

To all marrow edition 6 notes and other latest notes,click below

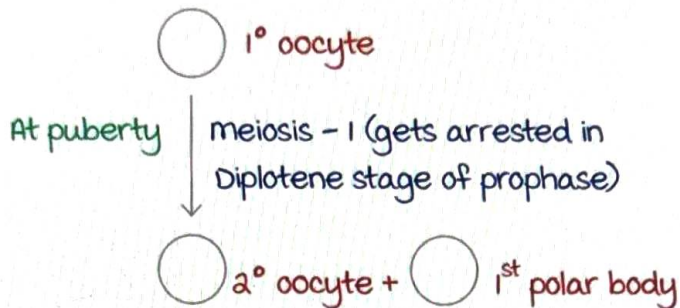
[Click here](#)

**Gynaecology**

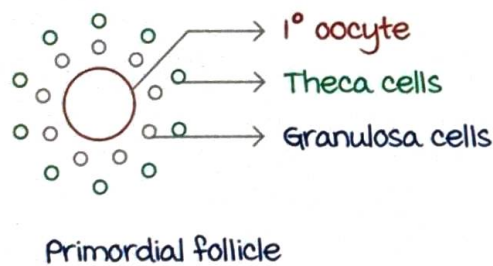
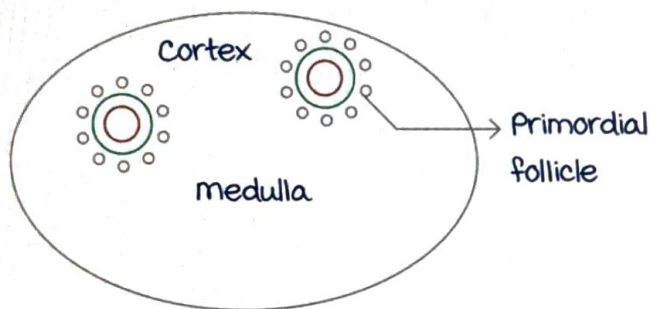
# MENSTRUAL CYCLE

## Oogenesis

00:01:24



Structure of Ovary:  
Before puberty:



Cortex : Primordial follicle  
Granulosa cell

medulla : Blood vessels  
Theca cells

Number of follicles :

- maximum : At 5<sup>th</sup> month of intrauterine life (6-7 million).
- At birth : 1-2 million follicles.
- At puberty : 4-5 lakh follicles.

Initial recruitment of follicles is Hormone independent.

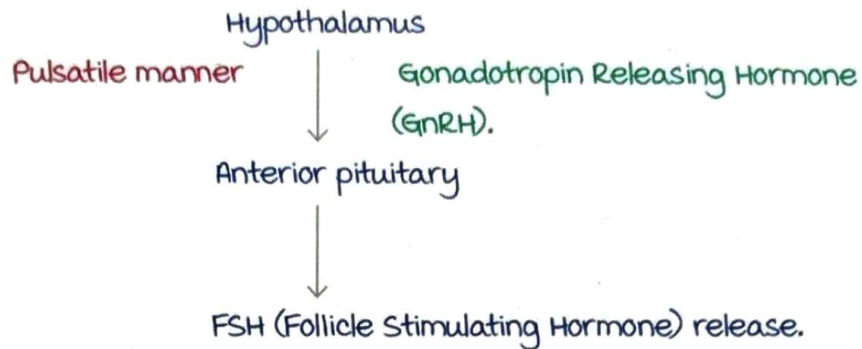
Active space

To get all ed6 notes and latest neet pg notes, [click here](#)

## Role of FSH

00:08:55

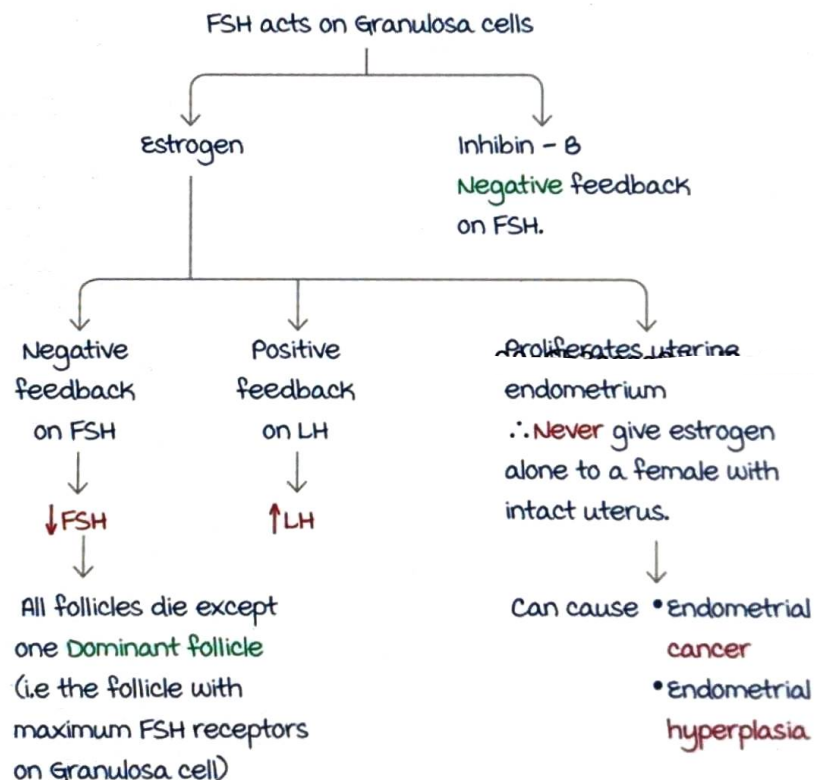
At puberty, Hypothalamus - Pituitary - Ovarian - Axis (HPOA) becomes functional.



Functions of FSH :

- Prevents the follicles from undergoing atresia.
- Stimulates follicles.

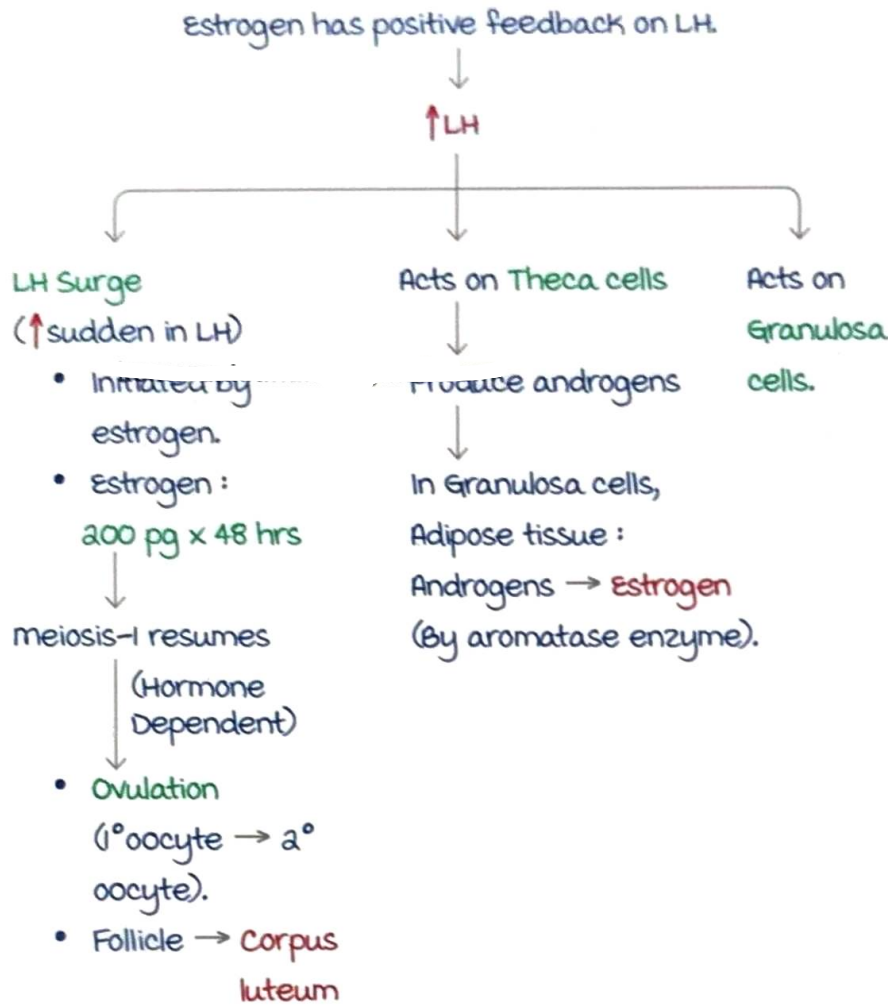
Role of FSH :



1. FSH receptors are present on Granulosa cells.
2. Granulosa cell tumour of ovary : **Feminizing tumor**.
3. Tumor marker for Granulosa cell tumor of ovary : **Inhibin - B**.

## Role of LH

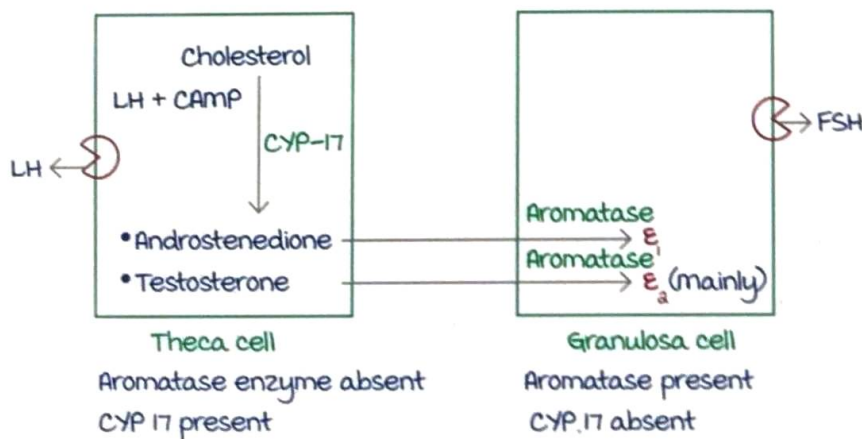
00:18:36



## Two cell two gonadotropin theory

00:24:38

Granulosa cell :



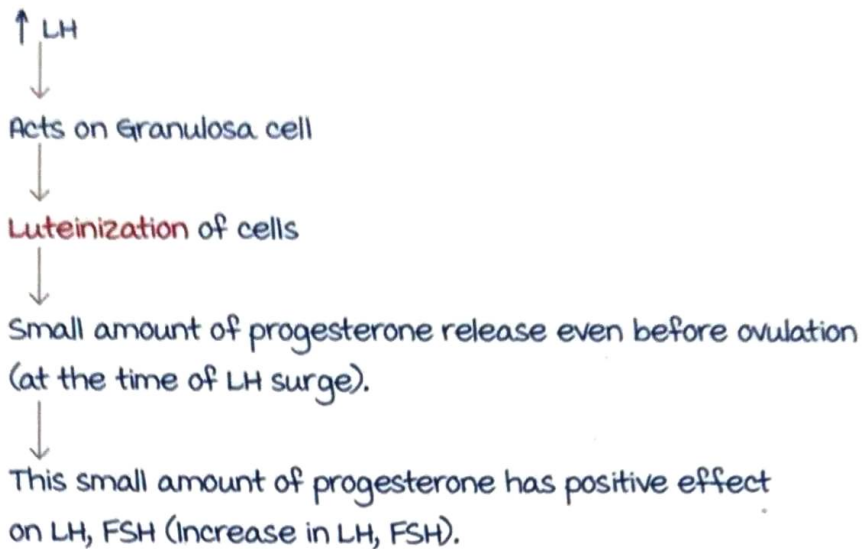
Adipose Tissue :  
Androstenedione  $\xrightarrow{\text{Aromatase}}$  E<sub>1</sub>.

Active space

To get all ed6 notes and latest neet pg notes, [click here](#)

### Role of LH granulosa cell

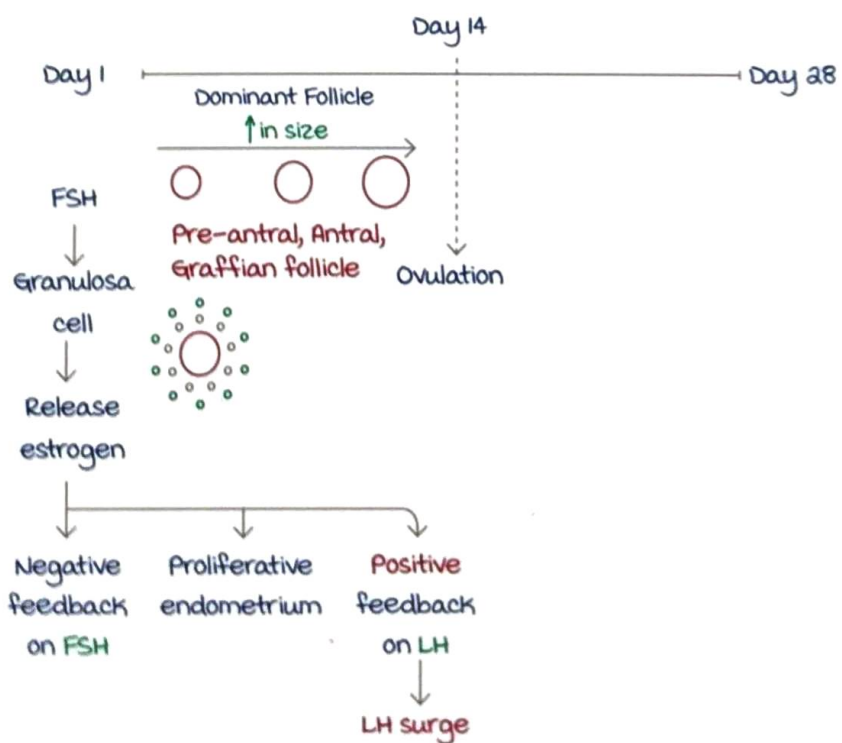
00:30:21



- In females, LH receptors are present on Theca cell, Granulosa cell.
- Progesterone appears earliest in menstrual cycle at LH surge (32-36 hrs before ovulation).
- There is LH and FSH surge before ovulation.

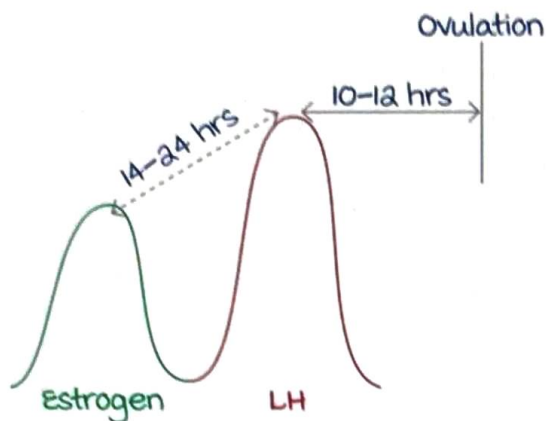
### Follicular/Proliferative phase menstrual cycle

00:35:40



Active space

- Ovarian cycle is initiated by FSH.
- Size of follicle, just before ovulation : 18 - 20 mm.
- For LH surge to occur, Estrogen levels : 200 pg x 48 hrs.
- LH surge  $\frac{32 - 36 \text{ hours}}{\text{or}}$   $\frac{24 - 36 \text{ hours}}$   $\rightarrow$  Ovulation.
- LH peak  $\frac{10 - 12 \text{ hours}}{\text{or}}$   $\rightarrow$  Ovulation.

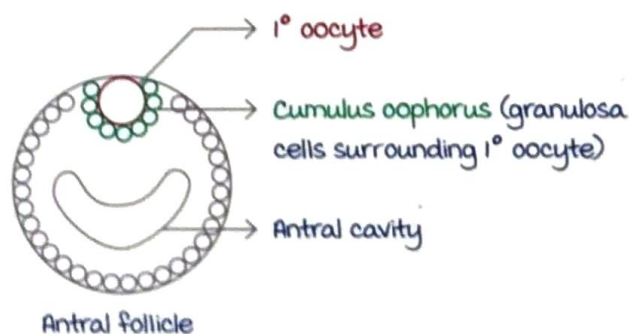


- Time interval between estrogen peak to LH peak : 14-24hrs.
- Time interval b/w estrogen peak to ovulation : 24-36hrs.
- LH Surge is initiated by estrogen.
- LH Surge is maintained by both estrogen and progesterone.
- Before ovulation there is LH and FSH surge.
- Ovulation is due to LH surge only.
- meiosis-I is resumed due to LH surge (32-36 hrs before ovulation).

## Ovulation

00:48:42

1° oocyte :



Active space

To get all ed6 notes and latest neet pg notes, [click here](#)

Normally :

- **Antral cavity fluid** : Estrogen + Growth factor + LH.
- LH appears in the antral cavity fluid only toward mid cycle.

Anovulation :

If LH appears in antral cavity fluid early in the cycle :

- Leads to atresia of follicle.
- Decreases mitotic activity of granulosa cell.



Leads to Anovulation

### Secretory phase of menstrual cycle

00:53:02

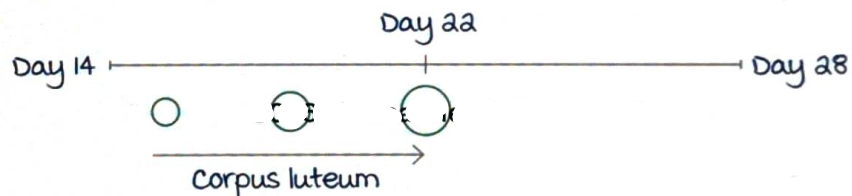
1° oocyte → 2° oocyte.

Follicle → Corpus luteum.

LH : maintains corpus luteum in a non-pregnant female.

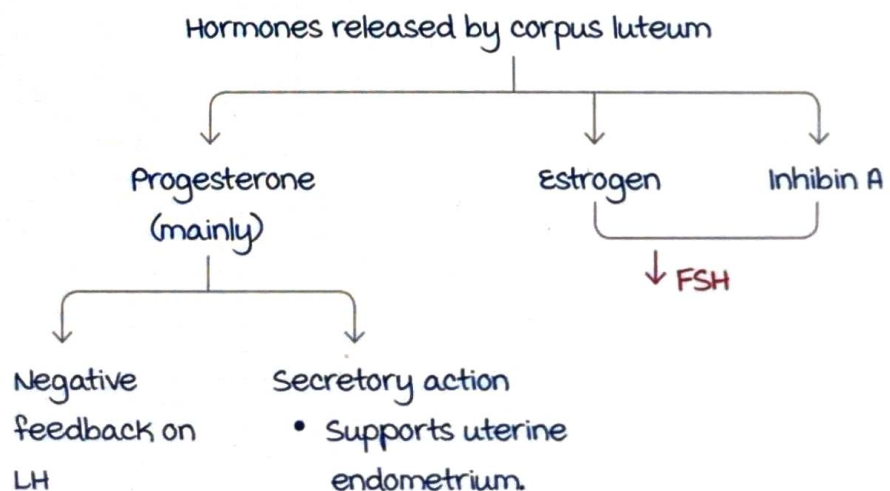
Corpus luteum :

- Corpus luteum starts growing under the effect of LH.
- **Day 22** of cycle/**8 days** after ovulation :  
Attains maximum size and activity.



### Hormones produced by corpus luteum

00:56:36

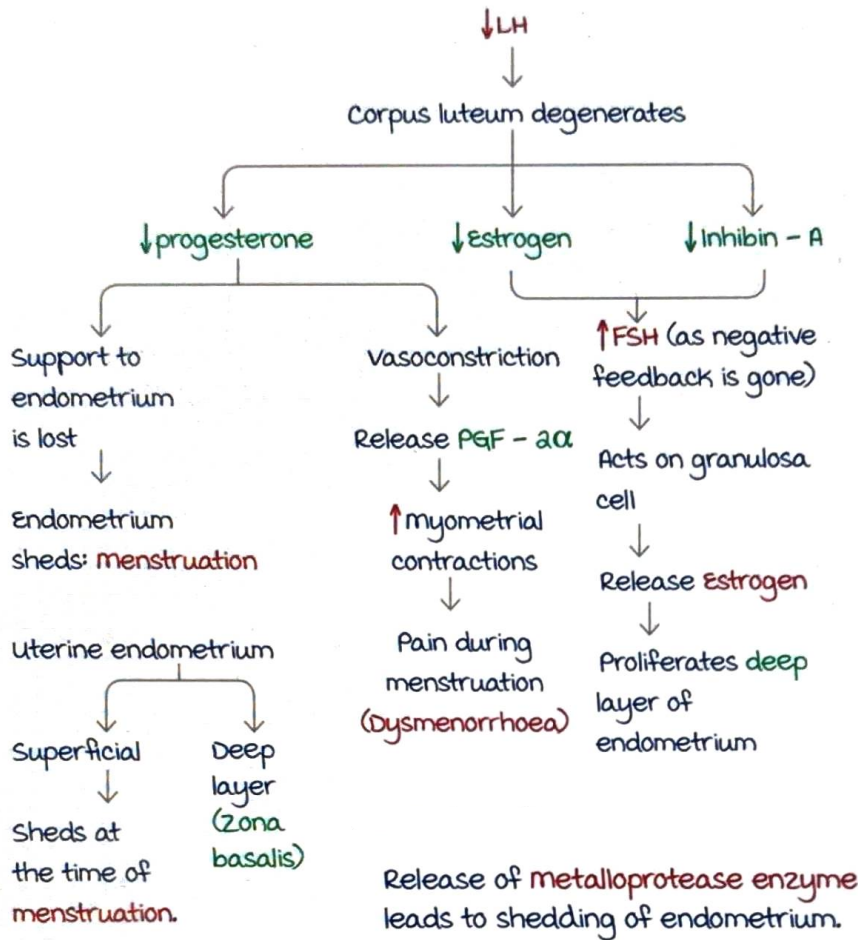


At low concentration of progesterone :  $\uparrow$  LH,  $\uparrow$  FSH.

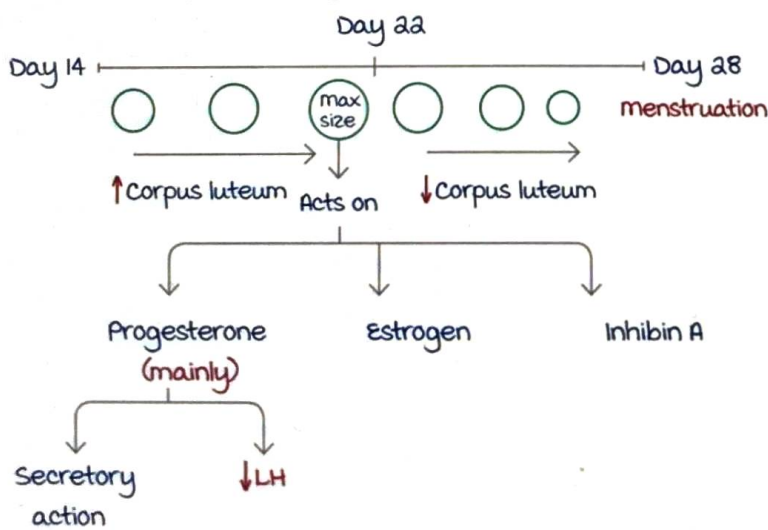
At high concentration of progesterone :  $\downarrow$  LH,  $\downarrow$  FSH.

**Corpus luteum degeneration**

01:01:42



Deep layer is responsible for regeneration of entire endometrium in next cycle.



2<sup>nd</sup> half of menstrual cycle : Luteal/Secretory phase.

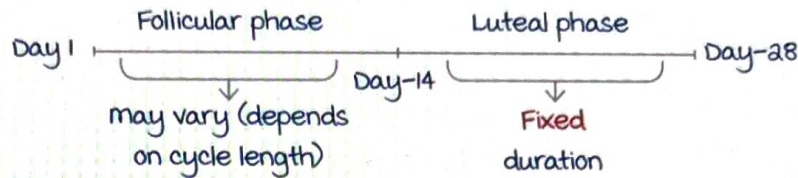
Active space



## One liners in menstrual cycle

01:13:22

- main hormone in :  
1<sup>st</sup> half of the cycle : **Estrogen**.  
2<sup>nd</sup> half of cycle : Progesterone.



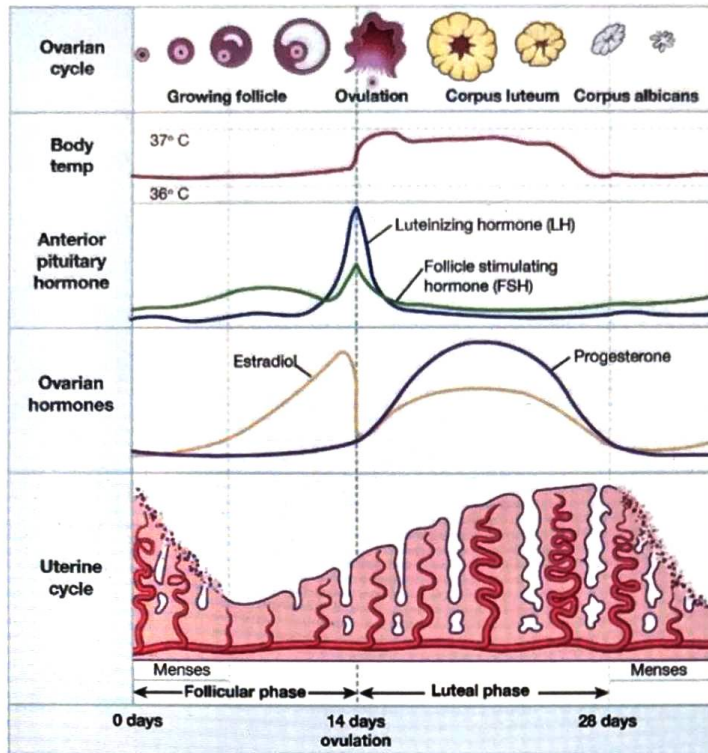
- Day of ovulation : Count 14 days backwards from the date of next menstruation.  
or  
Ovulation = Total length of cycle - 14  
(Eg : 26 day cycle, day of ovulation = 26 - 14 = Day 12)

- Corpus luteum :  
Hormone that maintains corpus luteum in non - pregnant female : **LH**.  
Hormone that maintains corpus luteum in pregnant female : **hCG**.  
Life span of corpus luteum in non-pregnant female : **10-12 days**.  
Life span of corpus luteum in pregnant female : **10-12 weeks**  
Hormone that protects corpus luteum from undergoing luteolysis : **hCG**

## Levels of hormones

01:23:14

All hormones peak at time of ovulation (LH, FSH).  
**Estrogen** peaks just before ovulation (24 - 36 hrs)  
**Progesterone** peaks at day 22 of cycle (8 days after ovulation).



At Day 22 :

- Progesterone peaks.
- Size of corpus luteum : **maximum**.
- All tests for ovulation : Done at day 22 of cycle.

At high concentration of progesterone : **Negative feedback** on  
LH, FSH.

Level of LH, FSH : minimum in **secretory phase/Day 22** of  
cycle/ **1 week before** menstruation.

**Mittelschmerz Syndrome** :

midcycle abdominal pain, or  
Pain in the abdomen at the time of ovulation

## Characteristics of menstrual cycle

01:33:48

Initially : High levels of progesterone support  
Endometrium

Eventually : Progesterone level decrease and support of  
Endometrium is lost.

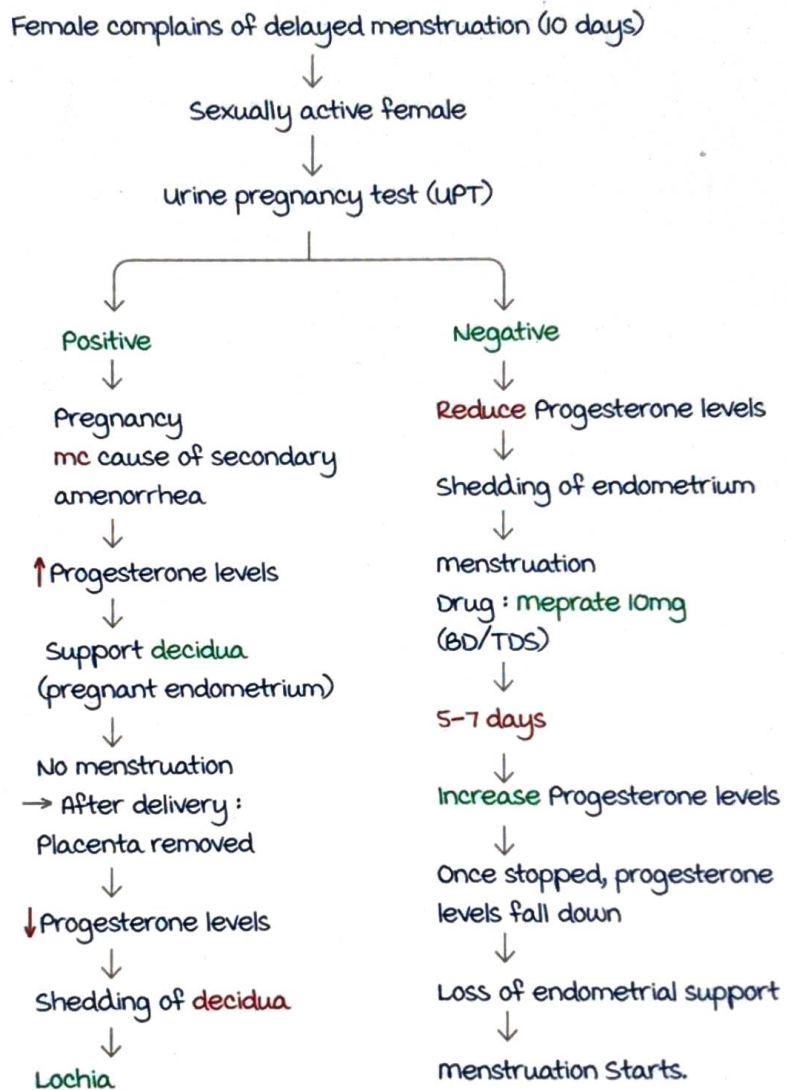
↓  
menstruation

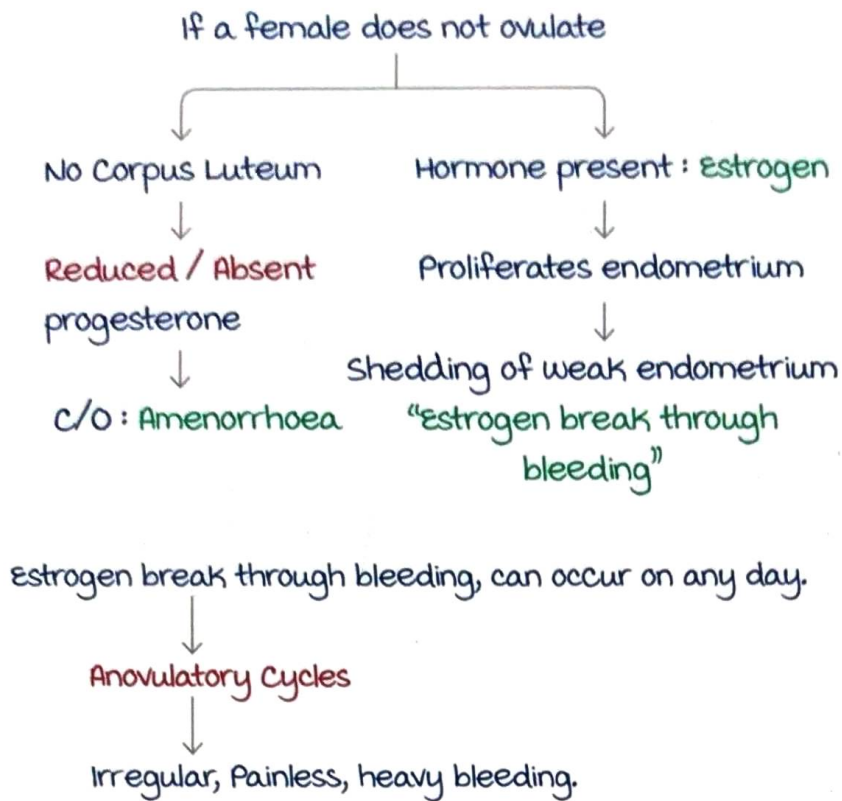
most important hormone needed for menstruation :  
**Progesterone.**

Active space

Progesterone cannot act unless endometrium is primed with Estrogen.

In case of postponing/preponing the menses :  
 2-3 days before expected date of menstruation.  
 Start **Progesterone** (Eg : 5 mg Primolut-N TDS).  
 High progesterone levels.  
 Once stopped, levels of progesterone will go down.  
 Menstruation starts after 2-3 days.

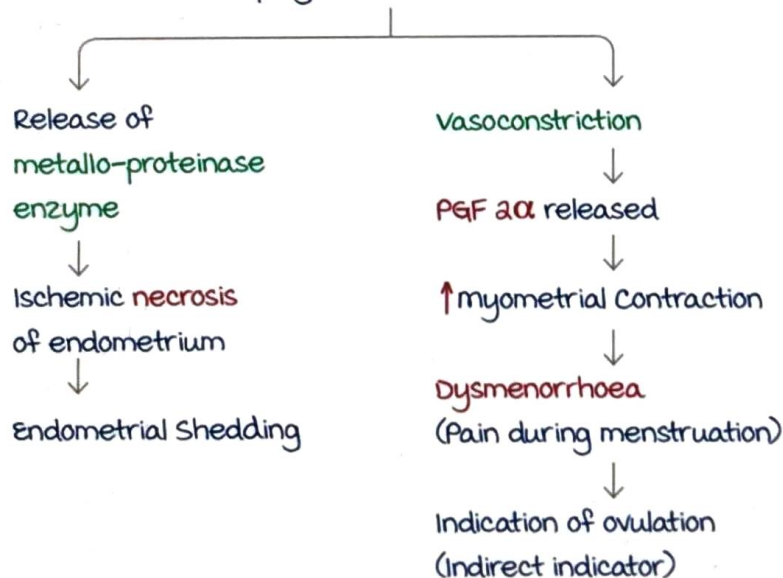




## Normal menstrual cycle

01:49:05

Sudden decrease in progesterone levels



Active space

## ATYPICAL UTERINE BLEEDING : PART 1

### New guidelines given by FIGO & adopted by FOGSI

00:02:41

menstrual cycle : Described in 4 subheadings.

1. **Frequency** of menses : In days.
2. **Regularity** of menses : Cycle to cycle variation over months.
3. **Duration** of flow in days.
4. **Volume** of monthly blood loss : In ml (rough estimation).

Characteristic	Normal limit	Abnormal	Old term	New term (AUB)
Frequency of menses	24-38 days	< 24 days	Polymenorrhea	Frequent cycles
		> 38 days	Oligomenorrhea	Infrequent cycles
Regularity : Cycle to cycle variation	2-20 days			Regular
		No bleeding		Amenorrhoea
		> 20 days		Irregular
Duration of flow	4.5-8 days	< 4.5 days	Hypomenorrhea	Shortened bleeding
		> 8 days	menorrhagia	Prolonged bleeding
Volume of blood loss (ml)	20-80 ml	< 20 ml	Hypomenorrhea	Light bleeding
		> 80 ml	menorrhagia	Heavy bleeding

Consider a female who had her DI of periods as follows :

1<sup>st</sup> march  $\xrightarrow{20 \text{ days}}$  20<sup>th</sup> march  $\xrightarrow{22 \text{ days}}$  11<sup>th</sup> April.

She has frequent cycles, as the duration of cycles is less than the normal cycle length of 24 - 38 days.

Cycle to cycle variation is of 2 days. For cycles to be irregular, the variability should be more than 20 days. (Normal : 2-20 days).

Hence, the patient's cycles are frequent and regular.

Earlier : Term metrorrhagia included,

- Irregular cycles.
- Intermenstrual bleeding.

Now : Irregular cycles, intermenstrual bleeding are used respectively.

Recently in 2018 : Federation Of International Gynaecologists And Obstetricians (FIGO) has again proposed following criteria for AUB which has not been adopted by FOGSI.

1. Regularity :

- Originally : 2 - 20 d days variation (normal).
- Now (new proposal) : 7 - 9 days.

2. Duration of bleeding :

- Originally : 2 - 8 days.
- Now : uptill 8 days.
  - ≤ 8 days : Normal.
  - > 8 days : Prolonged.

## Atypical uterine bleeding/AUB

00:16:45

Bleeding which does not follow the above normal characteristics.

It could be :

- Structural lesions (mnemonic : PALM).
- Non-structural lesions (mnemonic : COEIN).

Structural lesions	Non-structural relations
AUB-P : Polyps. AUB-A : Adenomyosis. AUB-L : Leiomyoma. AUB-m : malignancy/ hyperplasia.	AUB-C : Coagulopathy. AUB-O : Ovulatory dysfunction (anovulation not due to drug intake). AUB-E : Endometrial causes. AUB-I : Iatrogenic (due to OCP, IUCD). AUB-N : Not otherwise classified.

AUB - P : Polyps. Both endometrial & endocervical polyps are included.

AUB - A : Endometrial tissue is present in myometrium, at least 2.5 mm beyond endomyometrial junction.

AUB - C : most common is inherited von-Willebrand disease.

AUB - O : Commonly due to **anovulation**.

Can lead to oligomenorrhea (due to low progesterone) or HMB (Heavy menstrual Bleeding due to increased estrogen), now referred to as infrequent/ irregular cycles or amenorrhea.

AUB - I : Breakthrough bleeding during use of OCP, IUD.

AUB - N : Not otherwise classified.

Example : Chronic endometritis, AV malformation.

- Earlier : Heavy, noncyclic bleeding unrelated to the structural lesions of uterus, infections or systemic disease is known as **Dysfunctional uterine Bleeding (DUB)**, mostly due to **anovulation**.
- Now the term DUB is obsolete and **anovulation** is considered as a **part of AUB-O**.







Atypical uterine bleeding :

- Acute AUB : Episodes of heavy bleeding that is sufficient in quantity to require **immediate intervention** to prevent further blood loss.
- Chronic AUB : Bleeding from uterine corpus that is abnormal in **volume, regularity &/or timing**, and has been present for past 6 months.

### Identification of patients with heavy bleeding 00:27:58

1. Pictorial blood assessment chart (**PBAC**) : The chart is given to female with complaints of AUB, scoring done.  
Score :  $\geq 200$  indicates HMB  
(under normal circumstances, score :  $\leq 100$ ).
2. If Hb  $< 10$  g/dl.
3. If soakage of pad **every 2 hours**.
4. If bleeding is interfering with day to day life (ACOG criteria : American College Of Obstetricians and Gynecologists use this criteria for HMB).

PBAC Chart : month : \_\_\_\_\_

Date	Pads			Tampons			Clots		Flooding	Score
	Light  (1 pt each)	medium  (5 pts each)	Heavy  (20 pts each)	Light  (1 pts each)	medium  (5 pts each)	Heavy  (10 pts each)	50 paise coin size (1 pt each)	1 rupee coin size (5 pt each)		
1										
2										
3										
4										
5										
6										
7										
8										
9										
10										
11										
12										
13										
14										
15										

In case of coagulopathy, investigations like bleeding time, clotting time, PT and aPTT should be done.

Criteria for positive screen for coagulopathy :

Any of the following :

1. History of heavy bleeding starting at menarche.
2. Any one of the following :
  - Postpartum hemorrhage.
  - Bleeding associated with dental work.
  - Surgery related bleeding.
3. At least 2 of following symptoms:
  - At least 1 episode of bruising per month.
  - At least 1 episode of epistaxis per month.
  - Frequent gum bleeding.
  - Family history of bleeding disorders.

Active space



## Clinical vignette of AUB

00:36:44

Based on history :

- History of intermenstrual bleeding/metrorrhagia : Polyp, endometrial cause (intermenstrual spotting).
- History of HMB, marked dysmenorrhoea : AUB-A.
- History of prolonged uncontrollable bleeding : Fibroid (submucous).  
Intramural fibroid : Variable amount of bleeding.  
Subserous fibroid : Asymptomatic.
- History of heavy bleeding at menarche, family history of bleeding : AUB-C.
- History with signs of anovulation/oligomenorrhoea/signs of insulin resistance : PCOS (AUB-O).
- History of copper T insertion : AUB-L.

Based on examination :

Uterus : Normal in size	Uterus : Enlarged		
1. Polyp. 2. Coagulopathy. 3. Ovulatory disorders. 4. Endometrial disorders. 5. Iatrogenic disorders.	much enlarged, irregular ↓ Fibroid	Uniformly enlarged, up to 12 weeks size ↓ Adenomyosis. (Globular uterus, uterine tenderness ±)	Normal to mildly enlarged with restricted mobility ↓ AUB-m : malignancy/ hyperplasia (mobility restricted due to adhesions)

PALM : These are structural lesions where the size of the uterus could be abnormal except in polyp.

COEIN : These are non-structural causes, where the size of the uterus is normal.

## Case presentation of AUB

00:46:14

History :

1. menstrual history :
  - Age of menarche.

- LMP.
  - menses : Frequency, regularity, duration, volume.
  - Intermenstrual bleeding/post coital bleeding.
2. Symptoms of anemia like fatigue, malaise etc.
  3. Sexual & reproductive history :
    - Past pregnancy & mode of delivery.
    - Future desire of pregnancy.
    - Subfertility.
    - Concurrent desire of contraception.
    - Previous STI.
    - Previous pap smears.
  4. Associated symptoms :
    - Pain : Dysmenorrhea.
    - Discharge.
    - Bowel & bladder pressure symptoms (for fibroid).
  5. Systemic :
    - Weight change.
    - Coagulopathy history.
    - PCOS, liver, renal, thyroid disease.
    - Drug history.
  6. Family history :
    - Venous thromboembolism.
    - TB.
    - malignancy.

#### Examination :

1. BP.
2. BMI.
3. Goitre.
4. Pallor.
5. Signs of hyperandrogenism.
6. Hepatosplenomegaly.
7. Per speculum/bimanual examination :
  - Per rectal examination if appropriate.
  - Adnexal mass, size of uterus, anteverted/retroverted.
  - Retroverted, fixed uterus : Endometriosis.
  - Chocolate cyst : Adnexal mass in endometriosis.

## Investigations recommended by FOGSI in case of AUB

00:51:08

### Lab investigations :

1. Complete blood count : Recommended for all females with AUB.
2. UPT if pregnancy is suspected in reproductive/ perimenopausal/ **adolescent females**.
3. BT, CT, PT, PTT done if there is positive screening for coagulopathy.  
Further investigation for **von-willebrand disease** is recommended in consultation with hematologist.
4. TSH.
5. Serum ferritin.

Investigations included in von-willebrand panel : vWF, Factor VIII activity, etc., should be done **before starting hormonal treatment** for AUB or **7 days after oestrogen has been stopped**.

### Imaging :

1. USG :
  - Should be done in all AUB patients **except in adolescent females** with excessive bleeding (**puberty menorrhagia**).
  - Because causes for puberty menorrhagia are anovulation & bleeding disorder (USG is not helpful in diagnosis).  
First investigation in AUB is UPT followed by TVS.
2. Doppler ultrasonography : On suspecting,
  - AV malformation.
  - malignancy.
  - To differentiate between fibroid & adenomyomas.
3. For intracavitary lesions :

Normally uterine cavity is a potential cavity with anterior and posterior walls collapsed.

**Distention media** should be used before inserting

- hysteroscope to distend the uterine cavity.
- SIS (Saline Infusion Sonography)  
Distention media should be used before SIS.
  - 3D-USG.
4. MRI : To differentiate between fibroid & adenomyosis.
5. Endometrial sampling : Investigation of choice for assessing endometrium.  
OPD procedure.  
Can be done by :
- Endometrial Biopsy : Using Endometrial Biopsy (EB) curette.
  - Endometrial aspiration cytology : IOC  
Worldwide : Done using Pipelle/vabra aspirator.  
In India : Done using Karmann's cannula.

Indications for endometrial sampling :

1. All females > 40 years (National Guidelines),  
FIGO : > 45 years, with complaints of AUB irrespective of USG findings.
2. All females < 40 years, complaints of AUB & who have high risk factors for Endometrial carcinoma :
  - Obesity.
  - Hypertension.
  - PCOS.
  - Diabetes.
  - Endometrial thickness > 12 mm on USG.
  - Family history of ovary/breast/colon carcinoma.
  - Use of Tamoxifen.
3. AUB unresponsive to medical management.
4. In post-menopausal females, Endometrial thickness  $\geq 4$ mm on USG.

### Fractional curettage (D&C) & hysteroscopy 01:05:22

This is the gold standard method to assess the endometrium.  
Done in OT under anesthesia.  
Hysteroscopy is done for focal lesions.

Fractional curettage or D & C : For all generalised endometrial thickness.

uterus is divided into different sections like fundus, body, isthmus, cervix and sample is curetted from each section. This is known as fractional curettage.

Indications :

- If on endometrial biopsy report : **Endometrial hyperplasia with atypical cells.**  
Endometrial hyperplasia with atypia : Chances for endometrial cancer is high. Management is hysterectomy.  
Fractional curettage + Hysteroscopy should be done before hysterectomy to rule out endometrial cancer.
- If endometrial biopsy report says **insufficient endometrial tissue.**
- In case of **tightly closed internal os.**
- If endometrial biopsy report is normal but **patient continues to bleed.**

Indications for therapeutic D&C :

1. Removal of retained product of conception.
2. Treatment of GTD (molar pregnancy) : Done only if **suction evacuation** is not possible.
3. management of acute AUB in patients with unstable vitals.
4. Bleeding unresponsive to medical treatment.

### Cervical cytology/PAP smear


01:16:34

- Carcinoma cervix has a **bimodal peak** : 35 - 39 years, 60 - 64 years.
- So in female presenting with AUB specifically if complaints of post coital bleeding, post menopausal bleeding : **Pap smear should be done.**

## ATYPICAL UTERINE BLEEDING : PART 2

### Ultrasonogram (USG) findings in AUB

00:00:18

USG finding	Clinical condition
Echogenic smooth intracavitary mass.	Polyp 
Heterogeneous texture of endometrium & obscuring of endometrial-myometrial junction.	Adenomyosis
Well defined solid mass with whorled appearance with echogenicity similar to myometrium.	Fibroid
Thick endometrium ≥ 12mm in reproductive age ; ≥ 4mm in post menopausal women.	Endometrial hyperplasia/ Endometrial cancer.
uterus is normal in size but fluid in endometrial cavity	AUB - E
Thick endometrium with polycystic ovaries.	AUB - O (Anovulation)
Normal uterus with normal findings. Sometimes a hemorrhagic cyst.	AUB - C (Coagulopathy)

### Management of AUB

00:05:07

management of AUB depends on

Cause.

Age of the female (adolescent, reproductive, perimenopausal & post menopausal women).

Severity of bleeding (mild, moderate, severe).

Active space

## General management of AUB :

Severity of bleeding	management plan
mild bleeding	No hormonal treatment needed. Reassure the patient and supplement with Iron & Folic acid (IFA) tablets & NSAIDS to control bleeding. maintain a menstrual diary Regular follow up
moderate bleeding	Hormonal treatment with OCPs (E+P) or Progesterone only pills.
Severe bleeding/ heavy menstrual bleeding	Dilatation & Curettage. IV Estrogen.

In normal menstrual cycle,

Day 1 - 14 : Estrogen proliferates the endometrium.

Day 14 : Ovulation.

Corpus luteum formed, releases progesterone that acts like a cement and supports the endometrium that has been primed by estrogen.

Progesterone cannot act on an endometrium that is not primed by estrogen.

Corpus luteum increases in size till day 22.

After that, progesterone has negative feedback on LH and size of corpus luteum decreases → support to endometrium lost and menstruation starts.

To prevent endometrial shedding (menstrual bleeding), Estrogen and Progesterone together (OCPs) or Progesterone only pills, can be given.

Estrogen proliferates the endometrium and Progesterone acts like a cement and supports the endometrium.

## Treatment of moderate bleeding

00:12:44

Treatment	Features
<p>Estrogen &amp; Progesterone (OCP pills):</p> <p>Estrogen proliferates endometrium and progesterone holds it together.</p>	<p>To control bleeding.</p> <p>1 pill per day OR start with 1 pill per 8-12 hours &amp; when bleeding stops</p> <p>↓</p> <p>One pill/ day.</p> <p>Advantages:</p> <p>Estrogen is hemostatic.</p> <p>Has contraceptive benefit.</p>
<p>Progesterone only therapy:</p> <p>In AUB -O (Anovulation):</p>	<p>Estrogen is contraindicated (or)</p> <p>Patient refuses OCP.</p> <p>To regularize cycles &amp; control bleeding:</p> <p>Start Progesterone, mid cycle for 10 - 12 days.</p> <p>In practice: Progesterone given from 1<sup>st</sup> - 10<sup>th</sup> day every month.</p> <p>When Progesterone is stopped on the 10<sup>th</sup> day, withdrawal occurs and menstruation occurs, excessive bleeding is controlled.</p>
<p>In AUB other than AUB - O:</p>	<p>Endometrium is exposed to high levels of progesterone → No menstruation.</p> <p>Given from Day 5 - 25 of every month for 3 months.</p>

Active space



Progesterone only pill can be given orally :  
 micronised Progesterone 200 mg/day OR  
 Norethindrone 2.5-5 mg /d OR  
 MPA 10 mg/d.

It can also be given as LNG - IUCD (Mirena).

Added advantage of LNG - IUCD : **Contraceptive benefit.**

In moderate bleeding : **OCP** > Progesterone only pills. -

### Severe/ heavy menstrual bleeding

00:20:14

In heavy menstrual bleeding (HMB)

↓  
Thin endometrium.

↓  
Due to less estrogen.

↓  
No priming.

↓  
No use in starting only Progesterone.

Vitals unstable :

Dilatation & curettage	IV Estrogen
manual removal of the shedding superficial endometrium.  <b>Temporary method.</b>	Hemostatic and primes endometrium. After bleeding stops ↓ OCP or Progesterone only pills.
	If bleeding does not stop ↓ IV Estrogen + Hemostatic agent (Tranexamic acid/ Epsilon aminocaproic acid) + Progesterone only (24 - 48 hrs) ↓ Bleeding stops ↓ OCPs/Progesterone.
Contraindication : <b>Adolescent females</b> to prevent <b>intrauterine adhesions</b> called <b>Asherman syndrome.</b>	High risk of thromboembolism. Given for <b>24 hours</b> only. may extend to 48 - 72 hours, only if absolutely needed.

Can be given in reproductive and perimenopausal age group women.	Can be given to adolescent females.
--	-------------------------------------

Vitals stable : High dose Estrogen and Progesterone pills  
(Estrogen > 50 mcg).

### Puberty menorrhagia

00:29:13

MC cause : Anovulation.

2<sup>nd</sup> MC : Bleeding disorder.

USG is not mandatory.

Done to rule out other pelvic pathologies.

Trans Abdominal (TAS) preferred over Trans vaginal (TVS)

USG.

management :

Hb ≥ 10 : mild/moderate bleeding.

Hb < 10 : Severe/heavy bleeding.

Severity	Treatment
<p>mild :</p> <p>Number of days of bleeding longer than normal &amp; short cycles for atleast 2 months.</p>	<p>Reassure.</p> <p>Supplement with Iron &amp; folate tablets &amp; NSAIDS.</p>
<p>moderate :</p> <p>Number of days of bleeding &gt; 8 or cycles every 1 - 3 weeks</p>	<p>OCP or only progesterone.</p> <p>Presently <b>bleeding</b> &gt; 8 days : 1<sup>st</sup> line : <b>OCP</b> since estrogen is hemostatic.</p> <p>Presently <b>not bleeding</b> : 1<sup>st</sup> line : <b>Progesterone</b> only pill for 10 days every month.</p>

Severe bleeding : Thin endometrium.

Stable vitals	Unstable vitals
<p>High dose Estrogen &amp; Progesterone pill. (Estrogen &gt; 50 mcg).</p> <p>Administer</p> <p>1 pill 4<sup>th</sup> - 6<sup>th</sup> hourly for 24 hours. 1 pill 8<sup>th</sup> hourly for 3 days. 1 pill 12<sup>th</sup> hourly for 3 weeks. 1 pill/ day to be continued till anemia resolves for 3 - 6 months.</p>	<p>IV Estrogen followed by maintenance therapy (OCP).</p>

### Maintenance therapy

00:37:47

OCP	Progesterone
Hb < 10 → Give continuously for 3 months and then withdraw.	Due to anovulation : Excess estrogen, excess bleeding.
Hb > 10 → Give in cyclical manner for 21 days, every month and then withdraw.	First 10 days every month for 6 months and stopped → withdrawal.
<p>Stable patient planned for OCPs with high dose estrogen : But estrogen is contraindicated.</p> <p>Progesterone that also contains estrogen : Norethindrone 5 - 10 mg/ twice or thrice a day followed by 5 - 10 mg once a day</p>	<p>Withdrawal bleeding controlled : As bleeding is due to progesterone withdrawal rather than presence of estrogen.</p>

**AUB in perimenopausal women**

00:43:39

MC cause : Anovulation.

Other causes :

Clinical conditions	Tests done to diagnose/rule out.
Pregnancy	Urine Pregnancy Test (UPT).
Fibroid & Polyp	Ultrasound (USG).
Thyroid, prolactin disorders	TSH, prolactin
Premalignant conditions : CIN Endometrial hyperplasia	PAP smear Endometrial sampling

National guidelines :

Females  $\geq$  40 years, irrespective of USG findings  $\rightarrow$  Do endometrial sampling.

management :

Severe bleeding with

Vitals stable	Vitals unstable
OCP with High dose estrogen ↓ Control bleeding ↓ Mirena	Dilatation & Curettage ↓ OCPs or IUCD : Mirena.  IV Estrogen
D & C preferred over IV estrogen because of increased risk of thromboembolism	

Medical management fails  $\rightarrow$  Surgical management :

Endometrial ablation.

In fibroids :

uterine artery embolization.

magnetic Resonance guided focused Ultrasound.

Surgery :

Hysterectomy.

myomectomy.

**Endometrial ablation (EA)**

00:47:15

Principle :

Surgical destruction of the uterine lining (basal layer) upto 4 - 6 mm deep.

D&C is not therapeutic as it removes only superficial layer which can regenerate back.

Permanent management.

For females who **do not desire future pregnancy.**

**Efficacy** of endometrial ablation : Comparable to MIRENA.

So, mirena preferred as it is non surgical.

methods of EA :

Non resectable EA	Resectable EA
uses disposable device inserted into the uterus : Commonly done now.	uses resectoscopic electrosurgical instruments.
Device delivers energy to uniformly destroy the uterine lining by either heating the endometrium to 60° C or cooling it to -65° C	Ablating or cut the endometrium.
Eg : 1. Cryotherapy 2. Bipolar frequency 3. Hydrothermal ablation : Circulation of hot water. 4. Microwave EA.	Eg : 1. Roller ball. 2. wire loop. 3. Vaporizing electrode. 4. Laser. 5. Transcervical Resection of endometrium (TCRE)

Active space

2 <sup>nd</sup> generation : Not done under hysteroscopic guidance.	1 <sup>st</sup> generation : Done under hysteroscopic guidance.
Complications : <b>No fluid overload.</b>	Under Hysteroscopy, distension medium used to dilate uterus with inlet & outlet. Distension media absorbed leading to fluid overload.

Indications for EA :

Ovulatory menorrhagia in perimenopausal females.

Acute AUB in hemodynamically stable patients in whom medical therapy is contraindicated or unsuccessful.

Contraindications of EA :

Absolute	Relative
<ol style="list-style-type: none"> <li>1. Pregnancy or desire to preserve fertility.</li> <li>2. Known/suspected endometrial hyperplasia/cancer.</li> <li>3. Active pelvic infection.</li> <li>4. IUCD in place.</li> <li>5. Previous trans-myometrial uterine suraeru</li> </ol>	<ol style="list-style-type: none"> <li>1. Size of <b>uterine cavity</b> &gt;10-12 cm (Disposable devices of Non resectable EA are small and cannot be used in a large uterus).</li> <li>2. Post menopausal women : Highest risk of endometrial hyperplasia &amp; cancer.</li> <li>3. Congenital uterine anomaly.</li> <li>4. Severe myometrial thinning.</li> </ol>

Always **endometrial sampling is done before EA** → Rule out endometrial hyperplasia/cancer.

Saline infusion sonography/ diagnostic laparoscopy → Rule out polyp & fibroid.

Complications :

- Uterine perforation.
- Hemorrhage.
- Hematometra.
- Pelvic infections.

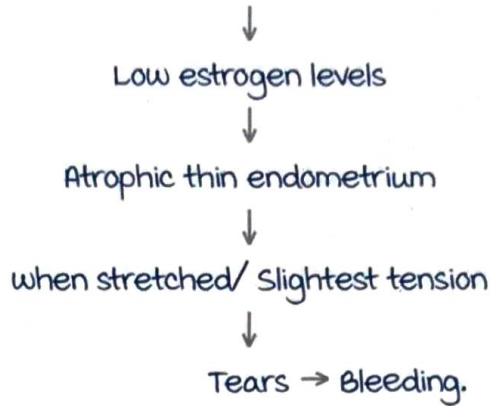
**Post menopausal bleeding (PMB)**

00:57:56

Definition : any bleeding that happens after menopause.

MC cause : Atrophic endometritis.

Mechanism : Post menopausal females



Other causes of PMB include :

- Hormone Replacement Therapy (HRT).
- Endometrial hyperplasia.
- Endometrial CA : Only 10% post menopausal bleeding.
- Cervical Cancer : Post coital bleeding more specific.
- Polyps.
- Atrophic vaginitis.

Investigations :

USG : To rule out fibroid, polyp.

measure endometrial thickness.

< 4mm	≥ 4 mm
Tranexamic acid & follow up:	Endometrial sampling by : Endometrial biopsy. Endometrial aspiration cytology.

PAP smear :

Post menopausal women → Rule out cervical cancer.

Endometrial thickness < 4mm + Persistent endometrial bleeding → Endometrial sampling to rule out Type 2 Endometrial cancer.

Endometrial cancer :

Type 1 (mc)	Type 2
Excessive estrogen ↓ Thick endometrium	Normal estrogen ↓ Thin endometrium (<4mm)

Active space

## DYSMENORRHEA

Dysmenorrhea is defined as pain during menstruation.  
It is usually cramping type of pain in the lower abdomen.

Dysmenorrhea is of two types :

1. Primary Dysmenorrhea.
2. Secondary Dysmenorrhea.

### Primary & Secondary dysmenorrhea

00:00:50

Primary/ Spasmodic dysmenorrhea :

Pain occurs during ovulatory cycle and it is because of the myometrial contraction.

Due to prostaglandin release :  $PGF_a$  alpha.

Not associated with any pelvic pathology.

Patient is usually a young female with complaints of pain during menstruation since 1-2 years after menarche.  
Initially no pain because the cycles were anovulatory.

more common in females who have,

- Early menarche.
- Increased inter-menstrual period.
- Increased menstrual flow.

Pain gradually decreases on its own after some physical activity, after marriage or childbirth and reassurance should be given.

Pain begins with menses or just before menses and gradually decreases within 72 hours.

Pain is Spasmodic in nature.

Pain is intermittent and varies in intensity.

Pain is centralized and in suprapubic region.

maybe associated with psychological factors.



Secondary/ congestive dysmenorrhea :

Pelvic pathology present,

- Endometriosis (most common cause).
- Adenomyosis.
- Fibroid.

Patient will be a female in reproductive age group > 30 years, with complaints of pain during menses present for the past few months.

Pain occurs much before the onset of menses and remains even after onset of periods.

Pain is Congestive in nature, intensity of pain keeps on increasing (Progressive dysmenorrhea).

Pain is localized.

Dysmenorrhea may be associated with dyspareunia and dyschezia.

## Management

00:08:51

Primary dysmenorrhea :

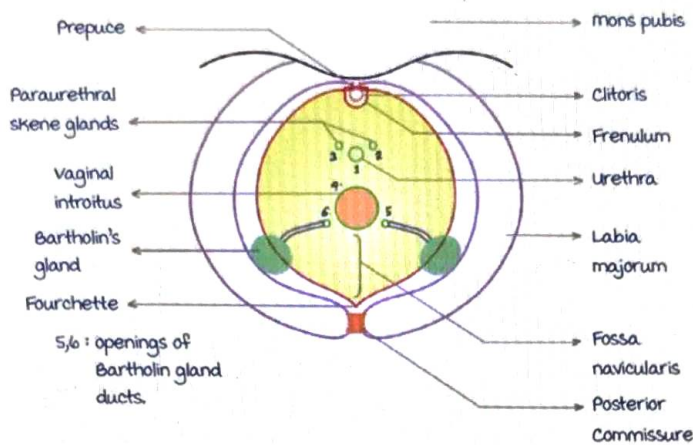
- NSAIDs.
- OCP : makes the cycle anovulatory, synthetic estrogen has negative feedback on FSH and synthetic progesterone has negative feedback on LH.
- vaginal rings can be given.
- Levonorgestrel (mirena) : makes the cycle anovulatory.

Secondary dysmenorrhea :

Treat the cause of dysmenorrhea.

Pain at the time of ovulation (mid cycle pain or 2 weeks before menses) is called as mittelschmerz syndrome.

## GYNAECOLOGY - ANATOMY INTEGRATION : PART 1



Female External Genitalia :

Also known as **vulva** or **pudendum**, consists of :

- **Mons Pubis/Venereum** : Hair bearing area of the vulva with underlying subcutaneous fat. This lies **ventral** to the pubic symphysis.

- **Labia Majora** : Outer lip like structures containing **hair** and **all glands** (sweat, apocrine, sebaceous glands).

**Posterior commissure** is the region where the posterior lips of the labia majora meet.

At the anterior 1/3rd of the labia majora, the **round ligament** and processes vaginalis are attached.

**Labia majora** is homologous to the **male scrotum**.

- **Labia Minora** : Known as the inner lips. The **medial part** of labia minora is lined by **non-keratinized stratified squamous epithelium** and the **outer part** is lined by **keratinized stratified squamous epithelium**.

**Hart's Line** : Is the line separating the **keratinized epithelium** from the **non-keratinized epithelium** on the inner lip (Labia minora).

The labia minor anteriorly forms a fold above and below the clitoris, enclosing it.

The fold above : Prepuce.

The fold below : Frenulum.

The labia minora has no hair and glands except sebaceous glands

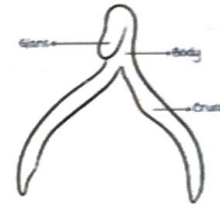
Fourchette is the region where the posterior lips of the labia minora meet.

- Clitoris : Is a vascular and an erectile organ. Clitoris is homologous to male penis.

The normal length of clitoris is 2 - 2.6 cm.

- Vestibule :

Space bordered by fourchette (posteriorly), labia minora or Hart's line (laterally) and clitoris (anteriorly).



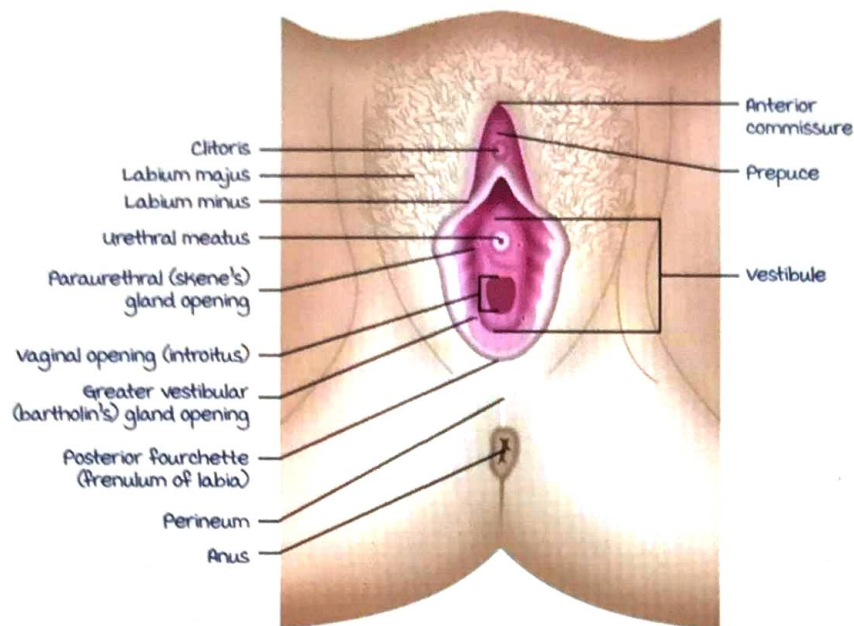
- 6 openings are found in the vestibule :

1. Urethra.
2. Skene Glands : Paraurethral glands found at 1 and 11'o clock position.  
These glands are homologues to prostate gland in males.
3. Introitus : Vaginal opening.  
Hymen covers the introitus.
4. Bartholin Ducts : Opens just outside the introitus in the vestibule at 4 and 8'o clock positions or 5 and 7'o clock positions.

But the Bartholin gland is present at the groove between the labia majora and labia minora.

These glands are homologues to bulbourethral glands.

- Fossa Navicularis : Shallow vestibular depression present in between the introitus and fourchette.



mons pubis/ mons venerum : Rounded fat pad which lies ventral to pubic symphysis, covered by hair.

Pubarche : Appearance of pubic hair on puberty and is dependent on androgens. This corresponds to Tanner stage 3.

Labia majora : Posteriorly it meets in the area called as posterior commissure. It has subcutaneous layer and hair, similar to the anterior abdominal wall.

The subcutaneous layer in mons Pubis and Labia majora is similar to the anterior abdominal wall. They too have :

- Camper's Fascia,
- Colle's Fascia or superficial perineal fascia (deep membranous layer).

Colle's fascia at the level of mons pubis and labia majora :

- Anteriorly : It is continuous with the anterior abdominal wall.
- Laterally : Attached to the ischiopubic rami firmly.
- Posteriorly : Attached to the perineal membrane.

These attachments prevent spread of fluid, blood or infection from superficial perineal space to thigh but anteriorly it can spread to anterior abdominal wall.

Round ligament is homologous to gubernaculum of testes.

The round ligament starts from the **cornua of the uterus**, passes through the inguinal canal to reach the anterior abdominal wall and attaches to the anterior 1/3rd of the **labia majora**. **Processes vaginalis** also attaches here.

Labia majora drains into **superficial inguinal lymph nodes**.

mass palpated on labia majora could be :

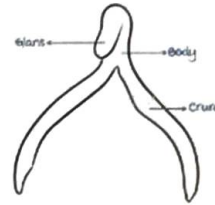
- **Leiomyoma** arising from round ligament.
- **Persistent processes vaginalis**.
- **Breast tissue** along distal milk line.
- **Indirect inguinal hernia**.

## Clitoris

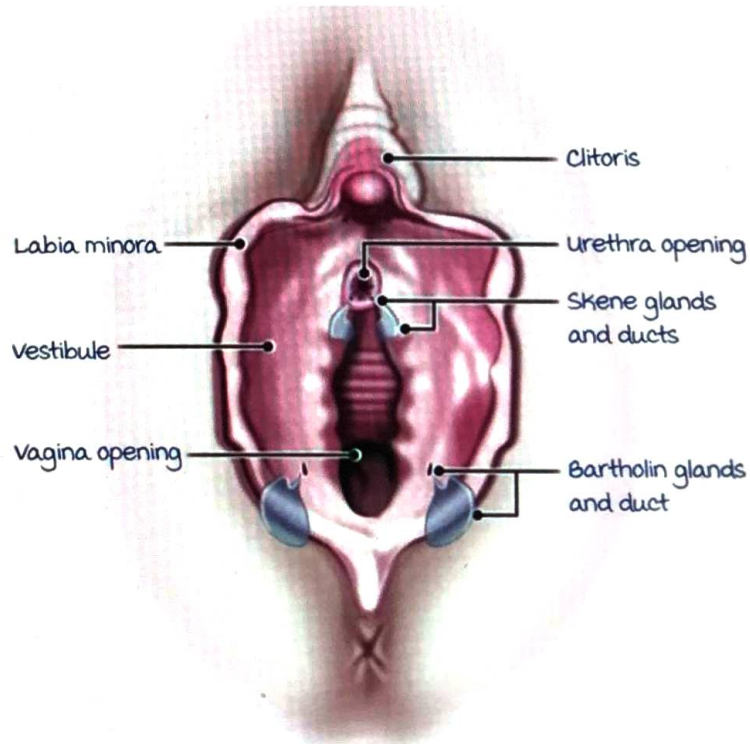
00:27:27

Clitoris has 3 parts :

- **Glans**.
- **Body**.
- **2 Crura**.



The glans of the clitoris drains into **deep inguinal lymph nodes** which is known as lymph node of **Cloquet/Rosenmuller** lymph node.



Skene's glands and Bartholin's glands

The body and the crura drains into the superficial inguinal lymph node then into the deep inguinal lymph nodes.

Clitoris is highly vascular. Normal length is 2-2.5cms.

Clitoromegaly : When the clitoris is >4 cm.

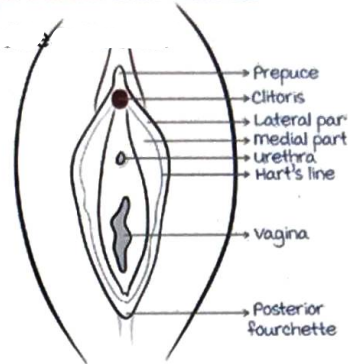
Clitoromegaly indicates ambiguous genitalia but needs further evaluation.

Vestibule area :

Bounded by clitoris above

Fourchette : posteriorly

labia minor/ hart line laterally.



Skene Gland :

Skene cysts formed by blockage of skene gland is usually found lateral to the urethral opening and is also known as urethral diverticulum. The position of these cysts are usually anterolateral.

## Bartholin Gland

00:32:40

Pea sized glands of racemose variety. Bartholin glands are normally not palpable.

The Bartholin gland is lined by columnar epithelium, therefore the most common variety of Bartholin cancer is adenocarcinoma.

But the Bartholin gland duct is lined by transitional epithelium and non keratinized stratified squamous epithelium.

Therefore a Bartholin carcinoma can be of any variety. Bartholin glands secrete alkaline mucus at the time of intercourse.

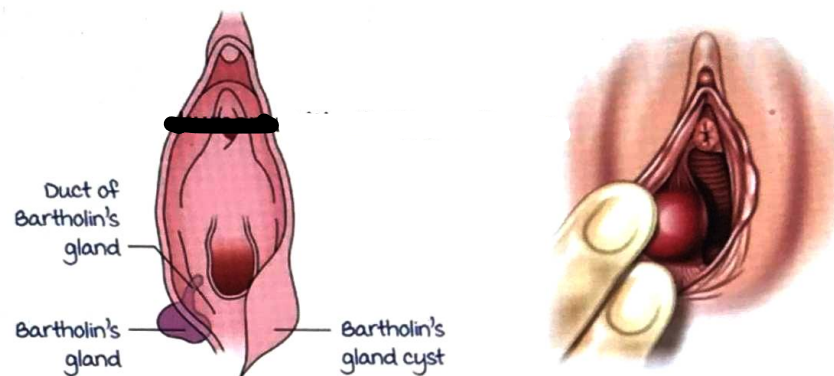
Bartholin glands are present in the superficial perineal pouch and Cowper's glands are present in deep perineal pouch.

Bartholin gland ducts open in the vestibule outside the hymen at the junction of anterior 2/3<sup>rd</sup> and posterior 1/3<sup>rd</sup>.

If this gland is blocked, a Bartholin cyst develops which can be present outside the hymen in the vestibule or in between labia majora or labia minora.

Clinical Case :

23y/o complains of 3cm intermittent painless mass on her vulva. The mass is aggravated by intercourse but goes away on its own. Pap smear results are normal and following cyst was seen on examination. What is the management ?



Presentation of Bartholin Cyst :

- Intermittent painless mass over the vulva.
- mass is aggravated by intercourse and resolves on its own.

The most common cyst in vagina : **Functional cysts.**

Functional cysts are located at 3'o clock and 9'o clock position. They are deeply located and management is by excision surgery.



Gartner's Cyst :

Typical present on the anterior wall of the vagina.

management of Bartholin Cyst :

- Biopsy of the cyst wall should be done in cases of :
  1. If age is  $>40$  years or
  2. Post menopausal or
  3. Solid mass or a solid mass fixed to a structure.

In these patients, Bartholin cancer should be suspected.

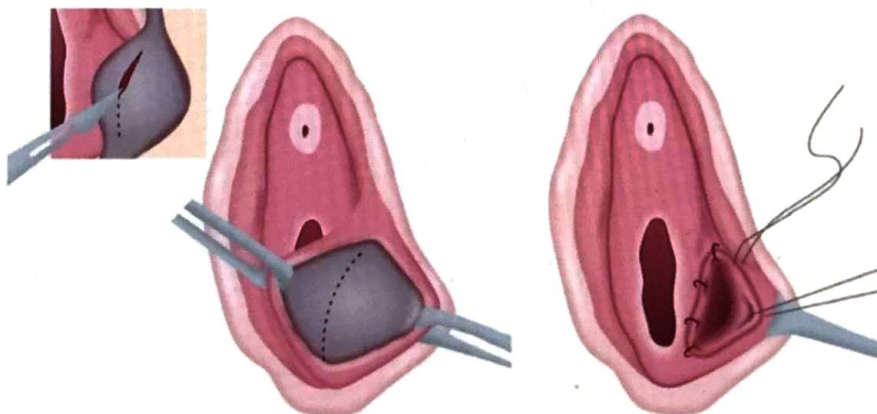
- For other cases :

The patients are classified into symptomatic and asymptomatic.

1. For symptomatic Bartholin cyst/abscess : Incision and drainage.
  2. For asymptomatic Bartholin cyst :
    - a) For size  $<3\text{cm}$  : Conservative management.
    - b) For size  $>3\text{cm}$  : Incision and drainage.
- If incision and drainage is done for a total of 3 times, then the next step would be marsupialization.

marsupialization :

The Bartholin gland is removed and the linings are exteriorized. This prevents recurrence of cyst.





Bartholin Abscess :

most common organism : **E.coli** > Gonorrhoea.

management : **Incision and drainage** followed by insertion of **word catheter**.

Bartholin Cancer :

Very rare cancer and most likely to be seen in **post menopausal** female.

An enlarged Bartholin gland in a post menopausal female should be **regarded as cancerous** unless proven otherwise.

most common variety : **Adenocarcinoma**.

most common symptom : **Vulval mass** > **Dyspareunia**.

**Honan criteria** is used to classify Bartholin cancer.

## Vulva

00:43:46

Blood supply of vulva : **Internal Pudendal Artery**.

Nerve supply : **Pudendal nerve (S2-S4)**.

Lymph Node drainage : First to **superficial inguinal lymph node** (Sentinel lymph node) then to **deep inguinal lymph node** (Femoral lymph node).

This is why in vulval cancer, **inguinofemoral lymph node** dissection is done.

Sentinel lymph node biopsy is done in : **Vulval cancer** > **Ca cervix**.

Homologous organs :

Organs in males and females with **same embryological origin**.

males	Females
Penis	Clitoris
Scrotum	Labia Majora
Penile urethra	Labia Minora
Prostate Gland	Skene Gland
Cowper's Gland	Bartholin Gland

Note:

Bartholin glands in females are homologous to Cowper's glands/bulbourethral glands in males.

If Bartholin ducts are blocked, the swelling, appears, at the junction of labia majora and labia minora or at the introitus, not at the wall of the vagina.

Active space

## GYNAECOLOGY - ANATOMY INTEGRATION : PART 2

### Surgical anatomy of internal genital organs

00:00:15

**Uterus** : Dome shaped.

uterus includes : Corpus (body) and cervix.

**Corpus** :

Dome shaped.

Prominent upper part is called as fundus.

Lower most part of uterus which is narrowest is called as **isthmus** lies just above the cervix.

**Angles of uterus** : Cornua of uterus.

Fallopian tube opens here.

Opening in which fallopian tube opens is called as **ostium**.

2 ostia : Right and left (sphincters) - Circular concentric muscle fibres.

At cornua, along with fallopian tube there are 3 tube like structures.

From anterior to posterior :

- Round ligament.
- Fallopian tube.
- Ovarian ligament : Connected to ovary.

If **ovaries** are visible clearly : It is **posterior view**.

From the top to bottom :

Superior most : Fallopian tube.

Ovarian and round ligament are at the same level.

Clinical importance : **Tubal ligation**.

Instead of fallopian tube, round ligament is ligated resulting in **failure of female sterilization**.

Structure typical to fallopian tube : Fimbriae.

Ovarian ligament attaches ovary to cornua of uterus.  
Round ligament from cornua of uterus, passes into anterior abdominal wall and via inguinal canal get attached to labia majora (1/3rd).

They pull uterus in forward direction, thus round ligament helps to keep uterus in **anteverted** position.

Angle between vagina and cervix : **Angle of anteversion - 90°.**  
Angle between cervix and uterus : **Angle of ante-flexion.**

**Normal position of uterus and majority of females :**  
**Anteverted and ante-flexed.**

In the lower part of uterus, broad uterine cavity becomes narrow near the cervical canal is called as **internal os** (i.e., anatomical internal os).

Uterus lined by high columnar epithelium.  
Cervix is lined by low columnar epithelium.

Gradual change in lining of uterus changing to lining of cervix : **Histological internal os.**  
Histological internal os is below the level of anatomical internal os.

Area between anatomical internal os above and histological internal os below is called as **isthmus of uterus.**

**Cervix :**

2 parts : Part above cervix and near to uterus is called as **endocervix/Supra vaginal part of cervix.**

Inside vagina, on per speculum examination a part of cervix lies inside vagina also is called as **exocervix/ectocervix/portio vaginalis.**

Opening visible at that point is called as external os.

Exocervix appears pink on PS examination.

Endocervix appears red colour on PS examination.

Endocervix : Columnar epithelium.

Exocervix : Stratified squamous epithelium.

Pockets seen between cervix and wall of vagina : Fornices.

Anterior, posterior and 2 lateral fornices are present.

Deepest : Posterior fornix.

Posterior wall of vagina is longer than anterior wall of vagina.

## Uterus

00:15:50

Has 2 parts : Corpus and cervix

Pyriform shaped/pear shaped

Corpus : Body of the uterus.

Prominent upper part in the corpus, broad and dome shaped

: Fundus of the uterus.

Lower most part of body, narrow and it lies close to cervix :

Isthmus.

uterus has 2 angles, known as cornua of uterus.

At the cornua of the uterus fallopian tube opens.

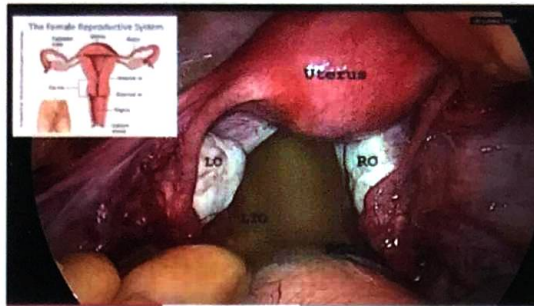
Opening of fallopian tubes are called as ostium.

**Ostia** : Identification landmarks for hysteroscopy (uterine cavity visualization).



while hysteroscopy, the examiner is at the foot end of the patient and looking towards tubal end.

uterus from outside is visualised by laparoscopy.



In laparoscopy, examiner stands on head end of the patient.

Pearly white structures : Left and right ovary.

At cornua of uterus, 3 tubular structures are attached :

- Round ligament.
- Fallopian tube
- Ovarian ligament.

From superior to inferior : Fallopian tube, round and ovarian ligament lies at same level.

Whereas, round ligament lies anterior to fallopian tube and ovarian ligament lies posterior to fallopian tube.

Laparoscope holds Round ligament.  
m/c reason for failure of tubal ligation  
is identification of wrong structure.  
This is prevented by tracing the tubes  
from fimbrial or distal end.



- 1 : Round ligament.
- 2 : Fallopian tube.
- 3 : Ovary.
- 4 : Ovarian ligament.

most superior site : Fallopian tube.

Fallopian tube + Ovary = Adnexa.



## Round ligament

00:26:31

Derived from gubernaculum.

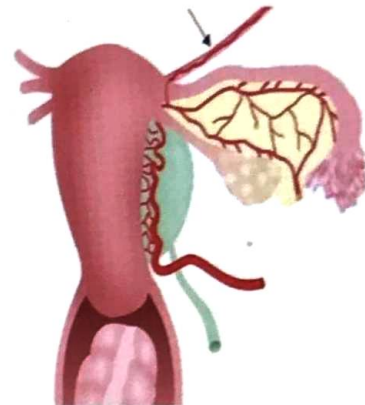
Attached to cornua of the uterus and inserted into anterior 1/3rd part of labia majora.

Function : Helps to maintain anterversion position of uterus.

Blood supply : Sampson artery - branch of uterine artery.

Identify the marked structure :

- Sampson artery.
- uterine artery.
- Obturator artery.
- Internal iliac artery.



Size of uterus : 3 X 2 X 1 inch.

Weight of the uterus :

- Non pregnant : 60-80 g.
- Pregnant : 1000 g.

Increase in weight and size of uterus during pregnancy :

Hypertrophy > Hyperplasia.

Volume of uterus :

- Non pregnant : 10 cc.
- Pregnant : 5 litres.

The place where broad uterine cavity becomes narrow cervical canal is called as anatomical internal os (Sphincters : Smooth muscles are arranged in concentric manner).

Lining of uterus : High columnar epithelium.

Lining of cervix : Low columnar epithelium.

The place where lining of uterus becomes lining of cervix is called as histological internal os.

Isthmus :

Part of uterus between anatomical internal os and histological internal os is called as isthmus.

Length of isthmus in non pregnant females : 0.5 cms.



Importance :

- Forms lower uterine segment in pregnancy.
- Length of LUS at term : 5 cm.
- Length of LUS during labor : 10 cm.
- LUS is identified by : Loose fold of peritoneum.

uterocervical length : 3 inches.

measured with the help of uterine sound.

## Corpus

00:33:52

After puberty, corpus is longer than cervix but before puberty, cervix is longer than corpus.

Age groups	Cervix : Corpus ratio
At birth	1 : 1
Before puberty	2 : 1
At puberty	1 : 2
Reproductive age	1 : 3/1 : 4
menopause	1 : 1 (both organs are atrophied).

3 layers :

Outermost : Serosa.

middle : myometrium.

- Smooth muscle.
  - Thickest layer.
  - Arranged in 3 layers :
    1. Outer layer : Longitudinal.
    2. middle layer : mesh wire fibres/criss cross fibres (also called as living ligature).
    3. Inner layer : Circular fibres.
- Innermost layer : Endometrium.

Thickness of endometrium :

After menstruation : 0.5 mm (average).

Around ovulation : 3 mm.

Secretory phase : 6 mm.

At the time of implantation : 10-12 mm.



**Endometrium** : It has glands and stroma.

Lining : Columnar epithelium.

m/c type of endometrial carcinoma : Adenocarcinoma.

2 layers : Superficial layer and basal layer.

**Superficial layer** : Is called as functional layer, shed at the time of menstruation.

**Deep layer** : Basal layer (basalis), responsible for regeneration of entire endometrium in next cycle.

Body of the uterus - uterine cavity (potential cavity).

- When the uterus is occupied : Cavity extends and walls moves away from each other.
- When it is empty : Walls lie opposed to each other.

While doing hysteroscopy, distension media is needed to look inside the uterus.

E.g., CO<sub>2</sub>, RL, NS, 5% dextrose, mannitol, etc.,.

If the basal layer of endometrium is destroyed (vigorous curettage).



There will be no regeneration.



Raw surface will be present.



Since it is a potential cavity, the walls get adhered.



Presence of intra uterine adhesions is known as **Ashermann's syndrome**.

## Position of uterus

00:44:30

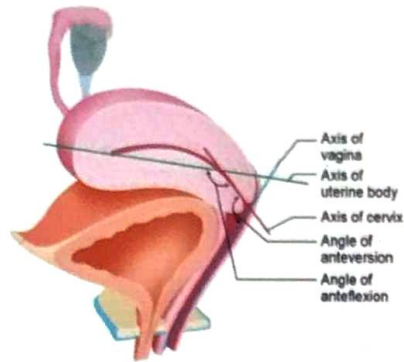
Angle between vagina and cervix : Angle of anteversion - 90°.

Angle between cervix and uterus : Angle of ante flexion - 120°.

At the level of internal os

Normal position of uterus and majority of females :

Anteverted and ante flexed.



In 20% females : uterus can be retroverted and retroflexed.

On PV examination :

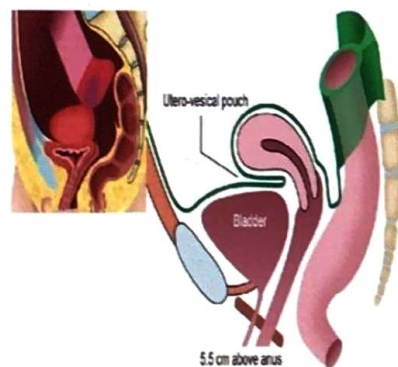
In anteverted uterus : Cervix posterior and fundus palpated anterior, easily palpable.

In retroverted uterus : Cervix anterior and fundus palpated posterior, not easily palpable.

Retrograde gravid uterus may lead to urinary retention.

Pessary used for retroversion : Hodge Smith pessary.

Peritoneal coverings of uterus :



From anterior abdominal wall, the peritoneum comes and reflected on to the anterior part of the bladder.

From anterior part of the bladder, it gets reflected on to the anterior side of the uterus.

From anterior side of the uterus it is reflected on to posterior side of uterus and also covers upper posterior part of vagina.

In uterus upper and posterior walls are covered by peritoneum.

In vagina, only posterior upper part is covered by vagina.

When peritoneum reflects, bladder to uterus a pouch or pocket is made : **utero-vesical pouch**.

Peritoneum reflecting between uterus and rectum : **Pouch of Douglas/ Cul de sac**.

This is the **most dependent part**.

**Clinical importance :**

- In case of **PID**, fluids come out of fimbrial end of tube and collected in pouch of Douglas.
- In case of **ectopic pregnancy**, blood is collected in POD. Can be accessed via posterior fornix.  
**Culdocentesis** : Aspiration of the collection of fluid from POD. Can aspirate non clotting blood from POD by passing a syringe through posterior fornix.
- In case of **pelvic abscess** : Opening in POD is made through which pus of pelvic abscess is drained - **Colpotomy**.

## GYNAECOLOGY - ANATOMY

### INTEGRATION : PART 3

#### Ligaments of the uterus

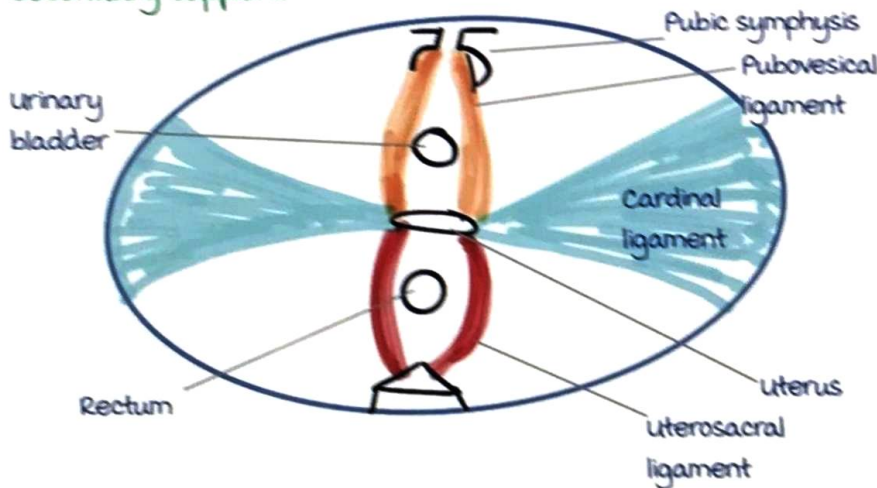
00:00:13

1. Round ligament : Helps to keep the uterus anteverted.
  2. Pubocervical ligament
  3. Cardinal ligament/ Mackenrodt/  
Transverse ligament.
  4. Uterosacral ligament.
- } Triradiate ligament  
(main supporting ligaments of uterus)

The uterosacral and transverse ligaments are also attached to the vagina.

While performing hysterectomy the ligaments are clamped and cut, their vaginal attachment can be spared.

Round ligament is not a direct support of the uterus, it is a secondary support.



5. Broad ligament :

misnomer : Not a ligament.

Does not support the uterus.

Fold of peritoneum : With anterior leaf and posterior leaf going over the utero-tubo-ovarian pedicle.

Parts :

1. mesosalpinx : Part which overlies the fallopian tube.
2. mesovarium : Part which overlies the ovary.

