UNIVERSITEIT VAN PRETORIA
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Faculty of
Health Sciences

Fakulteit Gesondheidswetenskappe
Lefapha la Disaense tša Maphelo

Make today matter

Infertility Endometriosis & Dysmenorrhoea

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Video Infertility

Impact of infertility

- Cuts across colour, religion, socio-economic, cultural lines

- Causes:
  - frustration
  - anger
  - fear
  - guilt
  - shame
  - isolation

Impact of infertility

- Infertility has impact in a couple's

  - Psychological
    - frustration/anger
    - anxiety/stigmatisation
    - high depression
    - suicide
  - Financial
  - Medical
  - Social wellbeing
    - divorces
    - intimate partner violence
    - stigma

Incidence

- In SA incidence is 15 – 20% (approx 1 in every 5- 6 couples)
- WHO has defined Infertility is a disease
- Infertility generates disability /an impairment of function
- Ranked the 5th highest serious global disability in population under 60
- Stats SA/ SADHS , 2016 – decline in fertility in SA

Impact of Infertility

South Africa

- Impact on South African economy

- Fertility has declined by about 1/2 between 1970 and 1996.

(An analysis of the 1996 Census and the 1998 Demographic and Health Survey)

- by 2040, fertility rates are expected to drop below the "replacement level“

(South African Institute of race relations, Jan 2012 report)

- The shrinking workforce + ageing population (improved life expectancy) =
  - harmful economic consequences
  - an increasing burden of dependency on the economically active population

The pain of “Barrenness amid plenty”

Overpopulation **Vs** **Childlessness**

Resources in SA

- Contraception
- TOP
- Other health priorities: HIV/TB/Cancer

Neglected

- Medical Insurance does not pay for ART services
- 3 State hospitals offer service

What is Infertility

- **Infertility** : (WHO) is a disease of the reproductive system

- defined by:
  - the failure to achieve a clinical pregnancy
  - after ≥**12 months**
  - of **regular** ,**unprotected** sexual intercourse

-after **1 Year** in women < **35yrs**

-after **6 months** in women **> 35 yrs**

Definitions

- **Primary infertility :** woman who has never conceived

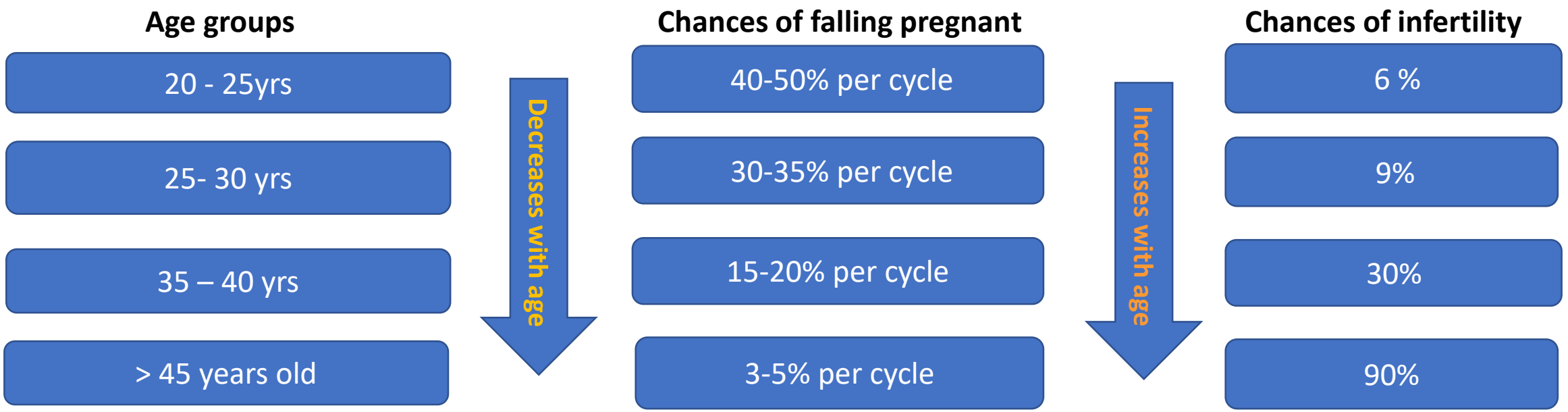
- **Secondary infertility :** woman with previous pregnancy

- **Subfertility**:
  -patients have a successful pregnancies after fertility treatment
  -term more preferable unless the couple has been proven to be sterile

- **Fecundity: -** means “fruitfulness”.
  - It is the probability to achieve pregnancy in 1 menstrual cycle

Normal fecundity rates

- 80-90 % of normal couples will conceive within the 1st year
- 5 – 15 % will conceive in 2nd - 12 months
- After 24 months - 95% of couples will have conceived



Reasons for decline in fertility

- High rates of anatomical causes
  - Tubal infections – causing occlusion
  - Myoma
  - Environmental factors

- Women delaying pregnancy for careers

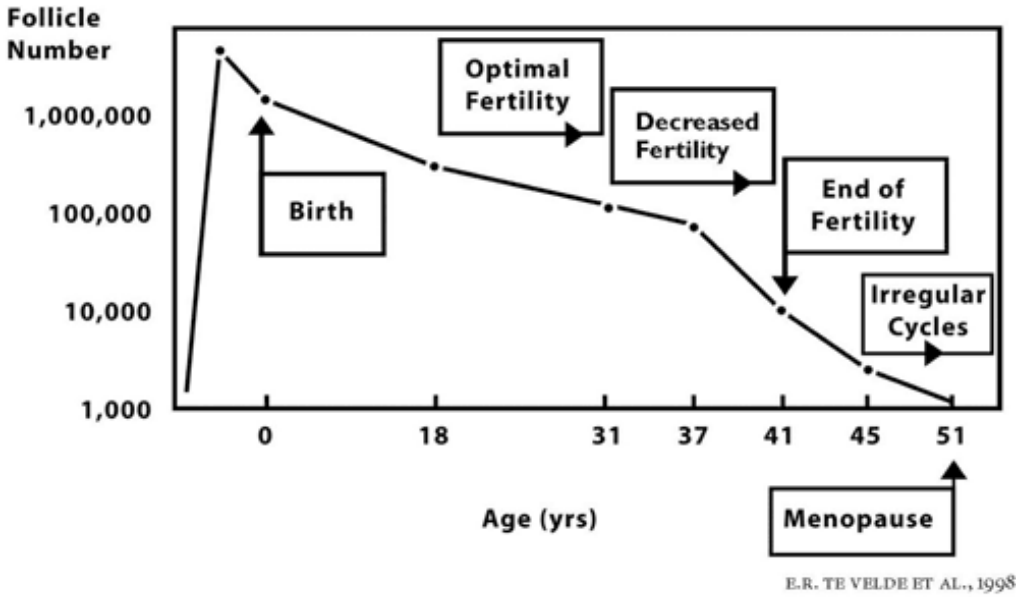
- Exorbitant cost of raising children – delay in 2nd child = 2^{o} infertility

- Increasing use of contraception

- Liberal abortion laws

- HIV/Aids – voluntary infertility

Age Related Decline in Fertility



- At **birth,** there are approximately **1-2 million oocytes**.
- There is a decline in the oocytes
- At **puberty**, there are **300 000.** Of these, 500 are destined to mature in the individual's lifetime, the rest undergo atresia/cell death
- By **menopause** there are only about a **1000 oocytes**.
- After 40 years old, follicle number falls rapidly until menopause

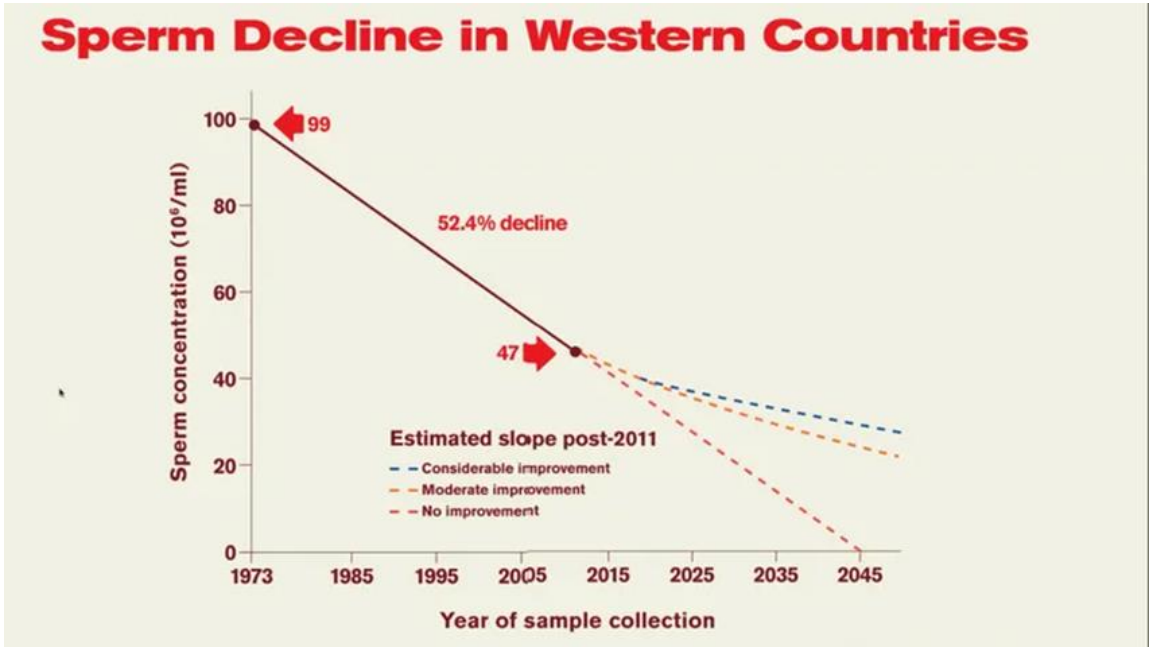
Infertility Crisis

Decreasing sperm quality: a global problem

- Worldwide, sperm counts have declined 50 % in males the past 50 years

Carlsen et al, BMJ,1992

- By 2045 median sperm counts in men are headed toward zero.



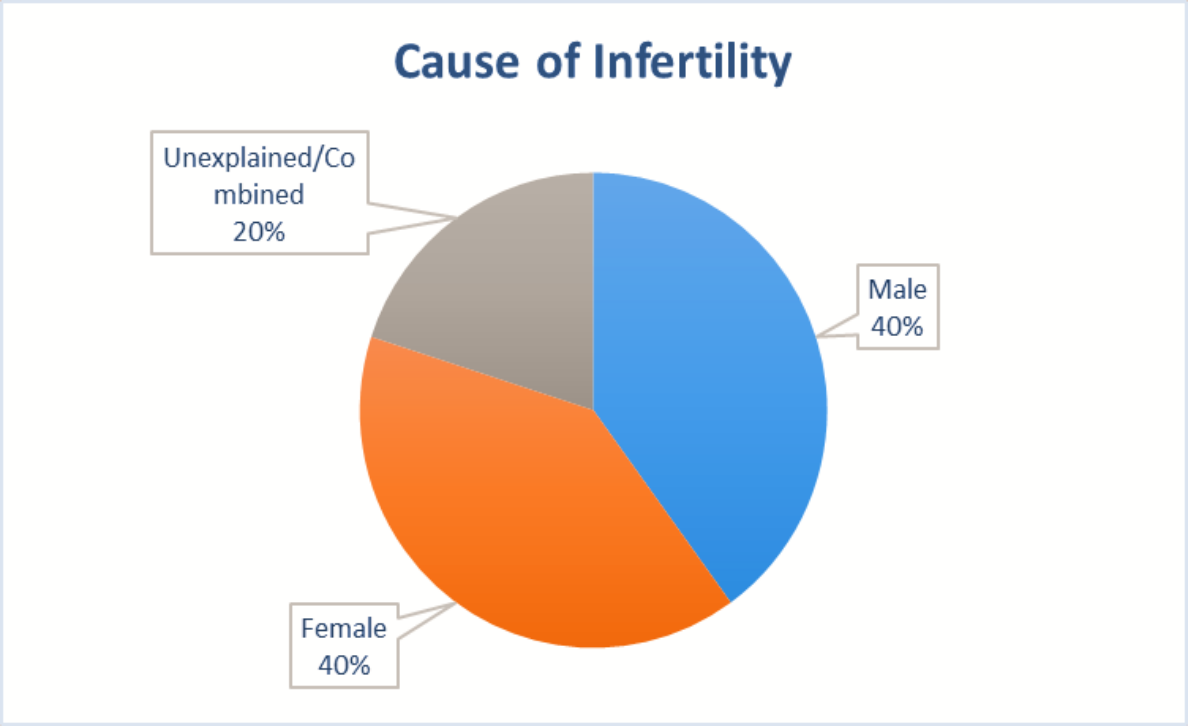
- Recent high-quality studies have demonstrated that there is indeed a decline in sperm parameters.
- No clear etiologic factors have been identified
- Potential causative factors include obesity, diet, chronic disease, smoking, marijuana, and environmental toxins.

Mann et al, Current opinion in urology, 2020

Causes of infertility

Causes of infertility vary in different regions

- Male factor 40%
- Female factor 40%
- Unexplained or Combined 20%



Nelson AL, Marshall JR. 2004

https://www.glowm.com/section_view/heading/psychological-issues-related-to-infertility/item/412

Aetiology of infertility

Male factors

- Pre-testicular
  - Endocrine (Hypothalamic, pituitary)
  - Coital disorders
  - Drugs
- Testicular
  - Genetic
  - Congenital
  - Infective
  - Vascular (torsion, varicocoele)
  - Immunological
  - Toxins (irradiation, drugs)
- Post-testicular
  - Obstructive
  - Surgical (vasectomy)
  - Congenital absence of the vas deferens (Cystic fibrosis)

Female factors

- Cervical factors
  - Cervical mucous immobilises sperm
  - Cervical lesions/stenosis due to LLETZ or DD&C
- Tubal factor
  - Chlamydia (PID) and genital TB
  - Endometriosis
  - Tubal ligation/Tuboplasty/Salpingectomy
- Ovulatory dysfunction
  - PCOS
  - Hypothalamic hypogonadism
  - Prolactinoma, thyroid disease
  - Premature ovarian dysfunction
- Uterine factor
  - Fibroids
  - Intrauterine adhesions
  - Polyps
- Peritoneal disease
  - Endometriosis

Fibroids and Infertility

- Fibroids are benign tumours of the smooth muscle of the uterus
- The aetiology is unknown
- Fibroids are found in 20–50% of women in reproductive age group
- Incidence of fibroids in women with infertility is 5-10%
- Malignant transformation is rare. The risk is estimated at less than 0.1%.
- May be asymptomatic or may cause non-infertility problems or obstetric problems

Non-fertility problem of fibroids

- They cause heavy menstrual bleeding
- Prolonged menstrual bleeding
- Pressure symptoms
- Pain (degeneration)

Obstetric problems

- Miscarriages
- Recurrent pregnancy losses
- Preterm labour
- Abruptio placentae
- Pain (red degeneration)
- Malpresentation
- Postpartum haemorrhage

Neuwirth, R, Moritz, J, *Glob. libr. women's med.*

https://www.glowm.com/section_view/heading/leiomyomas-of-the-uterus/item/7

Which Fibroids have an impact on infertility

- Not all fibroids cause infertility
- Submucosal fibroids have an impact
- Subserosal fibroids have NO impact
- Intramural fibroids - no consensus
  - ✓ Those that distort cavity have impact
  - ✓Those that are larger than 5cm in size
  - ✓Distance more than 5mm have no effect
- Surgery should be done only if it will improve fertility

