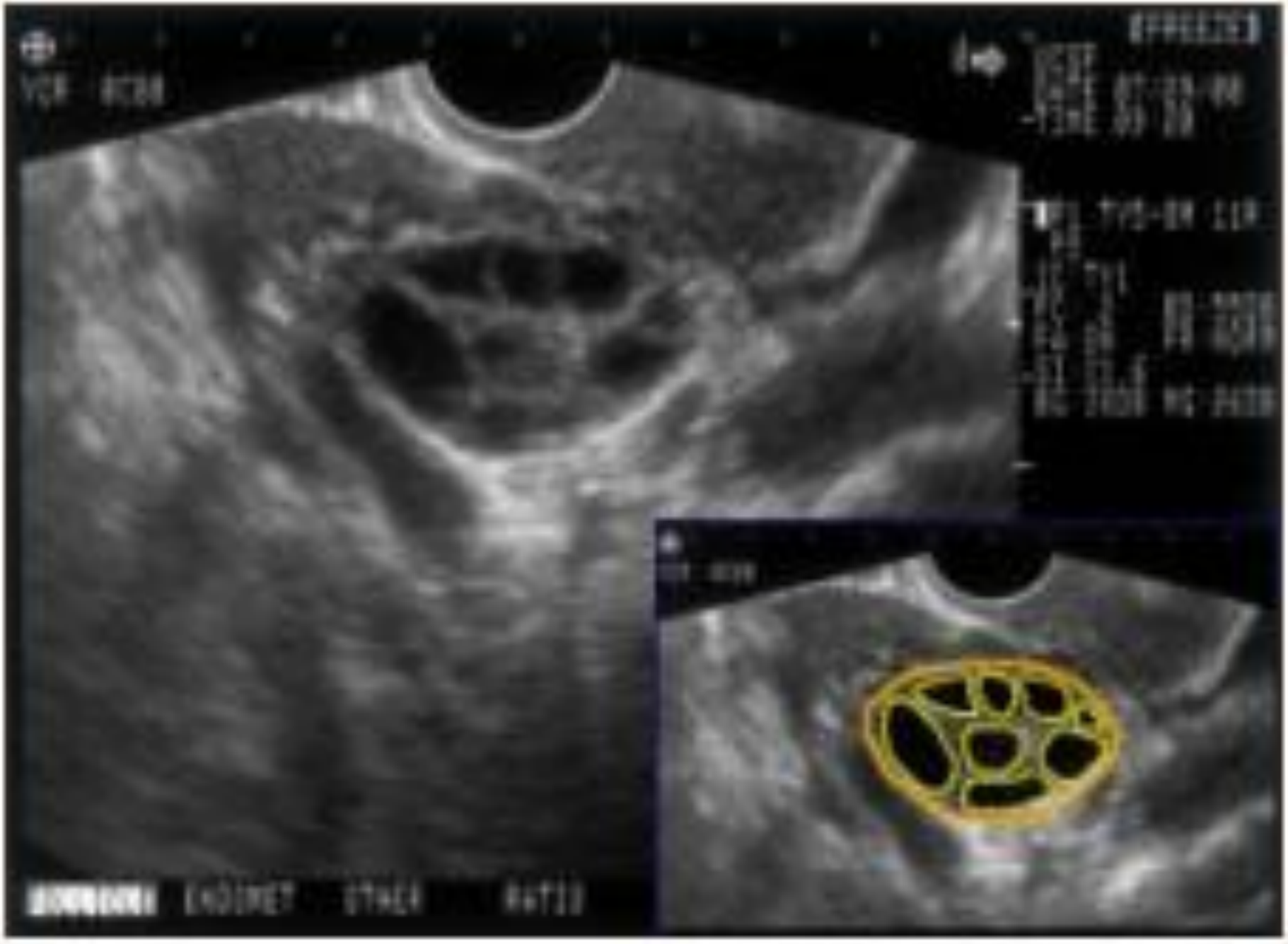
In Vitro Fertilization - History

- 1978 – First "test tube" baby was born in England
- 1981 – IVF in U.S.
- Started with GIFT and ZIFT
- 2008 - >98% IVF with transfer of embryo to uterus