3. mesometrium : Part which covers the uterus.

Contents : **BROAD**

Blood vessels :

uterine vessels and nerves.

Ovarian vessels and nerves.

Round ligament.

Ovarian ligament.

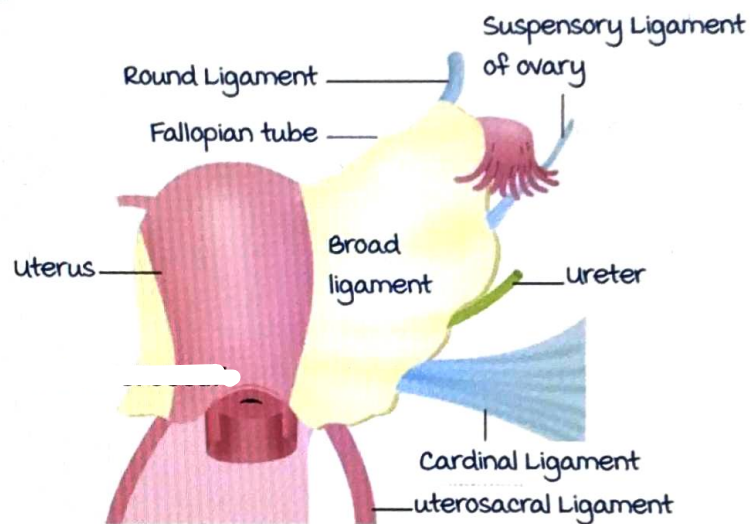
Artefacts : Epoochoron, paroophoron, Gartner's duct.

Oviduct : Fallopian tube.

New concept : Ureters are now considered to be a content.

Ureter lies in the medial border of broad ligament.

Ovary is not a content.



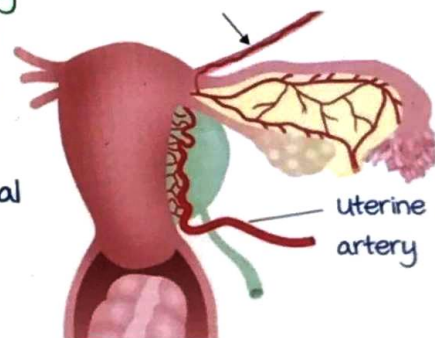
The ligaments that surround the uterus have been given a collective name : Parametrium.

### Blood supply of the uterus

00:10:07

1. 80% is from the uterine artery :

Arises from anterior division of internal iliac artery and moves transversely → Takes a sharp turn, 2 cm lateral to the internal os and supplies uterus.



2. 20% from Ovarian artery :

Branches of uterine artery ( from outside to inside) :

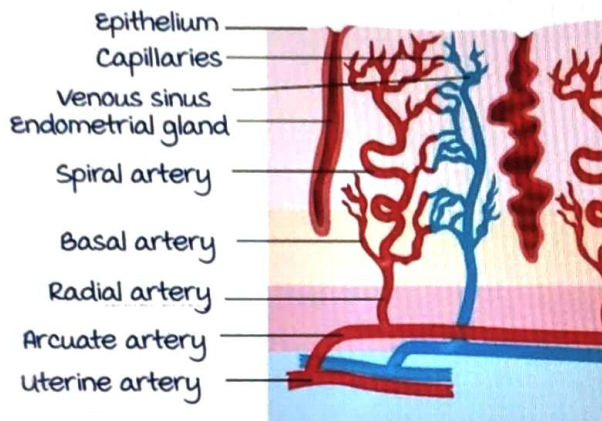
1. Arcuate artery : Supplies outer 1/3rd of myometrium.
2. Radial artery : Supplied inner 2/3rd of myometrium.

Gives off two branches :

- a. Basal artery : Supplies basal layer of endometrium.
- b. Spiral artery : Supplies functional layer of endometrium.

uterine arteries supplies :

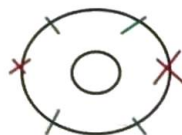
1. Fallopian tube.
2. uterus.
3. Cervix and vagina : via the descending cervical arteries.
4. Round ligament : Sampson artery.
5. ureter.



Blood vessel which constrict at menstruation : Leading the shedding of endometrium :

As superficial part of endometrium sheds : **Spiral artery constricts.**

Descending cervico-vaginal branch :



It is present at 3 o'clock and 9 o'clock position.

Hence a paracervical block is given either at 2 and 10 o'clock position or 4 and 8 o'clock position.

## Cervix

00:16:04

Part of the uterus.

Made up of connective tissue (mainly) : Collagen,  
and only 10% is smooth muscle.

In pregnancy/ at the time of labor, Cervix dilates and become short and thin.

Due to the break down of collagen and increased water content : Effacement.

The place where cervix opens to vagina : External Os.

It is also acts as a sphincter.

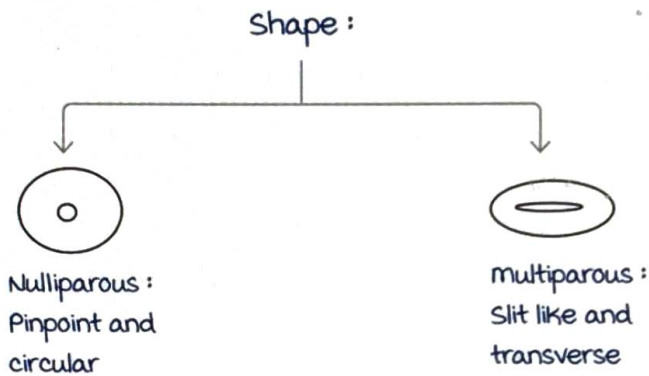
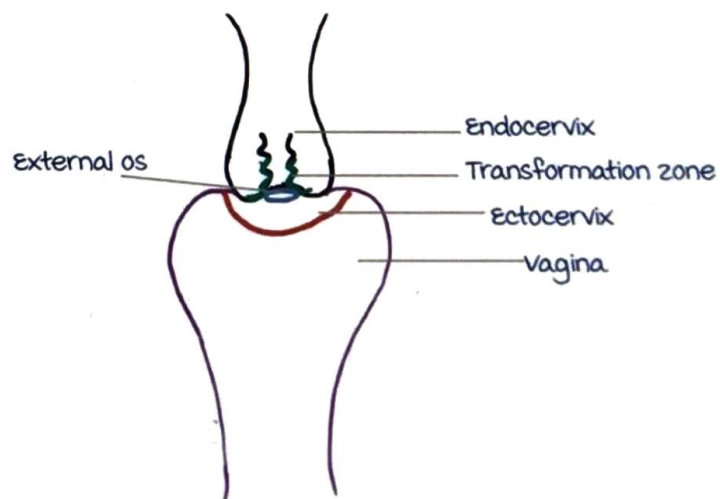




Diagram of cervix :

Endocervix/Supravaginal part of cervix : Lined by columnar epithelium and appears red on per speculum examination.

Ectocervix/ Portio vaginalis : Lined by stratified squamous epithelium, appears pink on per speculum examination.



Parts :

Endocervix		Ectocervix/Ectocervix
1.25 cm	Length of non pregnant cervix (2.5cm)	1.25 cm
2-2.5 cm	Length of pregnant cervix (4-5cm)	2-2.5 cm
Supravaginal part	Location	inside the vagina (portio vaginalis)
Columnar epithelium	Lining epithelium	Stratified squamous epithelium
Red in color	P/S examination	Pink in color
		

In all females, columnar epithelium of endocervix will change into squamous epithelium of ectocervix : metaplasia, which not a premalignant condition and is physiological.

This area is called as : Transformation zone.

Originally, this change occurs the level of external os.

This change happens gradually.

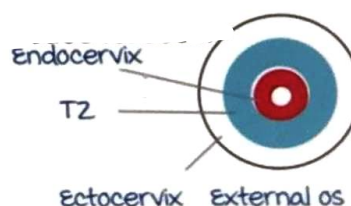
This TZ is not a static point and is a dynamic point.

The position keeps on changing because of :

1. Increasing age.
2. Change in hormones.

TZ will move out towards the exocervix at :

1. Puberty.
2. Pregnancy : Ectropion.  
Where endocervix moves out.
3. OCPs.





For ectropion : No biopsy,  
no intervention.

Tz moves inside, toward the endocervix : With increasing age.

When endocervix comes out, the glands present in columnar epithelium of the endocervix : Blockage of these cervical glands : Nabothian cyst/follicle.

No biopsy needed and no treatment.

MC variety of Cervical cancer : Squamous cell carcinoma.

Other types : Adenocarcinoma cervix.

MC site for SCC : Transformation zone/ Squamocolumnar junction.

MC site for adenocarcinoma : Endocervix.

Ectropion is not a premalignant condition.

### Nerve supply and lymphatic drainage

00:34:17

Uterus :

T10 - L1 : Franker Hauser ganglion.

Cervix and upper part of vagina : S2 - S4.

Perineum and lower part of vagina : Pudendal nerve (S2-S4).

Lymphatic drainage :

Body/corpus :

- |                          |   |                    |
|--------------------------|---|--------------------|
| 1. Internal iliac nodes. | } | Common iliac nodes |
| 2. External iliac nodes  |   |                    |

Fundus : Paraaortic nodes.

Cornua and round ligament : Superficial inguinal nodes.

Cervix :

1. Hypogastric / internal iliac nodes.
2. Obturator nodes.
3. Paracervical nodes : Sentinel lymph node.
4. External iliac nodes.

Cervix does not drain into superficial inguinal nodes.

## Per speculum examination

00:38:00

**Sim's speculum** : Retracts the posterior wall of vagina.

Not self-retaining. Anterior vaginal wall retractor has to be used.

**Anterior vaginal wall retractor** :

Has two loops which face different directions and have transverse serrations to fit into rugosities of the vagina.



Sim's speculum



Anterior vaginal wall retractor

**Cusco's self-retaining bivalve retractor**.

Drawback : Less area.



**Vulsellum** : To hold the anterior lip of cervix for non pregnant cervix.

Has small rat like teeth.

Sponge holding forceps for pregnant cervix. Upward concavity, with gap between the blades.



Vulsellum forceps

**Uterine sound** : To confirm

anteverted or retroverted uterus

and to measure the length of uterus.



Simpson's uterine sound

To perform any procedure this is used first.

It acts as the first dilator.

uterine sound	Bladder sound
1. Prominent curve 2. Calibrations present 3. Olive tip.	1. No prominent curve 2. Calibrations absent 3. No olive tip.

**Hegar's dilator** :

Cervix is dilated at the internal os.



Hegar's dilator

**Curette** :

Blunt and sharp curette for D & C.



Sim's curette

Active space

Blunt : Pregnant.

Sharp : Non-pregnant.

Sharp curette of pregnant uterus done  
in case of molar evacuation.

Anterior wall retractor	Curette
1. Loop is bigger 2. Serrations present	1. Loop is small 2. Serrations absent

Leech Wilkinson Cannula :

Typical funnel shaped end and wire  
like serrations at the proximal end.



Used to inject dye during hysterosalpingography.

Per speculum examination :

Retract posterior wall of vagina with Sim's speculum  
(narrow blade), inserted at right angles.



Retract the anterior wall of vagina with retractor.



Hold the anterior lip cervix with vulsellum

Opening : External os.

Remaining visible part is ectocervix.

## Vagina

00:50:21

It is the fibromuscular, distensible hollow tube connecting  
introitus and cervix.

Vagina makes an angle of  $90^\circ$  with cervix : Anterverted.

Vagina makes an angle of  $45^\circ$  with horizontal.

Cervix projects into the vagina making pockets : Fornices.

There four fornices :

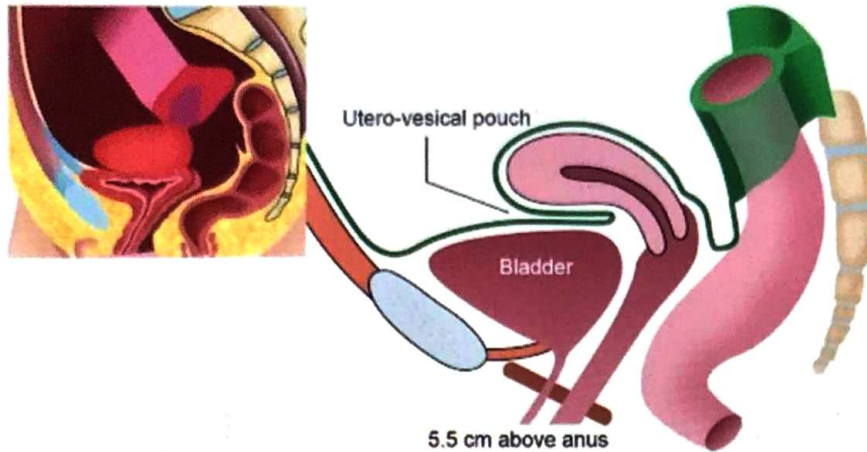
Anterior.

Posterior : Deepest.

2 lateral.

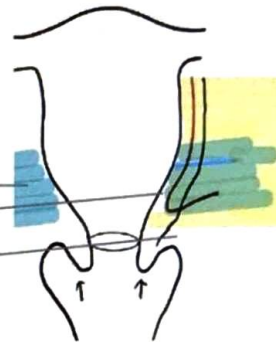
Posterior vaginal wall is longer than anterior vaginal wall by 2  
cm.

To do a culdocentesis : Pass syringe through posterior fornix.



Relations of Lateral fornices/ cervix :

1. Cardinal ligament.
2. Uterine artery.
3. Ureter.



Lining of the vagina : Non Keratinised, stratified squamous epithelium.

3 types of cells :

1. Superficial cells (Estrogen predominance).
2. Intermediate cells (Progesterone predominance).
3. Parabasal and basal cells.

No glands.

Vaginal secretions come from :

1. Cervical glands (mainly).
2. Endometrial glands.
3. Bartholin glands (only at the time of intercourse).

pH of vagina : Acidic.

pH of cervical secretions is alkaline.

Since vagina has inhabitant bacteria, **Doderlein bacilli** which are **lactobacilli**, convert **glycogen to lactic acid**.

Therefore, vaginal pH is acidic.

**Doderlein bacilli** appear at the time of puberty.

Disappear after menopause.

Acidic pH is body's natural defence against infections.

Only Candida can survive in acidic media.

Estrogen acts on superficial cells to make glycogen.  
The cells that have glycogen are called : **mature cells**.  
Hence, Superficial cells are mature cells.

The following two are essential to keep acidic pH :  
**Doderlein bacilli + Estrogen.**

Age	Factor	pH
At birth	some estrogen from mother present	Acidic
Children	No E and no doderlein	Alkaline (6.5-7.5)
At puberty	Both present	Acidic
Reproductive age	Both present	Acidic (3.5 - 4.5)
After menopause	No E or Doderlein	Alkaline (6.5 - 7.5)
Pregnancy	High E and Doderlein	Acidic = 4
menstruation	Blood in vagina, and is alkaline	Alkaline (6.5-7.5)

**mcc vaginitis is pregnancy : Candidiasis.**

## Ovary

01:04:17

Size : 3 X 2 X 1 cm.

volume : 6-7 cc

if volume > 10 cc : PCOS.

Location : Lateral pelvic wall in **fossa of Waldeyer**.

In intrauterine life : Located higher up in the abdomen.

Descends down with the help of the gubernaculum.

uterus prevents further descent of ovaries.

uterus divides the gubernaculum into :

1. Round ligament.
2. Ovarian ligament.

Ligaments in relation to the ovary :

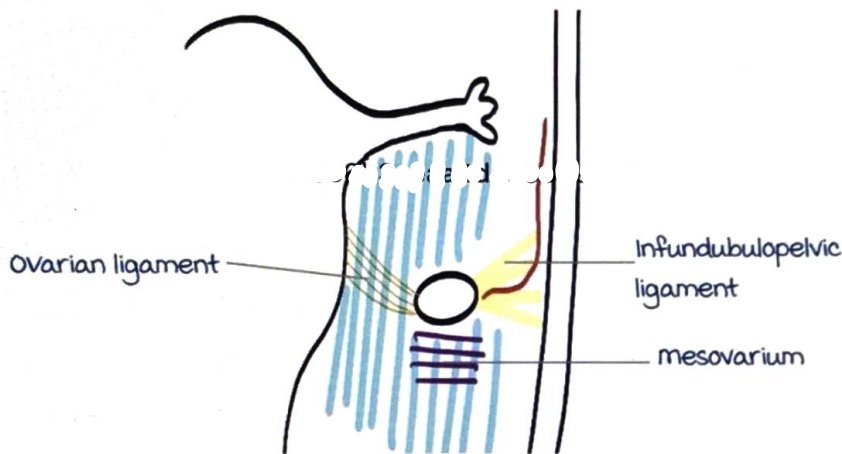
1. **Ovarian ligament** : Connects the ovary to the cornua of the uterus.

2. **Mesovarium** : Part of broad ligament lying behind the ovary.

3. **Suspensory ligament of ovary/infundubulopelvic ligament** : Connects the ovary to the lateral pelvic wall.

Ovarian artery and nerve lie in this ligament.

If during hysterectomy, ovaries are not to be removed, then do not cut this ligament.



Relations of the ovary :

Anterior/Superior : External iliac artery.

Posterior : ureter and internal iliac artery.

Lateral : Obturator nerve and infundubulopelvic ligament.

medial : Ovarian ligament.

In case of ovarian or adnexal mass → Presses on the obturator nerve → Pain radiating to the medial side of thigh.

Blood supply :

Ovarian artery : Branch of abdominal aorta at L2 level.

Venous drainage : Ovarian vein :

Left side ovarian vein drains into left renal vein and right side drains into inferior vena cava.

Nerve supply : Ovarian plexus.

Lymphatic drainage : Para-aortic LN.

## Fallopian tube

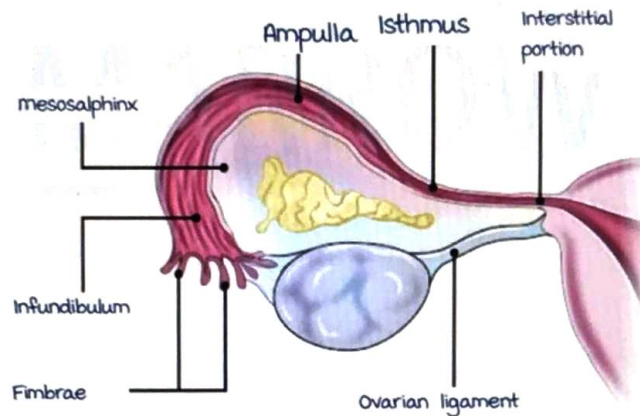
01:17:53

Length : 4 inches or 10–12 cm.

Parts of tube are:

**Interstitial** (intramural) : 1.25 cm long and 1 mm diameter (narrowest part of the tube).

It has no longitudinal muscles, only circular muscles are present and acts as anatomical sphincter by forming tubal ostia.



**Isthmus** : 2.5 cm long and 1 mm in diameter (second narrowest part).

It acts as **physiologic sphincter**.

From the broad ampulla the conceptus comes to narrow isthmus hence it's a physiological sphincter.

**Ampulla**: widest and longest part (5 cm) and fertilization occurs here.

It has mucosal folds called as plicae.

**Fimbria/infundibulum** : 1.25 cm long with a maximum diameter of 6 mm.

**Histologically** : Fallopian tube has peg cells and is lined by single layer of ciliated columnar epithelium.

**MC cancer** : Adenocarcinoma.

**Important questions on fallopian tube** :

m/c site for fertilization : Ampulla of fallopian tube.

m/c site for ectopic pregnancy : Ampulla of fallopian tube.

m/c site for tubal abortion : Ampulla of fallopian tube.

m/c site for tubal rupture : Isthmus of fallopian tube.

m/c site for tubal ligation : Isthmus.

Best prognosis for reversibility/recanalization of tube is if there is isthmo-isthmic anastomosis.

Anatomical sphincter : Interstitial part.

Physiological sphincter : Isthmus.

TB causes block in : Cornual end of the tube.

Gonococcus causes block in : Fimbrial end of tube.

Blood supply :

medial 2/3rd by branches of uterine artery.

Lateral 1/3rd by branches of ovarian artery.

Lymphatic drainage : Para aortic LN.

The interstitium or intramural part drains into superficial inguinal LN along with the cornua of uterus via round ligaments.

Nerve supply : T11, T12, L1.

### Origin of internal genitalia

01:22:25

Fallopian tube	}	mullerian Duct / Paramesonephric duct
uterus		
Cervix		
upper 1/3 rd vagina		

These are mesodermal in origin.

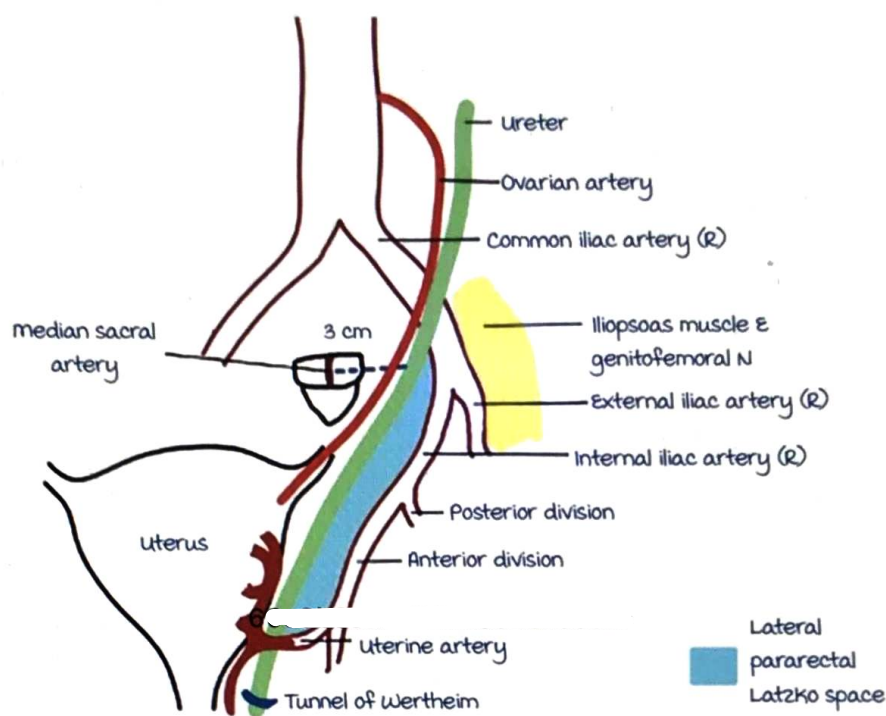
Lower 2/3rd vagina : Sinovaginal bulb of urogenital sinus and is endodermal in origin.



## GYNAECOLOGY - ANATOMY INTEGRATION : PART 4

### Course of ureter

00:01:25



ureter enters the pelvis from lateral to medial side crossing the common iliac artery.

It lies anteriorly to common iliac artery.

median sacral artery lies on the sacral promontory.

ureter is 3 cm away from the median sacral artery when it enters into the pelvis.

It enters the infundibulo-pelvic ligament after it enters the pelvis.

- Infundibulo-pelvic ligament is posterior and medial to it.

Once the ureter crosses the common iliac artery, divides to external and internal iliac arteries.

External iliac artery : Continues into the triangle of doom.

Internal iliac artery : Divides to anterior and posterior division.

- Anterior division gives the first branch : uterine artery.
- Posterior division : Goes posteriorly to supply the lower limb.

Lateral to external iliac artery : iliopsoas muscle with genitofemoral nerve.

Ovarian artery lies anterior to the ureter.

- Arises from the abdominal aorta at L<sub>4</sub> level.
- In salpingo-oophorectomy, the broad ligament has to be opened between round ligament and infundibulo-pelvic ligaments to gain access to the retroperitoneal space.  
Clamp must be applied only after visualizing the ureter.

m/c site for ureteric injury (gynecological surgery) : At the level of pelvic brim.

ureter lies in the medial part of the broad ligament.

At 2 cm lateral to the internal os, ureter is crossed by uterine artery.

- Takes a sharp upward turn to supply the uterus.
- Gives a descending cervical/ cervico-vaginal artery : supplies cervix and vagina.

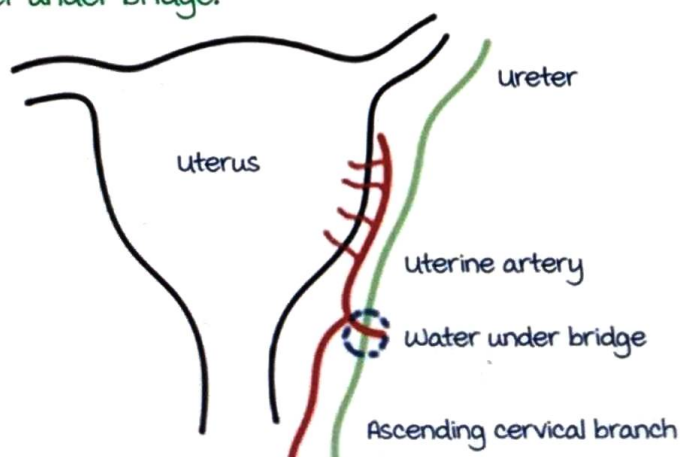
Water under bridge : uterine artery directly crosses over the ureter.

Bridge : uterine artery.

Water : urine in ureter.

While ligating the uterine artery : should remain as close to the uterus as possible to avoid injury to the ureter.

Second m/c site for ureteric injury in gynecological surgeries : water under bridge.



Branches of uterine artery (from outside to inside) :

- Arcuate artery
- Radial artery
- Basal artery
- Spiral artery.

Relationship of ureter to arteries :

Ovarian artery : Anterior to ureter.

Uterine artery : Anterior to ureter.

Common iliac artery : Posterior to ureter.

Internal iliac artery : Posterior to ureter.

Lateral pararectal / Latzko space boundaries :

medial : ureter.

Lateral : Anterior division of internal iliac artery.

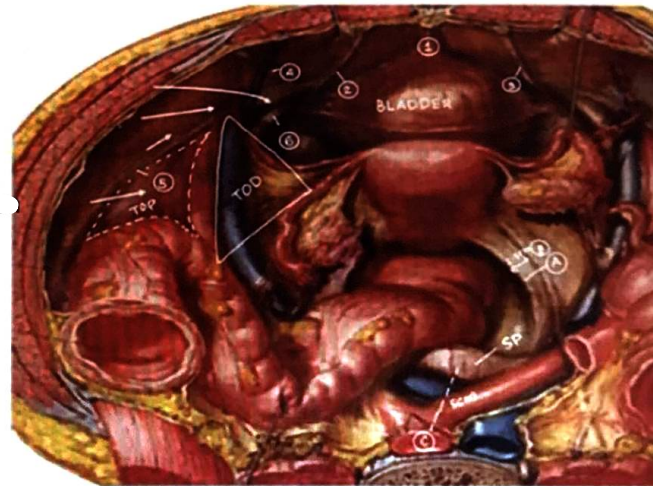
Below : uterine artery.

Ureter crosses the common iliac artery at right angles.

Visualization of peristalsis : Diagnostic of ureter during surgeries.

## Pelvis

00:15:22



1 : median umbilical ligament (always at 12'o clock position).  
urachal remanent.

2 & 3 : medial umbilical ligament (at 1'o clock & 11 o' clock  
position). umbilical artery remanent.

4 : Lateral umbilical ligament (2'o clock & 10 o' clock position).  
Inferior epigastric artery remanent.

S : Inguinal ligament.

G : Cooper's ligament.

SP : Sacral promontory.

C : ~~FORNO~~ Iliac axis.

A : uterosacral ligament.

B : ureter.

Bladder lies between the medial umbilical ligaments.

Hence, peritoneum should not be cut medial to medial umbilical ligament.

The camera of the telescope should be held in such a manner that the median umbilical ligament lies in the 12 o' clock position.

Lateral umbilical ligaments are commonly injured in gynecological surgeries.

- Important for surgeons as they determine if the hernia is direct or indirect.

m/c vessels injured in laparoscopic gynecological surgeries : subcutaneous vessels.

m/c vessel to get injured in laparoscopic gynecological surgeries leading to complications : inferior epigastric vessels.

median, medial and lateral umbilical ligaments are false ligaments : Peritoneal folds.

Inguinal ligament :

True ligament.

From pubic tubercle to anterior superior iliac spine (ASIS).

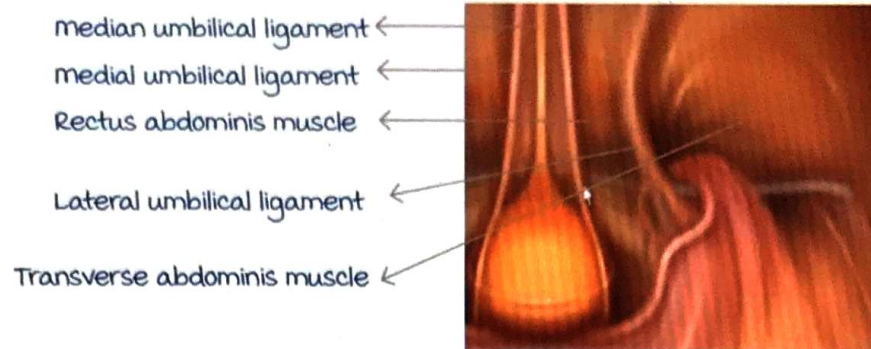
Important for surgeons.

Cooper's ligament :

Also called as light house : Pearly white in color and reflects light.

Also called as pectineal/iliopectineal ligament.

In Burch colposuspension : Suspend the urethra to the Cooper's ligament.



Triangle of doom :

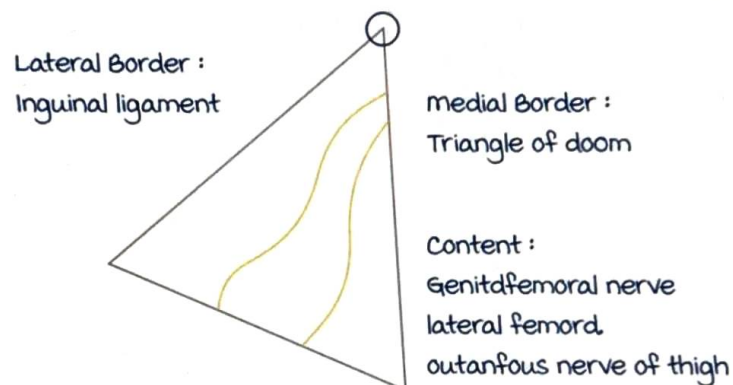
Apex : Deep inguinal ring.

medial border : Round ligament in females and vas deferens in males.

Lateral border : Sampson artery in females and spermatic vessels in males.

Contains : External iliac artery (lateral) and external iliac vein (medial and superficial).

Apex : Deep inguinal ring



During salpingo-oophorectomy, remain in anteromedial part.

- Posterior : Ureter present.
- Laterally : Triangle of doom present.

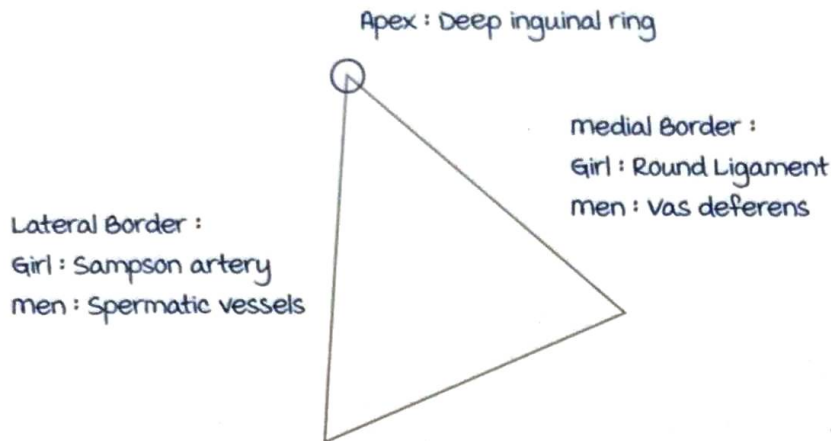
In most cases, the sigmoid colon covers the triangle of doom on left side : Sigmoid colon needs to be mobilized for surgeries like salpingo-oophorectomy, ectopic surgery or tubal ligation.

Triangle of pain :

Apex : Deep inguinal ring.

medial : Triangle of doom.

Lateral : Inguinal ligament.



Contains two nerves :

- **Genitofemoral nerve :**

Supplies to **mons pubis** in females and **scrotum** of males.

Surgery for endometriosis, endometrioma removal or lymph node dissection leads to injury to genitofemoral nerve resulting in hyperesthesia/paresthesia to mons pubis.

Can **regenerate** within a couple of months.

- **Lateral femoro-cutaneous nerve of thigh :**

Supplies **upper lateral aspect of the thigh**.

Surgery for endometriosis : Injury to lateral cutaneous nerve of thigh resulting in paresthesia or burning sensation on the lateral aspect of thigh.

**Does not regenerate.**

**Immediate** complaint : **Permanent** damage.

**Delayed** complaint : Due to inflammation and edema (**reversible damage**).

median sacral artery :

Lies on sacral promontory.

While doing **sacral colpopexy** (for vault prolapse) :

**Injury** to the artery leading to **massive bleeding** as it is a direct branch of the abdominal aorta.

**5 cm above** sacral promontory : **Aorto-iliac axis** - Right and left common iliac arteries lie.

3 cm lateral to median sacral artery : Ureter crosses common iliac artery.

Common iliac artery divides into internal and external iliac arteries.

Pelvis is separated from perineum by levator ani muscle.

Aka pelvic diaphragm.

Has 2 parts : Pubococcygeus (arise from pubic bones) and iliococcygeus (arise from iliac bones).

Ischiococcygeus is not a part of levator ani muscle.

Aka coccygeus muscle.

Pubococcygeus named according to location :

Puborectalis/ puboanalis : Part near to the rectum.

Pubovaginalis : Part near the vagina.

Pubourethralis : Part near urethra.

Levator ani is covered by superior and inferior fascia →

Superior and inferior fascia of the pelvic diaphragm → Arcus tendinous fascia.

Arcus tendinous fascia : De Lancey's level 2 support.

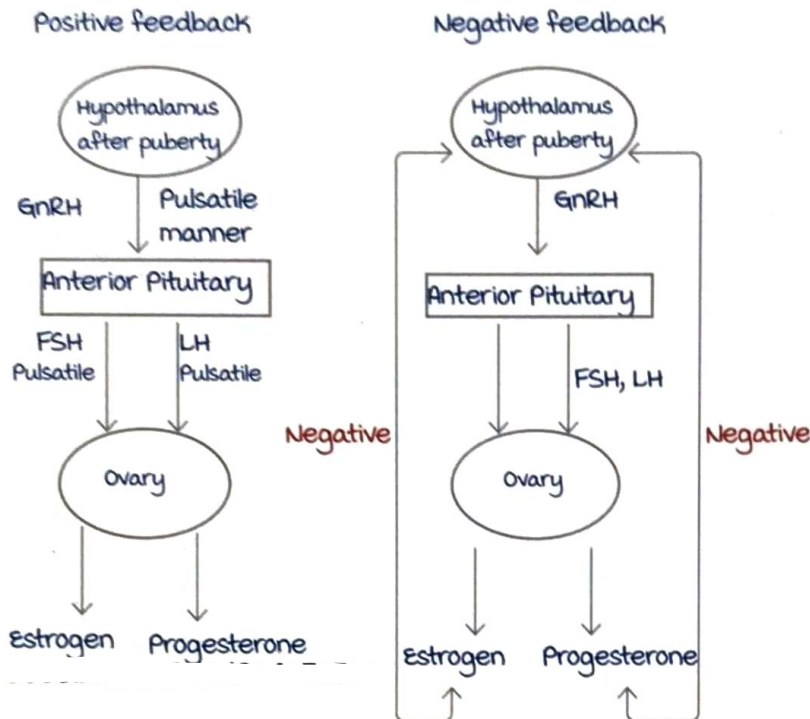
Levator ani muscle : De Lancey's level 3 support.

# GYNAECOLOGY AND PHYSIOLOGY

## INTEGRATION : PART 1

### Hypothalamo-pituitary-ovarian axis

00:01:46



### GnRH

00:05:14

- Decapeptide hormone.
- Formed & released by paraventricular nucleus of hypothalamus.
- $t_{1/2}$ : 3-4 minutes.
- Acts on anterior pituitary and stimulates release of FSH and LH from anterior pituitary.
- GnRH receptors are membrane bound receptors.

GnRH levels in blood cannot be checked directly due to short half-life.

Hence, GnRH is indirectly checked by measuring the levels of LH and FSH.

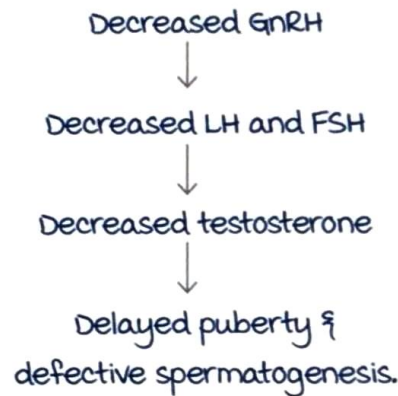
Decreased levels of LH and FSH indicates decreased levels of GnRH & vice versa.



The neurons which release GnRH are derived from **olfactory placode**. These neurons migrate from olfactory placode to hypothalamus in **close association with olfactory nerves**.  
**Defect in the neuronal migration** can lead to decreased GnRH leading to

- Decreased levels of LH.
- Decreased levels of FSH. } Anovulation/no folliculogenesis  
**Primary infertility**
- Decreased levels of estrogen : Delayed puberty.
- Decreased levels of progesterone (no corpus luteum) :  
 Primary amenorrhea.
- Anosmia.  
 Primary amenorrhea and anosmia known as **Kallman syndrome**.

In males :



Clinical presentation : Infertility with anosmia.

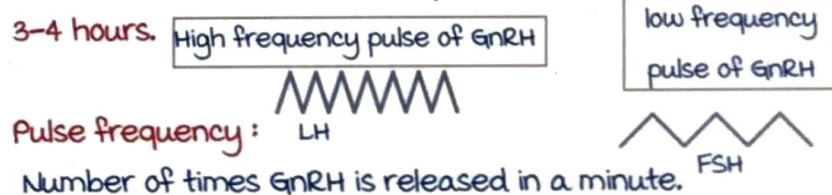
Kallman syndrome is **more common in males** than females.

Anovulation : no primary oocyte converted into secondary and no corpus luteum formation . hence levels of progesterone decrease causing amenorrhoea later to infertility.

Estimation of GnRH levels :

Estimated indirectly by measuring LH or FSH (**LH > FSH**).

Half-life of LH is **20 minutes** (preferable) and that of FSH is **3-4 hours**.



- If pulse frequency of GnRH release is low → FSH is preferentially released.
- If pulse frequency is high → LH is released.

Hormones that control GnRH :

- Estrogen and progesterone : Negative feedback on GnRH.
- Prolactin : Negative feedback on GnRH.  
This is the basis of lactational amenorrhea & 2° amenorrhea in patients with increased prolactin.

Lactating females have high prolactin levels → Negative feedback on GnRH → Decreased levels of LH and FSH → No oestrogen & progesterone → absence of ovulation & menstruation - ..

Prolactin is secreted by acidophilic cells of anterior pituitary.

## LH and FSH

00:18:45

- Peptide hormones.
- Secreted by basophilic cells of anterior pituitary.
- Secreted in a pulsatile manner.

Receptor location is membrane bound :

	LH	FSH
male	Leydig cells : Testosterone	Sertoli cells : Inhibin B
Female	<ul style="list-style-type: none"> <li>• Theca cells : Produces androgen (testosterone)</li> <li>• Granulosa cells : In late proliferative phase, LH receptors appear on luteinized granulosa cells and stimulate release of progesterone.</li> </ul>	Granulosa cells

Functions of FSH :

- Selection of cohort of follicles every month.
- Growth of follicles.
- Selection of dominant follicle.
- Responsible for collagen breakdown at the time of ovulation. Hence, there is LH & FSH surge just before ovulation.

Functions of LH :

- main hormone responsible for ovulation.
- Responsible for maintenance of corpus luteum in non-pregnant females.

hCG prevents luteolysis (degeneration) of corpus luteum. Hence, hCG is responsible for maintenance of corpus luteum which releases progesterone in early weeks of pregnancy.

### Estrogen and progesterone

00:23:34

	Estrogen	Progesterone
Nature of hormones	Steroid	Steroid
Type	C18 steroid	C19 steroid
Receptors	Intracellular	Intracellular
Location of receptors :	Intranuclear	Intracytoplasmic
Action :	Intranuclear	Intranuclear
Naturally occurring	$E_1$ : Esterone $E_a$ : Estradiol $E_3$ : Estriol	Progesterone
Synthetic	Ethinyl Estradiol (in OCPs)	Progestin
Potency	$EE > E_a > E_1 > E_3$	

Naturally occurring estrogens :

most common naturally occurring estrogen in reproductive age & in post-menopausal female are  $E_a$  and  $E_1$  respectively.

most specific for pregnancy :  $E_3$ .

most common estrogen in pregnancy :  $E_a$ .

$E_a$  :  $E_1$  is normally 2 : 1

In a post-menopausal female



Adrenal glands produce androgens  $\xrightarrow{\text{Aromatase}}$  Estrogen ( $E_2$ )  
Hence, the most common estrogen in post-menopausal female is  $E_1$  in adipose tissues.

In obese PCOS females, excessive androgens will get converted to estrogen in peripheral tissues.

$E_a$  :  $E_1$  becomes 1 : 2.

Due to high  $E_2$ , hyper-estrogenic conditions are common in obese females such as :

- Fibroid.
- Endometrial Cancer.
- Ovarian cancer.

Letrozole (aromatase inhibitor) is used in all hyper estrogenic conditions.

$E_3$  : Estriol.

Produced in placenta.

Requires fetal DHEA sulfate for its production.

Sources of Estrogen	Sources of Progesterone
$E_a$ : • Granulosa cells in ovary • Corpus luteum	After ovulation : Corpus luteum.
$E_1$ : Androgens in adipose tissue	Before ovulation : Luteinized granulosa cells.
$E_3$ : Placenta (requires fetal DHEA)	During pregnancy : Placenta.

Action on each other's receptors :

Estrogen	Progesterone
Upregulates progesterone receptors on uterus. Progesterone cannot act on uterus unless primed by estrogen	Downregulates the Estrogen Receptors (ER) on uterus. Hence, progesterone has antiproliferative effect.

Action of Estrogen on endometrium :

- Proliferation of endometrium.
- Leads to endometrial hyperplasia and endometrial cancer.
- In all females with intact uterus, never give estrogen alone. Give estrogen + progesterone.

## Action of progesterone on endometrium

00:35:40

- **Antiproliferative effect** : Protects against endometrial cancer.
- **Secretory effect** : Supports the endometrium.
- If given for long time, causes **endometrial thinning**.

In female with uterus estrogen is never given alone but as **estrogen+ progesterone**.

Progesterone containing contraceptives like **MIRENA (LNG-IUCD)** causes thinning and atrophy of endometrium leading to decreased blood loss and ultimately amenorrhea.

Copper containing IUCD causes increased bleeding.

- A female with history of menorrhagia who needs contraception : **Treatment of choice is MIRENA**.
- Patients with excessive bleeding (due to thick endometrium) can be given Progesterone alone or Estrogen + progesterone combinations like OCPs.
- Thick endometrium means estrogen is present i.e., uterus is primed.
- In patient with **thin endometrium** (estrogen is absent) : Progesterone alone cannot stop bleeding as endometrium is not primed by estrogen. Hence the patient should be given : **OCPs** or **Estrogen first** which is then followed by progesterone.

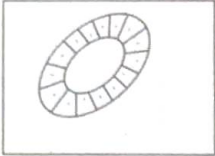
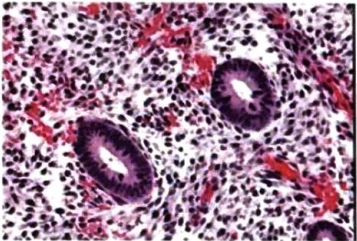
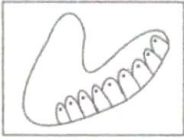
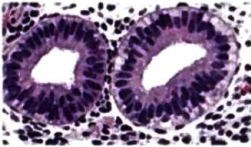

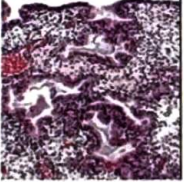
Type of bleeding :

Estrogen	Progesterone
<ul style="list-style-type: none"> <li>• Anovulatory cycles : progesterone is absent</li> <li>• Estrogen will proliferate the endometrium, and the absence of supportive progesterone can cause break down of the weak endometrium : <b>Estrogen breakthrough bleeding</b>.</li> <li>• <b>Heavy and irregular</b></li> <li>• <b>Painless</b> due to absence of prostaglandins.</li> </ul>	<ul style="list-style-type: none"> <li>• In normal menstrual cycle, bleeding occurs due to progesterone withdrawal.</li> <li>• Progesterone is a smooth muscle relaxant.</li> </ul> <p>Decreased progesterone ... ..            → vasoconstriction → <b>PGF-<math>\alpha</math></b> release → Dysmenorrhea.</p>

Active space

# Endometrial biopsy

00:47:16

Estrogen	Progesterone
<ul style="list-style-type: none"> <li>• Proliferative phase :</li> </ul> <p>Simple tubular glands.                      Pseudostratification : Nuclei present at different levels.                      Telescoping of glands.</p>  	<ul style="list-style-type: none"> <li>• Early secretory phase :</li> </ul> <p>Indicator of ovulation :                      Subnuclear vacuoles present : vacuoles present beneath nucleus and nucleus is pushed to apex of the cell.</p>  <p>Subnuclear vacuolation is earliest sign of ovulation on biopsy. Occurs at Day 17 of cycle.</p>  <p>2<sup>nd</sup> best answer : Biopsy taken at time of ovulation.</p> <ul style="list-style-type: none"> <li>• Late secretory phase</li> </ul>  <p>High progesterone causes coiling of glands, corkscrew or sawtooth appearance of glands. Secretions present within the gland.</p> 

Active space

Effect on myometrium :

Estrogen	Progesterone
<ul style="list-style-type: none"><li>• Growth of non-pregnant uterus (predominant)</li><li>• Increases uterine contractions.</li><li>• In patients of <b>Turner syndrome</b>, because of decreased estrogen their uterus resembles that of infants : <b>infantile uterus</b> or <b>hypoplastic uterus</b>.</li></ul>	<ul style="list-style-type: none"><li>• Growth of pregnant uterus. (predominant)</li><li>• Decreases uterine contractions as it is a smooth muscle relaxant. Hence, progesterone can be used for preventing preterm labor.</li><li>• Progesterone receptors decrease at onset of labor : <b>Functional withdrawal of progesterone</b>.</li></ul>

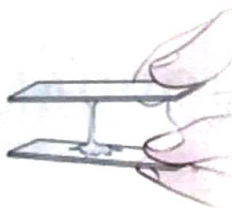
# GYNAECOLOGY - PHYSIOLOGY

## INTEGRATION : PART 2

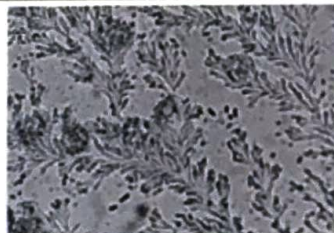
### Effect of estrogen and progesterone on cervical mucus

00:00:12

Estrogen on cervical mucus	Progesterone on cervical mucus
Thin, watery	Thick, viscous
Copious	Scanty
Elastic → Stretched between fingers : Spinbarkeit.	Not elastic → Breaks on stretching : Tack.
Under microscope : Fern like appearance (due to increased estrogen, increased sodium chloride and acellularity of mucus).	Under microscope : Ferning is absent.
<p>Applications :</p> <ul style="list-style-type: none"> <li>Used as a test for ovulation : Absence of ferning on day 22 of cycle indicates ovulation &amp; presence of Progesterone. Presence of ferning indicates non-ovulation as estrogen predominates. Insler score is used to assess suitability of cervical mucus for fertility.</li> <li>Natural method of contraception : Billing's method (avoidance of intercourse till estrogenic mucus is present).</li> <li>Physiological discharge (Leukorrhoea) Could be thin &amp; watery in the first half of the cycle (estrogen) or thick &amp; scanty in the second half of the cycle (Progesterone) in normally ovulating females. 2 characteristics to differentiate from discharge due to vaginitis : No foul smell. No itching. maximum discharge is seen at just before ovulation (maximum estrogen).</li> <li>After menopause → Decreased estrogen → Decreased cervical discharge → vaginal dryness : Senile vaginitis/atrophic vaginitis. Now called Genitourinary syndrome of menopause.</li> </ul>	<p>Applications :</p> <ul style="list-style-type: none"> <li>All progesterone containing contraceptives make cervical mucus thick (one of the mechanisms of action).</li> <li>Progesterone makes cervical mucus thick → Decreases sperm ascent → Decreased risk of PID. MIRENA (Progesterone containing IUCD): Decreased risk of PID. Decrease in blood loss.</li> </ul>



Spinbarkeit test



Fern like appearance of cervical mucus under the effect of estrogen.

Active space



Ferning appears by **day 8** and disappears by **day 18** of the cycle.

- Amniotic fluid shows fern like appearance under microscope in **premature rupture of membrane** (Fern test).
- Amniotic fluid ferning is **thin** and cervical mucus ferning is **thick**.
- In pregnancy, cervical mucus does not show ferning (as progesterone is predominant). If ferning is present in pregnancy, it indicates presence of amniotic fluid (thin, delicate ferning).
- All tests for ovulation are done on day 22 in women with regular cycle because maximum activity of corpus luteum is seen only 8 days after ovulation.
- Nature of cervical mucus is checked using a tissue paper every morning.
- PID is a sexually transmitted disease. Acquired through ascent of sperms (**most common route** of spread).
- There is increased risk of PID (**most common organism** is actinomyces) and blood loss with copper IUCD. Risk of PID and blood loss is less with MIRENA.
- menopause → no ovarian follicles → no granulosa & theca cells → estrogen level drops.
- vaginal dryness seen as vagina does not have glands and depends on cervical mucus.

### Effect of estrogen and progesterone on vaginal mucosa

00:14:19

vaginal epithelium has 3 types of cells : Superficial, intermediate and parabasal/basal cells.

**Superficial cells** (predominates under estrogen effect) :

**Eosinophilic**, polygonal with pyknotic nuclei.

**Intermediate cells/navicular cells** (predominates under progesterone effect) :

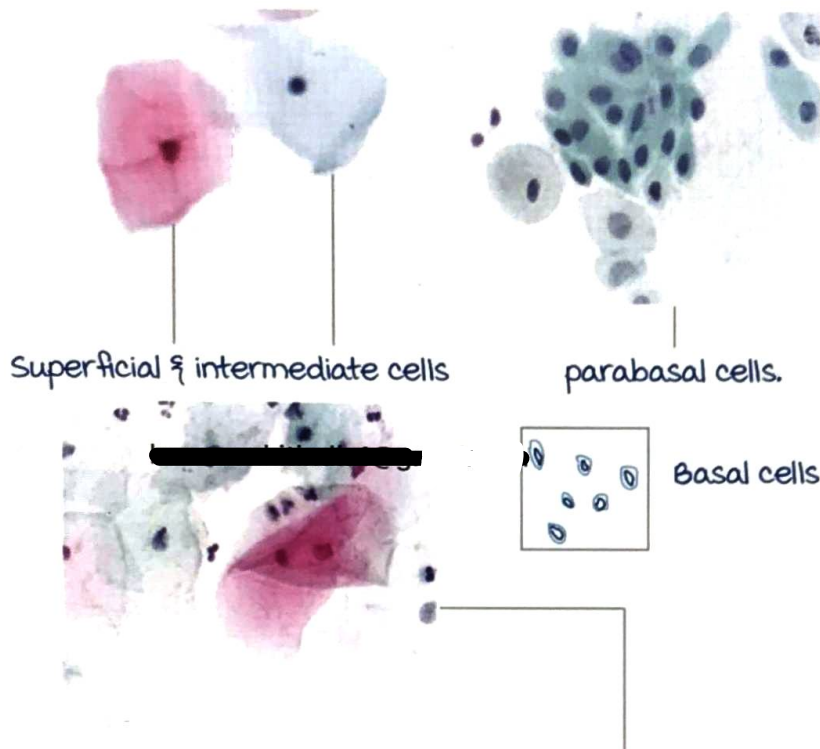
**Basophilic** with slightly bigger nuclei than superficial cells.

**Parabasal cells** are **basophilic**. They are smaller than

superficial and intermediate cells, with blurred margins and larger nuclei than other 2 cells.

Basal cells are very small. They appear in clusters with big nuclei.

Parabasal/basal cells are of same category. Seen in absence of hormonal predominance.



Smear predominantly basophilic (blue) : Secretory phase.  
 Smear predominantly acidophilic (pink) : Proliferative phase.

**Clinical application :**

Ovulation can be determined based on vaginal cytology. On day 22, if predominant cells are pink, it indicates no ovulation (no progesterone). Normally, smear taken on day 22 should have intermediate cells due to progesterone.

**maturation index :**

Ratio of parabasal (a) : intermediate (b) : superficial cells (c) in a smear with 100 cells.

Estrogen	Progesterone
0 : 30 : 70 (Proliferative phase)	0 : 70 : 30 (Secretory phase)

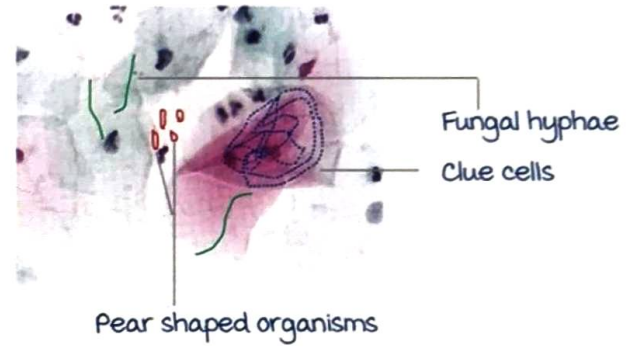
Active space

0 : 10 : 90 (Late proliferative phase : Just before ovulation)	0 : 90 : 10 (Around day 22 of cycle or in pregnancy)
--	--

- maturation index 100 : 0 : 0 -> **menopause/before puberty/after delivery.**
- Vaginal cytological smear for hormonal study is taken ~~from the cervix~~ **of vagina.**  
These cells are also seen in exocervix.

Abnormalities in cytology :

- In pap, if vaginal epithelial cells are rough/unclear, it indicates adherence of bacteria : **Clue cells in bacterial vaginosis.**
- If thin threads are seen, it indicates hyphae of fungus **candida infection.**
- If pear shaped organisms are seen, it indicates **trichomonas infection.**
- Cells with big nuclei (increased nuclear cytoplasmic ratio) are dysplastic. Seen in **cervical cancer.**



**Effect of estrogen and progesterone on fallopian tube**

00:30:40

	Estrogen	Progesterone
Fallopian tube	Increases motility	Decreases motility (Failure of Progesterone containing contraceptives increase the risk of <b>ectopic pregnancy</b> ).
Salt and water	Retention	Excretion
Breast	Increases fat deposition and leads to ductular development at the time of puberty.	<b>Glandular development.</b> OCPs slightly increase the risk of breast cancer due to <b>progesterone component.</b>

Active space

Bone	<p>Closure of epiphysis and increase in bone mass.</p> <p>Application :</p> <ul style="list-style-type: none"> <li>menopause/ovarian failure : Decreased bone density, Increased chances of fracture (osteoporosis).</li> <li>Drugs that decrease estrogen can cause osteoporosis (continuous GnRH/Letrozole).</li> <li>Precocious puberty : Premature closure of epiphysis causing short stature.</li> </ul>	No effect.
Clotting factors	<p>Increases 2, 7, 8 and 10 → Procoagulant → Increases the chances of thromboembolism.</p> <p>Application :</p> <p>HRT and OCP are <b>contraindicated</b> in females with h/o of coronary artery disease/venous thromboembolism/stroke/risk factors of venous thromboembolism such as prolonged immobility or prolonged surgery.</p>	<p>Progesterone has no effect on clotting factors.</p> <p>Application :</p> <p>Progesterone only contraceptives can be given to females with h/o of coronary artery disease/venous thromboembolism/stroke.</p>
Lipid profile	<p>Increases HDL and decreases LDL: Cardioprotective in nature.</p> <p>Application :</p> <ul style="list-style-type: none"> <li>Chances of coronary artery disease are less in premenopausal females and more in pos menopausal women.</li> <li>Exogenous estrogen &amp; progesterone (HRT) does not decrease the risk of coronary artery disease (CAD). There is slightly increased risk CAD with HRT due to progesterone component.</li> </ul>	Decreases HDL and increases LDL.
Basal body temperature	No effect	<p>Slightly increases basal body temperature.</p> <p>Application :</p> <ul style="list-style-type: none"> <li>To determine ovulation (slight increase in temperature)</li> <li>As a natural method of family planning.</li> <li>Symptothermal method : Combination of 2 natural methods of family planning to increase efficacy. Example : Cervical mucus method + Basal body temperature method.</li> </ul>
Effect on FSH	Always have <b>negative effect</b> .	<p>Low levels → Positive effect.</p> <p>High levels → Negative effect.</p>

Effect on LH	Low to normal estrogen → Negative effect on LH. High levels of estrogen (>200 pg for 48 hours) → Positive effect on LH	Low levels → Positive effect. High levels → Negative effect.
--------------	---	---

In Turner's syndrome, there is decreased estrogen but short stature due to mutation in **SHOX gene**.

## Androgen production in females

00:42:09

Androgens are produced from puberty onwards by ovary. Androgens are **C19** steroids & their receptors are present **intracellularly**.

**50%** from peripheral conversion of androstenedione.

**25%** from adrenal glands.

**25%** from ovaries (Theca cells).

Maximum androgen produced by ovaries is

Androstenedione > Testosterone > DHEA.

Ovaries do not produce :

- DHEA-S → Produced by adrenal glands.
- Dihydrotestosterone → Produced by peripheral conversion of testosterone.

Estrogens are **C18** steroids.

Natural progesterones are **C21** steroids.

Synthetic progesterones are **C19** steroids (have androgenic side effects).

- majority of androgens and estrogens bind to **sex hormone binding globulin (SHBG)** mostly. Remaining bind to albumin.
- majority of progesterone binds to albumin. Small amount to cortisol binding globulin. Never to SHBG.
- Testosterone (androgens) has higher **affinity** for SHBG.
- When androgens bind to SHBG, it decreases SHBG synthesis.
- When **estrogen** binds to SHBG, it increases SHBG synthesis.

Role of androgens in females :

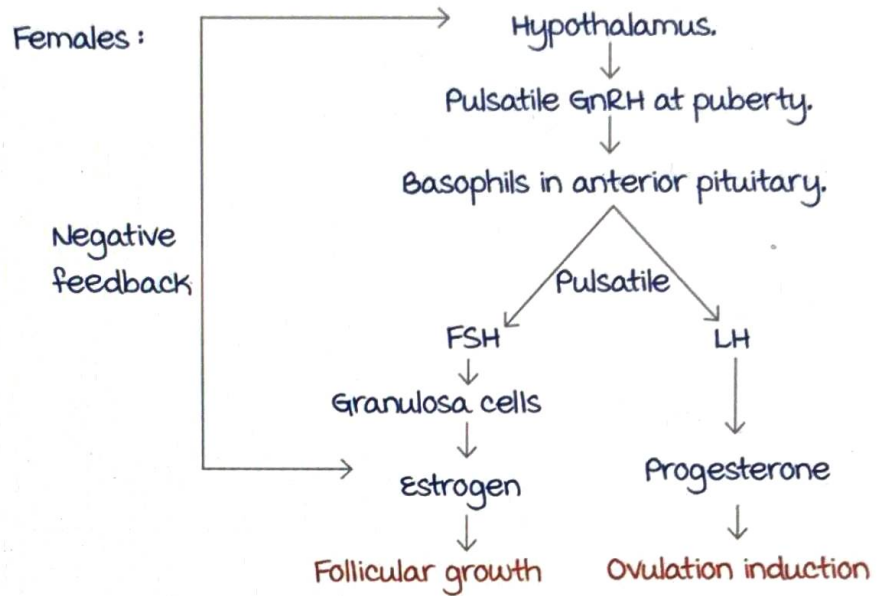
- Responsible for pubic and axillary hair growth (pubarche at the time of puberty).
- Responsible for libido/sexual drive.

Folliculotoxic if local concentration increases in ovaries. In patients of PCOS, increased androgens arrest the growth of the follicles (immature follicles) → Appear as cysts on the ultrasound.

# GYNAECOLOGY - PHARMACOLOGY INTEGRATION : PART - 1

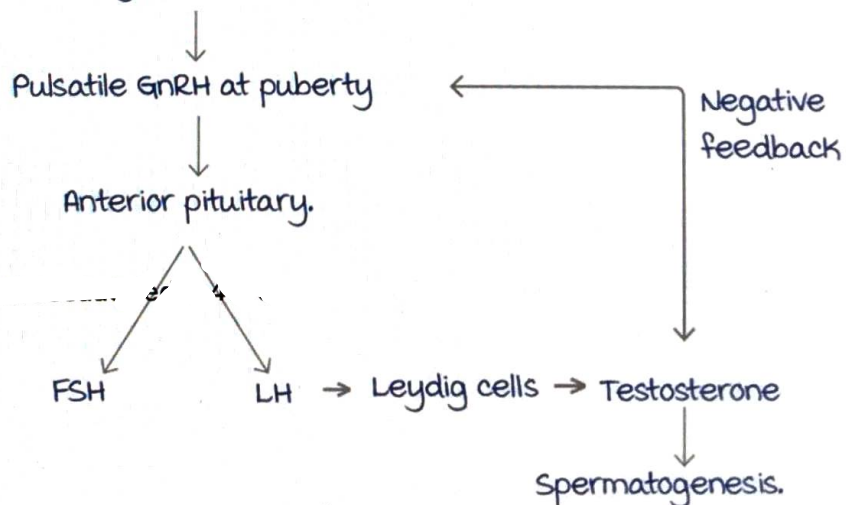
## Reproductive physiology

00:02:00



Estrogen has positive feedback on LH only during LH surge.  
Gonadotropin → FSH + LH (High estrogen)  
(Responsible for estrogen and Progesterone synthesis)

males : Hypothalamus



Active space

Hypogonadotropic Hypogonadism → Decrease in GnRH →  
Decrease in estrogen.

Gender	Condition	GnRH	FSH	LH	Estrogen
Female	Hypothalamic pathology : Decreased GnRH.  Anterior pituitary pathology : Decreased estrogen.	Decreased	Decreased	Decreased	Decreased
	Hypogonadotropic Hypogonadism.				
Female	Normal hypothalamus. Normal pituitary. Abnormal ovaries (e.g, Ovarian failure). Hypergonadotropic hypogonadism.	Increased	Increased	Increased	Decreased

**Deficiency of LH and FSH**

00:09:54

Females	males
Anovulation	Oligospermia (Decreased testosterone)
Delayed puberty (Decreased estrogen)	Delayed puberty

Excessive LH and FSH with normal ovaries and testes :

Females (excess estrogen)	males (excess testosterone)
Precocious puberty	Precocious puberty
Fibroid	Prostate cancer
Endometriosis	
Endometrial cancer	
Ovarian cancer	

Physiology :

LH acts on theca cells to produce androgens in females.  
So, increased LH → increased testosterone → Hirsutism.

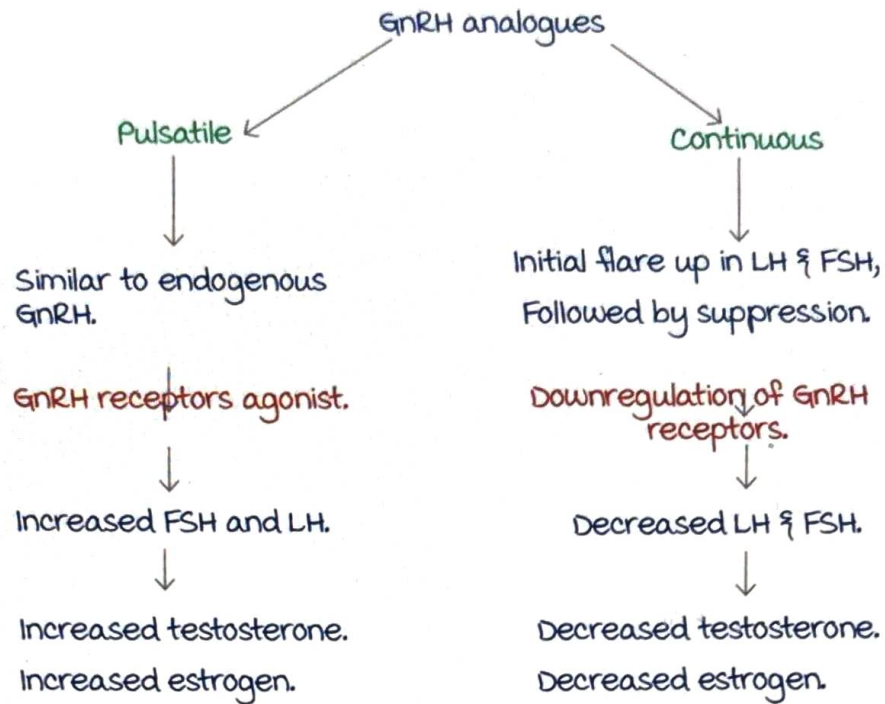
Active space



**GnRH analogues/synthetic GnRH**

00:15:00

GnRH : Paraventricular cells of the hypothalamus.



Indications for pulsatile GnRH	Side effects (excess FSH & LH)
Delayed puberty	Multiple ovulation
Hypogonadotropic Hypogonadism	Ovarian Hyperstimulation Syndrome (OHSS)
Kallmann syndrome. Decreased GnRH + Anosmia. (males > females)	Ovarian Cancer : Due to excess estrogen.
Anovulation	Theory of incessant ovulation : more the ovulation, more the chances of developing cancer
Sexual infantilism	

Active space

**Continuous GnRH/ GnRH antagonists**

00:24:48

Indications :

- Precocious puberty.
- Fibroid.
- Endometriosis.

- Hirsutism.
- Prostatic cancer.
- Estrogen-positive breast cancer.
- Theoretically, it can be given in ovarian & endometrial cancer, but surgery is preferred.

GnRH analogues and antagonists :

GnRH analogues	GnRH antagonists/ Continuous GnRH
Leuprolide Goserelin Buserelin Nafarelin Triptorelin	Ganirelix Cetrorelix (mc used) Relugolix, Elagolix (recently approved).
Inactive orally due to high 1 <sup>st</sup> pass metabolism.	Orally active.
Route of administration : Subcutaneous injection. Buserelin & Nafarelin : Intranasal.	Oral but very expensive.
Act as both activators & suppressors based on pattern of administration.	Always suppressors.
Causes initial flare up.	No flare up reaction.
	Adverse effects (Decreased FSH & LH) : males (decreased testosterone) loss of libido, impotence, reduced muscle mass. Females (decreased estrogen) : Infertility Osteoporosis Hot flushes } Symptoms similar to post menopausal women.

Applied :

Young girl with precocious puberty :

Give GnRH analogues continuously → Infertility, hot flushes, osteoporosis occurs.

To prevent this, add back therapy with Norethindrone (1<sup>st</sup> generation progesterone) → Small amounts of estrogen given.

## Synthetic LH & FSH

00:33:30

Human menopausal Gonadotropin (HMG)/ menotropin.

Obtained from the urine of post menopausal women.

Component : 75 IU LH + FSH.

Action : Increases FSH & LH.

Increases ovulation & estrogen.

Uses :

Ovulation induction in females with decreased LH & FSH (Hypogonadotropic hypogonadism).

In PCOS : LH increased, FSH normal. So, HMG 2<sup>nd</sup> line drug for ovulation induction.

In IVF cycles : To hyperovulate, therefore better chances of conceiving.

Draw backs :

30% chance of multifetal pregnancy (triplets & so on).

(Clomiphene → more chances of twin.)

Ovarian cancer.

5 - 15% chance of OHSS.

## Human chorionic gonadotropin

00:41:20

Human Chorionic Gonadotropin (hCG) is similar to LH.

Obtained from the urine of pregnant women.

Uses :

- Triggers ovulation with Clomiphene.

Dose of hCG : 5000 IU IM administration.

- Luteal phase support :

hCG helps in maintaining corpus luteum of pregnancy.

In patients with infertility due to decreased LH & FSH (Hypogonadotropic hypogonadism).

↓  
For infertility : HMG is administered.

↓  
Conceived after ovulation occurs.

↓  
hCG 2000 IU every 3 - 4 days or Progesterone.

## GYNAECOLOGY - PHARMACOLOGY INTEGRATION : PART 2

Recombinant FSH : Follitropin  $\alpha$ ,  $\beta$  and Delta.

Recombinant LH : Leutropin  $\alpha$ .

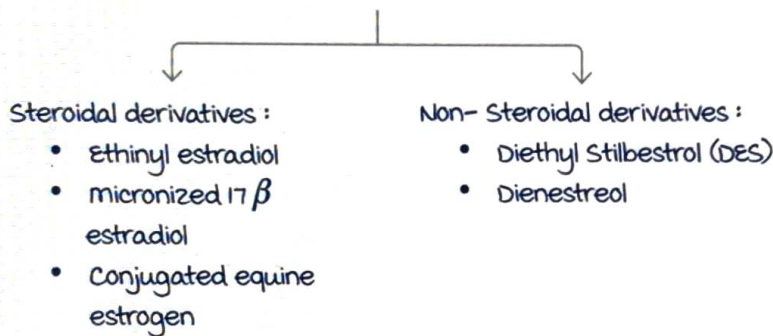
Recombinant hCG : Choriogonadotropin  $\alpha$ .

Recombinant FSH, LH, hCG are more purified but expensive than hCG.

Patients who have both LH, FSH deficiency : HMG is preferred due to cost.

### Synthetic estrogens

00:01:33



DES : No longer used as it lead to a number of congenital malformations in fetuses.

Female fetus : Clear cell Ca of vagina and cervix, hypoplastic uterus, T shaped uterus.

male fetus : Renal anomalies, cryptorchidism.

most potent : Ethinylestradiol (EE), hence used in OCPs.

$EE > E_a > E_1 > E_n$

Depending on the amount of Ethinylestradiol in OCPs :

- High dose pills : EE > 50 mcg (not used now as it can lead to thromboembolism).
- Low dose pills : EE < 50 mcg, ~ 30- 35 mcg.
- very low dose pills : < 20 mcg.
- Lowest possible dose of EE which exerts contraceptive effects is 10  $\mu$ g.

- Lowest dose is used to minimize risk of thromboembolism.

All preparations of synthetic estrogen are derived from plant sources except **Conjugate equine estrogen (CEE)** which is derived from urine of pregnant mares.

CEE has mainly Esterone ( $E_1$ ).

Dose equivalent :

0.625 mg of CEE = 1 mg of micronized  $17\beta$  estradiol.

5 mcg of EE.

0.05 mg of transdermal estradiol.

Uses :

1. Contraception (OCP, vaginal rings : **NUVA ring**, transdermal patches).
2. Hormone Replacement Therapy :
  - To treat hot flushes (vasomotor symptom).
  - **Osteoporosis** as estrogen increases bone mass.
  - Genitourinary symptoms like dry vagina that occurs due to scanty cervical mucus production.
3. Atypical uterine bleeding.
4. Non contraceptive benefits of OCPs.

Route of administration :

**Oral :**

- Have high first pass metabolism.
- High portal vein estrogen concentration leads to increased production of proteins in the liver like Sex Hormone Binding Globulin (SHBG), triglycerides, HDL & clotting factors.
- **Increased clotting factors** → Increased risk of venous thromboembolism.

These effects are not seen :

**Transdermal estrogen :**

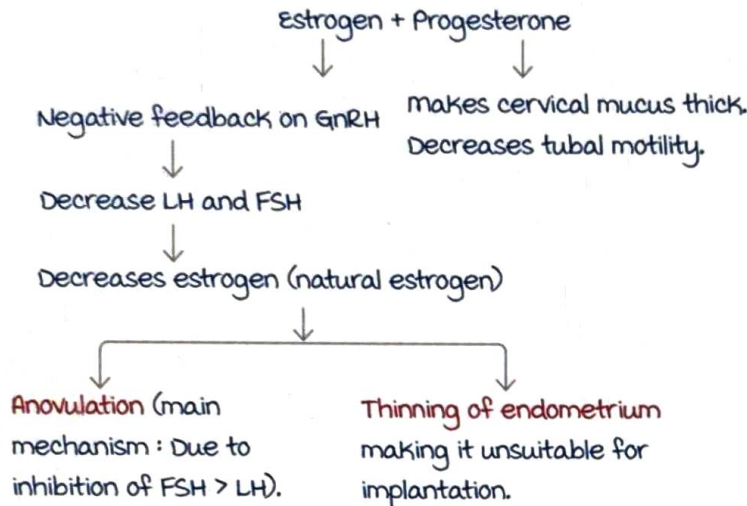
- As effective as oral estrogen.
- Associated with lower risk of venous thrombosis and stroke.
- Less effect on serum lipid concentration.

Hence, transdermal patch is the preferred route of HRT in post-menopausal females.

**Topical vaginal estrogen** : used to treat genitourinary symptoms like dyspareunia, senile vaginitis in post-menopausal females.

## Oral Combined Pills

00:14:36



Ethinyl Estradiol pill → Low dose pill (30 µg)

OCPs started on **day 1** of cycle → Given for **21 days** → **1 week pill-free interval**.

On taking OCPs : Exogenous estrogen and progesterone will be present, endogenous hormones will be reduced.

When the patient stops taking OCPs, there will be a sudden drop in the amount of estrogen and progesterone in her body, which causes menstruation.

Non contraceptive benefit of OCPs :

- Regularizes menstrual cycles : **DOC** for irregular cycles.
- Decrease menstrual blood loss : Decreased amount of estrogen and progesterone causes limited proliferation of endometrium, forming thin endometrium.
- **DOC** : **Puberty menorrhagia** :

Occurs due to anovulatory cycles in puberty

Excessive estrogen is **not** balanced by progesterone.

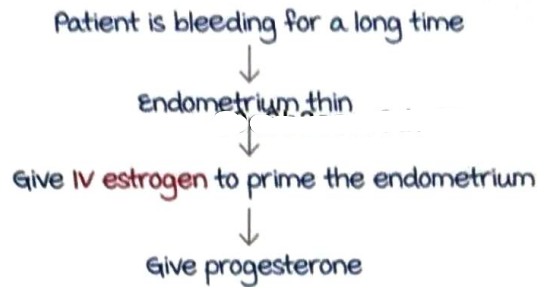
Excess estrogen proliferates endometrium.

Causes **breakthrough bleeding**.

Vitals stable : Give OCPs

- Progesterone can act only on estrogen primed endometrium.
- On taking OCPs : Progesterone **cements** the endometrium and prevents it from shedding.

Vitals unstable :



- OCPs suppresses ovary → Can be used for **managing simple ovarian cysts**.
- OCPs → Decrease LH → Decrease androgens → **DOC for hirsutism**.

In **idiopathic hirsutism**, androgen levels are normal, OCPs may or may not be effective.

Adverse effects of estrogen :

- Nausea and vomiting.
- Increase clotting factors → Increase thrombosis. Hence **contraindicated** in patients with history of thrombosis, stroke, CAD, conditions which predispose to thrombosis e.g., prolonged immobility, lupus anticoagulant present.
- Estrogen stimulates RAAS → Increased aldosterone → Salt and water retention → mild hypertension. Hence, OCPs/ HRT are contraindicated in patients with **severe uncontrolled hypertension** (BP ≥ 160/110 mmHg). In medically controlled hypertension, OCPs/ HRT are not contraindicated.
- Cancers :
  1. Uterus : **Endometrial cancer** (due to estrogen component).
  2. Liver : **Hepatic adenoma** (estrogen component).

3. Breast : Slight increases chances of breast cancer (due to progesterone component).

- In females **with uterus** requiring HRT, give **estrogen + progesterone**.  
Progesterone (anti-proliferative) is added for protecting the endometrium.
- In females **without a uterus** requiring HRT, give **only estrogen**.

Oral HRT is used **only for severe hot flushes** that interferes with daily life.

Advantages :

- Increases bone mass.
- Reverses dryness of vagina.
- Relieves vasomotor symptoms.

### Selective Estrogen Receptor Modulators

00:39:33

Act as agonist of estrogen at certain sites and antagonist at certain organs.

- Clomiphene.
- Tamoxifen.
- Raloxifene.
- Ospemifene.
- Ormifloxifene.
- Bazedoxifene.

Clomiphene :

Non-steroidal triphenyl-ethylene derivative.

Has 2 stereoisomers :

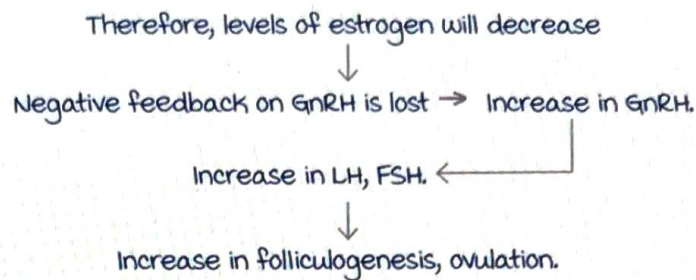
Zuclomiphene	Enclomiphene
38%	62%
CIS isomer	TRANS isomer
Less potent	more potent : <b>greater antiestrogenic activity</b> , primarily responsible for follicular development
Longer half-life	Shorter half-life

Active space



mechanism of action :

Acts on estrogen receptors in hypothalamus for a prolonged time and down-regulates them.



Side effects :

- Hot flushes due to reduced estrogen. (most common side effect).
- Dryness of vagina.
- Multifetal pregnancy (broad range : 4-7%, narrow range : 6-8%) : Due to increased folliculogenesis. Leads to increase in twin pregnancy.
- Ovarian hyperstimulation syndrome (mild and rare).
- Increase in ovarian cyst formations. (Second most common side effect).

Due to central action :

- Headache due to central action of clomiphene.
- Blurring of vision (stop the drug).

Prerequisite for clomiphene to act :

Functional Hypothalamo-Pituitary-Ovarian axis : Check FSH, LH.

When there is decreased FSH, LH (hypogonadotrophism) indicates problem in hypothalamus or pituitary, clomiphene cannot be used.

Clomiphene can be used for infertility only when FSH, LH levels are normal or increased.

Conditions where clomiphene is used :

- PCOS for infertility treatment. LH increased, FSH decreased.

DOC : Letrozole.

2<sup>nd</sup> DOC : Clomiphene citrate.

- unexplained infertility :

Clomiphene + Intrauterine insemination for 3 cycles.

DOC for anovulation in PCOS : Letrozole.

DOC for anovulation due to any other cause with normal LH, FSH : Clomiphene citrate.

Causes of anovulation where HPO is not intact :

- Hypogonadotropic hypogonadism.
- Kallman's syndrome (absent GnRH).
- Pituitary ablation.

For these causes, treatment is pulsatile GnRH or HMG.

Starting dose of clomiphene citrate : 50 mg OD for 5 days.

Maximum dose is 150 mg OD.

Clomiphene citrate can be started any day between

Day 2 to Day 5.

Usually given on Day 5, given for 5 days (up to Day 9)

LH surge is seen 5 to 12 days after stopping the drug.

Any one of the following advice to be followed :

- Have intercourse daily after 5 days of stopping the therapy till 1 week (from Day 14 onwards).

- Use urinary LH kits to predict LH surge :

The test will be positive once LH surge occurs →

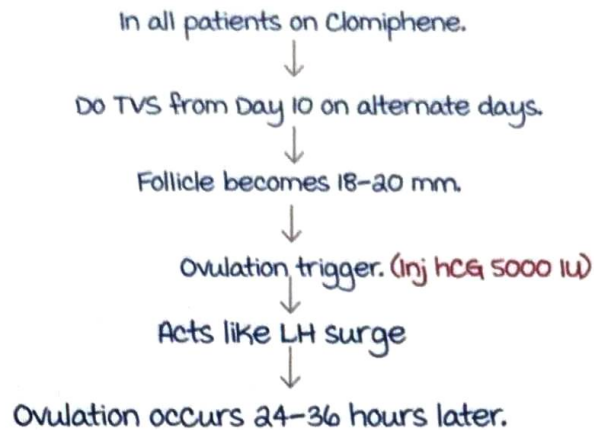
Ovulation occurs 48 hours later.

Hence patient is advised to have intercourse daily for 4-5 days once the test becomes positive.

- Follicular monitoring : From Day 10 onwards follicular monitoring is done by TVS on alternate days.

Once the follicle size becomes  $\geq 15\text{mm}$  → Advised to have intercourse daily for 4-5 days.

Clinical :



Inj. hCG is not mandatory in all patients on clomiphene.  
(Inj. hCG 5000 IU used for LH surge)

Ovulation rate : 80%

Pregnancy rate : 30-40%

Since all SERMs have antagonistic action on uterus,  
vagina, and cervix.

uterus : Endometrium will become thin and becomes  
unsuitable for implantation. Cervical mucus becomes  
thick.

HMG is preferred for IVF as it increases estrogen whereas  
Clomiphene decreases estrogen.

Side effects → Headache, blurring of vision.

Effects **not seen** with Clomiphene citrate :

- Does not increase risk of teratogenicity.
- Does not increase risk of CA Breast.
- Does not increase risk of CA Ovary.

Success rate of clomiphene is decreased when :

- Age > 35 years.
- BMI > 25 → 75 g 2-hour OGTT → Insulin resistance present → **Clomiphene citrate + metformin**.
- Hyperandrogenism : **Clomiphene citrate + Glucocorticoids** (which do not cross the placenta like prednisolone or hydrocortisone).

maximum number of cycles in which clomiphene can be tried  
is **6 cycles**.

## GYNAECOLOGY - PHARMACOLOGY INTEGRATION : PART 3

### Tamoxifen and Raloxifene

00:00:10

**SERM** (Selective estrogen receptor modulators) :

Organ	Tamoxifen effects	Raloxifene effects
Breast	Antagonist. 1 <sup>st</sup> line for ER+ breast cancer in premenopausal women for both treatment and prophylaxis.	Antagonist. ER+ breast cancer.
Vagina	Antagonists : Vaginal dryness. Cannot be used for senile vaginitis, dyspareunia in post menopausal women.	
Uterus	Agonist. Increased risk of endometrial cancer,	Antagonist. No risk.
Ovulation induction	Not used.	
Bone	Agonist. Not used because of side effect.	Agonist. Osteoporosis.
Clotting factors	Increased → Increased risk of venous thromboembolism.	
Hot flashes (due to lack of estrogen)	Common side effect. Should <b>not be used</b> to treat hot flashes. Treatment : Ethinyl estradiol + Bazedoxifene (decreases the risk of endometrial cancer due to estrogen) in post menopausal women.	

### Other important SERMs

00:10:24

- 1). **Ospemifene** : Can be used for vaginal dryness, senile vaginitis, dyspareunia in post menopausal women.
- 2). **Orniloxifene** : Active component of centchroman, a non steroidal contraceptive agent.

Approved by Government of India to be a part of National family planning program by the name chaya (earlier called as sahel).

Active space

Hyper estrogenic conditions :

- Endometriosis.
- Fibroids.
- Endometrial carcinoma.
- Ovarian carcinoma.

Risk factors	Protective factors
Obesity. Increased peripheral conversion of androgen to estrogen in adipose tissues.	Physical exercise. Reduces adipose tissue, reduced production of estrogen.
Nulliparity	multiparity.
Early menarche, late menopause as both lead to increased exposure to estrogen.	<b>Smoking</b> : Inhibits aromatase. <div style="text-align: center;">           Androgens            ↓ Aromatase            Estrogens.         </div> Smoking also protective in pregnancy induced hypertension).

### Management of hyper Estrogenic conditions

00:15:38

Decreases estrogen levels.

**Best** : Continuous GnRH.

**1<sup>st</sup> Line** : Progesterone.

Others :

Letrozole : Aromatase Inhibitor.

Danazol : Progesterone like effects + androgen like side effects (hirsutism). ~~sa. not used in women.~~

Gestrinone : Similar to progesterone.

**Letrozole** : DOC for **PCOS Infertility**.

mechanism of action : Inhibits aromatase in the periphery (adipose tissue) and decreases conversion of androgens to estrogen.

Decreased estrogen in periphery

No Negative feedback → Increased FSH → Folliculogenesis & increased LH → Ovulation.

Dose : 2.5 mg for 5 days from day 3 of menstrual cycle.

In PCOS with amenorrhoea, rule out pregnancy and start Letrozole.

### Letrozole v/s Clomiphene

00:23:38

Clomiphene	Letrozole
Centrally acting via hypothalamus.	Peripherally acting.
Overall decrease in estrogen.	Peripheral decrease in estrogen.
Thinning of endometrium.	Maintains endometrial thickness leading to increased pregnancy and live birth rates.
Hot flashes ++.	Hot flashes decreased.
Risk of OHSS.	No chance of Ovarian Hyperstimulation Syndrome (OHSS).
Risk of multifetal pregnancy are comparable.	
Can be used only in the presence of a functional HPO axis.	

Letrozole does not increase the risk of fetal congenital malformations.

	Condition	Drug Of choice (DOC)
1	Infertility due to PCOS.	Letrozole
2	unexplained infertility.	Clomiphene citrate
3	Infertility with decreased LH, decreased FSH. MRI : Normal pituitary.	Injection HMG

4	Infertility with decreased LH, decreased FSH. MRI: Absent pituitary (empty sella tursica).	Injection HMG or pulsatile GnRH
5	Infertility with decreased LH, decreased FSH + anosmia (Kallmann syndrome).	Pulsatile GnRH

## Progesterone

00:29:29

Generation	Names of progesterone
1 <sup>st</sup>	Norethindrone (estrogen + androgen action). medroxy Progesterone Acetate (MPA) (androgen action).
2 <sup>nd</sup>	Levonorgestrel (less androgenic action).
3 <sup>rd</sup> (least androgenic action).	Desogestrel (MC used in OCPs). Gestodene. Norgestimate. Etonorgestrel.
4 <sup>th</sup> (anti-androgenic).	Drospirinone. Dienogest. Cyproterone acetate. Drospirinone. Dienogest. Cyproterone acetate.

### Applications of progesterone :

1. Norethindrone : Add back therapy in long term GnRH therapy.

2. In PCOS :
 

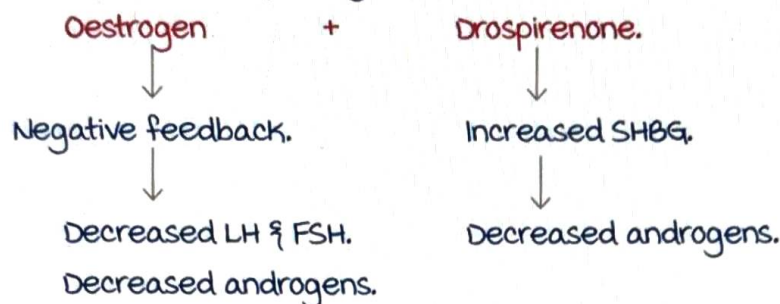
PCOS	}	menstrual irregularity	}	OCPs (3 <sup>rd</sup> /4 <sup>th</sup> generation only).
		Hirsutism		

3. Drospirinone :

- Derived from Spironolactone → Aldosterone antagonist → Diuretic activity.
- Salt and water excretion → Excretion of Na<sup>+</sup> and

retention of  $K^+$  → use in caution in renal disease patients.

- Estrogen → Retention of salt and water. Antagonized by Drospirenone.
- Patients who develop fluid retention on OCPs/ mild hypertension, give OCP + Drospirenone.
- Anti androgenic effect : Increases Sex Hormone Binding Globulin (SHBG) → Decreased free testosterone.
- In PCOS with hirsutism and in patients with hirsutism who need contraception, give



3<sup>rd</sup> and 4<sup>th</sup> generation progesterone do not alter lipid metabolism.

## Uses of progesterone

00:38:19

1. menstruation regulation : MPA for 7-10 days, then suddenly withdrawn.  
Sudden decrease in progesterone → menstruation.
2. Delay periods : Take progesterone (primolut - N 5mg TDS) 2-3 days before periods. She will menstruate once she stops taking progesterone.
3. Endometrial thinning : used in endometriosis, fibroid, endometrial hyperplasia without atypia.
4. Contraception.
5. Hormone replacement therapy along with estrogen to protect the endometrium in females with intact uterus.
6. Obstetrics : In luteal phase defect and to prevent preterm labour (smooth muscle relaxant).