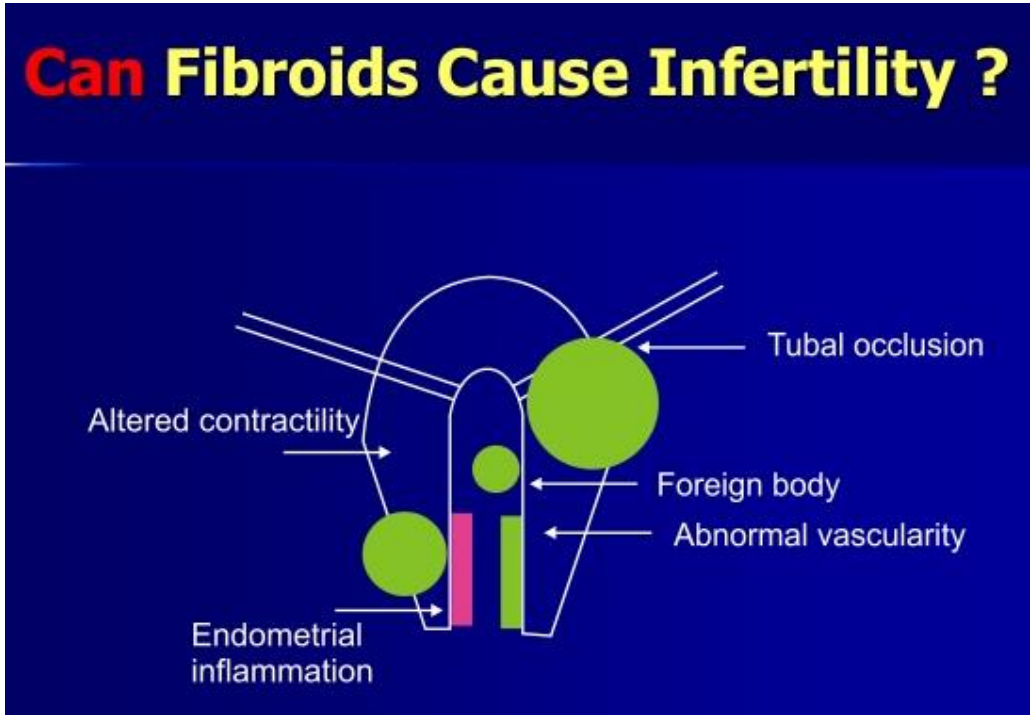
Leiomyoma Subclassification System

S – Submusosal	0	Pedunculated intracavitary
	1	< 50% intramural
	2	≥ 50% intramural
O – Other	3	Contacts endometrium; 100% intramural
	4	Intramural
	5	Subserosal ≥ 50% intramural
	6	Subserosal < 50% intramural
	7	Subserosal pedunculated
	8	Other (specify e.g. cervical, parasitic)

Hybrid leiomyomas (impact both endometrium and serosa)	Two numbers are listed separated by a hyphen. By convention, the first refers to the relationship with the endometrium while the second refers to the relationship to the serosa. One example is below	
	2-5	Submusocal and subserosal, each with less than half the diameter in the endometrial and peritoneal cavities, respectively.

Mechanisms:

1. **Effect on fertilization Interference with sperm or ovum transport.**
   a. Enlargement& deformity of uterine cavity
   b. Uterine contractility
   c. Distortion of the cervix
   d. Distortion or obstruction of tubal ostia



2. **Effect on implantation (possible mechanisms - not confirmed)**
   a. Alteration of the endometrial contour
   b. Persistence of intrauterine blood or clots
   c. Focal endometrial vascular disturbance
   d. Endometrial inflammation
   e. Secretion of vasoactive substances
   f. Enhanced endometrial androgen environment

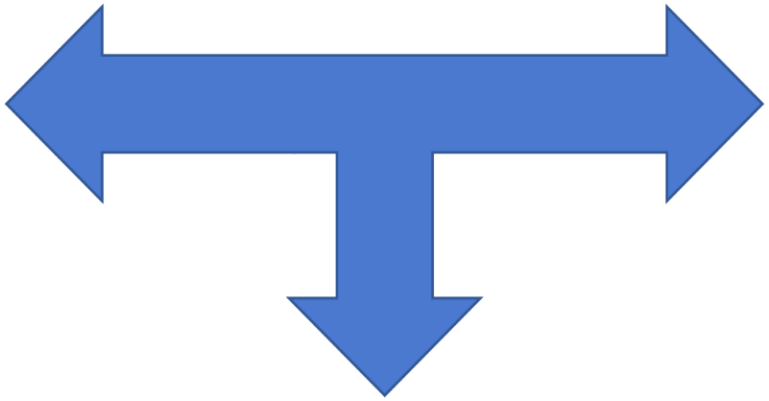
3. **Effect on fertilization Effect on implantation**
   a. Anatomic distortion of the cervix
   b. Altered endometrial development
   c. Altered uterine contractility

Management of Fibroids

Medical options

For symptomatic bleeding and pain:
- Combined oral contraceptives
- Progesterone only contraceptives - Pill, LNG-IUS
- NSAIDS
- Tranexamic acid

For decrease in fibroid size and symptoms:
- GnRHa
- sPRMs



Surgical Options

1. Myomectomy
   - Hysteroscopic
   - Laparoscopic
   - Laparotomy
2. Hysterectomy
   - Not for fertility

Other options

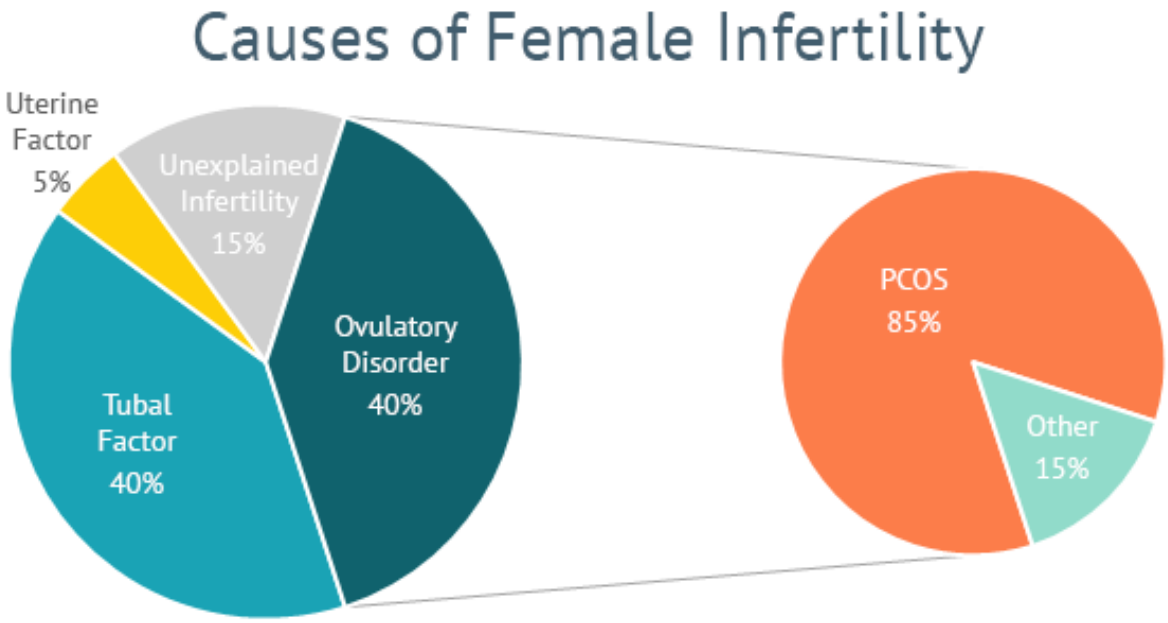
- Uterine Artery Embolisation (UAE)
- MRI guided focused ultrasound (MRgFUS/HIFU)

All medical options except NSAIDS prevent pregnancy

UAE and MRgFUS - not enough evidence to recommend in women who desire fertility

Ovulatory Disorders

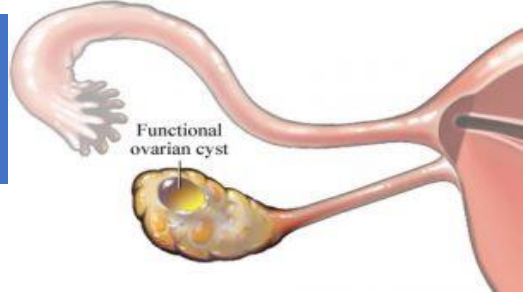
- **Polycystic Ovarian Syndrome (PCOS)**
  - ✓ Menstrual abnormalities/Anovulation
  - ✓ Hyperandrogenism (Clinical/Biochemical)
  - ✓ Polycystic Ovaries



- Rottedam Criteria
  - ✓ 2 out of 3 of above
  - ✓ Exclude other causes

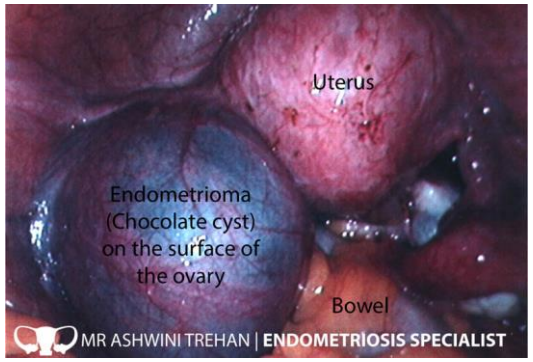
    (CAH/Androgen secreting tumours/Hyperprolactinaemia)

Ovarian Cysts



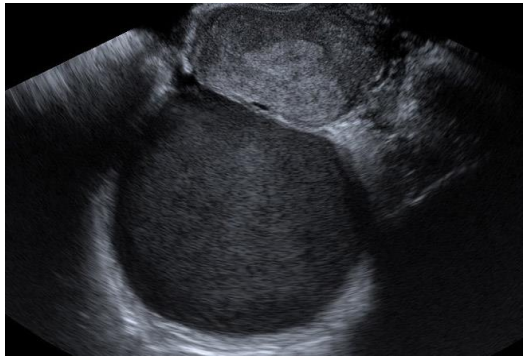
- Most ovarian cysts are asymptomatic and are harmless

- There are two types of functional cysts:
  1. Follicular cyst.
  A follicular cyst begins when the follicle doesn't rupture or release its egg, but continues to grow.
  2. Corpus luteum cyst.
  The corpus luteum forms after ovulation. Fluid can accumulate inside the follicle, causing the corpus luteum to grow into a cyst



- The majority disappears without treatment within a few months

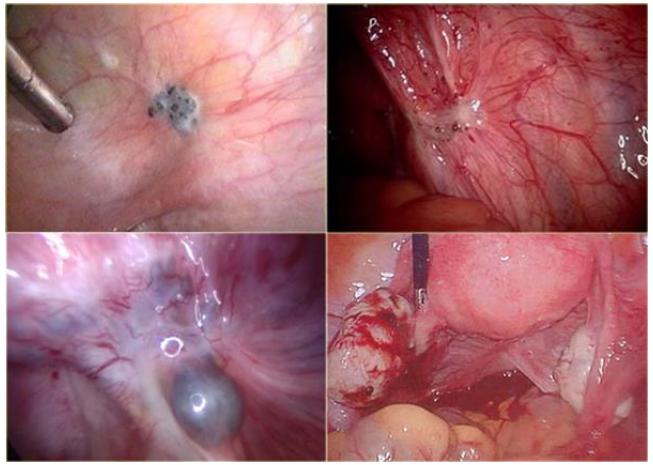
- Cysts cause pain if
  - ✓ Ruptured
  - ✓ Undergoe torsion
  - ✓ Haemorrhagic
  - ✓ Large
- Other cysts
  Dermoid cysts/ teratomas. Contain tissue, such as hair, skin or teeth, because they form from embryonic cells.
  Cystadenomas. These develop on the surface of an ovary and might be filled with a watery or a mucous material.
  Endometriomas. These develop as a result of endometriosis



Endometriosis

Definition

- Presence of endometrial tissue (both glands & stroma) outside the uterine cavity



➢oestrogen dependant disease

➢ found in women in the reproductive age group

➢rare in pre-pubertal girls and postmenopausal

Prevalence:

3-10% - in reproductive years

30% - with infertility

30% - with chronic pelvic pain

Aetiology

Aetiology is unknown

There are many theories

1. Sampson's theory of Retrograde menstruation (most accepted)

- Endometrial fragments are transported to peritoneal cavity through tubes
- Viable cells implant & grow

2. Coelomic Transplant theory

- Irritating factors transform derivatives of coelom into endometrium
- under certain conditions embryonic cells can develop into endometrial tissue

3. Hematologic /Lymphatic Spread

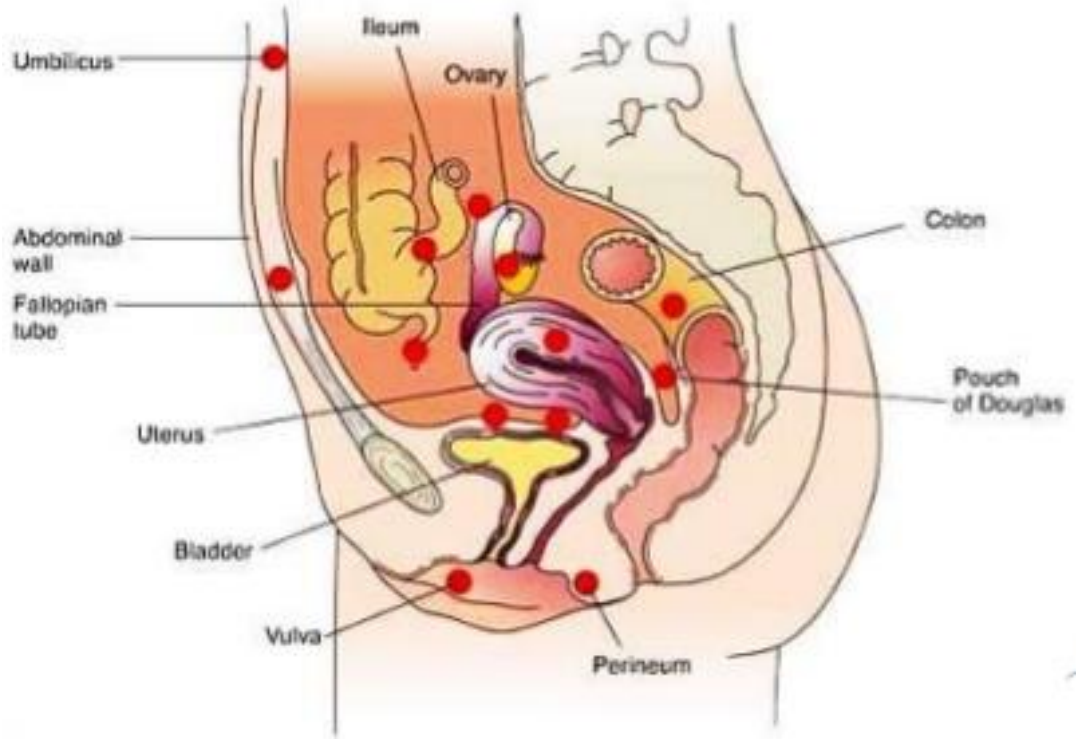
- distant sites of endometriosis can be explained by this process