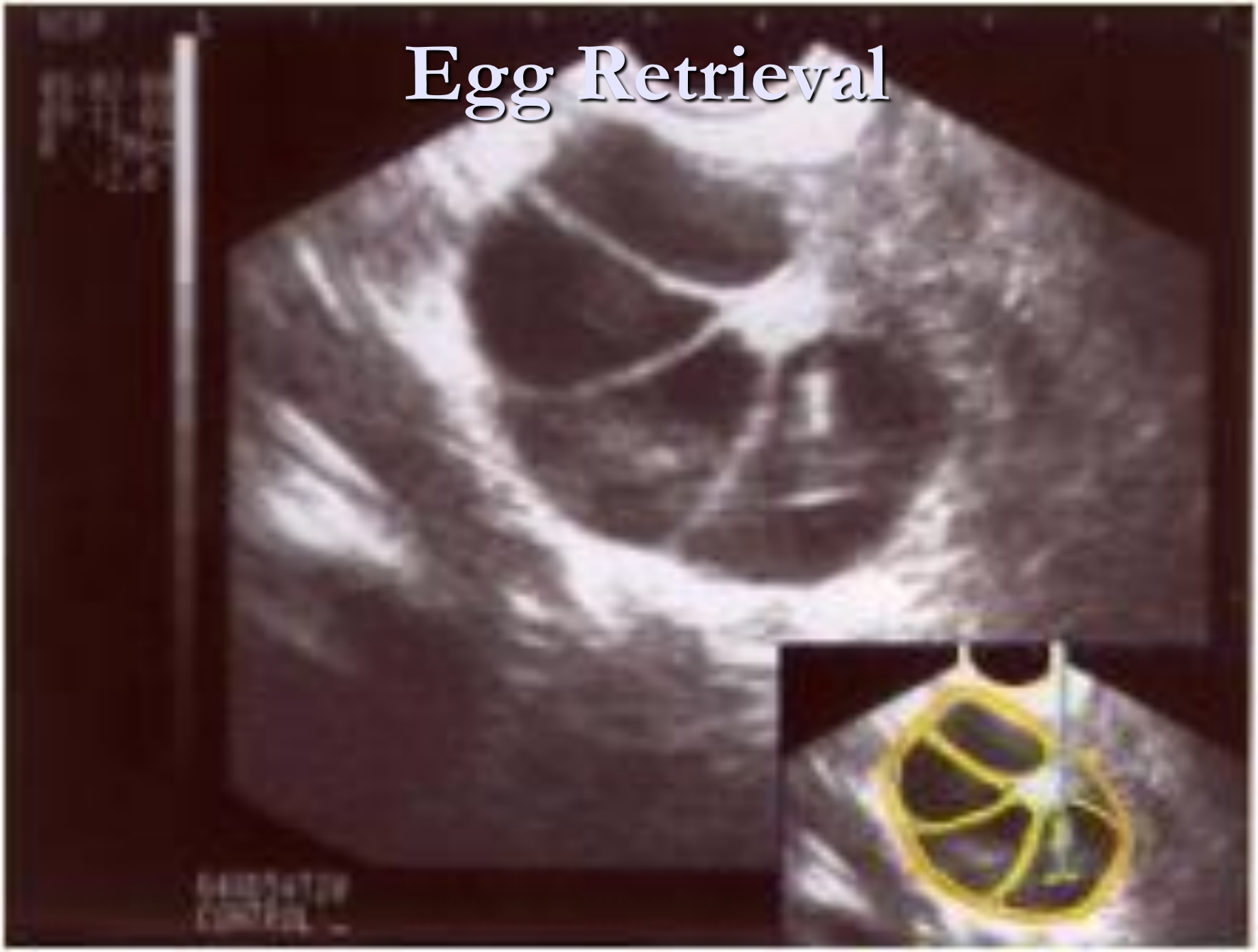
In Vitro Fertilization (IVF)