Selective progesterone receptor modulator :

Ulipristal → Blocks progesterone effects → Blocks ovulation →

Emergency contraception.

Dose : 30 mg single dose.

Severely hepatotoxic.

Progesterone antagonist :

mifepristone/RU 486 : Decreases progesterone.

Used in medical abortion.

## Anti-androgens

00:43:42

1. Spironolactone : Diuretic with anti-androgenic activity.

Dose : 50-100 mg BD.

Uses : Hirsutism.

Side Effect : Hyperkalemia, orthostatic hypertension, loss of libido (in both men and women).

2. Finasteride : 5 $\alpha$  reductase inhibitor. used for hirsutism & androgenic alopecia.

3. Flutamide : Hepatotoxic.

4. Topical eflornithine : Inhibits ornithine decarboxylase → Arrests hair growth.

management of hirsutism :

DOC : OCP with drospirinone for 6 months.

If it fails :

- Spironolactone.
- Cyproterone Acetate.
- Flutamide.
- Finasteride.
- Topical eflornithine.
- Continuous GnRH.

Danazol can never be used to treat hirsutism as it causes hirsutism.

# GYNAECOLOGY PATHOLOGY

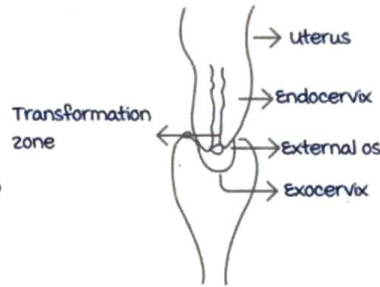
## INTEGRATION : PART 1

### Applied anatomy of cervix

00:01:20

#### Endocervix :

- Closer to the uterus.
- Lined by **columnar epithelium** : Can give rise to adenocarcinoma of cervix.
- Per speculum examination : Appears **red**.



#### Exocervix :

- Lies inside the vagina.
- Also called as portio vaginalis.
- Lined by **stratified squamous epithelium**.
- Per speculum examination : **Appears pink**.

Cervix opens into vagina at **external os**.

Area where columnar epithelium of endocervix changes into squamous epithelium of exocervix is called as **transformation zone**.

Transformation zone lies near to the external os. It is a **dynamic point** : Can move inside or outside based on hormonal status.

Transformation zone is the **pale area** between endocervix and exocervix on per speculum examination.

#### Per speculum examination :



Active space

most common site for cancer of cervix : Transformation zone.

most common cancer in cervix : Squamous cell carcinoma.

most common site for adenocarcinoma of cervix : Endocervix.

Pap smear :

- It is a cytology based test which detects current cellular changes in the cervix.
- 2 samples should be taken from transformation zone and endocervix.
- These changes are most prominent in superficial layers (douching/intercourse to be avoided before a pap smear).
- Used as a screening test for cancer cervix. It can detect certain infections as well.

methods of doing pap smear :

1. Conventional method :

Slide is prepared using Ayers spatula (wooden or plastic)/endocervical brush.

2. Liquid based cytology :

Specimen obtained by cervical broom is put in fixative directly. Ayers spatula (plastic)/endocervical brush can obtain specimen but wooden spatula cannot be used.

Advantages :

HPV DNA testing can be done from the same sample. Smaller area to screen and quality of slide is better.

Instruments used in pap smear :



Ayers spatula and endocervical brush

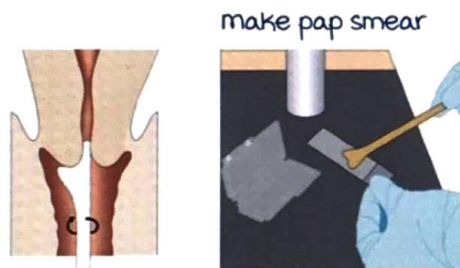


Cervical broom

### Conventional pap smear

00:10:22

**Transformation zone** : First sample is taken at the level of external os using Ayers spatula from bifid end. Concavity of the spatula fixes into the transformation zone. Smaller limb is kept at the level of external os, and the longer limb is placed inside endocervix. Spatula is rotated 360 degrees for 2-3 times and sample is smeared on a slide.



make pap smear

**Endocervix** : Endocervical brush is placed in endocervix and rotated 180 degrees 2-3 times. Sample is smeared on the same slide.

- As thin as possible
- Properly labeled



Slide should not air dried. It should be dipped into fixative : 95% ethyl alcohol  $\pm$  5% ether. Ether is not used nowadays as it is highly inflammable.

Active space

Note :

Any friable/raised lesion seen on cervix (except nabothian cyst) during pap smear should be biopsied.

For conventional pap smear, satisfactory sample should have 8,000 to 12,000 well visualized squamous cells/10 HPF + at least 10-12 endocervical cells.

Liquid based cytology :

2 methods : SurePath method and ThinPrep method.

**SurePath method :**

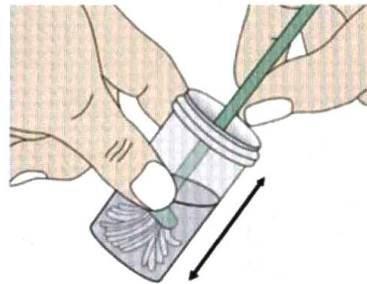
A single cervical brush is used to take the sample from the transformation zone and endocervix.

Longer bristles go into endocervix and shorter bristles rest on the transformation zone.

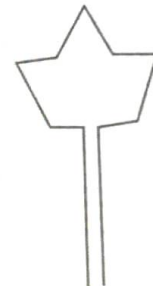
Cervical brush is rotated 5-6 times and sample is put in a container with fixative.

Cervical brush head is broken into fixative.

Lid is closed and shaken. A smear is prepared.



Liquid based cytology



Cervical brush

**ThinPrep method :**

Ayers spatula and endocervical brush are used to take the sample from the transformation zone and endocervix.

The specimen obtained is put directly into fixative (methanol).

Fixative is filtered to get the concentrated specimen. A smear is prepared using concentrated specimen.

Satisfactory smear should have 5000 squamous cells/10 HPF + at least 10-12 endocervical cells.



Liquid based cytology



Conventional pap smear

Active space

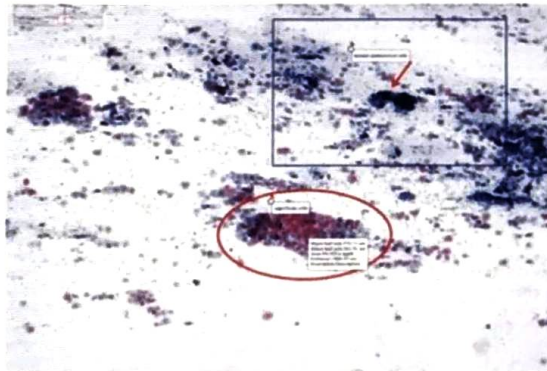
Important points :

- Do **not** do P/V examination before pap smear.
- Instruct patient against **vaginal douching**, use of **vaginal lubricants**, **intercourse** at least 48 hours prior to pap smear.
- Bleeding is not an absolute contraindication for pap smear. If blood is present at external os, remove with cotton swab and perform the test.
- Active bleeding in **menstruation** is a relative contraindication for conventional pap smear. Bleeding does not interfere at all with liquid based cytology.
- If patient is having discharge, wipe it off and take a pap smear.
- Obscuring factors of pap test :
  - Blood.
  - Air artefacts.
  - Inflammation.

If **> 75%** of smear is obscured by any of these, sample is called as inadequate.

- Interfering substances are **semen** and **lubricants**.

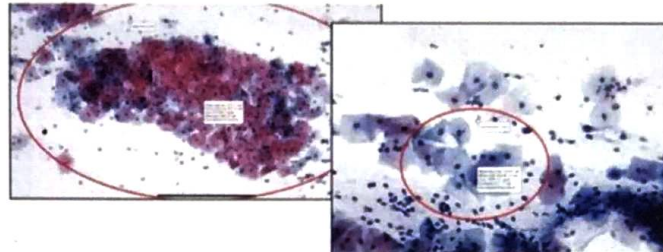
Normal pap smear :



4 types of cells :

- Superficial cells** : Pink colored eosinophilic cells, polygonal, pyknotic nuclei.  
~~Seen under~~ the influence of **estrogen**.
- Intermediate cells** : Blue colored cells, polygonal, slightly bigger nucleus.  
Seen under the influence of **progesterone**.

- C. **Parabasal cells & basal cells** : Basophilic small rounded/elongated cells with slightly bigger nucleus. Seen when there is no hormonal predominance.
- D. **Endocervical cells** : mucin filled cells arranged in **honey comb appearance** or **picket fence arrangement**.

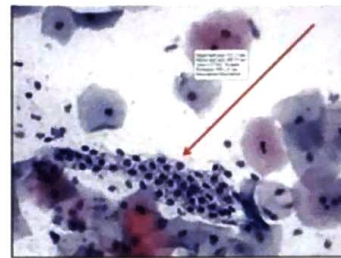


Superficial cells

Intermediate cells



Parabasal cells



Endocervical cells

**maturation index** :

100 cells count : Percentage of parabasal/intermediate/superficial cells.

**Karyopyknotic index (KPI)** : Number of mature superficial squamous cells divided by intermediate + basal cells.

Higher the level of **estrogen**, higher the karyopyknotic index.

Proliferative phase : KPI >25%.

Secretory phase : KPI is very low.

KPI peaks just before ovulation/on day of ovulation.

### Pap smear in cervical premalignancy

00:29:06

**Abnormalities** :

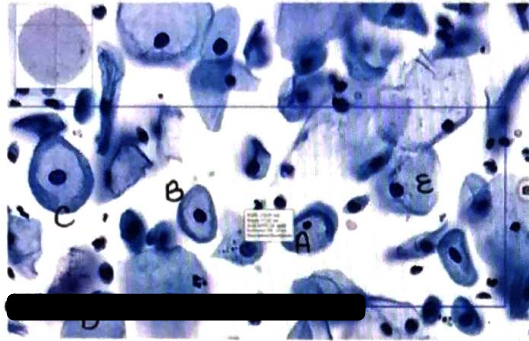
- **Nucleus enlarged** : Typical.
- **Paranuclear halo/clearing** : Typical.
- Nuclei become bifid.
- Hyperchromatic nuclei.

These changes in superficial and



intermediate cells indicate HPV infection.

HPV infected cells are called as **koilocytes**, and changes are called as **koilocytosis**.



Cells A, B and C : Perinuclear halo.

Cell D and E : Typically showing eccentric nuclei with perinuclear halo.

**metaplasia :**

In cervix, columnar cells of endocervix changes into squamous cells of exocervix at transformation zone.

It is physiological.

If this metaplasia occurs in a disorganized manner, it is called as **dysplasia**.

It is **pre-malignant and pathological**.

Characteristic of dysplastic cells :

Increased nucleus : Cytoplasmic ratio.

Bethesda system :

Dysplasia could be :

- LSIL : Low squamous intraepithelial lesion.
- HSIL : High squamous intraepithelial lesion.

Note :

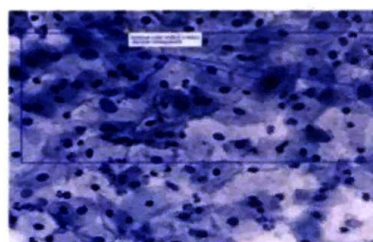
If on pap smear, koilocytes + nuclear abnormalities : LSIL.

LSIL :

Dysplastic cells.

Increased nucleus : cytoplasmic ratio but ratio is **< 1 : 3**.

Hyperchromatic nuclei (darker





than surrounding cytoplasm of cell).

No nucleoli

margins of nuclei are irregular (raisin clusters).

(If koilocytic changes are seen, include in LSIL).

HSIL :

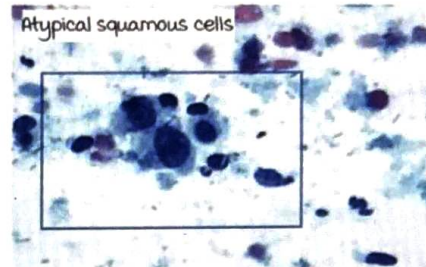
Increased nucleus :

cytoplasmic ratio.

Nucleus is  $\geq 50\%$  of  
cytoplasm.

Hyperchromatic nuclei.

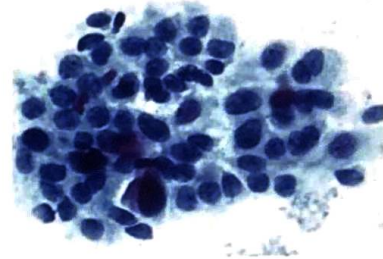
Nucleoli may be seen.



Atypical glandular cells :

Clumps of cells with increased  
nuclear cytoplasmic ratio.

Nucleus is hyperchromatic but  
is see through. Nucleoli can  
be seen.



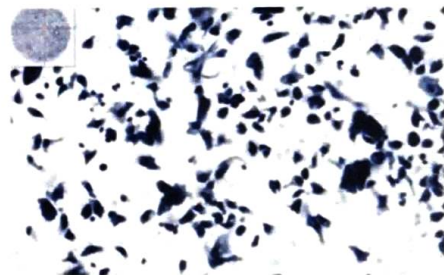
Squamous cell carcinoma :

Irregular bizarre cells :

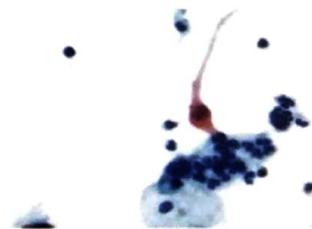
Tadpole cells.

marked hyperchromatism :

It seems as if entire slide  
is smudged with ink.



Tadpole cell (orange color is due  
to keratinization) : Indicates  
well differentiated keratinized  
squamous cell carcinoma.



## Vaginal flora

00:43:32

Normally lactobacilli (doderlein bacilli) converts glycogen in  
vaginal epithelium into lactic acid and maintains acidic pH of  
vagina.

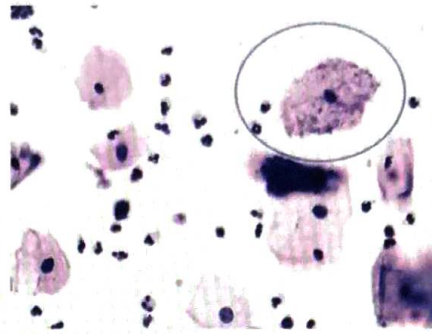
These lactobacilli may be visible on pap smear as small rod  
like organisms.

Alteration in normal vaginal flora :

Bacteria (cocci/bacilli) are  
adhered to epithelial cell :

Clue cells.

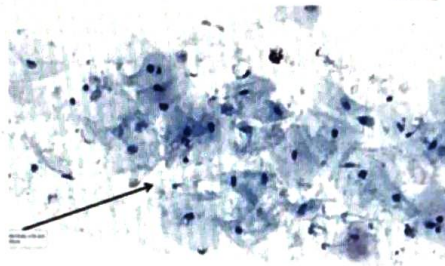
≥ 20% clue cells are seen in  
bacterial vaginosis.  
In bacterial vaginosis,  
lactobacilli are absent.



Note : This pap smear is taken in proliferative phase.

Thread like structures :

Leptothrix associated with  
trichomonas infection.

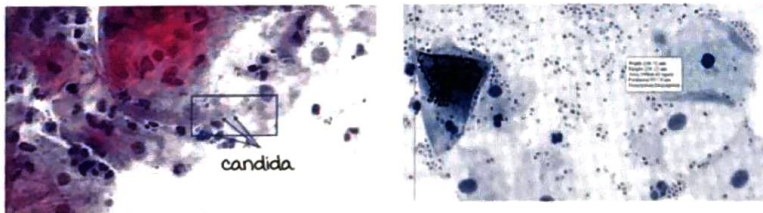


Note : This pap smear is taken in secretory phase or  
pregnancy.

### Infective organisms seen on pap

00:47:52

Candida spores :



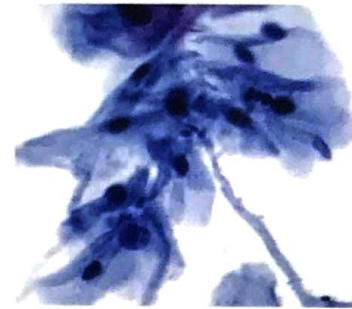
Small organisms which are smaller than the nucleus of  
epithelial cells.

Pseudohyphae of candida in  
liquid based cytology.

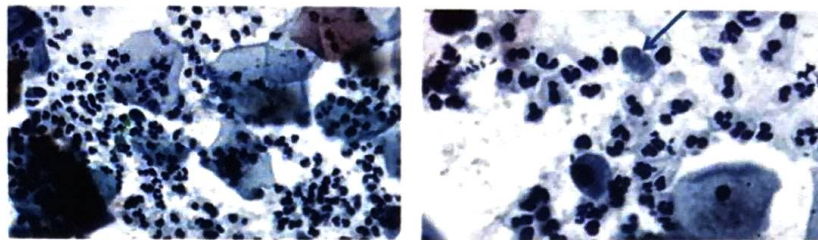


Active space

The squamous epithelial cells are adhered to pseudohyphae :  
 Shish kebab/seekh kebab appearance.



Trichomonas :



Pear shaped organism which is smaller than the cell (roughly size of nucleus of epithelial cells).

Has eccentric nuclei.

Trichomonas is commonly associated with leptoithrix :

Spaghetti and meat ball appearance.

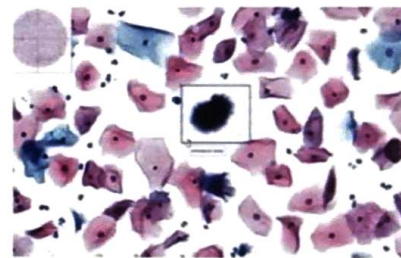
Actinomyces :

Cotton wool appearance :

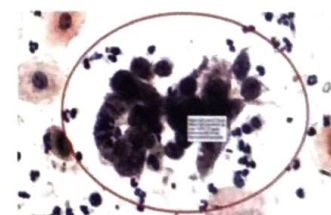
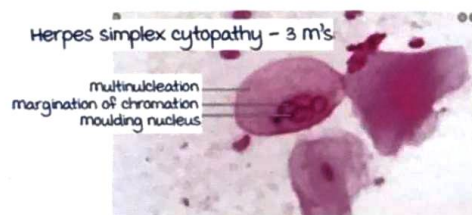
Actinomyces.

most common infection in

IUCD users.



Herpes simplex virus :



3 m's :

~~multinucleation~~

margination.

moulding (overcrowding of nucleus).

Also shows hyperchromatism, big nuclei.

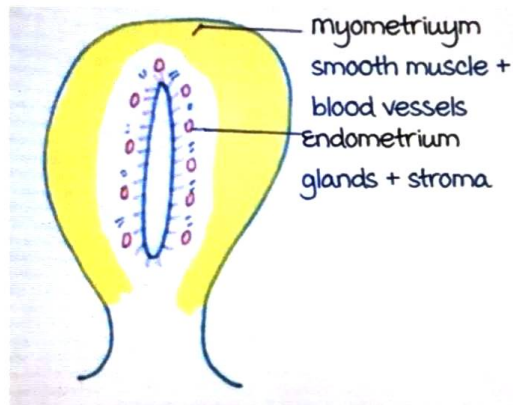
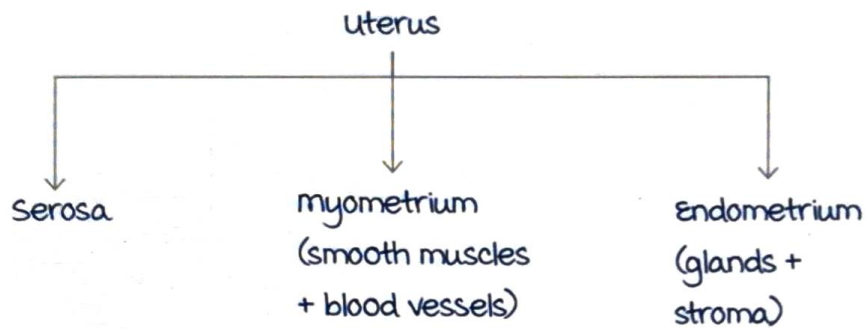
Active space

# GYNAECOLOGY PATHOLOGY

## INTEGRATION : PART 2

### Cultivation of bacteria

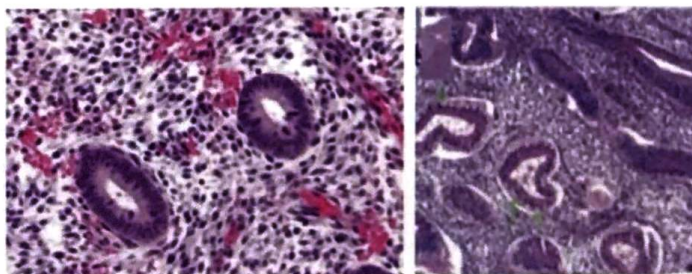
00:04:38



### Endometrial biopsy

00:00:43

endometrial biopsy has glands and stroma.



Proliferative phase

Early secretory phase

Active space

<p>Simple, tubular glands. Resemble Hen's egg. <b>Pseudostratified</b>: Nuclei appear to be at multiple layers.</p>	<p>Glands have begun to coil. <b>Sub-nuclear vacuoles</b> present. (First sign of ovulation on endometrial biopsy) Piano sign. Seen on <b>Day 17</b> of cycle.</p>
---	--

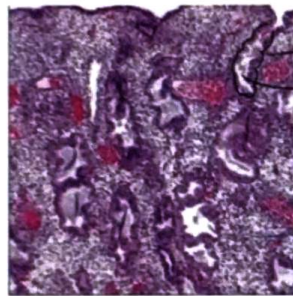
Late Secretory Phase :

**Saw-tooth/ Cork-screw appearance** of glands.

White areas within these highly coiled glands represent their secretions.

Spiral arterioles and decidualisation of cells are represented by the pink areas.

**Decidualisation**: Cells around the spiral arterioles acquire abundant pink cytoplasm.



Late secretory phase

**Endometrial hyperplasia**

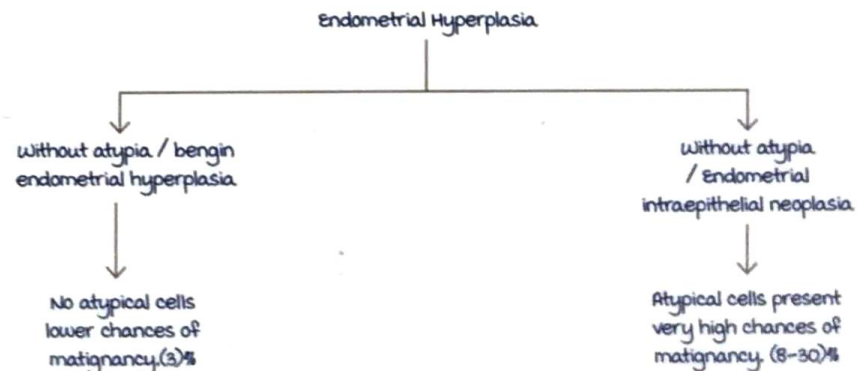
00:04:11

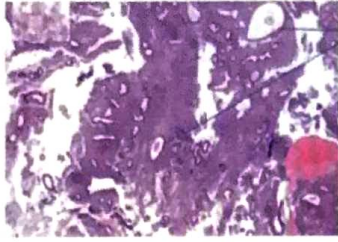
Normal Endometrium :

(Gland : Stroma) : (1 : 3)

In case of Endometrial hyperplasia the number of glands increase significantly resulting in overcrowding of glands and leads to the increase in the (Gland : Stroma) ratio.

Active space





Endometrial Hyperplasia with  
out Atypia.

Dilated glands.  
Normal Epithelium.  
Number of glands is more than  
usual.



Endometrial Hyperplasia with  
Atypia.

Overcrowding of glands.  
Nuclear Abnormalities are seen.

### Endometrial carcinoma histology :

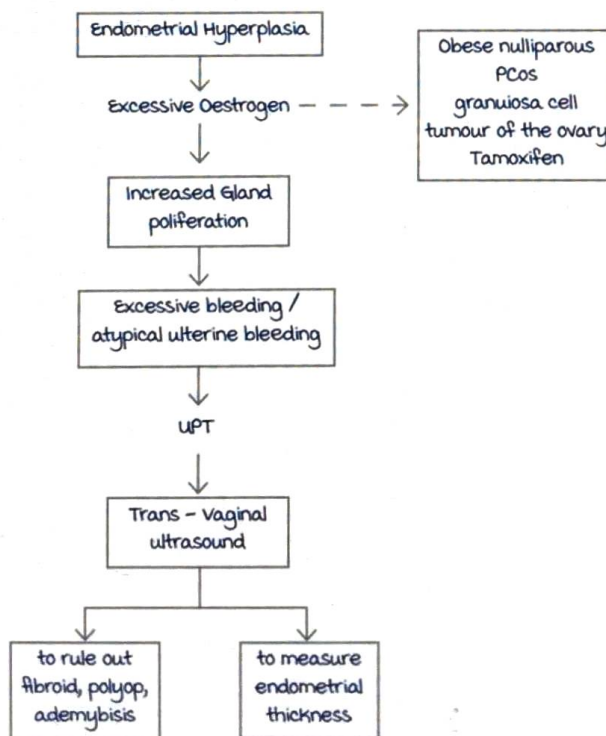
Gland overcrowding increases significantly ; Back-to-back  
arrangement.

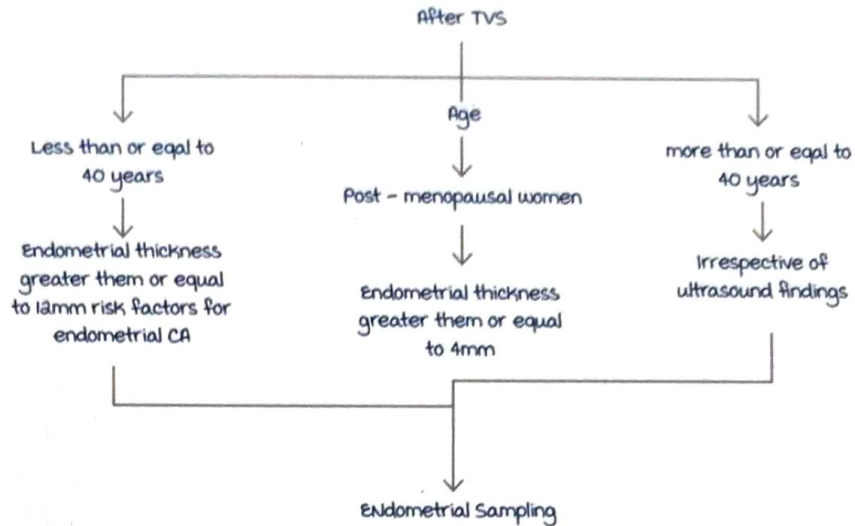
mitotic figures are seen.

Nuclei appear hyperchromatic.

Various nuclear abnormalities are observed.

### Endometrial hyperplasia clinical presentation 00:08:46

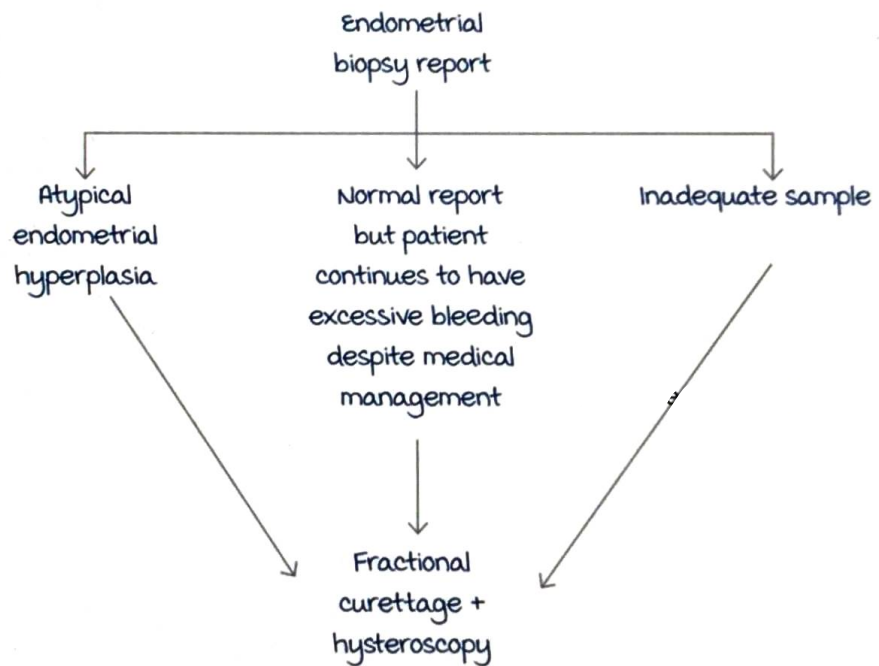




Endometrial Sampling could either be done Endometrial Biopsy or Endometrial Aspiration Cytology both of which are OPD procedures.

**Endometrial biopsy report**

00:15:58



Investigation of choice for assessing Endometrium/  
Endometrial Hyperplasia/Endometrial CA :

**Endometrial Sampling**  
**(Endometrial Biopsy/Endometrial Aspiration Cytology)**

Active space

Gold Standard for assessing Endometrium / Endometrial Hyperplasia / Endometrial CA :

(Fractional Curettage + Hysteroscopy)

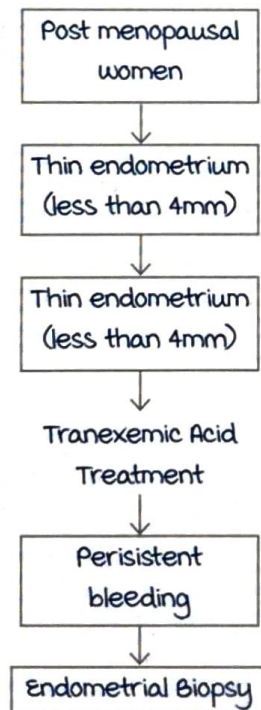
**Fractional Curettage** : The procedure involves obtaining samples of the uterus in sections with each section being assessed separately.

Hysteroscopy is highly effective for detecting Intra-cavitary focal lesions.

Curettage is better in cases where we see a uniform distention of the uterus.

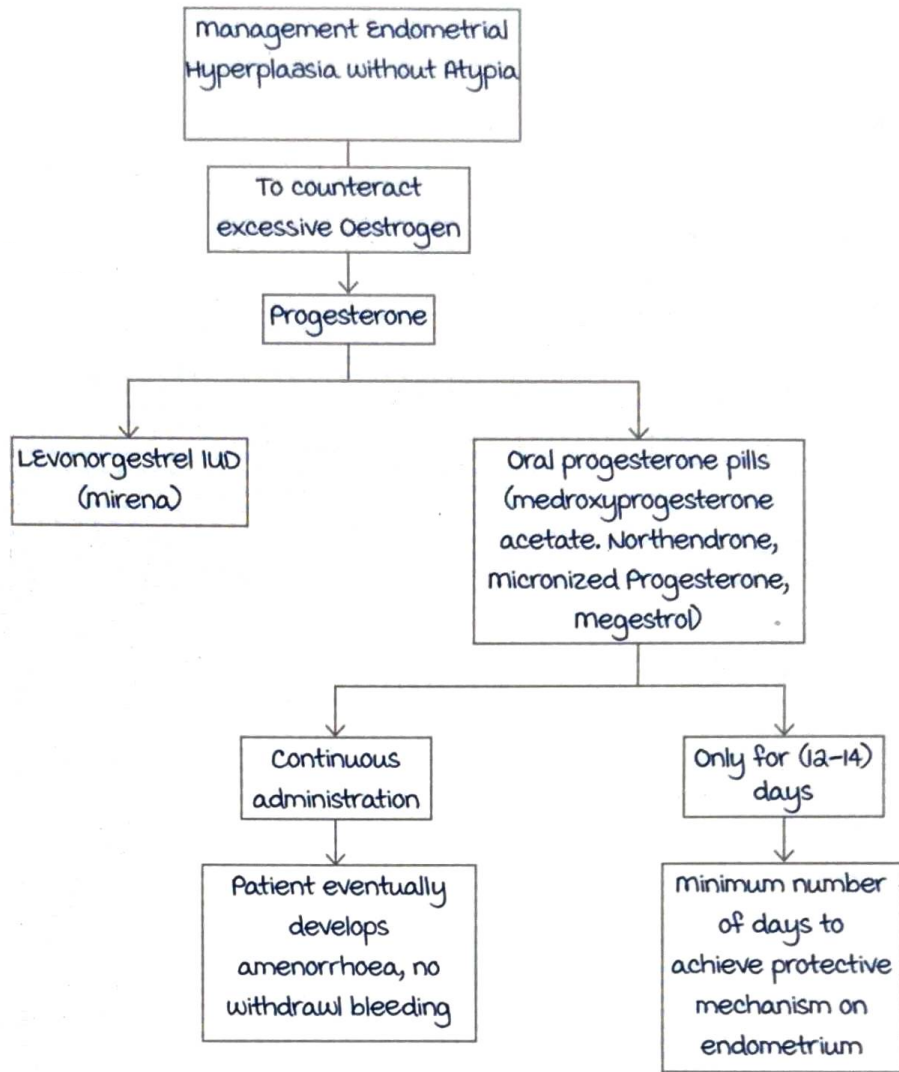
If the patient continues to have excessive bleeding despite medical management, endometrial biopsy is taken **irrespective of age**.

This holds good even in post-menopausal women with persistent bleeding despite medical management even though they have an atrophied endometrium.



Active space

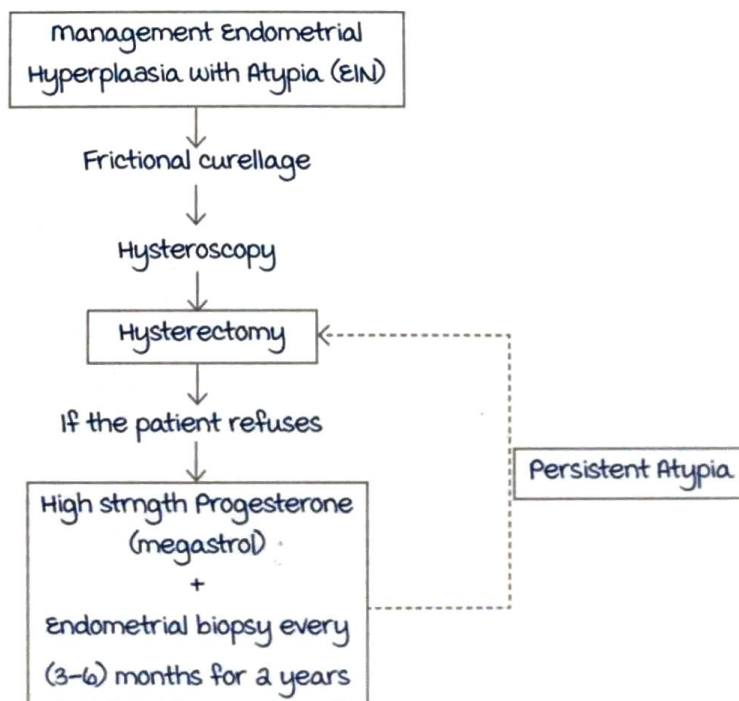




**Management of endometrial hyperplasia**

00:18:35

Active space



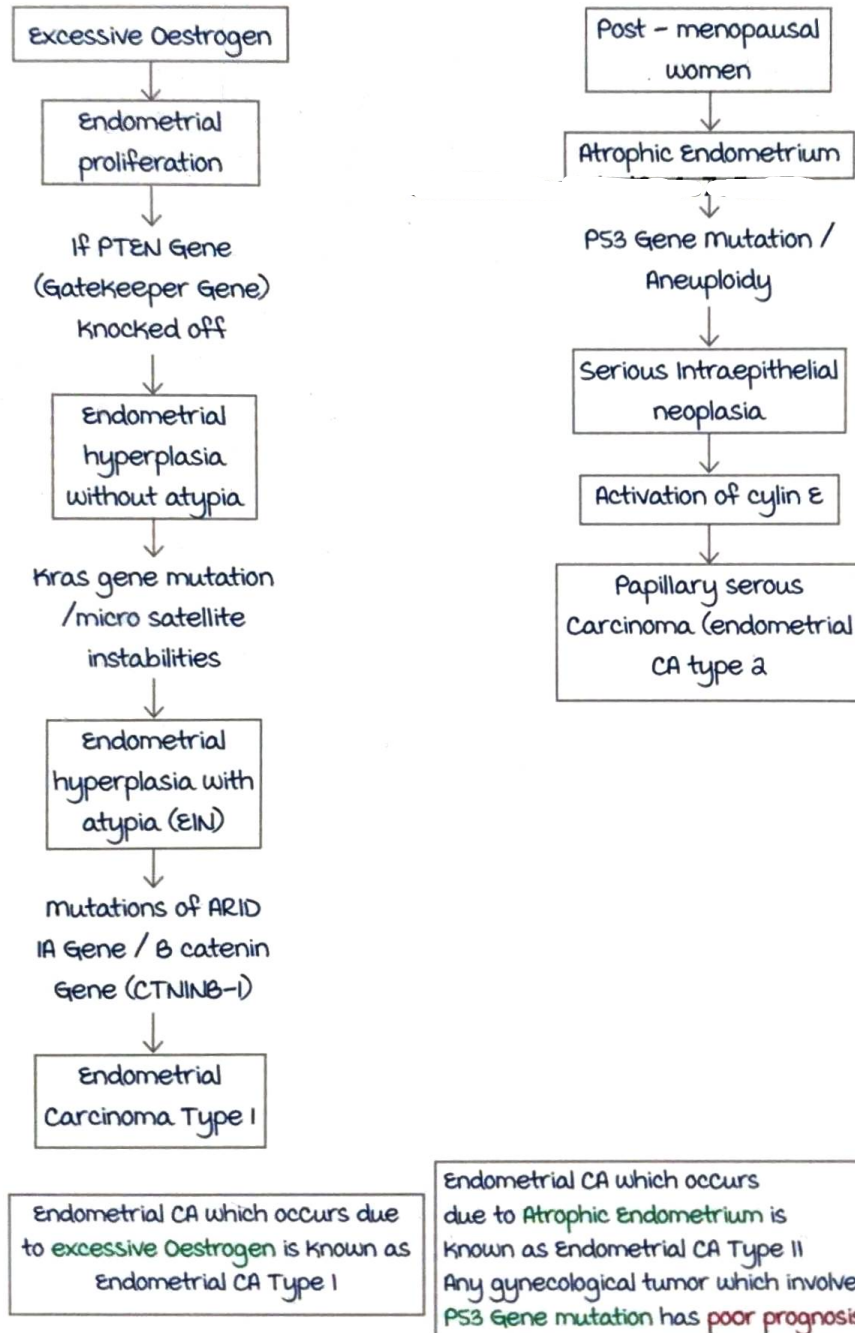
management strategies for both endometrial hyperplasia without atypia and EIN differ in approach and are given as follows.

The definitive treatment of endometrial intra-epithelial neoplasia remains to be **hysterectomy**.

## Gene mutations in endometrial

### CA Type I and Type II

00:23:27



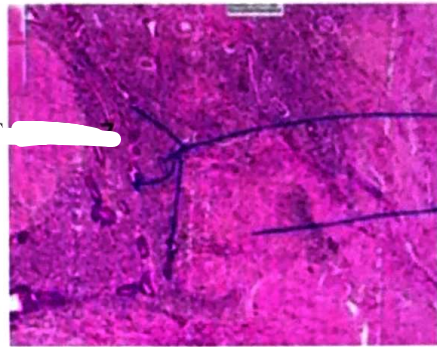
### Adenomyosis

00:30:55

When normal endometrial glands are seen deep within the myometrial tissue.

The endometrial glands need to be at least **2.5mm** deep in the myometrium to be called adenomyosis.

Also known as 'endometriosis interna'.

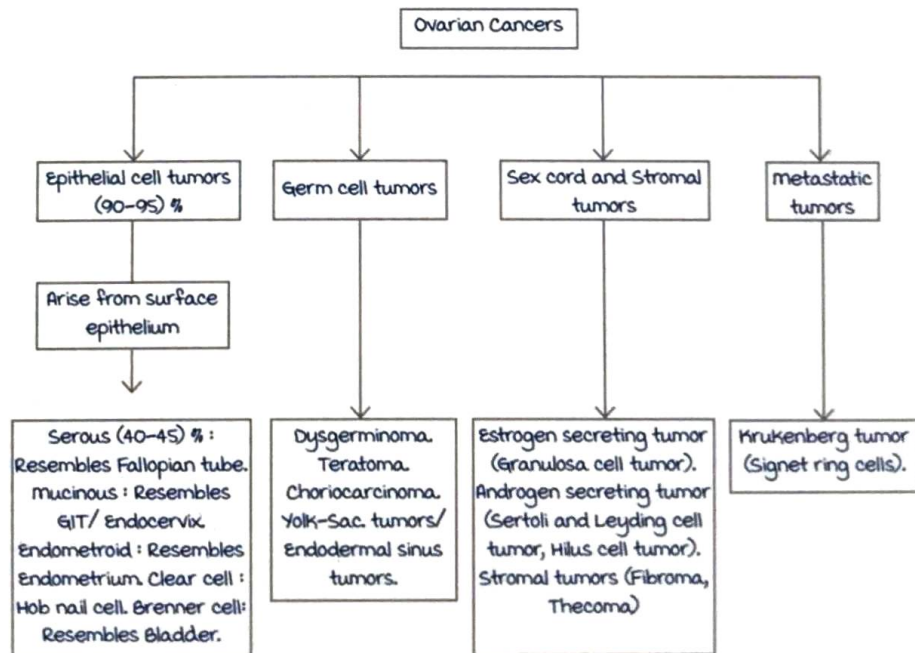


Adenomyosis

### Ovarian cancers

00:32:56

Classification of Ovarian cancers :



Active space

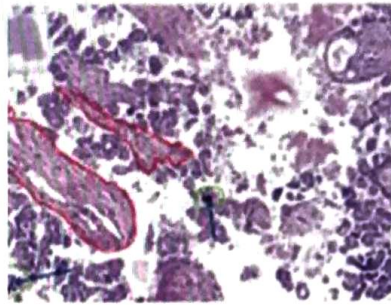
Each ovarian cancer will be discussed under the following headings :

- Histopathological characteristics
- Gene mutations
- Tumor marker

### Serous cell tumors

00:36:15

most common type of epithelial cell tumor comprising around (40 - 45) % of ovarian tumors.  
Either uniloculated or biloculated.



Serous Cell Tumor

Benign : No proliferation ; No invasion into stroma.  
Borderline : Proliferative ; No invasion into stroma.  
malignant : Both Proliferative and invades the stroma.

Histopathological characteristics :

**Psammoma body** : Papillary outgrowths with calcified laminated bodies.

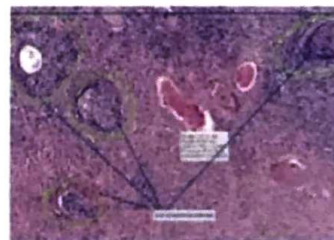
Gene mutations : BRCA 1, BRCA 2 and p53 mutations

Tumor marker : CA125

### Brenner tumor

00:38:46

Benign solid tumor of the ovary.  
Normal ovarian stroma with nests of cells resembling bladder epithelium,



Brenner Tumor

Histopathological Characteristics :

**Walthard cell nest** : Foci of transitional epithelium.

**Coffee bean nuclei** : Grooved nuclei (Also seen in Granulosa cell tumor).

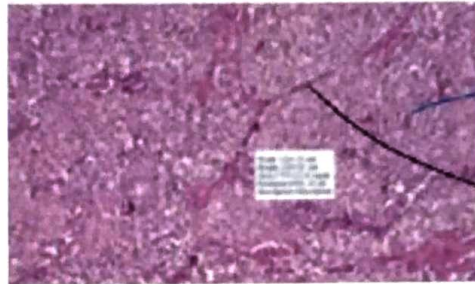
**Dysgerminoma**

00:40:28

Histopathological characteristics :

Sheets of cells separated by fibrous septa,  
These septa are filled with inflammatory infiltrate.  
Fried egg appearance

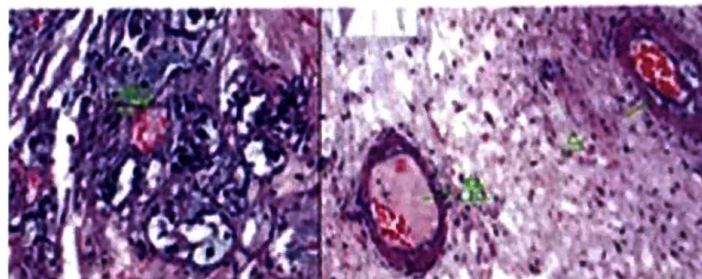
Tumor marker : LDH, Placental Alkaline Phosphatase, **HCG**



Dygerminoma

**Yolk sac tumor/ endodermal sinus tumor**

00:42:21



Yolk-Sac tumor

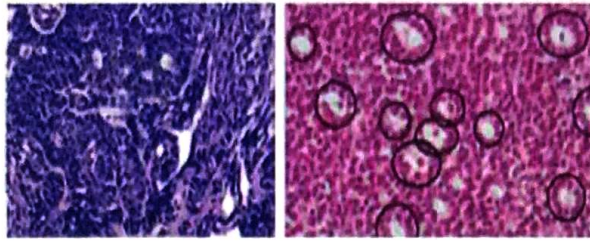
Histopathological characteristics :

**Schiller Duval Bodies** : Central capillary structure with a purple basement membrane surrounded by a layer of cells.

Tumor marker : **Alfa Feto Protein**

## Granulosa cell tumor

00:44:45



Oestrogen-secreting tumor

Granulosa cells secrete Oestrogen and Inhibin.

Histopathological characteristics :

**Call Exner Bodies** : Central eosinophilic material surrounded by cells giving it the appearance of a follicle,

**Coffee bean nuclei.**

Tumor marker : Inhibin B, Anti-muellerian Hormone.

## Teratoma

00:47:31

Histopathological characteristics :

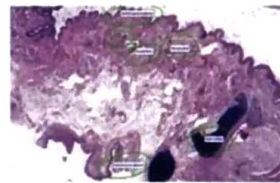
Cartilage, Bone, Teeth, Hair,

Sebaceous gland surface

epithelium are seen.

Essentially derivatives of **all three germ layers.**

most common derivative is ectodermal component.



Teratoma

mature Teretoma : Benign ; Dermoid cyst.

Immature Teratoma : malignant (**most common malignant germ cell tumor of the ovary**).

## Krukenberg tumor

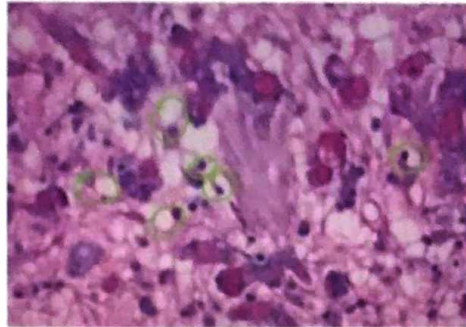
00:49:03

metastatic tumor

most common primary site is Pylorus of stomach from which the cancer reaches the ovary through **retrograde lymphatics.**

Histopathological characteristics :

**Signet ring cells** : white mucin-filled cells with the nucleus pushed to one side.



Krukenberg tumor

### Important gene mutations

00:50:47

Serous cell tumor :

Low Grade : KRAS.

High Grade : p53 ; BRCA 1 and BRCA 2.

Mucinous tumor : KRAS.

Endometrioid tumor : Beta-Catenin ; PTEN.

Both Endometrioid tumor and Granulosa cell tumor can lead to Endometrial CA.

Endometrioid tumor because of PTEN and B-Catenin gene mutations.

Granulosa cell tumor because it's an oestrogen producing tumor.

Granulosa cell tumor : FOX L-2

# MENOPAUSE

## Definition

00:00:51

Permanent cessation of periods/menstruation for 12 months.

Age :

Worldwide : 51 years.

India : 47 years.

Perimenopause :

Period of 4-5 years before menopause where menopausal transition occurs.

Premature menopause :

menopause at <40 years.

Primary ovarian insufficiency (POI) is the new term used to denote premature menopause.

Delayed menopause :

- menopause  $\geq 55$  years.
- Females with delayed menopause will be exposed to increased estrogen for a longer time  $\rightarrow$  Increased risk for endometrial and ovarian cancer.

Cause of menopause :

Follicles are maximum at 5<sup>th</sup> month of intrauterine life (6-7 million).

At the time of birth : 1-2 million follicles.

At the time of puberty : 4 lakh follicles.

Every month 1000 follicles undergo atresia.

In females, number of follicles are limited. Follicles undergo programmed cell death  $\rightarrow$  Apoptosis  $\rightarrow$  Every month, number of follicles deplete  $\rightarrow$  When no follicles left in ovary  $\rightarrow$  menopause.



Changes in female physiology during late reproductive age.

- Inhibin B : **Decreases.**
- FSH : **Slightly increases.**
- Estrogen (E<sub>2</sub>) : **Normal.**
- Progesterone : **Slightly decreases.**
- Females have difficulty in conceiving.
- menstrual irregularity : Short follicular phase i.e. Short cycles (Around 40 years).

Changes in female physiology during perimenopause age :

- menopausal transition begins : **Intermenstrual cycle length increases  $\geq 7$  days.** Example : If initial cycles occur at 25-30 days, cycles occur at 40-50 days during perimenopause.
- Late perimenopause  $\rightarrow$  **Amenorrhea  $\geq 2$  months.**
- FSH : **Increases.**
- Estrogen (E<sub>2</sub>) : **Decreases.**
- Inhibin B : **Decreases.**

### Tests for ovarian reserve

00:12:48

- **FSH (day 3)** : Increase in FSH indicates decreased number of follicles/ovarian failure.
- **E<sub>2</sub>** : Decreased estrogen in ovarian failure.
- **Anti-mullerian hormone** : Decreases in ovarian failure.
- **Antral follicle count** : Decreased count in ovarian failure.
- Best test for ovarian reserve : **Anti-mullerian hormone** (less cyclical variation).
- **Inhibin B** is not a test for ovarian reserve. It is used as a marker for granulosa cell tumor of ovary.
- **Straw staging** divides the entire period of woman's life into various phases such as early reproductive age, reproductive age, late reproductive age, early menopausal transition, late menopausal transition, and menopause.

menopause pathophysiology :

- No more follicles in ovary.
- Decreased estrogen  $<20$  pg. most common estrogen in menopausal females is  $E_1$ .
- Inhibin B decreases.
- FSH ( $\geq 40$  IU) and LH increase due to decrease in inhibin B and estrogen.
- Anovulation  $\rightarrow$  Decreased progesterone  $\rightarrow$  Amenorrhea.
- Decreased androgen  $\rightarrow$  Decrease in libido.
- Increased FSH and LH are excreted in postmenopausal females. HMG injection (menotropin) is produced from urine of a postmenopausal female.
- Parabasal and basal cells predominate on vaginal cytology in menopausal females.
- maturation index in menopausal female : 100/0/0.

### Symptoms of perimenopause

00:22:48

- menstrual irregularity due to anovulation. Initially persistent difference of  $\geq 7$  days in consecutive cycles. Later, amenorrhea of  $\geq 2$  months.
- most common symptom is hot flashes.
- Decreased estrogen  $\rightarrow$  vaginal dryness (senile vaginitis/atrophic vaginitis/genitourinary menopausal syndrome).
- mood swings.
- Sleep disturbances.

Symptoms of menopause :

most common and most prominent symptom : Hot flashes.

Hot flashes :

- Begin as sudden sensation of heat on upper chest and face (due to vasodilation) that rapidly becomes generalized. The sensation lasts for 2-4 minutes, is associated with profuse sweating and occasionally palpitations. It may also be associated with shivering and anxiety.
- Hot flashes usually occur several times a day but are most common at night : Night sweats.

- Hot flashes are mediated by **thermoregulatory dysfunction** at the level of hypothalamus.
- Thermoregulatory center at hypothalamus regulates thermoneutral zone. Thermoneutral zone is **narrowed** in perimenopausal and menopausal females. When body temperature is increased by 0.4 °C, mechanisms for hot flashes are generated to dissipate heat.
- Thermoregulatory center is innervated by **Kisspeptin, neurokinin and dynorphin neurons (KNDY neurons)**. Estrogen inhibits KNDY neurons. After menopause, estrogen decreases. So, the negative effect goes, and thermoregulatory dysfunction occurs in the form of hot flashes.
- main cause of hot flashes : **Decrease in estrogen.**
- Best management for hot flashes : Replace the estrogen : Give **hormone replacement therapy (HRT)**.
- mild hot flashes : **Reassurance and vitamin E.**
- moderate to severe hot flashes (Hot flashes interfering with day to day life) : **HRT.**
- Hot flashes coincide with LH surge.

### Hormone replacement therapy (HRT)

00:33:43

Systemic and local HRT.

Systemic HRT :

Female with intact uterus : **Estrogen + Progesterone.**

Female without uterus (undergone hysterectomy) : **Estrogen.**

Combined estrogen + progesterone :

- Increased risk of venous thromboembolism.
- Increased risk of breast cancer.
- Increased risk of coronary heart disease.
- Decreased risk of **endometrial cancer.**

Estrogen alone :

- Increased risk of venous thromboembolism.
- Increased risk of endometrial cancer if uterus is intact.

HRT is not given to all menopausal females.

Potential candidates :

- No more follicles in ovary (post-menopausal).
- Ovary removed/destroyed.
- Ovary not functioning (Turner's syndrome).

Indications :

Premenopausal females :

HRT (systemic) to be given till the normal age of menopause.

- Gonadal dysgenesis/Turner's syndrome (Initially estrogen followed by estrogen + progesterone).
- Female in whom oophorectomy/pelvic irradiation done (most sensitive pelvic organ to radiation is ovary).

Postmenopausal females :

Females < 60 years and should be <10 years have passed from attainment of menopause.

- moderate to severe hot flashes : Systemic HRT should be given till 60 years of age or <5 years.
- Genitourinary symptoms : Local estrogen.

HRT never given to females >60 years of age.

First line management of genitourinary symptoms is lubricants and moisturizers.

## Estrogen

00:45:45

- Route : Transdermal (Similar efficacy to oral estrogen and decreased chances of venous thromboembolism).
- Preparation : micronized  $17\beta$  estradiol (resembles the estrogen produced by ovary).
- Start with lowest dose of estrogen.
- maximum dose is 1mg of oral micronized  $17\beta$  estradiol/0.5 mg of transdermal patch. Exception is a young female who requires HRT due to surgical oophorectomy : maximum dose is 2mg oral/0.1 mg transdermal.
- Dosing equivalent : 1 mg of oral micronized  $17\beta$  estradiol/0.5 mg of transdermal patch is equivalent to 5 mcg of ethinyl estradiol.

Progesterone :

- Added to protect against **endometrial cancer**.
- Nowadays, natural micronized progesterone is used.
- Dose : **200 mg/day for 12 days in luteal phase of each cycle OR 100 mg/day continuously.**
- Earlier, medroxyprogesterone (MPA) was used. Women's health initiative study showed use of MPA was associated with increased incidence of breast cancer and coronary heart disease.

Other points on HRT :

HRT is used for management of menopausal symptoms like **hot flashes and genitourinary syndrome** but not for prevention of coronary heart disease, osteoporosis or dementia.

HRT decreases the risk of **colorectal cancer**. There is no effect on cervical cancer.

Estrogen + Progesterone :

**Progesterone component** : Increased risk of breast cancer and coronary heart disease.

**Estrogen component** : Increased risk of venous thromboembolism.

Studies have shown that if estrogen alone is given in HRT, incidence of breast cancer and coronary heart disease is not increased compared to combined estrogen and progesterone therapy.

Incidence of endometrial cancer increases if progesterone is not used in a female with uterus.

Contraindications for HRT :

Same as OCPs.

Case : Perimenopausal female around 45 years with hot flashes requests for contraception. What do you prescribe?

A : **Low dose/very low dose OCPs** to be given. At 50-51 years (47 years in India) taper OCP and put her on HRT. In obese perimenopausal females, **avoid** low/very low dose OCPs.

Note : Lowest possible effective dose of estrogen in a contraceptive pill is **10 micro grams**.

## Other drugs used to treat hot flashes

00:55:54

If patient has a history of venous thromboembolism :

- SSRIs like paroxetine, fluoxetine, venlafaxine.
- Gabapentin /pregabalin : Helpful for nocturnal hot flashes.
- Clonidine.

Selective estrogen receptor modulators (SERMs) are never used for the treatment of hot flashes except **Bazedoxifene**.

**Bazedoxifene + Estrogen** has been approved for the treatment of hot flashes and osteoporosis.

Phytoestrogens like flaxseeds.

Other symptoms of menopause :

- Vaginal dryness : Atrophic vaginitis/senile vaginitis (genitourinary syndrome of menopause).
- Decreased bone mass : Osteoporosis.
- Increased chances of depression.
- Sleep disturbances.
- Cognitive impairment.
- Dementia.

Genitourinary syndrome of menopause (GSM) :

- Due to decrease in estrogen.
- GSM includes vaginal dryness, dyspareunia, postcoital bleeding/postmenopausal bleeding, vulvovaginal burning and urinary symptoms such as urgency, dysuria, recurrent UTI.
- Unlike hot flashes, GSM gradually **increases with time**.
- Management :
  - 1<sup>st</sup> line** : Vaginal lubricant and moisturizers.
  - 2<sup>nd</sup> line** : HRT - Local estrogen cream. Systemic/oral/transdermal form should not be used.
  - 3<sup>rd</sup> line** : Ospemifene.

## Osteoporosis

01:02:12

- Bone density decreases due to decreased estrogen. It is a **qualitative defect** and not a quantitative defect.
- RANK-ligand interaction :  
Osteoblast forms **RANK ligand** which stimulates **osteoclasts**. Osteoclasts lead to resorption of bone → Increase calcium. Estrogen produces **osteoprotegerin protein (OPG)** : Binds to RANK ligand and prevents stimulation of osteoclasts. So, deficiency of estrogen causes decrease in bone mineral density
- As bone density decreases, risk of fractures increases.
- most common fractures seen are **vertebral** > **neck of femur** > **colles**.
- most common complaint of females with osteoporosis : **Backache**.
- Investigation of choice : **Bone mineral density by Dual X ray absorptiometry scan (DEXA) scan**. Unit of bone mineral density is **gram/cm<sup>2</sup>**.
- Indication for bone mineral density testing : **Females age ≥ 65 years**. If there is a **risk factor** such as rheumatoid arthritis, heparin use → test should be done at **≥ 60 years**.
- Site of measurement : **Proximal femur, first 4 lumbar vertebrae**.
- Bone mineral density scores :  
**T score** : Bone mineral density of old aged female is compared with the bone mineral density of young female. It is always negative. 0 to -1 is normal. -1 to -2.5 is osteopenia. **≥ 2.5** is osteoporosis.  
X-ray finding of lumbar spine in osteoporosis : **Cod fish appearance** (vertebra is biconcave).  
**Z score** : Bone mineral density of age matched population is compared. If decreased, it indicates some other reason for decreased bone mineral density.  
Example : Drugs.



Cod fish vertebrae

## Management of osteoporosis

01:12:00

1<sup>st</sup> line of treatment : **Bisphosphonates**. most common side effect is **severe gastritis**. Patient is instructed to sit upright for 30 minutes to 1 hour after taking bisphosphonates.

**H. pylori infection and history of gastric ulcer** should be ruled out.

Other drugs :

- Tibolone : Estrogen action on bone + Progesterone like action on endometrium + Androgen like action (increases libido).
- SERM : Raloxifene, Tamoxifen, Bazedoxifene + Estrogen.
- Denosumab : Binds to **RANK ligand** and prevents activation of osteoclasts.
- Teriparatide : Parathyroid hormone analogue. Should be given in low amplitude. **Acts on osteoblasts**.
- SAL-Calcitonin : used if the patient has severe backache along with vit D and calcium supplementation.
- Strontium ranelate : Acts by **activating osteoblasts**. Not used nowadays.

All drugs for osteoporosis act by inhibiting osteoclasts. Only 2 drugs act by activating osteoblasts : **Teriparatide and Strontium ranelate**.

Recommended calcium intake in a postmenopausal female : **1200 mg/day**.

Some calcium is taken in diet as supplement :

**500 to 1000 mg/day**.

Daily requirement of vitamin D : **800 IU/day**.

In all females with osteoporosis and osteopenia, **check calcium and vitamin D levels**. If low, supplementation should be given.

Active space



# PCOS : PART 1

## Introduction

00:01:08

Also known as **Stein-Leventhal syndrome**.

most common endocrine and metabolic disorder in women.

Incidence: 10%

most common cause of hirsutism in females.

most common cause of anovulation in females.

3 main components of PCOS :

1. Increased androgens.
2. Ovulatory dysfunction.
3. Polycystic ovaries.

Cyst meaning unruptured follicles in the ovaries.

Females at high risk for developing PCOS :

- Obese and or insulin resistance.
- Type 1, 2 DM.
- History of premature adrenarche.
- Ethnicity : mexicans/ Australian and South Asians.
- History of 1st degree relatives with PCOS.

Anti epileptic drug which has high risk for PCOS :

**Valproic acid** (Leads to androgen synthesis in ovary).

## Pathogenesis

00:06:18

main etiology : **Increased production of androgens by ovaries.**

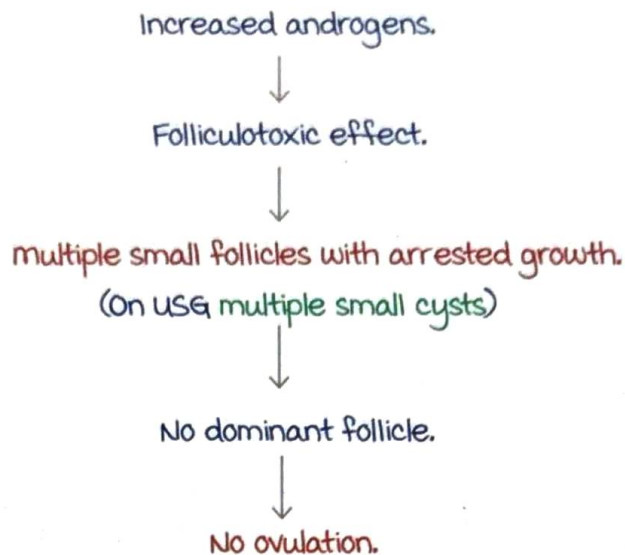
main pathological site of PCOS : Ovary.

Normal androgen level : <70ng/dl.

Levels of Androgens increase but never >200ng/dl.

Increased production of Androgens is due to ovary (Not adrenals).

Leads to **Theca cell hypertrophy.**



This forms the basis of diagnostic criteria for diagnosing PCOS → **Rotterdam criteria**.

In PCOS patients, some of the excess androgen may come from adrenal glands.

Thus, in few PCOS patients DHEA-S may be mildly raised.

### Pathophysiology of excessive androgens

00:12:15

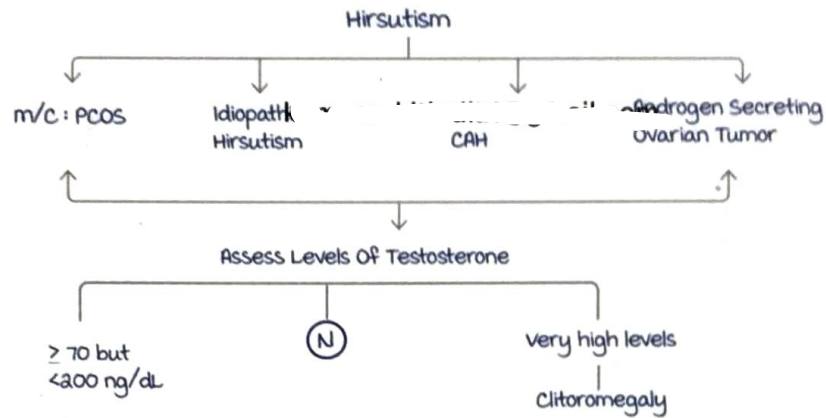
- Symptoms :
  - mild elevation of androgens (>70 but <200) leads to **Hirsutism**.
  - Folliculotoxic causing **Anovulation**.

Hirsutism.	Virilisation.
Occurs due to mildly elevated androgens.	Due to excessive androgens : very high levels.
Seen in PCOS.	Seen in Androgen producing tumour of ovary, Late onset CAH.
Includes : <ol style="list-style-type: none"> <li>1. Growth of coarse, terminal hair in male pattern. Sites : Lips, chin, periareolar region, chest, around linea nigra.</li> <li>2. Acne Not responsive to usual treatment. Scarring acne.</li> <li>3. Alopecia.</li> </ol>	Include : <ol style="list-style-type: none"> <li>1. Clitoromegaly (clitoris &gt; 1cm).</li> <li>2. Increased muscle mass.</li> <li>3. Deepening of voice.</li> <li>4. Breast atrophy.</li> <li>5. Temporal recession of hair line.</li> </ol>
modified Ferriman-Gallwey score. 9 sites to be checked. Each site scored between 0-4. Total score: ≥ 8 hirsutism present. ≥ 15 severe hirsutism.	Prader score.

Active space

4. Lab investigations :

- Increased LDL
- Decreased HDL } Dyslipidaemia
- Testosterone levels >70 but <200.
- DHEA : mildly elevated.
- LH elevated.
- SHBG : Decrease.



5. Future complications :

- Dyslipidaemia.
- High BP.
- Coronary artery disease.

most common cause of hirsutism in young female with history of rapid onset : **Androgen secreting ovarian tumor.**  
 most common cause of hirsutism in young female : **PCOS.**

In **obese** females :

Androgens in adipose tissue convert →  $\epsilon_1$  and elevates estrogen.

$\epsilon_1 : \epsilon_a$  ratio becomes **2 : 1** (Normally 1 : 2).

Future complications :

- Endometrial cancer.
- Ovarian cancer (may or may not be seen).

Active space

## Insulin resistance

00:28:18

Seen in 50-80% patients.

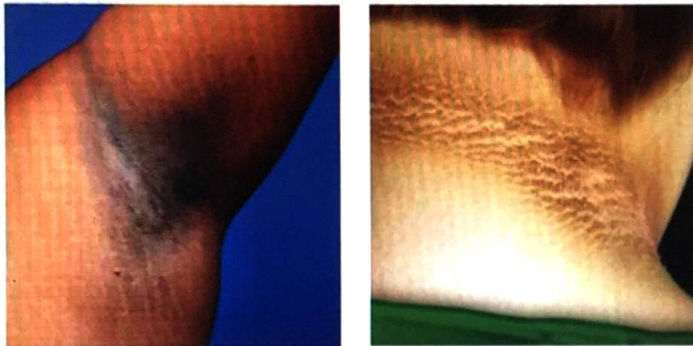
Further stimulates the theca cells to produce androgens.

Adds to dyslipidaemia.

H  
A } Hyperandrogenism

I  
R } Insulin resistance

A  
N } Acanthosis nigricans : Clinical manifestations of insulin resistance syndrome.



Future complications : may develop DM.

Lab investigation :

SHBG levels decrease.

2 hours OGTT : abnormal.

effects of anovulation :

1. Infertility due to anovulation and treatment.
2. Amenorrhea or oligomenorrhea : No corpus luteum formation, thus decrease progesterone.
3. menometrorrhagia : In obese females : Increased estrogen proliferates endometrium and low levels of progesterone are unable to support the endometrium.

Anovulation has decreased levels of Progesterone, so even if conceived, high chances of abortion.

Also there is poor endometrial receptivity.

	Obese PCOS female	Thin PCOS female
Insulin Resistance	Present	Present
Amenorrhoea	Less common	more common
Oligomenorrhoea and menorrhagia (<9 cycle/year)	more common	menorrhagia is not seen
Estrogen levels	High	Normal
$E_1/E_2$	Raised	Normal

### Diagnostic criteria for PCOS

00:41:37

#### Rotterdam criteria :

Any 2 of the following 3 should be present to make a provisional diagnosis of PCOS :

1. Increased androgen levels :

On biochemistry : hyperandrogenaemia or  
As hirsutism : hyperandrogenism.

2. Ovulatory dysfunction : As oligomenorrhoea/ amenorrhoea.

3. On USG :

1 or both ovaries : > 12 follicles ; 2-9 mm in size (< 1 cm).  
volume of ovary > 10cc.



Necklace pattern : Arranged towards periphery.

Is obesity a criteria to diagnose PCOS?

No

Is Insulin resistance a criteria to diagnose PCOS?

No

Can ovary be normal in patients of PCOS?

Yes

Case :

Female with hirsutism with irregular cycles. Raised testosterone levels. On USG ovaries are normal. Can be a case of PCOS. So, rule out late onset CAH. This is done on the basis of 17OH Progesterone.

Is USG mandatory to make a diagnose of PCOS?

No

Are there any cysts in ovary of PCOS?

No

most commonly the arrested follicles are arranged around the periphery of ovary giving a necklace appearance.

Is necklace appearance a criteria to diagnose PCOS?

No

Recommendation by PCOS international group to change the 3<sup>rd</sup> criteria from  $\geq 12$  follicles to  $\geq 20$  follicles has yet not been implemented.

Is the diagnosis of PCOS confirmed by Rotterdam criteria?

No.

Provisional diagnosis of PCOS by Rotterdam criteria is in close d/d with late onset PCOS.

For making a confirmational diagnosis, rule out CAH.

In adult onset CAH : Assess levels of 17OH Progesterone.

- $<200$  : Rules out CAH.
- $200-800$  : ACTH stimulation test to confirm CAH.
- $>800$  : Confirms CAH.

Case 1 :

18 year old female, during covid had periods of amenorrhea. She noticed hair growth on her chin and also has acne. Next step to be done : Assess testosterone levels.

Case 2 :

Provide a list of all investigation to be recommended to a female of reproductive age with suspected PCOS, with complaint of secondary amenorrhea.

- UPT.
- Thyroid and prolactin levels.
- LH, FSH.
- 17 OH progesterone.
- Testosterone.

In patients of PCOS

- UPT : Negative.
- TSH : Normal.
- Prolactin : Normal.
- LH : Raised.
- FSH : Normal.
- LH : FSH ratio - 2 : 1 or 3 : 1 (N= 1 : 1).
- Testosterone : Raised (<200).
- 17 OH progesterone : Normal.

Case 3. Diagnosis of PCOS is made in above patient.

Enlist further investigations for further management :

1. Lipid profile.
2. OGTT.
3. If Endometrium thickness > 12mm. Rule out endometrial cancer by doing endometrial aspiration biopsy. (EAB)

Short term complications	Long term complications
<ul style="list-style-type: none"> <li>• menstrual irregularities</li> <li>• Hirsutism</li> <li>• Alopecia</li> <li>• Infertility</li> <li>• Insulin resistance.</li> </ul>	<ul style="list-style-type: none"> <li>• Dyslipidaemia</li> <li>• High BP</li> <li>• CAD</li> <li>• Endometrial cancer</li> <li>• Ovarian cancer</li> <li>• DM</li> <li>• NASH</li> <li>• metabolic X syndrome</li> <li>• Sleep apnea syndrome</li> <li>• mood disorders : depression, anxiety.</li> </ul>

Pregnancy complications :

- Infertility : Due to anovulation. Easily treatable/ reversible.
- Increased abortions (due to decreased Progesterone).
- PIH.
- Gestational diabetes.
- Still birth.

## PCOS : PART 2

### Criteria for PCOM

00:00:35

Rotterdam criteria for PCOM/ Polycystic ovarian morphology :  
On USG :  $\geq 12$  follicles size = 2 to 9mm or volume  $> 10\text{ml}$  in one or both ovaries.

Asper ESHRE (Williams 4<sup>th</sup> edition) / European society of human reproduction and embryology and ASRM (American society for reproductive medicine) :

PCOM =  $\geq 20$  follicles, size = 2 to 9mm.

Volume =  $> 10\text{ml}$ .

AEPCOS : Androgen excess and PCOS society :

PCOM =  $\geq 25$  follicles (rest same).

### Management of PCOS

00:03:35

1<sup>st</sup> line management : Lifestyle modification.

Even a 5% weight loss can lead to ovulatory cycles.

Recommended in overweight + obese PCOS females.

Advice : Hypocaloric diet + Brisk walking & exercise.

metformin is not used for this indication.

Advantages of weight loss :

To decrease central fat & improved insulin sensitivity.

Increase Sex hormone binding Globulin/SHBG  $\rightarrow$  decreased

Androgen (free testosterone) levels.

In 5 to 10% females resumption of ovulatory cycles.

Q. Female has undergone Bariatric surgery  $\rightarrow$  Pregnancy should be delayed x 1 to 2 years. (As per rapid weight loss is during this period)  $\rightarrow$  IUGR & nutritional deprivation.



DOC for PCOS : In general, it is **Oral combined pills / OCP's** .

Progesterone should belong to 3<sup>rd</sup> or 4<sup>th</sup> generation.  
(Least androgenic Side effects).

For menstrual irregularities, OCPs given for : **3 weeks on & 1 week off.**

Exogenous Estrogen & Progesterone in OCP, has negative feedback on natural LH & FSH, hence **no natural Estrogen and Progesterone** in females body.

**Regularisation of cycles :**

OCPs are started at day 1 or within 5 days of the cycle.  
The levels of estrogen and progesterone are high for 3 weeks and when stopped results in menstruation.  
And is started again after she menstruates.

Progesterone reduces endogenous LH which acts on theca cells to produce Androgens.  
Hence **Hirsutism** is treated.

As natural/endogenous Estrogen is reduced, it leads to **thinning of the endometrium**. (Endometrial hyperplasia is prevented).

**menstrual irregularity / Oligo-anovulation in PCOS :**

Oligo-anovulation = **< 9 cycles/year**.

DOC = OCPs (3 weeks on + 1 week off).

or

Estrogen & Progesterone patches (new patch each week)  
/ Rings for 3 weeks on + 1 week off.

Alternative (if OCPs are contraindicated) :

Every 1 to 3 months (When they do not menstruate) : Give **progesterone withdrawal** :

medroxy progesterone acetate : Given 5 to 10mg daily orally for 12 days. This leads to menstruation  
It does not act as a contraception.  
They does not help in relieving Acne & Hirsutism.

DOC for Insulin resistance :

metformin : It is a category B drug.

Off label uses in PCOS :

Weight loss, restore cycles, and lower Hyperandrogenism.

Indications :

PCOS with IGT/ Impaired glucose tolerance.

Or  $\uparrow$  Fasting insulin.

Or Acanthosis Nigricans.

Or family history of Diabetes melitus.

Dose : 850mg BD or 500mg TID with meals.

Side effects : GI side effects (most common).

most Dangerous Side effect : Lactic Acidosis.

Not teratogenic.

PCOS patients :  $\downarrow$  Progesterone =  $\uparrow$  chances of abortion.

metformin =  $\downarrow$  Chances of abortion &  $\downarrow$  chances of Diabetes in pregnancy if used in PCOS patients during pregnancy.  
But now it is not recommended for this indication.

Patients with PCOS : may have Insulin resistance / Type 2 diabetes melitus.

In all patients of PCOS : 75gm OGTT / Oral glucose tolerance : done every 2 years.

In PCOS patients with Insulin resistance : Yearly 75gm OGTT.

IR/ Insulin resistance is defined as :

fasting Insulin :  $> 20$  mIU /ml.

1hr PP/Post prandial insulin :  $> 55$  mIU/ml.

2hr OGTT result in Non pregnant females :

Fasting : < 100.

1 hour PP : < 200.

2 hour PP : < 140.

Other insulin sensitizers :

Agonist of Glucagon like peptide 1 (GLP 1) receptor :

Can be used in PCOS patients.

But not if patient wants to conceive. (Category C)

Sodium glucose cotransporter 2 inhibitor : Empagliflozin  
(Jardiance)

Weight loss is more in comparison to metformin.

Category C drug.

Not recommended in females during pregnancy.

### Management of Hirsutism

00:22:26

mild : Removal of hair by mechanical methods :

Shaving, Plucking, Waxing, Laser.

moderate to severe :

moderate = Ferriman-Gallwey score  $\geq 10$ .

Severe = Ferriman-Gallwey score  $\geq 15$ .

DOC : OCPs with 4<sup>th</sup> generation Progesterone (Antiandrogens)

Drospirinone (Dose = 3mg; Ethenyl Estradiol = 35mcg)

Cyproterone (Dose = 2mg; Ethenyl Estradiol = 35mcg)

Egs : Diane 35, Dianette.

OCP = Estrogen + Progesterone

Estrogen binds to Sex hormone binding globulin and reduces free testosterone.

Progesterone has negative feedback on LH, which inturn reduces Androgens.

If the patient has high risk factors for **venous**

**Thromboembolism.**

Scenario : Female patient with hirsutism and history of venous thromboembolism.

use : **Norethindrone.** (Progesterone with estrogen action).

Estrogen leads to increase in clotting factors. Not used in patients with risk of venous thromboembolism.

Norethindrone is also used as an add back therapy for **GnRH agonists.**

Total duration of treatment with OCPs for hirsutism = **6 months.**

metformin : reduces insulin and androgens but not approved for treatment of hirsutism.

If in 6 months : No relief : 2<sup>nd</sup> line of management :

**Add antiandrogens.**

DOC : **Spirinolactone.** (or with OCPs).

Others :

Flutamide.

Finasteride.

Ketoconazole.

last resort : **Continuous GnRh.** (Decreased Lh, FSH. And decreased androgen production by ovaries).

Alternative : **Topical Eflornithine.**

Reversible inhibitor of **Ornithine decarboxylase enzyme** which is needed for cell division. It slows growth of facial hair.

(to be used for very long to get desired effect).

metformin also has slight antiandrogenic action.

Drug which is never be used to treat hirsutism : **Danazole** (side effect is hirsutism).

Important one liners :

Dose of spirinolactone : **50 to 100mg BD.**

Adverse effect : **Orthostatic hypotension.**

**Hyperkalemia.** (Caution in females with reduced renal function).

**Hirsutism :**

No significant reduction in hair growth may occur upto 6 months which is half life of hair follicle.

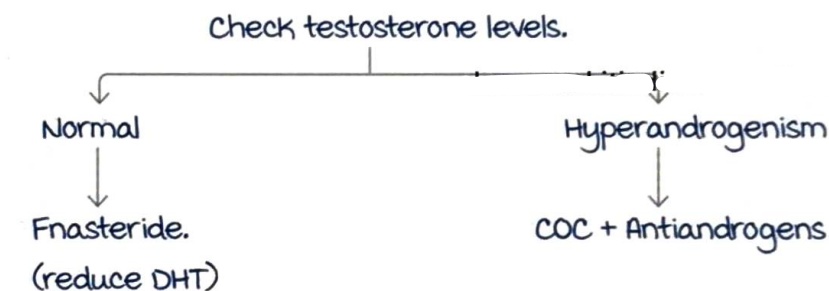
Treatment for hirsutism should be continued indefinitely or until the patient wants to conceive as problem of excess hair rarely goes away : It recurs following treatment discontinuation.

**Advice to patients on Antiandrogens :**

She should not conceive.

If she is carrying a male fetus and given antiandrogens.

It will lead to **ambiguous external genitalia**.

**management of females with alopecia.**

minoxidil : 5% local application

(side effect : Headacche).

**Management of Infertility**

00:33:23

Infertility is due to anovulation.

But even if they ovulate :

1. Egg quality is very poor.
2. Low endometrial receptivity.

1<sup>st</sup> line drugs :

DOC : **Letrozole**.

2<sup>nd</sup> DOC : **Clomiphene citrate**.

2<sup>nd</sup> line drugs :

HMG (75 units of LH and FSH).

or laproscopic ovarian drilling.

3<sup>rd</sup> line :

Pulsatile GnRh.

IVF.

Drug of choice for Anovulation in PCOS : **Letrozole** > CC.

DOC for Anovulation : **Clomifene Citrate** / CC.

DOC for unexplained infertility : CC + IUI (Intrauterine Insemination).

DOC used for ovulation stimulation during IVF : **HMG**.

	Letrozole	Clomiphene
mechanism of action	Aromatase inhibition (Androgen conversion to estrogen ↓) ↓ Estrogen ↓ GnRH ↑ ↓ FSH ↑	Selective estrogen receptor modulator / SERM : its antagonist properties predominate. ↓ Estrogen ↓ Negative feedback lost on GnRH (GnRH ↑) ↓ ↑ FSH & LH. ↓ multiple follicles grow.
T <sub>1/2</sub>	48 hours	weeks

Active space

	Letrozole	Clomiphene
Starting dose	2.5mg	50mg
maximum dose	7.5mg	150mg
Given from	Between Day 2 to day 5	Between Day 2 to day 5.
Before starting treatment	Do USG to see if there is no follicular cyst (> 20mm) from previous cycle & endometrium is <5mm.	Do USG to see if there is no follicular cyst (> 20mm) from previous cycle & endometrium is <5mm.
Do follicular monitoring	Day 10 onwards (everyday/alternate day)	Day 10 onwards follicle grows 1 to 3mm/day
when follicle is 18 to 20mm in size give ovulation trigger	Inj. hcg (5000 I/U)	Inj. hcg (5000 I/U)
Rate of ovulation	↑↑	↑
Singleton pregnancy rate.	↑↑	↑
Live birth rate.	↑↑ (27%)	↑ (19%)
Twin pregnancy rate	same (3 to 7%)	same (5 to 8%)
Pregnancy loss rate	same	same

Active space

most common side effect of Clomiphene citrate : **Hot flushes.**

other side effects of clomiphene citrate :

↓ Estrogen = **menopause symptoms.**

**Ovarian cyst** (↑ FSH → multiple follicles grow and some do

not ovulate → unruptured follicles remain as cyst.

Side effects because of which CC should be discontinued =  
Visual disturbances.

Letrozole Side effects : most common : Headache/ Cramps.  
Dizziness, Fatigue, less Hot flushes compared to CC, ovarian  
cyst formation.

Earlier Letrozole use was thought to cause Congenital  
anomalies : Cardiac & bone malformation. Now it is not proved.

Either Letrozole or Clomiphene citrate  
should be used for 3 to 6 cycles.



Next line of management

Alternatively :

Adjuvant therapy can be treated after 3 cycles :

1. Prednisolone = Sma : If androgens are high (DHEA).
2. metformin : If insulin resistance is present.

Although reports show : Clomiphene is not teratogenic but  
still it's use is not recommended during pregnancy & it is  
considered as Category X drug.

## HMG

00:51:24

(75 IU of FSH + LH) most common ovulation induction drug for  
IVF cycles. Indication :

1. If Clomiphene / Lactulose fail.
2. In IVF cycles.

3. In hypogonadotropic Hypogonadism.

(decreased GnRH → decreased LH & FSH → Anovulation/  
Infertility) seen in : Kallman syndrome  
Pituitary Ablation.



Clomiphene citrate & Letrozole can be used only if Hypothalamo-pituitary-ovarian axis is intact (in PCOS As HMG is given it replaces LH and FSH leads to ovulation.

4. In unexplained infertility; DOC : Clomiphene citrate + IUI.

Highest incidence of multifetal pregnancy (15%).

Associated with increased risk of ovarian hyperstimulation syndrome.

Maximum risk = Hmg > Clomiphene citrate > Letrozole.

Chances of pregnancy loss = increased with hmg = 20 to 25%.

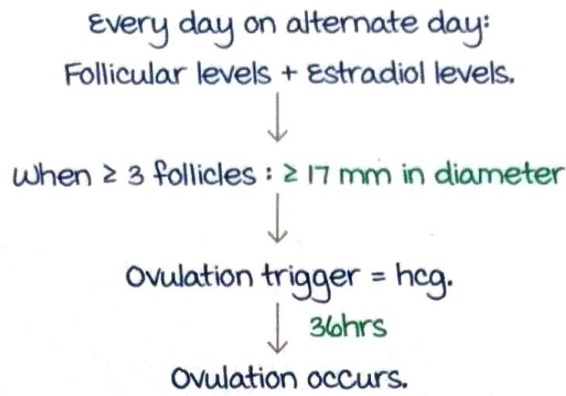
No risk of Congenital anomalies.

Use of Hmg :

In IVF : Female partner or PCOS patients as 2nd line management



If E2 levels are high it indicates a large number of follicles are growing which indicates **Ovarian hyperstimulation syndrome**.



For uniformity = hmg usually given = 5 to 8pm.  
E2 levels are measured = Early in morning.

As E2 levels rise :

Cycle fecundability increases (Because more follicles are formed, which mature).

But chances of multiple pregnancy & OHSS also increases.

Ideal E2 levels : Peak = 500 to 1500 pg/ml.

Chances of multiple pregnancy with hmg (15%) / OHSS :

Increases with increase in E2 levels.

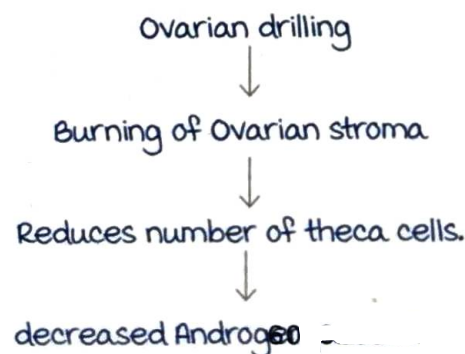
Increases with total number of developing follicles.

Reduces with increase in maternal age.

It does not correlate with number of large preovulatory follicles.

2<sup>nd</sup> line : Laproscopic ovarian drilling :

Principle =



Use is controversial : As it is associated with increased chances of ovarian failure and androgen formation.

In laproscopic ovarian drilling,

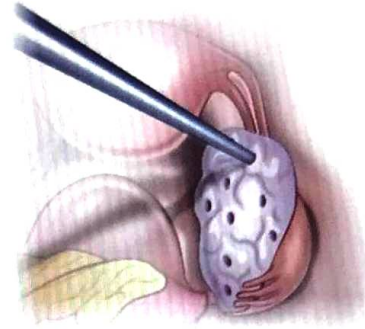
Rule of 4 :

Only 4 punctures

are to be done.

For 4 seconds.

At 40 watt.



Laproscopic ovarian drilling

Indication of IVF in PCOS :

If age of female > 35 years + PCOS + Other factors of infertility.

### Ovarian Hyperstimulation syndrome

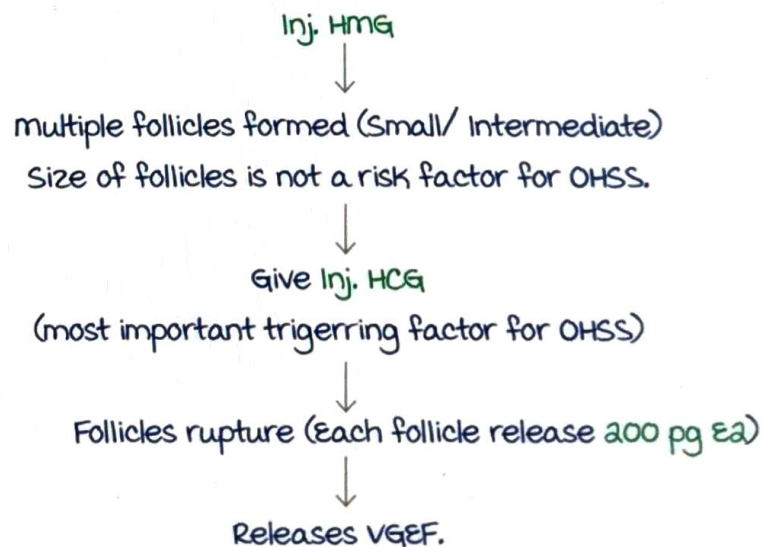
01:08:32

Iatrogenic complication seen with  
administration.

Less common with Clomiphene.

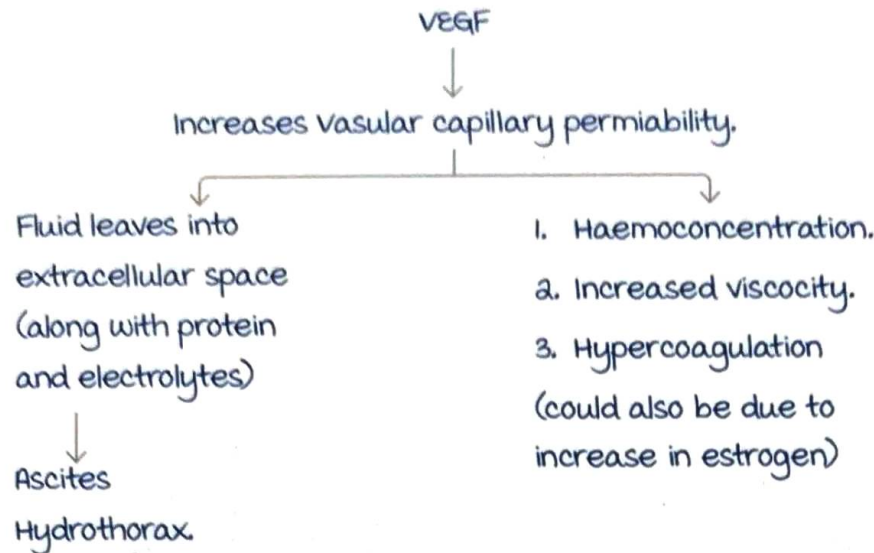
Not seen with Letrozole.