Endometriosis

TYPES OF ENDOMETRIOSIS

PELVIC ENDOMETRIOSIS	EXTRA PELVIC ENDOMETRIOSIS
• Peritoneal	• Gastrointestinal tract
• Ovarian	• Urinary tract
• Deep infiltrating	• Scar endometriosis
	• Vaginal endometriosis
	• Thoracic endometriosis

SITES



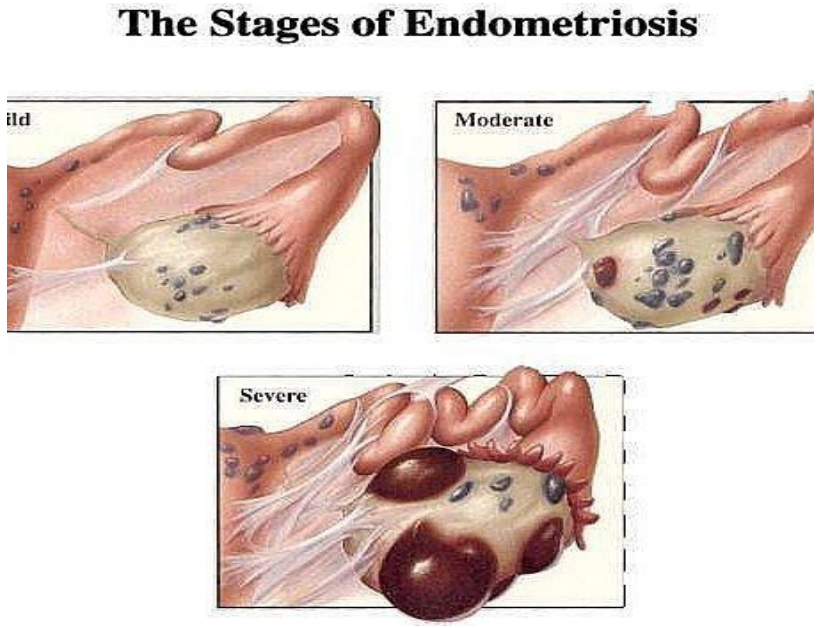
Clinical Presentation

- Dysmenorrhoea
- Dyspareunia (Deep)
- Subfertility
- Chronic pelvic pain
- Disorders of menstruation

Other Symptoms: related to site of endometriosis

- Bleeding umbilicus during menses
- Flank pain and haematuria- renal/ureteric endometriosis
- Dyschezia- painful defaecation- GIT endometriosis
- Catamenial haemoptysis – pulmonary endometriosis

Endometriosis & Infertility



Mechanism of pain

- Deep infiltration of endometriotic lesion
- Peritoneal inflammatory response with peritoneal leucocytes
- Adhesions
- Endometrioma
- Distension of ovary

Mechanical of subfertility:

- Adhesions cause anatomical distortion
- Tubal obstruction
- Block tubal motility and pick up of eggs

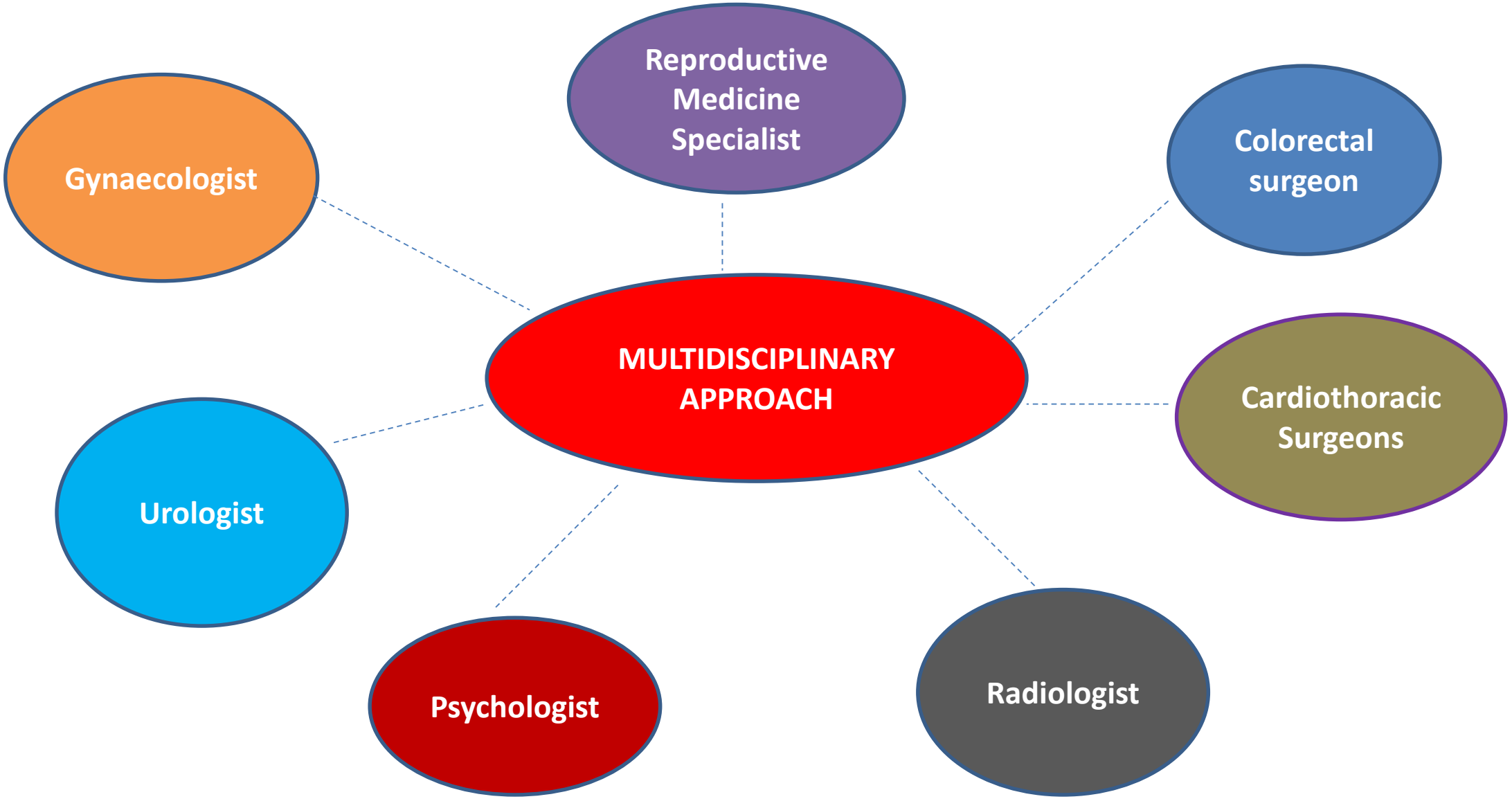
Ovulatory dysfunction :

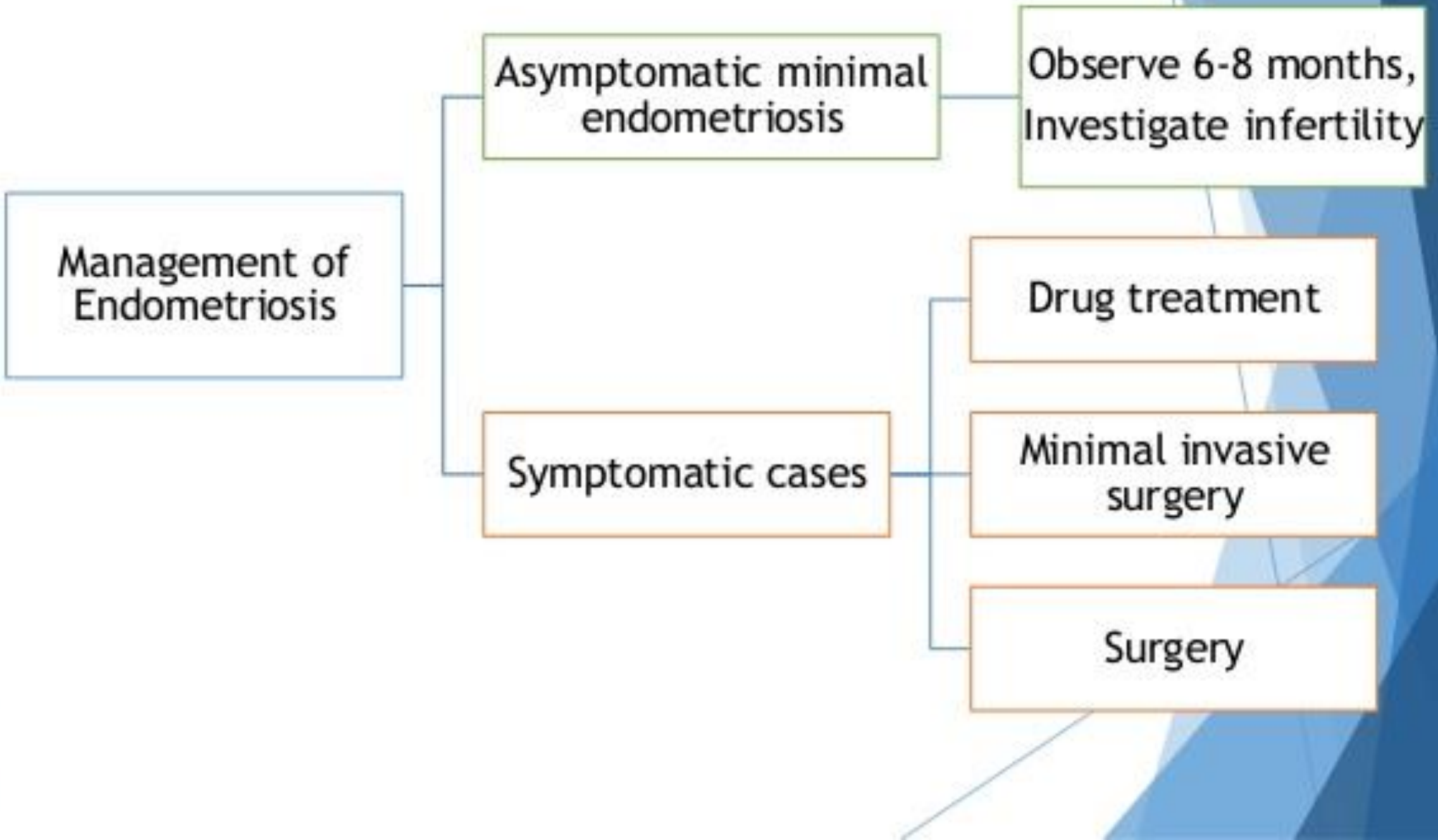
- ovarian damage or endometrioma
- adhesion cause unruptured follicle no release of oocyte

Peritoneal fluid : -has macrophages
- spermicidal and
- inhibit sperm function
- increases sperm phagocytosis
- reduce sperm motility

Prostaglandins and leuckocytes - inhibit fertilization

Management of Endometriosis




Management of Endometriosis
Asymptomatic minimal endometriosis
Observe 6-8 months, Investigate infertility
Symptomatic cases
Drug treatment
Minimal invasive surgery
Surgery

Medical Treatment

1. **COC's :** causes 'pseudo-pregnancy"

2. Progesterone: causes atrophy of the endometrial tissue

- MPA 30 mg po daily
- Depo Provera 150mg IMI every 3 months
- Mirena

3. Danazole: derivative of 17α – ethinyl testosterone

- induces pseudo-menopause
- expensive
- severe S/E - high androgen (hirsutism, deep voice)
  - low oestrogen (hot flushes, ↓ breast size)

4. **Aromatase inhibitors** : Inhibit oestrogen production

Anastrozole 1.0mg daily

Letrozole 2.5mg daily

5. GnRH Analogues:

suppress ovarian steroid production by inhibiting pituitary gonadotropin (FSH,LH) secretion

- Nasal spray : Nafarelin 400-800mg daily
- Depot injection: Goserelin (zoladex) 3.6mg subcut. monthly

Leuprolide 3.75 mg monthly intramuscularly

S/E : hot flushes, ↓ bone density

6. Mefipristone : RU486, Antiprogestin

- Inhibits ovulation
- disrupts endometrial intergrity
- induces amenorrhoea

100mg per day for 3/12

Surgical Management

- **Indication** :
  - ➢ severe endometriosis
  - ➢ to improve fertility

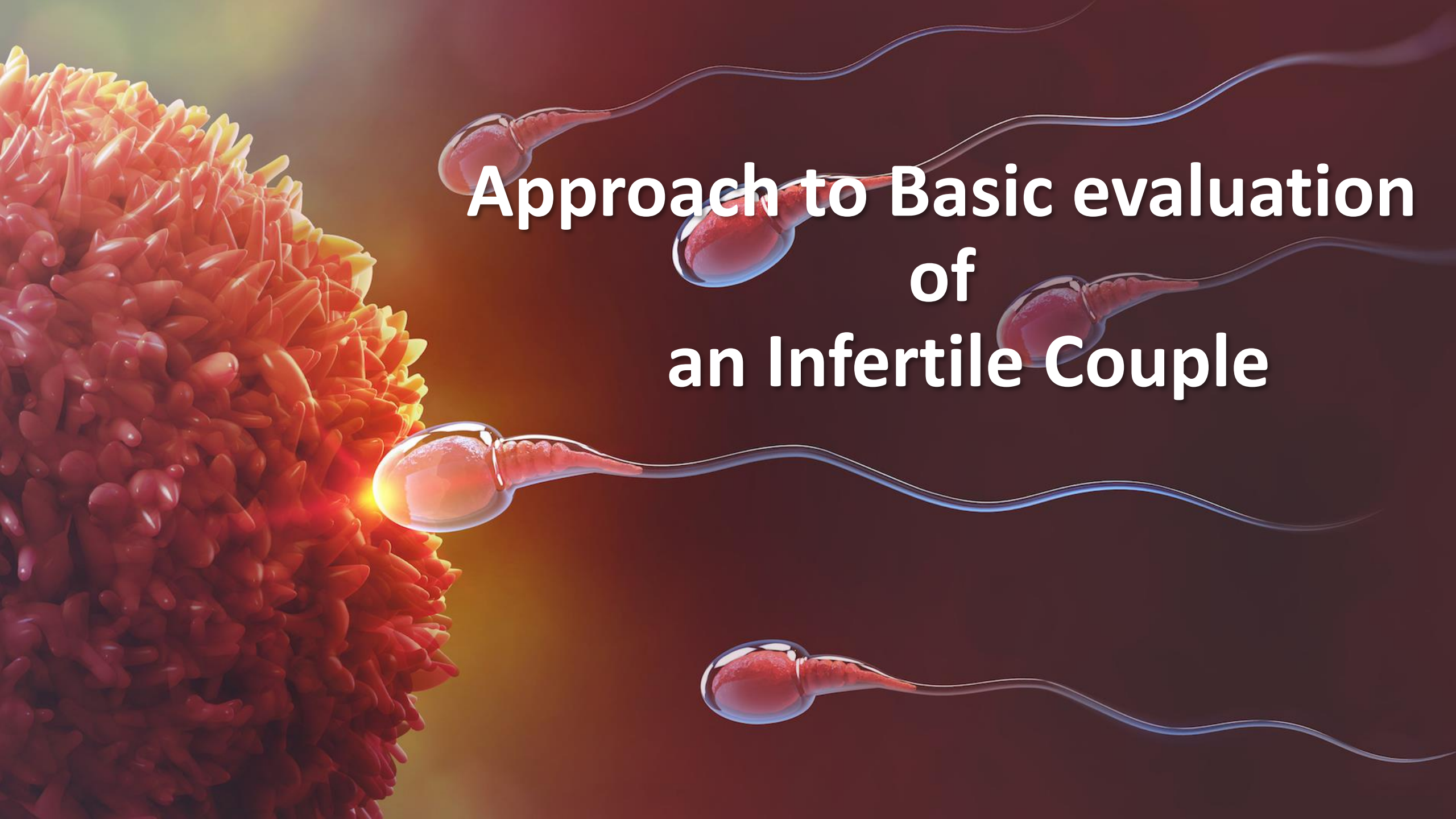
- **Objective** :
  - ➢ to restore anatomy
  - ➢ to remove as much endometriosis as possible