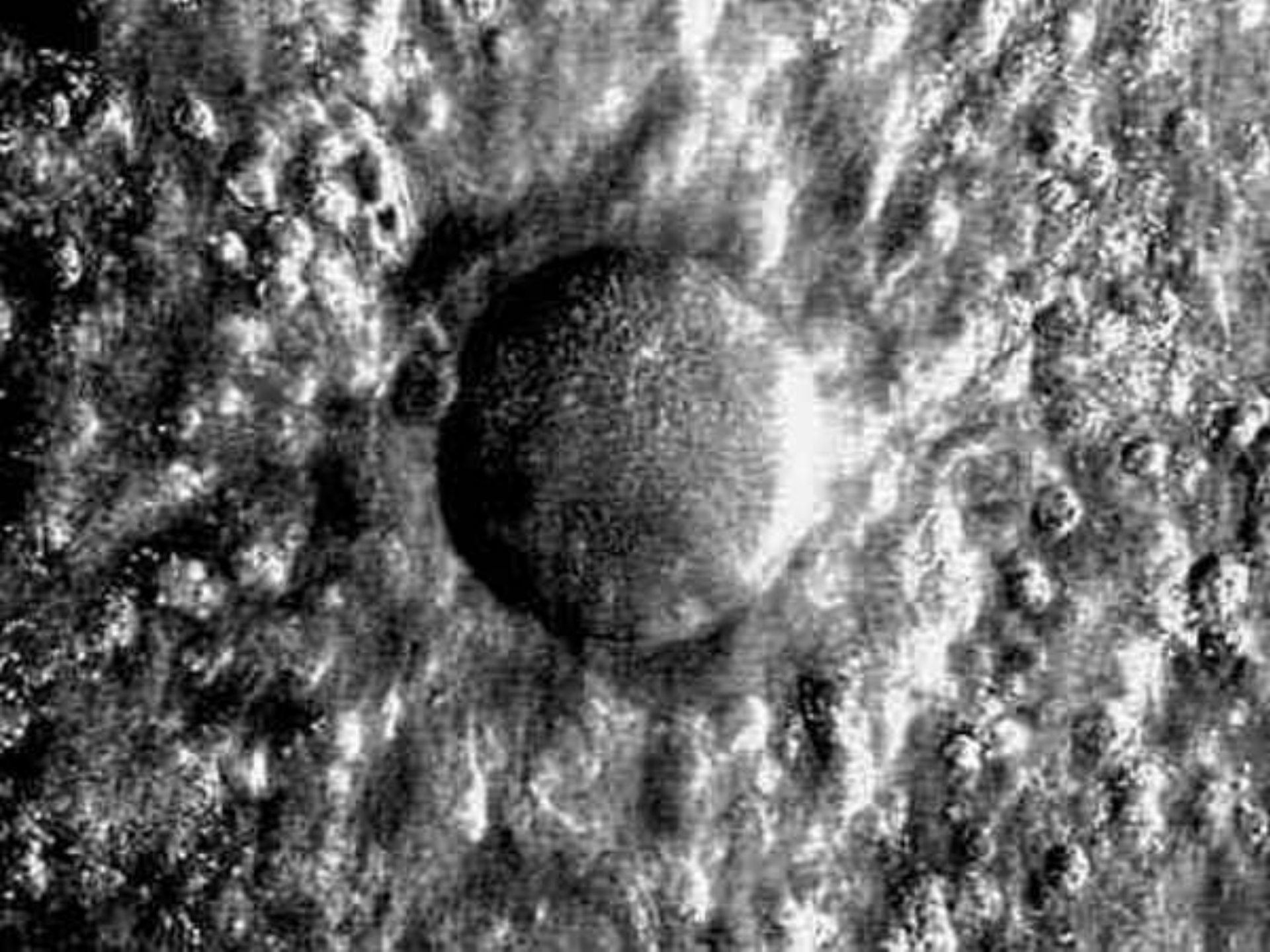


In IVF, eggs are harvested from the woman's ovary and fertilized in the laboratory with sperm. The embryos are then transferred into the uterus.