Pathophysiology :



hmg (LH and FSH) → Increase FSH → multiple follicles in ovary.

Hence Inj. HCG should not be given.



In these patients: Due to enlarged ovaries and accumulation of peritoneal fluid.  
Patient complains

Do TVS = multiple follicular cysts + Ascites (Seen in OHSS).  
But still OHSS → Clinical diagnosis.

OHSS ultrasound:



Big follicles seen in OHSS

Classification of OHSS:

Grade 1: Abdominal distortion/ discomfort.

2: Grade 1 + Nausea/vomiting

+ USG = Ovaries enlarged 5 to 12 cms.

3: USG = Ascites.

4: Clinical evidence of ascites/ Hydrothorax/

Difficulty in breathing.

5: Grade 4 + Haemoconcentration + reduced renal

perfusion and coagulation.

**management :**

mild : Grade I & 2 : Analgesics and Avoid strenuous activities & Intercourse.

2 reasons :

Risk of ovarian rupture.

If she conceives → Increase hcg production.

It leads to worsening of symptoms.

In moderate to severe Diseases :

Rest

- maintain electrolyte balance.
- maintain fluid balance with isotonic fluid = NS  
Otherwise untreated Hypocalcemia can lead to renal / hepatic failure.
- Prophylaxis for thrombocytes.
- For ascites → Paracentesis.

If patient has conceived : Admit her.

OHSS :

Early = < 9 days after giving hcg = due to exogenous hcg.

Late = > 9 days = due to endogenous hcg produced during pregnancy. (triggering factor).

Risk factors of OHSS :

Patient :

- Young females : High number of follicles.
- Previous history of OHSS.
- PCOS female.
- Thin females.

Ovary :

- Large number of follicles.
- ↑ Antral follicle count.
- ↑↑ AMH (> 3.3)
- ↑ Ea levels (> 2500pg/ml).

Preantral & antral follicles release AMH after puberty.

HCG :

- HCG for luteal phase support.
- Pregnancy.

methods to prevent OHSS :

- monitor number of follicles.
- monitor E<sub>2</sub> levels.
- With hold hcg if E<sub>2</sub> > 2500 and cancel the cycle.
- Dopamine agonist = Cabergoline (0.5mg) decreases VEGF concentration and can be started at trigger of ovulation to reduce chances of OHSS.
- If risk of OHSS is present → delay embryo transfer so that pregnancy does not occur.
- For luteal phase support : Give progesterone instead of HCG.

HCG for trigger.

Either with hold it.

Reduce dose.

use leuprolide 0.5 to 1 mg for trigger.

Q. A 25 years old woman underwent induced ovulation . On usg, ovary showed 8 follicles, serum estradiol level 880 pg/ml. what is the next step ?

- Retrieve follicle
- Cancel cycle
- Withhold hcg
- Give cabergoline

Per follicle 220 pg is released, hence out of 8 follicles, 4 to 5 are maturing. (more than 2500 pg/ml).

Ovarian drilling :

lesser risk of OHSS.

To be done only at 4 sites in each ovary.

Can lead to premature ovarian failure.

# ENDOMETRIOSIS

## Endometriosis

00:00:41

Endometrial tissue (glands + stroma) present outside the uterus.

Ectopic endometrial tissue is hormonally active → Every month, cyclical changes occur → Bleeding → No passage to be released outside → Inflammatory markers released → Inflammation.

This causes :

1. Pelvic pain (dysmenorrhea/dyspareunia).
2. Infertility (due to adhesions).

Progesterone is anti inflammatory in nature & so used in the management of endometriosis.

Symptoms of endometriosis regress during pregnancy.

macrophages (inflammatory cells) released → Ingest RBCs → Blood and blood products inside the macrophages → various pigmented lesions (red, blue black) & adhesions (due to inflammation) seen during laparoscopy in patients of endometriosis.

Therefore, endometriosis is :

1. Benign condition.
2. Inflammatory condition.
3. Oestrogen dependent condition.
4. Undergoes regression in post menopausal females.  
As oestrogen levels go down → Endometriotic implants undergo regression.

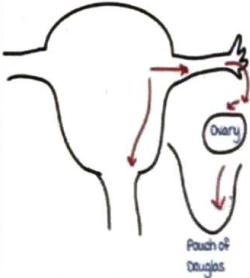
## Site of endometriosis

00:07:02

- Can occur anywhere in the body (even in CNS & spleen).

- most Common sites :  
**Ovary** → Pouch of douglas → Posterior leaf of the broad ligament → uterosacral ligament → Fallopian tubes → Pelvis.
- It can be seen in all sites except spleen (as it is the rarest site).
- Can also be seen in surgical scars : **Scar endometriosis**.

Theories explaining endometriosis :

Theory	Proposed by	Theory explains	Conclusion
Theory of implantation or theory of retrograde menstruation.	Sampson.	<p>Normally in females, menstruation occurs in forward direction.</p> <p>In females with endometriosis, both forward + retrograde menstruation occurs.</p> <p>Superficial layer of endometrium to be shed also comes from the fallopian tubes, ovary and the pouch of douglas.</p> <p>↓ endometrial implantation.</p> <p>↓ Endometriosis in these sites.</p> 	<p>Retrograde menstruation is seen mostly in conditions like imperforate hymen/uterine congenital anomalies (outflow obstruction) → Increased chances of endometriosis.</p> <p>Explains how ovaries and pouch of douglas are the most common sites.</p> <p>This theory does not explain :                      Occurrence of endometriosis at site like pleura/ lung /diaphragm/ umbilicus.</p> <p>Occurrence of endometriosis in premenarchal females (rare).</p>

Active space



Lymphatic theory.	Halban.	Similar to cancer cells, endometrium undergoes metastasis.	Explains occurrence of endometriosis in umbilicus.
Theory of coelomic metaplasia.	Ferguson & Ivanoff.	mesothelial cells → Derived from coelomic epithelium → Present at various sites → metaplasia → Endometriosis.	Explains how : • Endometriosis occurs in other sites like lungs, pleura etc. • Can also occur in prepubertal female.
Genetic theory.	K-Ras gene involved.	If there is a female whose first degree relative has endometriosis, she has 6-7 times more chances of having it.	
Immune mediated.		Females with endometriosis have deficient cell mediated and humoral immunity.	Explains the involvement of immune component with endometriosis.

### Types of endometriotic lesions

00:15:50

#### 1. Superficial lesions :

Histiocytes and macrophages engulf blood → Appear pigmented.

- Red : Red flame lesion.
- Black : Gun shot or powder burn appearance.

#### 2. Chocolate cyst or endometrioma :

- MC site is ovary, where blood while shedding, gets collected as a hematoma → Surrounded by duplicated ovarian parenchyma, called chocolate cyst (filled with chocolate tarry coloured fluid which is altered blood).

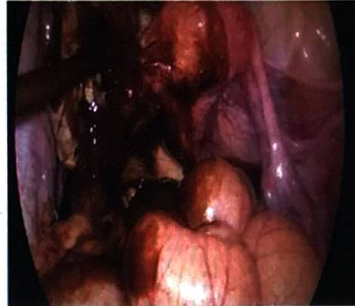
may or may not appear brown in colour.

### 3. Deep infiltrating endometriosis :

- Solid endometriotic mass → Situated > 5 mm deep to the peritoneum.
- more Common in bladder/bowel/rectovaginal septum or rectum.
- Leads to maximum pain.

Pain in endometriosis related to the depth of the lesion.

Bursted chocolate cyst



## Chocolate cyst vs haemorrhagic cyst of the ovary

00:22:17

Chocolate cyst	Hæmorrhagic cyst
Endometrial glands + stroma + Endometrial lining.	Not seen.
Surrounded by fibrotic tissue.	Not lined.
Surface adhesions +	Absent.

Risk factors for endometriosis :

1. Increased levels of oestrogen (hyperestrogenic conditions) :
  - Nulliparity.
  - Early menarche.
  - Late menopause.
2. All factors leading to increased bleeding (more retrograde flow) :
  - Short, frequent cycles.
  - Heavy menstrual bleeding.
  - Conditions which obstruct out-flow tract : Imperforate

### hymen & Congenital uterine conditions.

#### 3. Females with low BMI :

Thin females (increased consumption of trans unsaturated fats).

#### 4. White and Asian females.

#### Protective factors :

1. Multiparity.
2. Late menarche.
3. OCPs → Anovulation. → Decreased blood flow.
4. Consumption of omega 3 fatty acids.
5. Smoking → Inhibits aromatase. → Prevents conversion of androgen to oestrogen. → Less oestrogen.

- most common age group of endometriosis : 25 to 35 years (reproductive age).
- Also seen in pubertal and perimenopausal age group.
- Endometriosis in pubertal woman : Rule out congenital malformations of uterus (mullerian malformations).

### Clinical presentation

00:28:25

#### Triad :

1. Pain (secondary dysmenorrhea/dyspareunia) : most common symptom (80 % patients).
2. Infertility : Second most common symptom (25 %).
3. Adnexal mass (20 % patients) : Seen on per vaginal examination.

#### Less common symptoms :

1. Atypical uterine bleeding (hormonally active causing heavy or prolonged bleeding).
2. Pain while urination, cyclical hematuria, increased frequency/urgency : Bladder endometriosis.
3. Painful defecation, constipation, diarrhoea : Bowel endometriosis.
4. Painful abdominal mass, vicarious menstruation (bleeding during menstruation from umbilicus /any site)

other than vagina due to endometriosis) : Abdominal endometriosis.

5. Catamerial pneumothorax/hydrothorax (during menstruation) : Chest wall/pleural endometriosis.

Differential diagnosis :

1. Bleeding is more prominent : Fibroid.
2. Heavy menstrual bleeding + Dysmenorrhea : Adenomyosis.
3. Dyspareunia/dysmenorrhea + Adnexal mass + Infertility : Endometriosis.

### Per vaginal examination in endometriosis 00:32:25

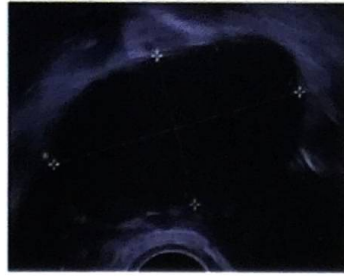
1. Uterus : Fixed and retroverted (Due to adhesions : Fundus pointing towards sacral promontory).
    - In normal women with retroverted uterus, it can be manually corrected.
    - In endometriosis, it is fixed.
  1. Adnexal mass (due to chocolate cyst).
  2. Tenderness in pouch of Douglas : Due to deep infiltrating endometriosis leading to adhesion formation.
  3. Nodules felt in the posterior fornix.
- Tender uterus is seen in adenomyosis.

These findings can also be absent in females with endometriosis.

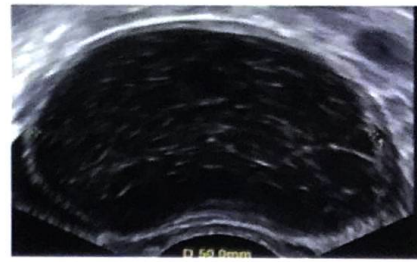
Hence lack of these findings doesn't exclude endometriosis.

### Investigations 00:37:07

1. Ultrasound : TVS /Trans vaginal Sonography (First investigation).
  - Normal.
  - Adnexal mass : Chocolate cyst/Endometrioma (20 %).
  - Bladder nodules.
  - Rectovaginal nodules.



Internal homogenous echoes  
(ground glass like appearance):  
**Chocolate cyst/endometrioma.**



White thread like structures: Thin  
strands of fibrin (net like  
appearance): **Haemorrhagic cyst.**

#### 2. CA 125:

- Non specific marker.
- **Raised in endometriosis** ( $\geq 35$  IU).
- Not used for diagnostic purpose.

#### 3. MRI Scan:

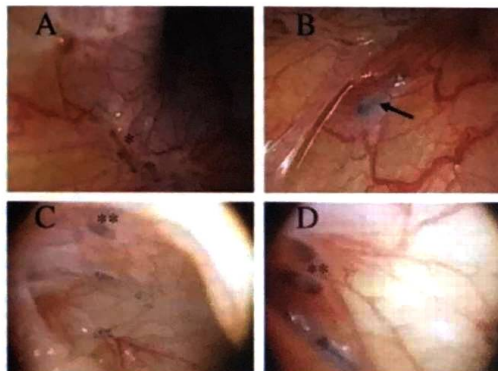
- Not done routinely.
- Done to accurately diagnose **deeply infiltrating endometriosis**:  
Bowel endometriosis.  
Thoracic endometriosis.  
Rectovaginal endometriosis.  
Bladder/ureter endometriosis.
- Done prior to laparoscopy.

#### 4. Laparoscopy:

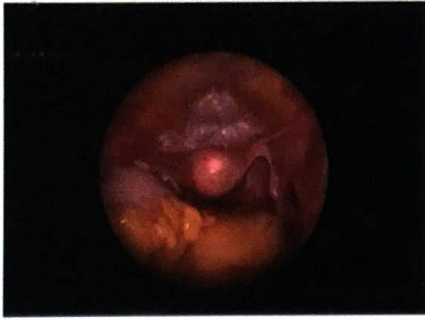
- **Investigation of choice** for endometriosis.
- Diagnostic, therapeutic (adhesiolysis) + for staging of endometriosis.
- While doing laparoscopy, sample sent for histopathology

Histopathology: **Gold standard** for diagnosing endometriosis.

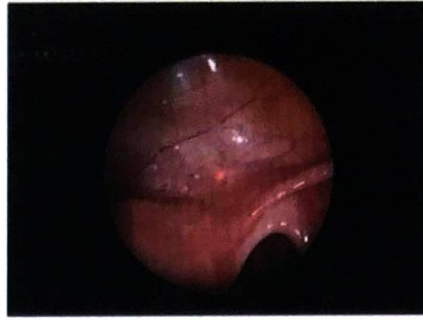
Endometrial lesions:



A: Red flame like lesions (new), B: Powder burn/gunshot  
appearance (chronic lesion), C & D: Peritoneal defect.



E1 : Laparoscope is introduced



E2 : Translucent blebs are seen. Endometriosis can appear in the form of white opacification.

Staging of endometriosis :

- Adhesions seen from stage 3.
- Deep implants seen from stage 3.

	Stage 1	Stage 2	Stage 3	Stage 4
	minimal	mild	moderate	Severe
Implants : Characteristics	Isolated implant.	Multiple superficial implants <5 cm scattered on peritoneum.		Distorted pelvic anatomy.
Adhesions	No adhesions.	No adhesions.	Adhesions seen (peritubal & periovarian).	Endometriomas. Adhesions seen.
Implants depth	Superficial.	Superficial.	Superficial & deep.	Superficial & deep implants

Management of endometriosis

00:47:37

Based on symptoms :

Pelvic pain :

- m/c symptom.
- m/c variety of pelvic pain :
  - Secondary dysmenorrhea > Chronic pelvic pain > Dyspareunia.
- Pain due to :
  1. Inflammation - Rx : NSAIDs.
  2. Neurological dysfunction - Oestrogen leads to :

Active space

- Increased nerve fibers at the site of endometrial implants.
- Imbalance of the sympathetic and sensory nerve fibers at the site of implant.
- Increased PGE<sub>2</sub> at the site of endometrial implants.

Rx: Decrease oestrogen using:

1. Progesterone (suppresses the activity of oestrogen).
2. Continuous GnRH.
3. GnRH antagonist.
4. Aromatase inhibitors (letrozol).
5. Danazol.

Secondary dysmenorrhea:

- Dysmenorrhea occurring d/t pelvic abnormality.
- MC cause of secondary dysmenorrhea: **Endometriosis**.
- Investigation -  
 Ultrasound:  
 Rule out other causes.  
 To detect endometrioma (surgery is the only treatment).

medical management of Dysmenorrhea (progressive) -  
 minimal/ mild pain:

1. First line: **NSAIDs + OCP's**.

- Oral Combined Pills (OCPs) → will make the cycles anovulatory.  
 Can be given as 3 weeks on, 1 week off (withdrawal bleeding) OR as Continuous regime.  
 Continuous regime - No menstruation / Retrograde menstruation.
- Only **NSAIDs** given if patient wants to conceive.

2. Second line: **Progesterone**:

Given continuously:

- Oral progesterone - MPA (100mg for 6 months).  
**Norethisterone acetate (2.5mg daily upto 20mg daily).**
- DMPA injection (3 monthly).
- LNG IUCD mirena.
- Nexplanon

Anti proliferative & anti inflammatory.

Advantages of progesterone :

- Progesterone → Decidualization of endometrial implants  
→ Endometrial atrophy, when used for long time (both endometrium and ectopic endometrium) → Amenorrhea  
→ Decreased retrograde menstruation.

3. Third line : GnRH agonist : Continuous.

Leuprolide (3.75mg IM monthly / 11.25mg 3 monthly).

First line treatment in severe endometriosis.

Continuously given → Decreased FSH & LH

(downregulates HPA axis) → Decreased oestrogen →

Hypoestrogenic environment.

Also reduces cox-2 levels in patients of endometrium.

Drawbacks :

It is expensive & has more side effects.

Patient will have menopause like symptoms → Add back therapy needs to be given.

Add back therapy - small amounts of oestrogen however will still create hypoestrogenic environment.

Alternative : Instead GnRH antagonist can be given like Elagolix (Nonapeptide ; orally active).

4. Laparoscopy : If medical management is not working.

moderate to severe pain :

1. First line drug : Continuous GnRH agonist or GnRH antagonist → No relief → Laparoscopy
2. Laparoscopy (directly).

Other drugs for endometriosis :

1. Aromatase inhibitors - Letrozole (decreases estrogen as aromatase is required to convert androgens to estrogen).  
Negative feedback on GnRH is lost → Increased FSH & LH  
→ Formation of cysts.

Letrozol is usually combine with OCPs or progesterone.

2. Progesterone receptor modulators -

Progesterone antagonist : mifepristone leads to immediate endometrial atrophy. Only approved by FDA for medical abortions.



Also leads to unopposed estrogen → Increases chances of endometrial hyperplasia or PAEC (Progesterone associated endometrial changes).

Selective Progesterone receptor modulator - **Ulipristal**.

FDA approves it as emergency contraceptive, however similar to mifepristone, not approved for use in endometriosis

3. **Danazol** - Has androgenic side effects (Hirsutism) & hence not used.

### Laparoscopy in endometriosis

01:10:43

**Investigation of choice** in endometriosis.

Helps in diagnosing & staging of endometriosis.

Sample can be taken simultaneously & sent for HPE.

Can also be used in surgical /therapeutic management of pain.

Indications :

1. Not relieved by medical management.
2. Deeply infiltrating endometriosis, not responding to medical treatment or leading to obstruction.
3. Endometrioma > 5 cm.

Surgical management of pain :

Adhenolysis.

Fulguration of implants of endometriosis.

Presacral neurectomy.

Laparoscopic uterosacral nerve ablation (LUNA).

Total abdominal hysterectomy (prevents new lesions from forming).

**Oophorectomy is not recommended.**

Even after laparoscopic surgery, patients will require some medical management.

Adolescents <16yrs - **OCPs**.

Adolescents >16yrs - **OCPs or GnRH agonists**.

Adult - **OCPs or GnRH or Progesterone**.

## Management of Endometrioma

01:16:57

Principles :

- **No role** of medical management.
- Endometrioma decreases fertility of female & AMH levels.  
Injury to follicles may occur unknowingly due to removal causing more infertility.  
If endometrioma is not removed :  
Risk of endometrioma -  
Increase in size → Leads to more pain & increased risk of torsion.  
Increased risk of ovarian malignancy.

management of Chocolate cysts :

- If patient wants to conceive -  
Irrespective of size , do expectant management.  
Do not remove endometrioma.
- If patient does not want to conceive :
  1. Size of cyst < 5 cm and asymptomatic : Follow up 6 monthly / 1 yearly with TVS.
  2. Size of cyst ≥ 5 cm : Laparoscopic cystectomy.

management of Infertility :

In minimal/mild endometriosis -  
multiple factor like defective folliculogens, defective pick up/implantation → Decreased fertility rate → **Unexplained Infertility.**

Treatment :

1. Clomiphene citrate + IUI (intra uterine insemination) :  
3 cycles.
2. If 3 cycles failed, IVF.

moderate to severe endometriosis : Adhesions are present.

Treatment : IVF.

Steps of laparoscopic cystectomy :

- Ovaries are identified (usuallu pink/pale).
- staging can be done.
- Ovary needs to be mobilised (freed from underlying adhesions).

- cyst may rupture from its weakest point (welcome sign).
- Injury to follicles can be avoided.
- Suction of the entire brown fluid from the pelvic cavity as it obscures the vision & may lead to adhesion formations.
- **Thorough lavage** of pelvic cavity by normal saline.
- Remove the cyst wall completely & preserve ovarian cortex (as just aspiration may lead to recurrence - 80%).
- **Injection vasopressin** can be used to cause vasoconstriction (less blood loss), bring clear plane of separation between cyst wall & ovarian cortex.
- With careful dissection, cyst wall is separated till hilum (blood vessels enter here) where maximum blood loss may happen.
- Cauterize the blood vessels at hilum & cut the cyst wall from underlying tissue.
- Gentle cautery for remaining ovarian bleeders.
- Reconstruct the ovary.
- Similar steps on the other side.
- Explore the entire pelvic cavity to fulgrate the remaining implants if any.

# FIBROIDS

## Introduction

00:00:25

- most common pelvic tumor in females.
- most common benign tumor in females.
- Aka Leiomyoma. They are smooth muscle tumors originating from myometrium.
- Fibroid which is present inside the myometrium is called as intramural/interstitial fibroid.
- To begin with all fibroids are intramural fibroid.
- Each fibroid/leiomyoma originate from a single myocyte (monoclonal in origin).

Fibroid is an estrogen (mainly) & progesterone dependent tumor. Major growth of fibroid occurs in the reproductive age (30-40 years). After menopause, the fibroid shrinks and its development is infrequent.

If the size of fibroid increases in menopause, it points towards malignancy.

Fibroid is most common in obese female (hyper estrogenic stage). more common in reproductive age (30-40 yrs).

more common in patients with early menarche, Nulli parous women and African American females.

Females with PCOS have increased risk of fibroid.

Protective factors :

- Smoking inhibits aromatase, thus decreasing estrogen.
- Physical exercise.
- Pregnancy (Absent ovulation).
- Multiparity.
- Breast feeding.

## Effect of OCP and Pregnancy on Fibroid

00:08:49

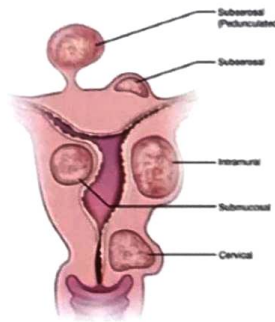
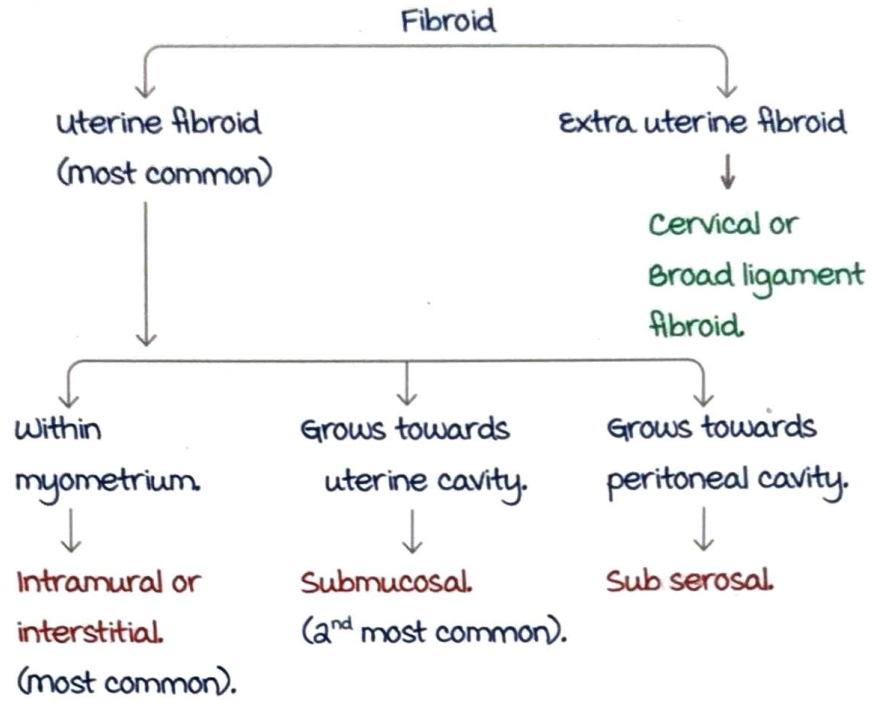
Use of OCP has no effect on size of fibroid.

The more the female becomes pregnant, more the anovulation and that is a protective factor.

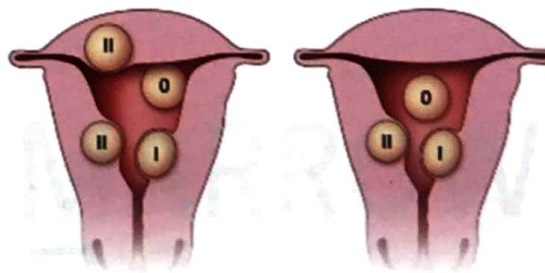
Active space

Patient with fibroid getting pregnant : Pregnancy has no effect on size of fibroid.

Types of fibroid :



Hysteroscopic classification of submucous fibroids



Wamsteker's classification

Adopted by ESGE

- 0 - Fibroids totally in cavity
- 1 - More than 50% in cavity
- 2 - Less than 50% in cavity

Active space

Sub serosal fibroid can be pedunculated or non-pedunculated.

## Broad ligament fibroid

00:14:05

Can be of two types : True broad ligament (BL) fibroid or Pseudo BL fibroid.

- True BL Fibroid : Arises from the broad ligament; Fibroid is present lateral to the ureter.
- Pseudo BL Fibroid : Sub serosal fibroid which grows into the broad ligament; Fibroid is present medial to the ureter.

Broad ligament Fibroid : Polycythemia (release of erythropoietic factor due to compression of ureter).

FIGO classification :

Fibroid classification : 8 varieties.

- Sub mucous fibroid : Type 0 (Completely within uterine cavity), Type 1 (< 50% in the myometrium / > 50% in the uterine cavity), Type 2 ( $\geq$  50% inside the myometrium / < 50% in the uterine cavity).
- The Hysteroscopic classification of sub mucous fibroid : Wamsteker's classification. Type 0 and type 1 can be removed hysteroscopically.
- Intramural fibroid : Type 3 and type 4.
- Sub serosal fibroid : Type 5, 6 and 7.
- Extra uterine fibroid (broad ligament & cervical) : Type 8.

## Presentation in a fibroid

00:22:15

most common presentation : Asymptomatic (incidental finding).

most common symptom : menorrhagia.

In endometriosis : Pain, dysmenorrhea, dyspareunia.

In polyp : Irregular bleeding or inter menstrual bleeding.

MC fibroid to cause menorrhagia : Submucosal fibroid.

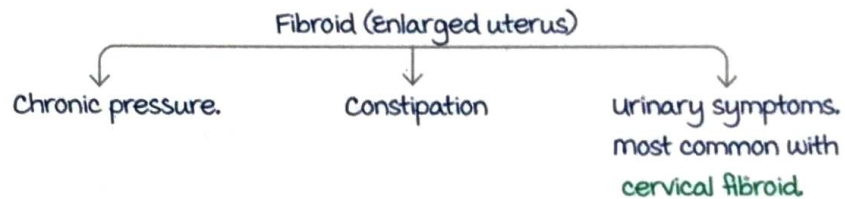
Fibroids can cause dysmenorrhea but can never be the chief complaint.

Fibroids can never cause dyspareunia.

Pain in fibroid:

- Indicates the fibroid is undergoing degeneration.
- Pedunculated subserous fibroid: Torsion.

Pressure symptoms: MC cause is Subserous fibroid.



Anterior cervical fibroid: ↑ urinary frequency.

Posterior cervical fibroid: urinary obstruction.

Infertility and recurrent abortion:

- MC fibroid causing this is sub mucous fibroid.
- It is due to prevention of implantation of sperm. Fibroid as a sole cause of infertility is seen in 1-3% of cases.

### Structure of fibroid

00:30:30

- white/off white in color resembling myometrium.
- Cut surface: Rough, whorled appearance, uneven.
- Broad base.
- Surrounded by pseudo capsule (Enucleated easily).
- more vascular at the periphery, least vasculature at the center. Hence degeneration begins from center of fibroid. (Polyp: vasculature at center).



- most common degeneration : **Hyaline degeneration**.
- Least common (0.2 to 0.5% chance) : Sarcomatous change/ malignancy (Leiomyosarcoma).
- most common fibroid undergoing **sarcomatous change** : **Submucous fibroid**.  
Changes occurring : Becomes painful and size increases, On HPE,  $\geq 10$  mitosis per HPF & the pseudo capsule is lost.
- Degeneration is more common in the center except **calcific degeneration** which is more common in the **periphery**.
- maximum chance for calcific degeneration is seen in **sub serous fibroid**.

**Wandering fibroid** : **Pedunculated subserous fibroid**. Lost its connection with the uterus.



## FIBROID : PART 2

### FIGO classification of fibroid

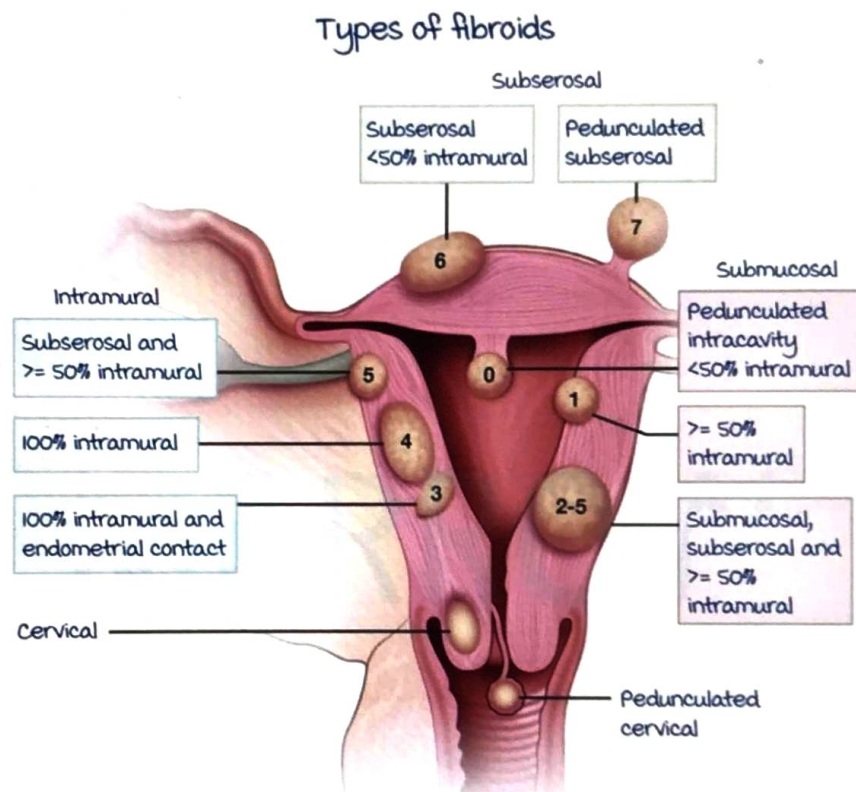
00:00:55

Type 0, 1, 2 : Varieties of sub mucous fibroid.

Type 3,4 : Varieties of intramural fibroid.

Type 5, 6, 7 : Varieties of subserosal fibroid.

Type 8 : An extra uterine fibroid (can be a broad ligament fibroid which could be a cervical fibroid).



FIGO classification of fibroid :

Type 0 : Fibroid is entirely in the uterine cavity.

Type 1 : more than 50% is in the uterine cavity (less than 50% is intramural).

Type 2 : more than 50% is intramural and less than 50% is in the uterine cavity.

Type 3 : Fibroid is 100% is intramural except for the edges that touch the endometrium.

Type 4 : Fibroid is 100% intramural. The edges do not touch

the endometrium.

Type 5 : Is a sub-serosal fibroid which is  $> 50\%$  intramural.

Type 6 : Is sub-serosal which is  $< 50\%$  intramural.

Type 7 : 100% sub-serosal.

Example :

Type a/s :

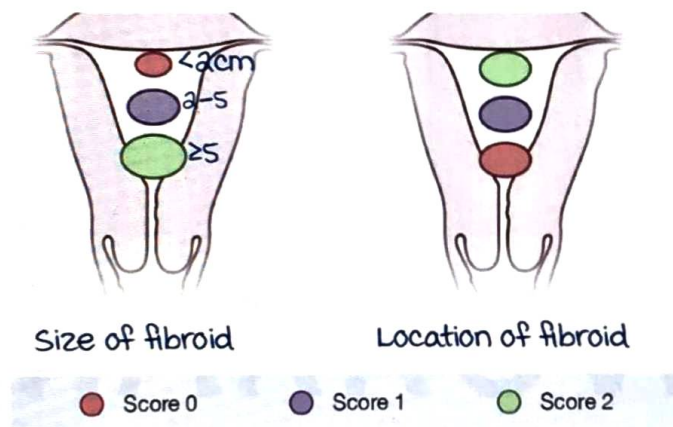
a inner boundary : Submucous fibroid which is  $\geq 50\%$  intramural.

s outer boundary : Subserosal fibroid which is  $\geq 50\%$  intramural.

According to Figo classification hysteroscopic myomectomy can be done in :

Type 0 and type 1 varieties of sub mucous fibroid.

Step w classification :



Helps to know if hysteroscopic myomectomy is possible.

Criteria used to assess the fibroid :

Location :

Upper-0.

Body-1.

Lower part-2.

Higher the score lesser are the chances of removal through hysteroscopic myomectomy.

This means that a fibroid which is located in the upper part

of uterus can be easily removed using hysteroscopic myomectomy.

Size :

< 2 cm easily removed : 0.

2-5cm : 1.

>5 cm score of 2.

This classification also includes other 3 criteria.

If the total score is 4 : Then hysteroscopic myomectomy is possible.

If the score is between 4-6 : Then GnRH administration can be done (decreased size of fibroid), followed by hysteroscopic myomectomy.

If score is > 6 then hysteroscopic myomectomy is not possible.

### Investigations

00:07:53

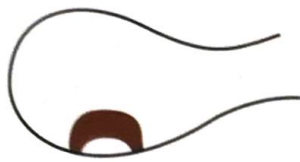
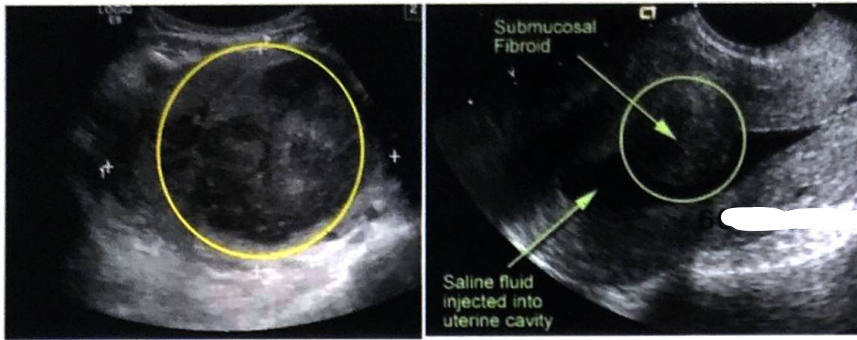
Investigation of choice : **USG**.

Findings :

- Intramural fibroid is seen in the USG
- It is a well-defined (because of the **pseudocapsule**) mass inside the myometrium.
- Centrally located.
- Homogenous in appearance.
- Appearance is similar to that of the **myometrium**.

For submucous fibroid : A better investigation than a plain USG is saline infusion ultrasound.

Features that differentiate a submucous fibroid from a polyp in a USG.



Submucous fibroid  
Base is broad



Polyp base is narrow



Fibroid

vessels in the periphery



Polyp

Feeder vessel sign

Submucous fibroid has a **broad** base while a polyp has a **narrow** base.

For a better clarification a **Doppler USG** can be used.

Fibroid : Covered by pseudo capsule and the blood vessels supplying are also in the pseudocapsule.

Polyp : Has a single vessel coming up till its centre. This is called the **feeder vessel** sign.

In this USG :

Subserous fibroid is arising from the uterine fundus.

Blood vessels can be seen around the periphery of fibroid.

These blood vessels are arising



Bridging vessel sign

Active space

from uterus and passing to subcutaneous fibroid.

This sign is called the **bridging vessel sign**.

It helps to differentiate between a mass arising from uterus from a mass arising from bowel.

Feeder vessel sign : Seen in polyp. Has a very narrow base of attachment

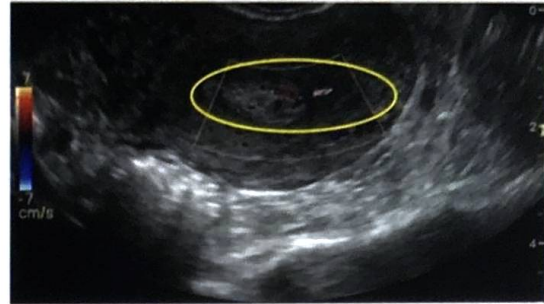
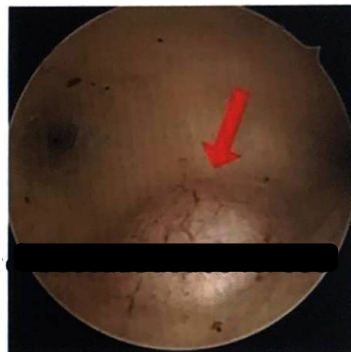


Image of polyp showing feeder vessel sign

Hysteroscopic image of a submucous fibroid.

- White/pale colour.
- Broad base.
- Surface vessels.



## Management of Fibroid

00:16:53

A patient with fibroid can come for treatment for one of the following symptoms :

1. Heavy or prolonged **bleeding**.
2. **Bulk symptoms** (abdominal protrusion, bladder or bowel dysfunction, early satiety).
3. Reproductive dysfunction (**infertility due to submucous fibroid** or recurrent pregnancy loss).

Pain : Pain in fibroid is very uncommon.

Can either be painful menstruation (dysmenorrhoea)

or non-menstrual pain causes include :

- Infection.
- In pregnant females : Red degeneration.
- Fibroid has undergone malignant transformation.
- Torsion of a pedunculated fibroid (very rare).

Pre-treatment evaluation :

Investigation of choice is : USG.

In case of a submucous fibroid a saline infusion sonography can be done.

Transabdominal scan :

- If the fibroid is palpable per-abdominally TAS is done.
- Can get additional information about other organs.
- Can detect the presence of ascites.

Transvaginal scan :

- If the fibroid is not palpable per-abdominally TVS is done.
- TVS is used for fibroid mapping in order to know the location, size and number of fibroid.

Pressure symptoms:

If the fibroid is located ;

- Anteriorly, then it irritates the bladder and the micturition frequency.
- Posteriorly, then it blocks the urethra and the bowel leading to urinary retention and constipation respectively.
- Laterally, it can press on the ureter leading to hydronephrosis or hydroureter. (TAS can give this information)

**Pseudo meig syndrome :**

It is when a fibroid/ovarian tumor other than Fibroma, Thecoma, Brenner's tumour or Granulosa cell tumour are associated with right sided pleural effusion and ascites.

If fibroma, thecoma, Brenner's tumour or granulosa cell tumour are associated with right sided pleural effusion and ascites, it is called **meig syndrome**.

Evaluate for :

## 1. Anaemia :

Correct the anaemia before surgery as myomectomy and hysterectomy both lead to increase blood loss as fibroid is an hyper-oestrogenic condition (vascularity of the uterus is increased).

Correction :

2. Infertility : **Rule out** other causes.

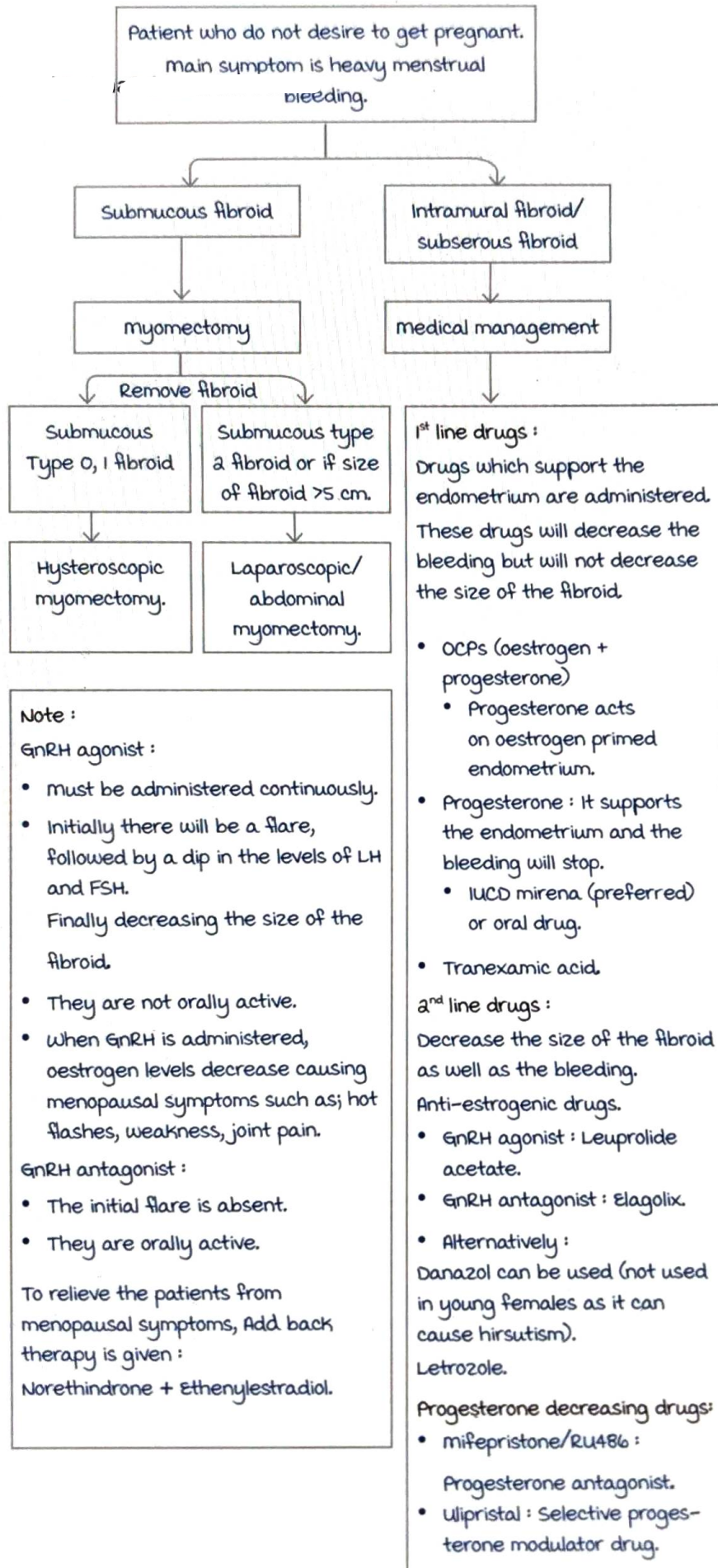
Semen analysis of the partner.

## 3. Endometrial carcinoma : Since fibroid is a hyperestrogenic condition it can predispose to endometrial cancer. Rule out endometrial cancer before conservative surgery is done by doing an endometrial biopsy.

**Treatment**

00:26:48

For treatment purpose patients can be divided into 2 categories :





The drug preferred initially, is **GnRH antagonist** as they are orally active and does not cause flare.

If this fails, GnRH agonist is administered continuously.

If patient denies either therapy or if both fails or not available, then the 2<sup>nd</sup> line management is uterine artery embolization.

Indications for GnRH agonist/antagonist in the management of fibroid :

1. In **heavy menstrual bleeding** :

Intramural/ Submucous fibroid : If the first line measures fail.

2. In patients with complaints of **pressure symptom**

As first line drug as it decreases the size of the fibroid.

3. In patients with fibroid and **anaemia** who doesn't respond to iron supplements (course of 3-6 months).

In such cases a course of GnRH + Iron is beneficial before surgery.

The GnRH agonist/antagonist will decrease LH/FSH causing amenorrhoea (Bleeding stops).

4. As a **transitional therapy** in patients moving from perimenopause to menopause.

uterine artery embolization :

It is a preferred 2<sup>nd</sup> line management in situations where oral GnRH antagonist is not available.

Principle :

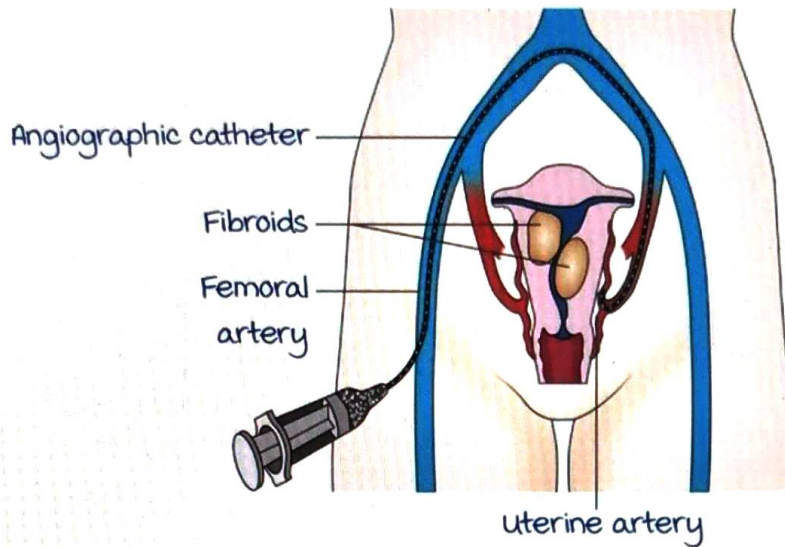
uterus is supplied by uterine artery which is a branch of anterior division of internal iliac artery.

By decreasing the blood supply to the uterus, the blood supply to the fibroid also decreases subsequently.

As a result of which, the size of the fibroid decreases and the symptoms are relieved.

Procedure : Is done via femoral artery the **contralateral uterine artery** is being embolised, using polyvinyl alcohol.

The ipsilateral artery is not ligated as it can result in kinking of the catheter resulting in a failed embolization.



Ideal candidate should have all of the characteristics :

- Heavy menstrual bleeding or dysmenorrhoea caused by intramural fibroid.
- Premenopausal.
- No desire for future fertility.

It is also used as a treatment option for adenomyosis and is very beneficial in patients with adenomyosis and fibroid together.

Absolute contraindications include :

- Pregnancy.
- PID.
- malignancy.
- Symptomatic fibroid.
- Desires future pregnancy.

Relative contraindications :

Post-menopausal female :

- After menopause size of fibroid decreases.
- Increased chances of leiomyosarcoma.

Pedunculated submucous/sub-serous fibroid with a narrow stalk :

- Their stalks may get necrosed and such fibroids may detach.

Side effects :

most common post procedural pelvic pain due to necrosis of fibroid.

2<sup>nd</sup> most common side effect is vaginal discharge.

### 3<sup>rd</sup> line of management of heavy menstrual bleeding in intramural/subserous fibroid

00:46:39

1. Focused ultrasound surgery : HIFU (High intensity focused ultrasound)/MRg FUS (magnetic resonance focused ultrasound).
2. Endometrial ablation :  
Not much use : Except if fibroid with heavy menstrual bleeding with associated bleeding disorder.
3. Hysterectomy : 2 types :  
Vaginal hysterectomy : Non descent vaginal hysterectomy (descent vaginal hysterectomy is done in patients with prolapse).  
Often done in uterus with fibroid <12 weeks size.  
Can be done up to 16 weeks size.

Advantages :

- Cosmetically better.
- Less painful.
- Less chances of incisional hernia.
- Less chances of paralytic ileus (bowel is not being handled).

Abdominal hysterectomy can be further classified into :

- Total abdominal hysterectomy.
- Laparoscopic hysterectomy.

High intensity focused ultrasound :

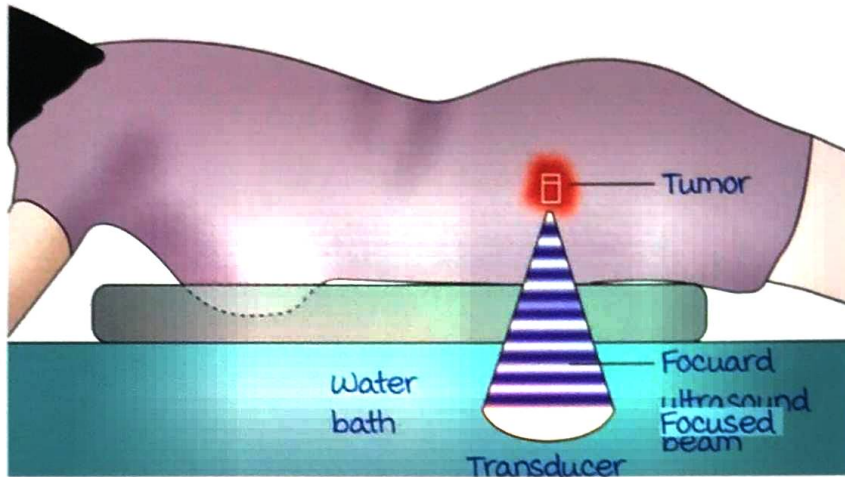
Patient lies supine and USG rays are focused on the fibroid causing coagulating necrosis of the fibroid.

magnetic resonance focused ultrasound :

Patient lies on MRI machine.

Source of radiation is inside the machine.

Here also there is coagulating necrosis of the fibroid.



Indications:

- If the number of fibroid  $< 3$ .
- Size of the fibroid  $< 10\text{cm}$ .
- Fibroid not calcified.

All the 3 conditions must be fulfilled.

Pressure symptoms (most common 2<sup>nd</sup> complain):

Intramural/subserous fibroid due to increase in the size of the fibroid.

management: **Decrease the size** of the fibroid.

- GnRH agonist/GnRH antagonist.
- Perimenopausal: uterine artery embolization.

Infertility:

most commonly seen in **submucous fibroid**.

Type 0, 1: Hysteroscopic myomectomy.

Type 2 submucous or any other fibroid: Laparoscopic myomectomy or abdominal myomectomy.

Rule out other causes of infertility before proceeding with these surgeries.

Expectant management of fibroid :

- Perimenopausal female : Asymptomatic.
- Post-menopausal female : Asymptomatic.
- Reproductive age female with asymptomatic fibroid < 12 weeks pregnant uterine size.

Follow up :

TVS x 6 months.

- If patient has rapid growth of fibroid.

OR

- If patient develops pain.

If the following features are present then surgery must be done.

### Myomectomy

00:57:00

It is the **enucleation** of the fibroid.

Blood loss during the procedure is intense as the uterus is highly **vascular**.

Steps taken to decrease blood loss during myomectomy :

1. Preoperative : GnRH analogues plus iron to increase haemoglobin levels.
2. Intraoperative :
  - Keep blood ready in case the need for transfusion arises.
  - Hypotensive anaesthesia.
  - Vasopressive drugs are injected into the capsule of fibroid.
  - Bonney's myoma **clamp/tourniquet** at the level of uterine artery.

Vascular clamp : At the infundibulo pelvic ligament (ovarian vessels supply the ligament).

Complications :

**Haemorrhage.**

**Adhesion formation** : It is more if the incision is made on the posterior surface of the uterus.

Persistent myomas despite doing myomectomy.

The ideal time to conceive after myomectomy is **6 months**, but she may conceive between 3-6 months.

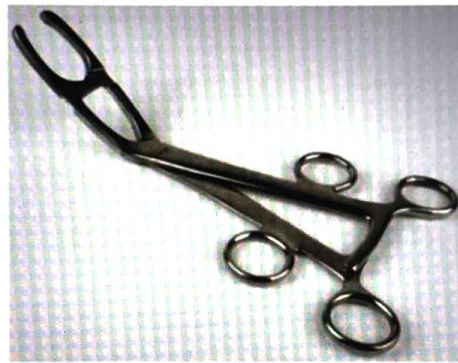
Following myomectomy, **symptomatic relief** occurs in 80% of the patient.

Subsequent surgeries are done in **10-25%**.

Important instrument for myomectomy :



Bonney's myoma screw



Bonney's myoma clamp

Bonney's myoma screw is used to hold the fibroid during myomectomy.

Bonney's myoma clamp is used to decrease blood loss during myomectomy.

	UAE	mRg FUS	myomectomy
Absolute C/I	malignancy	malignancy	malignancy
	Current pelvic infection	Current pelvic infection	Current pelvic infection
	Pregnancy	Pregnancy	Pregnancy

Relative C/I Size of uterus	> 20 - 24 weeks	> 24 weeks	Hysteroscopic myomectomy
pregnancy	Desires preg- nancy	Desires pregnancy	Type 0,1 fi- broid
menopause	Yes	Yes	Best = Size < 3cms of fibroid
Pedunculated subserous fibroid	Yes	Yes	Laparoscopic size < 10cm.
	Coagulopathy. Renal impair- ment. Distorted anatomy due to previous salpingecto- my or radia- tion.	Fibroid > 10cm Fibroid >12cm deep from skin. No. of fibroid >4. Calcified fi- broid.	No. of fibroid < 3.

Between UAE & MRg FUS :

Preferred is UAE, as re-intervention rate is high in MRg FUS.  
Symptomatic improvement is less with MRg FUS.

New Technique : For fibroid = Radiofrequency ablation.

Should not be used for submucous Type 0, Type 1, Fibroid.

Desire of future pregnancy is not a contraindication.

Best suited for fibroid < 6 to 10 cms and uterine size < 16 weeks.

Rare manifestations of fibroid :

If weight of fibroid > 1000g → DVT.

Increased RBC count due to excessive erythropoietin → myomatous erythrocytosis syndrome.

Mutation in Fumarate Hydratase gene leading to Hereditary Leiomyomatosis & renal cell Ca. / HLRCC syndrome or Reed Syndrome.

Rarely : Extrauterine smooth muscle tumors may develop in females with fibroid → Leiomyomatosis.

### Case presentation

01:11:50

History :

1. Presenting complain :

Heavy menstrual bleeding :

Number of days since bleeding.

Passage of clots.

Feeling of tiredness/fatigue.

Dysmenorrhoea.

Pressure symptoms :

- Abdominal distention.
- Difficulty in passage of stools.
- Difficulty in micturition.
- Varicose vein oedema.

Site :

Anterior.

Lateral : most common.

Posterior.

2. Negative histories :

- Post coital bleeding indicates cervical cancer.
- Intermenstrual bleeding : Polyp.
- Dyspareunia : Endometriosis.
- Bleeding from other sites : Epistaxis, gum bleeding,



bruises.

- History of anticoagulant drug intake.
- History of IUCD insertion (not OCP intake).
- Symptoms of Thyroid disease.
- Abdominal distention :  
To differentiate between fibroid and adenomyosis.  
It can also be an ovarian malignancy (granulosa cell tumour).
- Loss of appetite/weight loss : malignancy.
- History of preceding amenorrhoea : Pregnancy and AUB-O (metropathia haemorrhagica).
- History of discharge P/V, fever : PID.

### 3. Menstrual history :

- Age of menarche :  
The importance of age of menarche is that since fibroid is a hyperestrogenic condition they are more common in females with **early menarche**.
- LMP.

### Past and present cycle :

- Cycle length.
- Day of flow.
- Number of pads used.
- Passage of clots.

### 4. Obstetric history :

Fibroid is more common in **nulliparous** females.  
mention if the patient has the desire to conceive in the future as the treatment options can be chosen accordingly.

### 5. Contraceptive history :

Temporary methods.  
Tubectomy/vasectomy.

#### 6. Past history :

Chronic disease :

- Diabetes mellitus.
- Hypertension.
- Asthma.
- TB.
- Thyroid diseases.
- Bleeding disorders.
- Previous surgeries.
- Previous blood transfusions.

#### 7. Family history :

Strong genetic association.

more common in 1<sup>st</sup> degree relatives.

Examination :

##### 1. Palpation :

Location.

Consistency : Firm with irregular surface borders.

Borders: mention which borders can be felt.

mobility of the mass : **Transverse mobility** is achieved in case of fibroid.

##### 2. Percussion :

Dull on percussion.

##### 3. Auscultation :

Normal bowel sound is heard.

##### 4. Bimanual examination findings :

Enlarged, mobile uterus with irregular contour.

A fixed retroverted uterus is a typical finding of **endometriosis**.

D/D : Adenomyosis.

Adenomyosis :

It is the growth of the endometrium inside the myometrium as a result of which there is symmetrical enlargement of the uterus.

Whereas in the case of a fibroid there is asymmetrical enlargement of the uterus.

Per-vaginal findings : Symmetrically enlarged globular uterus which is **not more** than 12-13 weeks uterus size.

### **Steps of vaginal hysterectomy**

01:22:46

Advantages of Vaginal hysterectomy over Abdominal Hysterectomy :

Takes less time (Less anesthetic complications).

No scar (Cosmetically better).

No possibility of incisional hernia.

Less operative complications (injury of ureter/bowels).

Post operative recovery is quicker (Pt can be discharged earlier/ Pain is lesser).

Bowel hand handling does not happen : Less chances of paralytic ileus.

Disadvantage : Other organs cannot be explored.

Indications of Vaginal Hysterectomy :

Prolapse.

Fibroids (Non descent vaginal Hysterectomy) can be done if :

No adhesions.

Size is less than 16 weeks pregnant uterus size.

Anatomy of Uterus :

Uterus is held in position by number of ligaments, starting from bottom :

Uterosacral & macanrod's ligament.

Uterine artery. (At level of internal OS).

Round ligament, Fallopian tube & Ovarian ligament (At level of Cornua).

Before the surgery the patient's bladder must be emptied using a foleys catheter or a metal catheter.

Expose the cervix, retract the posterior wall of vagina.

Step 1 : Hydrodissection : 1ml Adrenaline mixed with 2ml of NS, Infiltrate over the cervix and vagina, at angle of 15 to 30°

Step 2 : An incision has to be given at the cervicovaginal junction. This junction is 1.5 cm above the external os.

Step 3 : Pubocervical fibres are cut using a sharp scissors.

Step 4 : Once sharp dissection is done it is followed by blunt dissection using fingers to create space between cervix and bladder so that bladder does not get injured.

Step 5 : Clamping the ligaments. There are several techniques.

One technique is, by clamping the uterosacral ligament complex on one side, cutting and ligating it (vicryl 1-0 suture is used)

Step 6 : Pouch of Douglas is opened so that space is created.

using Kocher's forceps the pouch is held and with the help of scissors the pouch is opened. Then moving on to the contralateral uterosacral ligament ligation.

Step 7 : uterine artery ligation. The landmark for uterine artery is at the level of internal os. With the help of sharp scissors the artery is cut . After this the vessel is ligated. The same process is done on the other side.

Step 8 : Deliver the uterus.

The uterus is cut in the centre and all the fibroids are enucleated.

The fibre of pseudo capsule is then removed.

Step 9 : Once the fibroid is removed a last clamp is put at the cornual end of the uterus it is then cut and ligated. The same procedure is done on the other side.

At the cornual end the round ligament, ovarian ligament and

fallopian tube is present.

Step 10 : The uterus is then removed.

Step 11 : The vault of the vagina is sutured.

Step 12 : Saline irrigation is done to look for fresh bleeding.

Other techniques :

- Another technique is, by opening the pouch of Douglas first.
- While some open the uterovesical pouch first.

### Instruments required for vaginal hysterectomy

01:37:58

1. Foleys catheter/metal catheter :

2. Instruments required for a speculum examination.

Sims double blade speculum :

It is a non self-retaining speculum used to retract the posterior wall of the vagina.

Owards self-retaining weighted speculum.



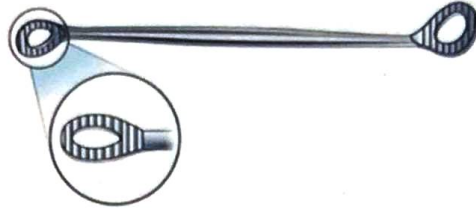
Sim's speculum

3. Anterior vaginal wall retractor :

There is a loop on either end. One is facing upwards while the other faces downwards.

It has transverse serrations that help fix into the rugosities of the vagina.

used to retract the anterior wall of the vagina.



Anterior vaginal wall retractor

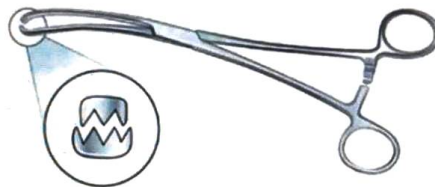
4. Vulsellum :

The anterior lip is held using a vulsellum.

It has 2 concave blades with a gap in between them.

It has a ratchet like lock.

The end has multiple rat like teeth.



vulsellum forceps

5. Tenaculum :

This is also used to hold the anterior lip of cervix.

This is not used in vaginal hysterectomies as it has a single tooth therefore increase chances of bleeding.

6. Blade no. 22 and BP handle no.4 :

This is used to make an incision at the cervicovaginal junction.



## Scalpel blade sizes and shapes

## 7. Deaver's retractor :

used to retract the posterior wall.

Question mark shaped retractor.

It has a narrow end and long handle.



Deaver's retractor

## 8. Landon's retractor:

used to push the bladder up.

L shaped retractor.



Landon vaginal retractor

## 9. Kocher's forceps :

It is used to hold the pouch of douglas.

It does not have space between the blades.

It has multiple transverse serrations on both the blades.

On one side it has a single tooth and on the other it has 2 teeth.

It must be differentiated from vulsellum (has space between the blades).



Kocher's hemostatic forceps

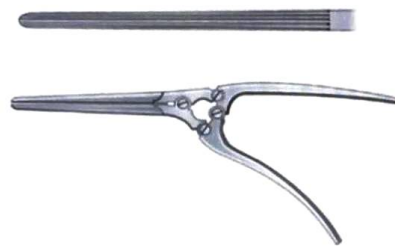
#### 10. Clamps :

Straight or curved clamps.

Used to clamp the uterosacral and mackenrodt ligament complex pedicle.



Doyen's intestinal occlusion clamp



Payr's crushing clamp

#### 11. Vicryl I-0 :

Suture material most commonly used for hysterectomies.

Pedicles that are ligated : uterosacral pedicle, mackenrodt pedicle, uterine artery pedicle, cornual pedicle.

#### 12. Needle holder :

The blades have a groove to hold the needle.





Needle holder

### 13. Allis forceps :

To hold any **hard tissues**.



Allis tissue forceps

### Other surgical instruments :

- Doyen's retractor :  
used to retract the bladder in abdominal surgeries.



Doyen's retractor

- Czerny's retractor :  
It is a Z shaped retractor.  
It is used to retract the skin to view the rectus sheath.



Czerny's retractor

- Cheatle forceps :  
It has a peculiar curved beak shaped end.  
It doesn't have a ratchet lock.  
(ovum forceps which is a spoon shaped forceps also doesn't have a ratchet lock).  
used to take out instruments.



Differentiate between the two :

uterine sound	Bladder sound
It has a well-defined curve	Does not have a well-defined curve
Olive tip is present	Olive tip is absent
Calibrated	Not calibrated

Allis forceps	Kocher's forceps
Gap present between the blades	No gap between the blades
No serrations	multiple transverse serrations are present on the blade
multiple rat like teeth	On one side it has a single tooth and on the other it has 2 teeth

Allis forceps	Vulsellum
Rat like teeth present	Rat like teeth present
Small in size	Large in size
Blades : Straight	Blades : Concavity facing upward

### Abdominal hysterectomy

01:52:50

Although the principle of both vaginal and abdominal hysterectomy are same, there is a difference in the **sequence of clamping**.

First clamp : At the cornual angle enclosing the round ligament, ovarian ligament and the fallopian tube.

Second clamp : At the level of internal os where **uterine artery** is clamped.

Third clamp : At the **uterosacral and cardinal ligament complex**.

Fourth clamp : At the **angles of the vagina**. This is because uterine artery gives a very important branch which is the descending cervical artery that supplies the cervix and the vagina. In order to prevent bleeding a clamp is placed at the angle of the vagina.

Once the uterus is removed the vault is sutured. To prevent vault prolapse the uterosacral ligaments are sutured at the angles of the vault.

This is called **uterosacral suspension or vault suspension**.

Steps of total abdominal hysterectomy :

Step 1 : A low transverse incision is made called the **Pfannelstiel incision**.

All the layers including the skin, subcutaneous tissue, the rectus sheath and all the muscles are cut. After the rectus sheath is cut, the muscles are separated using hands.

Once this is done the **peritoneum** is cut and the uterus is delivered out.

Several subserous fibroids can be seen.

To this fibroid, omentum is attached.

Step 2 : First clamp is at the **cornual angle** enclosing the round ligament, ovarian ligament and the fallopian tube.

Once the clamp is placed it is then cut and ligated.

Step 3 : The peritoneum is cut at the level of the **utero-vesical pouch**. The loose fold of peritoneum has been identified and the utero-vesical pouch is cut.

Step 4 : The bladder is pushed downwards and the uterine artery is clamped, cut and ligated.

The clamp is placed at the level of internal os.

The same procedure is repeated on the other side.

Step 5 : Clamping the uterosacral and the cardinal ligament complex is clamped, cut and ligated.

Same procedure is repeated on the other side.

Once this is done, a clamp is used to hold the vagina and to clamp the descending **cervicovaginal artery**. The clamps are placed at the angle of the vagina.

Step 6 : The uterus is removed.

Step 7 : When the uterosacral ligament was ligated a long thread was left behind on both the sides so that the ligament can be attached to the angles of the vault.

Step 8 : Vault is repaired.

Suture material used is Vicryl 1-0.

The total abdominal hysterectomy is also called simple hysterectomy or type I extra facial hysterectomy or type A hysterectomy.

Total abdominal hysterectomy with bilateral salpingo-oophorectomy.

First clamp : Is placed at the **infundibulopelvic ligament**.

Wertheim's hysterectomy/type 2 hysterectomy/modified radical hysterectomy/type B hysterectomy.

The difference between this and total abdominal hysterectomy is the **removal of parametrium** (ligaments that surround the

medial half of cardinal ligament, medial half of uterosacral ligament, fallopian tube and the ovaries

The third clamp : Is placed mid-way between the **origin and the insertion** of cardinal and uterosacral ligament.

The cardinal ligament originates in the uterus and inserts in the pelvic side wall.

The uterine artery clamp is placed at the level of internal os after it has given origin to the ureteric branch.

maximum incidence of **ureteric injury**.

Radical hysterectomy/Type 3 hysterectomy/Type C hysterectomy.

Here the entire cardinal ligament and uterosacral ligament along with the uterine artery are removed.

The third clamp is placed at the level of their **insertion**.

The uterine artery clamp is placed at the **origin** of the uterine artery.

It originates from the **anterior division of internal iliac artery**.

## Hysteroscopic resection of a submucous fibroid

02:03:20

Only type 0 and I can be easily removed by hysteroscopy.

Where > 50% of the fibroid is coming inside the cavity.

Hysteroscope is introduced, distention media is already there.

The **osteal openings** can be seen.

A submucous fibroid can be appreciated.

To know the accurate percentage of fibroid in the cavity the intrauterine pressure must be **lowered**.

When the intrauterine pressure is lowered the size of the fibroid will **gradually increase**.

The vessels can be seen in the **pseudocapsule**.

Once the size is confirmed, a **resectoscope** (22FR) is used to cut through the fibroid and the pieces are removed.

Once the fibroid is removed the pink endometrial lining can be seen.

Removal of all the pieces of fibroid is done using a **in-bag morcellator** or the ports.

Earlier morcellation was done where the fibroid was cut into pieces and the parts were removed through the vagina but few cases of leiomyosarcoma was reported.

**In-bag morcellator :**

It is a **stomach shaped bag** and comes with an inserter.

The bag is rolled with the inserter and placed inside the uterus with the help of the resectoscope through the port.

Once it is placed, the bag is **unfolded**.

the fibroid is put in the bag.

The entire bag is **removed** through the port insertion

(one end from one port and tail end through the other port).

## POLYP AND ADENOMYOSIS

### Polyp

00:00:57

One of the most common causes of abnormal uterine bleeding (AUB) in premenopausal and postmenopausal women. Localised hyperplastic overgrowth of endometrial glands & stroma around a vascular core which forms a sessile or pedunculated projection from surface of endometrium. A polyp has blood vessel running in its center.

Grossly :

Polyp appears :

Narrow.

Beefy red in colour.

Generally pedunculated with thin base (narrow).

Soft and friable to touch.

A dilated gland can be visualised sometimes.

Smooth surface.

Fibroid :

White in colour.

Irregular contour.

Whorled appearance.

Risk factors : OATS.

Obesity .

Increasing Age.

Tamoxifen use (higher chances of a polyp becoming malignant).

Syndromes :

Lynch syndrome.

Cowden syndrome.

All these are also risk factors for endometrial cancer.

Clinical manifestations :

AUB (most common).

In premenopausal female :

- Intermenstrual bleeding.
- Irregular bleeding.

In post menopausal : Post menopausal bleeding.

Generally bleeding is less (not heavy).

Bleeding may not respond to medical treatments (rule out polyp).

may be a cause of infertility.

Do not lead to adverse pregnancy outcomes like abortion, pregnancy loss.

95% cases benign.

If malignant should be treated like endometrial carcinoma.

Diagnosis : AUB.

UPT : Advised and if negative .

Transvaginal scan (First investigation) :

Polyp : Hyperechoic mass with narrow base.

Fibroid : Hypoechoic mass with broad base.



Doppler :

Polyp :

**Feeder vessel sign** : A single blood vessel running upto the centre.

Fibroid : Surface blood vessels.

Hysteroscopy :

Investigation of choice.

Should be done for patient planned on surgical & medical management (to rule out malignancy).

**Diagnostic & therapeutic.**



Polyp appears :

Smooth reddish/beefy structure.

Pedunculated.

No surface vessels.



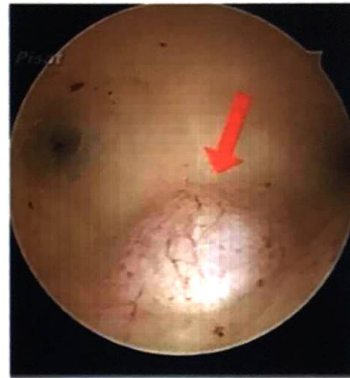
Gold standard investigation : After removal of polyps it should be sent for histopathological examination.

Hysteroscopic view of submucous fibroid :

White colour/pale.

Broad base.

Surface vessel.



Management :

Hysteroscopic polypectomy.

Indicators for removal : In all post menopausal women irrespective of symptoms (higher chance of carcinoma).

In premenopausal women with :

- AUB.
- Infertility.
- Multiple polyps.
- Size of polyp > 1.5 cm.
- Prolapsed polyp.
- Recurrent polyp.

In premenopausal women :

If polypectomy not done

↓  
Should do diagnostic hysteroscopy

↓  
Then put patient on progesterone/continuous GnRH (polyp is an overgrowth of endometrium).

Generally **bleeding recurs** after the treatment is stopped.

## Hysteroscopy

00:12:07

Telescope which is inserted into the uterus via cervix and vagina.

Used to visualise :

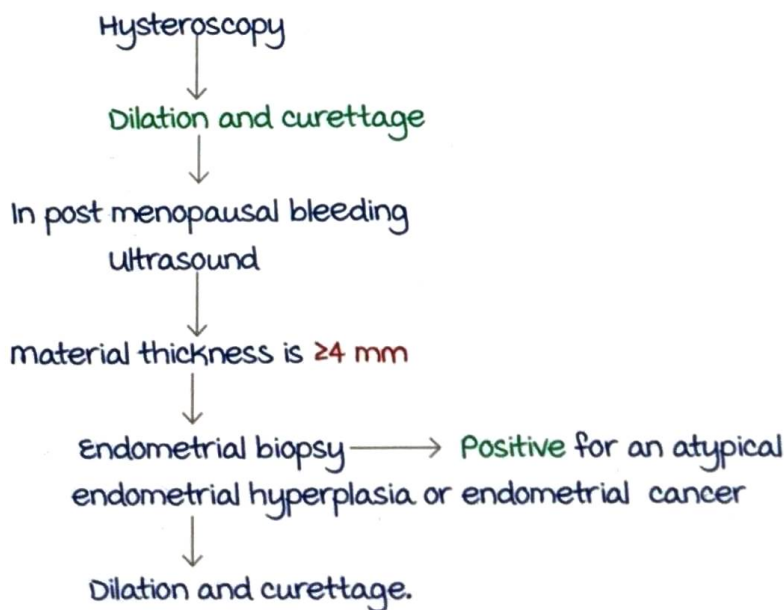
- Endometrial cavity.
- Cervix.
- Endocervical canal.
- Tubal ostia.

Diagnostic and therapeutic.

most common indication : Infertility.

Indications :

- Atypical uterine bleeding.
- Post menopausal bleeding.
- Infertility.
- Recurrent early pregnancy loss : Because hysteroscopy visualise sub mucous fibroids
- Atypical uterine bleeding.  
material biopsy is done and if endometrial biopsy comes out to be positive.



Diagnostic and therapeutic indications done in case of :

- Asherman syndrome.

- Polyps. Polypectomy
- Uterine septum → Hysteroscopic resection of the septum.
- In case of blocked tubes on HSC on hysteroscopy

Bilateral cornual block

Laparoscopic chromo perturbation right + insert hysteroscope

Through scope pass a thin guidewire

Any spasm of the tubes will get relieved

- Mullerian anomalies.
- Lost copper T : Aids in removal.

Position of the patient during hysteroscopy :

**Lithotomy :**

Head in neutral position neither should head be elevated  
neither should head be in a low down position.

Level of vagina at the level of the elbow.

Pain relief during hysteroscopy :

Regional anesthesia (multiple operative) : Less preferred.

**IV sedation and paracervical block is preferred.**

uterine cavity is a potential cavity (anterior and posterior wall of the uterus opposed to each other).

uterine cavity walls separate on insertion of distention media (to see clearly).

1<sup>st</sup> distention media : Carbon dioxide.

Now carbon dioxide is not used these days **except for diagnostic hysteroscopy** as :

On passing current → the temperature increase → increases smoke (visibility is not there).

Chances of air embolism.

On hysteroscopy the pressure inside the uterus : maintained around 75 to 80 mm.

may be increased to 125 to 150 mm Hg especially in nulliparous females.

Do not exceed : 150 mmHg.

Fluid distention media :

2 types of fluids :

Electrolyte deficient fluid :

- 1.5% glycine.
- 3% sorbitol.
- 5% mannitol.

Electrolyte rich media :

- Ringer lactate.
- Normal saline : Diagnostic + operative.

Both of them are used for operative hysteroscopy .

Electrolyte deficient media can be used with monopolar and bipolar instruments.

Electrolyte rich media can be used : Only with bipolar instruments.

**Not use** with **monopolar** instruments as : Electrolytes gets spread and can lead to shock & burns.

Drawbacks of electrolyte deficient media :

- Lead to water intoxication.
- most of the electrolyte deficient media are hyposmolar and Lead to hyponatremia **except for mannitol** (as iso osmolar).

Fluid distention media is absorbed by the patient's body.

Input = Fluid which is put inside.

Fluid which has come outside = output.

Fluid absorbed/deficit : Input-output.

For example :

Input : 3l of normal saline.

Output : 2.5 litre of normal saline.

Fluid deficit is 500 ml (absorbed by patient's body).

Stop procedure when using :

Electrolyte deficient media with **IL** fluid deficit (early water intoxication possibility).

Electrolyte rich media with 2.5 L fluid deficit.

### Complications :

uterine perforation.

Fluid overload :

Symptoms :

Nausea.

Vomiting.

Headache.

Visual symptoms.

Prevention :

Restrict operating time to 1 hour.

Calculate fluid deficit.

IUP not be  $\geq 180$ mm Hg.

Air embolism.

Hyponatremia (delirium, confusion).

### Contraindication :

Viable intrauterine pregnancy.

Current pelvic infection/herpes infection.

Carcinoma cervix/carcinoma endometrium.

## Hysteroscopic instruments

00:28:06

Telescope : Standard size : 4 mm, 30° telescope.

mini telescope :

1.8 mm, 0° telescope.

Office hysteroscope (used in OPD):



Diagnostic hysteroscopy :

The telescope is inserted into a smooth sheath → goes inside cervix → visualise uterine cavity.

Single channel sheath with an obturator (5 mm sheath).

Diagnostic sheath is put over telescope.

Retraction of walls of vagina → Cervix held with tenaculum →

Cervix dilated with Hegar's dilator (up to 5 number) or

misoprost 200 micrograms 12 hours before the procedure.

Have only one channel for entry of fluid.

No exit channel.

Carbon dioxide, normal saline could be used.



For operative hysteroscopy : Sheath will have 4 channels.

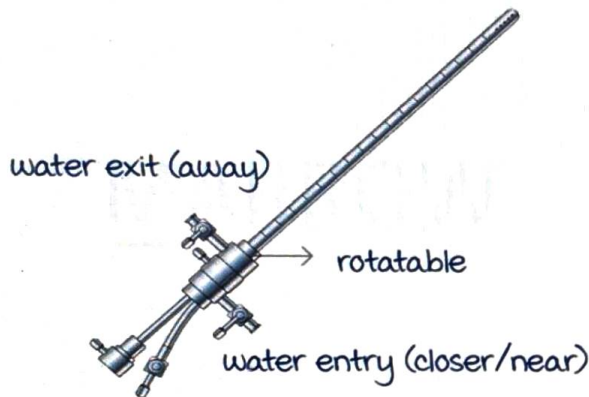
4 channels :

1 : Telescope.

2 : Instruments like scissors, grasper, biopsy forceps depending on the procedure.

3 & 4 : For fluid.

The near one is for fluid entry and away is for fluid exit.



Instruments inserted through channel no.2 :

Various cutting and grasp instruments.

These instruments are very flexible.



Uses :

Adhesolysis in Asherman syndrome

Remove lost IUCD.

Take biopsy.

Chromopertubation/hysteroscopic cannulation.

Falloscopy.

Active space

**Drawback :**

No provision to pass current.  
Cannot cauterise.

In Diagnostic hysteroscopy, laparoscopic is not required.

In operative hysteroscopy :

Like in treatment of Asherman syndrome.

Laparoscopy is simultaneously done with hysteroscopy.

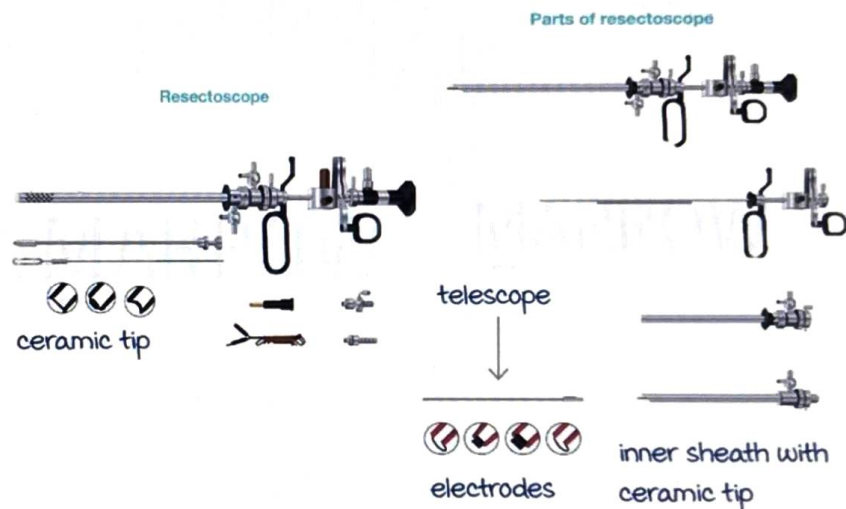
Hysteroscopy + Laparoscopic = **Pelviscopy**.

For electro surgical procedures :

Use **resectoscope**.

Assembled resectoscope.

Disassembled resectoscope with its parts.

**Parts :**

- Working element.
- Outer sheath.
- Inner sheath with ceramic tip : Act as insulator.
- Telescope.
- Electrodes.

**Procedures performed :**

Submucous myomectomy.

Polypectomy.

metroplasty.

Resection of septum.

Trans Cervical Resection of Endometrium (TCRE).

## Adenomyosis

00:40:08

Condition where endometrial glands and stroma are present in myometrium.

> 1 HPF or  $\geq 2.5$  cm below myometrium.

Resulting in hypertrophy of surrounding myometrium  
Symmetrical enlargement.

Case seen in multiparous woman (4<sup>th</sup>-5<sup>th</sup> decade).

condition can coexist with fibroid > endometrium.

m/c complaint :

Heavy menstrual Bleeding (HMB) + Dysmenorrhea.

m/c : Heavy menstrual bleeding > dysmenorrhea.

Chronic pelvic pain.

Per vaginal examination :

uterus :

mobile, symmetrically enlarged : Globular uterus.

Never > 12 weeks enlarged.

uterus is soft/boggy.

Tenderness + : Halban sign.

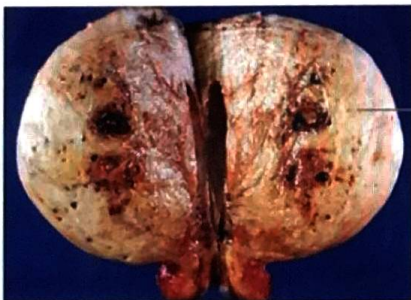
No adnexal mass/tenderness.

Differential diagnosis :

Clinical differences :

In endometriosis : uterus fixed & adnexal mass +.

In fibroid uterus : Irregular enlargement/firm/non tender.



Haemorrhage in endometrial gland present in the myometrium.

↓  
Globular : symmetrically enlarged uterus.

Investigation :

Presents with AUB.

UPT suggested → negative → Transvaginal scan (TVS).

Active space

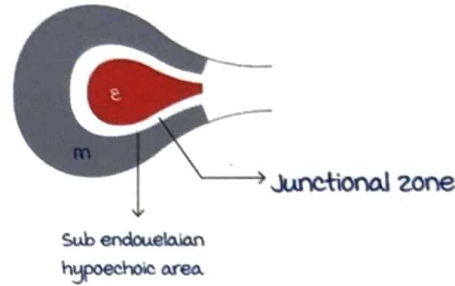


Normal endometrium in TVS :

Between endometrium and myometrium there is a subendometrial hypoechoic area.

Subendometrial hypoechoic area represents the junctional zone.

endometrium and myometrium appear as hyperechoic area.

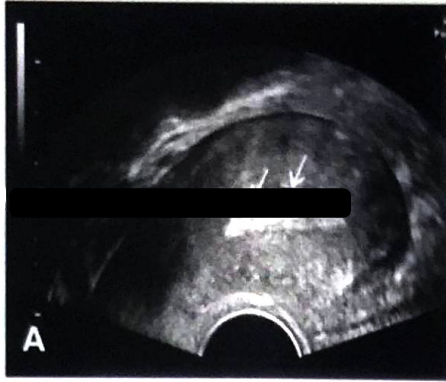


morphological uterine sonographic assessment (MUSA) criteria for diagnosis of adenomyosis :

Active space

Description	Drawing
1. Asymmetrical myometrial thickening	
2. myometrial cyst	
3. myometrial island	
4. Fan shaped shadowing	
5. Echogenic subendometrial lines / buds	
6. ↑ vascularity in cervix	
7. Irregular junction zone	
8. Absent junction zone	

Fan shaped shadowing/Venetian blind appearance.



myometrial cyst



Venetian blind appearance :  
Alternate dark & light bands.

management :

If pregnancy not desired :

Total abdominal hysterectomy : Preferred.

Alternatives :

uterine artery embolisation (UAE).

High-intensity focused ultrasound (HIFU)/magnetic

Resonance-guided Focused Ultrasound (MRgFUS) .

If pregnancy desired : LNG -IUCD.

Alternative :

Oral dienogest.

Continuously GnRH analogues.

GnRH antagonist : Elagolix.

Letrozole.

	Fibroid	Polyp	Adenomyosis
	Benign tumor	mucosal growth	Endometrium inside the myometrium

Active space

Presenting symptom	Seen in repr age female- females more than 30 years (35 years)	Can be seen in reproductive age/ perimenopausal age/post menopausal female	Seen in females $\geq 45$ years
	menorrhagia	Irregular/ intermenstrual bleeding	menorrhagia and dysmenorrhea
Size of uterus	Size enlarged, may go upto 20 weeks preg uterus size uterus is irregular enlarged	Normal size uterus	10-12 weeks preg uterus size uterus is symmetrically enlarged, globular
On examination	uterus non tender except if its very big in size when it undergoes degeneration or torsion or in pregnancy : red degeneration	No tenderness	Painful, tender (halban sign)

Feature	Fibroid	Polyp	Adenomyosis
USG	1. Hypoechoic 2. Well circumscribed due to pseudo capsule 3. Broad base 4. intramural - inside myometrium and it's echogenicity resembles that of uterus 5. DOPPLER- peripheral blood vessels	Hyperechoic Narrow base Doppler- feeder vessel sign	myometrial cysts myometrial islands venetian blind appearance

Active space

IOC	USG	Hysteroscopy	MRI Gold standard- HPE after hysterectomy
mgt	-	Hysteroscopic polypectomy	TAH

Clinical concept :

Q. 45 year old female complains of irregular bleeding . On P/V examination, uterus is normal in size and tenderness is absent. What is the most probable diagnosis ?

A : Polyp.

Q. 42 year old female complains of excessive bleeding. She has dysmenorrhea also. On P/V examination - uterus is 12 weeks in size and globular. Tenderness is present. What is the next step ?

A : Transvaginal scan (TVS).

Q. A 42 year old female , para 2 complains of severe progressive secondary dysmenorrhea and menorrhagia. Pelvic examination demonstrates a tender diffusely enlarged uterus of around 12 weeks pregnant uterus size with no adnexal tenderness. Results of endometrial biopsy are normal. The patient most likely has :

Adenomyosis.

Q. A 40-year-old female complains of heavy menstrual bleeding and dysmenorrhoea. On USG-an echogenic area of 20 weeks of pregnancy is seen in the uterus. Tenderness is present. most likely diagnosis is :

A. Fibroid uterus.

B. Adenomyosis.

C. Endometriosis.

D. PID.

Note : Tenderness due to red degeneration in fibroid.

## CONGENITAL MALFORMATIONS OF THE UTERUS

### Relevant anatomy

00:00:43

The female genital tract is formed by the **paramesonephric ducts (mullerian ducts)**.

In males : From **Wolffian duct (mesonephric duct)**.

mullerian ducts are an invagination of **coelomic epithelium** (at 6 weeks) and grow downwards alongside mesonephric ducts enclosed in peritoneal folds that later give rise to **broad ligament of the uterus**.

In early intrauterine life, both mullerian duct and wolffian duct are present in both the sexes, enclosed in broad ligament.

Remnants of the mesonephric duct (Wolffian Duct) :

Epooophoron, Para-oophoron and Gartner's duct are contents of broad ligament.

mullerian duct (MD) grows in females due to lack of Anti-mullerian hormone (AMH) in intrauterine life.

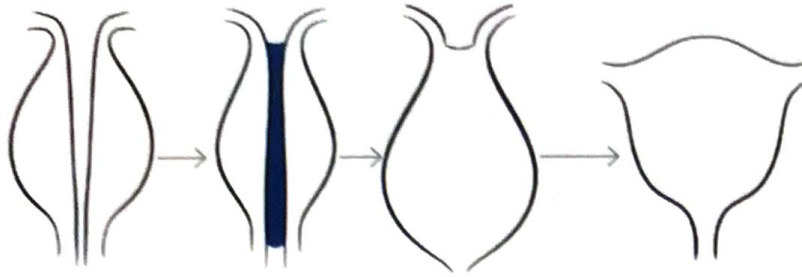
In males, AMH is formed by the sertoli cells of the testis.