5-year recurrence rate after surgery is 20 %

Conservative : Laparoscopic –excision, adhesiolysis

Laparatomy – for recto-vaginal nodule

Radical : Removal of Uterus, tubes and ovary



Approach to Basic evaluation of an Infertile Couple

History Taking

- Age of each patients
- Primary or secondary infertility
- Previous reproductive history
- Duration of infertility and previous infertility treatment
- Menstrual history
  - -menarche
  - - regularity
  - - length of cycle
  - - dysmenorrhoea
  - - volume of blood
- Sexual history
  - - coital frequency
  - - dyspareunia
  - - use of lubricants
  - - sexual dysfunction (erectile problems, vagismus ejaculation)

- Previous contraception
- Pelvic infections
- Other infections
- Breast development , galactorrhoea, tenderness
- Skin Abnormalities - acne, hirsutism
- Weight gain/loss
- General systemic Enquiry
- Surgical history
- Trauma (to testes)
- Social history: smoking, alcohol, socioeconomic factors, work history
- Exposure to toxins
- Family history

Examination of a female

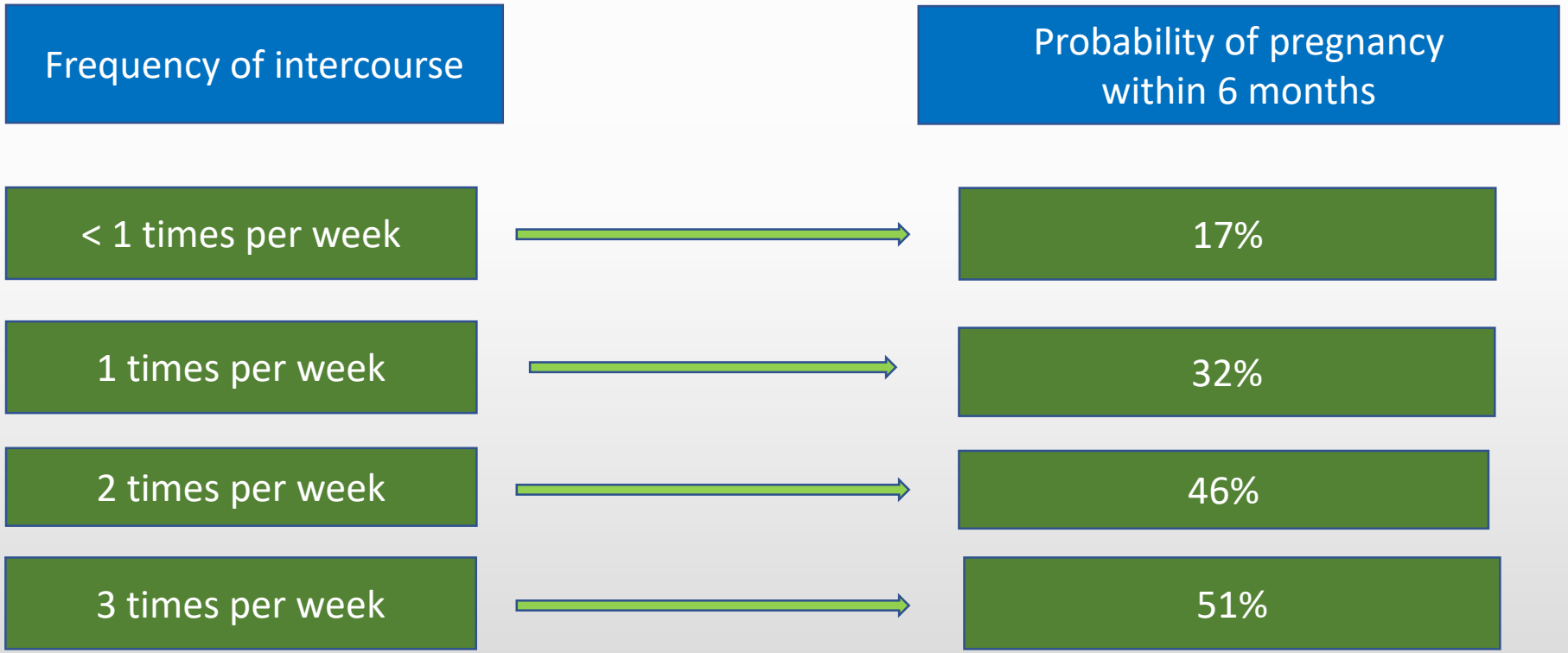
- Stature, height, weight, and calculate BMI
- Secondary characteristics and hair distribution
- Thyroid enlargement
- Breast development, exclude galactorrhoea
- Abdominal exam: surgical scars, masses

- Complete gynaecological exam
- Rectovaginal exam – to exclude rectovaginal nodule (endometriosis)
- Papsmear must be done
- Ultrasound:
  - uterine myomas
  - uterine cavity abnormalities
  - ovarian cysts
  - Antral Follicle count

What is adequate sexual intercourse

- Coital frequency is positively correlated to pregnancy rate
- Intercourse every 2 to 3 days optimizes the chance for pregnancy

NICE Guideline 2013, Updated 2017



Hatcher RA, Trussell J, Stewart F, et al. Contraceptive Technology. 1994.

MacLeod J, Gold RZ. Fertil Steril. 1953.

Cycle Evaluation and Ovulation Prediction

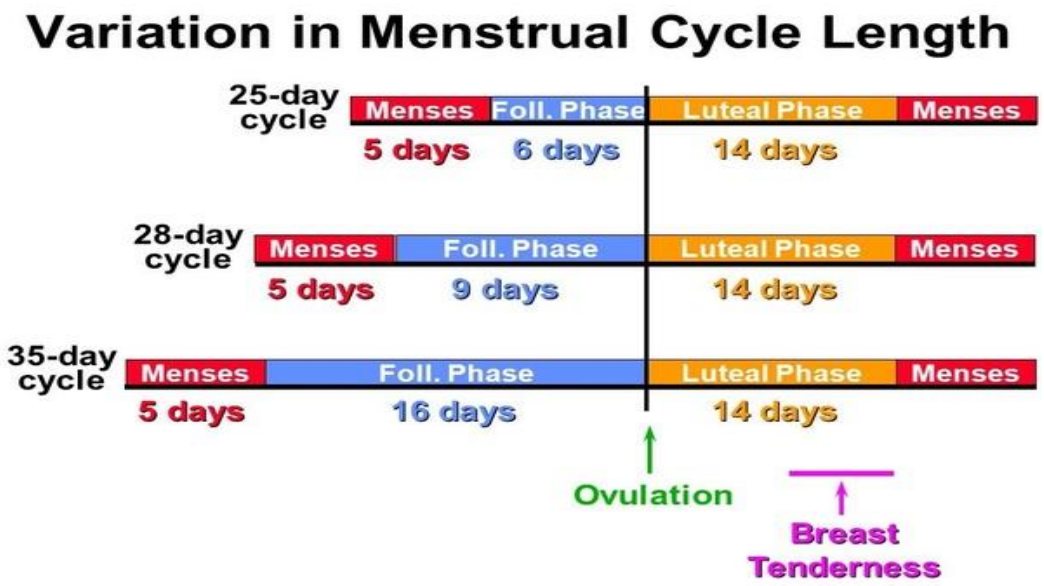
- The average menstrual cycle lasts 28 days
- Not all women have a 28 day cycle

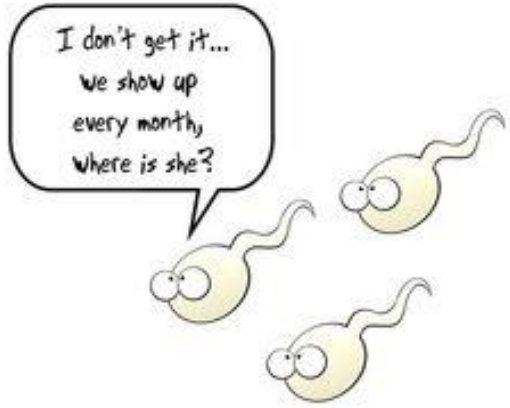
- Variation of the menstrual cycle
  - ✓ length of cycle
  - ✓ timing of ovulation and
  - ✓Implantation

- Follicular phase - shows variability

- Luteal phase - constant/remains the same

- Important when monitoring cycle to predict ovulation





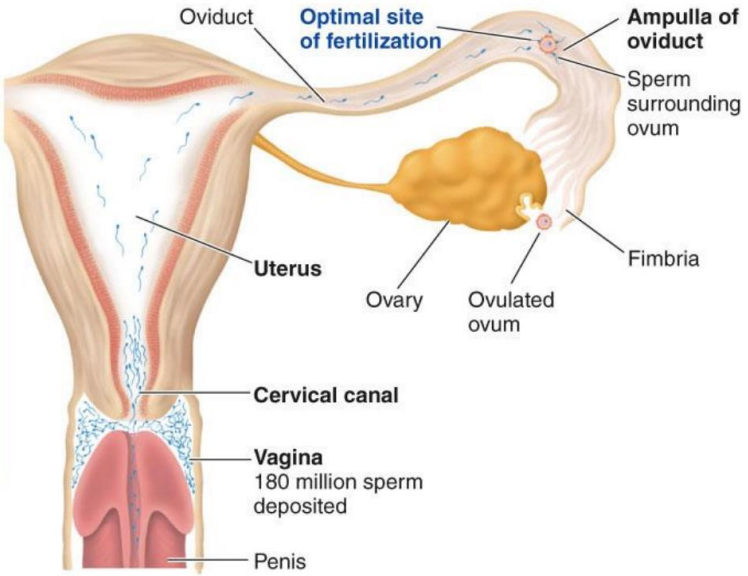
Factors affecting infertility

- Intercourse just before ovulation maximises chances of pregnancy
- Sperm survives for 3 - 5 days in the female genital tract
- Some sperm will live for a shorter time, depending on the conditions in the vagina, fallopian tubes and uterus.
- The Ovum life expectancy is about 24 hours (1 day) if not fertilized
- Intercourse more than a day after ovulation will therefore usually not result in fertilization
- Sperm should be available in the female genital tract at ovulation or shortly before ovulation

Transport of Sperm in the Female Reproductive Track

Location	Time of appearance (min after ejaculation)	Percent of ejaculated sperm*
Fertilization site (upper third of oviduct)	30–60	0.001
Uterus	10–20	0.1
Cervical canal	1–3	3
Vagina	0	100

*Based on data from animals. Sperm and ovum enlarged.



100% to vagina, then 3% to cervical canal, then 0.1% to uterus, then only 0.001% reaches fertilization site

Examination of the Male

- General body habitus
- Virilisation
  - facial hair
  - Voice
  - Hair line
  - Muscle mass
  - Fat distribution
- Height
- BMI
- Smell – hyposmia/anosmia
- Vision/visual field defects
- Gynaecomastia

External genitalia

- Tanner staging – pubic hair
- Penile length(cm)
- Scrotal skin: pigmented with rugosity

Testis size and consistency

- Palpate
- Testicular volume

Epididymis

presence of Vas deference

Prader orchidometer

Investigations

3 Basic test for infertile couple

1. Tests for Ovulation
2. Tests for Tubal patency
3. Semen analysis
   - ❖ Sperm count
   - ❖ Motility
   - ❖ morphology

Evaluation of the Female

- History
- Physical examination
- Cycle evaluation
- Ovarian reserve testing
- Test for tubal patency

1. Tests for ovulation:

(limited clinical use)

- Basal body temperature : easy, cheap
  - drawback in interpretation, and retrospective
  - Not recommended

- Urinary ovulation prediction kit – detect LH surge
  - 5-10% false pos and false negative rates

- Ultrasound monitoring of dominant follicle – until ovulation
  - labour intensive

- Endometrial biopsy: - evaluates secretory changes in endometrium and
  - indirect evidence that ovulation has taken place
  - It is invasive, expensive

- Mid luteal phase Progesterone - >10 nmol/l
  or >3 ng/ml = recent ovulation

  - in ♀ with 28 day cycle should be done on day 21 of a 28 day cycle)

Tests if Irregular menstruation

- Women with Irregular menses should have serum test of gonadotropins and Estradiol
- Day 2/3 serum FSH,LH and estradiol levels
- Normal values:
  - FSH < 10
  - LH < 10
  - Estradiol <80 pg/mL
- Variation between cycles
- Must be taken D2/D3

Tests for Ovarian Reserve

❖ **Anti-mullerian hormone (AMH)** - >1.1 ng/ml

- good ovarian reserve

- more reliable

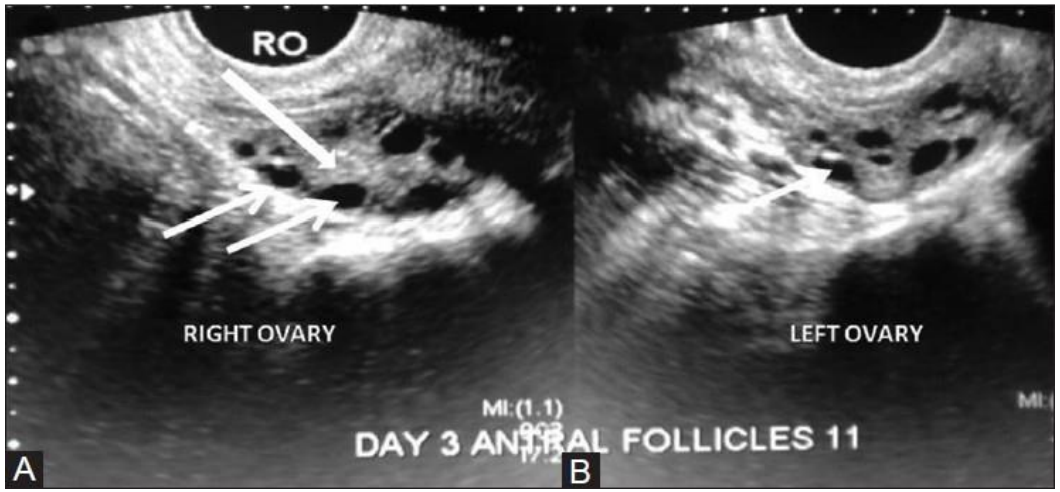
- AMH <0.5 ng/mL = reduced ovarian reserve
- AMH <1.0 ng/mL = borderline ovarian reserve
- AMH >1.0 ng/mL - <3.5 ng/mL = a good response
- AMH >3.5 ng/mL predicts a high response, caution - avoid ovarian hyperstimulation syndrome

❖ **Antral Follicle Count (AFC)**

– with transvaginal sonar

- 2-9 mm

- < 5 = poor ovarian reserve



Investigations: Tests for tubal patency

1st line :