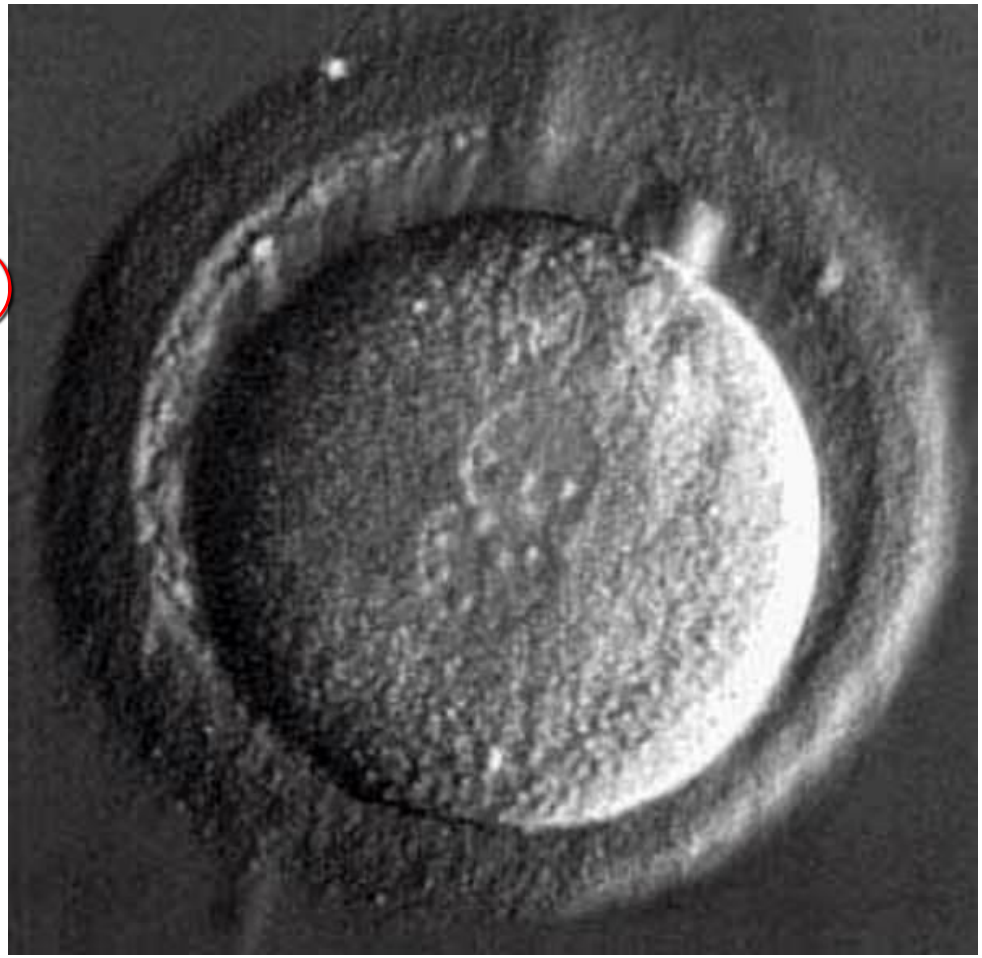


Egg Retrieval

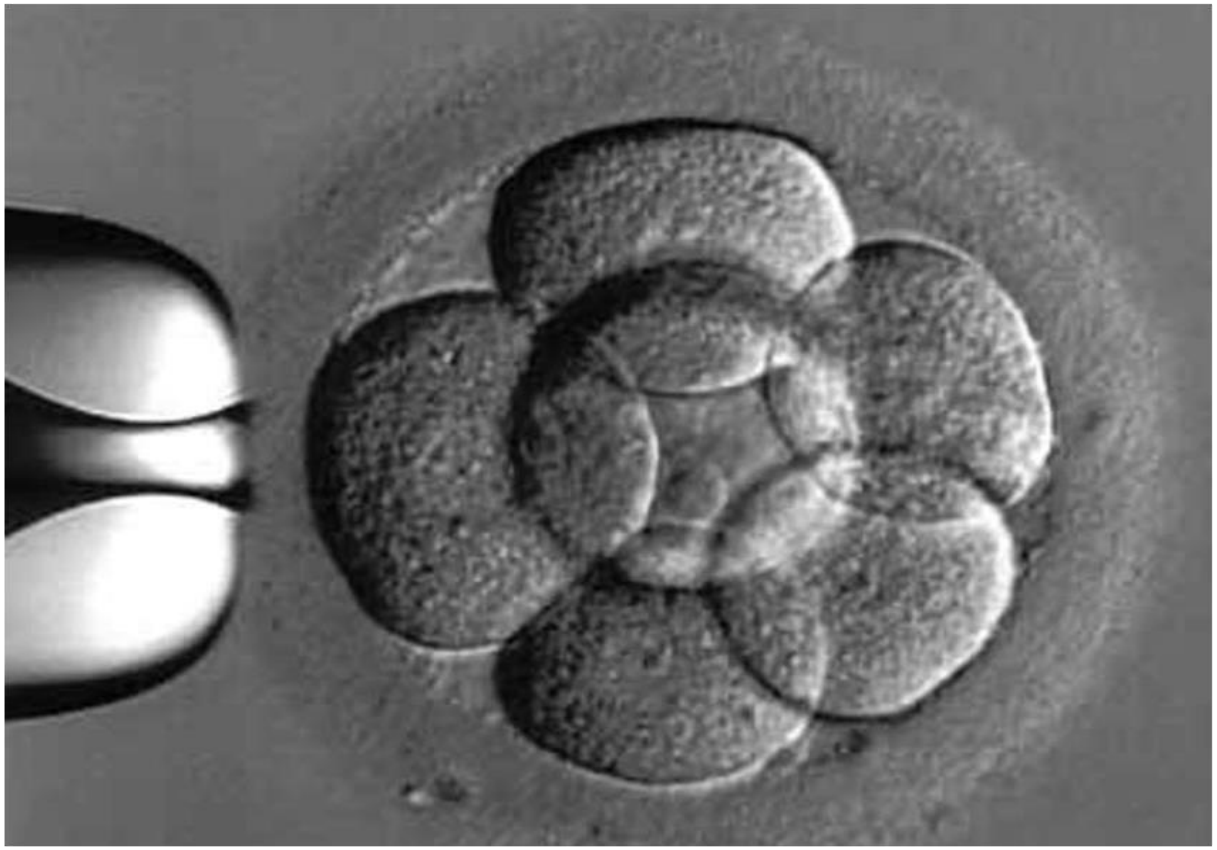




- 2 Pronuclei (2PN)
- 1 day after egg retrieval



Day 3 Embryo



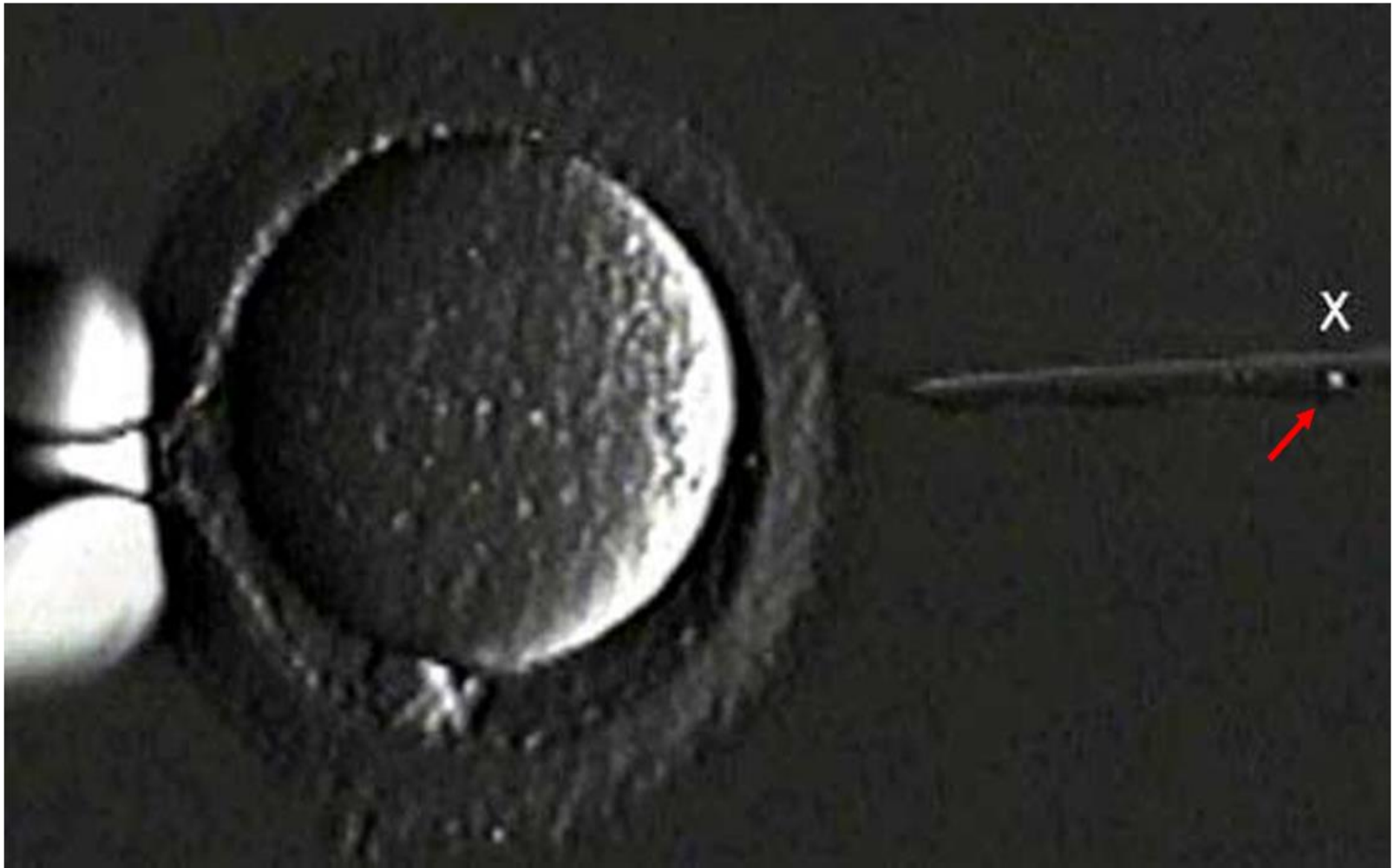
Pre-Implantation Genetic Testing Stage

Special IVF Procedures

- Assisted hatching
- Intracytoplasmic sperm injection (ICSI)
- Preimplantation genetic diagnosis (PGD)
- Freezing
- Egg donation
- Surrogacy

Assisted Hatching

ICSI



Oxidation-reduction potential of semen: what is its role in the treatment of male infertility?