During Paramesonephric duct elongation, ~~certain HOX genes~~ genes or HOX genes in group 9-13 play an important role on development.

- HOX 9 : Fallopian tube.
- HOX 10, 11 : uterus.

**At 10 weeks** : The two distal parts of MD approach in the midline and fuse to form **uterovaginal canal/septa**.

**At 12 weeks** : mesonephric duct regresses.



Both MD approach each other and fuse (Fusion begins from below upwards direction)

Septa is formed (uterovaginal canal)

Septa dissolves and a single uterine cavity is formed by 20 weeks (from below upwards)

Fundus becomes dome shaped

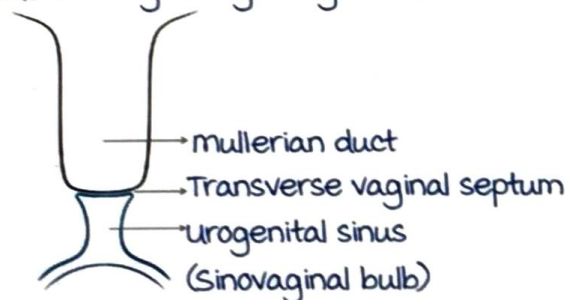
Each MD gives rise to :

- One side fallopian tube.
- 1/2 of uterus.
- 1/2 of cervix
- 1/2 of upper part of vagina.

Vaginal development :

- Upper part (2/3<sup>rd</sup> or 1/3<sup>rd</sup>) : mullerian duct.
- Lower part (1/3<sup>rd</sup> or 2/3<sup>rd</sup>) : Sinovaginal bulb part of urogenital sinus.

Transverse vaginal septa is formed by fusion which dissolves by 20 weeks forming a single vaginal canal.



Complications in a female with mullerian malformations :

1. Recurrent pregnancy loss (RPL).
2. Abortion.
3. Preterm labor.
4. malpresentations.
5. Ectopic pregnancy : unicornuate pregnancy.

- Gynaecologic complications :
  1. Infertility.
  2. Endometriosis.
  3. Dysmenorrhea : Generalised (U/L dysmenorrhea : Unicornuate uterus)
  4. Outflow tract obstruction : Hematometra.

In young pubertal females with C/O endometriosis : Always rule out mullerian malformations.

MC complaints : Obstetrics complications (recurrent pregnancy loss) > infertility.

1<sup>st</sup> Investigations : Incidental finding on USG (RPL) / HSG (infertility)

HSG is not the IOC because : It cannot differentiate between septate and bicornuate uterus as it cannot visualise the outer contour/fundus of the uterus.

Hysterosalpingography (HSG) :



A water soluble iodinated radioopaque dye is passed inside the uterus with the help of Leech-Wilkinson cannula (funnel shaped with transeverse serrations).

Followed up with serial X-rays.

IOC of mullerian malformations : 3D USG.

Gold standard : MRI.

Last resort : Laparoscopy + Hysteroscopy.

MC indication for doing surgery in mullerian malformations : RPL.

## Congenital malformations of uterus

00:16:57

Class I : mullerian agenesis/MRKH syndrome/MURCS syndrome

Description : Both mullerian ducts are absent

- No Fallopian tube (distal part present).
- No uterus.
- No cervix.

- No upper vagina (Generally complete vaginal agenesis)
- Ovaries are normal (development is from genital ridge)

Associated problems :

- **Renal anomalies** (30-50%) : Renal agenesis, Horse-shaped kidney.
- **Skeletal anomalies** (10-15%).

So in all cases of MRKH syndrome, intravenous pyelography (IVP) and skeletal X-rays must be done.

MRKH syndrome D/D : Androgen Insensitivity syndrome (AIS)

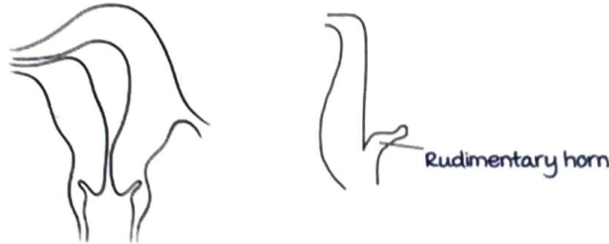
Obstetrical complications :

- Primary amenorrhea.
- Infertility.

MRKH : **Mayer-Rokitansky Kuster Hauser syndrome.**

MURCS : mullerian agenesis, Renal anomalies, Cervical somites.

**Class 2 : Unicornuate uterus**



Description : Only one side mullerian duct is present

- Fallopian tube : 1
- Uterus, cervix, upper vagina : 1/2

Other side either **complete agenesis** or **rudimentary horn** (communicating or non-communicating)

Associated problems :

Non-communicating horn with active endometrium present :

- Cyclical w/L dysmenorrhea.
- w/L hematometra.

Overall increased chances of :

~ Endometriosis:

- Infertility.
- **Ipsilateral renal anomalies** (2<sup>nd</sup> MC mullerian malformation associated with renal anomalies).

Obstetric complications :

- Increased spontaneous abortion.



- Increased preterm deliveries.
- If pregnancy occurs in rudimentary horn : uterine rupture (prior to 20 weeks).
- Ectopic pregnancy in the rudimentary horn.

mullerian malformation associated with increased risk of ectopic pregnancy : Unicornuate uterus.

Normal HSG :

- 2 FT (thin and tortuous)
- Single uterus.
- Single cervix.
- Single vagina.
- Bilateral spillage of the dye (can be used to check patency of tubes).

Normal



Unicornuate uterus on HSG :

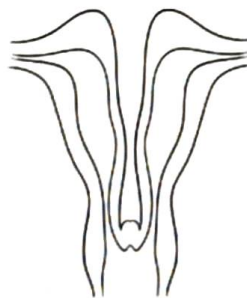
- Single FT (unicornuate uterus).
- U/L spillage of dye.
- Banana shaped uterus.



Communicating rudimentary horn should be obliterated to prevent ectopic pregnancy and uterine rupture in the horn.

### Class 3 : Uterine didelphys

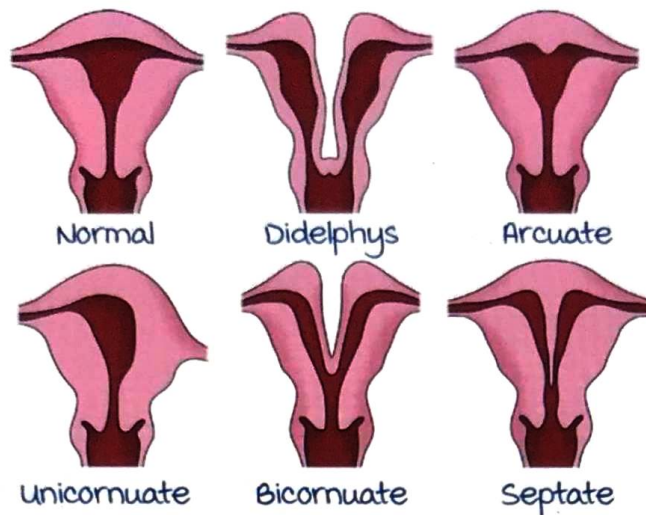
00:27:02



Description : Failed fusion of the paired mullerian ducts  
Fallopian tubes, uterus, cervix, upper part of vagina : 2.  
2 Leech wilkinson canula needed to visualise the uterus.

↳ come when compared to other mullerian anomalies.

Obstetric complications : RPL, fetal growth restriction.



#### Class 4 : Uterus bicornuate :

Description : Incomplete fusion of Mullerian duct.

- Fallopian tube, uterus : 2
- Cervix : 1 or 2
- Always **single vagina** (because fusion occurs from below upwards.)

Bicornis unicollis : 2 uterus 1 cervix

Bicornis Bicollis : 2 uterus 2 cervix

Distinguishing feature :

To distinguish between bicornuate uterus and septate uterus

: Look at fundus of the uterus.

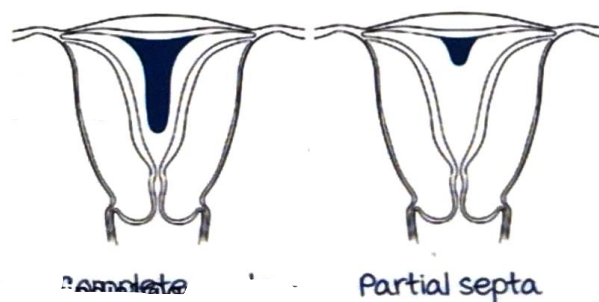
Normal fundus : Septate uterus

**Depression on the fundus (divided)** : Bicornuate uterus.

The two cannot be distinguished on HSG (Hence not IOC).

#### Class 4 : Septate uterus

00:32:56



Complete or partial septa (always at the top of uterus).

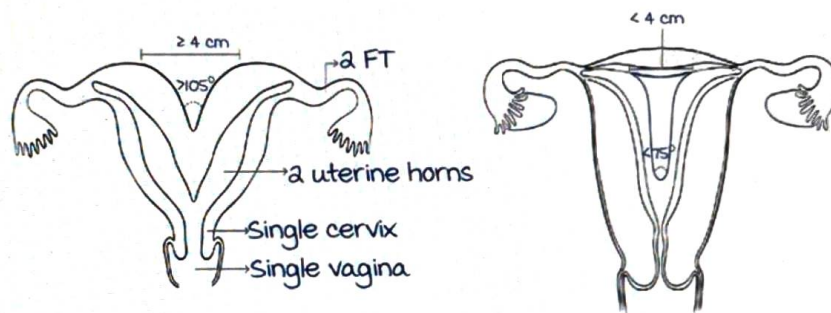
Septate uterus results when both MD fuse, septa is formed but septa fails to resolve partially or completely. Outwardly, the uterus appears normal, but a septa is present inside the uterus

Bicornuate uterus vs septate uterus :

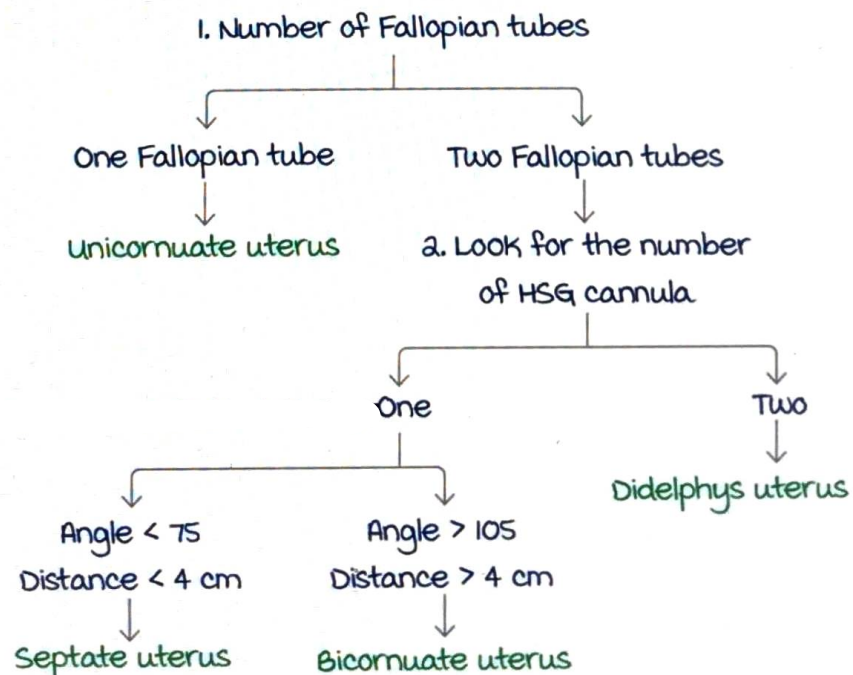
Should be distinguished by looking at fundus of the uterus.

On HSG :

	Bicornuate uterus	Septate uterus
External contour	Divided	Normal
Intercornual angle	$> 105^\circ$	$< 75^\circ$
Distance between 2 horns	$\geq 4$ cm	$< 4$ cm



Algorithm to diagnose mullerian malformations :





Bicornuate uterus



Septate uterus

Bicornuate uterus :

Obstetric complications :

- RPL.
- PTL.

Case of RPL : Surgery indicated for bicornuate uterus

**Straussman metroplasty.**

Pregnancy after repair; deliver by C-section.

Septate uterus :

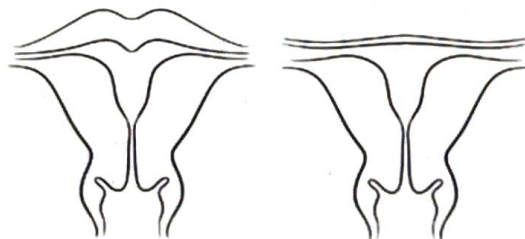
Obstetric complication :

- MC uterine anomaly leading to 1<sup>st</sup> trimester abortion
- Possibly congenital malformation.
- In case of RPL : Surgery - **Hysteroscopic resection of the septum.**
- MC uterine anomaly associated with infertility.

### Class 5 : Arcuate uterus

00:42:06

Associated problem : Entire uterus is formed except there is  
Slight indentation of fundus/flat topped uterus



Indentation of fundus

Flat topped fundus

Obstetric complication : Overall best reproductive outcome.

Class 6 : Diethylstilbesterol (DES) induced reproductive tract abnormalities :

DES is a synthetic non-steroidal estrogen which was prescribed to millions of pregnant females earlier.

Led to abnormal development of the reproductive tracts of daughters of the pregnant females :

- T-shaped uterus.
- Clear cell adenocarcinoma of the vagina and cervix (due to suppression of WNT-4 gene; HOX gene).
- Vaginal adenosis.
- Cervical collar.
- Genitourinary malformations.
- Fallopian tube abnormalities like absent fimbriae.

These females in adulthood showed :

- Earlier menopause.
- Increased risk of Breast Ca.

males exposed to DES :

- Increased incidence of cryptorchidism.
- Testicular hypoplasia.
- Hypospadias.
- micropallus.
- Renal anomalies.

Renal anomalies were not associated in females exposed to DES (previously believed, newer studies shows otherwise)

DES is no longer used.

management of mullerian malformations :

Surgical management :

Indications : RPL

- Bicornuate uterus : Straussman metroplasty.
- Didelphic .
- Septate uterus : Hysteroscopic resection of septa (earlier John-Tompkins metroplasty).

# PROLAPSE

Herniation of content from its normal anatomical position.

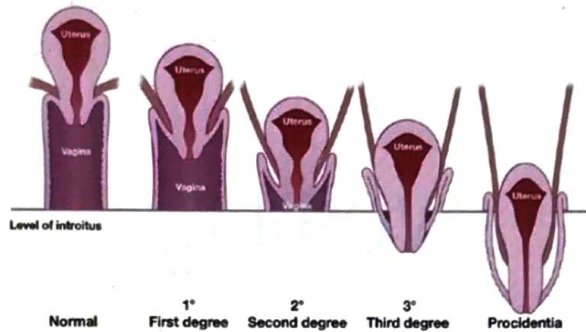
uterocervical prolapse

Vaginal prolapse

## Uterocervical prolapse

00:00:57

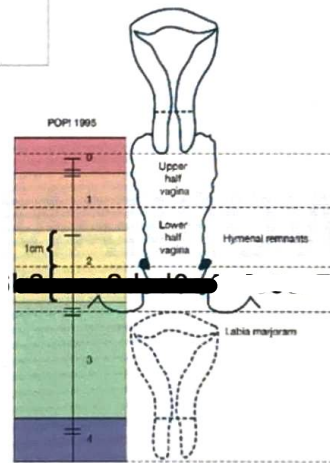
Shaw classification :



Uterine descent:
1°--Descent of cervix into vagina
2°--Descent of cervix into introitus
3°--Descent of cervix outside the introitus
Procidentia- All of the uterus outside the introitus

POP-Q classification :

- Pelvic Organ Prolapse Quantification classification.
- Reference point : **Hymen.**



Baden Walker classification :

- Reference point : **Hymen.**

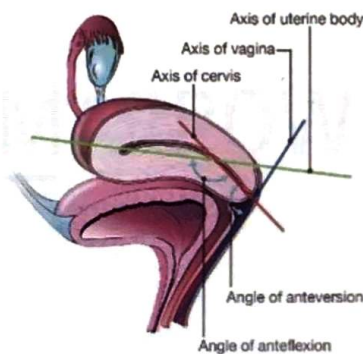
## Anatomy: Supports of the Uterus

00:09:43

mechanical support :

- Angle of anteversion :  $90^\circ$
- Angle of ante flexion :  $120^\circ$
- 1<sup>st</sup> step in prolapse : **Retroversion of uterus.**

Anteversion and ante flexion of the uterus

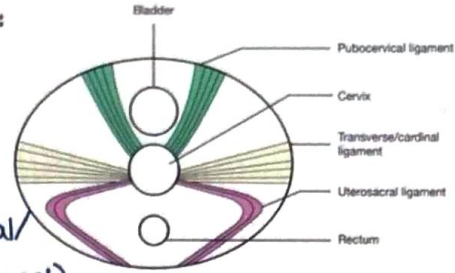


Active space

Ligaments supporting uterus :

Primary support :

1. Pubocervical ligament.
2. Uterosacral ligament.
3. Cardinal/Transverse cervical/mackenrodt's ligament (Strongest).

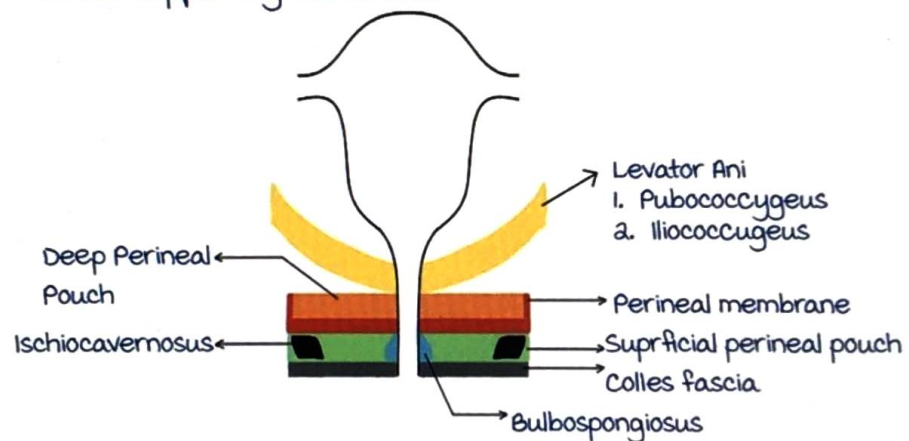


All these three are referred to as Triradiate ligament.

Secondary support : **Round ligament.**

- Ligament which does not support uterus : **Broad ligament.** (Peritoneum of uterus).
- Ligament which helps to keep the uterus in anteverted position : **Round ligament > Uterosacral ligament.**
- Ligament which helps to keep the uterus in retroverted position : **Uterosacral ligament > Round ligament.**

Muscles supporting the uterus :



Muscle which is not a part of Levator ani : **Ischiococcygeus.**

Muscles which are not in midline/ muscles not attached to Perineal body/ muscles which do not support uterus :

- **Ischiocavernosus muscle.**
- **Ischiococcygeus muscle.**

Most important support of uterus : **Levator ani**

(main - **Pubococcygeus**)

Other muscles : Superficial transverse perineal muscle.

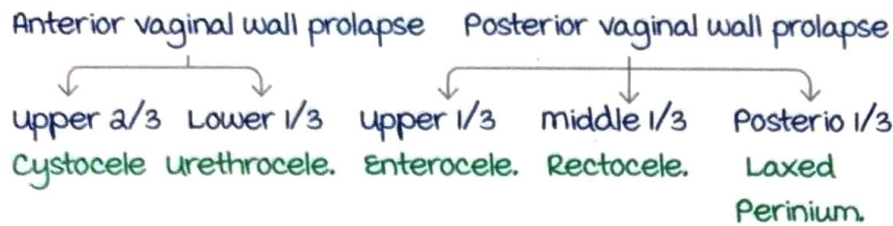
Deep transverse perineal muscle.

Bulbococcygeal muscle.

External urinary sphincter.

## Vaginal prolapse

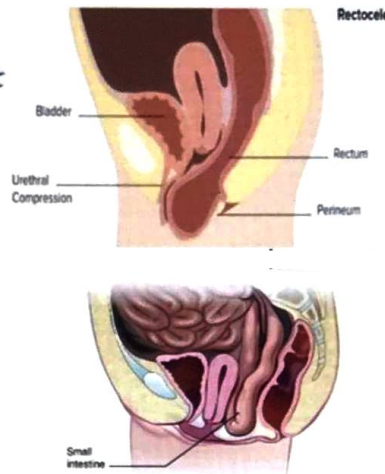
00:26:13



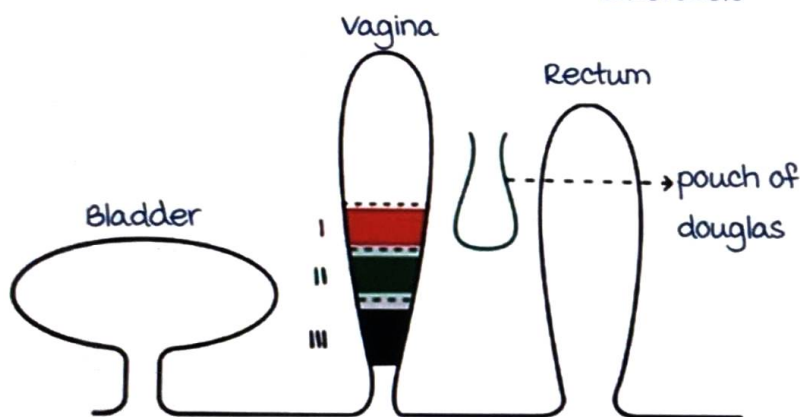
Differentiating between an Enterocele & Rectocele :

Clinically :

- P/R examination - Bulge felt  
On the tip of the finger :  
Enterocele  
On the pulp of the finger :  
Rectocele
- Transillumination test :  
(+) : Enterocele  
(-) : Rectocele



De Lancey's level of supports :



Level I : upper 1/3<sup>rd</sup> of vagina

- Structures supporting : uterosacral ligament.  
Cardinal ligament.
- Defect leads to :  
Enterocele (Posterior defect).  
Apical/ Vault prolapse (Central defect) :  
Leads to elongation of cervix.

Level II : middle 1/3<sup>rd</sup> of vagina

- Structures supporting : Arcus tendinous fascia.
- Defect leads to : Cystocele (Anterior defect)

Active space



## Rectocele (Posterior defect).

Level III : Lower 1/3<sup>rd</sup> of vagina

- Structures supporting : Perineal body & muscles attached to it.
- Defect leads to : Urethrocele (Anterior defect).

Laxed perineum (Posterior defect).

Characteristics of prolapse

00:37:04

Prolapse occurs when muscles/ ligaments become weak d/t :

1. menopause (Elderly)
2. Repeated child birth (multiparous) :
3. Especially with obstructed labour, prolonged labour, perineal tear, instrumental delivery.



Other risk factors for prolapse :

- Cigarette smoking.
- Chronic increase in intra-abdominal pressure.
- Spinal cord injury.
- Connective tissue disorder.

Symptoms of prolapse :

- Feeling of something coming out of vagina.
- Pressure.
- Decubitus ulcer on the prolapsed part :  
Due to venous congestion.

management :

Packing with **Acryflavine** (antiseptic) & **Glycerin** (hygroscopic).Management of Prolapse

00:50:26

management of vaginal prolapse

- **Not dependent on age / parity**
- Cystocele } Anterior colporrhaphy
- Urethrocele }
- Enterocele - moschowitz repair } Outdated
- Halban repair }
- mccall cudopalsty }

- Rectocele
  - Laxed perineum
- Posterior colpoperineorrhaphy

management of uterine prolapse :

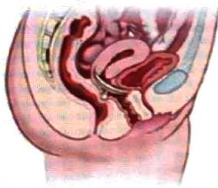
Surgical management

- **Best management.**
- Permanent.
- Done in 2° & 3° prolapse.
- Depends on : Age & parity of the patient.

Conservative management

- **Kiegel's exercise** (Perineal exercises) : Prevents prolapse. Prevents progression of prolapse. Done in 1° prolapse. Advised to all pregnant women, during & after pregnancy.
- **Pessary**

Pessary :



Gellhorn pessary



Doughnut pessary

A space occupying device.

Principle : Doesn't allow uterus to prolapse.

MC used : **Gellhorn, Doughnut**

Disadvantage : Not a permanent cure.

Should be changed every month.

Helps to manage : Uterocervical prolapse and Cystocele.

Indications : Prolapse in a pregnant female.

In postpartum period.

C/I to surgery or if patient refuses surgery.

## Surgical management of prolapse

00:58:34

Case 1 : If a female is 40 years, she has completed her family.

2°/3° degree prolapse + cystocele + rectocele.

Vaginal  
hysterectomy

Anterior  
colporrhaphy

Posterior  
Colpoperineorrhaphy

Pelvic floor repair

Active space

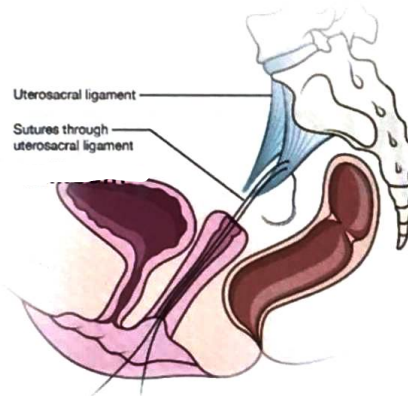
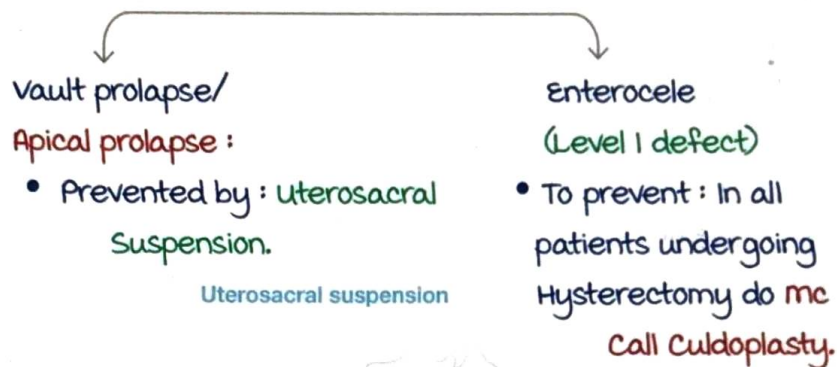
Ward Mayo hysterectomy = vaginal hysterectomy + Pelvic floor repair.

Order of clamping in vaginal hysterectomy :

1. Uterosacral ligament.
2. Cardinal ligament.
3. Uterine artery.
4. Tuboovarian ligament, Round ligament pedicle.

Order in case of abdominal hysterectomy : 4,3,2,1 (Reversed).

After vaginal hysterectomy, there are chances of :



Hysterectomy :

- Preferred hysterectomy : vaginal.
- Hysterectomy with maximum risk of ureteric injury : Wertheim's hysterectomy > Radical hysterectomy.
- maximum chance of injuring the ureter : Laparoscopic hysterectomy > Abdominal hysterectomy > Vaginal hysterectomy

Case 2 : Post-menopausal female (Age : 60 - 65 years).

Some contraindication to surgery (Diabetes/ hypertension).

Not safe to give anesthesia for a long time.



**Lefort's Colpocleisis :**

Not done in young patients :

- Coital function is hampered.
- No space for menstrual blood to come out.

used for managing vault prolapse.

Case 3 : Elderly post-menopausal female with comorbidities.

Anesthesia cannot be given at all.



**Pessary**

**Prolapse in reproductive age group**

01:15:45

1. **Sling surgery/ Colpocleisis :**

Pre requisite : **utero cervical length should be normal.**

2. **Fothergill's repair.**

TOC for prolapse :

- In a female of reproductive age group/ Nulliparous female/ Female who wants a future child : **Sling surgery.**
- In a female of reproductive uterocervical length increased : **Fothergill's surgery.**
- In a female of reproductive age group, Child bearing complete : **Fothergill's surgery.**  
Child bearing not complete : **Sling surgery.**

Case 4 : A female of reproductive age group with child bearing complete/ reproductive age group with increased utero cervical length.



**Fothergill's repair.**

Fothergill's repair :

1. **Cervical amputation** (Therefore the surgery is done when the uterocervical length is increased).

Complications : Cervical incompetence.

Cervical stenosis.

Cervical dystocia.

2. **Plication of Cardinal ligament.**

Shirodkar modification of manchester surgery/ Fothergill's repair :

- Only step 2 of Fothergill's repair is done. (Don't perform step 1).
- This surgery can also be done in females who want a future child.

Case 5 : Female of reproductive age group with Incomplete child bearing/ Congenital prolapse.

Congenital prolapse is seen in a nulliparous female.



Sling surgery (utero cervical length should be normal)

Female of reproductive age group with incomplete child bearing but her,

uterocervical length has increased.

Child bearing is completed first.



Fothergill's repair

Sling surgery :

Principle : Supports the uterus and cervix

material of sling : mersilene tape.

Types :

1. Anterior : Dynamic sling.

One end : Attached to anterior part of isthmus.

Other end : Attached to rectus sheath.

Female should have good abdominal tone.

Complications : Less.

Success rate : Less.

Eg : Purandare sling.

2. Posterior : Static sling.

One end : Attached to posterior part of isthmus.

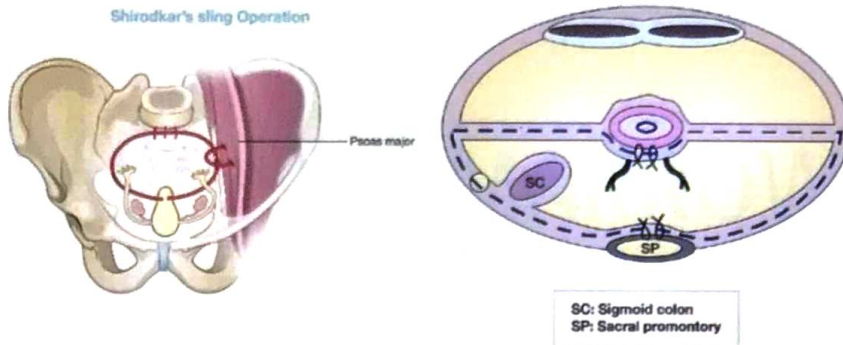
Other end : Attached to ligaments attached to sacrum.

Complications : more

Success rate : Better

eg : shirodkar sling - mostly done these days

khanna's posterior sling (Not done these days)



Complications of Shirodkar sling :

most common on left side.

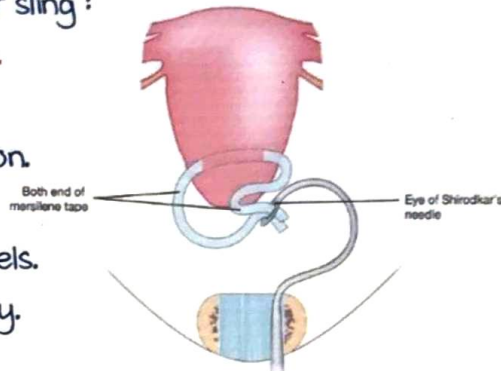
Eg :

Obstruction of sigmoid colon.

ureteric injury.

Injury to mesenteric vessels.

Genitofemoral nerve injury.



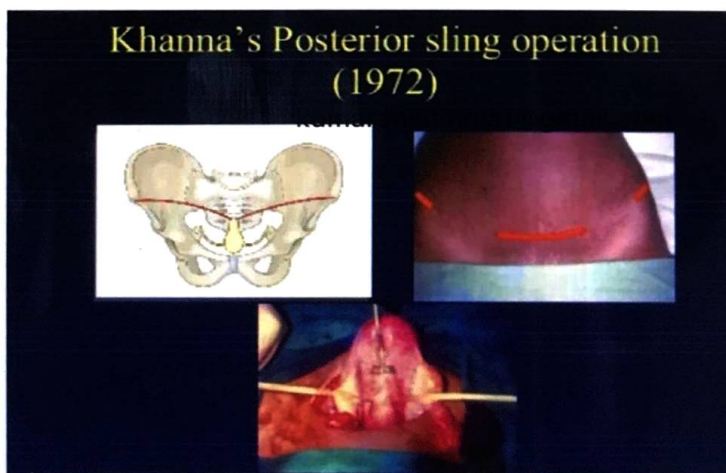
Shirodkar needle  
(Question mark shaped)

Virkud/ Composite sling :

- On right side : Shirodkar sling.
- On left side : Purandare sling.

Khanna's posterior sling operation :

- One end : Attached to posterior part of isthmus.
- Other end : Attached to ASIS



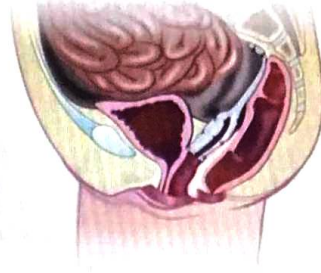
Case 6 : Vault prolapse.

To prevent vault prolapse during hysterectomy :  
uterosacral suspension.

management :

Abdominal surgery : **Sacral colpopexy.**

- Best option : Surgery.
- But difficult to perform.
- mesh used.
- One end is attached to sacrum.
- Other end is split into 2.  
One part : Anteriorly to vagina.  
Other end : Posteriorly to vagina.
- It heals with fibrosis, attaches vagina permanently to sacrum.



Vaginal surgery :

1. **Uterosacral suspension :**  
Can be done to prevent/ treat vault prolapse prophylactically.  
Can be done vaginal/ abdominal.
2. **Sacrospinal fixation :**  
Sutures between apex of vagina & sacrospinous ligament.
3. Leforts colpocleisis.

# STRESS URINARY INCONTINENCE

## Stress Urinary Incontinence [SUI]

00:00:25

Involuntary escape of urine when intra-abdominal pressure is increased as in sneezing, coughing, or laughing.

most common type of urine incontinence in women accounting for 50 to 70% of cases.

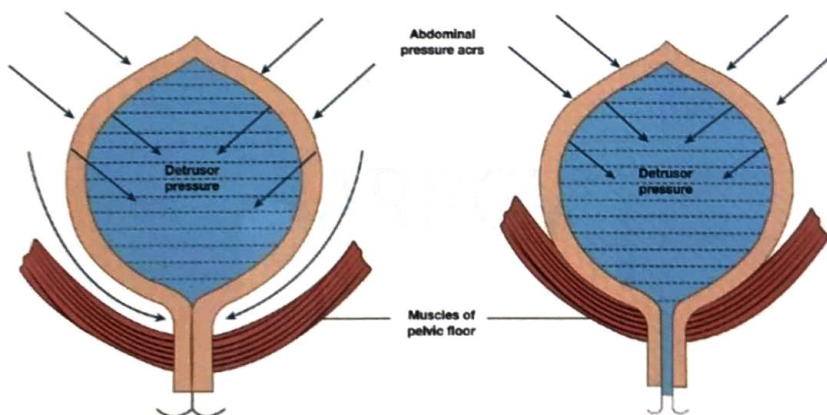
Cause :

1. Bladder neck descent (including urethral hypermobility) : 75-80%.
2. Intrinsic sphincter defect : 20-25%.

**mechanism :** In normal conditions

↓  
 ↑ in intra-abdominal pressure → Compresses the upper urethra (Continence).

↓  
 But in bladder neck descent → Compression does not occur (incontinence).



**management :**

A. Earlier concept :

- Anatomic hypermobility of the urethra : Colposuspension.
- Intrinsic sphincter deficiency : Pubo-vaginal sling surgery (E.g. Aldridge, mc Guire)

B. New concept : Colposuspension (no separate surgeries for different causes).



Burch Colposuspension	mmk (marshall-marchetti-Krantz)
Proximal urethra suspended to Cooper's ligament. ↓ Gold standard for SUL.	Proximal urethra suspended to pubic symphysis. ↓ Not done (Complication: Osteitis pubis).

Both are abdominal surgeries.

In both proximal urethra is suspended.

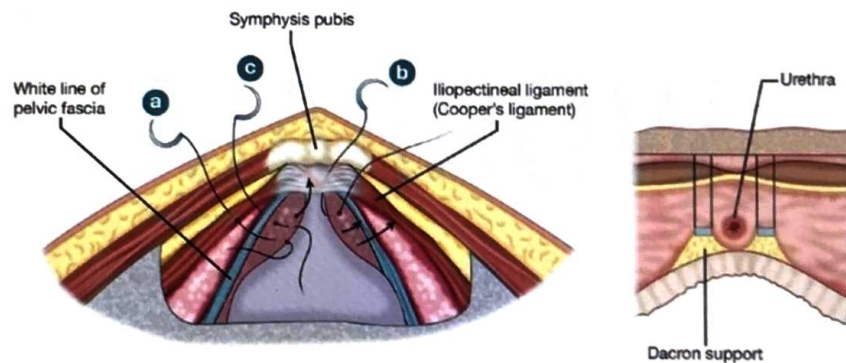
Earlier tests for SUL (Q tip & Bonney test) are outdated now. Urodynamic studies are needed in urge incontinence (not in stress incontinence).

## Surgeries

00:08:03

Colposuspension procedure :

### Colposuspension



Colposuspension (Burch operation).

a = Burch Colposuspension,

b = mmk procedure,

c = Colposuspension using the white line of pelvic fascia

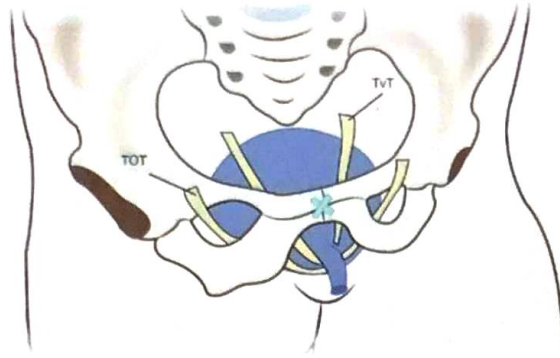
Newer surgeries for SUL :

TVT and TOT.

Daycare surgeries.

Vaginal surgeries.

Mid-urethra is suspended.



TVT : Tension-free transvaginal tapes (enter retropubic space).

TOT : Tension free trans-obturator tapes (via obturator foramen).

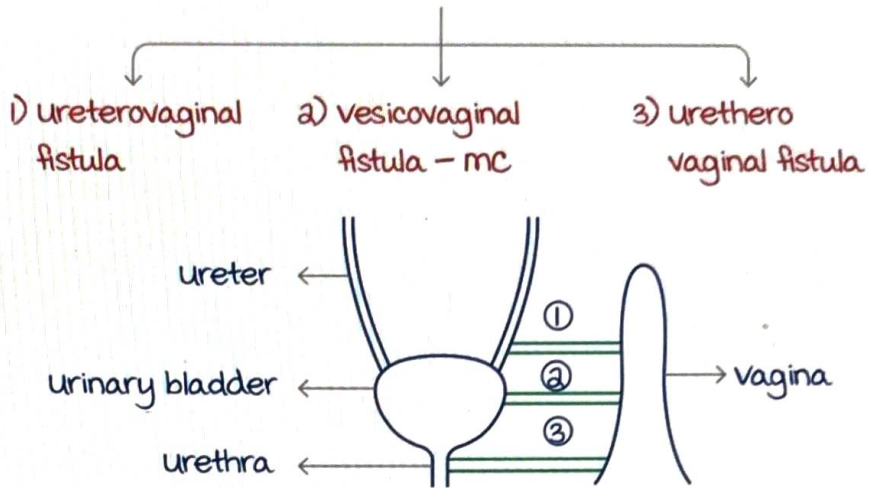
TOT is better as there is **no need to enter** the **Space of Retzius** (retropubic space) → Fewer complications.

Best surgery for SUI : TOT > TVT > Burch Colposuspension.

# URINARY FISTULA

## Types of urinary fistulae

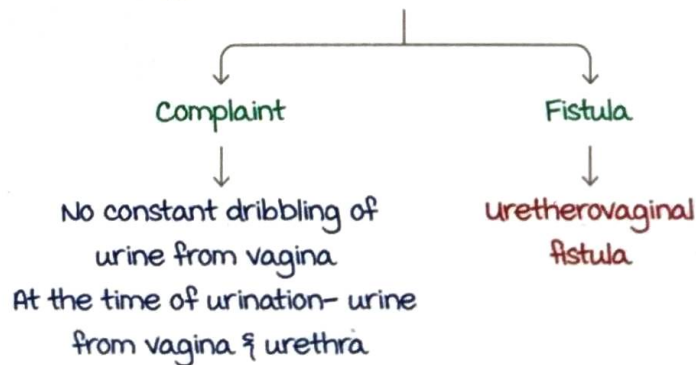
00:00:18



ureterovaginal fistula and Vesicovaginal fistula (VVF) :

Complaint	Fistula
1. Constant dribbling of urine from vagina + Normal urination.	Ureterovaginal fistula.
2. Constant dribbling of urine from vagina + No Normal urination.	VVF.

urethrovaginal fistula :

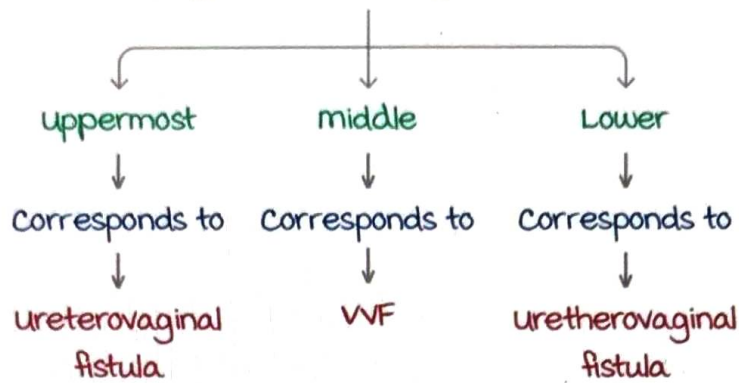


Active space

## Methylene blue three swab test

00:06:34

- Three cotton plugs – Placed in vagina.



- With the help of Foleys catheter

↓  
Put methylene blue dye in bladder + urethra, wait.

Observation	Interpretation
<ul style="list-style-type: none"> <li>• If the uppermost cotton swab wet with urine but <b>not blue</b> in colour.</li> </ul>	ureterovaginal fistula.
<ul style="list-style-type: none"> <li>• If middle <del>cotton swab</del> (middle + lower) is wet + <b>blue</b> in colour.</li> </ul>	
<ul style="list-style-type: none"> <li>• If <b>only</b> Lower cotton swab is wet + blue in colour.</li> </ul>	urethrovaginal fistula.

## Vesicovaginal fistula

00:13:09

- **m.c** urinary fistula.
- **m.c** cause :
  - In developed countries** – Surgery (Hysterectomy).
  - Developing countries** – Obstructed labor.
- **I.O.C** : Cystoscopy.
- Best method to collect urine in VVF patient : **Suprapubic catheterisation.**

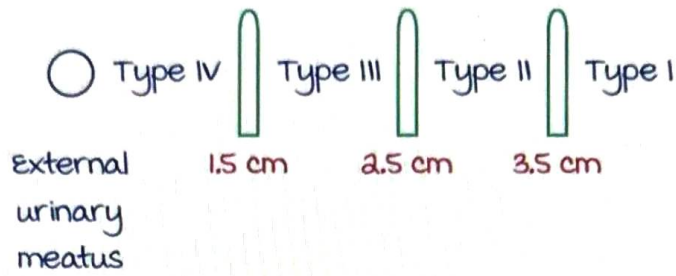
Active space



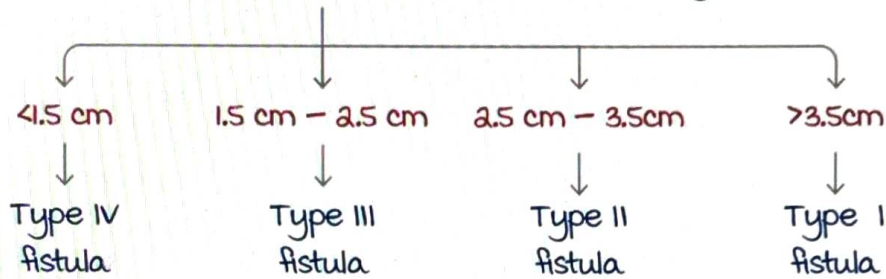
## New classification of genitourinary fistulae

00:25:10

- Depending on **distance** of fistula from external urinary meatus.



If the distance of fistula from external urinary meatus is



a → < 1.5 cms in diameter.

b → 1.5 to 3 cms in diameter.

c → > or = 3 cms in diameter.

Active space

## NORMAL SEXUAL DEVELOPMENT

Genetic sex :

If Y chromosome is present : Foetus is male sex.

If Y chromosome is absent : Female sex.

As per genotype :

Turner syndrome (45X0) : Female babies.

Klinefelter syndrome (47XXY) : male babies.

Gonadal sex :

If Y chromosome is present : gonads - testes.

If Y chromosome is absent : gonads - ovary.

For proper development of ovaries, both the X chromosomes should be present although both the X chromosomes are not needed for presence of ovary.

In Turner's syndrome (45X0) :

Y chromosome - Absent, Gonads - Ovaries.

only one X chromosome present, ovaries undergo accelerated atresia.

At birth these ovaries are replaced by fibrous streak called as streak gonads.

Phenotypic Sex :

Depends on external genitalia and secondary sexual characters.

In normal sexual development, Genetic, Gonadal and Phenotypic sex are in accordance to each other.

### Y Chromosome

00:07:32

SRY gene /Sex related region /Sex determining factor.

Present in distal end of the short arm of Y chromosome adjacent to pseudo allele region.

Sex of the baby is determined by the SRY gene.  
micronutrient required for functioning of SRY region is Zinc.

Regulators of SRY gene :

- most important : SF -1/Steroidogenic Factor 1.
- WT-1 (Wilms Tumour) gene.
- GATA-4 gene

In males :

SRY gene on Y chromosome activates Sox-9 gene which leads to testis formation.

For testis formation

most important gene : SRY gene.

and most important gene : Sox-9 gene

In Females :

SRY gene is absent, this absence activates :

- Wnt4 gene.
- RSPO-1 gene.
- DAX-1 gene.
- $\beta$  Catenin gene.

## Development of gonads

00:12:45

Gonads develop from Genital Ridge.

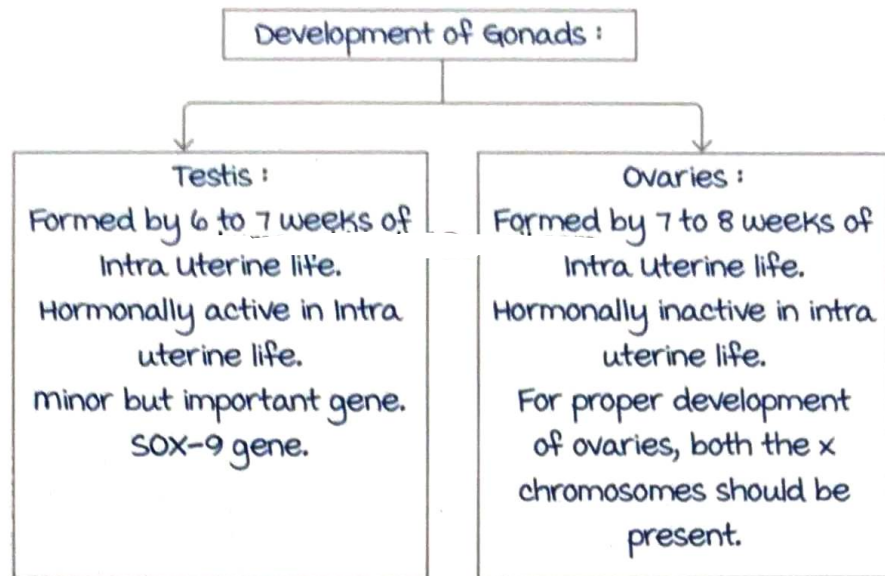
Genital ridge is formed by 5 weeks of intra-uterine life (IU life).

Genital ridge is derived from intermediate mesoderm.

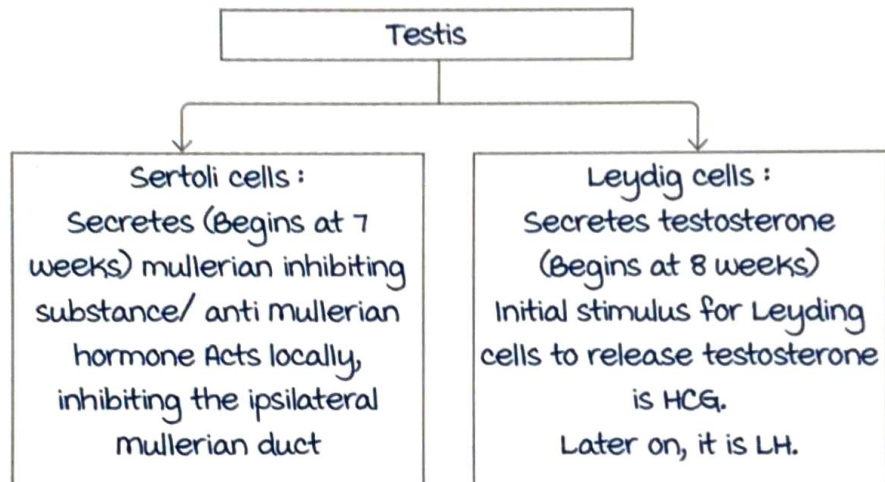
Till 6 weeks of intrauterine life, the gonads are bipotential i.e., undifferentiated.

SRY gene determines the development of the Genital ridge into either ovaries or testis.





In males :



Sertoli cells :

- 1<sup>st</sup> cells to develop.
- Only cell type in males to express **SRY gene**.
- They also express **SOX-9 gene**.
- SOX -9 gene which regulates secretion of Anti mullerian hormones (AMH).
- SOX -9 gene is **marker for developing sertoli cells**.
- Prostaglandins that helps in differentiation of sertoli cells - **PGD-2**
- Sertoli cells forms a barrier between growing germ cells and blood.

Cells that lie outside the blood testis barrier : **Leydig cells**.

1<sup>st</sup> ultrasound feature of growing testis : presence of **Testicular cords**.

Even if germ cells are absent, still testicular cords will develop.  
Thus testis differentiation is directed by **somatic cells**.

Descent of Testis :

Initially testis are abdominal organ. Later, they descend into scrotum.

With the help of : Elongated diverticulum of peritoneal cavity called : **Processes vaginalis / Gubernaculum**.

It is regulated by :

- Anti-mullerian hormone : majorly for abdominal descent.
- Testosterone : majorly for scrotal descent.
- Insulin like factor 3.

In Females : Ovaries.

No Sertoli cells. Hence, no AMH in IU life.

No Leydig cells. Hence, no testosterone in IU life.

But after puberty, AMH is formed from the small granulosa cells of growing follicles, estrogen from ovaries and androgen from theca cells.

Ovaries are ...

1<sup>st</sup> sign of ovarian differentiation is absence of Sertoli cells/ testicular cords by **6 to 7 weeks**.

Ovarian primordial follicles are identifiable after **13.5 weeks**.

## **Barr bodies**

00:23:50

Number of barr bodies = Number of X chromosomes - 1.

Sample taken - Buccal mucosa.

Condition	Number of barr bodies
males 46XY	0
Females	1
Turners syndrome	0
Klinefelter's syndrome	1

Sex determination :

External genitalia (most common)

Ambiguous genitalia : By looking at genitalia, cannot differentiate as male or female.

Number of Barr bodies.

Best method : **Karyotyping.**

~~and presence~~ or absence of Y chromosomes.

**Germ cell differentiation :**

In males :

SRY gene is present, germ cells become **spermatogonia.**

Spermatogonia immediately stops mitosis.

resume proliferation from puberty.

In females :

SRY gene is absent, germ cells become **oogonia** and continue mitosis.

They reach a peak at **20<sup>th</sup> week** of gestation : 5 to 7 million.

They get converted to **primary oocytes.**

Some primary oocytes enter meiosis and become **primordial follicles.**

The meiosis gets arrested.

Rest of primary oocytes degenerate to undergo apoptosis.

At birth ovaries will have **1 to 2 million** oocytes.

### **Formation of internal genital organs**

00:29:08

Internal genital organs are formed by ducts.

Initially in both males and females, till **8 weeks** of life **2 pairs** of ducts are present :

A pair of **mullerian duct (MD)**/paramesonephric duct.

A pair of **Wolffian duct (WD)**/mesonephric duct.

Wolffian duct appears earlier than the mullerian duct.

WD appears from the **intermediate mesoderm.**

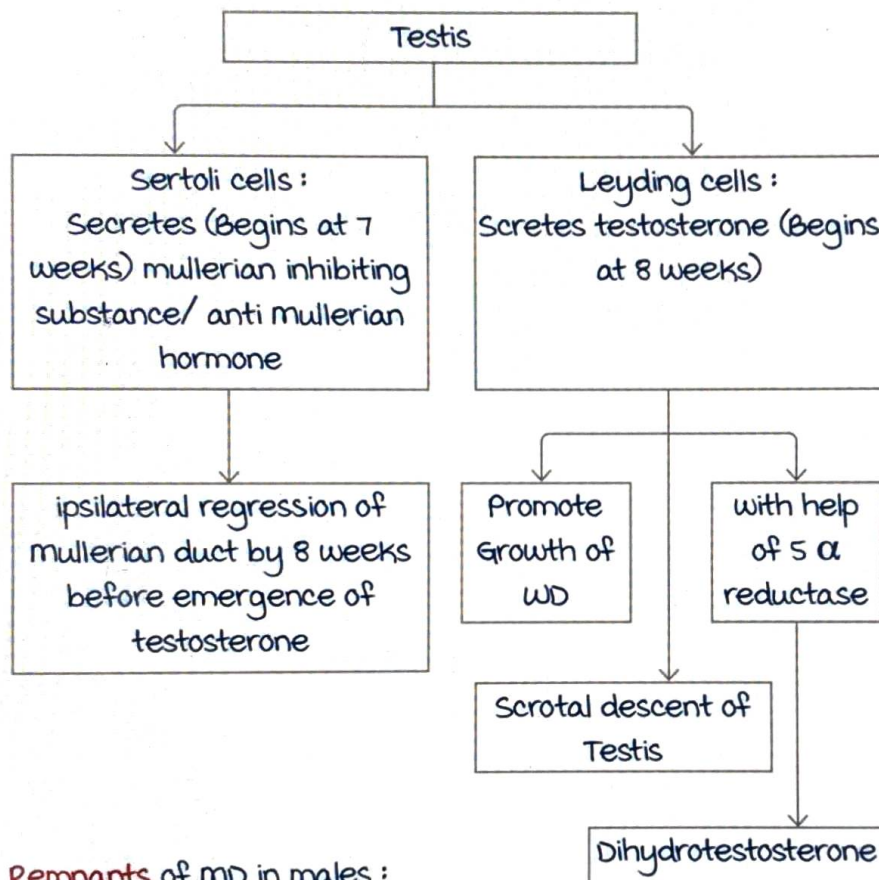
MD appears after WD as a cleft in the coelomic epithelium.

At 9 weeks one pair of them will disappear.

At 10 weeks internal genitalia are formed from these ducts.

### Formation of internal genital organs in males 00:31:13

Presence of y chromosome, thus SRY gene is present also gonads will be testes.



Remnants of MD in males :

- Prostatic utricle.
- Appendix of testis.

Sertoli cells also secrete **Inhibin B**

Function : Negative feedback on FSH.

Testosterone :

Promotes the development of the Wolffian duct.

The Wolffian duct is responsible for the development of internal genitalia in males,

Internal genitalia include the following in males :

Mnemonic : SEED

Seminal vesicles.

Epididymis.

Ejaculatory duct.

vas Deferens.

They need a high local concentration of testosterone to develop.

Di hydro testosterone :

Responsible for male external genitalia to look like male external genitalia.

One liners :

Gene encoding AMH : Present on Chromosome 19.

AMH g<sup>-</sup> ..... by SOX -9 gene on sertoli cells.

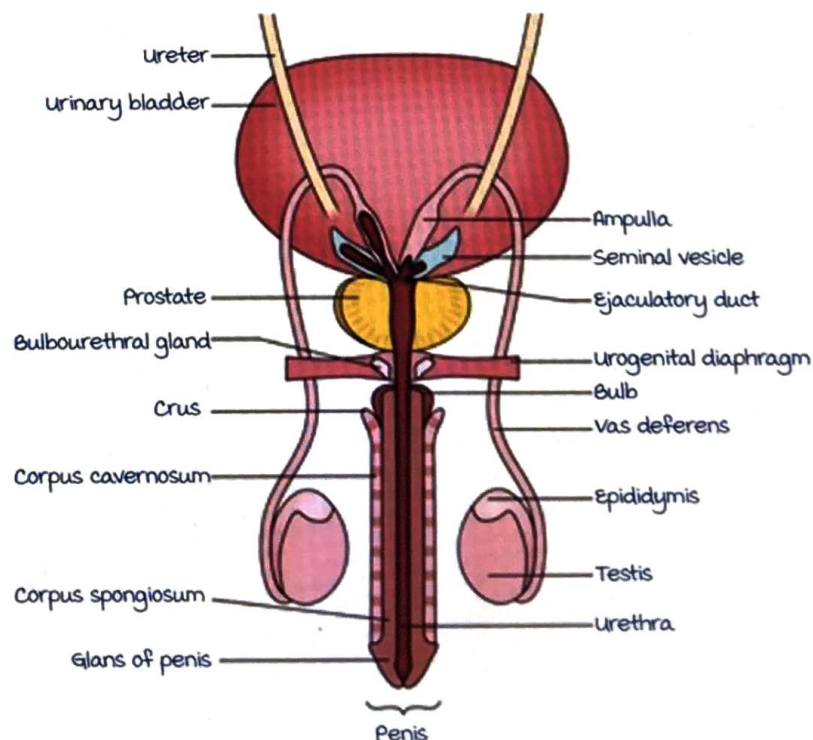
Gene involved in regression of wolffian duct is WT-1 gene.

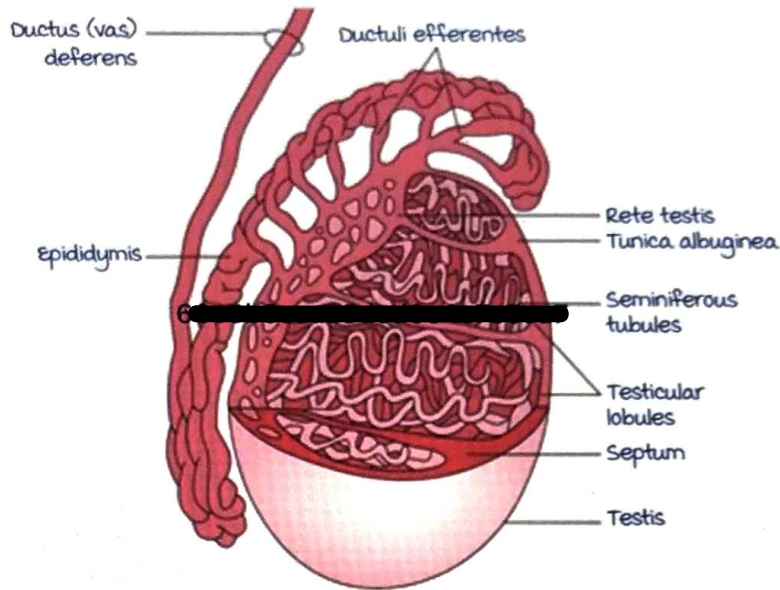
markers for Sertoli cells :

Gene marker : SOX-9.

Hormonal markers : Anti mullerian hormone and inhibin B.

Diagram of male internal genital organs and testis





Prostate glands in males are a part of external genitalia & not internal genitalia.

mesonephric tubules In males lead to formation of **efferent Tubules**.

most potent Testosterone is : Dihydrotestosterone.

Both testosterone and DHT act through **same receptors**.

Receptors for Androgen receptors are located on **long arm of X chromosome**.

Appendix of testes is a remnant of mullerian ducts

Appendix of Epididymis is a derivative of Wolffian duct.

Applied question.

In male **anencephalic foetus**, pituitary gland is **hypoplastic**.

Decreased or **absent LH**.

Hence testosterone secretion is decreased.

Abnormal internal genital and External genital organs.

In females, with exposure to androgen in IU life :

Due to : Congenital adrenal hyperplasia, maternal androgens  
E.g., Pregnancy luteoma.

Still, WD does not develop as for the development of WD **high local levels** of androgens are needed.

In XY individuals, MD can be seen which leads to the formation of the uterus.

In XX individuals, always WD will be absent, male internal genital organs are **never seen**.

### Formation of internal genital organs in females

00:48:56

No AMH in IU life, hence mullerian duct will develop in females. mullerian duct will lead to the formation of female internal genitalia :

Fallopian tube.

Uterus.

Cervix

upper 1/3<sup>rd</sup> of vagina.

No testosterone in IU life,

hence WD regresses, leaving remnants :

Epooophron.

Paraoophron.

Gartners duct.

Hence no DHT in IU life,

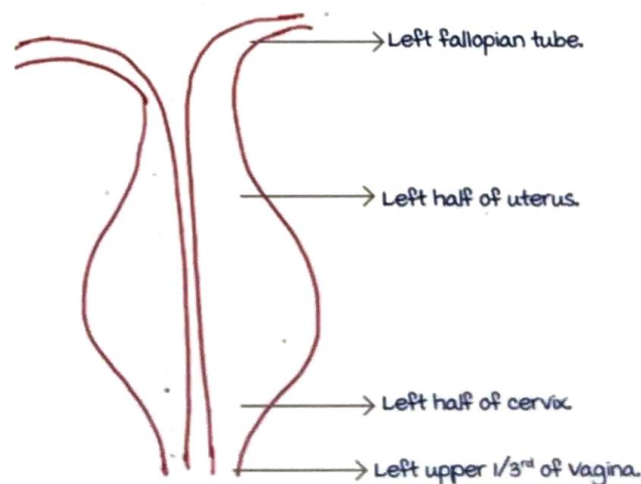
External genitalia appear like female external genitalia.

Formation of internal genital organs :

The two mullerian ducts **cross** the wolffian ducts and come in the midline.

Then the 2 MDs fuse.

Left MD leads to formation of :



Same on each side.

The unfused parts leads to formation of fallopian tubes.

Fused parts leads to formation of :

~~uterus~~

Cervix

upper 1/3<sup>rd</sup> of vagina.

uterus is formed by 10 weeks. (solid organ)

**Canalization** of uterus/ cervix/ vagina : Fusion of MD forms a septa, which resolves, resulting in formation of a cavity.

Occurs by 18 to 20 weeks.

uterus is formed by mullerian duct.

But for proper growth of uterus, estrogen is needed at puberty.

Applied aspect :

In Turner syndrome : 45X0.

Gonads : Ovaries, but streak Gonads.

So they produce low Estrogen.

So in turners syndrome, uterus remains hypoplastic/infantile uterus.

upper 1/3<sup>rd</sup> of vagina is formed by MD.

Lower 2/3<sup>rd</sup> of vagina is formed by sinovaginal bulb, which is a part of urogenital Sinus.

entire female reproductive tract is mesodermal in origin.

except, parts which are derived from urogenital Sinus (endodermal).

Vaginal epithelium is derived from endoderm of urogenital sinus.

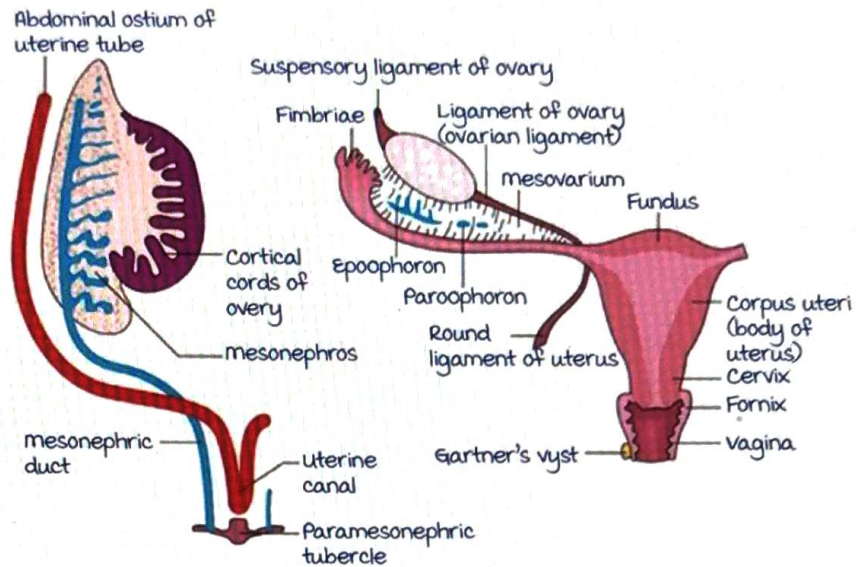
Remnants of WD in females :

Are present in broad ligament.



Remnants of mesonephric tubules

- 1. Cranial end = epooophoron.
- 2. Caudal end = paraophoron. } If blocked = Paratubule cyst.



Remnant of mesonephric duct : Gartner's duct.

If blocked : Gartner's cyst :

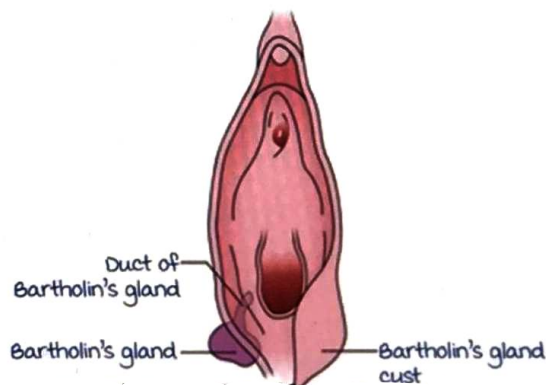
Is present in anterior lateral wall of vagina.

D/D : Bartholin cyst :

Present at location of bartholin gland (between labia majora and labia minora).

Bartholin duct is located at the groove between hymen and labia minora posteriorly.

Cyst is not formed on walls of vagina.



Active space

most common cyst in vagina : Inclusion cyst.

male and female internal genitalia can be differentiated by 10 weeks.

male and female **external genitalia** can be differentiated by 12 weeks.

On USG (external genitalia is observed not internal), the sex of the foetus can be earliest determined by 12 weeks.

## Development of external genitalia

01:03:46

In both male and female fetuses in early IU life, there is an indifferent analge

In absence of any external hormonal influence :  
Differentiates in to **female external genitalia**.

Suppose in XY genotype :

Testis is not functioning, no DHT/testosterone.

Or is completely resistant to androgens : Complete Androgen Insensitivity Syndrome/ AIS. Here the external genitalia will be female external genitalia.

Formation of **male** external genitalia occurs :

In presence of **proper DHT**.

Ambiguous genitalia :

When testosterone is **partially present**.

XY genotype with **partial AIS**.

XX genotype is exposed to androgens in IU life :

Here testosterone is not converted to DHT.

Embryonic structure	In absence of any Hormone - females	In presence of DHT - males	In presence of partial testosterone. <b>Ambiguous Genitalia</b>
Genital tubercle	Clitoris	Glans penis	<b>Clitoromegaly / micropenis</b>
Genital swelling	Labia majora	Scrotum	<b>Labioscrotal fold</b>

Genital fold	Labia minora	Penile urethra + shaft of penis	Hypospadias.
--------------	--------------	---------------------------------	--------------

### Homologous organs :

Those organs in males and females with the same embryological origin.

males	Females
Glans penis	Clitoris
Scrotum	Labia majora
Penile urethra + shaft of the penis	Labia minora
Prostate gland	Skene glands/paraurethral glands
Copper gland/bulbourethral gland	Bartholin gland
Gubernaculum	Round ligament

### Development of secondary sexual characters at puberty :

#### Females :

most important character : Development of breast/thelarche.

Hormone responsible for thelarche : Estrogen.

Other characters : Axillary hair, pubic hair - Testosterone/Androgens.

#### In males :

Deepening of voice.

Increase in muscle mass.

Axillary hair and pubic hair.

Hormone responsible : Androgens.

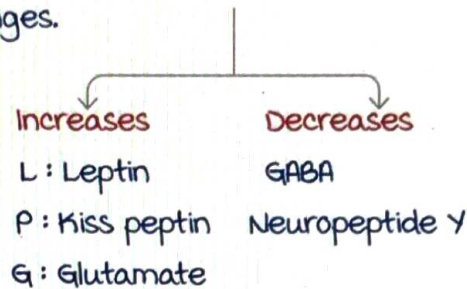
# PUBERTY

## General Points

00:00:15

Age at which males or females start having secondary sexual characteristics.

Hypothalamic pituitary axis gets activated (neurotransmitter changes) → Hormonal changes.



### Arcuate nucleus

↓  
 GnRH released in a pulsatile manner.  
 ↓  
 Initially GnRH released only at night.  
 ↓  
 Pulsatile release of LH at night.  
 ↓  
 Then later cycle becomes more stable.  
 ↓  
 Both LH & FSH released at day and night.  
 ↓ acts on ovary  
 Release oestrogen (-ve feedback on LH) & progesterone (-ve feedback on FSH).

mainly estrogen responsible for the development of secondary sexual characteristics.

**GABA**: Neurotransmitter that keeps the hypothalamus dormant before puberty.

**Kiss peptin**: Neurotransmitter responsible for pulsatile release of GnRH leading to puberty.

**Leptin**: Neurotransmitter which acts as a somatic stimulus for the onset of puberty (permissive role).

Active space

## Puberty in Female vs Male

00:05:09

Female	male
<p><b>10.5 years.</b></p> <ul style="list-style-type: none"> <li>• 1<sup>st</sup> sign : <b>Growth spurt</b> (initiation of skeletal growth).</li> <li>• 1<sup>st</sup> visible sign : Thelarche. Breast budding (most specific sign).</li> <li>• Pubarche : Appearance of Pubic hair &amp; axillary hair.</li> <li>• Peak height velocity.</li> <li>• <b>menarche</b> : Onset of menstruation (~ 12.5 yrs).</li> </ul> <p>Chromosome <b>6 &amp; 9.</b></p>	<p><b>11.5 years.</b></p> <ul style="list-style-type: none"> <li>• 1<sup>st</sup> sign : Testicular enlargement.</li> <li>• Penile enlargement.</li> <li>• Pubarche.</li> <li>• Peak height velocity.</li> </ul>

most important 2<sup>o</sup> sexual characteristics in females : Breast development (**Oestrogen**).

**Pubic hair and axillary hair** : Dependant on **androgens** (in females also).

**Tanner staging** : For breast and pubic hair development.

**5 stages** :

- Stage 1 & 2 : Initial stages/less developed
- Stage 4 & 5 : Fully developed breast & pubic hair.

## Precocious puberty and Delayed puberty

00:11:00

Precocious puberty	Delayed puberty
<p>In females : <b>&lt;8 yrs</b> of age (breast budding appears).</p> <p>In males : <b>&lt;9 yrs</b> of age (testicular enlargement occurs).</p> <ul style="list-style-type: none"> <li>• most common cause : <b>Idiopathic</b>. more common in girls.</li> <li>• Due to excess estrogen.</li> <li>• <b>DOC</b> : GnRH (<b>continuous</b>).</li> </ul>	<p>In females : 2<sup>o</sup> sexual characteristics have not appeared by <b>13 years</b> of age.</p> <p>In males : Testicular enlargement has not occurred by 14 years.</p> <ul style="list-style-type: none"> <li>• most common cause : <b>Constitutional delay</b>. more common in boys.</li> <li>• In females delayed puberty is generally pathological.</li> <li>• <b>DOC</b> : GnRH (<b>pulsatile</b>).</li> </ul>

Precocious menstruation : when menarche occurs at < 10 years of age.

## Precocious Puberty

00:14:43

Central (True precocious puberty)	Peripheral
<ul style="list-style-type: none"> <li>Premature activation of HPO axis.</li> <li>↑ LH.</li> <li>↑ FSH.</li> <li>↑ estrogen.</li> <li>Due to increase in estrogen.</li> </ul> <p>Puberty is always <b>isosexual</b>.</p> <p>Causes :</p> <ul style="list-style-type: none"> <li>90% : Idiopathic.</li> <li>10% : Brain tumor (Hamartoma of tuber cinereum).</li> </ul> <p>Always do MRI of brain.</p>	<ul style="list-style-type: none"> <li>Due to exogenous production of estrogen.</li> <li>Isolated ↑ estrogen &amp; ↑ androgen.</li> </ul> <p>↓ -ve feedback on LH &amp; FSH.</p> <p>↓ LH &amp; ↓ FSH.</p> <ul style="list-style-type: none"> <li>Can be due to : ↑ estrogen    ↑ androgen</li> </ul> <p>↓                      ↓ <b>isosexual      Heterosexual</b></p> <p>Causes :</p> <p>↑ Estrogen :</p> <ul style="list-style-type: none"> <li>Granulosa cell tumor.</li> <li>Hypothyroidism (α subunit similar to LH &amp; FSH).</li> <li>McCune Albright syndrome.</li> </ul> <p>↑ Androgen :</p> <ul style="list-style-type: none"> <li>Sertoli Leydig cell tumor (Androgen secreting tumor of ovary).</li> <li>CAH (Congenital adrenal hyperplasia).</li> </ul>

**McCune Albright syndrome :**

- Café au lait spots.
- Polyostotic fibrous dysplasia.
- Precocious puberty.

MCQs :

Q. Which of the following pubertal events in girls is not estrogen dependent ?

- A. menses.
- B. vaginal cornification.
- C. Hair growth.

Active space

- D. Reaching adult height.
- E. Production of cervical mucus.

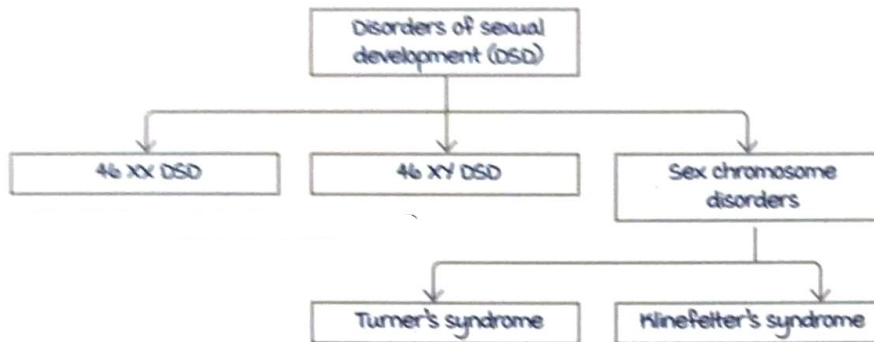
Q. A 9 year old girl has breast and pubic hair development. The evaluation demonstrates a pubertal response to a GnRH stimulation test and a prominent increase in luteinizing hormone (LH) pulses during sleep. These findings are characteristic of patients with which of the following?

- A. Theca cell tumors.
- B. Iatrogenic sexual precocity.
- C. Premature thelarche.
- D. Granulosa cell tumors.
- E. Central precocious puberty.

# DISORDERS OF SEXUAL DEVELOPMENT -I

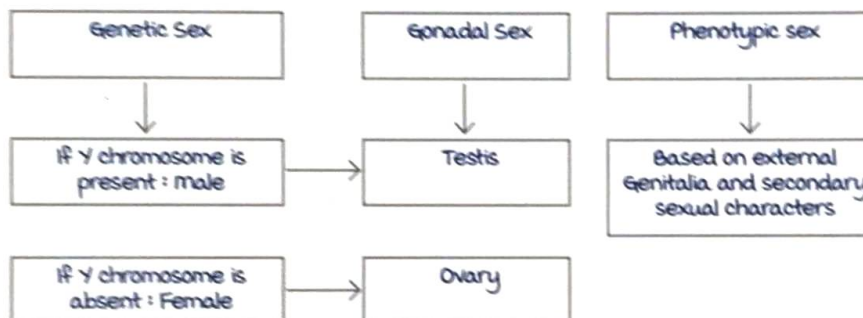
## Outline

00:00:49



## Sex of an individual

00:01:25



Best method for sex determination : Genetic sex :

Karyotyping.

If there is a discrepancy between in any of the above it is called as a disorder of sexual development (DSD).

For example : A 46XX individual with gonads as testis and exact female looking external genitalia is still having a disorder of sexual development. Hence we do not use terms as 'male' and 'female'.

46 XX :

Normal : Ovary.

Abnormal :

Ovotestis.

Streak gonads.

Testes + ( 46 XX reversal).



Normal : uterus.

Abnormal : uterus absent : mullerian agenesis.

Normal : Female looking external genitalia.

Abnormal : Ambiguous genitalia.

46XY :

Normal : Testis.

Abnormal : Testis do not function :

A. Testicular Regression syndrome.

B. Swyers Syndrome.

Ovotestis.

Normal : wolffian duct.

Abnormal :

1. wolffian duct absent : Androgen insensitivity syndrome.

2. mullerian duct present :

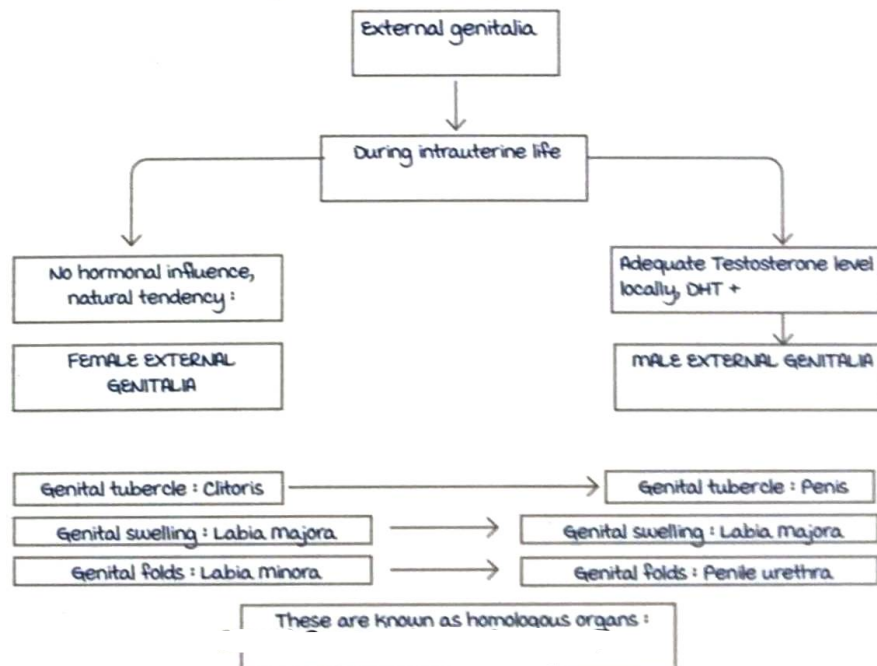
Swyers syndrome.

Persistent MD syndrome.

Normal : male external genitalia.

Abnormal : Female looking genitalia or ambiguous external genitalia.

Therefore, disorders of sexual development can be present even without ambiguous external genitalia.



Active space

Other homologous organs :

Skene glands/ paraurethral gland in female = Prostate gland in males.

Bartholin gland/ greater vestibular gland in female = Cowper's gland in males.

Round ligament in females = Gubernaculum in males.

46 XY : Testis descend into the scrotum and are palpable ( in either scrotum or inguinal canal).

Whenever gonads are palpable → 46 XY karyotype.

Ovaries are never palpable.

Hence whenever gonads are not palpable → 46XX karyotype.

Testosterone and dihydrotestosterone (DHT) act by the same receptors.

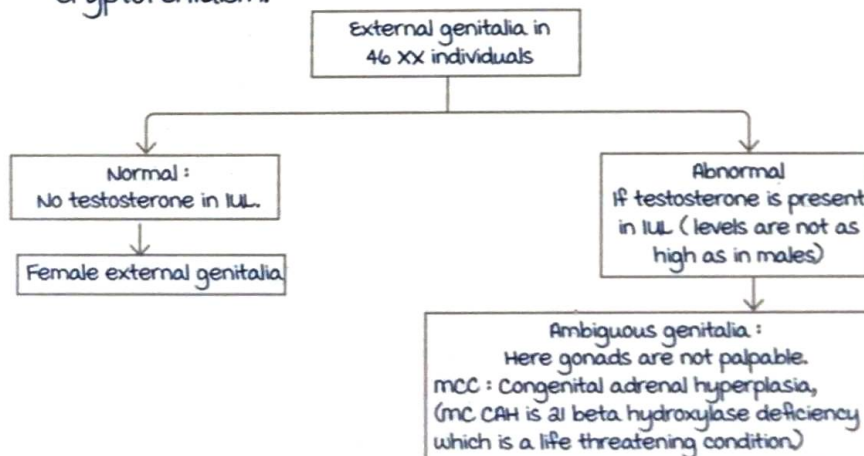
If testosterone levels in intrauterine life is low can lead to ambiguous genitalia.

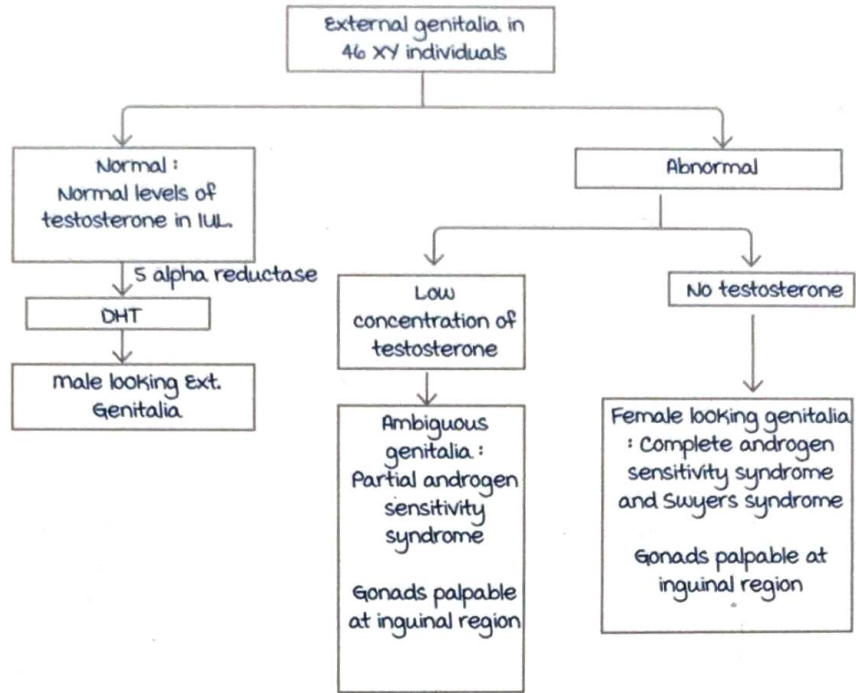
### When to suspect ambiguous genitalia

00:11:07

Ambiguous genitalia suspected :

- Clitoromegaly, if clitoral width > 6mm or length is > 9mm.
- Labioscrotal fusion.
- micropenis, if stretched length of penis < 2.5cm.
- Severe hypospadias.
- Hypospadias associated with unilateral or bilateral cryptorchidism.

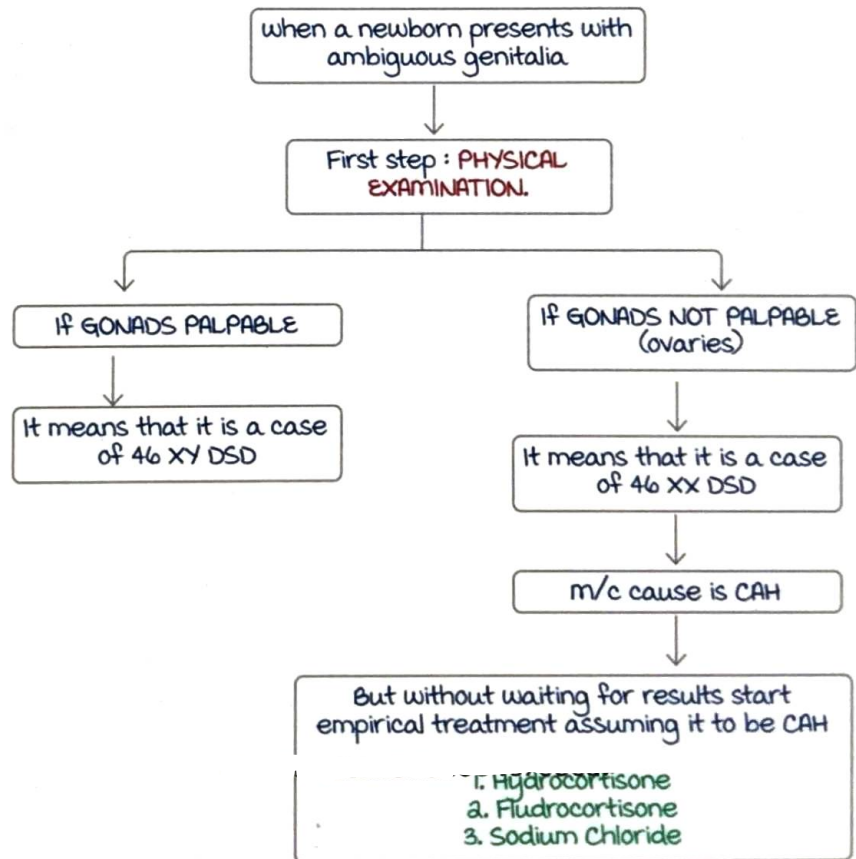




Incomplete descent in these testes is associated with high malignancy Gonadoblastoma.

MC malignant tumor seen in them : Dysgerminoma.

They are indications to do a gonadectomy.



Active space

Best investigation in ambiguous genitalia : **Karyotyping**.  
For a faster result : **FISH**.

**Causes of Ambiguous genitalia :**

- Serum electrolyte levels.
- 17-OH- progesterone levels.
- Karyotyping/ FISH.
- Hormonal study : FSH and LH.
- Pelvic USG : 1. Presence of uterus.  
2. Gonads and location  
3. Associated malformation.

#### 46 XX DSD : Ovotestis

00:26:37

Earlier known as **true hermaphrodite**.

Testis (usually on right side)		Ovary (usually on the left side)	
Duct	Wolffian duct	Duct	mullerian Duct
Internal genital organs	S E E D	Internal Genital Organs	Female
Hormone	Testosterone and DHT produced only by one testis, hence partially present	Hormone	Oestrogen
External genitalia	Ambiguous Genitalia		
At birth	mostly taken as male child		
most common karyotype	46 XX (and MCC in 46 XY)		
Gynecomastia	Since ovary produces estrogen : 3/4 <sup>th</sup> of them present with gynecomastia.		
menstruation	1/4 <sup>th</sup> of them menstruate		

## 46 XX sex reversal

00:31:21

Problem	SRY gene translocation to X chromosome Or mutation in SOX-9 gene SF-1 gene	
Gonads	These mutations lead to formation of testis These testis have normal Leydig and Sertoli cells	
Hormones	Sertoli Cells	Leydig Cells
	Produce AMH	Produce Testosterone Hence DHT also present.
Internal Genital Organs	mullerian duct regresses  Therefore no female internal genital organs	Promotes growth of wolffian duct  male internal genital organs present
External Genitalia	Due to presence of DHT : male looking External Genitalia.	
Secondary Sexual Characters	male type due to presence of testosterone at puberty	

Complete sex reversal : A 46 XX individual with

- Testis.
- male Internal
- male phenotype.

But for proper spermatogenesis both intact Y chromosome and testosterone are required

Therefore these individuals have :

- Infertility.
- Cryptorchidism.
- Short stature.

m/c type of DSD : 46 XX individual with gonads as ovaries and ambiguous external genitalia.

Earlier known as female pseudohermaphroditism.

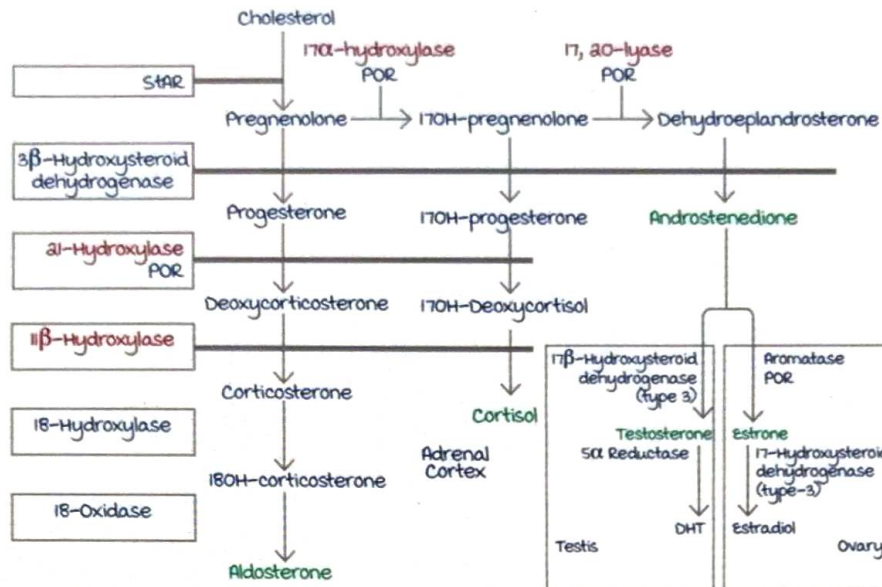
MCC of female pseudohermaphroditism : CAH.