- **Hysterosalpingography (HSG)**

  -assess tubal patency

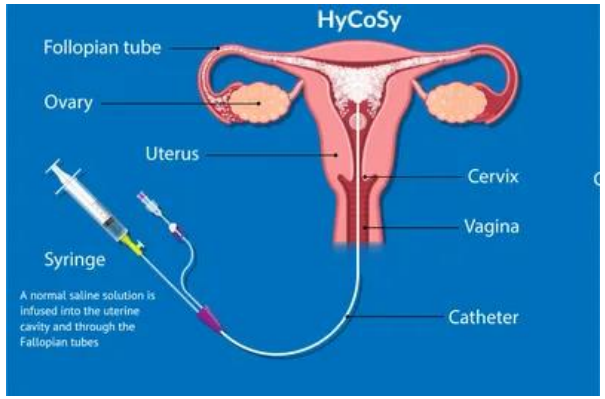
  -assess uterine cavity

- **Hysterosalpingo-contrast sonography**

  - HyCoSy (Foam Test)

  - transcervical injection of echogenic contrast media

  - ultrasound to view cavity and tubes



2nd line: invasive

- **Laparoscopy and chromopertubation**

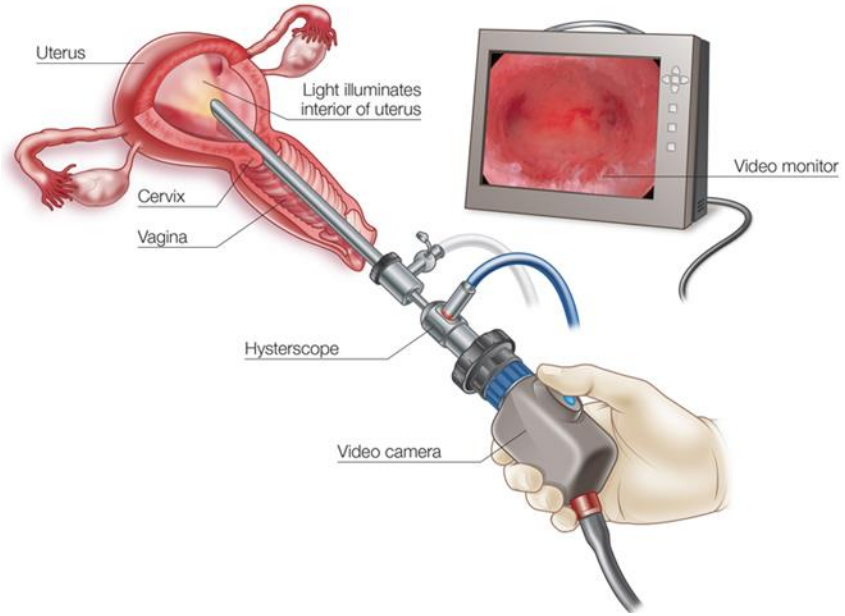
  - if other pathology suspected 1st line – e.g.endometriosis

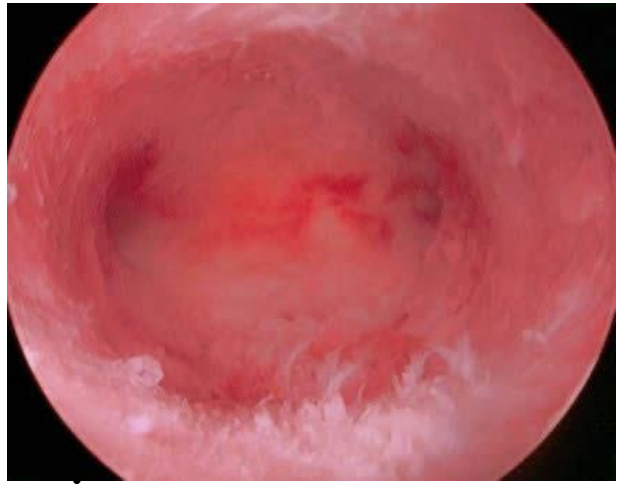
Investigation: Hysteroscopy for evaluation of the uterine cavity

- To evaluate cavity
- To treat at time of diagnosis

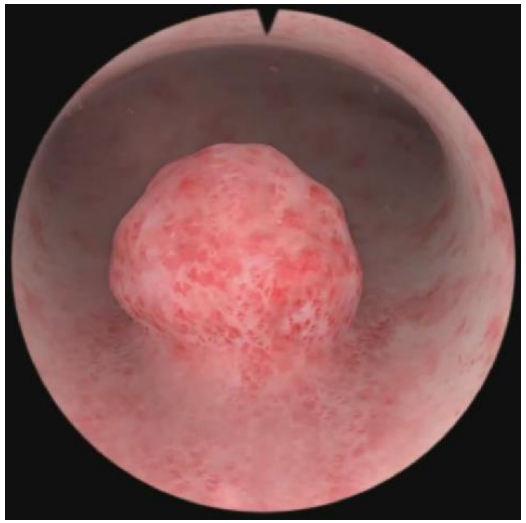
Indications for hysteroscopy

1. Intra cavitary Pathology
   - ✓ Sub mucous Fibroids
   - ✓ Endometrial Polyps
   - ✓ Uterine Septum
   - ✓ Intrauterine • Adhesions
2. Recurrent miscarriages
3. Recurrent IVF failure
4. Unexplained infertility





Normal Hysteroscopy

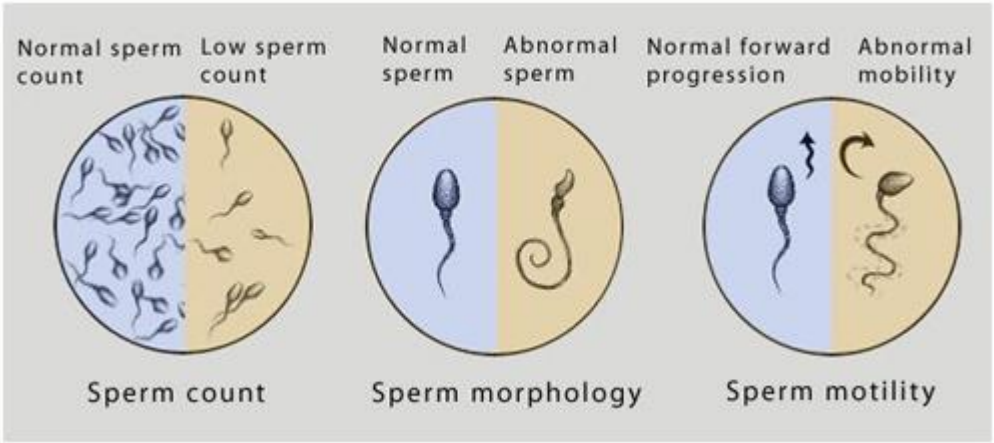


Abnormal Hysteroscopy

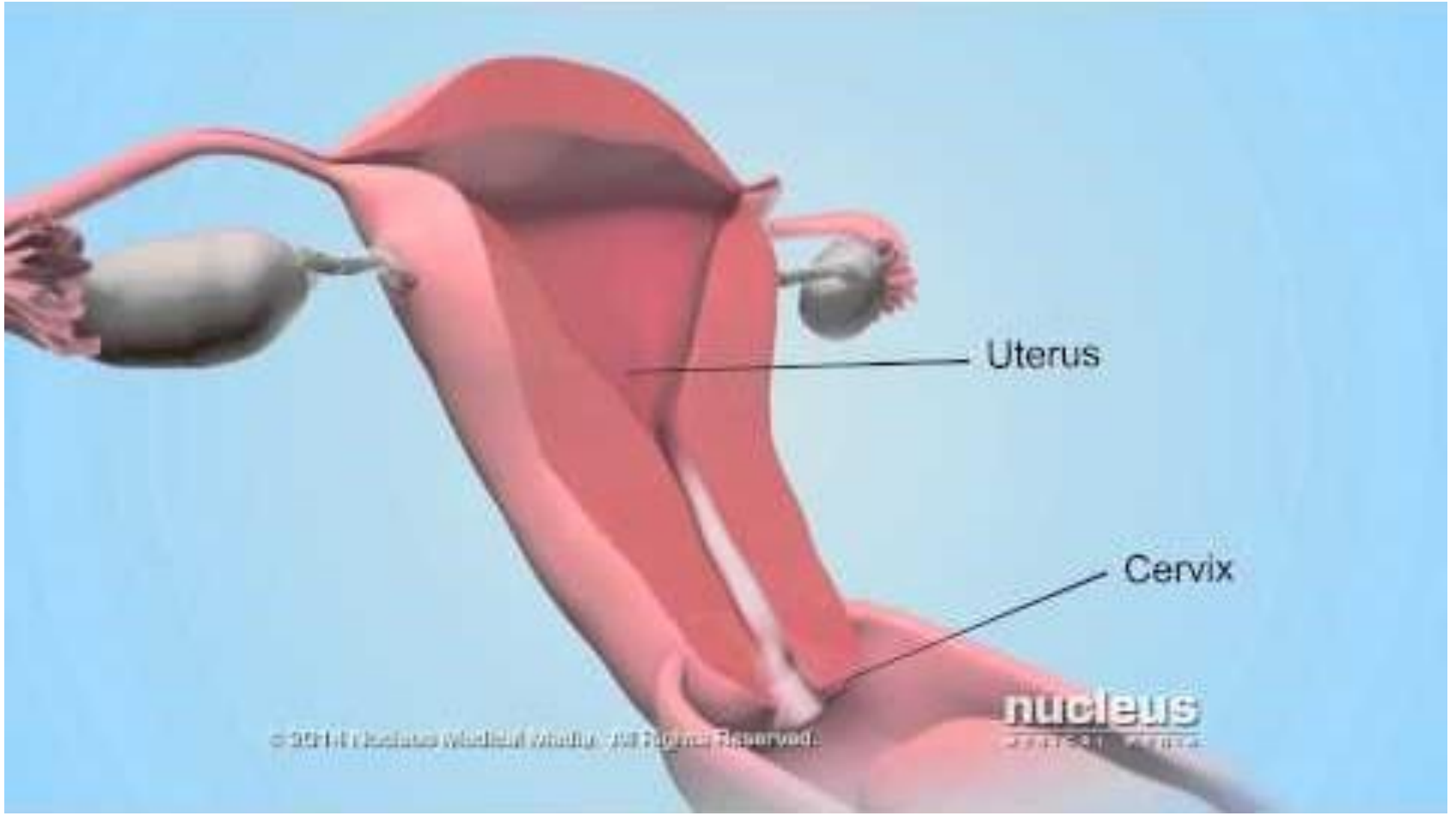
Evaluation of the Male

Semen analysis should be performed and interpreted according to the 2010 WHO semen criteria

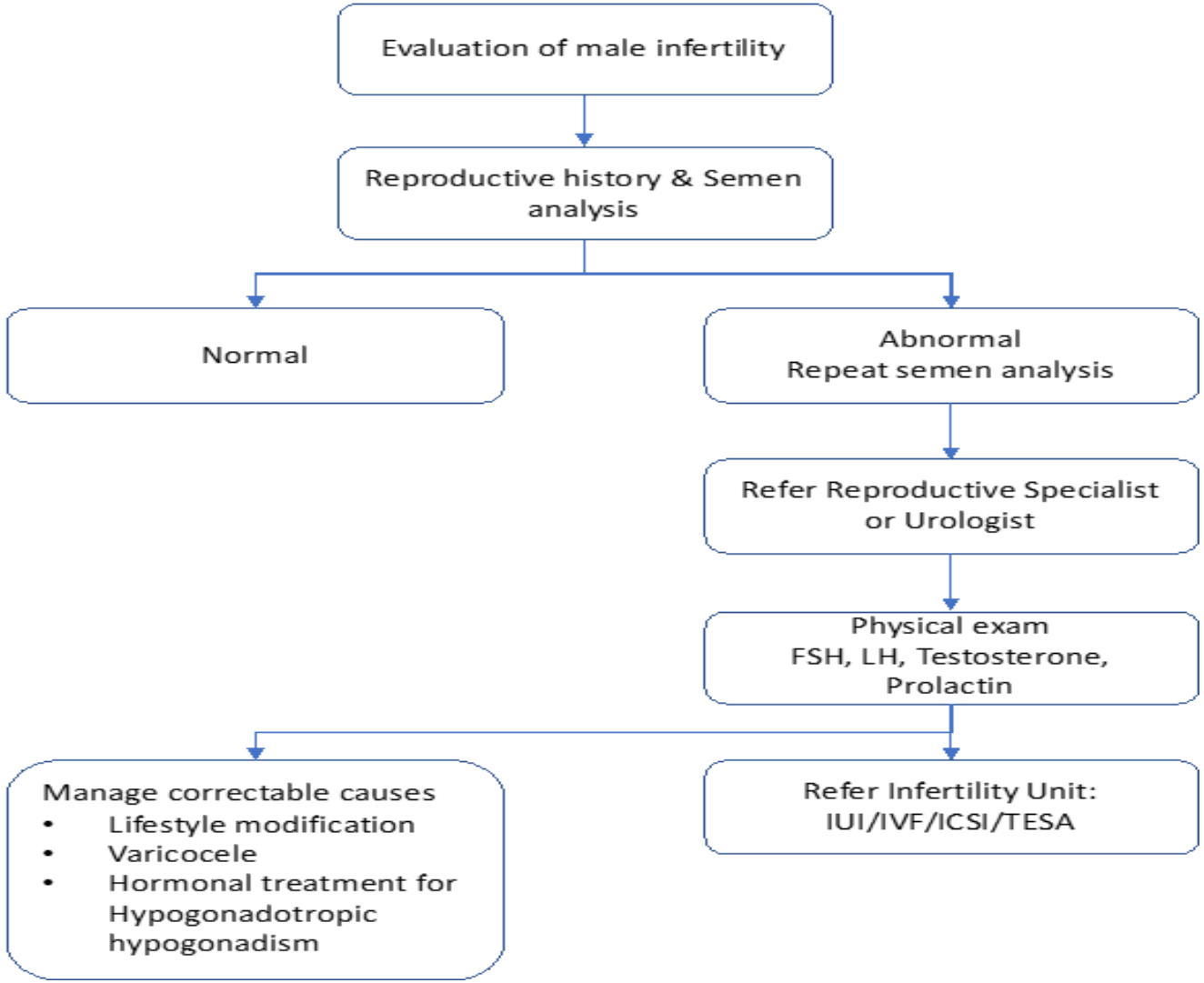
Parameter	Reference value
Ejaculate volume	1.5 ml
pH	7.2
Sperm concentration	15 x 10^6 spermatozoa/ml
Total sperm number	39 x 10^6 spermatozoa/ejaculate
Percentage motility	40%
Forward progression	32%
Normal morphology	4%
Sperm agglutination	Absent
Viscosity	≤2 cm thread after liquification



Video of Semen Analysis



Summary of Approach to Male Infertility



Management of Infertility

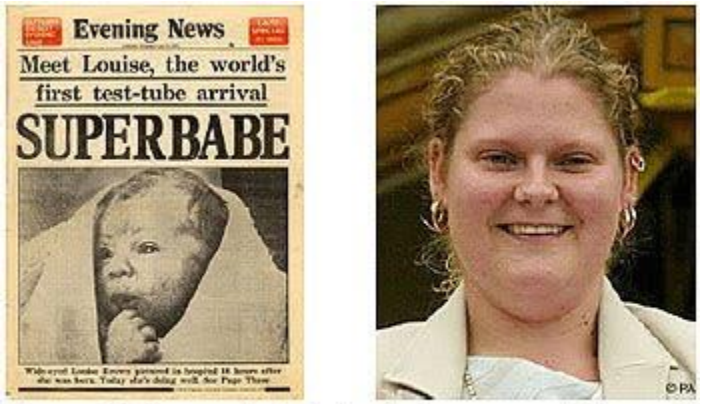
Prevention of infertility

- Holistic “Reproductive lifespan” approach
- Safe sexual practices – Prevent STI’s
- Maintain healthy weight
- Avoid delaying pregnancy
- Avoid smoking, drugs and alcohol
- Avoid steroids in men as it affects semen parameters
- Avoid exposure to certain environmental toxins, pesticides and chemicals

Factor	Impact on fertility
Obesity (BMI >35)	Time to conception increased 2-fold
Underweight (BMI <19)	Time to conception increased 4-fold
Smoking	RR of infertility increased 60%
Alcohol (>2 drinks/d)	RR of infertility increased 60%
Caffeine (>250 mg/d)	Fecundability decreased 45%
Illicit drugs	RR of infertility increased 70%
Toxins, solvents	RR of infertility increased 40%

Assisted Reproductive Technology (ART)
&
ART Procedures

Assisted Reproductive Technologies (ART)



The world's first test tube baby, Louise Brown, turned 30 years old in 2008.