Director, Andrology Center and American Center for Reproductive Medicine, Lerner College of Medicine, Cleveland Clinic, 10681 Carnegie Avenue, Desk X11, Cleveland, OH 44195, USA

- Oxidative stress is one of the major mediators in various etiologies of male infertility.
- it has deleterious effects on spermatozoa, including DNA damage.
- Alleviation of oxidative stress constitutes a potential treatment strategy for male infertility.
- Measurement of seminal oxidative stress is of crucial role in the identification and monitoring of patients who may benefit from treatments

Oxidation-reduction potential of semen: what is its role in the treatment of male infertility?

- Various tests including reactive oxygen species (ROS) assay, total antioxidant capacity (TAC) assay or malondialdehyde (MDA) assay used by different laboratories have their own drawbacks

- The MiOXSYS™ System is a novel technology based on a galvanostatic measure of electrons.

•NATURAL ANTI-OXIDANT SUPPLEMENTATION PRIOR TO INFERTILITY TREATMENT RESULTS IN EXCELLENT CLINICAL OUTCOMES FOR INFERTILITY PATIENTS WITH PRIOR IVF FAILURES

Fertility and Sterility, Volume 106, Issue 3, Supplement, September 2016, Page e265

L.A. Munkwitz, W.B. Schoolcraft, M. Katz-Jaffe

- Preliminary results indicate improvements in clinical IVF outcomes following the supplementation of a highly active anti-oxidant prior to ovarian stimulation. The restoration of the balance between oxidants and anti-oxidants in the ovary during the early stages of oocyte development may account for the clinical improvements observed. Ongoing investigations into the factors associated with oocyte quality will contribute to improved success for women with a history of IVF failures.

Female dietary antioxidant intake and time to pregnancy among couples treated for unexplained infertility

Elizabeth H. Ruder, Ph.D., M.P.H.[a, ,], Terryl J. Hartman, Ph.D., M.P.H.[b], Richard H. Reindollar,M.D.[c], Marlene B. Goldman, Sc.D

- Shorter TTP was observed among women with BMI <25 kg/m^2 with increasing vitamin C, women with BMI ≥25 kg/m^2 with increasing β-carotene, women <35 y with increasing β-carotene and vitamin C, and women ≥35 y with increasing vitamin E

•Male infertility: Decreased levels of selenium, zinc and antioxidantS

Journal of Trace Elements in Medicine and Biology, Volume 28, Issue 2, April 2014, Pages 179-185

Silver Türk, Reet Mändar, Riina Mahlapuu, Anu Viitak, Margus Punab, Tiiu Kullisaar

- Male partners of infertile couples had reduced level of antioxidative activity, selenium and zinc in their seminal plasma. Most importantly, reduced selenium levels were evident in all patient groups regardless of inflammation status. Therefore, these patients might gain some benefit from selenium supplementation

•Quantifying the effectiveness and cost-efficiency of food supplementation with antioxidants for male infertility

Reproductive BioMedicine Online, Volume 23, Issue 3, September 2011, Pages 361-362

Frank Comhaire, Wim Decleer

- In male infertility, complementary treatment with antioxidant-containing food supplements quadruples the spontaneous pregnancy rate and reduces the cost per pregnancy by 60%

Combination clomiphene citrate and antioxidant therapy for idiopathic male infertility: a randomized controlled trial

Fertility and Sterility, Volume 93, Issue 7, 1 May 2010, Pages 2232-2235
Hussein Ghanem, Osama Shaeer, Amgad El-Segini

- The combination of clomiphene citrate as an antiestrogen and vitamin E as an antioxidant can significantly increase the pregnancy rate and improve sperm count and progressive sperm motility in cases of idiopathic oligoasthenozoospermia

•DHEA improves the antioxidant capacity of endometrial stromal cells and improves endometrium receptivity via androgen receptor

European Journal of Obstetrics & Gynecology and Reproductive Biology, Volume 198, March 2016, Pages 120-126

Aiping Qin, Jinchun Qin, Yufu Jin, Wei Xie, Li Fan, Lingyun Jiang, Fuhua M

- Low concentration of DHEA improves the antioxidant capacity of decidual ESCs. DHEA treatment may also improve endometrium receptivity via AR