MCC of ambiguous genitalia in females : CAH.

## Congenital adrenal hyperplasia (CAH)

00:35:25

Steroid biosynthesis in the adrenal gland :



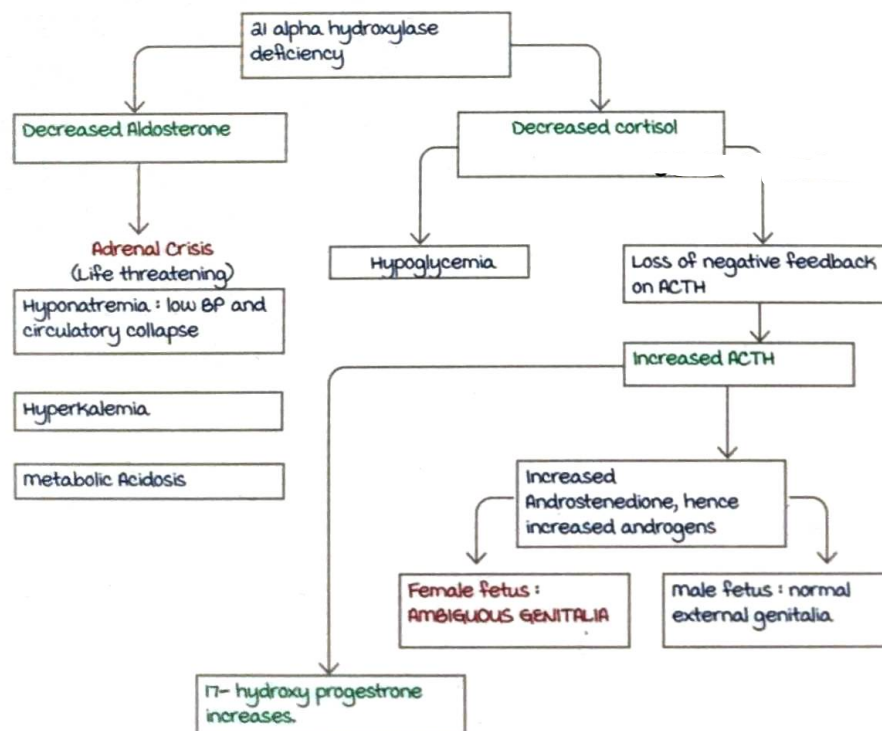
DHT- dihydrotestosterone, POR- P450 oxidoreductase; STAR, steroid acute regulatory protein

Adrenal glands, under the influence of ACTH produces aldosterone, Cortisol and Androstenedione in both males and females.

Once formed **Cortisol** has negative feedback on ACTH.

## 21 alpha hydroxylase deficiency

00:51:57



Active space

This is the most common enzyme deficiency in CAH.

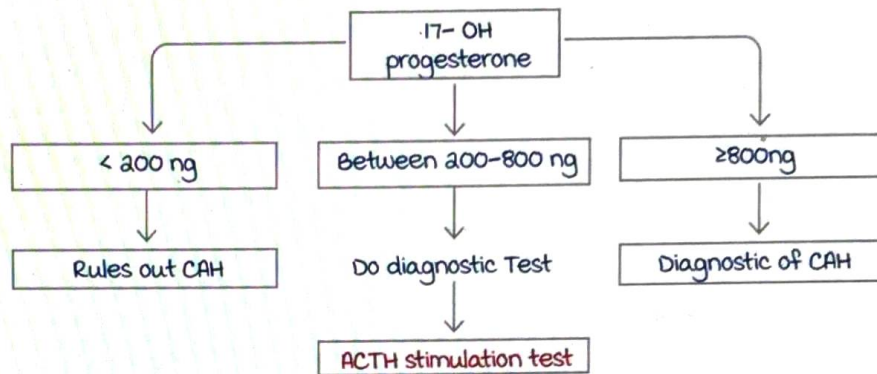
21  $\alpha$  hydroxylase is involved in synthesis of aldosterone and cortisol, hence not produced in the adrenal glands.

21  $\alpha$  hydroxylase is not involved in synthesis of sex hormones.

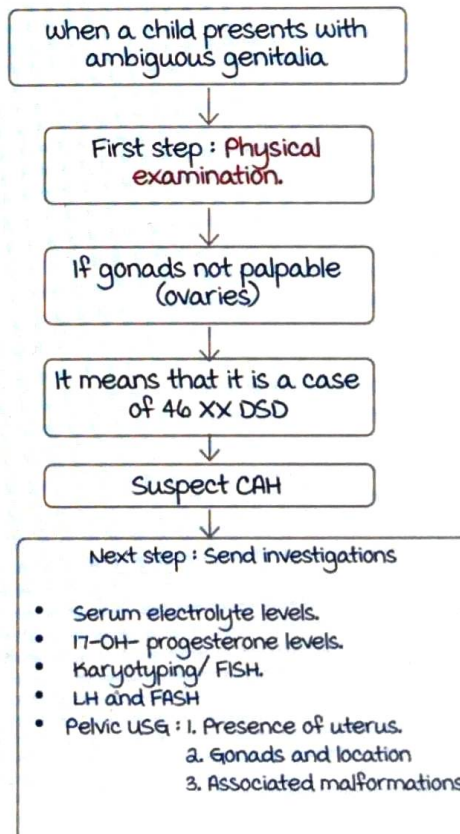
CAH due to 21 alpha reductase deficiency :

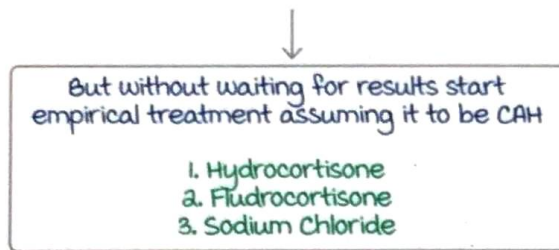
Doesn't affect external genitalia of male foetus.

Since precursor 17 hydroxy progesterone has increased due to increased ACTH, it is used as a screening test for CAH.



- CAH due to 21- $\alpha$ -hydroxylase deficiency is an Autosomal recessive disorder.
- Gene involved is CYP 21A located on chromosome 6.





Once diagnosis is confirmed :

- Continue hydrocortisone.
- Continue fludrocortisone.
- Perform reconstructive surgery for external genitalia as early as possible.

DOC for treatment of CAH : normally : Hydrocortisone.

Pregnant female with female fetus with CAH :

Dexamethasone.

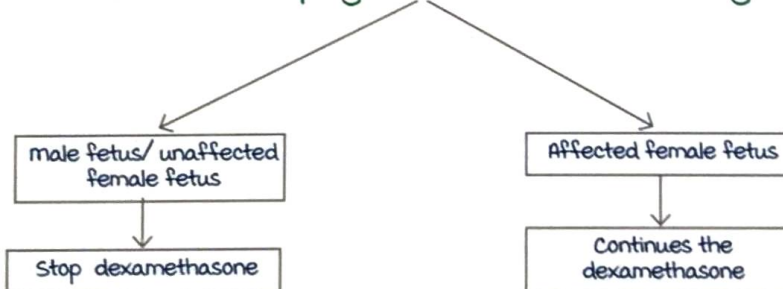
If pregnant woman with previous history of CAH baby or both the partners are known to be heterozygous for one of the severe mutations of CYP21A gene.

↓

Initiate dexamethasone as soon as pregnancy is confirmed

↓

After starting dexamethasone, at 10 weeks perform a  
chorionic villus sampling/ cell free fetal DNA testing.



## 11-beta-hydroxylase deficiency.

00:59:00

Second most common enzyme deficiency

11 beta hydroxylase is required for formation of aldosterone and cortisol.

Aldosterone is decreased.

No Cortisol to provide negative feedback on ACTH and there

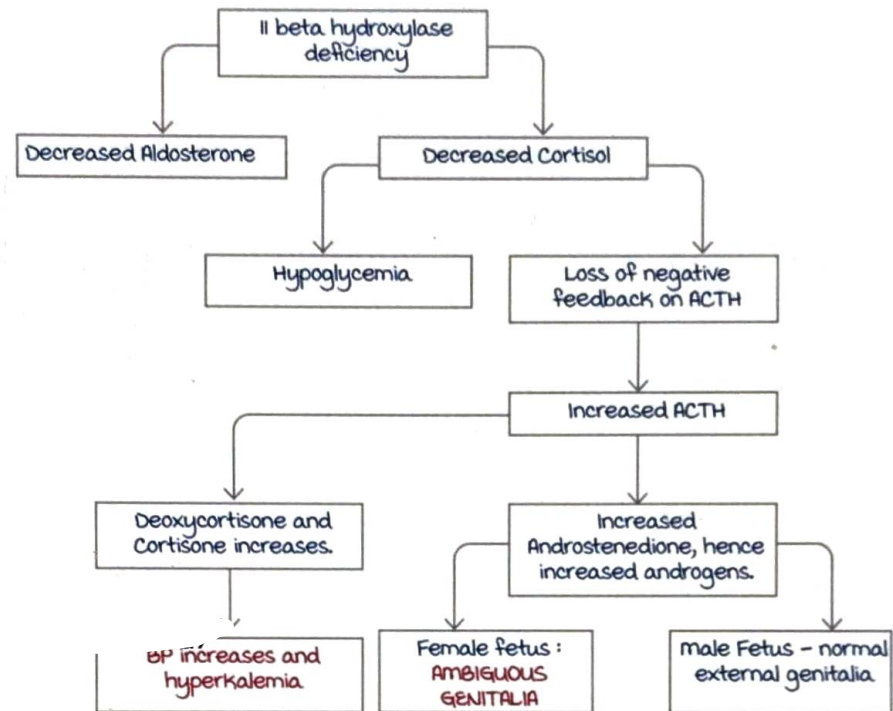


will be increased androgens.

All precursor substrates will increase- like Deoxycorticosterone.

Deoxycorticosterone has mild mineralocorticoid properties.

Hence, BP will increase. (Accumulation of deoxycortisone).



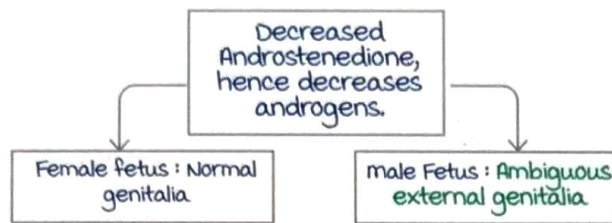
### Deficiency of 17-alpha hydroxylase or 17, 20 Lyase

01:00:41

These enzymes are not required in the production of aldosterone.

Ultimately DHEA and androstenedione decrease.

Hence production of androgens is decreased.



male fetus will present with ambiguous genitalia.

In 17 alpha hydroxylase deficiency

↓  
Decreased cortisol production

↓  
Loss of negative feedback on ACTH

↓  
Increased ACTH

↓  
This increases the aldosterone level and causes hypertension.

### Deficiency of 3-beta hydroxysteroid dehydrogenase

01:02:14

Since this enzyme is required in the production of all hormones.

All 3 hormones decrease.

Decreased aldosterone.

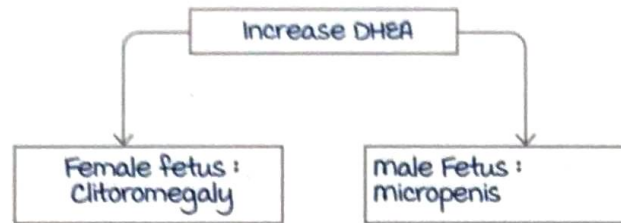
Decreased cortisol.

Decreased testosterone.

ACTH increases (loss of negative feedback).

Precursors like Pregnenolone and 17-OH-pregnenolone increase.

Increased DHEA.



male fetus : ambiguous genitalia, since DHEA although increases it's a weak androgen.

Female fetus : There is ambiguous genitalia as there is presence of an androgen (DHEA) : Clitoromegaly.

In neonates with 3 beta HSD deficiency : 17-OH-pregnenolone is increased.

### Newly diagnosed CAH

01:03:28

Deficiency of P450 oxido-reductase enzyme (OR enzyme)

P450 Or enzyme is located on chromosome 7.

This enzyme is an electron donor for many enzymes involved in the steroid pathway.

Therefore leads to ambiguous genitalia in both males and females.

Only DSD associated with skeletal abnormalities like

Craniosynostosis

Radio ulnar synostosis

midfacial hypoplasia

Choanal atresia.

Antley Bixler Syndrome.

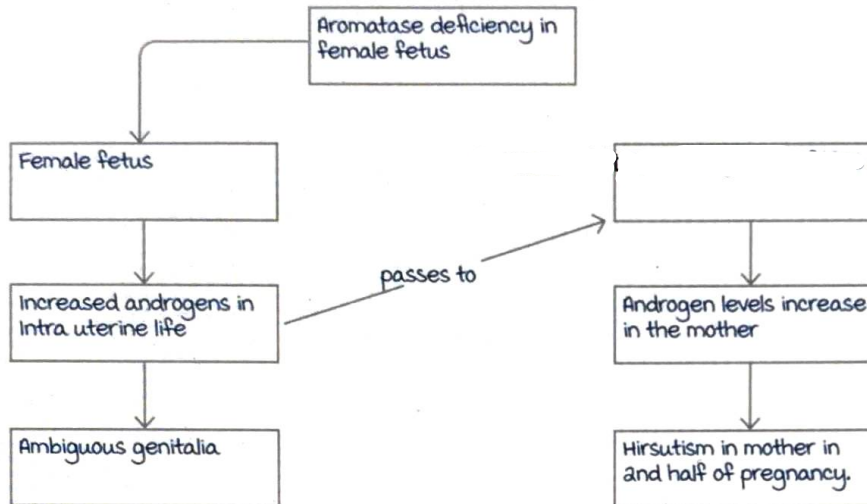
Aromatase Deficiency :

Another reason for 46 XX genotype with ambiguous genitalia.

Aromatase enzyme converts androgens into estrogen.

These androgens are produced by the adrenal glands of the fetus.

Placenta secretes aromatase during pregnancy (also produced by adipose tissue, brain and gonads).



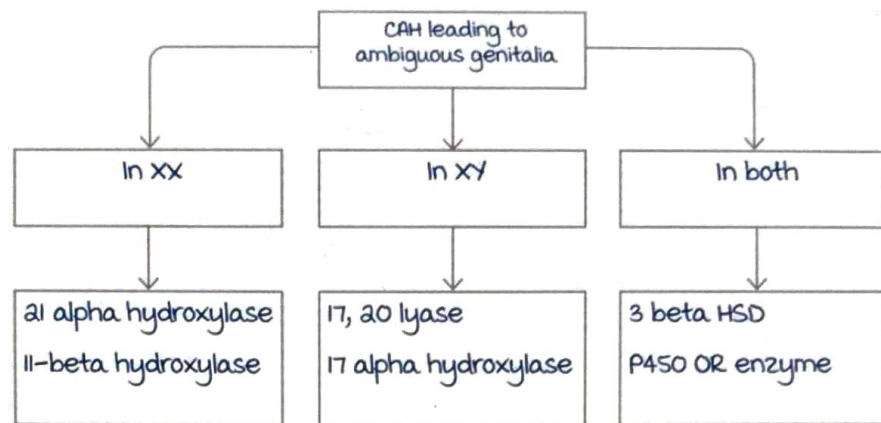
Therefore, if female fetus has ambiguous genitalia with history of hirsutism in mother during pregnancy : Aromatase deficiency is the cause.

Revision :

Causes of Ambiguous genitalia/clitoromegaly in 46 XX

Karyotype :

1. CAH due to :
  - I alpha hydroxylase deficiency (m/c).
  - II beta hydroxylase deficiency.
2. Ovotestis.
3. Aromatase Deficiency.
4. Maternal exposure to androgenic drugs.
5. Maternal overproduction of androgens (in luteomas and theca lutein cysts).
6. CAH : 3 beta HSD deficiency.
7. CAH : P450 OR deficiency.

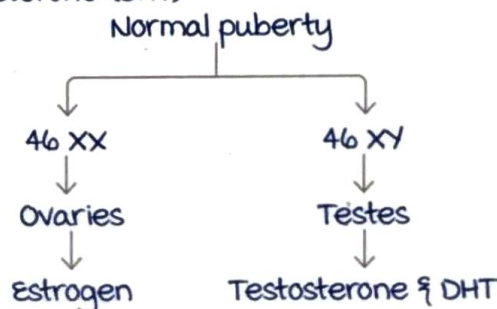


Active space

## DISORDERS OF SEXUAL DEVELOPMENT : PART 2

### 46 XY Disorders of Sexual Development (DSD) 00:00:08

- Abnormal testicular development :
  1. Pure gonadal dysgenesis/Swyer's syndrome (46 XY).
  2. Partial gonadal dysgenesis.
  3. Ovotestis.
  4. Testicular regression syndrome.
- Problem in androgen production/androgen receptors :
  1. Androgen insensitivity syndrome (AIS)
    - a. Complete AIS.
    - b. Partial AIS.
    - c. Reifenstein syndrome.
  2. Decreased androgen production :
    - a. Congenital Adrenal Hyperplasia → 17  $\alpha$  Hydroxylase deficiency & 17, 20 Lyase deficiency.
    - b. CAH : 3  $\beta$  HSD deficiency.  
P450 OR deficiency.
  3. Problem in the receptor :
    - a. Defective Anti mullerian Hormone (AMH) receptor → Persistent mullerian duct syndrome
    - b. Defective HCG/LH receptor → Defective testosterone production.  
The first stimulus for the testis to produce testosterone is by HCG.
  4. 5  $\alpha$  reductase deficiency → Decreased production of Dihydrotestosterone (DHT)



Estrogen :

- Development of 2° sexual characteristics (Breast).
- Proper growth of uterus, cervix and vagina.
- No role in the development of external genitalia.

The growth of axillary hair and pubic hair in females is dependent on testosterone, source :

- Theca cells of ovary.
- Adrenal glands.

Testosterone & DHT :

- Development of 2° sexual characteristics in males like deepening of voice, increased muscle mass, facial hair growth etc.

### Swyer's syndrome

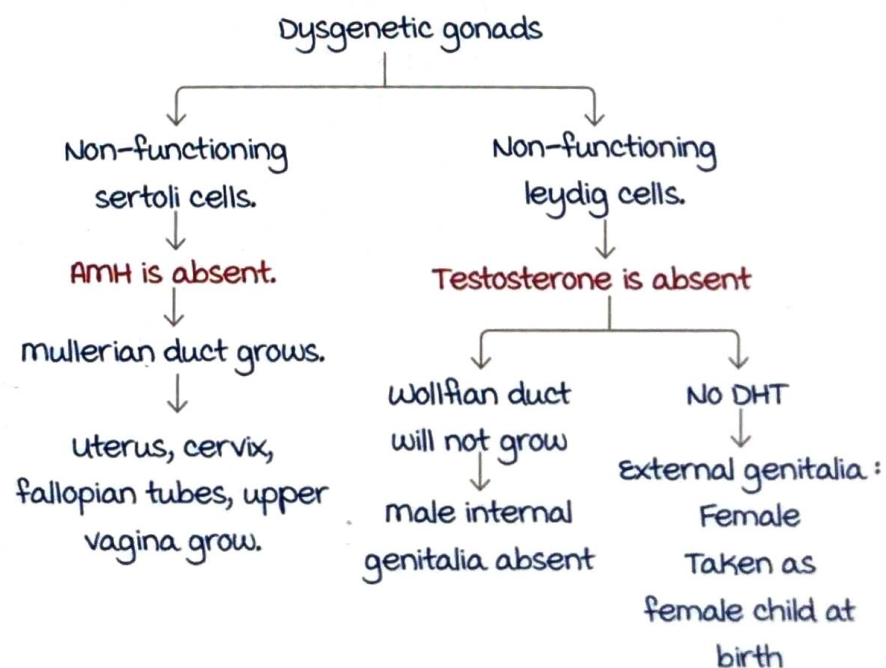
00:09:18

AKA Pure gonadal dysgenesis.

Genotype → 46 XY

Gonads dysgenetic/non-functional testes, due to :

- SRY gene mutation.
- SOX-9 gene mutation.
- NRSA-1 gene mutation.
- DAX-1 gene mutation.
- SF-1 gene mutation.



Testes are undescended (due to absent AMH, testosterone and DHT) : Palpable in the inguinal area.

- Present as inguinal hernia.
- Have increased chances of malignancy.

46 XY child with female looking phenotype and genitalia, suspect a DSD if :

- Palpable gonads.
- Karyotyping should be done.

Indication for karyotyping :

- Palpable gonads with female like external genitalia.
- Non-palpable gonads and male external genitalia.

When this child grows → At puberty → Non-functioning testes  
→ No testosterone → No secondary sexual characteristics of males.

No estrogen :

- No secondary sexual characteristics of females (no breast development).
- Uterus remains infantile.
- No menarche.
- Presents with C/O primary amenorrhea or delayed puberty.

Negative feedback on GnRH will be lost → Increased levels of  
LH and FSH.

USG :

- Uterus present.
- Undescended testes.

Lab investigations :

- Low testosterone (Leydig cells) and inhibin B (Sertoli cells) levels.
- Increased LH & FSH levels.

LH → Leydig cells → Testosterone → Negative feedback on  
LH & GnRH.

FSH → Sertoli cells → Inhibin B → Negative feedback on FSH.



management :

- Let them be females.
- Gonadectomy as soon as possible.
- Hormone replacement therapy :  
estrogen (1 year) for breast development.  
estrogen & progesterone (after 1 year) till the age of normal menopause (51 years).
- If problem in intercourse → vaginoplasty.  
Vecchiotti technique (laproscopic) / Davydov's technique.  
Performed just before or after marriage.

### testicular regression syndrome

0:22:39

Genotype → 46 XY (normal testis).

In early intrauterine life :

- Testes are normal.
- Testosterone & AMH production is normal.
- Internal and external genitalia are normal.

Later in intrauterine life (probably due to testicular torsion) :

**Testes regress** & anorchia is seen.

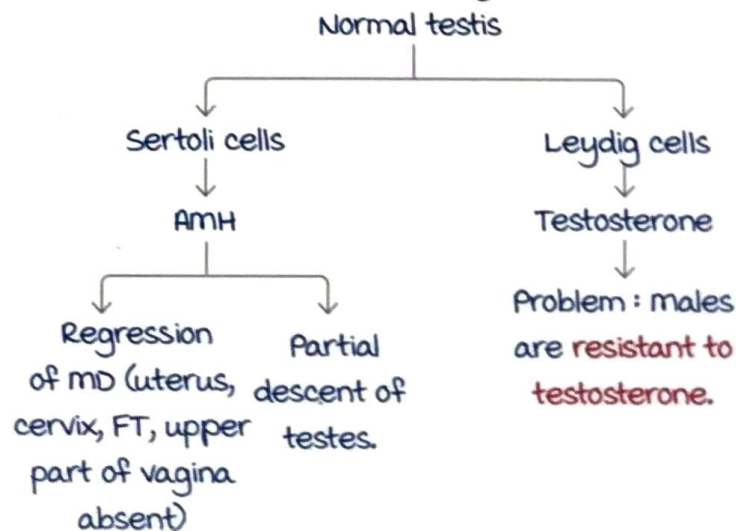
But by that time external and internal genitalia are already formed.

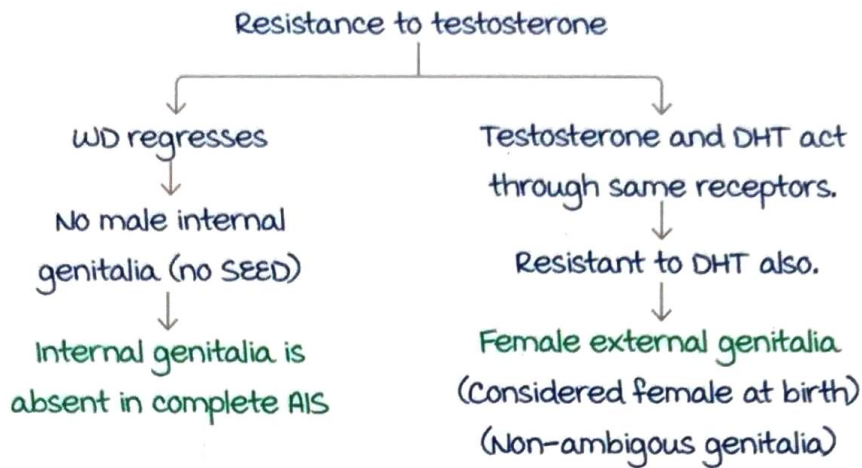
### Complete androgen insensitivity syndrome

00:24:30

X-linked recessive disorder ; Genotype → 46 XY.

Gonads → Testis (normal functioning).



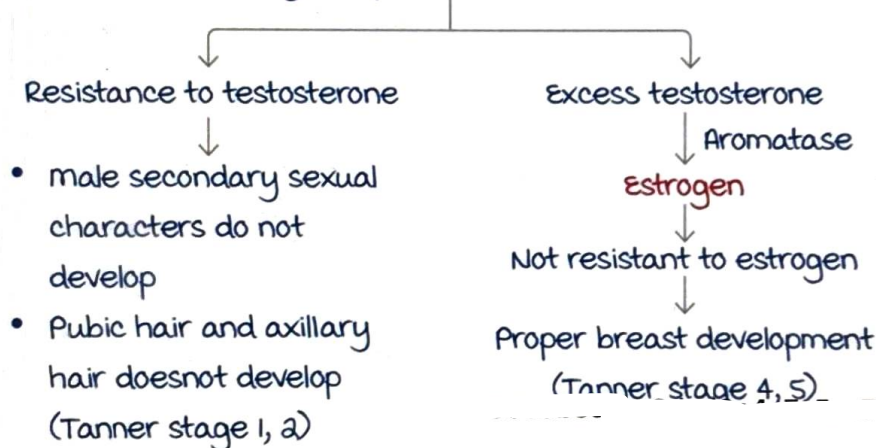


Testis is undescended :

- Palpable at inguinal region (can be detected at birth).
- Increased chances of malignancy.

When they reach puberty :

Testis → Functioning and produce testosterone but



Presents with **primary amenorrhea**/inguinal hernia.

Q. A female with C/o primary amenorrhea, her breast development corresponds to Tanner stage 4 or 5. She has scanty pubic hair/ axillary hair, uterus is absent, inguinal hernia is present.

Answer : Complete androgen insensitivity syndrome.

Lab investigations :

- **Testosterone** → **Increased** (corresponds to male levels)
- Due to resistance to testosterone → **LH is increased.**
- Sertoli cells → Inhibin → Negative feedback on FSH → **FSH levels are normal.**

D/D: **mullerian agenesis (46 XX)** with no uterus development.  
Confirmatory test → Karyotyping.

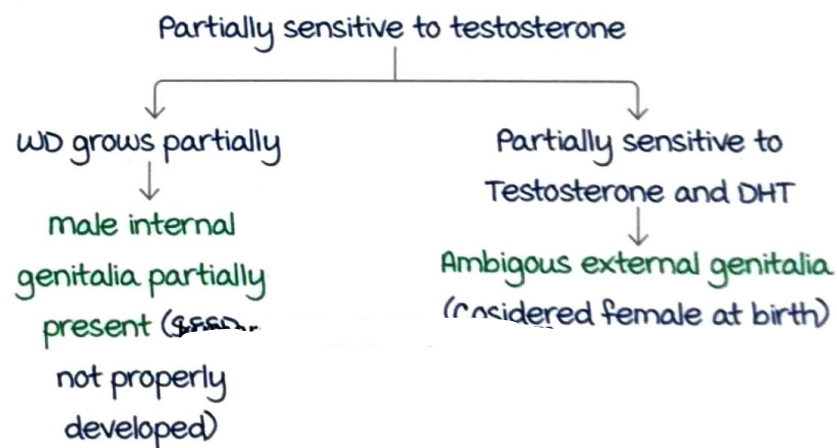
management:

- Let them be females.
- Gonadectomy (Only after pubertal development is complete → 16-18 years of age)
- After gonadectomy → HRT in the form of estrogen (only estrogen as uterus is absent)
- Perform vaginoplasty.  
Technique → Vecchietti/Davydov's procedure (laproscopic)  
McIndoe vaginoplasty (conventional technique).  
Time → Just before/ after marriage.
- These patients cannot have their biological children.

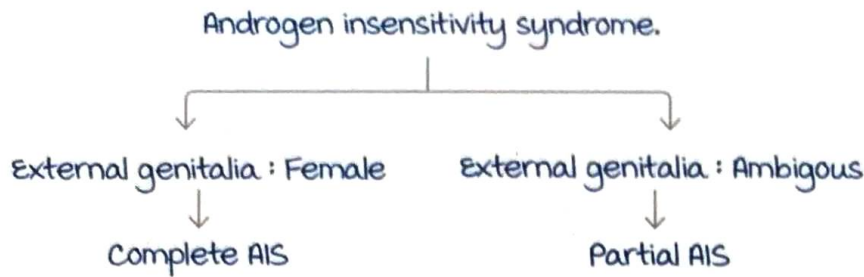
### Partial AIS syndrome

00:38:15

Everything is similar to complete AIS except these males are **partially sensitive to androgens**.



Q. A female with C/O primary amenorrhea; breast development corresponds to Tanner stage 4 or 5; axillary and pubic hair corresponds to Tanner 1 or 2; presence of inguinal hernia



management of partial AIS :

- Same as complete AIS.
- Difference : Perform gonadectomy ASAP to prevent virilization of external genitalia.

### Reifeinstein syndrome :

Present as undervirilized males.

Better form of partial AIS.

Presents as male who are infertile with a bifid scrotum, perineoscrotal hypospadias.

management :

- Give testosterone.
- Gonadectomy is done only if cryptorchidism is present

There is a 46 XX condition which closely resembles AIS (46 XY) in both these conditions :

- Female phenotype.
- Absent uterus.
- Presents with primary amenorrhea.

The condition → mullerian agenesis (46 XX).

### Mullerian agenesis

00:43:41

Genotype → 46XX

Ovary → Normal .

External genitalia → Normal female-like.

Problem → **Both MD are absent.**

So uterus, cervix, fallopian tubes, upper vagina are absent.

In some females :

- Distal FT may be seen.
- Complete vaginal agenesis (upper & lower part absent).
- A rudimentary uterine horn may be seen.  
(Endometriosis, dysmenorrhea).

These females at puberty :

Ovary normal :

- Estrogen is normal → Breast development normal.
- Ovulate normally.
- Androgens normal → Pubic hair and axillary hair normal.

In AIS :

Breast → Corresponds to Tanner 4/5

Pubic & axillary hair → Tanner 1/2

Mullerian agenesis → Breast, pubic & axillary hair → **Tanner 4/5**

These females can have primary amenorrhea

And after marriage → Coital difficulties.

Associated problems in Mullerian agenesis :

- **Renal anomalies (MC)** → Renal agenesis, Horse-shoe shaped kidneys.
- **Skeletal anomalies** → Hemivertebrae

Only Mullerian agenesis → **MRKH (Mayer Rokitansky Kuster Hauser syndrome) type I.**

(Mullerian agenesis + Renal anomalies + Skeletal anomalies)

→ **MRKH type 2 / MURCS syndrome (Mullerian agenesis, Renal anomalies, Cervical somite).**

IVP & skeletal X-rays should be done in all patients of MRKH.

Investigation of choice to differentiate AIS & Mullerian

agenesis → **Karyotyping.**

Levels of LH and FSH in Mullerian agenesis → Normal.

Management :

- These females cannot menstruate.
- Make them capable of having intercourse by vaginoplasty  
Technique : Vecchietti/Davydov's procedure (laproscopic)  
mc Indoe vaginoplasty (conventional technique).  
Time → Just before/ after marriage.
- These females can have their own biological children as they ovulate normally (IVF + Surrogacy).

## 5 $\alpha$ reductase deficiency

00:51:04

Genotype  $\rightarrow$  46 XY.

Normal testis

- Sertoli cells are normal  $\rightarrow$  AMH Normal  $\rightarrow$  MD regresses.
- Leydig cells are normal  $\rightarrow$  Testosterone normal  
WD grows  $\rightarrow$  Internal genitalia is male (SEED present).  
**Unable to convert to DHT**  $\rightarrow$  Female external genitalia  
(Considered female child at birth)

At puberty :

- Leads to the development of male secondary sexual characters like deepening of voice, increased muscle mass, increased libido.
- Some virilization of male external genitalia (not at birth)  $\rightarrow$  Clitoromegaly
- Breast tissue  $\rightarrow$  Absent.
- No DHT :
  - Less body hair.
  - Less acne.
  - Less temporal hair line recession.

Investigations :

(Testosterone : DHT) ratio :

- $> 10$   $\rightarrow$  In infants
- $> 20$   $\rightarrow$  Older children & adults.

Q. MC cause of **male pseudo hemaphrodite** :

Genotype  $\rightarrow$  male (46 XY)

External genitalia  $\rightarrow$  Female

Answer : Complete AIS.

Other  $\rightarrow$  Swyer syndrome.

5  $\alpha$  reductase deficiency.

MC cause of 46 XY with ambiguous genitalia  $\rightarrow$  Partial AIS.

Overall causes of ambiguous genitalia/clitoromegaly at birth :

46 XX :

- CAH.
- Ovotestis.
- Aromatase deficiency.
- Maternal exposure to androgens.

46 XY :

- Partial AIS.
- CAH.

# PRIMARY AMENORRHOEA

## Amenorrhoea

00:00:40

### Primary amenorrhoea :

No menarche by 15 years of age in the presence of secondary sexual characters (breast budding present).

(or)

No menarche by 13 years of age in the absence of secondary sexual characters.

### Secondary amenorrhoea :

Absence of menstruation for 90 consecutive days (or 3 months) in a female who was previously menstruating normally or absence of menstruation for 6 months in a female who previously had irregular cycles.

MC cause of primary amenorrhoea : Gonadal dysgenesis.

MC type of gonadal dysgenesis : Turner's syndrome.

2<sup>nd</sup> MC cause of primary amenorrhoea : Mullerian agenesis (MRKH syndrome).

MC cause of secondary amenorrhoea : Pregnancy (due to high progesterone)

MC cause of pathological secondary amenorrhoea : PCOS.

### menstruation :

- Hypothalamus releases GnRH in a pulsatile manner (at puberty)
- GnRH acts on anterior pituitary.
- From anterior pituitary, FSH and LH acts on ovary.
- From ovary, they produce estrogen and progesterone.
- Estrogen and progesterone acts on uterine endometrium.
- menstruation is shedding of endometrium.
- For shedding of endometrium, the outflow tract should be normal.

Causes of primary amenorrhoea based on the following :

Hypothalamus	Hypothalamic failure : Kallmann syndrome.
Anterior pituitary	Craniopharyngioma.
Ovary	Gonadal dysgenesis : Turner's syndrome (45X0) : MC cause Swyers syndrome (46XY) Pure gonadal dysgenesis (46XX)
uterus	Mullerian agenesis (46XX) : 2 <sup>nd</sup> MC cause Androgen insensitivity syndrome (46XY).
Outflow tract	Obstruction to outflow tract : Cryptomenorrhoea. Imperforate hymen Vaginal agenesis Transverse vaginal septum.

### Algorithm for primary amenorrhoea

00:10:21

1. Physical examination :
  - Breast : Tanner staging.
  - Pubic and axillary hair : Tanner staging.
  - Uterus present : P/R examination.
  - External genitalia
  - Inguinal area : Undescended testis.
2. Urine pregnancy test.
3. Pelvic USG :
  - Uterus : Present or absent.
  - Gonads.
4. LH or FSH.

Best or confirmatory investigation : Karyotyping.

Case 1 : A case of primary amenorrhoea with uterus present.

- Kallmann syndrome (46XX)
- Gonadal dysgenesis :
  - Turner syndrome (45X0)
  - Swyer's syndrome (46XY).
- Cryptomenorrhoea (46XX).

Case 2 : A case of primary amenorrhoea with absent uterus.



- Mullerian agenesis (46XX)
- Androgen insensitivity syndrome (46XY) : Complete/partial.

### Kallmann syndrome

00:14:29

Genotype : 46 XX

Gonads : Ovary

Disorder : Failure of migration of GnRH neurons from olfactory epithelium to the hypothalamus.

- Pulsatile release of GnRH is absent.
- Decreased GnRH, LH and FSH.
- Resulting in decreased estrogen.
- Secondary sexual characteristics absent (breast absent), axillary hair & pubic hair are sparse (due to decreased androgens).

This is called as hypogonadotropic hypogonadism.

Clinical features :

- Primary amenorrhoea.
- Infertility.
- Anosmia.

Height : Normal.

External genitalia : Female.

Internal genitalia : Uterus, cervix, vagina are present but infantile or hypoplastic (as for their growth, estrogen is needed).

Defect in gene : KAL-1 gene.

Inherited condition as X linked recessive disorder.

MC : males > females.

Management :

GnRH analogues given in pulsatile manner.

### Gonadal dysgenesis

00:21:17

Turner syndrome :

Genotype : 45 XO.

Gonads : Ovaries.

Only 1 X chromosome : Ovaries undergo accelerated atresia leading to **streak ovaries**.

Due to non-functional ovaries, there is no ovulation and progesterone secretion is absent.

No negative feedback on LH, i.e, **high levels of LH**.

No estrogen levels leading to

- Absent breast development : Secondary sexual characters are absent.
- Uterus : Infantile or hypoplastic.
- **FSH** : Negative feedback lost and levels are **high**.

High FSH and LH but no estrogen : **Hypergonadotrophic hypogonadism**.

**mutation in SHOX gene** : Short stature (most characteristic feature).

External genitalia : Normal female like.

Additional characteristics :

- Webbing of neck.
- Low posterior hairline.
- Shield shaped chest.
- Widely spaced nipples.
- Cubitus valgus.
- Congenital heart disease : **Bicuspid aortic valve** > coarctation of aorta.
- Diabetes mellitus, Hashimoto's thyroiditis.
- Short 4<sup>th</sup> metacarpal.

Life span : Slightly reduced due to cardiovascular complications.

**IQ** : Normal.

management :

- Estrogen : 1 year for breast development.
- Estrogen + progesterone as hormone therapy.
- Streak ovaries do not have chances of malignancy, no gonadectomy.
- Growth hormone : Height.

Karyotyping should be done to rule out mosaic (45XO/46XY).  
Female phenotype : Y chromosome is an indication of gonadectomy.

For conception : Donor egg + IVF.

Pregnancy is a contraindication only in cardiac complications of turners syndrome.

### Swyer's syndrome

00:30:07

Type of gonadal dysgenesis.

Genotype : 46 XY.

Inactivation of SR-Y gene leads to dysgenetic testis.

- They do not descend and presents as inguinal hernia.
- There is increased chance of malignancy.

Height : Normal.

Internal genitalia : Mullerian Inhibiting substance is absent causing growth of mullerian duct, uterus, fallopian tube, cervix and upper vagina will be present.

External genitalia : Testosterone and DHT are absent; external genitalia resembles exactly like a female.

Increased levels of LH and FSH (due to absence of inhibin and testosterone secretion from testes)

No estrogen : Breast development absent.

Management :

Estrogen for 1 year for breast development followed by estrogen + progesterone.

Gonadectomy as soon as possible.

Dysgenetic testis have increased chances of malignancy.

Pure gonadal dysgenesis :

Genotype : 46 XX.

Though 46 XX karyotype, gonads are streaked.

Everything is same as Turner's syndrome except,

Normal height and additional features are absent.

Common features in all 3 categories :

- Levels of estrogen are decreased : Absent breast development and infantile uterus.
- LH and FSH levels are high.
- Female external genitalia.

## Cryptomenorrhoea

00:37:10

It is a condition where female menstruates normally but menstrual blood fails to come out due to an **obstruction in the outflow tract**.

Causes of obstruction :

- MC cause : **Imperforate hymen**.
- Transverse vaginal septum.
- Vaginal agenesis.

In cryptomenorrhea : The entire **HPO axis is intact**.

LH : Normal, FSH : Normal.

Gonads : Normal ovaries.

Normal estrogen levels.

Normal breast development.

Normal ~~ovulation~~.

Internal genital organs :

- Normal female organs; obstruction present.
- These female menstruates but menstrual blood fails to come out leading to :  
Collection of blood in uterus : **Hematometra**.  
Collection of blood in cervix and vagina : **Hematocolpos**.  
Increased chances of retrograde menstruation resulting in **endometriosis**.

**C/O cyclical pain** in abdomen every month but no menstruation.

Sometimes female can present with **urinary retention**.

P/A examination : uterus may be palpable (if increased size due to hematometra)

P/V examination (Not done usually in virgin female) : enlarged uterus.

P/R : Preferred, enlarged uterus.

L/E :

**Vaginal agenesis** : Absent vaginal opening.

**Imperforate hymen** : Tensed bluish bulging hymen, cough impulse present, opening in hymen is absent.

Upper part of vagina (1/3rd) : Develops from mullerian duct.

Lower 1/3rd of vagina : Develops from sinovaginal bulb/urogenital sinus.

Septa resolves by 20 weeks.

If septa fails to resolve

**Transverse vaginal septum**.

MC site for transverse vaginal septum : upper part of vagina.

L/E :

Vaginal opening present.

Thicker membrane in the vagina.

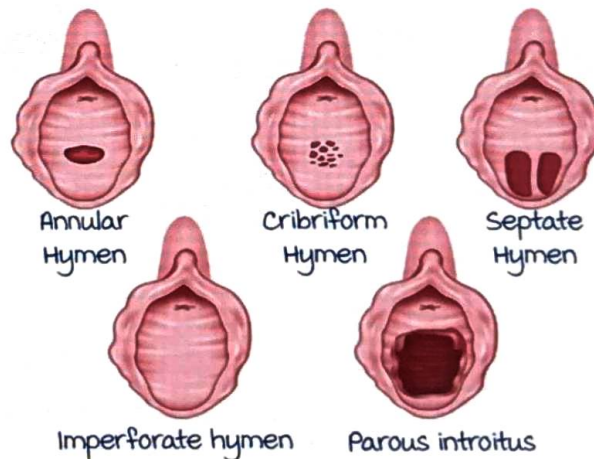
Absence of tensed bluish bulging hymen.

Cough impulse absent.

If doubt even after local examination, do USG and MRI.

management of imperforate hymen :

Cruciate (X shaped incision) on the hymen.



Kallman's syndrome : Levels of LH and FSH decreased.

Gonadal dysgenesis : Levels of LH and FSH high.

Cryptomenorrhoea : Levels of LH and FSH are normal.

Primary amenorrhoea with absent uterus, it is either a case of mullerian agenesis or androgen insensitivity syndrome.

Features	mullerian agenesis (MRKH syndrome)	Androgen insensitivity syndrome
Genotype	46 XX	46 XY
Gonads	Ovaries : Normal	Testis : Normal.
Hormone produced	Estrogen	Testosterone
Defect	Both mullerian ducts are absent	Individuals are resistant to testosterone.
Breast	Normal and corresponds to tanner stage 4 and 5	Testosterone converted to estrogen leading to breast development corresponding to tanner stage 4 or 5.
Axillary and pubic hair	Normal and corresponds to tanner stage 4 or 5.	Sparse corresponding to tanner stage 1 or 2.
Internal genital organ	Uterus : Absent Vagina : Complete	AMH present : mullerian duct absent and uterus absent. Blind vaginal pouch.
External genital organ	Female	Complete : Female Partial : Ambiguous genitalia.
Testosterone	Equivalent to female levels	Compared to a normal female, levels are high.
LH and FSH	Normal	Sertoli cells producing inhibin, FSH normal. Insensitive to testosterone, LH levels are higher.

Best investigation to differentiate between AIS and mullerian agenesis : Karyotyping.

management of mullerian agenesis :

- Vaginoplasty :  
Done just before or just after marriage.  
Conventional technique : mcIndoe.  
New technique : Vecchiatti.
- For pregnancy : IVF followed by surrogacy.

management of AIS :

- Let them be females.
- Gonadectomy (due to high risk of malignancy) is done after pubertal development is complete i.e., by 16-18 years of age (for breast development).

- After gonadectomy, HRT in the form of estrogen due to absent uterus.
- For child : Adoption (Reproduction outcome : Worst in AIS)

Key points :

Y chromosome with female phenotype : Increased chances of malignancy : Do gonadectomy.

Gonadectomy should be done in :

- Complete AIS around 16-18 years of age.
- Partial AIS as soon as possible.
- Swyer's syndrome as soon as possible.

Not done in streak gonads (Turners syndrome) except if it is mosaic.

## SECONDARY AMENORRHEA

Amenorrhoea :

**Primary amenorrhoea** : No menarche by 15yrs of age in presence of secondary sexual characteristics (breast budding present).

OR

No menarche by 13 yrs of age in absence of secondary sexual characteristics.

**Secondary amenorrhoea** : Absence of menstruation for **90 consecutive days** (or 3 months) in a female who was previously menstruating normally. OR

If females had previously irregular cycles absence of menstruation for 6 months.

**Primary amenorrhoea (William's)** :

- Absence of menstruation by 15 years. OR
- Absence of menstruation within three years of thelarche. OR
- Female has not menstruated by age 14 and shows signs of hirsutism, excessive exercise or eating disorder. (ACOG 2017)

**Secondary amenorrhoea** : Absence of menstruation for 3 months in a previously menstruating female.

Note : **<9 cycles /year** also needs to be investigated.

Categories of amenorrhoea based on gonadotropin & estrogen.

Types of hypogonadism	LH/FSH	Oestrogen	Primary defect
Hypergonadotropic	High	Low	Ovary
Hypogonadotropic	Low	Low	Hypothalamus/pituitary
Eugonadotropic	Normal	Normal/Low	Varied

Hypothalamus → Releases GnRh (pulsatile manner) → Acts



on anterior pituitary → Releases LH & FSH → Acts on ovary  
→ Estrogen and progesterone are released.

Estrogen has a negative feedback on FSH & GnRH.

If defect is in ovary & estrogen levels are decreased →  
Negative feedback on FSH will be lost → Hypergonadotropic  
hypogonadism.

If defect is in Hypothalamus/ Pituitary, levels of GnRH : Low  
→ FSH : Low → Estrogen : Low → Hypogonadotropic  
Hypogonadism.

FSH levels are usually checked.

### Secondary amenorrhea

00:06:44

MC cause : **Pregnancy** (Increased Progesterone levels).

Other physiological causes of secondary amenorrhea :

1. Lactation :

During lactation → Increased prolactin → Negative  
feedback on GnRH → Decreased levels of LH & FSH →  
Secondary amenorrhea.

Applied : Hyperprolactinaemia can cause secondary  
amenorrhea → Hypogonadotropic ammenorrhea.

In Hypogonadotropic ammenorrhea, prolactin levels are **not**  
**always** increased.

E.g Sheehan syndrome (Decreased LH, FSH, Prolactin).

### Physiology

00:10:31

Normally,

Hypothalamus → Releases peptides like GnRH, TRH, CRH →  
Stimulates pituitary → Pituitary releases LH, FSH, TSH &  
ACTH.

In case of prolactin :

Hypothalamus releases (arcuate nucleus) → Dopamine →  
Inhibitory effect on release of prolactin.

Dopamine agonists are used for the treatment of hyperprol-

actinemia

Prolactin releasing factors include :

- TRH.
- Vasopressin.
- Vasoactive intestinal peptides.
- Acetylcholine.

Dopamine receptors : D1 & D2.

Cells on anterior pituitary gland primarily have D2 Receptors. Therefore, drugs with better role in testing for hyperprolactinemia : D2 specific > Non-specific dopamine agonist.

D2 receptors specific : Cabergoline > Bromocriptine (Non specific dopamine agonist).

Cabergoline has longer t<sub>1/2</sub> : can be given weekly or twice weekly and has lesser side effects.

Bromocriptine given daily, has more side effects like nausea and vomiting.

TRH releases TSH & prolactin from pituitary.

Applied :

Hashimoto's thyroiditis → Decreased circulating thyroid levels (hypothyroidism) → Compensatory increase in TRH → Increases TSH & prolactin (this explains link between hypothyroidism & secondary hyperprolactinemia).

Therefore, in all patients with increased prolactin TSH must be measured.

If TSH and prolactin levels (both) are increased → Treat TSH first.

Hyperprolactinemia causes :

- Due to physiological activities :
  1. Pregnancy (10 times).
  2. Sleep.
  3. Eating.
  4. Coitus.
- Following chest wall stimulation :

1. Suckling.
2. Breast exam.
3. Chest wall surgery.
4. Herpes zoster infection.
- Cranial lesions :
  1. Cranial Tumors.
  2. Radiation.
  3. Sarcoidosis.
  4. TB.
- Hypothyroidism.
- Prolactin secreting tumors : Prolactinoma.

measure Prolactin in morning.

Prolactin has a negative feedback on GnRH → Decrease LH and FSH.

Prolactin → Normal :  $< 20\text{ng/ml} - 25\text{ng/ml}$

If prolactin is mildly elevated → Repeat a 2<sup>nd</sup> sample → Confirm increased levels → MRI (to detect and measure size of prolactinoma).

- microadenoma :  $< 1\text{cm}$ .
- macroadenoma :  $> 1\text{cm}$ .

**MC** symptom of prolactinoma → Amenorrhoea >> Infertility.

Other symptoms : Galactorrhoea, Delayed puberty, Anovulation, Oligomenorrhoea.

macroadenoma can invade surrounding structures :

- Optic chiasma : Bitemporal hemianopsia.
- Cavernous sinus : CV syndrome (headache, visual disturbances, cranial nerve 3,4,6 palsy).

Prolactinoma is a prolactin secreting pituitary adenoma, may release other hormones of pituitary as well.

Symptoms due to excessive hormones : Hyperprolactinemia, acromegaly, cushing disease.

There can be spontaneous hemorrhage into adenoma leading to pituitary apoplexy.

management :

Asymptomatic microadenoma :

manage conservatively.

Serial MRI and serial prolactin levels every 1 to 2 yrs.

Patient should be advised to report even mild changes in menstrual cycle as it is a risk for hypoestrogenism.

Chances of progression to macroadenoma < 10%.

Indication for managing prolactinoma :

Asymptomatic macroadenoma (may lead to neurological defect).

Symptomatic prolactinoma of any size.

Infertility due to increased prolactin (non pregnant female uterus).

Treatment : medical management.

DOC for prolactinoma in non-pregnant female → Cabergoline  
> Bromocriptine.

After 1 month, measure prolactin levels :

Normal range : Continue same dose.

Increased / Not decreased : Titrate dose.

Prolactin should be monitored every month.

If prolactin  $\geq 50$  persistently → Indication for surgery.

After 4 months, Do MRI :

Tumour shrunk : Continue same treatment.

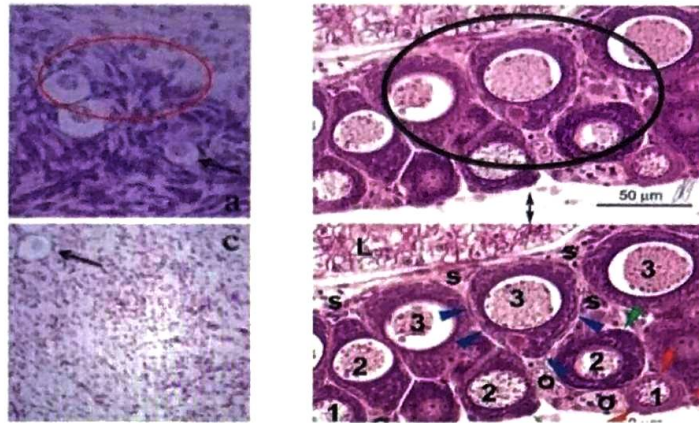
Tumour size Increased / Not decreased L Surgery.

a. menopause (India -  $\geq 47$  yrs ; Worldwide -  $\geq 51$  yrs)

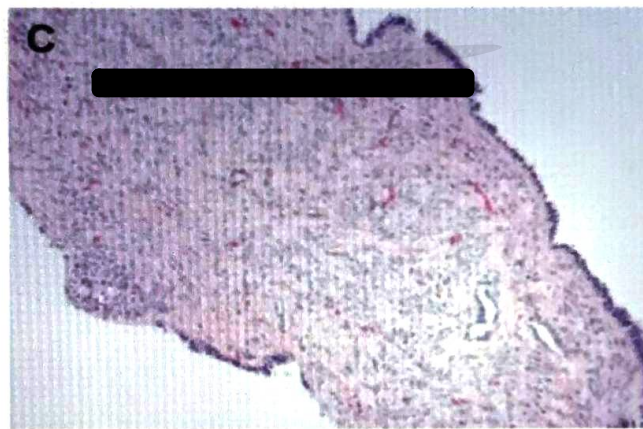
Applied :

If Ovarian failure occurs at <40 years → Premature  
menopause / primary ovarian insufficiency .

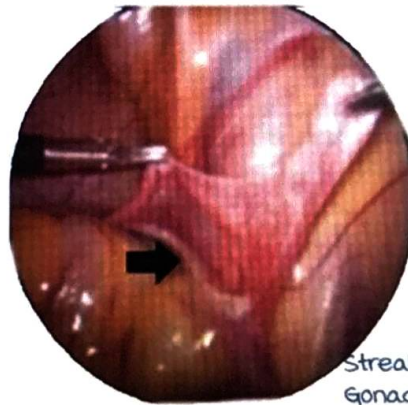
Primary ovarian insufficiency Leads to secondary  
amenorrhea generally but may also be cause of primary  
amenorrhea.



Follicles



primary ovarian insufficiency



Streak Gonads

Eg Turner syndrome → Streak gonads → primary ovarian insufficiency.

**Premature menopause / primary ovarian insufficiency**

00:33:49

Ovarian failure occurs at <40 years.

Causes :

Active space

- Radiation exposure : Ovary is the most sensitive organ in the pelvis.
- Chemotherapeutic drugs.
- Chromosomal anomaly :
  1. **Turner syndrome** : Accelerated atresia of ovaries.
  2. **Fragile X syndrome**.
  3. **Cyp 17 mutation**.
  4. **Perrault syndrome**.
- Autoimmune disorders.
- Viral diseases : **mumps**.
- Galactosemia.

Note :

**Fragile X syndrome** :

Triple repeat sequence CGG.

MC Inherited cause of mental retardation & autism.

Females → Primary ovarian insufficiency.

**Cyp 17 mutation** :

Congenital adrenal hyperplasia due to 17 $\beta$ , **Hydroxylase / 17-20 Lyase deficiency** → Decreased cortisol, androgen → Decreased estrogen (**sexual infantilism** → Absent breast Development, scanty axillary and pubic hair, Small/infantile uterus).

male ambiguous genitalia can be seen.

Decreased cortisol → Increased ACTH → Increased mineralocorticoids → Increased BP & hypokalaemia.

**Perrault syndrome** :

Sensory neural hearing loss ovarian dysfunction (ranges from ovarian dysgenesis/ Primary amenorrhea /primary ovarian insufficiency) + Neurological dysfunction (ranges from learning disability to cerebellar ataxia).

Confirmatory test :

measure **FSH levels** on 2 separate occasions (1 month apart)

→ levels **≥40 IU** → primary ovarian insufficiency.

Other investigations :

- Karyotyping especially if patient **<30 years**.

- Bone mineral density.

Treatment of choice (TOC) :

- **Hormone Replacement Therapy** (oestrogen + progesterone) till natural age of menopause.
- For **infertility** : Donor egg & IVF.

**Causes of secondary amenorrhea**

00:41:59

Endocrinal causes : Hypogonadotropic hypogonadism	Hypothalamus	Excessive exercise, stress, eating disorders, destructive process like tumors, trauma, radiation, infection.
	Pituitary	Prolactinoma, Sheehan syndrome, destructive process like tumors, trauma, radiation, infection.
Endocrinal causes : Hypergonadotropic hypogonadism	Ovaries	Primary ovarian insufficiency. Diagnosis : 2 readings of FSH $\geq$ 40IU. Suggestive : 2 readings of FSH $\geq$ 25IU.
Anatomical cause	uterus	Asherman syndrome (Estrogen, LH & FSH : Normal).

Note :

FSH  $\rightarrow$  Normal :  $<10$  IU/day.

In Hypogonadotropic hypogonadism, levels are low/Normal (1-2 IU/day).

In patients with amenorrhea, FSH can be done on any day (done on **day 2-3** of menstruation).

Causes of Eugonadotropic amenorrhea :

- PCOS (FSH : Normal)
- Non classical congenital adrenal hyperplasia.
- Thyroid disorders.

Active space

Hyperprolactinemia causes secondary amenorrhoea.

Investigations done in case of secondary amenorrhoea in cases of females with normal pelvic anatomy :

1st step → UPT (urine pregnancy test).

2<sup>nd</sup> step → Hormonal investigations :

- Thyroid stimulating hormone (TSH) levels :  
Hyperthyroidism and hypothyroidism both cause amenorrhoea.
- Serum prolactin levels.
- Follicle stimulating (FSH) levels.
- Clinical assesment of Estrogen levels.
- Vaginal USG : Helps in differentiating primary ovarian insufficiency (no follicles) & PCOS (≥ 20 follicles).
- MRI : if prolactinoma increases / if hypothalamic/ pituitary defect is suspected.

Excessive exercise → Excessive weight loss → Amenorrhoea.

**Female athlete triad :**

- menstrual dysfunction.
- Low energy availability.
- Low bone mineral density.

Excessive exercise → Release of endogenous opioid β endorphins → Alters pulsatility of GnRH → Secondary amenorrhoea.

## **Sheehan syndrome**

00:51:39

**Necrosis of anterior pituitary gland** due to excessive blood loss after delivery.

Due to severe PPH → Abrupt severe hypotension → Sheehan syndrome / pituitary apoplexy (severe cases).

Sheehan syndrome :

**LH** and **FSH** will **decrease** (1st hormones).



Decreased growth hormone.

ACTH levels are decreased.

Prolactin levels are decreased.

TSH levels (last hormones) are decreased.

Clinical features :

- Secondary amenorrhoea.
- Failure to lactate.
- Loss of sexual & axillary hair.
- Hypothyroidism.

Pituitary apoplexy :

Sudden onset headache, nausea, visual defect and hormonal dysfunction.

Note :

Female with complain of secondary amenorrhoea + Failure to lactate : Sheehan syndrome.

Female with complain of Galactorrhea + amenorrhoea + Headache + visual symptoms : Prolactinoma.

### Asherman syndrome

00:54:53

Presence of intra uterine adhesions or synechiae.

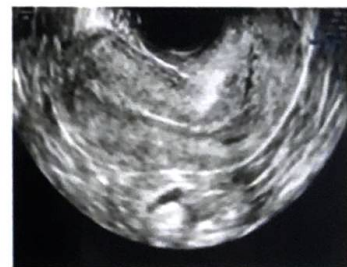
Due to the destruction of endometrium, upto the basal layer.

It is unable to regrow.

Normally, in a non-pregnant uterus the anterior and posterior walls are apposed

Causes :

- Excessive uterine curettage (highest risk : Curettage in postpartum period).
- multiple D & C
- Genital TB, schistosomiasis.
- uterine surgery : metroplasty, myomectomy, C-section.



Thin endometrium

Clinical presentation :

- menstrual irregularity → MC symptom group (Secondary Amenorrhea > Hypomenorrhea).
- Infertility → single MC symptom (infertility > Secondary Amenorrhea > Hypomenorrhea).
- Dysmenorrhea.
- Recurring pregnancy loss.

First investigation → Ultrasound :

thin, defective, heterogenous endometrium is seen.

Saline infusion sonography

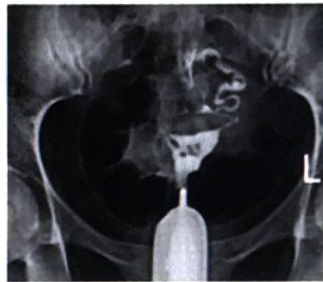
(non invasive) is better.

Screening test → HSG :

Small irregular multiple filling defects → moth eaten appearance.

If well-defined, regular filling defects are seen on HSG →

Fibroid

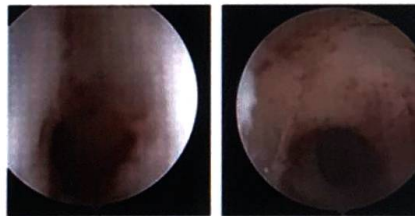


Hysterosalpingogram

Diagnostic test :

Hysteroscopy

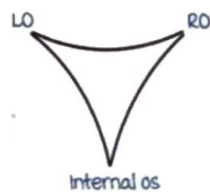
(invasive) : Investigation of choice.



hysteroscopy

3 landmark ports for hysteroscopy :

- Left ostia
- Right ostia
- Internal os



Asherman syndrome

Active space

Due to adhesions, there is dipping of fundus and in drawing of lateral walls in Asherman syndrome.

management :

- By doing **hysteroscopic adhesiolysis** for Asherman syndrome, the small contracted space → a bigger cavity where the foetus can grow.
- Followed by prevention of adhesions by :
  1. **Paediatric foleys catheter number 8 /10** in uterine cavity.
  2. **Cooks intrauterine balloon catheter** (not available in India).
  3. **Hyaluronate gel** (not available in India).
- Followed by hormonal replacement therapy (E+P) for 3 months to build the endometrium.

### Algorithm for diagnosis of secondary amenorrhea

01:07:05

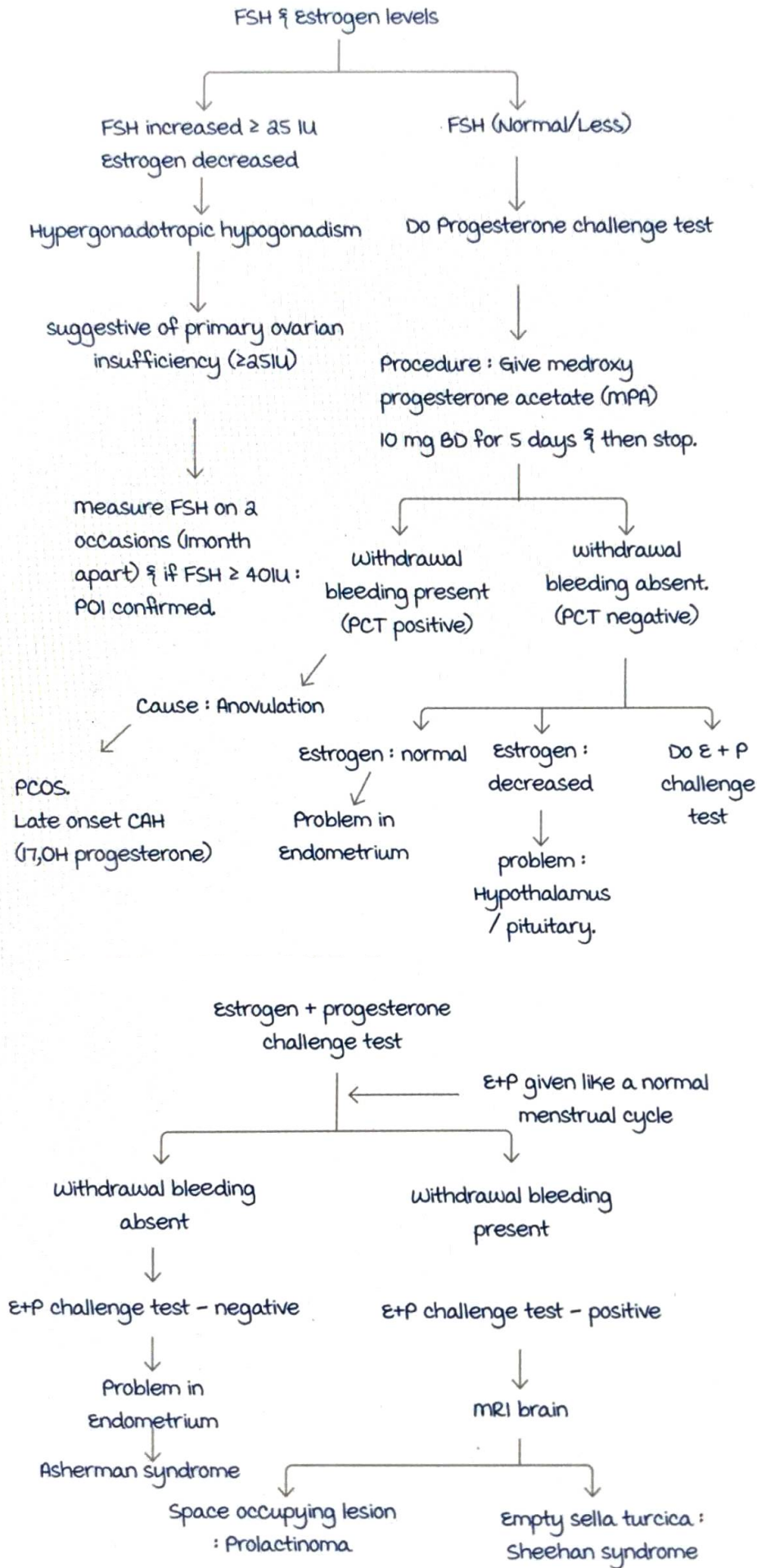
Note : In all females complaining of secondary amenorrhea/ infertility & all males complaining of infertility - Always measure TSH & Prolactin.

Secondary Amenorrhea



Investigation :

1. UPT.
2. TSH.
3. Prolactin.
4. FSH.
5. Estrogen levels.



Active space

If everything is normal : Hypothalamic amenorrhoea.

### Novaks updates 17th edition

01:21:02

Primary amenorrhoea	Both	Secondary amenorrhoea
Mullerian agenesis.	POI	Sheehan syndrome
AIS	Pregnancy	Asherman syndrome
Gonadal dysgenesis.	PCOS	Cervical sclerosis.
Physiological delay.	Increased Prolactin	Infections
Kallman syndrome.	Thyroid disease	Pituitary lesions
Transvaginal septum.	Cushing disease.	
Imperforate hymen.	Empty sella syndrome	

POI : Do tests :

FmRI premutation.

Karyotype in all females ( especially if in young female).

Test for CAH.

In POI : Decreased AMH ; FSH : increased.


PCOS : Increased AMH ; FSH : Normal.

	Overall	India NOVAKS (17 ed. pg 888)
MC cause of primary amenorrhoea.	Gonadal dysfunction. (Turners > Swyer syndrome)	Mullerian malformation.
2nd MC cause	Mullerian agenesis	Gonadal dysfunction. (Swyer > Turner's syndrome). Genital TB can also lead to primary amenorrhoea (6-8%).




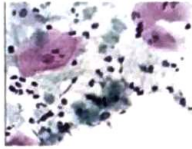


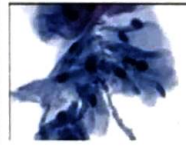
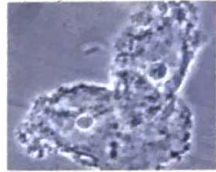
# VAGINITIS

Vaginitis

00:00:33

	Trichomonas vaginitis	Candidiasis	Bacterial vaginosis
MC organism	Trichomonas vaginalis (Flagellated Protozoa)	Candida albicans (Fungus)	Normal Döderlein bacilli (Lactobacillus) is replaced by <b>Gardnerella</b> (most important), mycoplasma, ureaplasma, peptostreptococcus, mobilincus. <b>No inflammation.</b>
Chief complain	Foul smelling frothy discharge	Pruritis	Foul smelling discharge.
Other symptoms	Dysuria. Dyspareunia. Pruritis.	Scanty discharge. <b>Splash dysuria.</b> Dyspareunia is generally absent.	<b>No pruritis, dysuria, dyspareunia.</b>
Discharge	<b>yellowish green.</b> Frothy. Foul smelling. pH >4.5	Curdy white or cottage cheese like discharge. Scanty. pH = 4-4.5 (<4.5)	Off white/ gray color discharge. Foul smelling. Profuse. >4.5
Per speculum examination	Strawberry cervix 		

Active space

Sexual transmission	+	+/-	-
Treatment of partner	Done	Done only if symptom is present.	Not done
IOC	Saline microscopy.  motile flagellated organism.	Saline microscopy.  Pseudohyphae in KOH staining or spore.	Saline microscopy.  Clue cells (vaginal epithelial cell to which bacterial cells adhered)
Pap smear	 Size of the organism is same as nucleus of epithelial cells.	 Hyphae identified.  Spores : Smaller than nucleus of epithelial cell.  Shish Kebab appearance	 Clue cell
Gold standard investigation	Culture	Culture	Gram staining: Nugent score (7-10)  (Done only of diagnosis can't be done clinically or on saline microscopy)

Active space

Whiff test : 10% KOH is added to discharge gives fishy odor.	+/-	-	Characteristic for BV.  Amsel's criteria: Any 3 present → BV. 1. Off white/ gray color discharge. 2. pH > 4.5 3. Clue cell ≥ 20% of entire epithelial cells 4. Add 10% KOH → fishy odor (whiff test positive)
Treatment	metronidazole 500 mg BD for 7 days or 2g Stat.  Pregnancy : same	Fluconazole 150 mg oral stat.  Pregnancy : Oral azole not given. Give topical miconazole or clotrimazole.	metronidazole 500 mg BD for 7 days or  Clindamycin 300 mg BD for 7 days.  In pregnancy : same

Recurrent candidiasis :

≥ 4 episodes in a year.

Treatment : Oral fluconazole 150 mg on day 1, 4, 7.

Maintenance dose : 150 mg weekly for 6 months

Bacterial vaginosis :

MC cause of vaginal discharge among reproductive age group.

In pregnancy can lead to preterm labor.

Ratio of polymorphonuclear cell : epithelial cells <1.



# PELVIC INFLAMMATORY DISEASE

## Introduction

00:00:08

Infection of the upper female genital tract :

- Fallopian tubes : Salpingitis.
- Ovary : Oophoritis.
- uterus : Endometritis.
- Peritoneum : Peritonitis.

Cervicitis and vaginitis are not included in PID.

PID one-liners :

most common cause of PID : Polymicrobial infection.

and most common : Chlamydia > Gonorrhoea.

most common cause of acute PID : Gonorrhoea.

most common cause in virgin females : Genital TB

(hematogenous spread).

most common cause in IUCD users : Actinomyces.

## Management of PID

00:02:29

According to the NACO Guidelines :

Syndromic management of PID is followed.

Principle : Least investigations followed by initiation of treatment.

Diagnosis of PID : Based on history.

- most common symptom : Lower abdominal pain.
- vaginal discharge :
  - Thick purulent : Gonorrhoea.
  - Thin watery : Chlamydial.
- Abnormal uterine bleeding.
- urinary symptoms.
- Secondary dysmenorrhoea.

Examination findings :

- uterine tenderness.
- Adnexal tenderness.
- Cervical motion tenderness ( Also a specific symptom of ectopic pregnancy).

If UPT positive : Ectopic pregnancy.

If UPT negative : PID.

Syndromic diagnosis : Lower abdominal pain syndrome.

management :

Yellow kit/kit 6 :

- Doxycycline 100mg BD for 14 days.
- Cefixime 400mg OD for 1 day.
- metronidazole 400mg BD for 14 days.

PID is a sexually transmitted disease ( Except : Genital TB).

So the male partner should also be treated but with grey kit/  
Kit 1 :

- T. Azithromycin 1 g.
- T. Cefixime 400 mg.

Other indications of grey kit :

- Cervicitis.
- Urethritis.
- Anorectal discharge.
- Scrotal pain syndrome.

If the yellow kit fails to resolve the patient's symptoms :

Laparoscopy is done as it is the gold standard for the  
diagnosis of PID.

\_\_\_\_\_ is taken for :

- TB : Culture and PCR.
- PCR/NAAT for Chlamydia and Gonorrhoea.
- Culture and sensitivity tests.

### CDC criteria for the diagnosis of PID

00:11:39

minimum criteria :

Lower abdominal pain with any one of the following three :

- Cervical motion tenderness.
- Uterine tenderness.
- Adnexal tenderness.

Additional criteria :

- Fever.
- mucopurulent discharge / friable cervix.
- microscopy of discharge : Abundant WBCs.
- Raised ESR and CRP.

- Lab tests positive for *N. gonorrhoea* or *C. trachomatis*.

#### Specific criteria :

- Endometrial biopsy.
- TVS or MRI.
- Laparoscopy.

#### Investigations in patients of PID (according to CDC) :

- UPT.
- Microscopy of discharge : Raised WBCs in the discharge.
- CBC : Raised WBC counts.
- Raised CRP and ESR.
- Tests for STDs like HIV, hepatitis B, syphilis etc.
- Lab tests for chlamydia and gonorrhoea.
- Imaging studies.

#### Imaging studies :

##### USG : General signs :

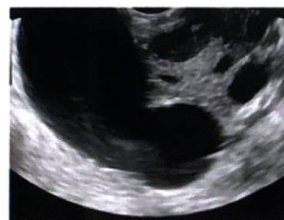
- Adhesions inside the tube.
- Adhesions in the peritoneal cavity.
- Hydrosalpinx.

#### Specific signs on USG :

- Beads on string appearance.
- Waist sign.
- Cogwheel sign.



Beads on string appearance



Waist sign



Cogwheel sign

Beads on string appearance on USG : PID.

**Beaded appearance on HSG : Genital TB.**

Endometrial biopsy : Endometritis.

Gold standard investigation : Laparoscopy.

Advantages of laparoscopy :

- Tubes and adnexa can be visualized directly.
- Can obtain peritoneal fluid for testing.

- Scoring for conception can be done : **Boer miesel score**.
- In 10% of PID cases, **violin string appearance** is seen (due to perihepatitis, which leads to right upper quadrant pain).



violin string appearance

### Fitz-Hugh Curtis syndrome :

Adhesions formed between liver capsule and anterior abdomen which have violin string appearance.

This is seen both in PID due to **Chlamydia** > Gonorrhoea.

Overall incidence : 10%.

Staging of Acute PID can be done : **Gainsville staging**.

Stage 1	No peritonitis
Stage 2	Peritonitis present
Stage 3	Tubo-ovarian mass / abscess
Stage 4	Ruptured tubo-ovarian mass

Long term complications :

- **Infertility** : most common.
- Ectopic pregnancy.
- Hydrosalpinx.
- Chronic pelvic pain.
- Recurrent PID.

management of PID :

Infection	CDC recommendation in non-pregnant
Trichomonas / bacterial vaginosis	metronidazole 500mg BD for 7 days
Candida	T. Fluconazole 150mg stat. Alternative : Ibrexafungerp 4 tabs of 150mg each, 2 with breakfast and 2 with dinner.

Infection	CDC recommendation in non-pregnant
Chlamydia	T. Doxycycline 100mg BD for 7 days. Alternative : T. Azithromycin 1gm.
Gonorrhoea	Inj. Ceftriaxone 500mg im single dose (dual therapy with Doxycycline to be used only if chlamydia infection cannot be ruled out). Alternative : T. Cefixime 800 mg single dose.

Syndromic management of vaginal discharge :

Green kit/kit 2.

- T. Fluconazole 150mg.
- T. Secnidazole 2gm.

Partner need not be treated.

Important indications of diagnostic laparoscopy :

- Chronic pelvic pain.
- Unresolved PID.
- medical treatment failure in endometriosis / Secondary dysmenorrhoea or in case of chocolate cyst.

## GENITAL TUBERCULOSIS

A secondary infection.

MC primary site : Lungs.

Lungs, lymph node

↓ hematogenous spread

Fallopian tube (MC site)

MC : Ampulla.

Least common : Intramural part.

MC symptoms : Infertility.

and MC site : Endometrium.

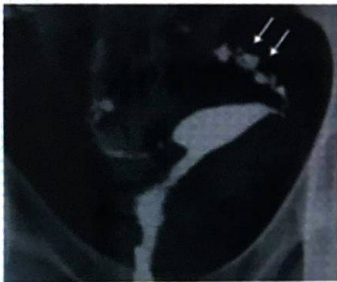
MC route of spread of genital TB : **Hematogenous.**

MC route of endometrial TB : Direct spread from Fallopian tube.

Least common site of genital TB : Vagina and vulva.

In genital TB, HSG is contraindicated.

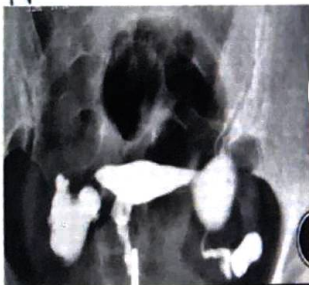
If HSG is done, following characteristic features will get.



(Beaded appearance of tube/ beads on string appearance)



(pipe stem appearance/ lead pipe appearance)



(Tobacco pouch appearance)



(Golf club appearance)

Other :

moth eaten appearance,

B/L cornual block : MC is physiological spasm of tube.

MC pathological is genital TB.

## Endometrial TB

00:0:54

Clinical features :

### A. Asherman syndrome :

Intrauterine adhesions are present.

Endometrium is very thin and defective.

Cause : Vigorous curettage.

Curettage done in postpartum period.

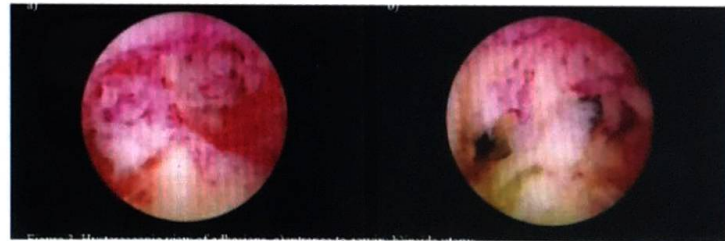
Genital TB.

Schistosomiasis.

MC presentation : menstrual irregularities  
(amenorrhoea).

MC single problem : Infertility.

IOC : Hysteroscopy (diagnostic and therapeutic).



Scared tissue/ adhesion is seen.



(multiple filling defect with irregular lining)

USG :



(Adhesion)

Treatment : Hysteroscopic adhesiolysis.

+

Pediatric foley's catheter inserted

+

Estrogen and progesterone.

### B. Pyometra :

Pus inside uterus.

MC cause : Senile endometritis.

MC cancer causing pyometra : Cancer cervix > cancer endometrium

Note : MC cause of hematometra : Imperforate hymen.

Diagnosis of genital TB :

Endometrial biopsy just before menstruation (1-2 days).

menstrual blood can be used for doing endometrial biopsy.

management of genital TB :

ATT for 6 month.

Treatment of infertility in genital TB : IVF.

Note :

MC menstrual irregularities seen in genital TB :

Polymenorrhea > secondary amenorrhea.

MC pelvic finding in TB : Normal.

2<sup>nd</sup> MC pelvic finding in TB : Adnexal tenderness.

MC pelvic finding in adolescent girl in genital TB : B/L

adnexal mass.



## FEMALE INFERTILITY

### Definition of infertility

00:00:27

Infertility is the inability of a couple to conceive even after 1 year of unprotected intercourse.

A patient <35y is asked to start investigations after 1 year.

If the age of the patient is  $\geq 35y$  : Begin investigations after 6 months.

If the age of the patient is  $\geq 40y$  : Begin investigations after 3 months.

The term infertility is now replaced by the term sub-fertility.

Both the partners contribute to infertility.

Female partners contribute 40-55% cases of infertility.

Male partners contribute 20-40% cases of infertility.

Rest is unexplained and that accounts for approximately 10% of infertility.

Basic investigations in infertility :

1. Semen analysis.
2. Ovulation test.
3. Tubal patency test : Hysterosalpingography.

**Fecundability** : Probability to achieve pregnancy in one cycle.  
20% for 1<sup>st</sup> cycle.

**Fecundity** : Probability to achieve live birth in one cycle.  
15-20% for 1<sup>st</sup> cycle.

Primary infertility : No h/o pregnancy in the past.

Secondary infertility : H/o pregnancy in the past, irrespective of outcome of the pregnancy.

## Female infertility

00:04:07

Causes :

- MC are ovarian causes.
- 2<sup>nd</sup> MC tubal factor infertility.
- Uterine cause.
- Cervical cause.
- Unexplained cause of infertility.

WHO CLASSIFICATION OF OVARIAN CANCER			
Class	Mechanism	Hormone levels	Site/causes
Class 1	Hypogonadotropic Hypogonadism : anovulation.	Decreased FSH, Oestrogen. Prolactin : Normal	Hypothalamus Pituitary (e.g. Kallman's syndrome)
Class 2 (MC ovarian cause of infertility)	Normogonadotropic Normogonadism	FSH, Oestrogen : normal. Prolactin : Normal	PCOS (MC cause of anovulation).
Class 3	Hypergonadotropic Hypogonadism	FSH ↑, ↓ oestrogen (due to -ve feedback) Prolactin : normal	Ovarian failure (premature menopause / primary ovarian insufficiency)
Separate category (some cases Class 4)		↑ Prolactin	

## Anovulation

00:10:00

MC ovarian cause of female infertility.  
most easily treatable cause.

Tests for ovulation :

1. Tests which predict time of ovulation.
2. Tests which tell if ovulation has occurred i.e., 1 week before menstruation / Day 22 of cycle.

Active space

It is measured on the day when progesterone is maximum (8 days after ovulation/ Day 22 of a cycle, when the size of corpus luteum is maximum).

Urine LH kits :

Similar to urine pregnancy kits.

Indicate urinary LH surge.

In urine when LH surge happens, ovulation occurs after 24 hours.

In serum when LH surge happens then ovulation occurs after 32-36 hours.

Drawbacks :

Does not predict ovulation, just indicates LH surge.

In patients with PCOS, levels of LH are high throughout cycle, hence not a reliable predictor of ovulation.

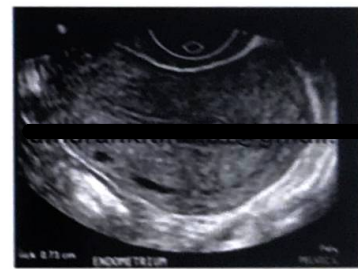
Follicular monitoring :

Done with the help of transvaginal scan, to study the follicle. Must be done from Day 10 of the cycle.

Patient must come daily or alternatively to measure the size of the follicle.

The size of the follicle increases 2mm/day.

- Once it reaches the size of 18-20 mm, the size of the follicle decreases (giving a crumpled appearance).
- Fluid in the pouch of Douglas occurs because there is release of fluid in the antral cavity.
- Endometrium appears triple layered called as the trilaminar appearance, seen in late proliferative phase/at the time of ovulation.



Trilaminar appearance

In early proliferative phase there is only a single echogenic line.

In secretory phase there is a thick echogenic endometrium.

Due to the presence of secretions in the glands,

there will be posterior acoustic enhancement (better marker for secretory phase).

All of these are signs of ovulation on USG.



## Tests which tell if ovulation had occurred

00:19:56

Based on the presence of progesterone on day 22 / the changes due to the presence of progesterone.

1. Vaginal epithelium study :  
If ovulation has occurred, (under the effect of progesterone) epithelial cells → Intermediate cell predominance.  
If ovulation has not occurred, (under the effect of oestrogen) epithelial cells → Superficial cells predominance.
2. Cervical mucous study :  
If ovulation occurred : Ferning is absent (progesterone is present).  
If ovulation has not occurred : Ferning is present (oestrogen is present).
3. Basal body temperature (immediately after waking up)  
If ovulation had occurred there will be mid-cycle increase in basal body temperature.
4. Serum progesterone levels on Day 22 :  
If  $\geq 3$  ng ovulation has occurred.
  - Non-invasive.
  - Reliable.
  - Best test.
5. Endometrial biopsy : Invasive.
  - To rule out genital TB.

In India, it's still preferred as incidence of endometrial TB is high.

It must be done in the pre-menstrual phase (2-4 days before the cycle) because in this phase the tubercles come to the superficial layer of the endometrium.

The sample is then divided into two parts :

1. Histopathological examination : Kept in formaldehyde.
2. Acid fast bacilli is kept in saline.

Report interpretation :

- Secretory endometrium → means ovulation has occurred.
- Proliferative endometrium → means ovulation hasn't occurred.
- A lag of  $\geq 2$  days between the endometrial dating and the patient history → means luteal phase defect → means decreased progesterone → can cause abortion.
- In a female with atypical uterine bleeding → For ruling out endometrial hyperplasia & endometrial cancer → Endometrial biopsy.

### Management of anovulation

00:26:54

- Drug of choice in PCOS :  
Letrozole : 2.5-5 mg on day 3-7.
- Drug of choice in other cases :  
Clomiphene citrate : 50-150 mg on day 3-7.  
Follicular monitoring must be done.  
Once it reaches 18-20 mm, for ovulation trigger → HCG injection dose : 5000IU IM (which acts as LH surge).
- Adjuvant therapy :  
Prednisolone : 5 mg if androgens levels are high (DHEA).  
metformin : If patient has insulin resistance.

Clomiphene / letrozole must be given for 3 cycles → if no ovulation occurs → Human menopausal gonadotropin (HMG) is indicated.

HMG :

MC ovulation drug for IVF cycles.

Indications :

- If clomiphene and letrozole fail.
- In IVF cycles.
- In hypogonadotropic hypogonadism to cause ovulation.
- In unexplained infertility.

HMG has high chances of Ovarian Hyperstimulation Syndrome (OHSS).

monitoring is essential when this drug is used.

monitoring done by :

- Serial measurements of oestradiol - If levels are  $>2500\text{picograms}$  → Do not give injection HCG.
- TVS : To monitor size and number of follicles.

Best test to detect ovulation : **Hormonal study.**

MC test done : **TVS/follicular monitoring.**

2<sup>nd</sup> cause of ovarian infertility /Class 3 category (hypergonadotropic hypogonadism) :

Diminished ovarian reserve/Premature menopause/ Primary ovarian insufficiency.

### Tests for ovarian reserve

00:34:14

Indications :

- Age  $\geq 35\text{y}$  : As age increases, reserve decreases.
- Chronic smoker.
- H/o premature menopause in family.
- Personal history of surgery, radiotherapy/ chemotherapy.
- Case of unexplained infertility.

Test	Principle	Done on	Result	Interpretation
Serum FSH levels (most common test done).	Poor ovarian reserve. FSH increases with negative feedback if Oestrogen is less.	menstruating : Day 3. If amenorrhea : can do the test any day.	<ul style="list-style-type: none"> <li>• 2-10</li> <li>• <math>\geq 15</math></li> <li>• <math>\geq 40</math></li> </ul>	<ul style="list-style-type: none"> <li>• Normal reserve.</li> <li>• Reserve.</li> <li>• Premature ovarian failure/ menopause.</li> </ul>
Serum AMH (anti-mullerian hormone)/ MIS <b>Best test</b>	Small follicles ( $<8\text{mm}$ - Pre-antral/antral) produce AMH from granulosa cells. AMH is directly proportional to ovarian reserve.	The levels donot fluctuate in the menstrual cycle.	<ul style="list-style-type: none"> <li>1-3.5ng/mL</li> <li><math>&lt;1\text{ng/mL}</math></li> <li><math>&lt;0.5\text{ng/mL}</math></li> <li>undetectable</li> </ul>	<ul style="list-style-type: none"> <li>• Normal.</li> <li>• Borderline.</li> <li>• ↓ reserve.</li> <li>• Premature ovarian Failure.</li> </ul>
Antral follicle count in both the ovaries. (size 2-10mm)	Done with TVS. Antral follicle ovarian reserve.	Day 3	$<10$ in both ovaries combined	↓ reserve

Active space

Other tests that are not routinely done for ↓ reserve :

1. Serum. Inhibin B levels : <45 pg on day 3 : Decreased reserve.
2. Clomiphene citrate challenge test.

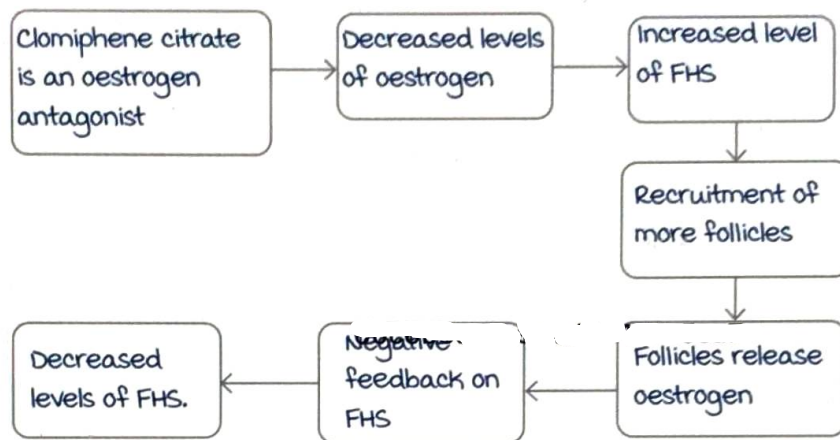
### Procedure for clomiphene citrate test

00:43:29

Day 3 : measure FSH levels.