- 1st IVF Baby
- Born July 1978
- England

- Was 28 when she had her own baby in 2008
- Spontaneous pregnancy
- 7 million pregnancies achieved with ART worldwide

Intrauterine Insemination (IUI)

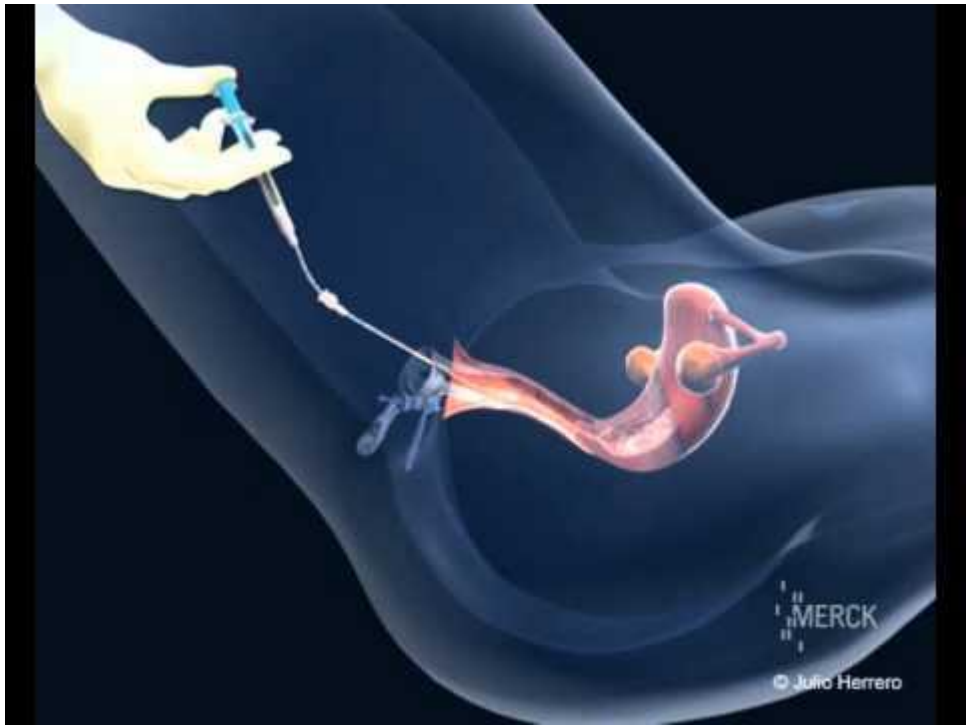
- IUI is a procedure in which processed sperm are placed directly inside the uterine cavity

Requirements for performing the procedure:

1. Ovulation

2. Patency of at least one fallopian tube

3. Insemination with an adequate number of motile sperm



IUI :Indications & Complications

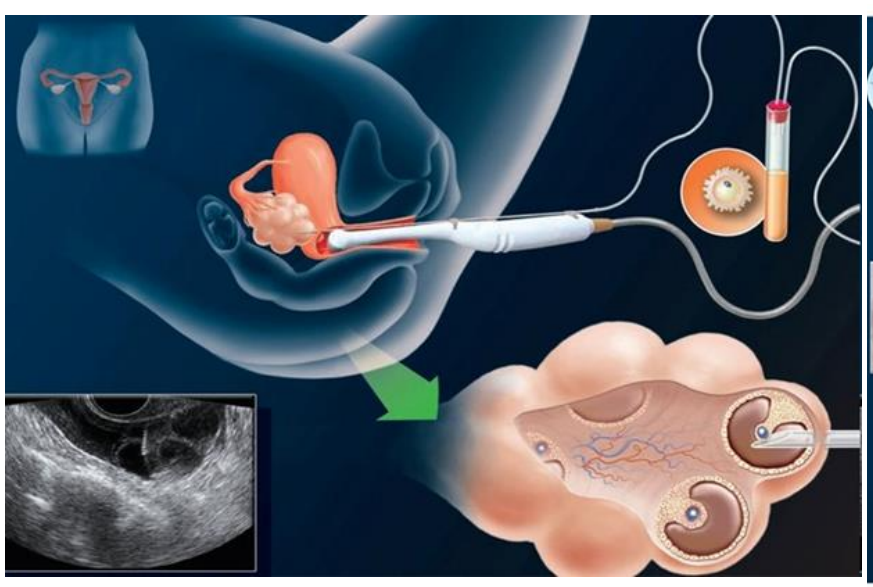
Indications

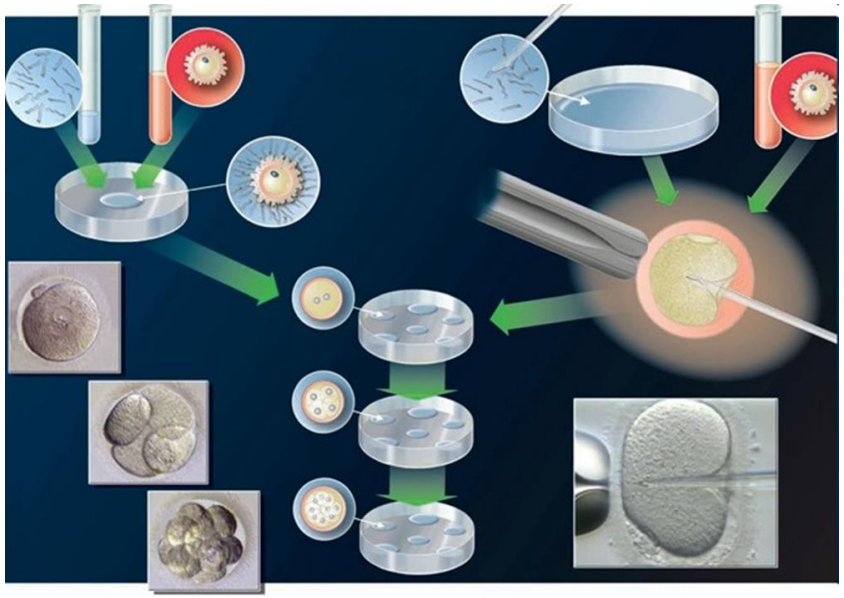
- Unexplained infertility
- Mild male factor
- Mild endometriosis
- Cervical factors
- Sexual disorders
- Same-sex/single persons

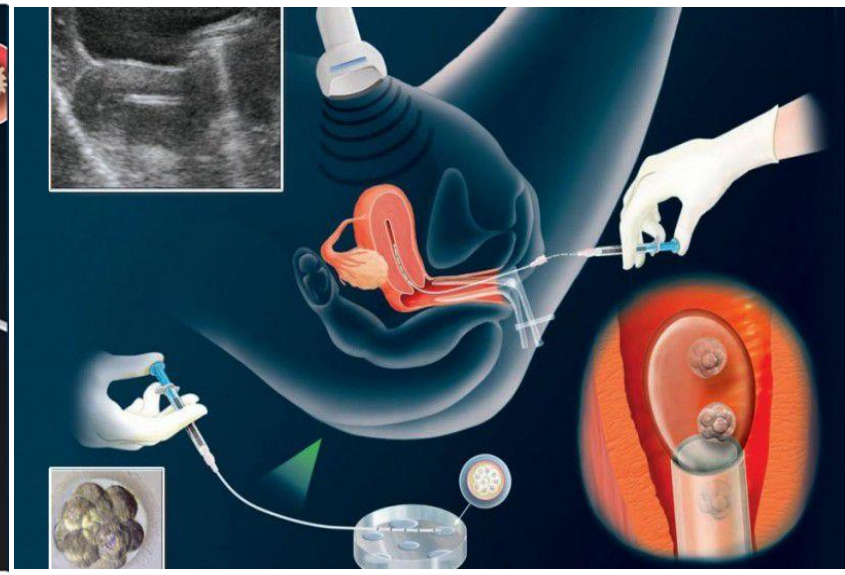
Complications

- Multiple pregnancies
- OHSS

InVitro Fertilisation (IVF)







- ovaries are stimulated with fertility drugs
- oocytes are then aspirated from ovarian follicles under ultrasound guidance
- These are fertilized in the laboratory ("in vitro")
- one or more embryo(s) are transferred into the uterine cavity

IVF Indications & Complications

Indications

- Tubal factor
- Failed IUI
- Severe endometriosis
- Diminished ovarian reserve
- Unexplained infertility

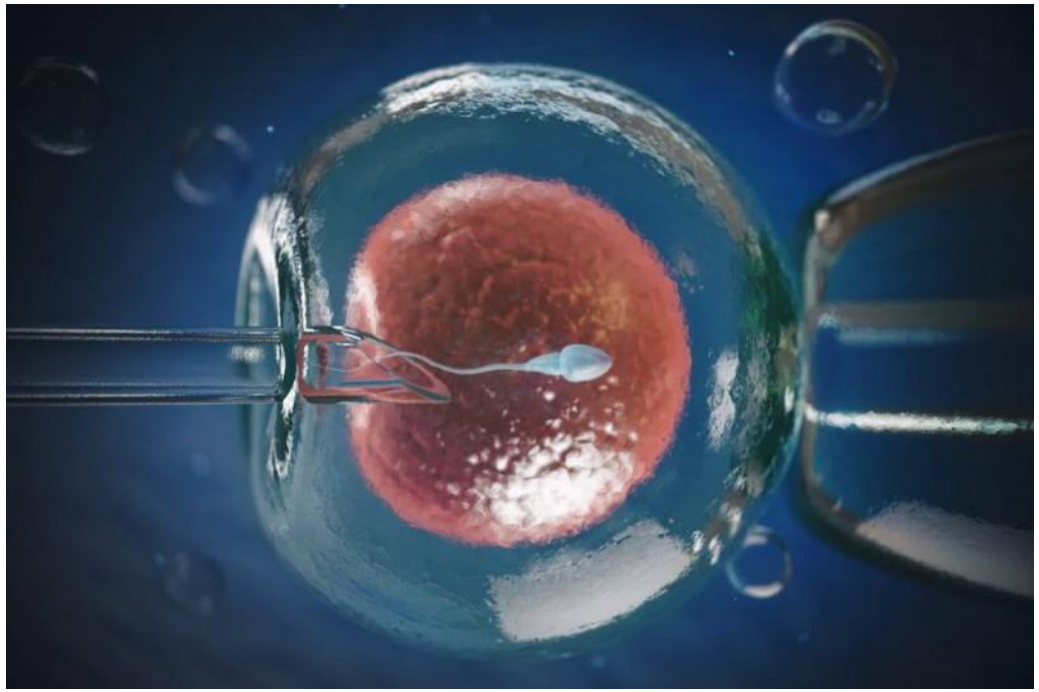
Complications

- OHSS
- Multiple pregnancies
- Side effects of drugs
- Egg retrieval procedure complications (pain, infection)
- Ectopic pregnancy
- Obstetric complications (multiple pregnancy/ PPH)
- Cost of treatment

Intracytoplasmic Sperm Injection (ICSI)

Intracytoplasmic sperm injection (ICSI)

- A technique in which a single sperm is injected directly into a mature oocyte.
- Assisting fertilization in men with abnormal semen parameters
- Sperm are retrieved from ejaculated semen or may be cryopreserved sperm
- Sperm may be surgically retrieved from the testes or male reproductive tract
- If the sperm used for ICSI have outwardly normal morphology and motility, the probability of fertilization is high



ICSI Indications & Complications

Indications

- Male factor
- Fertilisation failure with IVF
- Fertilisation with epididymal/testicular sample
- Fertilisation with cryopreserved sperm
- Fertilisation with immotile sperm

Complications

- OHSS
- Multiple pregnancies
- Side effects of drugs
- Egg retrieval procedure complications
- Ectopic pregnancy
- Obstetric complications
- Cost of treatment

Egg Retrieval Room

Embryo Transfer Room

Reproductive Biology

Third Party Reproduction

- Provides alternatives to “traditional” parenting

- “Third-party reproduction” refers to :
  - ✓ use of eggs, sperm, or embryos
  - ✓ donated by a third person to enable an infertile individual or couple to become parents

  “Third-party reproduction” includes:
  - ✓ Oocyte donor
  - ✓ Sperm donor
  - ✓ Embryo donor
  - ✓ Surrogates
  - ✓ Gestational carrier

- Donors may be known or anonymous to the intended recipient

Indications for Oocyte donation

Women with non-functioning ovaries

- Premature ovarian dysfunction
- Bilateral oopherectomy
- Ovarian agenesis/dysgenesis
- Menopause
- Hypogonadotropic Hypogonadism

Women with functioning ovaries

- Carrier of a genetic disease
- Poor ovarian reserve – age related
- Multiple failed ART cycles with poor oocyte/embryo quality
- Inaccessible ovaries

Indication for Sperm donation

Male infertility

- Azoospermia
- Severe oligospermia
- Ejaculatory dysfunction
- Oligoasthenospermia where partner declines ICSI
- Previous failed fertilisation after IVF
- Sperm or seminal fluid abnormalities (significant)

Non-fertility indications

- Genetic diseases
- Transmittable disease- cannot be eradicated
- ♀ Rh -ve and severely isoimmunized ♂RH +ve
- Same partner relationships

Surrogacy :Indications

Surrogacy is an arrangement that is supported by a legal agreement, whereby a woman (the surrogate mother) agrees to bear a child for another person or persons, who will become the child's parent(s) after birth

Indications:

- Absence of a uterus :Hysterectomy ,Congenital abnormality
- Severe uterine abnormalities
- Asherman;s syndrome
- Endometrial damage
- Medical conditions where pregnancy is contraindicated
- Chronic reproductive loss
- Same-sex male couples/single men

Surrogacy : Requirements & Complications

Requirements of a Surrogate

- Be competent to enter into the surrogate motherhood agreement
- Understand and accept the legal consequences of the agreement and the parental rights and obligations
- Not be using surrogacy as a source of income
- Undertake the surrogacy process for altruistic purposes only
- Have a documented history of at least one pregnancy that they carried to term
- Have the written consent of her partner (if any)
- The decision to terminate a pregnancy lies with surrogate mother for medical reasons

Requirements for commissioning parents

- Intended commissioning parent(s) are suitable persons to be parents.
- The commissioning mother has a condition, which is permanent and irreversible, that prevent her from carrying a pregnancy to full term
- A High Court application, in terms of Chapter 19 of the Children's Act, must be made to the Court in which you are domiciled (ordinarily resident)
- Commissioning parents become the rightful parents upon birth of the child