•Relation between seminal quality and oxidative balance in sperm cells

Acta Urológica Portuguesa, Volume 33, Issue 1, April 2016, Pages 6-15
António Patricio, Daniel Filipe Cruz, Joana Vieira Silva, Ana Padrão, Bárbara Regadas Correia, Luís Korrodi-Gregório

- It was concluded that the seminal quality is affected by the oxidative balance in sperm cells. The obtained results suggest that lipid peroxidation leads to a reduction in sperm concentration; antioxidant proteins protect the spermatozoa against protein oxidation and contribute to an increased sperm motility and normal semen viscosity. Thus, evaluation of oxidative parameters may be a useful tool for male infertility diagnosis and follow-up of antioxidant treatments.

Effect of antioxidant supplementation on sperm parameters in oligoasthenoteratozoospermia, with and without varicocele

- *Fertility and Sterility, Volume 106, Issue 3, Supplement, September 2016, Page e46*
- G. Busetto, M.A. Virmani, G. Antonini, G. Ragonesi, E. De Berardinis, A. Agarwal, V. Gentil

- r study, at the end of the treatment we observed a marked increase in quality parameters of sperm such as count and in total and progressive motility especially in varicocele patients. The supplementation was safe and no adverse events were observed. On this basis it can be established that the use of carnitines and other functional substances can form part of an efficacious strategy to handle male infertility.

•Protective effect of vitamin E on sperm motility and oxidative stress in valproic acid treated rats

Food and Chemical Toxicology, Volume 95, September 2016, Pages 159-167
Giovana M. Ourique, Etiane M.H. Saccol, Tanise S. Pês, Werner G. Glanzner, Sun Hee Schiefelbein, Viviane M. Woehl, Bernardo Baldisserotto, Maria A. Pavanato, Paulo B.D. Gonçalves, Kátia P. Barret

- Long-term administration of valproic acid (VPA) is known to promote reproductive impairment mediated by increase in testicular oxidative stress. Vitamin E (VitE) is a lipophilic antioxidant known to be essential for mammalian spermatogenesis. However, the capacity of this vitamin to abrogate the VPA-mediated oxidative stress has not yet been assessed. Thus, VitE protects the reproductive system from the VPA-induced damage, suggesting that it may be a useful compound to minimize the reproductive impairment in patients requiring long-term treatment with VPA.

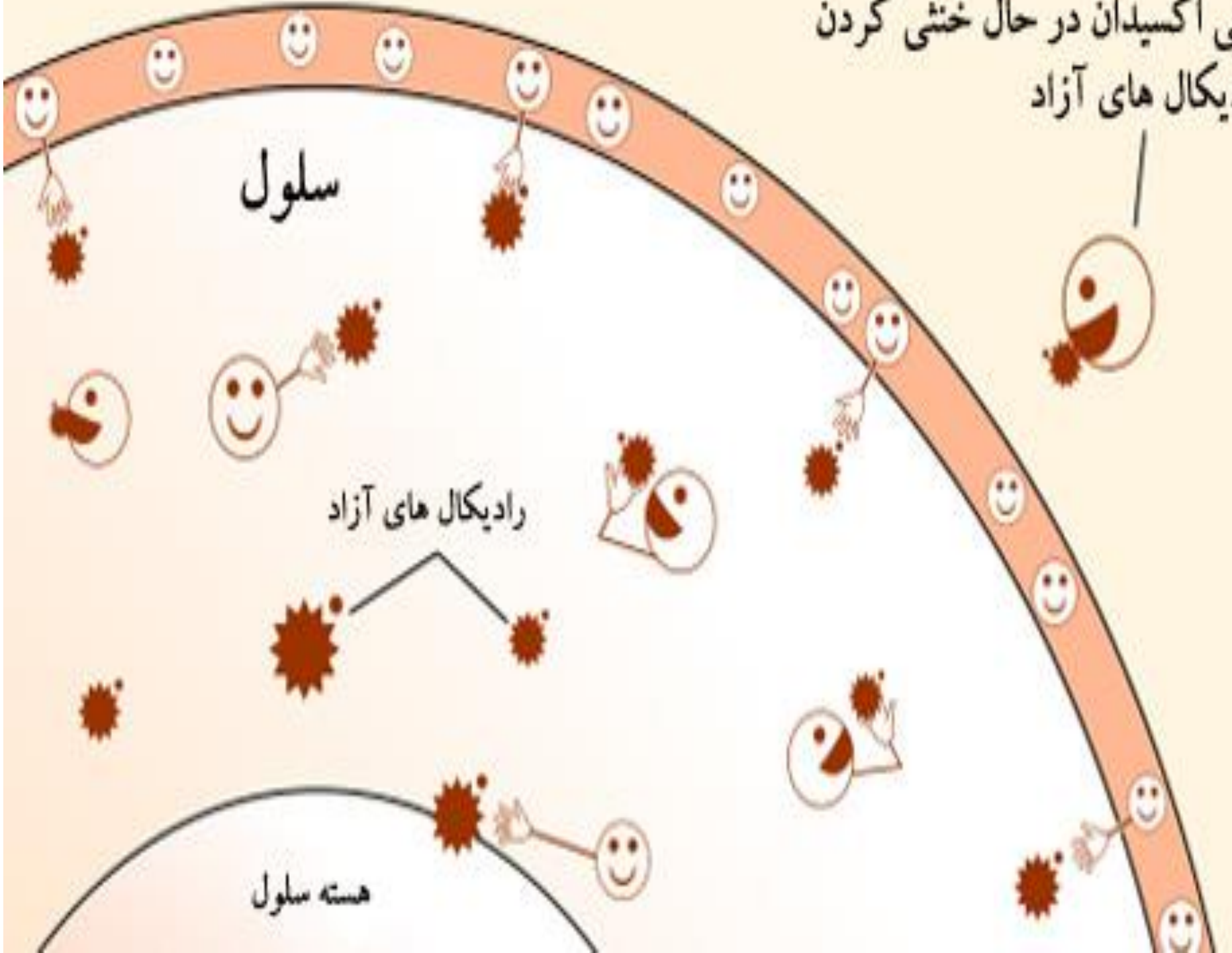
•Successful Treatment of Oligoasthenozoospermia Using Traditional Korean Medicine Resulting in Spontaneous Pregnancy