- If normal reserve : FSH is normal.
- If low on reserve : FSH is increased.

Day 5-9 : Give clomiphene citrate;



Levels of FSH on day 9 :

- If normal reserve : High.
- If low on reserve : High.

Levels of FSH on day 10 :

- If normal reserve : Normal.
- If low on reserve : High

Increased basal level of FSH which rises further on D 10 indicates poor reserve.

management of infertility due to decreased ovarian reserve : Donor Egg + IVF.

### Tubal factor infertility

00:48:34

It is due to tubal blockage caused by adhesion formation.

Investigation of choice to test patency of tubes :

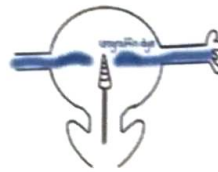
**Hysterosalpingography (HSG) :**

- It is an OPD procedure.

- It is not done under anaesthesia.
- It is slightly painful.
- Analgesia should be given 1/2 hour prior to the procedure.

HSG procedure :

- **urographin** is a radiopaque, iodine based, water soluble dye.
- The dye is inserted into the uterus via Leech Wilkinson Cannula (has a funnel shaped tip and serrations).
- Serial x-rays are done to see the spillage of the dye from the fallopian tubes.
- HSG is done in the pre ovulatory phase : Day 6-Day 11 (best time is day 7-10)
- Coincidental findings : mullerian malformation.



HSG findings if tubes are patent (normal) :

- Tubes are narrow ; do not appear straight or pipelike.
- Bilateral spillage of the dye is observed.

Abnormal findings on HSG :

- Straight lead pipe like tubes are seen in Genital TB.
- Hydrosalpinx.

Contraindications of HSG :

- Pregnancy.
- Genital TB.
- Active PID.



Normal HSG showing patent fallopian tubes

In genital TB and PID, dye can lead to spread of infection.

Drawbacks : Cannot see exterior of the tube.

Cannot see contour of uterus.

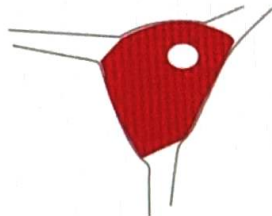
Sometimes due to pain on passage of dye → cornual spasm  
→ b/l cornual block.

MC cause of b/l cornual block : Physiological.

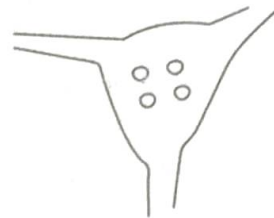


Findings on a HSG :

- Tube blockages : Proximal / midsegmental or distal.
- Distal block - the dye collects behind the block leading to dilatation of the tube → hydrosalpinx
- Mullerian malformations (accidental finding) : IOC 3D USG. Gold standard is MRI.
- Filling defects : Seen in 3 conditions
  1. Submucosal fibroids : Smooth and regular filling defect (broad base).
  2. Polyps : Smooth and regular filling defect (narrow base).
  3. Asherman syndrome : multiple irregular filling defects (moth eaten appearance).



Filling defect in Fibroid / polyp : smooth & regular



multiple, irregular defects in Asherman syndrome.

Honeycomb appearance on HSG seen in *Salpingitis Isthmica Nodosa*.

Findings of genital TB on HSG :

- Lead pipe appearance.
- Beaded appearance.
- Tobacco pouch like appearance.
- Golf stick appearance.
- Cotton wool appearance.



Hydrosalpinx



Straight lead pipe

Genital TB



Normal HSG showing patent fallopian tubes

Active space

Image A : Broad filling defect, smooth regular outline :  
 polyp/fibroid (confirmed by hysteroscopy).

Image B - moth eaten appearance : multiple irregular filling defects seen in Asherman syndrome.

HSG is not the gold standard test for tubal patency. Gold standard is laparoscopic chromoperturbation.

Laparoscopic chromoperturbation :  
 Dye : methylene blue/ Indigo carmine.

Laparoscope is inserted, dye is passed pv with the help of cannula.

Spillage is visualised.

It is gold standard because outside of the tube and spillage can be visualised.

HSG cannot visualise the outside of the tube.

If a patient has bilateral blockage of the tube on HSG :  
 It can be a proximal or distal block.

Bilateral cornual block : Dye has gone inside the uterus but the dye has not gone beyond the cornual of the uterus (or into the tubes).

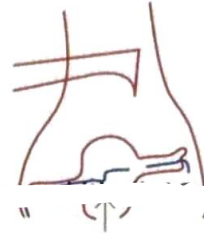
Causes :

Physiological - The MC cause is Cornual spasm while doing HSG.

Pathological - Genital TB.

If a patient gets diagnosed with Bilateral cornual block on HSG ;  
 the next step is Laparoscopic chromoperturbation + hysteroscopy.

While doing hysteroscopy, we pass a thin guidewire through the channel upto the cornua of the tubes so that if there is any



Bilateral cornual block

mucous plug causing obstruction or any spasm, it will be relieved.

This is known as **Hysteroscopic cannulation**.

Once the tests are done the chances of conception in the female becomes high and it is highest in that particular cycle only.

If the patient does not conceive despite this, the best management is **IVF** (in-vitro fertilisation).

unilateral tubal blocks cannot be treated with surgery/IVF.  
management :

**Clomiphene citrate** (controlled ovarian stimulation) + IUI.

If HSG is abnormal (proximal block), next step → **Hystero-laparoscopy** (together called **pelviscopy**).

B/L Distal block : Laporoscopic chromopertubation.

Laparoscopic chromopertubation advantages :

- Helps to confirm diagnosis.
- Assess the severity.
- Can treat simultaneously.

In this HSG, we can see that the dye has gone into the uterus → goes into both the tubes.

The tubes are then swollen → no free spillage of dye.

This is because of **B/L distal block** and hydrosalpinx (indicates severe disease and has worse reproductive outcome).

**Next step** is laparoscopic chromoperturbation (GS) + Hysteroscopy.

In this case the **best management** is IVF.

If there is b/l mild block : Fimbrioplasty → create new opening (neosalpingostomy).

However, if age of the female is > 35 yrs → decreased ovarian reserve → IVF

If block is severe IVF is done.



Bilateral distal block

## Management of hydrosalpinx

01:10:00

The fluid in the hydrosalpinx is **embryotoxic**.

During IVF the fluid present in the hydrosalpinx may trickle down and harm the implanted zygote.

To prevent fluid from entering uterine cavity :

Conventionally, we used to do b/l **salpingectomy** followed by **IVF**.

Nowadays, clips are applied at the proximal ends to prevent fluid entry into the uterine cavity followed by IVF.

mid segment block on HSG → Patient had prior tubal sterilization → now come for reversal (1-5% females come for reversal).

Success of reversal is higher if :

- Age of female <35yrs
- Type of tubal sterilization : Clips/ Fallope ring
- Type of anastomoses : Isthmo-isthmic.
- Length of reconstructed tube >4cm.

Note: Unlike vasectomy reversal, **length of duration between female tubectomies and reversal has no effect on outcome.**

## Uterine factor infertility

01:15:30

- Sub-mucosal fibroid (mc fibroid). Intramural fibroid can also lead to infertility if it distorts the cavity. A non distorting intramural fibroid > 5cms can lead to infertility.
- Endometrial polyp.
- Asherman syndrome.
- Chronic endometritis due to chlamydia.
- DES exposure leads to T shaped uterus, hypoplastic uterus.

Investigation :

Routine USG : **mullerian anomalies** may be picked up as incidental finding.

Gold standard for uterine infertility is **Hysteroscopy**.

Note: Saline infusion sonography has 100% sensitivity and specificity for polyps.

uterine malformations are more a/w recurrent pregnan-

Active space

cy loss than infertility. However, septate uterus can lead to infertility.

### Cervical factor infertility

01:17:30

Cervical stenosis, infections, presence of anti-sperm antibodies (immunological cause of infertility).

Immunologic infertility test : Anti-sperm antibodies present in the cervix- which make sperm immotile.

Test- Post coital test/Sims Huhner test (not used today)

Done on day 12-14 of cycle.

After intercourse, within 2 hours the female should reach the lab and cervical smear is prepared.

If sperm shows rotatory motion instead of progressive motility it suggests the presence of anti-sperm antibody.

management : Intrauterine insemination is done, bypassing the cervix.

### Unexplained infertility

01:19:34

management : Clomiphene citrate is administered ( day 2-5)

Follicular monitoring form day 10

When follicle  $\geq 17\text{mm}$   $\rightarrow$  inj. hCG

32-36 hours after hCG  $\rightarrow$  IUI.

Ideally IVF should be done.

IUI + CC x 3 cycles  $\rightarrow$  fails  $\rightarrow$  IVF.

### Procedure of laparoscopic chromopertubation

01:22:24

Advantage :

- Patient is under GA  $\rightarrow$  relaxed ; no spasm.
- Spillage and exterior of the tubes can be visualised

Procedure :

Introduce the HSG cannula and push the dye per vaginally.

Insert the laparoscope into the abdomen to visualise the spillage.

Sims speculum is used to retract the posterior wall of vagina.

Step 1 : The anterior lip of the cervix is held with a vassellum.

Step 2 : The internal os is dilated with the help of

Hegar's dilator and HSG canula is introduced

Step 3 : The methylene dye is introduced and spillage of the dye from both the sides can be visualised. (01:19:21)

Inference : Both the tubes are patent.

### **Procedure of fimbrioplasty**

01:24:23

Done in cases where fimbrial end is blocked.

Indication : If the disease is mild distal end blockage.

Here left side fimbrioplasty is already done.

Blue coloured methylene dye can be seen.

Procedure (right side) :

Step 1 : With the help of a Grasper we hold the right fimbrial end of the fallopian tube.

Step 2 : With the help of sharp scissor a small nick is made.

Step 3 : The dilatation of the ampullary part with the help of the scissors.

Step 4 : Laparoscopic chromopertubation is done. Spillage of the blue dye can be visualised out of the fimbrial end of the tube.

## MALE INFERTILITY

### Spermatogenesis

00:00:38

Spermatogenesis :

Begins at puberty.

Site : **Seminiferous tubules** in testis.

Time for spermatogenesis = **70 to 74 days**.

Additional time required by sperms to travel in the epididymis and entire ductal system = **12 to 21 days**.

Fertile male produces **100 to 200 million sperms** each day.

Hormonal support for spermatogenesis :

For spermatogenesis : **High local levels of testosterone** is needed.

Testosterone : Produced by **Leydig cells**.

1<sup>st</sup> stimulus needed by **Leydig cells** to produce testosterone in intrauterine life is **hCG/ Human chorionic gonadotropin**.  
Later **LH** acts on **Leydig cells** to produce testosterone.

Function of **FSH** :

Acts on **Sertoli cells** to releases **Inhibin B**, and **Androgen binding protein** which binds to testosterone and produces high local androgen levels.

**FSH** acts on **Leydig cells** to induce receptors of **LH** on them.

For spermatogenesis :

Testosterone : **main hormone**.

**FSH & LH** : **Contributory role**.

Temperature : **Lower than normal body temperature** is required.

Occupation with high temperature environment like **mining** can lead to defective spermatogenesis.

**Febrile illness** can lead to reduced sperm count.

Testicular volume :

Normal volume = **15 to 25ml**.

Normal length = **4cm**.

Small testicular volume : Indicates abnormal spermatogenesis.

Klinefelter syndrome : Testis are small and firm.  
 measurement of testis : Prader's orchidometer.

Spermatogenesis is also directed by Y chromosomes.

In Klinefelter's syndrome (47 XXY)  
 or microdeletion of Y chromosome  
 ↓  
 Defective Spermatogenesis

Karyotyping along with semen analysis to be done :  
 In case of male infertility with severe oligospermia (<5mil/ml)  
 or Non obstructive azoospermia.

Evaluation of the male partner : Semen analysis.

Semen analysis is the first and basic investigation to be done  
 for an infertile couple.

Best method to obtain sample : masturbation.

minimum abstinence of : 2 days.

maximum of : 7 days.

The sample should reach the lab within : 1 hour.

Analysis is done on : Liquefied semen.

Liquefaction time : 5-20 mins.

WHO parameters of semen analysis :

This represents the minimum criteria needed for conception  
 and not the average value.

pH	≥ 7.2
volume	≥ 1.5 mL
Total sperm count	≥ 39 million/ejaculate
Sperm concentration	≥ 15 million/ml
Total motility	40%
Progressive motility	32%
morphology	4% sperms should be absolutely normal (as per the strict tygerberg criteria)
vitality	58% of the sperms should be viable
WBC count	< 1 million/ml



Average sperm count : 50-100 mil/ml.

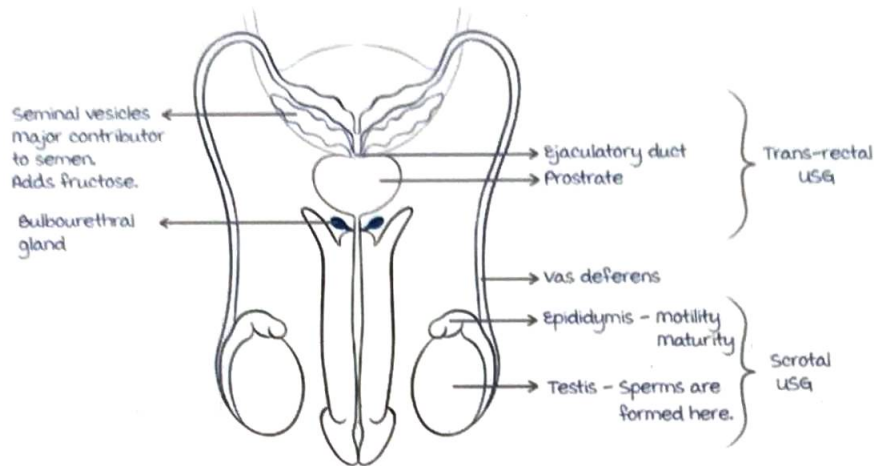
most important criteria :

morphology > motility > Sperm concentration.

Term	Definition	Seen in
Aspermia	No semen	Less semen volume if abstinence days are less
Oligospermia	Sperm concentration <15mil/ml	
Severe oligospermia	Sperm concentration < 5 million/ml.	
Azoospermia	No sperm in semen.	Klinefelter's syndrome. (Non obstructive azoospermia) Cystic fibrosis : (Obstructive azoospermia) Congenital b/l absence of vas deference and seminal vesicles.
Asthenospermia	Greater proportion of sperms with decreased motility or immotile sperms.	Kartagener's syndrome / Immotile cilia syndrome. Prolonged abstinence. Genital tract infection. Varicocele.
Teratozoospermia / Teratospermia	Abnormal sperm morphology	
Necrozoospermia	Increased non-viable sperms.	
Leucocytospermia	> 1 million WBC/ml	Chronic Prostatitis. Chronic Epididymis.  Treated by Doxycycline 100mg BD for 2 weeks
Asthenospermia + Oligospermia + Teratospermia		Varicocele. Chronic smoker.

## Sperm pathway

00:13:16



Spermatogenesis occurs in the testes. The testes formed in the seminiferous tubules pass through the epididymis to the vas deferens. The sperms attain :

**motility & maturity** in the epididymis.

The seminal vesicles pour their secretions into the vas deferens, which are :

Abundant.

Alkaline.

Rich in fructose.

The fluid from the seminal vesicles are the major contributors to the volume of semen.

The fluid from the seminal vesicle along with the sperms now pass through the ejaculatory duct to reach the prostate gland and receive prostate gland secretions which are rich in **prostatic enzymes** and is slightly **acidic**.

The bulbourethral glands produce their secretion at the time of intercourse.

Contributors of semen :

Seminal vesicle (major).

Prostate gland.

Bulbourethral gland/Cowper's gland.

Investigation of choice :

For testes and epididymis : **Scrotal US&** is done.

For seminal vesicle, ejaculatory duct (vas deference after seminal vesicles) and prostate gland : **Transrectal US&**.

Recently, **MRI** has become a preferred modality for imaging for male sex glands and ducts.

Major contributor to semen : **Seminal vesicle fluid.**

Semen contains : Sperms, Seminal vesicle fluid + Fructose, Prostatic fluid, Bulbourethral gland fluid.

If semen analysis appears abnormal, next step :

**Repeat the semen analysis** after a minimum of 1 week interval.

If both reports show azoospermia / oligospermia, next step :

**Hormonal Analysis.**

measure levels of **FSH** (most important), and **testosterone.**

Other hormones : **TSH & Prolactin.**

**TSH and prolactin** levels to be done in **both partners** of an infertile couple, both in male infertility as well as in female infertility.

In female partners, abnormal prolactin / TSH levels leads to ovulatory dysfunction.

In females with **secondary amenorrhoea**, hormonal evaluation is done including Prolactin, TSH and FSH.

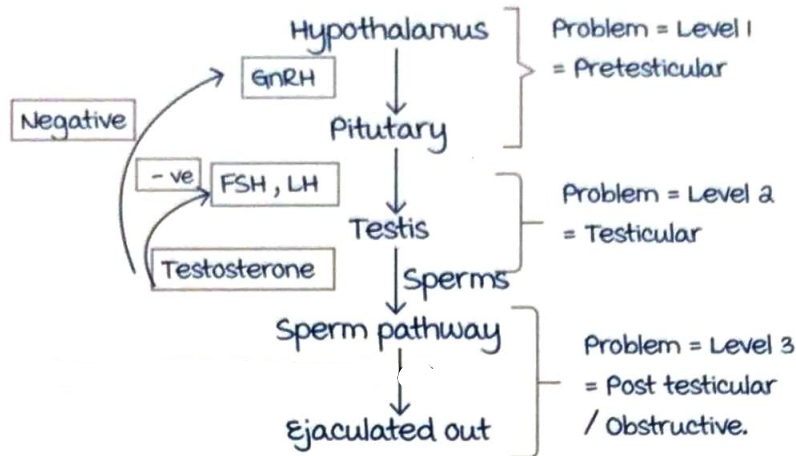
## Role of hormonal tests

00:19:38

Gives an idea about the **site of problem** :

Testosterone has a negative feedback on GnRH, it has **negative feedback** on LH and FSH indirectly.

Testosterone also has direct negative feedback on LH.



Azoospermia can be :

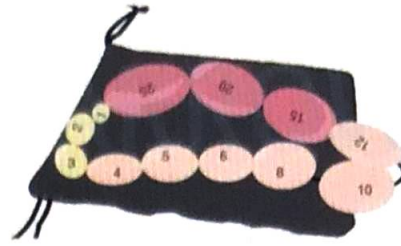
Pre-testicular/secondary hypogonadism/  
hypogonadotropic hypogonadism. (hypothalamus or  
pituitary involved).

Testicular azoospermia/primary hypogonadism (testes  
involved).

Post testicular azoospermia/obstructive azoospermia  
(ductal system involved) : Spermatogenesis can be normal.

	Pretesticular/ secondary hypogonadism	Testicular/ primary hypogonadism	Post testicular/ obstructive azoospermia
Defect in	Hypothalamus or pituitary	Testes	Sperm pathway
LH	↓	↑	Normal
FSH	↓	↑	Normal
Testosterone	↓	↓	Normal
Causes	Kallman syndrome (Hypothalamic failure), Hypothyroidism, Increased prolactin.	Klinefelter's syndrome, mumps orchitis, miners with heat exposure, Klinefelter syndrome	Tuberculosis, Congenital b/l absence of vas deferens associated with cystic fibrosis, varicocele

A **prader orchidometer** is used to measure the size of testes.



## Reifeinstein syndrome

00:26:20

A type of **partial Androgen Insensitivity syndrome**.

Therefore in Reifeinstein syndrome :

Testosterone : Normal (Resistant)

Negative feedback is lost = LH Increased.

FSH : Normal (because sertoli cells produce inhibin).

**LH and FSH levels** increase in testicular azoospermia because of lack of negative feedback by testosterone.

But in case of Reifeinstein syndrome, the levels of testosterone are normal therefore the levels of inhibin and FSH are normal.

For spermatogenesis to occur, testosterone is the major hormone required along with LH and FSH.

most common cause of ~~male infertility~~ **Primary Hypogonadism**.

Azoospermia with best prognosis : Obstructive Azoospermia.

Treated by relieving of obstruction by **resection and anastomosis**.

Klinefelter's Syndrome :

Genotype : 47XXY.

Seen in 1 in 500 men.

men are tall, undervirilised and have gynecomastia.

Testis are small & firm resulting in defective spermatogenesis.

In all males with severe oligospermia (< 5 mil/ml) or azospermia to rule out Klinefelter's syndrome/microdeletion :

**Karyotyping is to be done.**

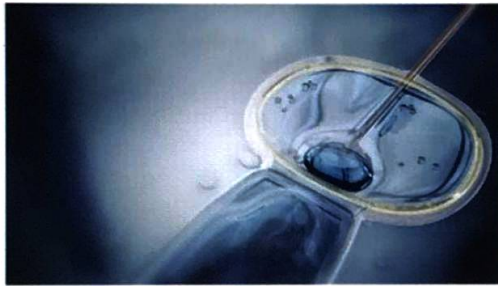
If Report of semen analysis is Azoospermia/ severe oligospermia : Although sperms are absent / less in semen. Viable sperms may be present in Testis/ Epididymis.

↓  
So testicular biopsy is done to determine whether viable sperms are present in seminiferous tubules or not.

If present, they are surgically retrieved by procedures like TESA / Testicular sperm aspiration or TESE / Testicular sperm extraction.

Or PESA / Percutaneous epididymal sperm aspiration.

These sperms are used for assisted reproductive technique called as ICSI/ Intracytoplasmic sperm injection :  
A secondary oocyte from female partner and with the help of special catheters, a single sperm is injected into the cytoplasm of the oocyte.



ICSI

management of testicular azoospermia/non-obstructive azoospermia :

Testicular biopsy : To check for sperms present in testes.

If sperms are present : Testicular sperm extraction is done by TESE (microsurgical testicular sperm extraction).

Intracytoplasmic Sperm Injection (ICSI) is done.

1 sperm/secondary oocyte needed.

If the block is at vas deferens or epididymis :

when the male ejaculates, the sperms won't be able to exit but the fluid from the seminal vesicle, prostate gland and Cowper's gland will be present in the ejaculate. Semen does not have sperms.

The volume of the semen, the fructose levels, and pH of the semen will be normal. i.e. the obstruction is above the level of seminal vesicles.

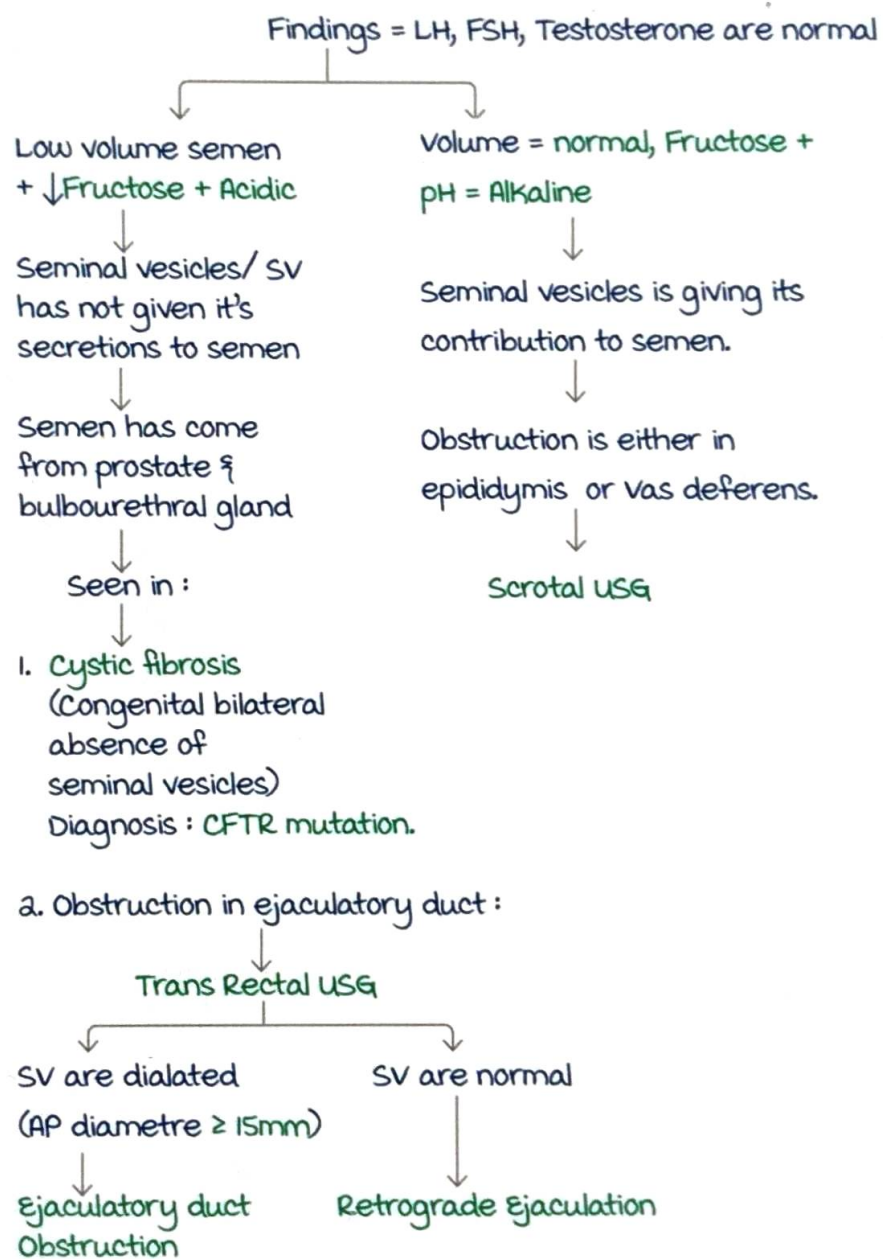
If the obstruction is at the level of ejaculatory duct :

Fluid from seminal vesicle and sperms won't be present in the semen. Only the fluids from the bulbourethral and prostate gland will be present.

Volume of semen is low, fructose absent and semen is acidic.

In case seminal vesicles and vas deferens are absent as in congenital bilateral absence of seminal vesicles, cystic fibrosis is to be suspected.

### Approach to obstructive azoospermia 00:40:50



## Intrauterine insemination

00:46:20

This is an OPD procedure.

~~Semen from the husband~~ is collected and liquified by keeping it on a heating block at 37 °C.

A droplet of the semen is taken and CASA (Computer Assisted Semen Analysis) is done.

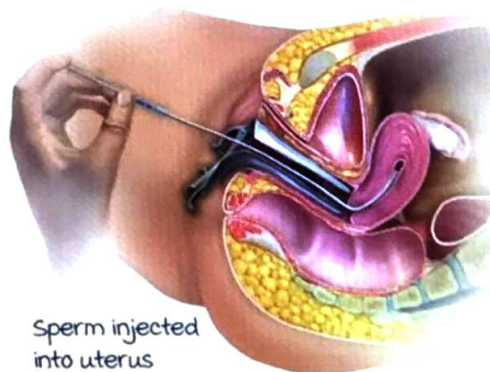
Sperm processing is done to get the most fertile and healthiest sperms free from impurities.

1. Semen is then taken and a buffer media added.
2. Centrifuge at very high speed for 12 mins.
3. The impurities float and the sperms settle down in the form of pellets.
4. Pellets are taken and place 2-3 drops of culture media over it.
5. Store inside an incubator for 45 mins to 1 hour.
6. The sperms with good motility and morphology swim up and reach the top of the media (swim up technique).
7. These sperms from the top layer are taken and again subjected to post wash CASA.

0.4-0.6 mL of the processed sperms are taken and inserted in the female in a lithotomy position with the help of an IUI catheter.



Sperm in sterile medium



Sperm injected into uterus

minimum sperm count needed for IUI : 10 mil/mL.

If IUI is done for Cervical factor infertility in females,

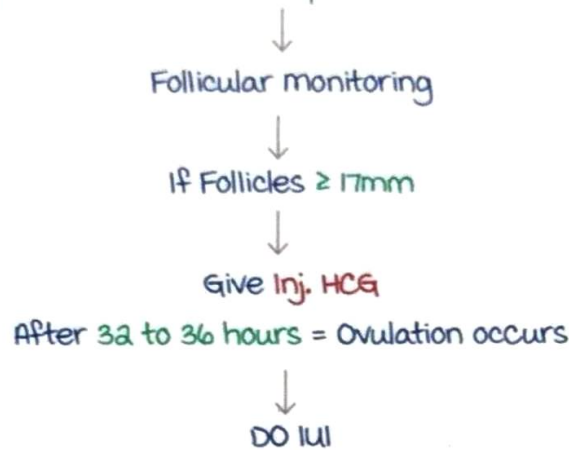
Timing of IUI should be determined by urinary LH Kit.

Correspond to time of ovulation.

Active space



In IUI done for unexplained infertility & male infertility.  
Do superovulation with Clomiphene acetate (D2 to D5).

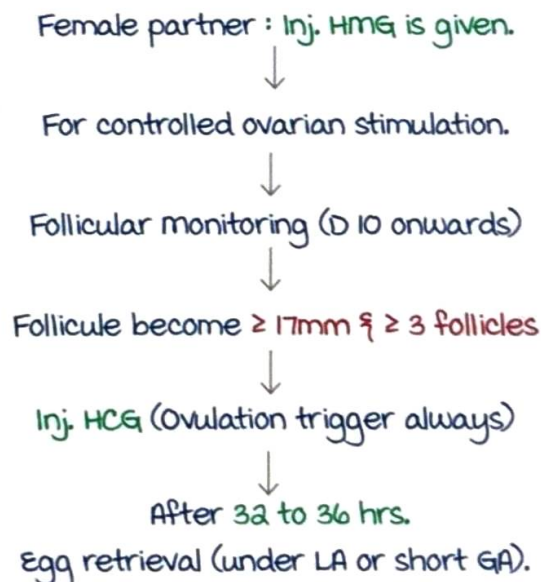


In case of retrograde ejaculation :

- sperms are collected & processed from a voided urine specimen after ejaculation.
- Oral Sodium bicarbonate is given to male prior to sperm collection to reduce risk of injury to sperms due to low urinary pH.

### Invitro Fertilization

00:49:34



On Doppler blood flow  $\geq 10\text{cm} / \text{sec}$   $\rightarrow$  mature follicles with healthy oocyte.

Oocyte pickup :

Done by special needles

under **USG guidance**.

The entire oocyte & follicular fluid is aspirated.

The oocyte picked up is incubated with sperms.

For each oocyte **50,000 to 1,00,000 sperm** are incubated.

Temperature = **37C**, in **5 to 20% O<sub>2</sub>**.

Time for **12 to 18 hours**.



Day 1 embryo



Day 2 ; 4 cell stage embryo



Day 5 blastocyst

Within 12 to 18 hours, Acrosomal reaction occurs.

**Cortical & Zona reaction** occurs.

Fertilisation occurs.

After 18 hours, Check for fertilisation by :

Female pronuclei, and male pronuclei.

and polar division occurs : **2 polar bodies** are seen in the **perivitelline space**.

Embryo transfer :

- **Day 3** : Cleavage embryo transfer.

- **Day 5** = Blastocyst transfer.

Is done under ultrasound guidance (bladder should be full).

Progesterone is given to make endometrium thick (atleast 7 to 9mm).

Embryo transfer can be done with the help of :

Fresh embryo.

Cryopreserved embryo. (brought to room temperature before transfer)

Using ~

Transfer done **2cm below the fundus**.

Success ratio = **20 to 30%**.

IVF cannot be done in :

- Azoospermia. (as required sperms is 50,000 to 1 lakh per oocyte)
- Asthenospermia (Sperms need to swim to reach oocyte)

## ICSI

00:49:34

Everything is same as IVF : till Oocyte retrieval.

Then instead of putting Oocyte and sperms together, Pick each oocyte and inject into cytoplasm = 1 sperm.

For each secondary oocyte : 1 sperm is needed.

management of male infertility :

If the sperm count is  $< 15 \text{ mil/mL}$  but  $\geq 10 \text{ mil/mL}$  :

Intrauterine insemination (IUI) can be done.

If the male partner has a sperm count between 5-10 mil/mL : IVF is done.

If sperm count is  $< 5 \text{ mil/mL}$  azoospermia/

Asthenozoospermia : ICSI.

Indications of IVF :

- Tubal blockage.
- Mullarian agenesis (IVF + Surrogacy).
- Decreased ovarian reserve/ Ovarian failure. (by donor eggs).
- Multiple IUI failures.
- Sperm concentration between 5 to 10mil/ml in male partner.

Indications of IUI :

- Cervical factor infertility.
- Vaginismus (Involuntary contraction of perineal muscles so that intercourse is not possible).
- unexplained infertility (Clomafine citrate + IUI).
- male Ejaculatory problems : Hypospadiasis, epispadiasis, retrograde ejaculation.
- Oligospermia (sperm count = 10 to 15 mil/ml).

Indications of ICSI.

= Indications of IVF + Severe Oligospermia  
+ Azospermia + Asthenospermia.

Success rate IVF and ICSI = 20 to 30%.

Complications of IVF and ICSI :

maternal :

- PIH.
- Placenta previa.
- Placental abruption.

Fetus :

- multifetal gestation (most common) : monozygotic and Dizygotic.
- Low birth weight.
- IUGR / Intrauterine growth retardation.

In IVF / ICSI conceived offsprings :

**Embryonal Hepatic Adenoma** is common.

Risk of congenital Anomalies are not increased.

Other techniques :

GIFT / Gamete intrafallopian transfer :

Here also, like IVF, Egg retrieval is done after controlled ovarian stimulation.

Unlike IVF, Fertilisation & early embryo development donot take place in lab.

Hence, egg and sperms are placed via a catheter into Fallopian tube.

It was done for  not tubal factor :

Now it is replaced by IVF.

### **Preimplantation genetic testing**

01:04:52

It is done to identify chromosomal abnormality or for HLA typing before embryo transfer.

PGT- A : PGT for Aneuploidies.

PGT - m : PGT for monogenetic / single gene defects.  
 PGT - SR : PGT for Chromosome structure rearrangement.

Specimen for PGT :

- Polar body

Advantage : Avoids removal of cell from developing embryo.

Disadvantage : Genetic abnormality of potential origin cannot be detected by PGT.

- Cleavage embryo stage.
- Blastocyst stage : Trophoectoderm. (Best way)

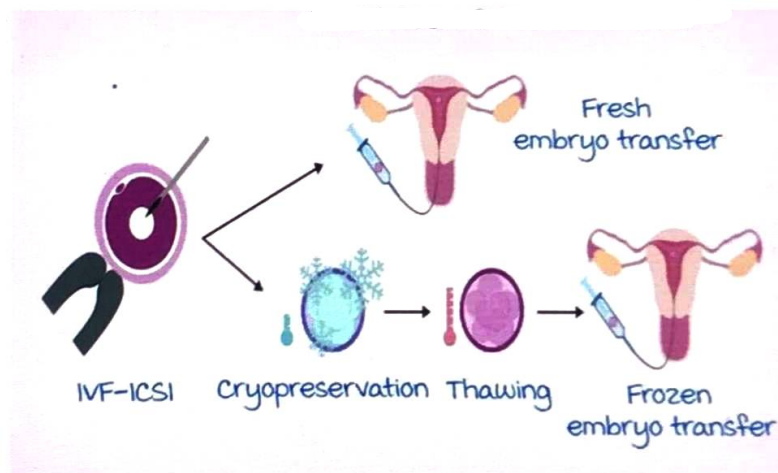
Recently :

Non invasive PGT can be done on cell free Fetal DNA.

Amplified using SEM media -> SEM media -> Spent embryo media.

### Miscellaneous

01:13:50



## NATURAL METHODS OF CONTRACEPTION

### Classification of contraceptive methods

00:00:57

Temporary methods.	Permanent methods.
<p>Natural family planning methods.</p> <p>Barrier methods.</p> <p>Estrogen + progesterone contraceptives :</p> <ul style="list-style-type: none"> <li>• OCP.</li> <li>• vaginal rings.</li> <li>• Transdermal patches.</li> </ul> <p>Progesterone containing contraceptives :</p> <ul style="list-style-type: none"> <li>• minipills.</li> <li>• Implants.</li> <li>• DMPA injection.</li> </ul> <p>IUCD :</p> <ul style="list-style-type: none"> <li>• Cu-T.</li> <li>• Mirena</li> <li>• Progesterone containing MIRENA.</li> </ul> <p>Centchroman : non-steroidal pill.</p>	<p>Females :</p> <ul style="list-style-type: none"> <li>• Tubal ligation.</li> <li>• Essure : hysteroscopic method of tubal ligation.</li> </ul> <p>Males:</p> <ul style="list-style-type: none"> <li>• Vasectomy.</li> </ul>

### Long-acting reversible contraceptives (LARC) :

- IUCD.
- Implants.
- Injections.

Active space

## Efficacy of contraceptives

00:04:33

measured with help of **pearl index**.

usual length of exposure : expressed in 100 women years.

Pearl index

$$= \frac{\text{Number of accidental pregnancies}}{\text{Number of females who used it} \times \text{years of use}} \times 100.$$

$$= \frac{\text{Number of accidental pregnancies}}{\text{Number of females who used it} \times \text{months of use}} \times 1200.$$

$$= \frac{\text{Number of accidental pregnancies}}{\text{Number of females who used it} \times \text{cycles of use}} \times 1300.$$

? X method was used by 50 females for 39 cycles. 10 of which became pregnant. Calculate pearl index?

$$\text{Ans: Pearl index} = \frac{10}{50 \times 39} \times 1300.$$

Factors affecting failure rate of contraceptives :

1. Type of Contraceptive.
2. Age of patient :
  - Teenage : Failure rate is more.
  - >30 years : Failure rate is low.
3. marital status :
  - married : Failure rate is low.
  - Unmarried : Failure rate is more.
4. Parity :
  - Nulliparous : Failure rate is low.
  - multiparous : Failure rate is more.
5. Intention towards future pregnancy :
  - Desirous : Failure rate is high.
  - Non desirous : Failure rate is low.

## Natural family planning methods

00:11:36

Based on time around ovulation : unsafe for intercourse.

Time of ovulation :  $\text{cycle length} - 14$ .

Time of ovulation can be assessed by certain characteristics :

- Cervical mucus.
- Basal body temperature.

### 1. Rhythm method :

Based on **Ogino Knaus theory**.

According to this method

- Female with regular 28-day cycle :

Safe period :

1<sup>st</sup> 7 days of cycle.

Last 7 days of cycle.

Unsafe period:

Day 8 - day 19 of cycle.

- Female with irregular cycle :

Unsafe period :

1<sup>st</sup> day of unsafe period :  $\text{shortest cycle} - 18$ .

Last day of unsafe period:  $\text{longest cycle} - 11$ .

## Tirumala method

00:16:26

### 2. Tirumala method:

Also known as standard day method or **cyclobead method**.

**32 beads** placed on a string.

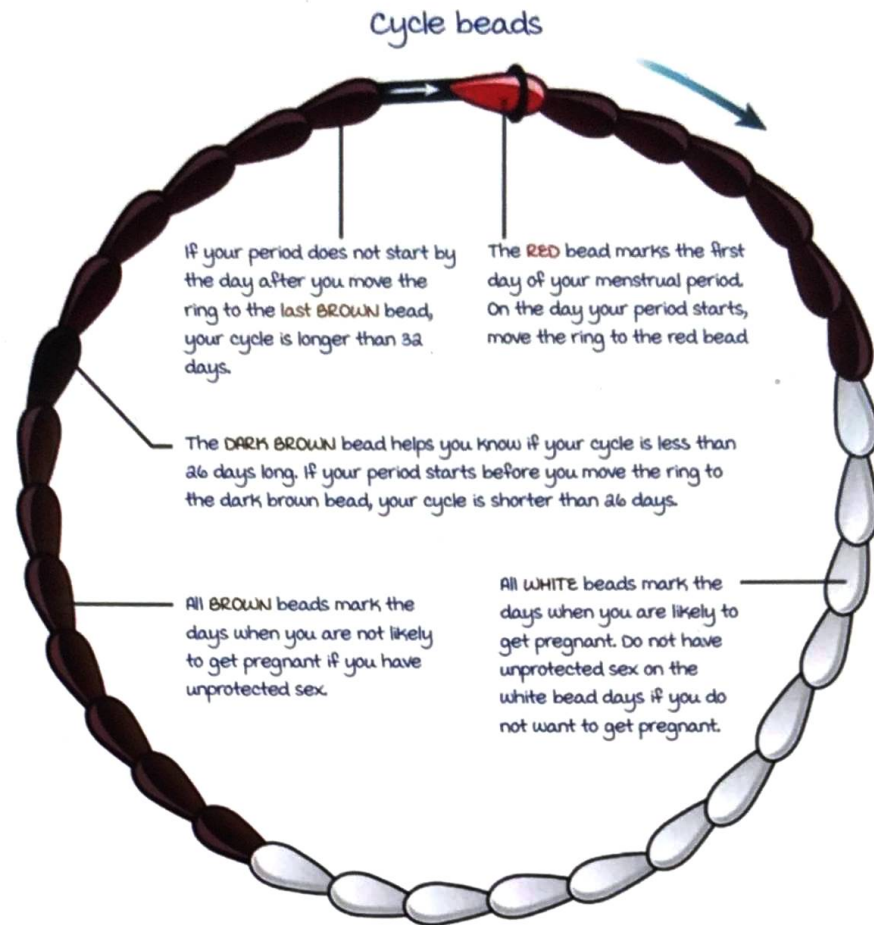
Present in 4 different colors:

- **Brown beads** : Safe period.
- **White beads** : unsafe period.
- **Red bead** : Day 1 of cycle.
- **Dark brown bead** : On day 27.

If female experiences bleeding before day 27 → then this method is not suitable for her.



Cyclobead method can only be used by females with a cycle length between 26-32 days.



### Cervical mucus method

00:21:55

#### 3. Cervical mucus method:

Also known as **billing method**.

under effect of estrogen :

- Cervical mucus is thin, watery, abundant, and elastic.
- mucus can be stretched between fingers :  
**Spinnbarkeit.**

under effect of progesterone :

- mucus is thick, scanty, viscus.
- Cannot be stretched between fingers.

Procedure:

- Every morning, wipe cervical mucus with tissue paper.
- Stretch cervical mucus between fingers and check.

Safe period:

- First 4 days of cycle : **dry days**.
- From 4<sup>th</sup> day after the peak cervical mucus.

unsafe period:

- From 5<sup>th</sup> day of her cycle → Day of peak cervical mucus → Till 3 days after it.

4. Basal body temperature method :

Progesterone increases basal body temperature by **0.4-0.8 °C** (0.5°C).

Procedure:

- Record basal body temperature every morning.

Safe period:

- First 4 days of cycle.
- From 4<sup>th</sup> day after the increase in BBT till end of cycle.

Unsafe period:

- From 5<sup>th</sup> day of her cycle → increase in BBT → 3 days after it.

5. Symptothermal method :

Combination of 2 methods :

- Cervical mucus method.
- Basal body temperature method.

## Lactational amenorrhea

00:28:16

6. Lactational amenorrhea :

**Best natural family planning method.**

Increased prolactin → negative feedback on GnRH →  
Decrease LH & FSH → No ovulation.

Prerequisites:

- Breast feeding should begin soon after delivery.
- Exclusive breast feeding.
- At least one feed at night.
- Frequency is more important than duration.

Active space

Failure rate :  $1-2/HWY.$

Other family planning methods  $>25 /HWY.$

most adopted natural family planning method : **Lactational amenorrhea.**

Natural family planning method with least failure rate:  
**Lactational amenorrhea.**

Ovulation resumes :

- Exclusive breast feeding female: **6 months.**
- Non breast feeding / partially breast feeding female: **6 weeks.**

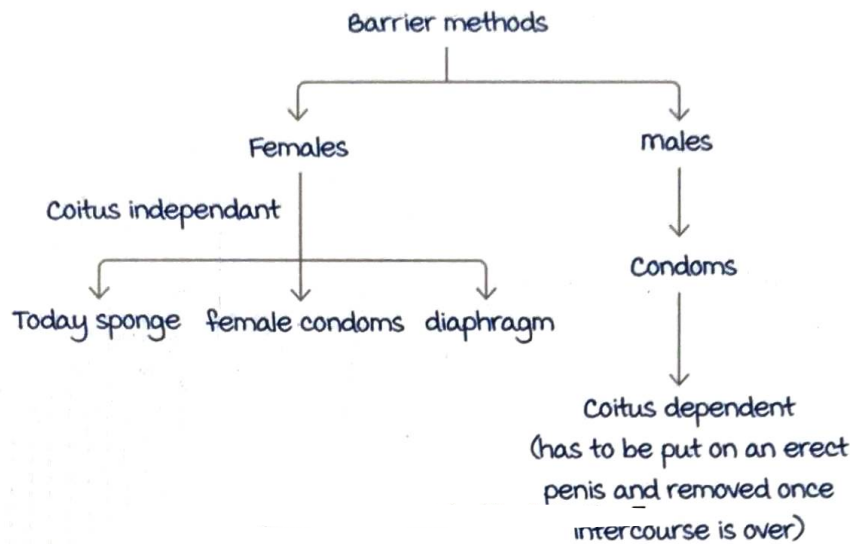
**Rule of 3 :**

- Contraception started by **3 months** in exclusive breast feeding female.
- Contraception started by **3 weeks** in partially breast feeding /non breast feeding female.

Disadvantages of natural family planning methods:

- Needs motivation.
- **Timed intercourse.**
- Suitable only for females with regular cycles.
- Associated with **high failure rate.**

## BARRIER METHODS OF CONTRACEPTION



Barrier methods are protective against :

- STDs/PID/ectopic pregnancy.
- HIV ( male condom > female condom).
- HPV infections, carcinoma cervix (male and female condoms).

None of the barrier methods can be used as emergency contraceptive.

male condom is included in National Family Planning Programs **Nirodh**.

Female condom (not included in NFPP ) is available under program **NACO** for female sex workers.

male condoms can only be used once.

Female condoms can be used up to **2 times** but it would be better to use them only once as the efficacy will be reduced.

Diaphragm can be used till **1 year** by washing and drying.

Today sponge can be used once when inserted up till **24 hours** ( independent of number of times intercourse occurs).

## Male and female condoms

00:05:13

male condom	Female condom
Has a single ring	Has 2 rings (single ring condoms are also available now)
They are long, narrow with a pointed edge.	They are short & broad like a pouch. No pointed ends.
Polyurethane condoms are used. Oil based lubricants cannot be used with latex condoms (earlier).	Polyurethane Condoms (FC-1) are used. FC-2 (Nitrile Condoms) → MC used now.
Failure Rate: 2-12 / Hundred Women Years (HWY)	5-20/HWY



Absolute contraindication for female condom: **Cystocele/rectocele.**

## Diaphragm

00:09:15

They are dome shaped cups with a flexible rim. Can be made of rubber/latex/silicone.

Spermicidal agents:

Spermicidal agents need to be used additionally as diaphragms are not sperm proof.

MC used spermicidal agent → **Nonoxynol 9.**

Spermicidal agents act by increasing the permeability of cell membrane → Leads to disruption of cell membrane.

Spermicidal agents - if used alone → failure rate 15-25%.

It can be used in conjunction with other barrier methods.

These agents are available in the form of creams, jellies &



diaphragm

suppositories etc.

The patient needs to wait for 20 minutes after using the spermicidal suppository as it takes time to disperse into the vagina once inserted.

Drawbacks :

- Some study show that HIV transmission is increased with the use of spermicidal agents like nonoxynol 9.
- Act on lactobacilli present in the vagina decreasing them and increasing the risk of colonization of E.coli → Bacteruria after intercourse.

Since diaphragms (any device) are dependent on spermicidal agents, they should not be removed before 6 hours after the intercourse.

Diaphragms can be used for 1 year by washing & drying. Chances of Toxic Shock Syndrome are present with diaphragm (not with today sponge).

Diaphragms should not be used with oil based lubricants.

They do not protect against HIV or herpes simplex infection but can protect against PID.

**Absolute contraindications :**

- Prolapse.
- Fistula.
- Eroded cervix.
- RV uterus.
- Recurrent UTI.

Female condom	Diaphragm
Can be used in puerperal and after abortion	Not to be used as rim can cause erosion, also uterine size keeps changing because of involution.
Does not need a spermicidal agent	Needs a spermicidal agent
Can be removed anytime after intercourse	Needs to be removed 6 hours later
Protects against HIV	Does not protect against HIV
Ideally should not be reused ; maximum reuse one time.	Can be reused till one year.

## Today sponge

00:16:28

mushroom shaped device  
having 1 gram nonoxynol 9  
(separate spermicidal agent is  
not required).  
once inserted they can be used  
up to 24 hours  
(maximum stay : 30 hours).



Today sponge

Chances of Toxic Shock Syndrome with today sponge is nil.

	Diaphragm	Sponge	Female condom
Insertion before coitus (maximum)	6 hours	24 hours	8 hours
Should be left after coitus	6 hours	6 hours	Can be removed immediately or after sometime (female's choice).
Maximum wear time	24 hours	30 hours	8 hours

## Vaginal pH regulator gel

00:18:48

Contains lactic acid, citric acid & potassium bitartrate,  
approved for contraceptive use in 2020.

The combination maintains a lower pH of 3.5 -4.5 (normal pH : 4-4.5) even in the presence of alkaline semen.

The adhesive properties allow this gel to coat the vagina and stay in place for up to 10 hours → Resulting acidic environment which immobilises sperms.

It does not contain any hormone, comes in a single dose, pre-filled vaginal applicators → Containing 5 gram of gel (90 mg lactic acid, 50 mg citric acid & 20 mg potassium bitartrate).

Each dose is inserted into the vagina not more than 1 hour prior to intercourse, dosing is repeated with every sexual act.

The gel can be used in addition to other forms of non hormonal barrier contraception however it is **not advised** to use along with **vaginal rings** (hormone containing).

Clinical question :

match column A with its appropriate property in Column B.

Column a :

1. Female condom
2. male condom
3. Diaphragm
4. Today sponge

Column b :

- Coitus dependent
- Can be reused for up to one year.
- Best suited for females who have multiple sex in 24 hours.
- Can be used in puerperal period.

Answer :

- Female condom - Can be used in puerperal period.
- male condom - Coitus dependent.
- Diaphragm - Can be reused for up to one year.
- Today sponge - Best suited for females who have multiple sex in 24 hours.



## ESTROGEN AND PROGESTERONE CONTRACEPTIVES

- Oral combined pills (estrogen + progesterone).
  - Transdermal patch (E+P).
  - Vaginal rings (E+P).
- } mechanism of action & absolute contraindications are same.

### Oral combined pills

00:01:14

Classification on the basis of dose of the pill (estrogen component : ethinyl estradiol) :

- High dose pills → if ethinyl estradiol (EE) >50mcg. (not used these days)
- Low dose pills → if EE <50 mcg (mostly 30mcg).
- Very low dose pills → if EE <20 mcg.

Minimum effective dose of EE in pills → 10 mcg, called **Loestrin**.

Classification on the basis of generation of the pill (progesterone component) :

- 1<sup>st</sup> generation
  - 2<sup>nd</sup> generation
  - 3<sup>rd</sup> generation
  - 4<sup>th</sup> generation
- } most important, as the generation increases, the androgenic effects of progesterone decreases.

3<sup>rd</sup> generation have the least androgenic effects while the 4<sup>th</sup> generation has anti-androgenic properties.

3<sup>rd</sup> generation OCPs :

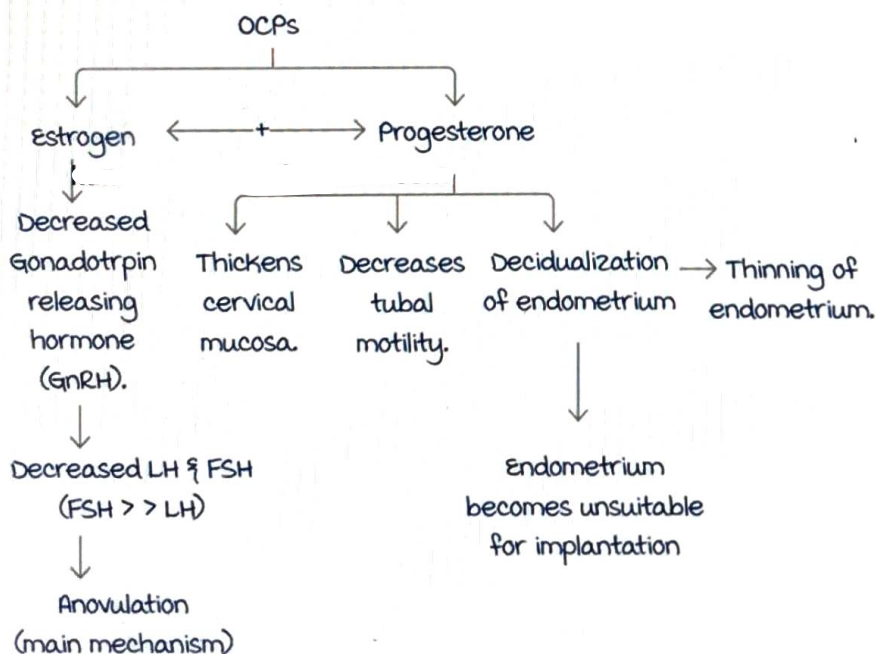
- Gestodene.
- Norgestimate.
- Desogestral : MC used progesterone in OCP.
- Etonorgestrel

4<sup>th</sup> generation OCPs :

- **Drospirenone** : A derivative of spironolactone.  
It is an **aldosterone antagonist** → diuretic action (when combined with estrogen, it antagonizes the salt & water retention caused by estrogen).  
Drospirenone has anti androgenic action as it increases sex hormone binding globulin → free testosterone decreases.  
Applied aspect : Patients with mild hypertension, salt and water retention caused by OCPs can be switched over to 4th generation OCP pills with drospirenone as it leads to excretion of sodium, retention of potassium (used carefully in patients with renal disease).
- **Dienogest**.
- **Nomegestral**.

### Mechanism of action

00:07:28



Active space

Composition of important pills :

Pill	Composition	Comment
Mala D	30 mcg EE + 0.15mg levonorgestrel (LNG)	Sold by Government of India at subsidised rates.
Mala N	30 mcg EE + 0.15mg levonorgestrel (LNG)	Distributed <del>free of cost</del> by Government of India.
Yasmin	30 mcg EE + 3 mg drospirenone	4th generation OCP.

Starting a pill :

- Start the pill on day 1 of the cycle.
  - Pills can also be started from day 1-5 of the cycle.
  - Still started post day 5 of the cycle → additional method of contraception should be used for 1 week.
- } No back up method required

One pill should be taken daily at the same time (approx) every day for 21 days.

The pill containing synthetic oestrogen and progesterone inhibit natural LH & natural FSH → no ovulation (no natural progesterone or oestrogen in the body).

Post 21 days when the pill intake is stopped, the synthetic oestrogen and progesterone decrease → patient menstruates after 3-4 days.

The patient starts bleeding again → day 1 of the next cycle. **Breakthrough bleeding** (most common side effect) → Due to missing of a pill dose → 24 pill packs (new) used to avoid breakthrough bleeding.

Uses of OCPs :

Non contraceptive uses :

- To regularise cycles in patients with irregular menstruation / in PCOS. (DOC)
- To prevent excessive bleeding / reduce blood loss in hyper estrogenic conditions like fibroids, endometriosis,

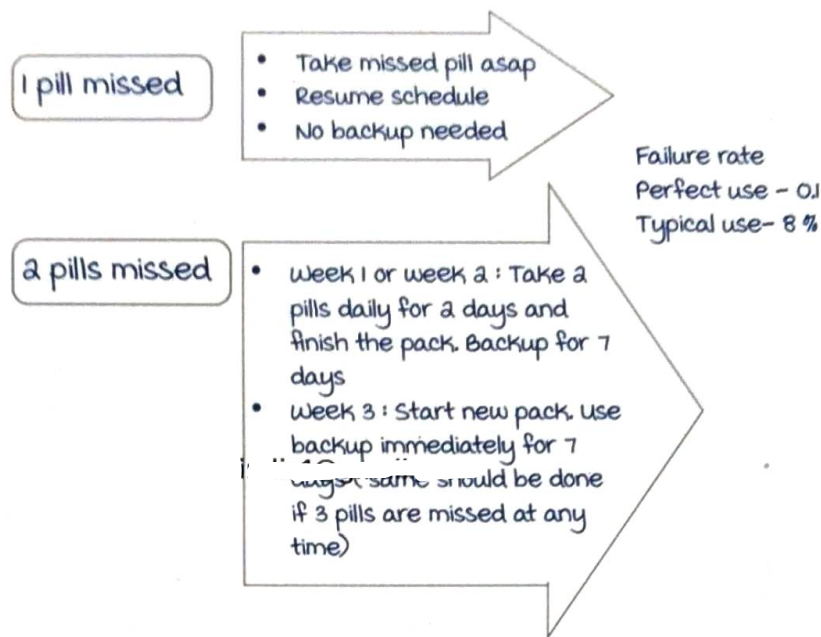
abnormal uterine bleeding / AUB (as oestrogen increases progesterone receptors & progesterone binds to them on endometrium, stopping the bleeding).

- To make cycles anovulatory to reduce pain in patients with 1° dysmenorrhea (DOC) / endometriosis.
- To manage (functional) ovarian cyst, menstrual migraine and mittelschmerz syndrome.
- To manage premenstrual syndrome (PMS) but not drug of choice. DOC: Fluoxetine (SSRI).
- Oestrogen component of OCP is used as hormonal replacement therapy (HRT) and management of Turner syndrome.
- Progesterone component of OCPs makes cervical mucosa thick → decreases chances of PID, STD and ectopic pregnancy.  
MC PID with OCP use → chlamydia.  
MC vaginitis with OCP use → candidiasis.
- To manage hirsutism (DOC), acne & hyperandrogenism.

(As they decrease GnRH, LH & androgens)

OCPc effect on cancers :

Increases	Relieves/Decreases	No effect
Hepatic adenomas.	Endometrial cancer.	Liver cancer.
Breast cancer in premenopausal females.	Ovarian cancer.	
	Ovarian cysts.	
Cancer cervix : Reversible; risk reduces as soon as the pills are stopped.	Benign breast diseases.	
	Colorectal cancer.	



### Absolute contraindications of OCPs

00:30:12

WHO category 4 :

Mnemonic: Banks Have Various Schemes To Provide Home Loans During May.

**Banks** : Known / suspected case of breast cancer.

**Have** : uncontrolled hypertension : severe (160/110).

(medically controlled hypertension, in a female who is non-smoker, of any age : Not a C/I for OCPs).

**Various** : undiagnosed vaginal bleeding.

**Schemes** : Smoker > 35 years of age.

**To** : Known or suspected case of thromboembolism or family history of idiopathic thromboembolism in parent or sibling or h/o CVA/MI, or conditions predisposing to it (Risk factor for thromboembolism e.g. malignancy, lupus anticoagulant present, prolonged immobility due to trauma or surgery → absolute contraindication).

**Provide** : Pregnancy or h/o peripartum cardiomyopathy.

**Home** : Severe hypercholesteremia, hypertriglyceridemia (>750mg/dl).

**Loans** : Presently impaired liver function / liver cancer / acute or chronic cholestatic liver disease.

During : Diabetes with vasculopathy.

may : migraine with aura.

Also contra-indicated in breast feeding & post-partum females (<21 days).

Absolute contraindication	Relative contraindication	Not a contraindication
Smoker (>35yrs) who quit smoking for < 1 year.	Sickle Cell Disease	Smoker who quit smoking for > 1 year.
Person using nicotine gums	Gall bladder disease	Varicose veins, obesity
Patient with present hepatitis (Till LFT becomes normal)	SLE (if lupus anticoagulant is present → absolute contraindication.)	Any age
Females with factor-5 leiden mutation.		Patients with CIN
		Past history of hepatitis
		Patient on anticoagulants (progesterone contraceptives preferred)
		CHD (if CHD is predisposing to thrombosis → contraindication)

In females who are older & obese, progesterone only pills are preferred.

Return of fertility :

Fertility returns within 3 months of stopping the pills.

OCPs are contraceptives of choice :

- Newly married couples staying together.
- After hydatidiform mole evacuation.
- For spacing of pregnancy.

Contraceptive rings

00:40:59

Other E and P containing contraceptives : RINGS

Rings Advantages over pills : Less estrogen exposure, less breakthrough bleeding.

Nuva ring 54mm diam, 4mm thick put it on day 1 of cycle

- E : EE (15mcg/d),
- P : Etonorgestrel (120mcg/d)
- Use same ring for 3 weeks then remove. After a week insert a new ring within 3 hrs of the stipulated time.

Annovera

- E : EE (13 mcg/d),
- P : Segesterol acetate (50mcg/d).
- use for 3 weeks and remove for 1 week → clean and reuse till 1 year.

Important points :

1. If a female removes ring during sexual activity, and reinserts it within 3 hr :  
Back-up contraception not needed
2. Annovera not used in females with BMI  $\geq 29$  d/t risk of embolism.

	NUVA ring	Annovera ring
EE dose	15mcg	13mcg
Progesterone	Etonorgestrel	Segesterol
Progesterone dose	120mcg	150 mcg



Contraceptive rings

Active space

Usage	Day 1	Day 1
	Ring stays in vagina for 3 weeks	Ring stays in vagina for 3 weeks
	1 week = no ring (removed)	1 week = no ring (removed)
	Day 1 of new cycle → new ring.	Day 1 of new cycle → old ring till 1yr.



Push into vagina Final position

Contraceptive rings have better compliance, lesser chances of break-through bleeding.

The rings need to be reinserted within 3 hours after removal during sexual activity → if reinserted within 3 hours : **No backup** contraception required.

If reinserted after 3 hours : **Backup** contraception needs to be used for **48 hours**.

**Annovera** rings are specifically contraindicated in females with **BMI ≥ 29**.

## Transdermal patch

00:46:10

Patch detachment :

If occurs <24 hours have passed → **reapply same patch**, no need for backup contraceptives.

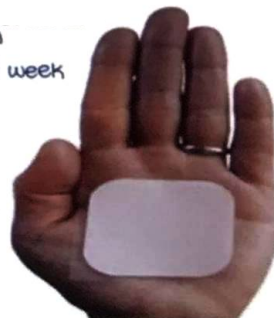
If occurs >24 hours have passed → **new patch**, new cycle begins, **backup needed for 48 hours**.

E : EE (20mcg/d) P : Norelgestromin (150mcg/d)

Apply new patch every week for 3 weeks : On same day, not same site and not same time. 1 week patch free.

Site : Lower abdomen, upper outer arm, buttock, upper torso, not breast.

Bathing, swimming, sauna etc donot lead to patch removal



Transdermal patch

Active space



## ONLY PROGESTERONE CONTRACEPTIVES

### Types

00:00:20

1. Progesterone only pills : Progesterone only pills (pops)/minipill.
2. Progesterone implants : Implanon.
3. Progesterone injection : Depot medroxyprogesterone acetate (DMPA).
4. Progesterone containing IUCD : mirena.

mechanism of action :

1. POPS : Thicken cervical mucus.
2. Implants, injections, cerazette (POP available in India),  
main mechanism : Anovulation.

Other mechanisms : Thicken cervical mucus and inhibit tubal peristalsis.

Progesterone containing contraceptives thicken the cervical mucus → Sperms cannot penetrate the thickened cervical mucus → Decrease the chance of Pelvic inflammatory diseases, sexually transmitted diseases and ectopic pregnancy.

They also decrease the tubal peristalsis and therefore a failure of the contraception, leads to increase chances of ectopic pregnancy.

Hence, absolute risk decreases but relative risk increases.

Progesterone containing contraceptives do not have any effect on :

1. Carbohydrate metabolism.
2. Lipid metabolism.
3. Clotting factors.
4. Breast milk.

Therefore, these contraceptives can be used by :

1. Breast feeding females.
2. Females with history of thromboembolism.
3. Smokers.
4. Age > 35 years.
5. Obese females.
6. Hypertension and increased cholesterol.
7. SLE on anticoagulant therapy.
8. Diabetes with vascular disease.

DMPA, implants and mirena can also be used to treat dysmenorrhea due to endometriosis.

Absolute contraindications for all progesterone containing contraceptives :

1. Undiagnosed vaginal bleeding.
2. Pregnancy.
3. Known or suspected breast cancer.
4. Benign or malignant liver tumors.

Previous history of ectopic pregnancy and PID are not a contraindication for POP, injections or implants.

most common side effect of progesterone containing contraceptives : Irregular bleeding.

mostly scanty bleeding which may ultimately lead to secondary amenorrhea (as it causes endometrial atrophy).

### Progesterone only pills

00:09:32

Contains low dose of progesterone.

mechanism of action : Cervical mucus thickening.

**Cerazette** : minipill available in India.

75 mcg of Desogestrel.

Acts by causing anovulation.

POPs must be taken at the same time every day, window period is 3 hours.

Cerazette has a window period of 12 hours.

Should be started on :

1. Day 1 of menses (No back up needed).
2. Quick start (from any day of the cycle, backup of 2 days needed).

If one pill is forgotten or window period is crossed :

Resume as soon as possible and back up contraception for 2 days.

If 2 or more pills are forgotten :

Stop the pills for the present cycle and restart once menses occurs.

In case she doesn't bleed in 4-6 weeks, do a urine pregnancy test.

Clinical decision to use minipill is made when :

1. Contraceptive of choice in lactating females.
2. Females over the age of 40 years.

Failure rate :

With typical use : 3%.

With perfect use : 0.5%.

## Implants

00:14:28

Single rod implant called Implanon is used.

If the implant contains barium sulphate it is called as Nexplanon.

Dimensions : 40mm X 20mm.

The core has Etonorgestrel + Barium sulphate + Ethylene vinyl acetate.

Etonorgestrel 68 mg present.

Rate of release : 60 mcg/day (gradually decreases).

Life span : 3 years.

If inserted within 7 days of menstrual cycle, then no back up is needed and it acts immediately.

If inserted after 7 days, back up needed for 3 days (or 7 days).

mechanism of action : Anovulation.

Insertion :

OPD procedure under local anesthesia.

Inserted on the medial side of non-dominant arm with the help of the inserter.



Implant with inserter

Removal :

OPD procedure under local anesthesia.

Small incision must be made.

Contraindications : Same as all progesterone containing contraceptives.

Implants are **not contraindicated** in the following conditions, but other methods are preferred :

1. Severe acne.
2. Severe vascular/migraine headache.
3. Severe depression.

Return of fertility : After removal, fertility returns in a month.

Fertility rate for implant : **0.05%** (most effective contraceptive).

Fertility rate for **Nexplanon** : **0.01%**.

**DMPA**

00:20:25

It is an injection.

Included by the name of *Antara* in National family planning program.

Composition : 150 mcg of MPA.

Injection should be taken once in 3 months.

Given in deltoid or gluteal region, intramuscularly.

Repeated every 3 months

Window period : 4 weeks.



In case of delay of  $\geq 4$  weeks in taking DMPA : **First perform a UPT.**

Once pregnancy is ruled out, inject DMPA and give a backup of 7 days.

mechanism of action : Anovulation.

most common side effect : Irregular bleeding.

Contraindications : Same as all progesterone containing contraceptives.

Given within 7 days of LMP and is effective within 24 hours.

Advantages :

1. Decrease seizure frequency.
2. Decrease sickling in sickle cell anaemia.

Therefore, the contraceptive of choice in epilepsy patients : DMPA.

The contraceptive of choice in sickle cell anaemia patients : DMPA.

Disadvantages :

1. Delayed return of fertility (takes 12-24 months).
2. Decreases bone mineral density.

Therefore, DMPA is not given to breast feeding females < 6 weeks postpartum.

Subcutaneous DMPA :

Comes as pre-filled syringe, dose of 104 mcg of mPA.

Patient can self-administer this injection subcutaneously.

Repeated every 3 months.

Failure rate :

With perfect use : 0.3%.

With typical use : 3%.



## IUCD

Classification of IUCD :

- 1<sup>st</sup> generation : Inert IUCDs.  
Eg. Lippes Loop.
- 2<sup>nd</sup> generation : Cu containing IUCD .  
Eg. Cu T, multiload devices.
- 3<sup>rd</sup> generation : Hormone containing IUCD.  
Eg. mirena.

The IUCDs included in National Family Planning Programme :

- CuT 380A - Paraguard.
- multiload 375 .

### CuT 380A - Paraguard

00:01:46

Also called as Paraguard.

T shaped device.

Copper is present on the vertical and also on the horizontal arms (indicated by A).

Area of copper is 380 mm<sup>2</sup>

Small ball of 3 mm<sup>2</sup> :

Prevents uterine perforation.

Thread : Polyethylene (monofilament).

Helps to assess if the CuT is in place.

Releases copper at 50 µg/day.

It can release copper up to 12 years but approved lifespan is 10 years.



## Multiload 375

00:04:04

Not T shaped and no copper on arms.  
 Arms are bent and have spurs on arms  
 thereby lessens expulsion.  
 Nylon thread present.  
 Live Span : 5 years.



## Mechanism of action of 2<sup>nd</sup> generation IUCD

00:05:19

Copper IUCD → releases copper → induces a  
 severe inflammatory reaction sufficient enough to be  
 spermicidal. → fertilization does not occur/  
 Inhibits implantation.

Prevents fertilization >> inhibits implantation.

No effect on ovulation. Not an abortifacient.

Time of insertion :

- If recently delivered :
  - Post placental : In 10 minutes of delivery.
  - Postpartum : After 10 minutes but within 48 hours of delivery.
  - Interval : Six weeks after delivery.
- If not recently delivered : Within first 10 days of cycle  
 ensures that patient has not become pregnant. After  
 10 days ovulation may occur and patient might have  
 conceived.

Government of India advises postpartum IUCD

Active space



## Risk of pelvic inflammatory disease (PID)

00:10:04

Earlier thought to have high risk of PID.

Now studies have shown risk of infection with IUCD **does not increase with long-term use**. Risk of infection is slightly increased within 1 month of insertion of IUCD that can be reduced by aseptic technique.

Past history of PID is not a contraindication but present history of PID is contraindicated.

Women at risk of STI.

Women with multiple sex partners  
 Women not in a stable relationship  
 Drug or alcohol abuse.



Advised to use **barrier method + IUCD** like in HIV patients.

In HIV patients,

For contraception : IUCD

Preventing transmission : Barrier method.

most common PID with IUCD is **Actinomyces**.

Treatment with oral Penicillin G 500 mg QID for 1 month.

method of insertion :

No Touch method.

Withdrawal technique.

## Risk of ectopic pregnancy

00:13:40

Absolute risk :

IUCDs have a high effective rate (high pearl index).

IUCD prevents any type of pregnancy including ectopic pregnancy.

Absolute risk of ectopic pregnancy decreases.

Relative risk :

**Increased**, if **IUCD failure** occurs there is a high risk of ectopic pregnancy.

Previous history of ectopic pregnancy :

It is not a **contraindication** as ideally chance of ectopic pregnancy decreases with IUCD.

**IUCD is the contraceptive of choice in :**

Diabetic patients.

Stable heart disease patients.

HIV patients.

Side-effects :

most common side-effect is **bleeding**.

most common cause of removal of IUCD is **pain**.

**Immediately fertility returns** after removal of IUCD.

### IUCD in nulliparous female

00:17:10

Preferably **frameless IUCD** as causes less pain and also lesser expulsion rate.

a type

- Gynefix (CuFix/Flexigard)
  - Have 6 Copper sleeves/cylinders.
  - It is **sutured to myometrium**.
  - A surgical polypropylene thread which is noted at one end .
  - Total Cu : is **330 mm<sup>2</sup> of copper**.

- Fibroplant :
  - Levonorgestrel (LNG) containing **frameless IUCD**.

a types :

- releases
  - 14 µg LNG (most common).
  - 20 µg LNG.



Active space

Fibroid used in :

In nulliparous female.

In perimenopausal or postmenopausal female.

Progesterone have anti proliferative activity hence it is used to treat endometrial hyperplasia without atypia.

Also used in perimenopausal or menopausal female with menorrhagia after ruling out carcinoma .

### In case of missing thread

00:20:30

Causes :

Thread coiled.

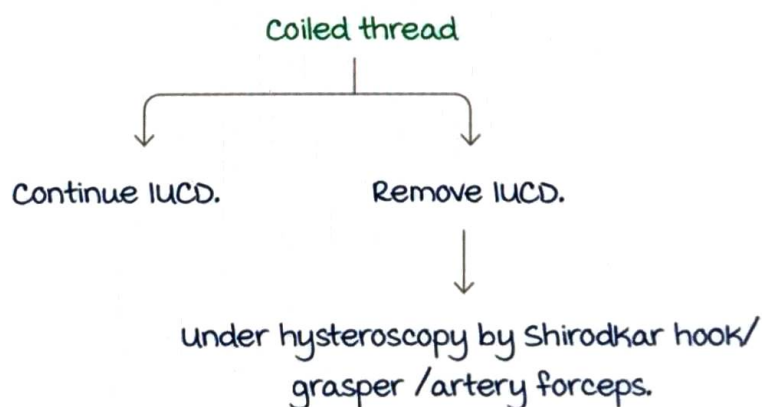
Patient has conceived (Size of uterus increased).

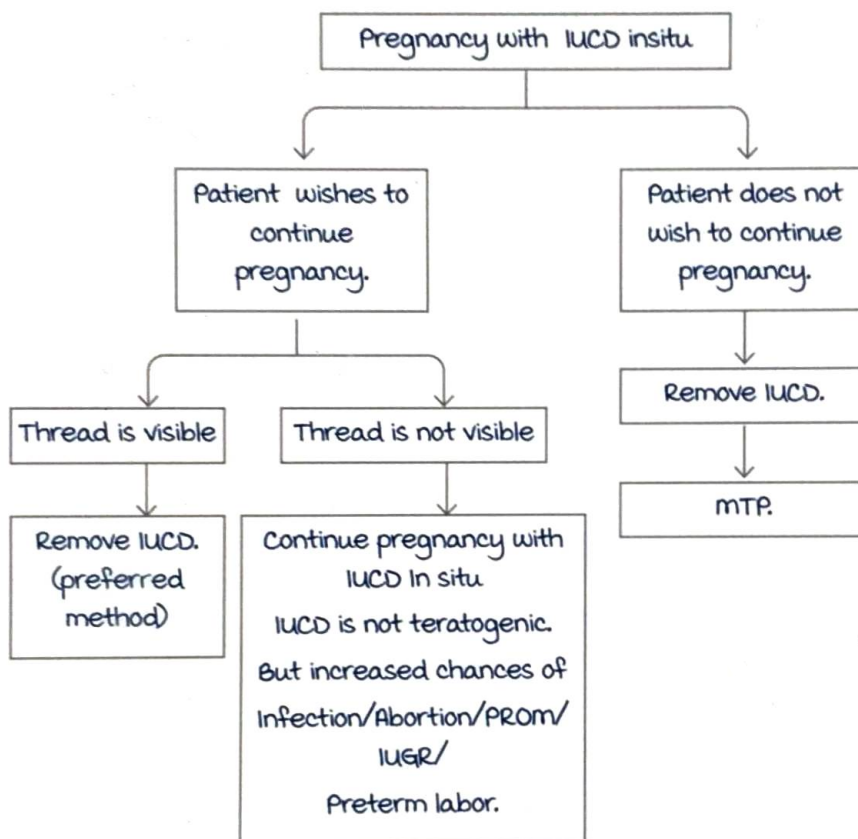
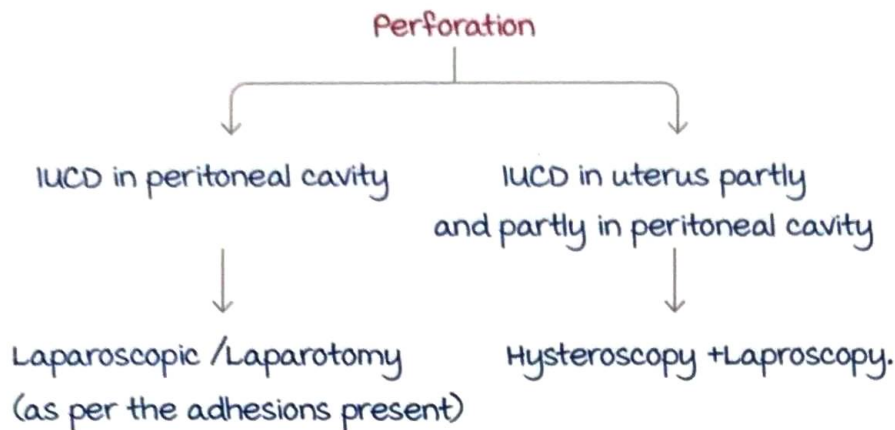
Perforation of uterus.

IUCD expelled .

First step to do is transvaginal scan :

→ Is not visible → Serial abdominal x-ray :  
IUCD is radio opaque  
Not preferred as first investigation as chances of patient being pregnant.  
(mostly) :





## LNG IUCD

00:27:10

### 3<sup>rd</sup> Generation IUCD

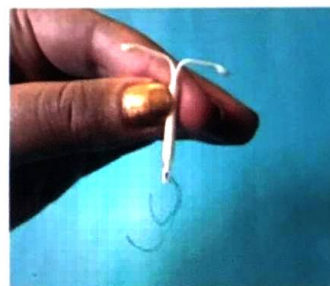
mirena : Available in India.

Not copper containing .

Contains progesterone -  
levonorgestrel (52 mg  
levonorgestrel ).

Releases 20 µg per day . So called as LNG -20.

Releases LNG for 7 years but approved life span is 5 years.



**Two newly approved hormonal IUD is by FDA** 00:28:26**Liletta :**

Similar in composition to mirena.

used up to 4 years (study still going on to see for 5 years).

It is low-cost .

**Skyla :**

13.5 mg LNG and approved for 3 years

mechanism of third generation IUCD :

**Prevent Implantation.**

Does not bring anovulation.

most common side-effects : Irregular bleeding.

Continuous use leads to endometrial atrophy and amenorrhea.

**Non-contraceptive benefits of 3rd generation IUCD** 00:30:27

- Decreased menstrual blood loss (progesterone stabilizes endometrium)

There by used in :

Abnormal Uterine Bleeding.

Fibroid.

Adenomyosis.

- Non contraceptive use of CuT:
  - CuT can be used as an emergency contraceptive (but mirena could not be used)
  - In Asherman syndrome to prevent adhesion formation after adhesiolysis/septum resection
- Levonorgestrel tablets are used as emergency contraceptive but mirena is

- **Anti-proliferative action** on endometrium.

Treatment of :

Endometrial hyperplasia without atypia

Endometriosis

**Prevention** Of endometrial carcinoma when patient on HRT/Tamoxifen therapy.

- makes cervical mucus thick.

Can prevent PID.

## Risks in Mirena

00:35:12

Absolute risk of ectopic pregnancy decreases with any IUCD so it decreases in mirena.

If failure occurs :

Increased chances of ectopic pregnancy by mirena >> CuT.

mirena is progesterone releasing and leads to **smooth muscle relaxation**.

morula moves from the fallopian tube to uterine cavity by peristalsis so the relaxation leads to **decreased peristalsis**, increasing chances of ectopic pregnancy.

Blood loss decreases in mirena (but increases in CuT).

Failure rate	Typical use	Perfect use
CuT	0.8	0.6
mirena	0.2	0.1

**minimum hemoglobin** of patient for use of IUCD is 7 g/dL.

IUCD should be disposed in red bag.

## Absolute contraindications to IUCD (Mirena + CuT) 00:38:41

Called as **WHO category 4** contraindications :

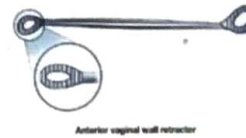
- Undiagnosed Vagina Bleeding.
- Distorted uterine Cavity :
  - Fibroid.
  - Endometrial Carcinoma.
  - Cervical Cancer.
  - Congenital Anomalies Of uterus.
- Current PID.

- Suspected Pregnancy.
- Only for CuT : Wilson's disease.
- Only for mirena : History of breast cancer.

### Instruments used for IUCD insertion

00:40:43

- Sim Speculum :  
For per speculum examination.  
Non-self retaining  
Double beveled.  
To retract posterior wall of vagina.
- Anterior vaginal wall retractor :  
To retract anterior wall of vagina.  
Have 2 loops with serrations/ fenestrations.
- To hold anterior lip of cervix 2 instruments can be used :



#### Vulsellum :

Posterior Part : Ratchet

Anterior : Concavity facing upwards & space between blades.

multiple rat like teeth on both ends helping in grasping the lip.

Hold vulsellum such that the concavity face upwards.

#### Tenaculum :

Have ratchet lock at posterior end

Anterior : Space between blades present but single tooth.

Lesser bleeding in vulsellum compared to tenaculum (post operative pain is same).

- Uterine sound :  
To measure uterine cavity :

Have sharp angle.  
Tip is olive tipped.  
Calibrated.

- Scissors : To cut of thread of CuT.

Procedure :

Before the insertion, pelvic examination is to be done.  
To assess for contraindications like undiagnosed vaginal bleeding, pelvic infection, uterine cavity distortion.

Position : Dorsal lithotomy  
No anaesthesia/analgesia.

Cleaning & draping



using sim speculum :  
Retract posterior wall of vagina



Anterior vaginal wall retractor :  
Retract anterior wall of vagina.



Vulsellum : Anterior lip of cervix.



uterine sound : measure length of uterine cavity.



Approximate length of CuT needed.



Loading of CuT .



maximum chance of infection during insertion so  
**No Touch method** used.

<p>Contents of CuT :</p> <p>CuT 380A</p> <p>Insertor (Transparent rod with depth gauge).</p> <p>Plunger (plastic rod) &amp; have thumb rest</p>
---



## Loading of CuT

00:49:34

Open halfway of packet → hold horizontal arms of CuT and squeeze it.

With the other hand pull the inserter rod little backward and hold it in pencil like manner.

Again move it forward so both horizontal arms slip inside the inserter tube.

Adjust length of inserter rod to that of uterine cavity.

Blue colored gauge (Flange) : white sheet have calibrations.

Flange set at same length of uterine length.

And then stabilized with thumb and inserter rod pulled in front so that tip of CuT coincides with the drawing of IUCD in the white packet.

After stabilizing plunger put into the inserter rod.

Loaded CuT taken inside vagina such that blue gauge lies at level of external os.

Then tenaculum and plunger stabilized.

Inserter rod withdrawn → The arms of CuT comes out → cut thread.

- misplaced CuT : Can be removed using hysteroscopic grasper.

## PERMANENT METHODS OF CONTRACEPTION

### Tubal ligation

00:00:41

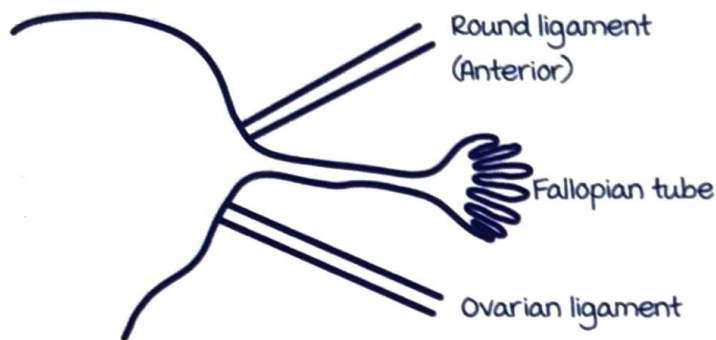
Permanent method of family planning for females.

Effective **immediately**.

Requires **only** the consent of the female, not of partner.

Site : **Isthmus** → junction of proximal and middle 1/3<sup>rd</sup>

Structures anterior to posterior



methods of tubal ligation :

- Laparoscopic tubal ligation.
- minilaparotomy.

Structures from anterior to posterior : mnemonic **RTO**.

**R**ound ligament.

**F**allopian tube

**O**varian ligament.

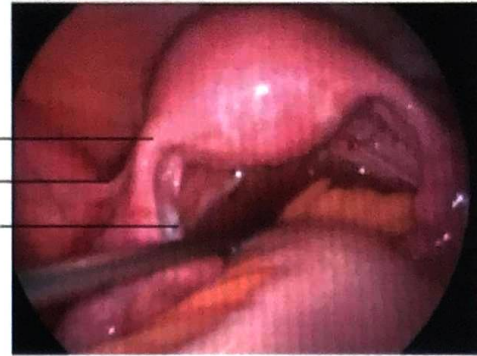
During laparoscopy, the patient's left coincides with doctor's left, same goes for right → stands at head end of the patient.

Fallopian tube is the **superior** ~~most~~ structure.

During hysteroscopy, patient's left coincides with doctor's right, right with doctor's left → standing at the foot end of the patient.

Active space

Left fallopian tube ←  
 Left round ligament ←  
 Left ovarian ligament ←

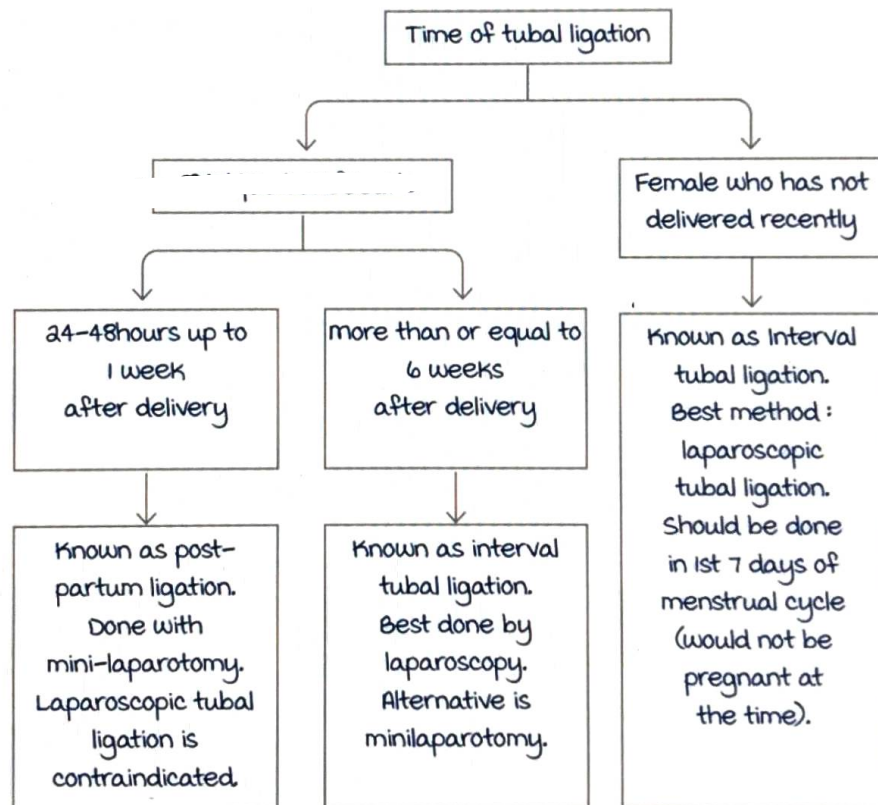


Failure rate : 1 in 200 pregnancies.

most cause of failure → identification of wrong structure.

Can be prevented by :

- Trace the tube from the fimbrial end.
- After tubal ligation, the resected specimen must be sent for histopathological examination.



Laparoscopic tubal ligation is contraindicated in immediate post-partum tubal ligation → uterus would be just below the umbilicus, and insertion of laparoscope can cause perforation of uterus.

Active space

If the tubal ligation is not done within 1 week of delivery, it is done after 6 weeks.

most common method of tubal ligation is laparoscopic method.

most common method of post-partum tubal ligation is minilaparotomy.

### Laparoscopic tubal ligation / sterilization

00:11:15

Gas used is CO<sub>2</sub>.

Pressure : 8- 12 mm of Hg (should always be <15mm of Hg).

maximum volume of gas for attaining pneumoperitoneum is 2L.

Pneumoperitoneum created by : Verres' needle.