Complications

- OHSS
- Side effects of drugs
- Depression

Costs involved in Surrogacy

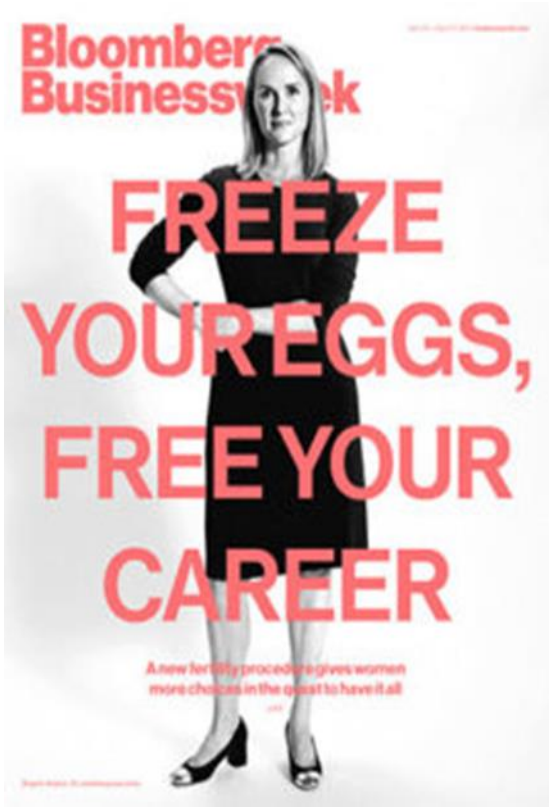
As an estimated range in ZAR (as of 2019):

- IVF Medical costs: R50 000 – R135 000
- Screening Costs: R 17 000 – R 25 000
- Legal Costs: R 60 000 – R 85 000
- Monthly compensation for expenses during the surrogate journey: R10 000 – R 15 000

- https://www.fertilitylaw.co.za/2019/12/06/becoming-a-surrogate-in-south-africa/

Egg Freezing

- Delay fertility
- Cancer treatment
- Early menopause



- Not insurance policy
- Best chance if freeze before Age 35yrs
- Must survive the thawing process
- Must fertilise

- Safe
- Not experimental

Safe Conception & Preconception Care

HIV and Infertility

- HAART has improved life expectancy of people with HIV
- HAART has ↓ MTCT to 1- 2%
  - If no intervention viral transmission : 15 – 30%
- Children born before there was provision of HAART/PMTCT program are now in reproductive age group – seek options
- No longer ethical to deny fertility Rx to HIV pos pt

Safe conception: what is the concern

- In HIV-serodifferent couples, there is a concern of transmission of HIV to the uninfected partner, especially if one partner is not suppressed on treatment
- In HIV-seroconcordant couples, there is a risk of possible transmission of drug-resistant HIV or superinfection.
- There is a risk of vertical transmission to the child when an HIV-positive female becomes pregnant
- An HIV-negative woman who seroconverts during conception attempts or pregnancy has a high risk of poor outcomes.

Infertility treatment in HIV pos patients

- People living with HIV should also have access to a full range of investigations
- Antiretroviral (ARV) therapy must be optimised before attempting to conceive
- Consistent use of ARVs is required, with good adherence to treatment
- Viral load must be undetectable < 50 copies/ml
- Monitoring of viral loads every 3-6 months to ensure sustained viral suppression
- Infertility treatment must be individualised, Offer ART when indicated

- Consider **condomless sexual intercourse** in those with no infertility diagnosis. Condomless sex should only be undertaken once adherence is confirmed, and the client living with HIV is virally suppressed
- All clients should be screened for active STIs. If there is evidence of an STI in either or both partners, both partners should be treated

- These guidelines are aligned with recommendations of the Southern African HIV Clinicians Society (SAHIVCS) guidelines and 2019 PMTCT guidelines ?

Reproductive options for people living with HIV

HIV+ woman HIV- man	HIV+ man HIV- woman	Both HIV+
• Antiretroviral therapy • Undetectable viral load < 50 copies/ml Fertility not an issue • Condomless sex • Timed condomless sex*/Self-insemination • Consider PrEP if female not on ARVs for at least six months and viral load > 50 copies/ml Infertility an issue • IUI/IVF/ICSI • Adoption	• Antiretroviral therapy • Undetectable viral load < 50 copies/ml Fertility not an issue • Condomless sex • Timed condomless sex* • Consider PrEP if male not on ARVs for at least six months and viral load > 50 copies/ml Infertility an issue • Sperm washing • IUI/IVF/ICSI • Donor sperm • Adoption	• Antiretroviral therapy • Undetectable viral load < 50 copies/ml Fertility not an issue • Condomless sex • Timed condomless sex* Infertility an issue • Sperm washing • IUI/IVF/ICSI • Donor sperm • Adoption

* Timed condomless sex -condomless sex acts limited to the peak fertile window, which occurs around the time that the female partner ovulates. Timed condomless sex is recommended if:

- Positive partner(s) not confirmed VL <200 copies/ml
- Viral load monitoring available
- Client preference
- No STI's

Levels of Care
&
Referral routes

Levels of Care: What can HCP do?

Level 1:

Primary health care clinic, community health care centres, District hospitals, General practitioner (GP)

- determine duration of infertility
- offer advise on prevention of infertility
- advise couple on the best time to have intercourse
- Refer rather sooner

Level 1/ GP	Action
Determine • Duration of infertility • Frequency of intercourse ✓ **1x per week** = chances of conception in 6 months= **17%** ✓ **3x per week** = chances of conception in 6 months = **50%** • Timing of intercourse • Alcohol/smoking/drug use • Obesity/low BMI • Folic Acid supplementation • Baseline hormone profile • Cycle evaluation • HSG • Semen Analysis ✓ If mild male factor- Prelox ✓ Repeat SA after 2 months	• Offer advice or • Timed intercourse Refer If: • > 1yr of regular unprotected intercourse in  <35yrs • > 6 months regular unprotected intercourse in  > 35yrs • Known cause of infertility • Irregular menstrual cycles

Specialist/Subspecialist

Level 2: Regional hospital (Gynaecologist support)
- Do hormone profile, HSG and semen analysis
- Do minor surgery

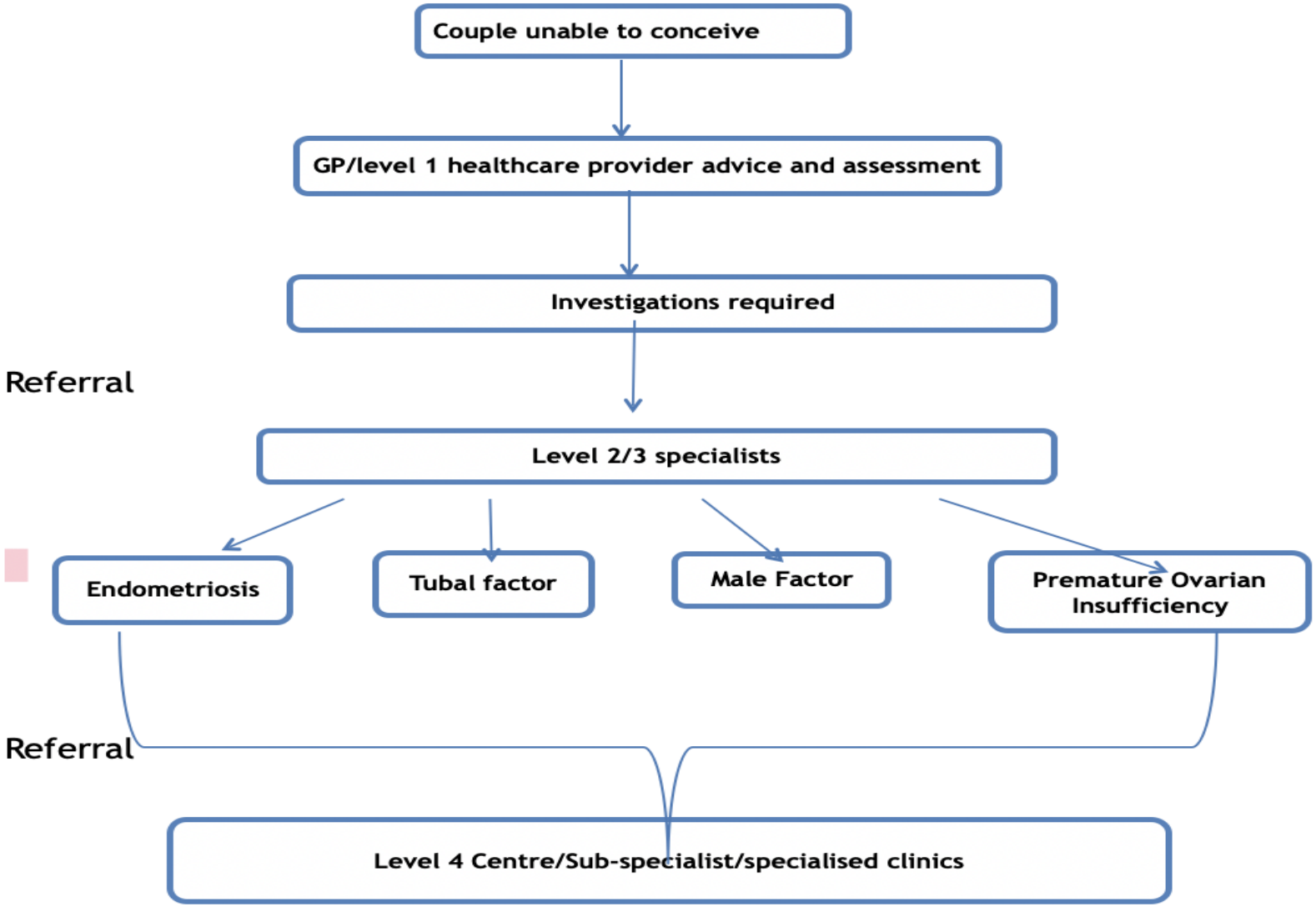
Level 3: Provincial Tertiary hospital (limited Reproductive Medicine Sub-specialist support)
- Do major surgery
- Do intrauterine insemination

Level 4: Specialised hospitals (Reproductive Medicine Sub-specialist support)
- Do IVF/ICSI
- Do specialized reproductive surgery

When to Refer:
- All patients with **known pathologies** (endometriosis, fibroids) and those who are **> 40 years** old should be **immediately referred to level 4**.
- Patients who are **> 35 years** old should be referred after **6 months of trying**
- Patients **<35 years** are evaluated **after 1 year** of trying

Level 2/3/ Specialist	Level 4/ Sub-specialist
• Major surgery • Specialised Reproductive surgery • Screening - e.g. cystic fibrosis/Karyotyping • IUI/Timed Intercourse	Offer Specialist services • Blocked tubes • Abnormal SA and Hormone profile • Specialised surgery to improve fertility • Sperm washing • IUI/IVF/ICSI • IVF/ICSI