Journal of Science and Healing, Volume 12, Issue 2, March–April 2016, Pages 136-138
Junyoung Jo, Myung Ja Kang

- This study represents TKM therapy including acupuncture and/or herbal remedies might be an option for infertile men (oligoasthenozoospermia). Further large-scale randomized controlled trials investigating the effects of TKM therapy for male infertility are needed.

Protective role of green tea on malathion-induced testicular oxidative damage in rats

- The results showed that total green tea extract improve oxidative damages against malathion group. Light photomicrograph of seminiferous tubules in malathion-treated group showed noticeable reduced height of germinal epithelium and disorganization of the tubules. An increased intestinal tissue was also observed. Primary spermatocytes were located distance from basal lamina indicating it induced damages to the intestinal tissue. While seminiferous tubules in malathion exposed and green tea extract-treated were normal


ی آکسیدان در حال خنثی کردن
یکال های آزاد
سلول
رادیکال های آزاد
هسته سلول

• Oxidative Stress in polycystic Ovary Syndrome

- papalou, Olga; M. Victor, Victor; Diamanti-Kandarakis, Evanthia
- **Source:** Current Pharmaceutical Design, Volume 22, Number 18, May 2016, pp. 2709-2722(14)

Oxidative Stress in polycystic Ovary Syndrome

- Polycystic ovary syndrome is a multifaceted disorder with a pathogen etic pathway that is not fully understood yet. Apart from hormonal derangements, insulin signaling defects and adipose tissue dysfunction, oxidative stress, defined as an imbalance derived from excessive formation of oxidants in the presence of limited antioxidants defenses, has been actively implicated in the etiology of the syndrome.
- Oxidative stress, in conjunction with the rest etiologic mechanisms of PCOS and the cardinal contribution of environmental factors, leads to an adverse redox status that stigmatizes the natural process of the syndrome.

Follicular fluid total antioxidant capacity levels in PCOS

- Journal of Obstetrics and Gynecology(2016)
- In this study, our aim was to assess total antioxidant capacity (TAC) levels in follicular fluid (FF) and their relationship to clinical pregnancy rates in PCOS patients undergoing assisted reproduction (ART).
- Twenty-two women with polycystic ovary syndrome (PCOS) (Group 1) and 41 women without PCOS (Group 2) were included in this study. Clinical and laboratory parameters and FF TAC levels were investigated.
- No statistically significant differences were found between the groups with regard to age and baseline parameters. Although we could not demonstrate a significant difference in FF TAC levels between the two groups (p=0.469), there was a significant positive correlation between FF TAC and clinical pregnancy rates, BMI, and the duration of infertility for the entire group