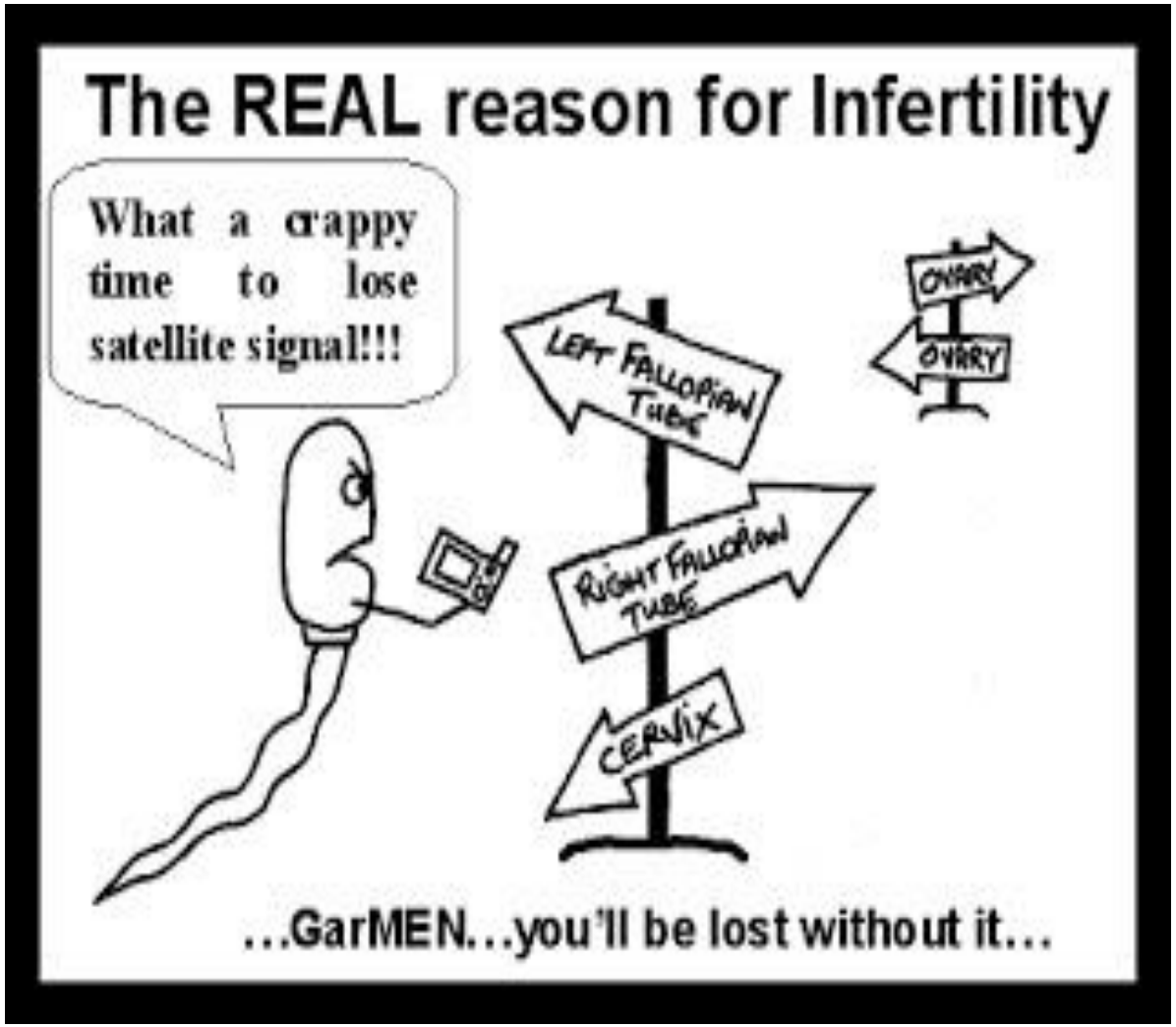
Levels of care/Referral routes



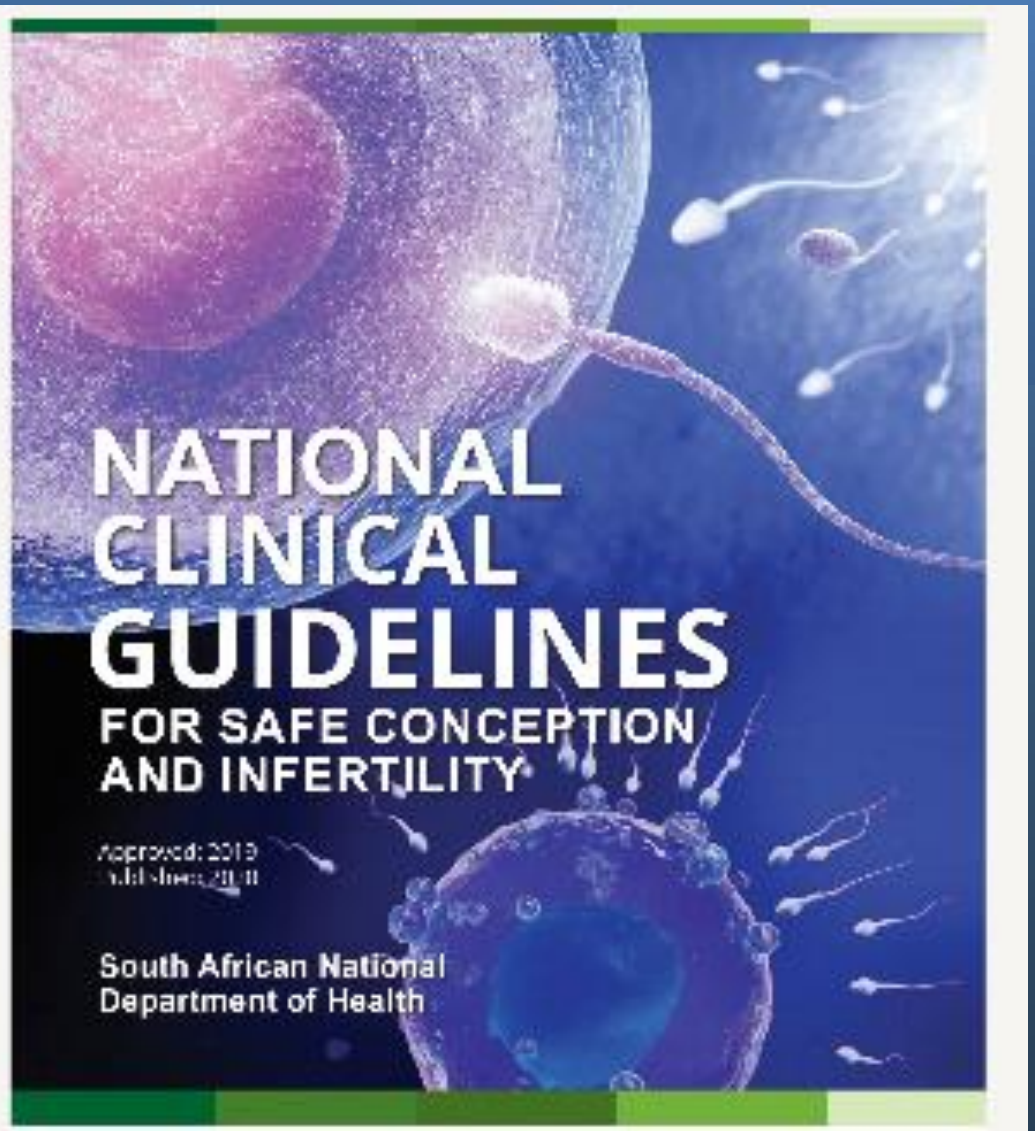
Success Rates & Cost

Procedure	Success Rate	Cost Public Sector	Cost Private Sector
IUI	12% -15%	R6 000 – R12 000	R12 000 – R 15 000
IVF	33% - 40%	R 25 000 – R 35 000	R 65 000 - R 80 000
ICSI	33% - 40%	R 25 000 - R 35 000	R 65 000 – R 90 000
Egg Freezing		N/A	Cost of Cycle + R 5000/year storage
Semen Decontamination		R 4 000 - R8 000	R 8 000
PGS/PGD	? May increase pregnancy Rate	R 18 000 – 25 000	

Conclusion



- Hope for couples
- Access to information
- Access to service
- Psychological Care
- SA Guidelines for Safe Conception & Infertility
- Right to have a child is a Human Rights Issue
- Help achieve family


NATIONAL
CLINICAL
GUIDELINES
FOR SAFE CONCEPTION
AND INFERTILITY
Approved: 2019
South African National
Department of Health

Thank You

Dysmenorrhoea

Definition

- Difficulty menstruation
- Painful menstrual cramps of uterine origin

Classification

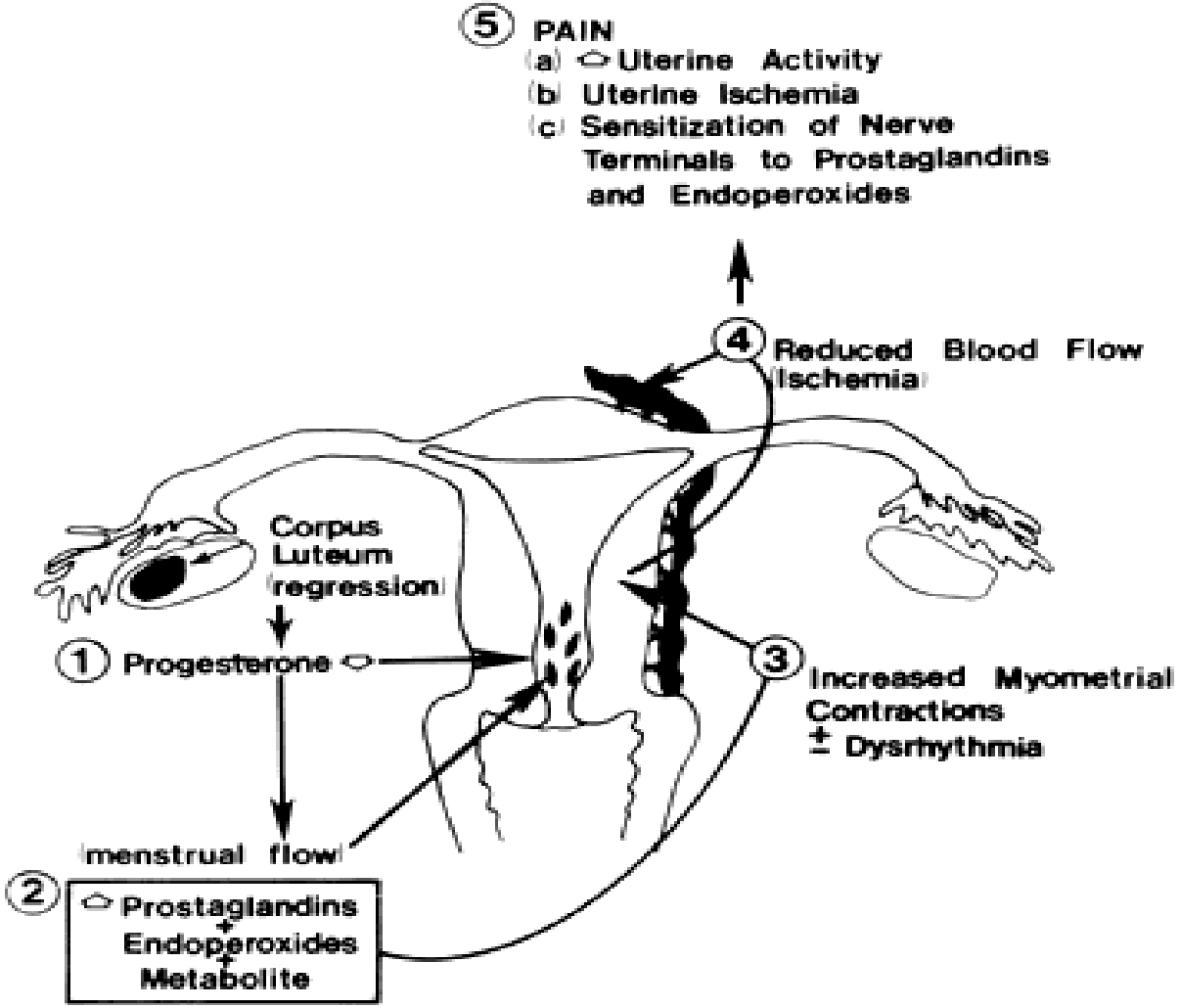
Primary

- No underlying pathology
- Starts shortly after menarche
- Starts within few hours of menstrual flow
- Intense in 1st and 2nd day and lasts 2-3 days
- Occurs in ovulatory cycles
- May be accompanied by nausea, vomiting, headache, dizziness

Secondary

- Underlying identifiable pathology
- Onset is > 2 yrs following menarche
- Or after the age of 25
- No previous history of dysmenorrhea
- Usually precedes menses by several days
- Lasts throughout menstruation

Pathophysiology



Management

Pharmacological

NSAIDs

- Ibuprofen 400 mg 6hrly
- Naproxen 500mg 6hrly
- Mefenamic Acid 500mg 6hrly
- Indomethacin 25mg 8hrly
- Oxicams (pyroxicam)

COX 2 inhibitors

- Inhibit COX I and II
- Cardiovascular effects led to their withdrawal

COC's

- 2nd line treatment
- Inhibits ovulation, thins the endometrium, therefore less menstrual flow, less prostaglandins
- Other hormonal treatment: norplant,Depo Provera

Mirena

- Thinning of endometrium
- Decreases dysmenorrhoea
- Causes amenorrhoea within 12 months

Non- Pharmacological Management

Other Treatment

- **TENS** – Transcutaneous Electrical Nerve Stimulation. Effective more than placebo
- **Acupuncture** – cochrane, 1 small study showing effectiveness
- **Heat Therapy** – heat patch. As effective as Ibuprofen
- **Lifestyle modification**
- **Exercise**
- **Psychological therapy**

Surgical

LUNA

- Laparoscopic Uterosacral Nerve Ablation
- Complete transection of Uterosacral ligament
- For severe pain not responding to medical Rx

LPSN

- Laparoscopic Presacral Neurectomy
- Disrupts sensory pathway from Uterus in hypogastric nerve plexus

Causes of secondary dysmenorrhoea

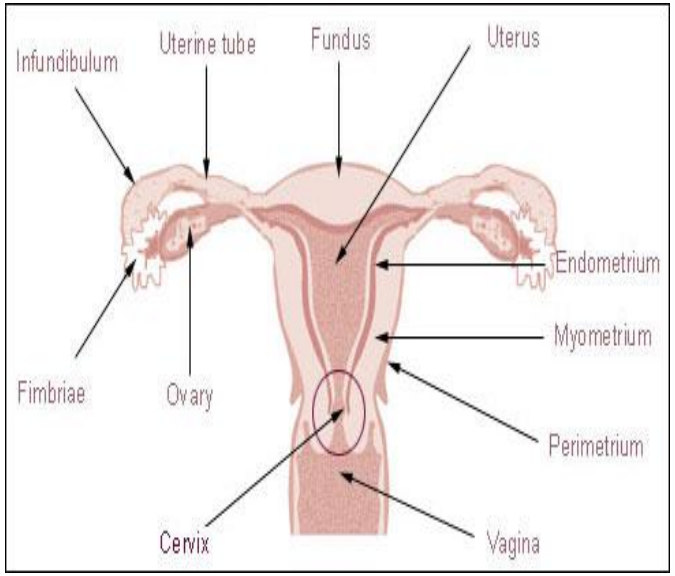
- Extrauterine
- Intramural (within myometrium)
- intrauterine(within cavity)

Extra-uterine

- Endometriosis
- Tumours – ovarian cysts
- PID
- Pelvic congestion syndrome
  - –Due to engorgement of pelvic vasculature

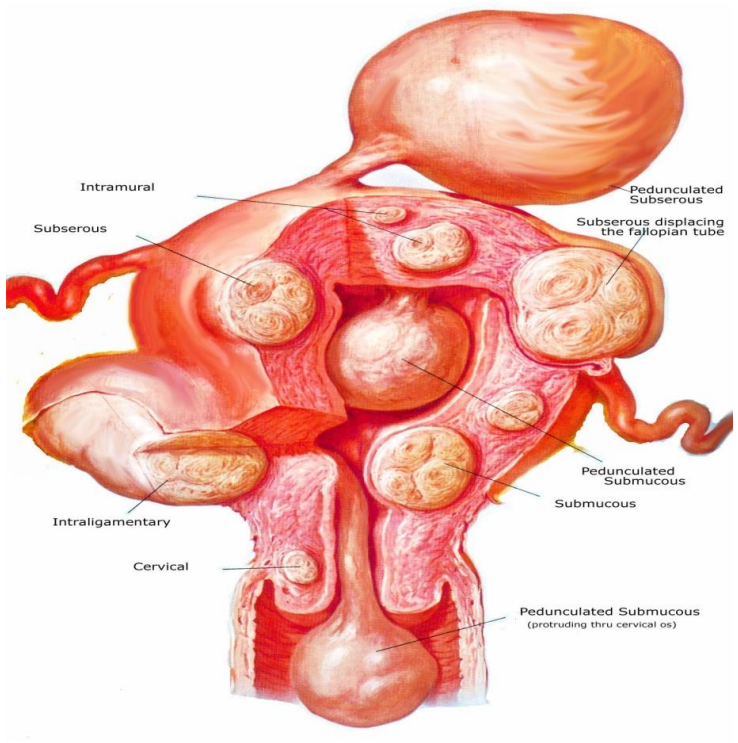
    Hx: burning, throbbing pain at night and after standing

    Dx: laparoscopic visualisation of engorged/varicosities of the broad ligament and pelvic sidewall veins
- Adhesions
- Psychogenic factors
- Mullerian tract anomalies



Intramural

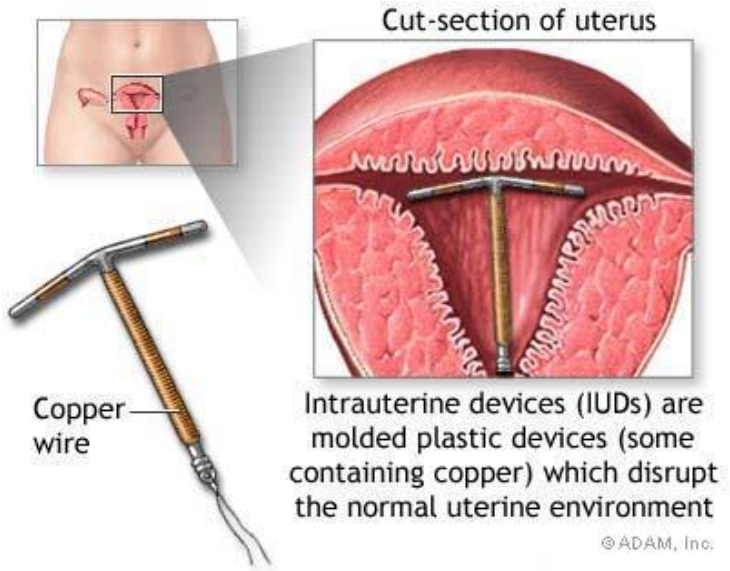
- Adenomyosis
- leiomyoma



Adenomyosis. Note thickened wall of uterus which can be mistaken for fibroids.

Intrauterine

- Submucous fibroid
- Polyps
- IUCD
- Cervical stenosis
- infections



Non-gynaecological

- GUT
  - Interstitial cystitis
  - Renal stones
  - Ureteral obstruction
  - Urethral diverticulitis
- GIT
  - Irritable bowel syndrome
  - Diverticulitis
  - Bowel obstruction
  - Appendicitis
- Orthopaedic
  - Spondylosis
  - Coccydynia
  - Fibromyalgia

Investigations

- Pelvic u/s
- Saline sonohysterography
- Urine mcs
- Vaginal swab mcs
- Hysteroscopy
- Laparoscopy

Treatment

- Treat the cause

Thank you !

.... Questions ?