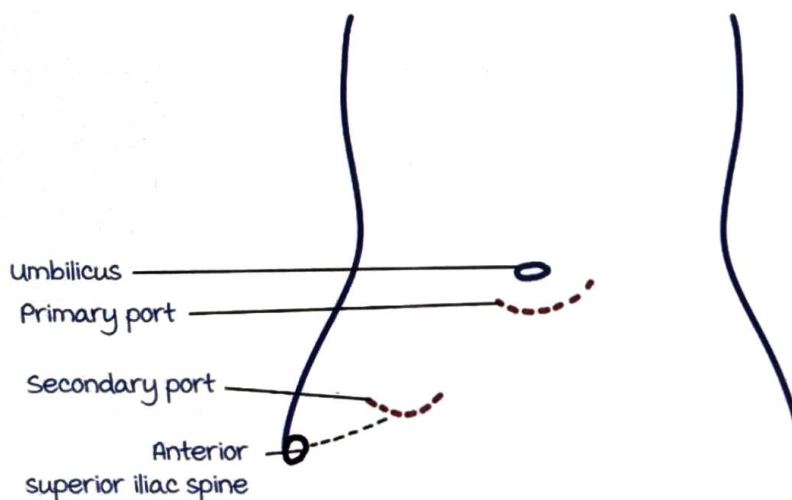
Incisions made :

Primary port → **Infraumbilical**: ~2cm below the umbilicus.

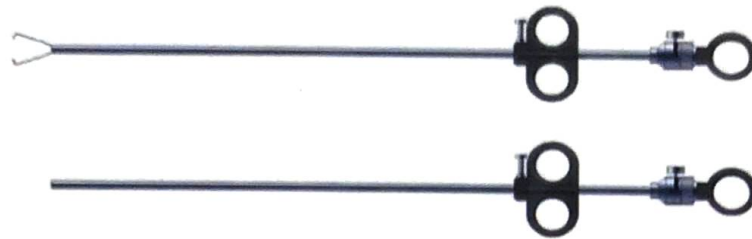
- Camera and laparoscope inserted.

Secondary port → 2cm above and 2cm medial to anterior superior iliac spine.

- Ring applicator loaded with two falope rings.



## Fallopian ring applicator



Extended tip

Extended tip  
with (1) silastic ringsExtended tip  
with (2) silastic rings

## Procedure :

Pneumoperitoneum is made.

The two incisions are made for primary and secondary ports.

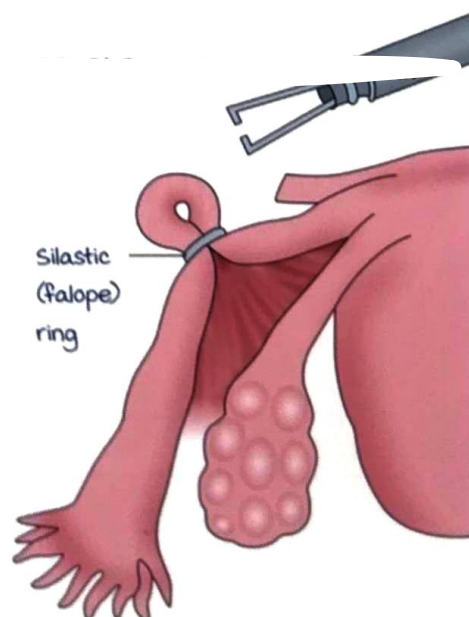
The ring applicator in the secondary port → grasps the isthmus of the tube, and releases the falope ring onto a 2.5cm loop of the tube.

Laparoscopic tubal ligation can also be done with :

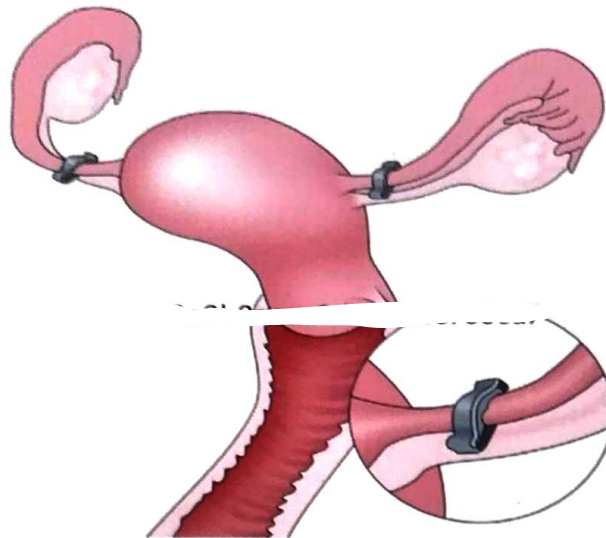
Hulka clip.

Filshie clip.

In India → falope rings are used.



Falope ring applied with ring applicator



Clips applied on the fallopian tube

Damage to the tube :

In ring applications → 3cm.

In clip applications → 4- 5mm.

- Less damage means easier reconstruction of tube.
- Preferred in young females who may need recanalization later.
- Preferred in tubectomy after abortion → the tubes are swollen on application → can cause the falope rings to become loose.

Laparoscopic tubal ligation cannot be done in post - partum period.

Done as a method of interval sterilization.

Another method of laparoscopic tubal ligation → electrocautery of the tube.

Bipolar or monopolar cautery is used.

Disadvantages are :

Thermal injury to adjacent structures like the bowel.

High risk for ectopic pregnancy.

## Minilaparotomy

00:17:44

Small incision (2-3cm).

Tubes delivered out of the incisions and ligated.

Can be done in post-partum period and interval sterilization.

Procedure :

Done under regional anaesthesia.

Patient's bladder should be empty.

Small incision given.

- Infraumbilical area in post-partum tubal ligation.
- 2 finger breadth above pubic symphysis in interval sterilization.

Open the abdomen through the incision.

Fingers of the surgeon are inserted into the opening → fundus of the uterus is traced.

Tube is palpated by tracing it laterally.

Fallopian tube is brought outside.

- ensure that it is fallopian tube by tracing it from the fimbrial end.

Procedure completed by tubal ligation, replacing the tube inside and suturing the wound.

methods of tubal ligation :

Pomeroy technique :

most commonly performed technique.

Loop of tube made at the isthmus area.

Base of the loop sutured with rapidly dissolving suture → single or double ligation.

The loop of tube is cut

Original Pomeroy method used chromic catgut sutures.

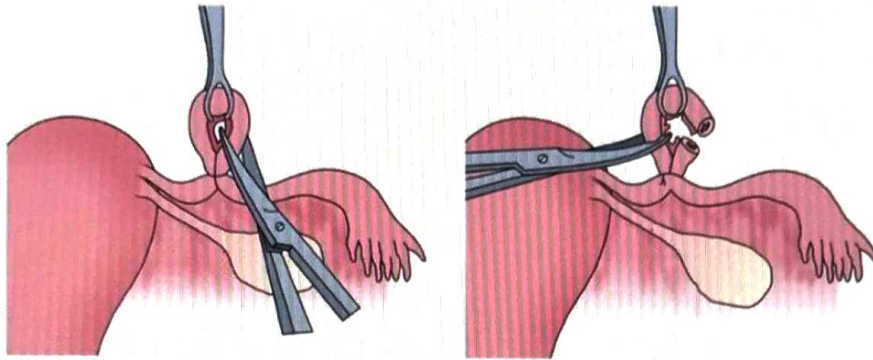
modified Pomeroy uses plain catgut → more rapid than chromic catgut.

Loop should be made such that 2cm of tube is removed.

Loop should be cut through entire thickness and lumen should be inspected.

Ends of the tube are separated after the suture dissolves.

Instrument used to hold the tube : Babcock's forceps.



Loop of tube removed after suturing

Parkland technique :

A window is created in the avascular region of the mesosalpinx.

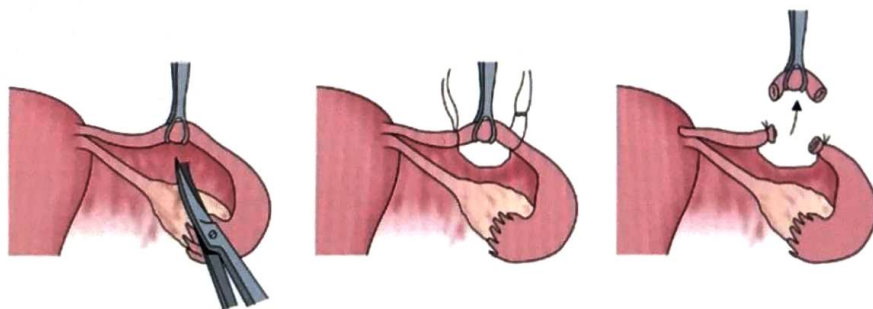
Loop of the isthmus made.

Double ligation done.

The segment between the double ligation (acm) is sharply incised.

Ends are immediately separated.

Chromic or plain catgut suture used.



mesosalpinx window made

Double ligation of tubes

Segment of tube removed

Less commonly preferred methods :

Irving method and uchida method.

Both techniques involve burying the tubal stump in a nearby structure.

Active space



Developed to minimise the tubo-peritoneal fistula formation and contraceptive failure.

Disadvantages :

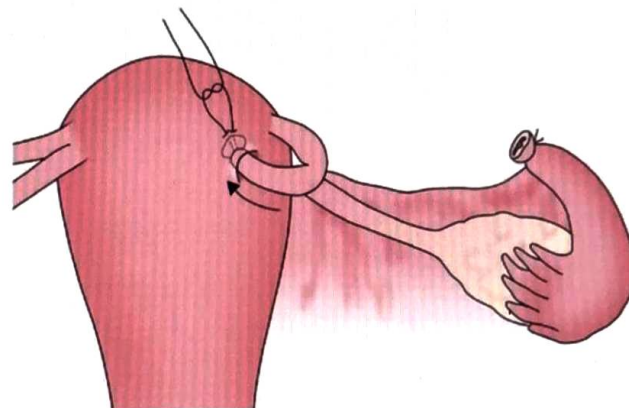
- more extensive dissection.
- Increased operative time.
- Increased chances of bleeding.
- Feasible only at the time caesarean section and not via mini-lap incision after vaginal delivery.

Irving method :

Double ligation and excision of the midportion of the tube.

Burying of proximal end of the tube into an incision made in myometrium.

The stump is sutured into the myometrium.



Irving's method of tubal ligation

Uchida method :

Hydro dissection is done → injecting serosa of the tube with normal saline and epinephrine.

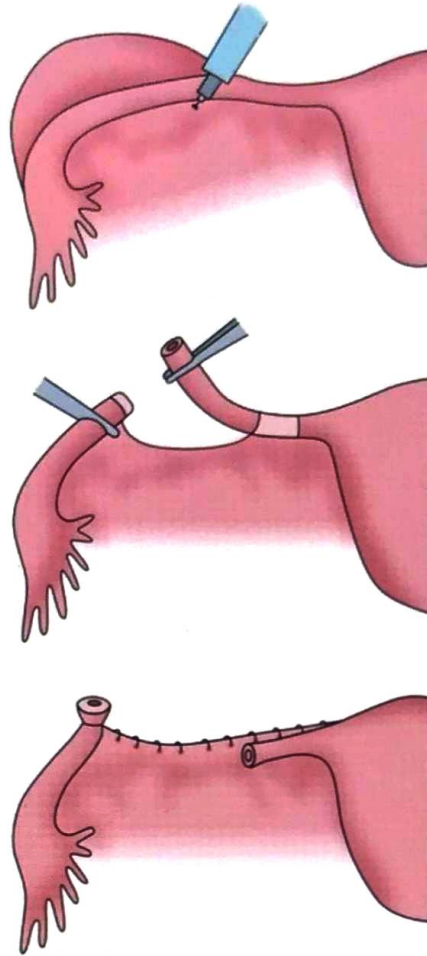
Serosa swells → incision at the antimesenteric border.

Muscular part of the tube is separated by Babcock's forceps.

Tube is cut.

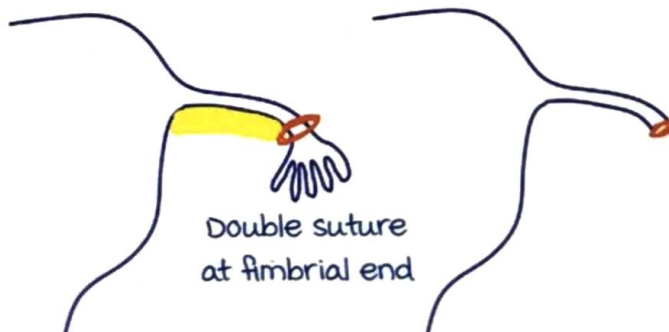
Proximal end is tied and left inside serosa → retracts and goes back into the uterus.

Distal end is stitched along with the serosa with purse string suture method.



uchida method of tubal ligation

Kroener's fimbriectomy :  
 Double ligation at fimbrial end.  
 Fimbrial end is then cut.  
 No longer done.



Least failure rate : cautery > uchida > Irving > modified Pomeroy > Pomeroy.  
 Chances of recanalization : Clips > Falope ring > Pomeroy > modified Pomeroy > Irving > uchida > Cautery.

Active space

Recanalization or reversal depends on :

At least 4cm of tube can be reconstructed.

Least possible tube is damaged.

- minimum with cautery as the damage to tube is maximum.

Isthmo - isthmic anastomosis has best prognosis.

### Essure device

00:33:19

Hysteroscopic method for permanent sterilisation.

Essure :

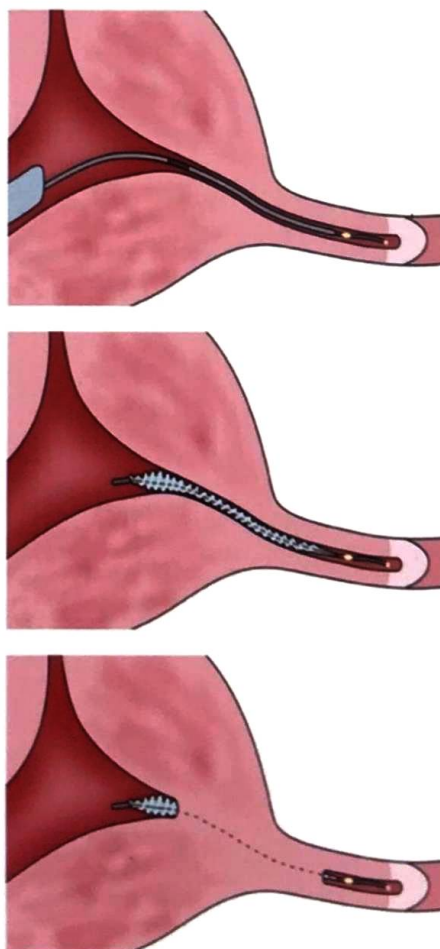
Spring like device.

Inserted in the intramural or interstitial part of the tube.

Done via hysteroscope.

Outer cylinder : nickel and titanium.

Inner cylinder : stainless steel.



Essure device and tubal blockage

mechanism of action :

Irritates the fallopian tube → initiates a tissue reaction → inflammation and blockage of the tube.

Blockage is **not immediate** → contraception is not immediately effective.

Back up contraceptive method needed for 3 months.

After 3 months, hysterosalpingography (HSG) done and bilateral blockage confirmed → back up contraceptives are stopped.

Success rate : **99%**.

To ensure proper placement of Essure → transvaginal sonography (TVS) or HSG.

To ensure **complete blockage** after 3 months → HSG.

Complications :

Could cause perforation of tube/ uterus.

Persistent pain.

Allergic / hypersensitivity reactions.

It is **irreversible**.

Contraindications:

Acute / recent ~~pericervicitis~~ ~~peritonitis~~ ~~infection~~

uterine / tubal pathology blocking access to tubal ostia.

**<6 weeks** after delivery.

Suspected unicornuate uterus.

Allergic to the metals.

## Vasectomy

00:37:59

method of male sterilization.

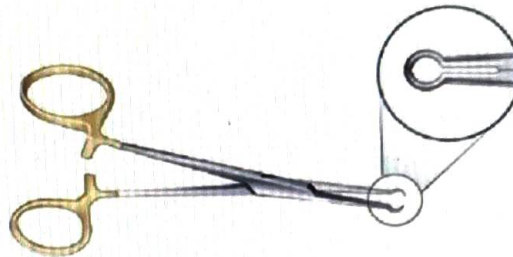
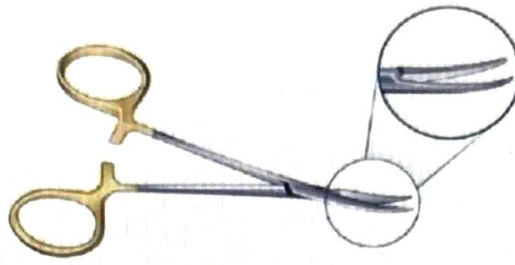
A segment of **vas deferens** is cut.

Conventional vasectomy : incision on scrotal skin.

No scalpel vasectomy :

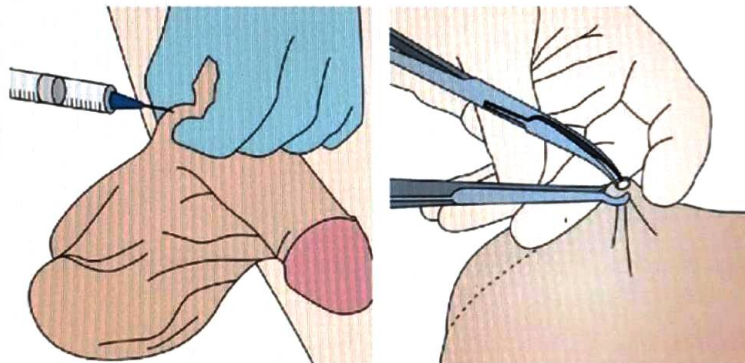
**No incision** in scrotal skin.

## Instrument used in non scalpel vasectomy



Skin is punctured using :

- Sharp dissecting forceps / hemostat.
- Ringed clamp.



under local anesthesia- no scalpel vasectomy

Forceps has ratchet lock at the end, unlike scissors.

Done under local anesthesia → ilioinguinal nerve and genital branch of genitofemoral nerve are anesthetised.

OPD procedure.

The scrotal skin is disinfected and covered with a sterile drape. After stabilising the vas deferens → vas deferens pulled → loop of vas made and ligated → either cut or cauterised.

Advantages of no scalpel vasectomy :

No incision on scrotum → patient can resume sexual

activity early.

Sexual activity can be resumed 7 days after no scalpel vasectomy.

No hospitalisation.

Chances of hematoma formation, infection, post operative pain are less than conventional vasectomy.

Failure rate : 0.1%.

males do not become sterile immediately after vasectomy. Sperms that remain in the ductal system would be ejaculated.

Back up contraceptive methods needed for 3 months / 15-20 ejaculates.

After 3 months semen analysis is done → azoospermia seen → back up contraceptives stopped.

Precautions after the procedure :

Scrotal support for 48hours.

Intermittent ice packing for 24- 48hours.

No weight lifting, exercise or sexual activity for 1 week (7 days).

Work involving light activities can be resumed from second day.

No hospitalisation, but advisable to have a bystander to drive them back home.

Reversal of vasectomy :

Done by microsurgery by vasovasostomy.

Post reversal :

- Fertility returns in 90%.
- Pregnancy occurs in 70%.

## Instruments

00:47:45

minilaparotomy by Pomeroy technique :

Babcock's forceps :

Hold the fallopian tube.

Proximal end is like a question mark (?).

There is a gap between the two ends.

Landon's retractor :

Retract skin and abdominal wall.

Narrow bladed.

L-shaped retractor.

If not available → Czerny retractor used.

metzenbaum scissors :

Distal part longer than the proximal part.

used to cut the loop.

Structures incised in conventional vasectomy :

From outside to inside.

- Skin.
- Dartos muscle and its fascia.
- External spermatic fascia.
- Cremasteric muscle and its fascia.
- Internal spermatic fascia.
- Spermatic cord with vas deferens and neurovascular supply to testis.

## MISCELLANEOUS CONTRACEPTION

### Centchroman

00:00:37

Non steroidal contraceptive pill.

Introduced in 1991 by SGPI Lucknow.

Earlier known as Saheli.

Nowadays by the name Chhaya :

Included in National family planning programme.

Active ingredient : Ormifloxifene (SERM).

Action:

It acts by making endometrium out of phase and inhibits implantation.

Important side effect :

- Delays menstrual cycle.
- Return in fertility occurs 6 months after stopping the drug.

It does not protect against pelvic inflammatory diseases.

Can be used as emergency contraception.

Dosage :

Contraceptive dose : Each tab 30 mg , twice a week for first 3 months and then weekly.

Long acting reversible contraceptives (LARC) methods :

- IUCD's.
- Implants.
- Injections : DMPA.

### Emergency contraception

00:02:28

If contraception is taken after unprotected intercourse : emergency contraception or interception.

No test needed before giving them.

mechanism of action :

Delays ovulation (not anovulation)

Inhibits implantation (second best answer).



Never act after implantation i.e they are not abortifacient.  
Ideally used within 72 hrs of unprotected intercourse but can be used uptill 120 hrs i.e 5 days.

- most effective emergency contraception : **Cu T.**
- most effective emergency contraceptive, On 5th day :  
**Cu IUCD.**
- most effective hormonal emergency contraceptive :  
**ulipristal** (30 mg single dose) > mifepristone (10-50 mg single dose) > Levonorgestrel (1.5 mg single or two divided doses 12 hrs apart).
- most common emergency contraceptive used :  
**Levonorgestrel.**
- Yuzpee method :  
use of OCP as emergency contraceptive.  
100 mcg Ethinyl estradiol initially, repeat after 12 hours.  
High dose pills (>50 mcg ethinyl estradiol) : 2 tabs initially, 2 tabs after 12 hours.  
Low dose pills : 4 tabs initially, 4 after 12 hours.
- **E pill** : contains levonorgestrel.
- Centchroman : 2 tabs (60 mg) initially, after 12 hrs a more tabs.
- most effective hormonal emergency contraceptive on 5th day : **ulipristal.**

Drugs not used as emergency contraceptive :

- Progesterone only pills.
- mirena.
- misoprostol.

**Post abortal contraception :**

Return of ovulation : Occurs within 21-29 days after procedure.

All females are advised to use contraception after first and second trimester abortion.

Timing :

All contraceptives can be started immediately after abortion (OCP, progesterone only pills, progesterone injection, implants, IUCD).

In case of surgical abortion :

- Started from **day of procedure**.
- **No backup** needed.

If started up till 7 days of procedure :

- Backup needed for **7 days** for all methods.
- Except for progesterone only pills : Backup of **2 days** needed.

Spontaneous abortion / medical abortion :

- Where exact day of demise of fetus is not known.
- Start as soon as one is sure that **uterus is completely evacuated** of the products of conception.
- Within one week (back up needed for **7 days**).

methods which cannot be used immediately after abortion :

1. Diaphragm.
2. Natural methods of family planning.

### Contraception in postpartum females

00:13:55

**Rule of three :**

- Non breast feeding female / partially breast feeding :  
**3 weeks** after delivery.
- Exclusively breast feeding female :  
**3 months** after delivery.

1. Condoms (male) can be used from Day 1.
2. IUCD insertion :
  - Can be inserted in **breast feeding & non breast feeding** females.
  - Post partum insertion : **within 48 hours** of delivery.
  - If not inserted within 48 hours, then **after 6 weeks** of delivery.
3. minilaparotomy :
  - Postpartum : **1 week** after delivery.
  - Thereafter : **6 weeks** post delivery.
4. Emergency contraception : **After 4 weeks** of delivery.

5. Centchroman :

- No contraindications.
- Can be used from **day 1** after delivery.

6. Steroidal contraceptives :

Estrogen - progesterone contraceptives :

2 concerns :

- Estrogen **decreases breast milk**.
- Estrogen **increases clotting factors** → Increased chance of venous thrombo embolism.
- Hence used with caution.

Progesterone only contraceptives :

Do not have the above disadvantages.

Contraception	Fully breast feeding	Partially breast feeding
OCP's	<ul style="list-style-type: none"> <li>• Absolutely contraindicated: <math>\leq 6</math> weeks of <del>breastfeeding</del> delivery.</li> <li>• Ideally started: <math>\geq 6</math> months of delivery.</li> </ul>	<ul style="list-style-type: none"> <li>• Absolutely contraindicated: <math>\leq 3</math> weeks of <del>breastfeeding</del> delivery.</li> <li>• Ideally started: <math>\geq 6</math> weeks of delivery.</li> </ul>
Progesterone only pills	<ul style="list-style-type: none"> <li>• Not contraindicated.</li> <li>• Can be started from <b>day 1</b> of delivery.</li> </ul>	<ul style="list-style-type: none"> <li>• Not contraindicated.</li> <li>• Can be started from <b>day 1</b> of delivery.</li> </ul>
Progesterone implants	<ul style="list-style-type: none"> <li>• Not contraindicated.</li> <li>• Can be started from <b>day 1</b> of delivery.</li> </ul>	<ul style="list-style-type: none"> <li>• Not contraindicated.</li> <li>• Can be started from <b>day 1</b> of delivery.</li> </ul>

DMPA injection	<ul style="list-style-type: none"> <li>• Contraindicated till <b>6 weeks</b> of delivery.</li> <li>• Causes <b>decrease</b> in bone mineral density.</li> </ul>	<ul style="list-style-type: none"> <li>• Not contraindicated.</li> </ul>
----------------	---	--

### Important conditions & contraception of choice

00:20:29

Condition	Contraception of choice
Female has hirsutism.	OCP's with <b>3<sup>rd</sup></b> or <b>4<sup>th</sup></b> generation progesterone.
HIV positive females/ women with multiple sex partners, who are greater risk of STI.	<ul style="list-style-type: none"> <li>• <b>IUCD + Barrier method.</b></li> <li>• Second best : IUCD.</li> <li>• Third best : Barrier.</li> </ul>
Pregnancy with cyanotic heart disease & pulmonary vascular disease.	<ul style="list-style-type: none"> <li>• <b>Implanon / IUCD mirena</b> are best.</li> <li>• Cu IUCD can be used, but is <del>not recommended</del> women who are anemic or cyanotic due to increased blood loss.</li> <li>• Tubal ligation can be done.</li> <li>• Depo provera is inappropriate for patients with heart failure due to its tendency to cause fluid retention.</li> <li>• OCP's can also be used only in patients with low risk of thrombotic events : Not preferred contraceptives.</li> </ul>
Female with SLE.	<b>Progesterone IUCD &gt; Implant.</b>

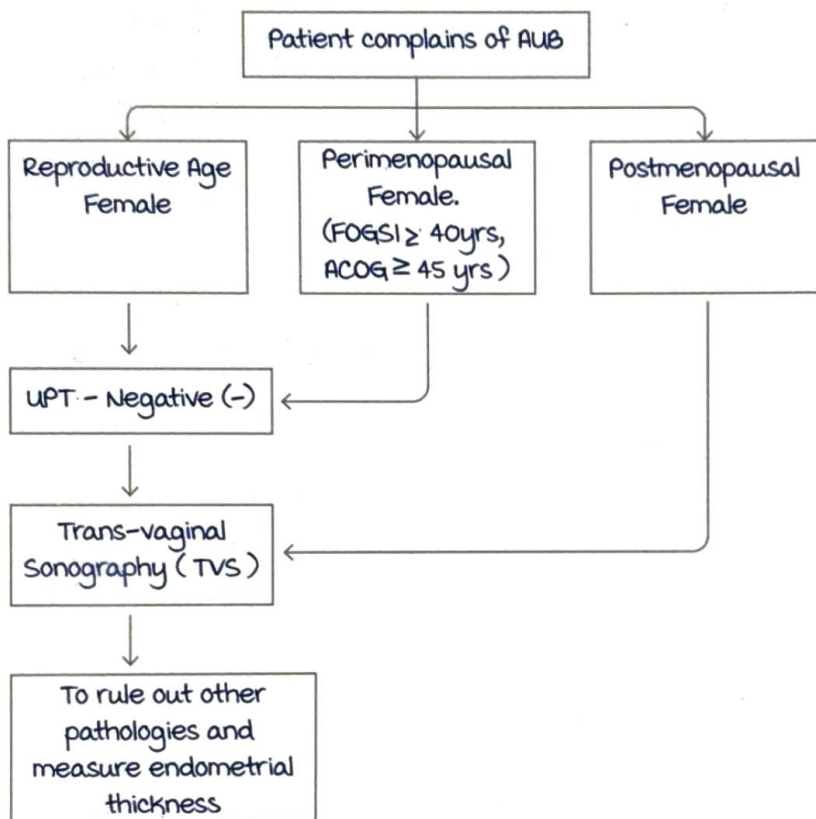
Active space

Female with endometriosis, pain and needs contraception.	Progesterone containing contraceptives : Implants, injections or IUCD.
Female with epilepsy / sickle cell anemia.	DMPA.
Obese female > 40 years.	Progesterone contraceptives: LNG IUCD better than Cu IUCD.
Female with menorrhagia or with bleeding disorder.	LNG IUCD.
Female on anticoagulants.	Progesterone containing contraceptives.
Lactating female.	Progesterone only pills. Govt of India recommends Post partum IUCD insertion.
Newly married couple living together.	Oral contraceptive pills.
Newly married couple living in 2 different cities.	Barrier methods.

## ENDOMETRIAL HYPERPLASIA

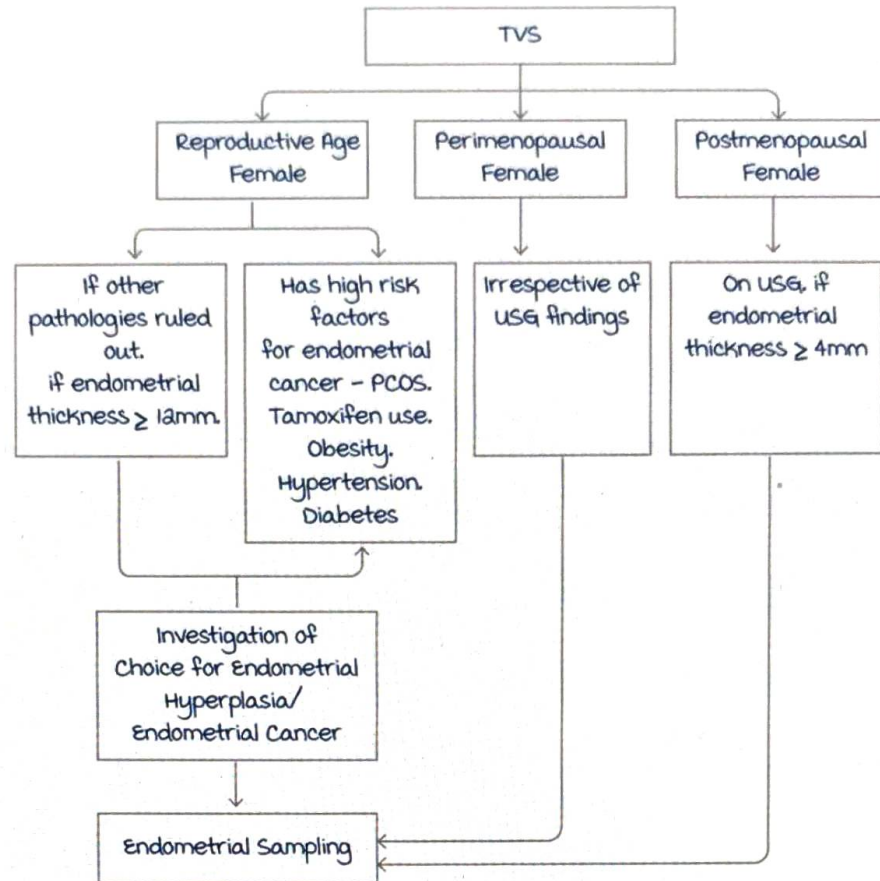
In endometrial hyperplasia, there is **excess proliferation of the uterine endometrium** due to excess **estrogen** → **AUB** (Atypical uterine bleeding).

Endometrial hyperplasia is histopathological diagnosis.



### Causes of AUB - PALM COEIN

- **P** - Polyp.
- **A** - Adenomyosis.
- **L** - Leiomyoma.
- **m** - malignancy and Hyperplasia (Endometrial).
- **C** - Coagulopathy.
- **O** - Ovulatory Dysfunction.
- **E** - Endometrial.
- **I** - Iatrogenic.
- **N** - Not otherwise classified.



## Method of Endometrial Sampling

00:07:09

methods : (Both are OPD Procedures , done without anaesthesia):

- Endometrial Biopsy.
- Endometrial aspiration cytology ( EAC ) : Preferred.
  1. Karman's Cannula (India).
  2. Pipelle / Vabra Aspirator.

Case Scenario :

A 46yr old female complains of AUB with UPT negative. On TVS, 3x2cm intramural fibroid is seen. Next step ?

In all postmenopausal bleeding patients, if endometrial thickness ( ET )  $\geq 4\text{mm}$   $\rightarrow$  Endometrial Sampling.

Along with Endometrial Sampling  $\rightarrow$  Do pap smear to rule out carcinoma cervix.

MC cause of postmenopausal bleeding : Atrophic vaginitis / Senile vaginitis.

Report of endometrial sampling :

New Classification -

- Endometrial Hyperplasia present without atypical features.
- Endometrial Hyperplasia present with atypical features → also called endometrial intraepithelial neoplasia.

Earlier Classification -

- Simple hyperplasia without atypical features : 1%  
Also known as cystic glandular hyperplasia
- Complex hyperplasia without atypical features : 3%
- Simple hyperplasia with atypical features : 8%
- Complex hyperplasia with atypical features : 30%

Chances of malignancy

Condition	Glandular stroma ratio	Overcrowding of glands	Atypical nuclear features
Normal endometrium	< 1:3	No	No
Endometrial hyperplasia without atypia	> 1:3	mildly crowded glands (dilated) with luminal outpouching.	No
Endometrial hyperplasia with atypia	> 1:3	Overcrowding prominent. Disorganised glands with luminal outpouching.	Present

Active space



MC presentation of endometrial hyperplasia : AUB.

Other less common presentations :

- On routine pap smear : AGUS ( Atypical glandular cells of unknown significance ).
- Suspect endometrial hyperplasia, endometrial carcinoma, adenocarcinoma of cervix → Endometrial sampling for diagnosis.
- Postmenopausal female with no complaints of bleeding, but on USG → endometrium is thick (incidental finding).
- Incidental finding on hysterectomy.
- metropathia haemorrhagica.

Examination :

- Per abdomen : Normal.
- Per Vagina : Normal.

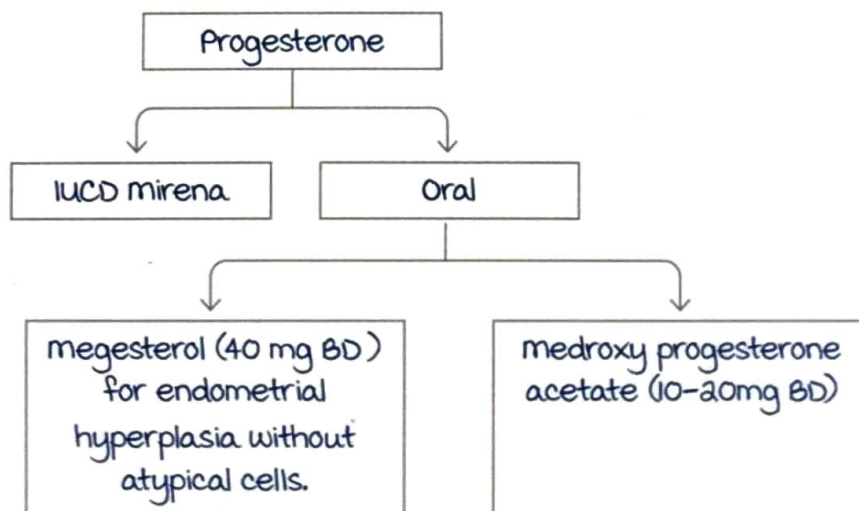
management of endometrial hyperplasia / EH without atypia (cystic glandular hyperplasia) :

- Chances of progression to cancer : <10%.
- Chances of concomitant cancer : <1%.

Best management / drug of choice :

Progesterone - has anti proliferative action , decidualisation action of endometrium making it thin.

2<sup>nd</sup> line drugs : Oral combined pills (OCP).



Preferred : mirena > oral progesterone (for EH).

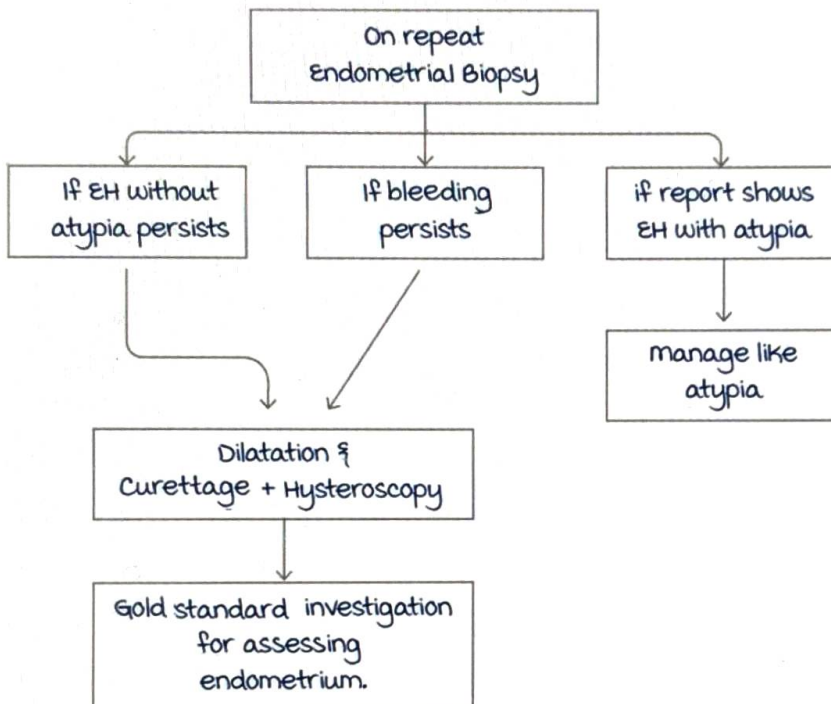
If patient denies using mirena / if contra-indications present → Oral progesterone (megestrol) is preferred.

Oral dosage :

- Continuous (preferred).
- Cyclical - progesterone given for 12-14 days in a month, no drug for the rest of the days.

Follow up :

Endometrial biopsy every 3 - 6 months for 1 year.



If a post-menopausal female with increased endometrial thickness on USG & no post-menopausal bleeding with Endometrial thickness (ET)  $\geq 11$  mm or Endometrial fluid is present & ET  $> 3$ mm } Endometrial biopsy.

If a post-menopausal female with endometrial thickness  $< 4$ mm on USG & has post-menopausal bleeding → Reassurance + tranexamic Acid.

If bleeding persists → Dilatation & Curettage + Hysteroscopy.

MC cause of post-menopausal bleeding : Atrophic endometritis / Senile endometritis.

## Dilatation & curettage & Hysteroscopy

00:27:04

Gold standard method to assess endometrium in :

- EH.
- Endometrial carcinoma.
- Post-menopausal bleeding.

**Fractional curettage** : uterus is divided into various fractions & each fraction is curetted separately.

**Fractional curettage > Dilatation & Curettage (D&C).**

**Dilatation & Curettage > Hysteroscopy.**

Hysteroscopy is best for focal lesions (see & take biopsy).

Dilatation & Curettage + Hysteroscopy are done in OT under anesthesia.

## Management of endometrial hyperplasia/EH with atypia

00:30:15

- Chances of progression to cancer : up to 40%.
- Chances of concomitant cancer : up to 40%.

So if report says EH with atypia : **D&C + hysteroscopy / Fractional curettage + hysteroscopy** (to make sure endometrial cancer isn't present).

Best management :

Premenopausal : **Total Abdominal Hysterectomy (TAH) / simple hysterectomy** (uterus + cervix).

Postmenopausal : **TAH + Bilateral Salpingo-Oophorectomy (BSO).**

If female  $\geq 45$  yrs : **TAH + BSO.**

Now, TAH + bilateral salpingo-oophorectomy (BSO) is not preferred in perimenopausal females.

Perimenopausal women : **TAH.**

Indications for **D&C + hysteroscopy / Fractional curettage + hysteroscopy** :

- Endometrial biopsy  $\rightarrow$  Atypical EH.
- Endometrial biopsy : Insufficient / inadequate sample.

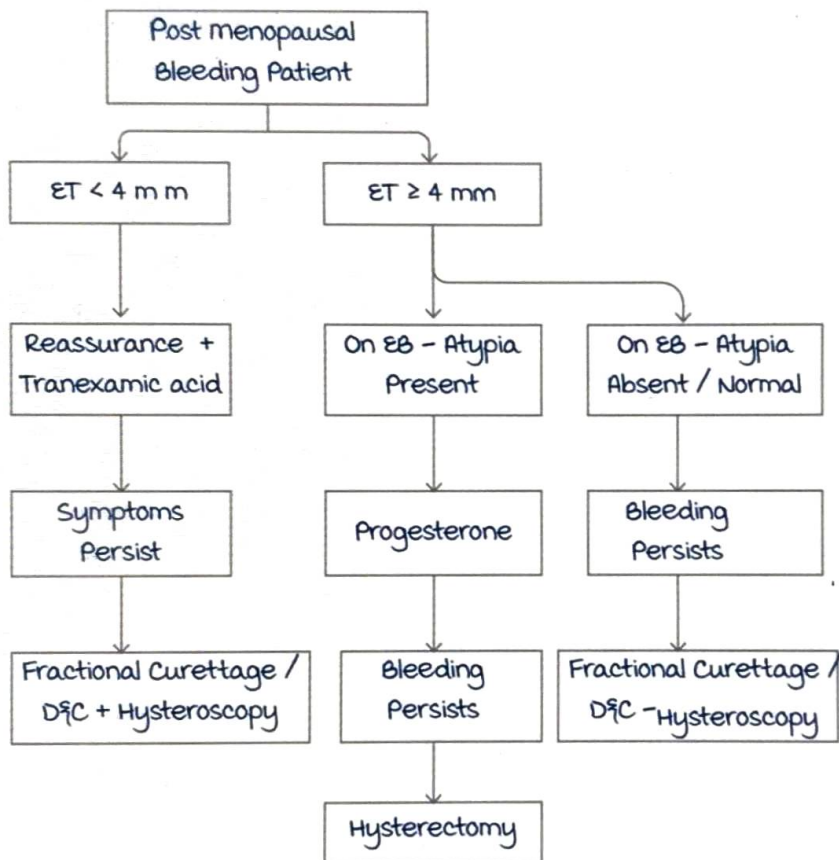
- In cases of cervical stenosis.
- If endometrial biopsy is normal but persistent bleeding.

If patients with AUB, on EB - EH with atypia, refuses hysteroscopy :

Drug of choice : Progesterone → mirena / megestrol.

Follow up - Endometrial biopsy every 3-6 months for 2 years.

Persistent Bleeding / EH with atypia : Hysterectomy.



## Metrorrhagia haemorrhagica

00:40:52

Seen in 40-45 yrs.

Female with a typical history of amenorrhea for 2 months (8 weeks) followed by excessive bleeding.

Cause - Anovulation.

On HPE of endometrium :

- Proliferative endometrium ; atypia absent.
- Swiss cheese appearance.

On USG, ET is increased.

It resembles Simple hyperplasia without atypia.

Risk of malignancy : 1%.

Treatment of choice : Progesterone (Mirena).

# ENDOMETRIAL CANCER

## Endometrial cancer

00:00:08

It is a **hyperestrogenic** condition.

Risk factors can be related to :

- Excessive **estrogen**.
- Increased **ovulation**.

Risk factors : mnemonic : **Family Has OLD AUNT**.

Family history.

Hypertension.

Obesity.

Late menopause & early menarche.

Diabetes mellitus.

Atypical endometrial hyperplasia.

Unopposed estrogen : **PCOS** or **granulosa cell tumor** of the ovary.

Nulliparity.

Therapies like :

- Tamoxifen therapy : Selective estrogen receptor modulator (SERM) used for managing breast cancer. It has **antagonist effect** on breast and **agonist effect** on endometrium.

Raloxifene does not lead to endometrial cancer → does not have any **effect** on the **genitourinary tract**.

- Hormone replacement therapy.

If **estrogen alone** is given, when uterus is intact → leads to **endometrial cancer**.

When **Estrogen and Progesterone** are given, it increases the risk of **breast cancer**.

**Corpus cancer syndrome** :

Increased chance of endometrial cancer in an **obese, diabetic, hypertensive female**.

Familial inheritance :

Presence of **Lynch II syndrome** : 60- 70% increased chances for endometrial cancer.

- Genes involved in Lynch II syndrome : **MLH- 1** and **MSH- 2**.
- The **most common** cancer associated with Lynch II syndrome : **Colon cancer**.
- The **second most common** cancer associated with Lynch II syndrome : **Endometrial cancer**.

Mutation in **BRCA1** and **BRCA2** also leads to endometrial cancer (most commonly associated with ovarian cancer).

**Cowden syndrome** :

Mutation of **PTEN gene** on **chromosome 10**.

Associated with endometrial cancer in 20- 30% cases.

**PTEN gene** : **Gatekeeper gene** for endometrial cancer.

Familial inheritance that causes endometrial cancer :

**Lynch II syndrome** > **Cowden syndrome**.

Protective factors :

Factors that **decrease estrogen** or **decrease ovulation**.

- Physical exercise.
- Smoking : Inhibits the enzyme aromatase, increasing the metabolism of estrogen.
- Multiparity.
- Pregnancy.
- OCPs.
- Breast feeding.

## Classification of endometrial cancer

00:09:22

Based on types : **Type I** and **Type 2**.

Based on histological variety :

- **most common** histological variety is **adenocarcinoma (endometrioid variety)**.
- **most malignant** one is the **clear cell variety** > **serous/ papillary serous variety**.

Based on the grade :

Grade 1 : Well differentiated.

Grade 2 : moderately differentiated.

Grade 3 : Poorly differentiated.

Type 1 (80%)	Type 2 (20%)
Includes adenocarcinoma grade 1 and grade 2	Includes : Adenocarcinoma grade 3. Clear cell carcinoma. Papillary serous tumors.
Related to increased estrogen.	Not related to estrogen.
more common in obese females. Associated with endometrial hyperplasia.	more common in thin females. Not associated with endometrial hyperplasia.
Gene mutation seen : KRAS, PTEN.	Gene mutation seen : p53.
Seen in comparatively younger females (50- 60years).	Seen in older females (65- 70years).
Good prognosis.	Bad prognosis.

In Cowden syndrome and HNPCC mutation/Lynch syndrome :  
Type 1 endometrial carcinoma.

MCQ :

Which of the following have the highest risk of endometrial cancer ?

- A. Lynch syndrome.
- B. Cowden syndrome.
- C. BRCA1 gene mutation.
- D. BRCA2 gene mutation.

Q. 45 years old female with Cowden syndrome complains of heavy menstrual bleeding. On EB-endometrial cancer was detected. What is the most likely histology of the cancer as stated in the report

- A. Endometrioid type 1 cancer.
- B. Endometrioid Type 2 cancer.
- C. Clear cell cancer.



D. Histology of cancer cannot be known through endometrial biopsy.

most common age for endometrial cancer is 60 years (5-7<sup>th</sup> decade).

most common symptom is irregular bleeding > post-menopausal bleeding.

most specific symptom is post-menopausal bleeding.

Only 10% of post menopausal bleeding is due to endometrial cancer.

## Investigations

00:18:43

1<sup>st</sup> investigation to be done is TVS.

Endometrial thickness is measured.

As the patient may be post menopausal, endometrial sampling is done if the endometrial thickness is :

- $\geq 5\text{mm}$  as per FIGO.
- $\geq 4\text{mm}$  as per ACOG.

(If both values are given : Endometrial biopsy is done when endometrial thickness  $>4\text{mm}$ ).

Endometrial sampling can be done by two techniques :

Endometrial biopsy.

Endometrial aspiration cytology (Less painful).

Both are OPD procedures and IOC.

The difference lies in the instrument used,

- Endometrial biopsy : Done using Endometrial biopsy curette.
- Endometrial aspiration cytology : Done using Karman cannula in India and a pipelle or Vabra aspirator in developed countries.

Endometrial sampling is the IOC in uniformly thickened endometrium (endometrial aspiration cytology > endometrial biopsy).

In a localized thick endometrium, the IOC after TVS is hysteroscopy and biopsy.

Indications for endometrial biopsy :

- Post-menopausal bleeding with endometrial thickness > 4mm.
- AUB patient with age  $\geq$  45 years.
- Reproductive age with endometrial thickness > 12mm.



Gold standard investigation : Fractional curettage with hysteroscopy.

Fractional curettage : OT procedure.

Divide the uterus into fractions and curetting is taken from each fraction of the uterus.

Each sample from the fractions are separately placed and labelled.

Fractional curettage is better than dilatation and curettage.

Dilatation and curettage : The entire uterus is curetted together and entire curettage sample is sent together for assessment.

Both procedures should be combined with hysteroscopy.

Indications of fractional curettage after endometrial biopsy :

- Report of endometrial biopsy: Tissue sample was inadequate.
- Report of EB says there is hyperplasia with atypia.
- EB report is normal but patient continues to bleed.
- If there is cervical stenosis.

MCQ :

Q. A 54-year-old female who had attained menopause 2 years back, complains of single episode of bleeding. TVS shows endometrial thickness of 4 mm with an area of focal thickness of 6 mm. What is the most appropriate next step in management?

- Perform fractional curettage.
- Perform hysteroscopy and biopsy.
- Perform pipelle aspiration.
- Renew in 3 months or earlier if bleeding recurs.

Other investigations :

PAP smear :

Done in **all patients** of endometrial cancer.

**1<sup>st</sup>** investigation done in a patient with **post coital bleeding**.

MRI :

Done to assess the **involvement** of the **myometrium**, **lower uterine segment** or **cervix**.

CT :

To assess the involvement of **pelvic lymph nodes**, other **pelvic structures** and to ascertain the presence of **metastasis**.

most common **route** of spread is **direct spread**.

most **common** site of **hematogenous** metastasis is **lungs**.

Serous variety :

Has **transperitoneal spread**.

- During staging, **omentectomy** should be done.
- **CA 125** levels will be **raised**.

### Staging for endometrial cancer

00:32:21

FIGO staging is used.

FIGO : International Federation of Gynecology and Obstetrics.

Stage 1 : Cancer is **limited to the uterus**.

A : **< 50%** myometrium involved.

B : **≥ 50%** myometrium involved.

Stage 2 : **Cervix stroma** and **glands** are involved.

When the endometrial cancer spreads to cervix, the stage changes from stage 1 to stage 2.

But in case of cervical cancer spreading to the uterus or endometrium, the stage does not change.

Stage 3 : Cancer spreads **beyond the cervix**.

Adnexa : Tubes and the ovary.

Parametrium : Ligaments surrounding the uterus.

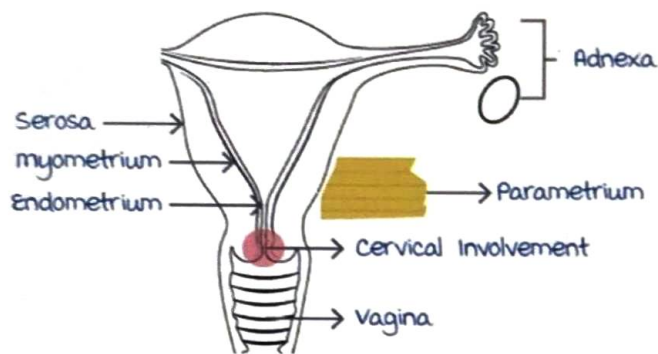
A : Cancer involves either the **serosa** or **adnexa**.

B : Cancer involves the **vagina** or **parametrium**.

C : **Lymph node** involvement,

C<sub>1</sub> : **Pelvic lymph nodes** involved.

C<sub>a</sub> : **Para aortic lymph nodes** involved.



Stage 4 : **metastasis**.

A : **Regional metastasis** to either **bladder** or **bowel**.

B : **Distant metastasis** or involvement of **inguinal lymph nodes**.

In cancer cervix, cancer ovary and cancer endometrium, **inguinal lymph nodes** are involved in **Stage 4B**.

Staging procedure : **Surgical staging**.

Also done for **ovarian cancer**.

A patient diagnosed with endometrial cancer by means of fractional curettage and hysteroscopy reports, is subjected to **surgery**.

The specimen is sent for **histopathology**.

Based on the **histopathology report**, which gives the **stage of the disease**.

The post operative management is planned according to the stage of the disease.

The steps are as follows,

- Do an MRI.
- TAH + BSO done in all stages.

Exceptions :

In cases where cancer has involved cervix or structures below the cervix : Stage 2 and above → Type 2 hysterectomy (Wertheim's hysterectomy) or Type 3 hysterectomy (radical hysterectomy) done.

- Lymph node dissection.
- Infracolic omentectomy with bilateral peritoneal biopsies from the pelvis, pericolic gutters and diaphragm done in serous variety, carcinosarcoma or clear cell variety.

### Lymph node dissection

00:42:57

In all cases : Pelvic and para-aortic lymph node dissection done.

Exception :

Type I endometrial carcinoma :

Adenocarcinoma grade 1 and 2.

MRI report shows involving <50% of myometrium (stage IA).

Based on the size of the tumor.

- <2cm : No lymph node dissection.
- ≥2cm : Pelvic lymph node dissection.

Stage	Surgery	Lymph node involvement	Post-operative therapy
Stage IA (adenoCA grade 1 and 2)	TAH + BSO	< 2cms : No ≥ 2cms : Pelvic LN	No post operative therapy
Stage IB	TAH + BSO	Pelvic and para aortic LN	Radiotherapy

Stage 2	Type 2 hysterectomy (Wertheim's hysterectomy) or Type 3 hysterectomy (radical hysterectomy)	Pelvic and para aortic LN	Radiotherapy
Stage 3	Type 2 hysterectomy (Wertheim's hysterectomy) or Type 3 hysterectomy (radical hysterectomy)	Pelvic and para aortic LN	Chemotherapy +/- radiotherapy
Stage 4	Debulking of tumor	Pelvic and para aortic LN	Chemotherapy +/- radiotherapy
Type 2 tumor (AdenoCA grade 3)	Surgery based on the stage.	Pelvic and para aortic LN	Chemotherapy + radiotherapy

### Piver Rutledge classification of hysterectomy 00:50:11

Type 1/Type A:

Simple hysterectomy: uterus + cervix are removed.

It is also called as total abdominal hysterectomy (TAH).

most common hysterectomy done for benign lesions.

Type 2/Type B:

Wertheim's hysterectomy/ modified radical hysterectomy.

Structures removed are:

uterus, cervix with both ovaries and tubes.

1cm of vagina.

medial half of cardinal ligament.

Half of uterosacral ligament.

Half of uterine artery.

Type 3/Type C :

Radical hysterectomy or modified Wertheim's hysterectomy.

Structures removed are :

uterus, cervix, both ovaries with tubes.

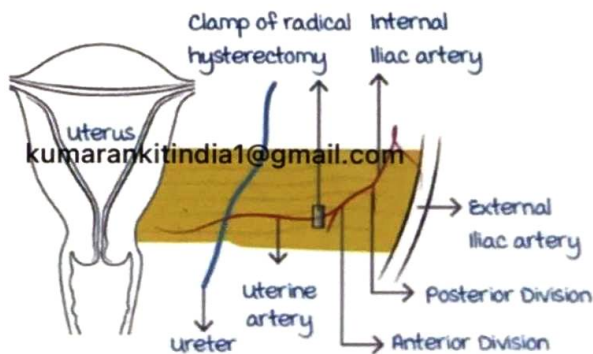
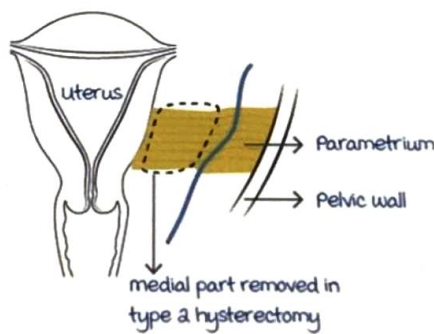
2cm of vagina.

Entire cardinal ligament.

Entire uterosacral ligament.

Entire uterine artery.

Type of hysterectomy	Parametrium OR Paracolpos	uterine vessals	uterosacral ligament	vagina	LN dissection
Type 1 : Simple hysterectomy / TAH	Not removed	Ligate at uterine isthmus.	Transected at uterine insertion.	Not removed	No
Type 2 : Wertheim's hysterectomy/ modified radical hysterectomy	medial half removed (medial to ureter)	Ligate at the level of ureter.	Transected midway between uterus and rectum.	1cm removed	Yes
Type 3 : Radical hysterectomy or modified Wertheim's hysterectomy	Entirely removed (medial to uterine vessels origin)	Ligate at origin from internal iliac vessels.	Transect near the rectum.*	≥2cm removed	Yes



Active space

Wertheim's hysterectomy has highest risk for injuring the ureter.

Chances for injuring the ureter is less in case of radical hysterectomy.

\*Removal of the entire uterosacral ligament resulted in high incidence of urinary retention. Therefore now, the entire uterosacral ligament is not removed.

### Post operative therapy

01:03:40

most often, the post operative therapy is radiotherapy.

Exception :

Stage IA grade 1 and 2 adenocarcinoma does not require any post operative therapy.

Chemotherapy +/- radiotherapy :

Carboplatin and Paclitaxel for 6 cycles.

Given in : Stage 3 and 4 of adenocarcinoma grade 1 and 2.

Type 2 tumors in all stages : Chemotherapy + radiotherapy.

Earlier regimen used : Paclitaxel + Doxorubicin + Cisplatin.

No longer in use due to increased risk of toxicity.

Fertility sparing management :

Hormonal therapy without hysterectomy is a management option in a young female with :

- Type 1 tumor.
- Only uterus is involved.
- No evidence of myometrial involvement on MRI.

Diagnosis by :

Hysteroscopy + dilatation and curettage (diagnosis of endometrial cancer).

MRI : myometrial involvement.



management : with Progesterone.

DOC : megestrol 160mg daily.

Alternatively : medroxyprogesterone acetate or levonorgestrel IUCD, mirena.

Follow up :

Every 3 months with endometrial biopsy or dilatation and curettage.

After completion of family or if the disease does not regress or if the disease progresses → Hysterectomy.

MCQs :

Q. A 65 year old women presents with postmenopausal bleeding. Biopsy shows grade I endometrioid carcinoma at the fundus of uterus. She has uncontrolled diabetes and hypertension. What is the most appropriate next step in management ?

- A. Perform MRI scan.
- B. Perform TAH + BSO.
- C. Perform TAH + BSO + pelvic and paraaortic lymph node dissection.
- D. Surgery followed by RT.

Q. A 54 year old female presents with postmenopausal bleeding. Biopsy shows endometrioid variety of endometrial cancer of 1 cm in the uterine fundus histology shows grade I tumor. MRI shows <50% of myometrial involvement. Next step in management is :

- A. TAH + BSO.
- B. TAH + BSO with pelvic lymphadenectomy.
- C. TAH + BSO with pelvic and paraaortic lymphadenectomy.
- D. TAH + BSO followed by RT.

Q. A 52 year old female has endometrial cancer of endometrioid variety stage IA grade 2 limited to endometrium. The tumor has not spread outside the uterus. Size of tumor is 3-4 cm. What is the most appropriate management?

- A. TAH + BSO.  
 B. TAH + BSO with pelvic lymphadenectomy.  
 C. TAH + BSO with pelvic and para aortic lymphadenectomy.  
 D. TAH + BSO followed by RT.

Q. True statements regarding investigation in endometrial cancer:

- A. MRI is superior to CT in detecting myometrial involvement.  
 B. CT is superior to MRI in detecting omental metastasis.  
 C. USG is initial investigation to be performed.  
 D. USG is the best investigation.

Updates :

most important risk factor for endometrial cancer : **Obesity**.

2<sup>nd</sup> most important risk factor : **Unopposed Estrogen**.

Tamoxifen :

Increases the risk for endometrial cancer.

Teratogenic : pregnancy should be avoided for 2 months after stopping the drug.

**Lynch syndrome :**

Autosomal dominant inheritance.

mutation in **MLH1**, **MSH2** and **MSH6** genes.

most common **extra-colonic manifestation** : **Endometrial cancer** (risk is 40-60%).

usually age for endometrial cancer : 6<sup>th</sup> decade (≥55years).

In patients of **Lynch syndrome**, endometrial cancer occurs in younger age group.

usually, **no routine screening** for endometrial cancer.

Exception : In cases of **Lynch syndrome**.

According to ACOG 2019, screening with **endometrial biopsy** every 1-2 years beginning at the age of 30-35 years.

Once the patient reaches 40 years and has completed her family, she is advised to undergo hysterectomy with BSO (Lynch syndrome also has 9-12% of ovarian cancer).

## CIN : PART 1

## Anatomy of cervix

00:01:04

Cervix is divided into 2 parts.

Endocervix : Lies close to uterus.

Aka supravaginal part of cervix

Lined by columnar epithelium.

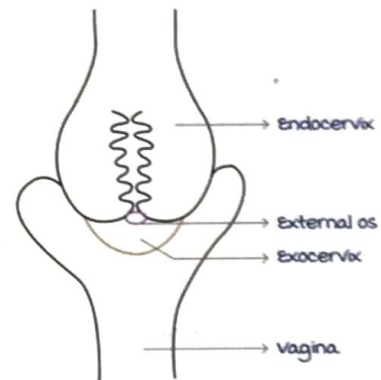
Appears red and velvety.

Exocervix : Lies within the vagina.

Aka portio vaginalis.

Lined by non keratinized stratified squamous epithelium.

Appears smooth and pink in colour.



External os : Cervix opens into vagina.

Cervix is derived from mullerian duct.

The epithelium of urogenital sinus which is non keratinized stratified squamous epithelium replaces the mullerian epithelium.

The migration continues till external os.

Original squamo columnar junction lies at external Os.

At puberty :

Estrogen is released from HPO axis.

Acts on columnar cells & increased glycogen content on squamous cells

Lactobacilli/Dodulein bacilli acts on glycogen and produce acidic pH.

The acidic pH acts as a stimulus for squamous metaplasia.

2 factors needed for acidic vaginal pH :

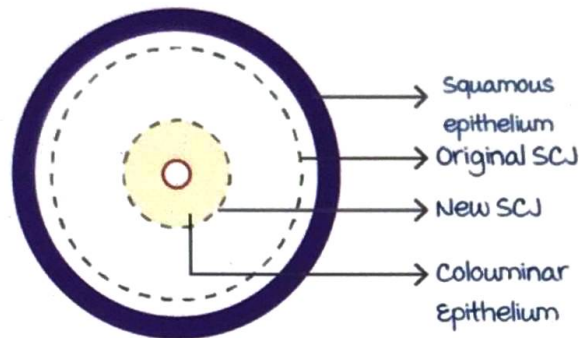
- Estrogen
- Lactobacillus

Squamous metaplasia : Replacement of columnar cells by squamous cells.

The undifferentiated reserve cells at SCJ

↓  
Change into squamous cells

↓  
Hence a new SCJ is formed



The zone between original SCJ and new SCJ is known as **Transformation zone**.

SCJ and transformation zone are not synonymous with each other.

This metaplasia occurs in all females.

It is physiological and not premalignant.

But these metaplastic cells are vulnerable to oncogenic effects of HPV and other oncogenes.

Hence MC site for carcinoma cervix is **transformation zone**.

MC type of CA cervix is **squamous cell carcinoma**.

and MC type of CA cervix is **adenocarcinoma**.

MC site for adenocarcinoma of cervix is **endocervix**.

The squamous metaplasia is most active during adolescence and pregnancy, hence early age of intercourse (coitarche) & 1st pregnancy are risk factors for cancer cervix.

### **Squamocoloumnar junction**

00:17:30

When squamous cells replace columnar epithelium, ducts are blocked and form nabothian cysts/follicles.

**Nabothian cysts** : Indicate columnar epithelium site.  
 These are blocked glands and hence does not require biopsy.

Pap smear is done if any lesion/friable mass on cervix.  
 It should be biopsied, except nabothian follicles.

**Transformation zone** : It is a dynamic area.  
 It moves towards ectocervix in response to estrogen :

- Adolescence.
- Pregnancy.
- OCP's.

Ectocervix ←  
 External os ←  
 Endocervix ←



It moves towards endocervix :

- menopause.
- Lactation.
- POP's.

Important points on transformation zone :

Sample for pap smear :

1st : **Ayer's saptula** = Transformation zone.

and best : **SCJ**.

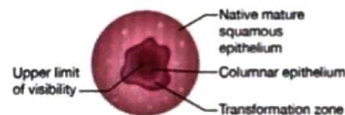
Endocervix brush = Endocervix.

**Per speculum examination** : 3 types of transformation zone.

Type 1 : Entire TZ is visible; TZ is entirely on ectocervix.

Type 2 : Entire TZ is visible; TZ has same endocervix component.

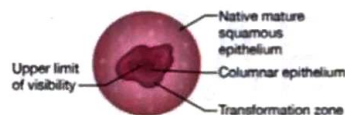
Type 3 : Entire TZ is not visible; TZ extends into endocervical canal.



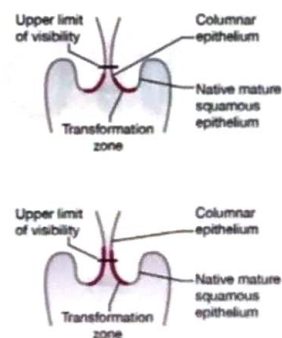
Type 1 TZ



Type 2 TZ



Type 3 TZ



Active space

## Dysplasia

00:28:22

metaplasia occurs in a **disorganized manner**.

Due to **presence of oncogenic stimuli**.

**Premalignant condition.**

Occurs in  $< 1/3$ rd of cervical thickness : CIN 1.

Occurs in  $1/3$  to  $2/3$  of thickness : CIN 2.

Occurs in  $\geq 2/3$  of thickness : CIN 3.

Occurs in entire thickness :

a. Overlying membrane is intact : Ca in situ

b. Overlying membrane is broken : Invasive Ca.

CIN is **diagnosed on HPE** i.e., biopsy.

In pap smear, only cells are examined.

It is a cytological test/study.

Squamous cells, glandular cell abnormalities are seen.

Diagnosis of CIN cannot be made by pap smear.

Pap smear is adequate when :

**Conventional** : No of squamous cells are 8000 - 12000/HPF +  
endocervical cells are 10-12.

**Liquid based cytology** : Squamous cells are 5000/10 HPF +  
Endocervical cells are 10-12.

Disorders detected by pap smear :

Squamous cell abnormalities :

1. Atypical squamous cells (ASC).
2. Low grade squamous intraepithelial lesion (LSIL).
3. High grade squamous intraepithelial lesion (HSIL).
4. Cancer in situ.

Glandular cell abnormalities :




1. Atypical glandular cells (AGC).
2. Adenocarcinoma in situ (AIS).
3. Adenocarcinoma.

LSIL report on pap smear : CIN I on HPE.

Active space

HSIL report on pap smear : CIN 2/3 on HPE.

LSIL and HSIL is based on Bethesda classification.

Area involved	Biopsy	malignant transformation risk	Bethesda classification according to Pap smear
<p>&lt; Lower 1/3<sup>rd</sup> thickness of the cervical epithelium.</p> 	CIN 1	1%	LSIL
<p>Lower 1/3<sup>rd</sup> to 2/3<sup>rd</sup> of thickness of cervical epithelium.</p> 	CIN 2	5%	HSIL
<p>&gt; Lower 2/3<sup>rd</sup> but not complete thickness of cervical epithelium.</p> 	CIN 3	12-20%	

Active space

## Risk factors of CIN/CA Cx

00:37:49

- HPV : **most important.**
- Early coitarche (< 18 years).
- Early age of 1st pregnancy (< 20 years).
- Multiple partners.
- Male partner with multiple partners.
- Immunocompromised states : **HIV.**
- Multiparity.
- Low socioeconomic status
- Smoking.
- OCPs.
- **Pre malignant conditions** : CIN, Vulval intra epithelial neoplasia, vaginal intra epithelial neoplasia.

### Oral combined pills :

Reversible risk.

Risk is more, if female has used OCP  $\geq$  5 years.

Earlier it was seen : OCP can lead to adeno carcinoma of cervix.

Now it is seen : OCP can lead to either adenocarcinoma of cervix or squamous cell carcinoma.

**Smoking** : Leads to squamous cell carcinoma.

Risk of cancer cervix is less in females with **circumscribed partner, barrier contraceptives (condoms), monogamous relationship or absent sexual life.**

Cancer cervix not related to :

- Early menarche/ late menopause.
- Genetic/ Familial history.

## HPV

00:42:23

ds DNA virus.

It is epitheliotropic : For completion of life cycle of HPV, it requires intact squamous epithelium.

Some of its genes :



Early genes : 'E' genes - expressed in basal and parabasal layers (E1,2,4,6 and 7).

Late genes : 'L' genes - expressed in surface layer (L1,2).

Hence, culture of HPV is not possible in vivo.

HPV leads to changes in epithelial cells

↓  
Koilocytosis

↓  
Corresponds to LSIL (CIN I/Koilocytosis)

E1,2 : Viral replication.

E6,7 : malignant transformation.

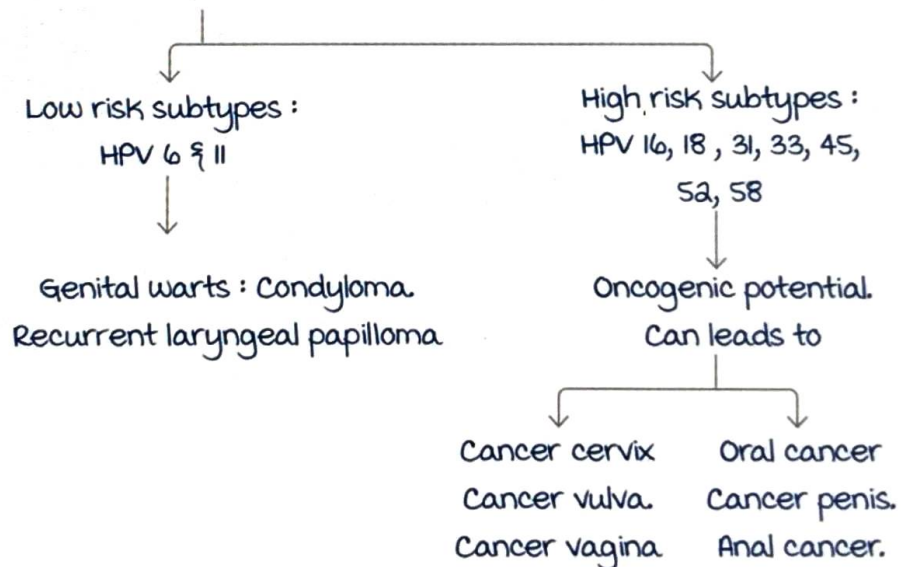
E6 : Knocks out p53 gene.

E7 : Knocks out Retinoblastoma gene (final step).

L1 : major capsid protein - HPV vaccines are made out of this.

L2 : minor capsid protein.

Has subtypes :



MC HPV leading to cancer cervix : HPV 16 (55% of CA Cx).

most specific HPV leading to cancer cervix : HPV 18.

and MC HPV leads to cancer cervix : HPV 18.

HPV 16 and 18 leads to 80% of CA Cx.

MC HPV leading to anogenital cancer/oropharyngeal cancer :

HPV 16.

MC HPV causing CIN 3 : HPV 16.

## Transmission of HPV infection

00:42:23

D) Sexually transmitted :

- Genital - genital intercourse.
- Oro - genital intercourse.
- Ano - genital intercourse.

HPV gets into basal layer through epithelial tract microabrasions.

**Applied aspects :** In all women with uterus; transgender males with uterus should be screened for cancer cervix.

Female who is in relationship with another female, chances of CA Cx rather than CIN.

a) Congenital HPV infection :

Seen in newborn, born to pregnant female with genital warts.

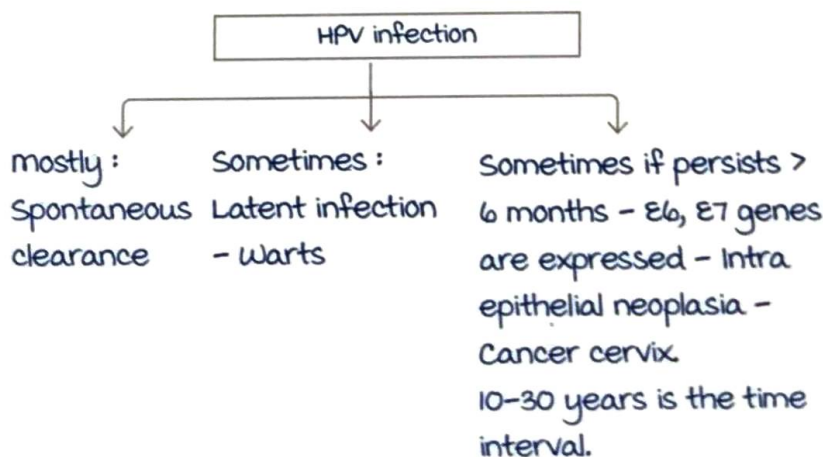
Transient infection.

No need for C-section in pregnant female with genital warts to prevent infection.

C-section should be done only if warts are large & obstruct vaginal delivery or may bleed during delivery.

## Course of HPV infection

00:42:23



Active space

Cancer cervix can be prevented by screening because :  
 It is MC female genital tract cancer.  
 Time period between infection to cancer is 10-30 years.

Therefore all females should be screened for cancer cervix :  
 Universal screening.  
 To prevent CIN/CA Cx : 2 strategies.  
 1) Screening for Ca Cx  
 2) HPV vaccines.

### HPV vaccines

00:56:00

Vaccine	Valent	Effective against	Protects from
Cervarix	Bivalent	HPV 16 and 18	Cancer cervix
Gardasil	Quadrivalent	HPV 6, 11, 16 and 18	Genital warts + Cancer cervix
Gardasil 9 (Available and MC used)	Non valent	HPV 6, 11, 16, 18, 31, 33, 45, 52 and 58	6 cancers + genital warts

These vaccines are prepared from L1 capsid protein.  
 Form virus like particles.

Regulation: Non infectious.

Highly immunogenic :

High levels of type specific humoral antibodies leading to prevention of entry of HPV into epithelial cells.

Hence gardasil 9 prevents against 6 cancers but it does not resolve precipitating HPV infection.

It doesnot resolve precipitating neoplasia.

Ideally these vaccines should be taken prior to sexual activity, when its benifit will be greatest.

but H/O prior sex act, HPV related disease or positive HPV test are not contraindication to vaccine.

HPV testing prior to HPV vaccine is not recommended.

If a female started vaccination schedule with 2V HPV or 4V HPV vaccine then it can be continued with vaccine : No need to restart vaccination.

If due to pregnancy or due to any reason, vaccine schedule is interrupted, no need to restart the series, just continue with the schedule when remembered.

vaccine is avoided in pregnancy but pregnancy testing is not recommended prior to administration of vaccine.

If unknowingly vaccine is given during pregnancy : No action is needed.

vaccine is safe during lactation.

Should not be given to patients with allergy to yeast or with recent febrile illness.

A female who has completed schedule with 2V HPV or 4V HPV vaccine : Should not repeat entire vaccination schedule with 9V vaccine.

Age group : 9-26 years.

Ideal : 11-12 years.

Extended age groups recommended by FDA : 27-45 years if gynecologist feels.

Under no circumstances, should this vaccine be given below the age of 9 years.

MC side effect : Syncope

## Dose schedule

01:06:25

> 15 years : 3 doses: 1st, 2nd and 3rd (1-2 month between 1st and 2nd dose, 6 months for 1-3rd dose).

< 15 years : 2 doses 1st - 2nd (6-12 months)

WHO - SAGE recommendation april 2022 :

- 9-14 years : 1 or 2 doses.
- 15- 20 years : 1 or 2 doses.
- ≥ 21 years : 2 doses (at 6 months interval).
- HIV +ve : 3 doses.

## CIN : PART 2

### Screening methods

00:00:11

3 methods :

- HPV DNA testing.
- Pap smear.
- Visual inspection with acetic acid.

Pap smear :

- Conventional.
- Liquid based cytology.

Specific but not sensitive.

Age  $\geq$  21 years.

Based on report of pap smear : Treatment cannot be given.

Report should be confirmed by colposcopic directed biopsy.

Then treatment should be given.

Can be repeated every 3 years.

Report of pap smear : Squamous cell abnormality.

1. ASCUS : Atypical squamous cells of unknown significance.

If age is  $<$  25 years : Repeat pap smear after 1 year.

If age is  $\geq$  25 years : HPV testing (Reflex test)  $\rightarrow$  If positive do colposcopy.

2. LSIL : Low squamous intraepithelial lesion.

If age is  $<$  25 years : Repeat pap smear after 6 months - 1 year.

If age is  $\geq$  25 years : Colposcopy.

3. ASC-H : Atypical squamous cells - HSIL cannot be ruled out.

4. HSIL : High squamous intraepithelial lesion.

In case of both 3 and 4 :

At any age : Colposcopy + Endocervical curettage.

## Colposcopy

00:07:02

Colposcope is a magnifying instrument.

Magnification : 30 times.

Focal length : 30.

- OPD procedure.
- Can visualize exocervix.
- Cannot visualize endocervix.
- Before colposcopy : UPT is performed if indicated.
- Do a bimanual examination : Cervix enlargement, malignancy, Intra uterine pathology.

Procedure :

Take a biopsy from :

- Rough area.
- Any area which is appearing white.

↓  
Apply acetic acid (3-5%) - If dysplastic cells are present (increased NC ratio) and take biopsy from aceto white areas.

↓  
Apply acetic acid to dysplastic cells.

↓  
Nuclear proteins coagulate.

↓  
Appears white in colour.

This is called as aceto white appearance.

Acetic acid to normal epithelium : Appears pink in colour.

Acetic acid to metaplastic epithelium : Appears grey in colour.

Colposcopy has green filter : Switch it on.

Helps to identify abnormal blood vessels like

- Punctate blood vessels.
- mosaic blood vessels.
- Reticular blood vessels.

Colposcopy cannot visualize endocervix.

To rule out lesion in endocervix, do endocervical curettage.

Pap smear can also detect glandular cell abnormalities :  
 Atypical glandular cells of unknown significance :  
 Should rule out cancer cervix and endometrial cancer.  
 It is done by : Colposcopy, endocervical curettage and endometrial biopsy.

In resource limited countries :

WHO recommends : See and treat method.

Pap smear cannot be used as primary screening test, because after pap smear a confirmatory test is needed and only then treatment can be done.

### HPV DNA testing

00:19:23

Recommended age :  $\geq 30$  years.

Can be done as early as  $\geq 25$  years.

Co test : HPV DNA test + Pap smear together.

Reflex test : If HPV DNA test is done after an abnormal report.

e.g., pap smear : ASCUS in a female  $\geq 25$  years.

HPV DNA test is a sensitive test.

Earlier, it was a part of screening test along with pap smear as a co test.

Now WHO recommends it as a primary screening test specially in resource limited countries.

Now HPV DNA test is used as primary screening test for see and treat approach by WHO.

If HPV DNA test is positive (Sample can be either provider collected or self collected cervix specimen), treatment is of a types :

**Ablation or LEEP.**

If HPV DNA test is negative : Repeat every 5-10 years in general population and 3-5 years in female who is HIV + or HIV + partners.

If HPV DNA test is positive :

High risk HPV DNA is present but it does not provide info about HPV subtype.

To know HPV subtype :

- High risk HPV DNA test (Partial test : 16, 18 sometimes 45).
- Cobas test.
- Onclarity test.

### Visual inspection with acetic acid

00:24:32

Also a primary screening test for see and treat approach.

WHO recommends **HPV DNA test** > VIA as as primary screening test for see and treat approach.

In VIA : 3-5% acetic acid is applied to cervix epithelium.

Normal epithelium : Appears pink.

Dysplastic epithelium : Has dysplastic cells - Increased NC ratio, in which nuclear proteins coagulate and appears white i.e., aceto white areas.



VIA as a screening test should be reported every 3 years.

Outdated test : VILI (Visual inspection with Lugol's iodine).

Normal cervix :

Has sufficient glycogen stores and when iodine is applied, it is stained as purple brown in colour.



**Dysplastic epithelium**: Glycogen is used up and appears as yellow (unstained).

ACOG recommendation for screening in resource rich countries:

Age to begin screening: **21 years** irrespective of sexual act.

method: **Pap smear**.

From  $\geq 30$  years: Co test - Pap + HPV DNA testing.

Repeat after 5 years.

Screening done upto age of:

**65 years**, if in previous decade normal screening report.

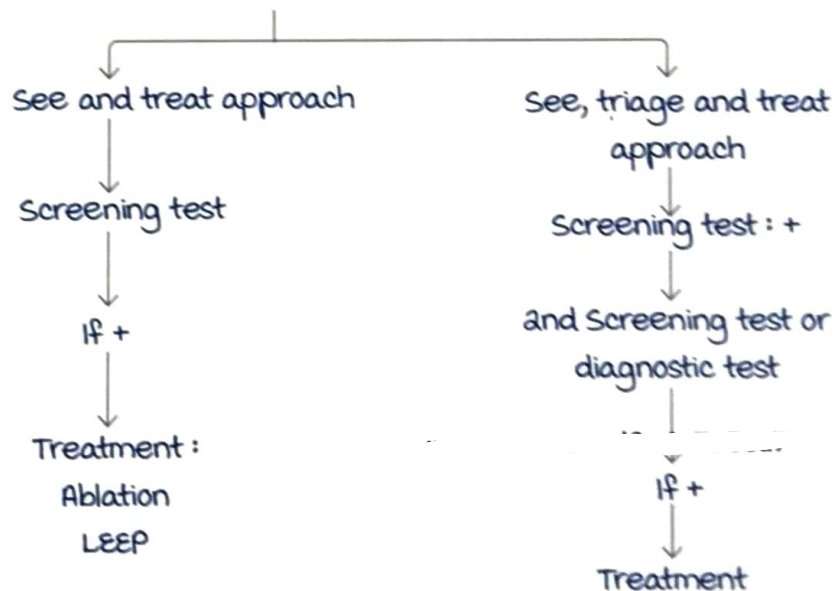
**75 years**, if in previous decade abnormal screening report.

As per pap smear report, further testing is done followed by diagnostic test and then treatment.

### WHO approach

00:32:32

Resource limited area:



Active space

### Screening and Treatment Approaches

- In the "screen-and-treat approach", the decision to treat is based on a positive primary screening test only.
- In the "screen, triage and treat approach", the decision

to treat is based on a **positive primary screening test** followed by a **positive second test** (a triage test), with or without histologically confirmed diagnosis.

Age to start screening (as per WHO) :

General population : **30 years** (as per ACOG **21 years**).

In female living with HIV positive : **25 years**.

Target population : **30-49 years**.

Age to stop screening : **50 years** (if previous 2 screening is normal).

WHO recommends : **See, triage and treat approach** > **See and treat approach**.

**HPV + VIA** > **HPV DNA** > **VIA**.

**HPV + VIA** : Best screening.

### See & treat approach

00:37:03

Test recommended by WHO.

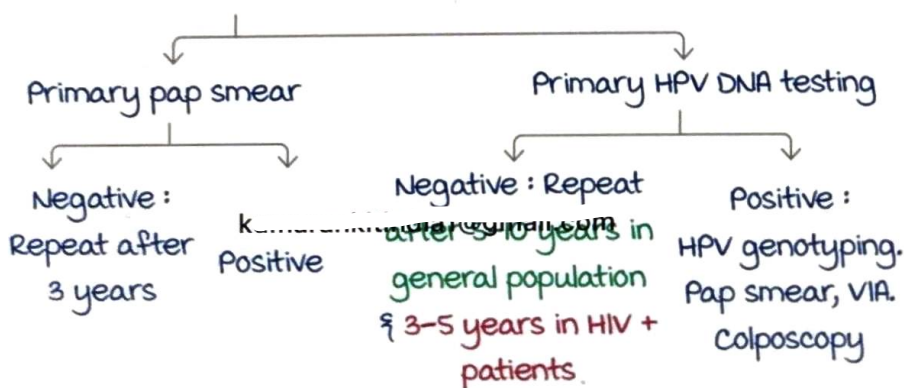
HPV DNA test - repeated after **5-10 years** (General population) and **3-5 years** (HIV patients).

VIA - repeated 3 years.

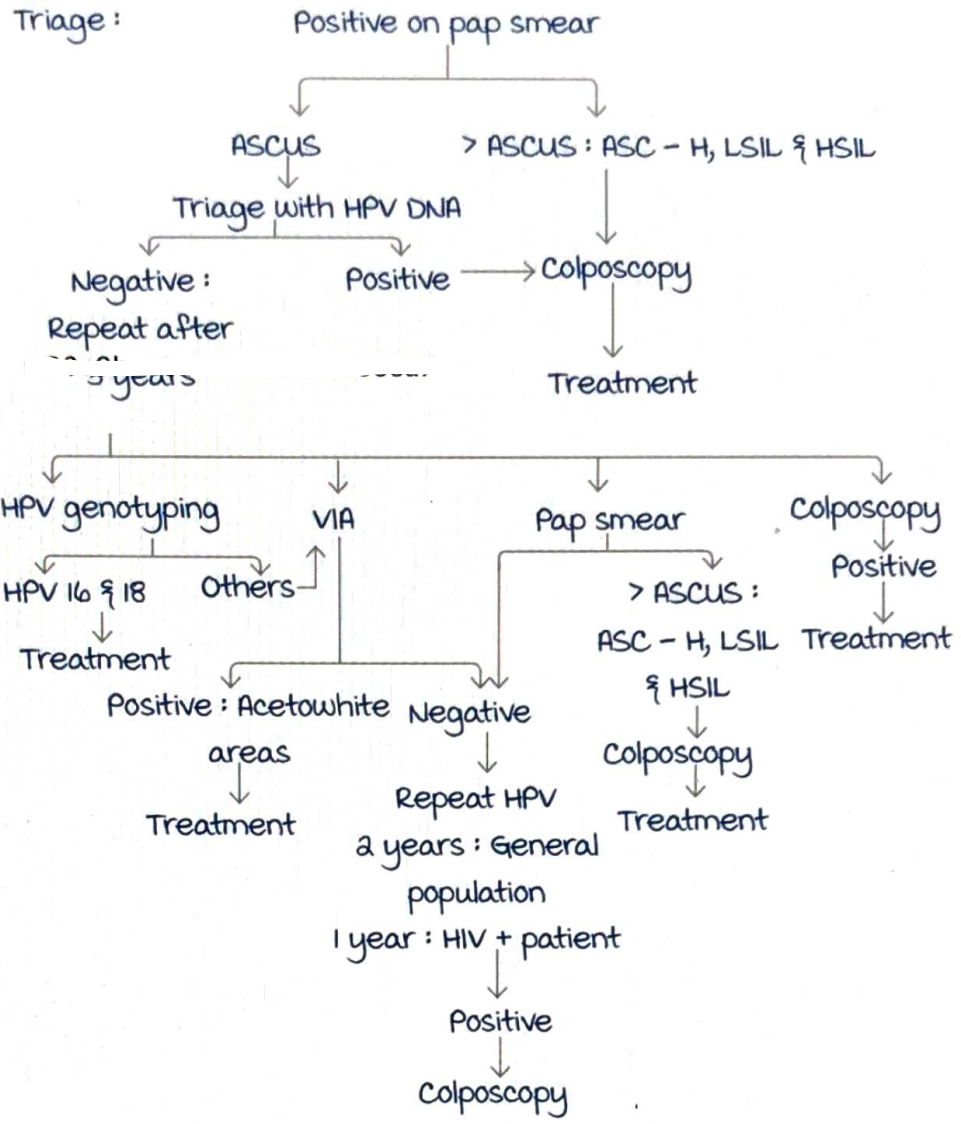
If positive, treatment and then followed by Follow up after 1 year with HPV DNA testing.

Treatment options are ablation and LEEP.

**See, triage and treat approach :**



Active space



Normally :  
**HPV DNA negative** : Retested 5-10 years as per WHO.  
 But if HPV DNA + and triage negative (VIA/pap smear) : HPV repeated after 2 years in general population and after 1 year in HIV + patients.

**Endocervical curettage** 00:52:10

Since colposcopy cannot visualize endocervix  
 To rule out lesions in endocervix

Indications for endocervical sampling as per ACOG 2018 :

- Transformation zone is not fully visible.
- Transformation zone is fully visible but no lesion is identified.
- Initial evaluation of HSIL, ASC-H, ASCUS or AI situ.

Active space

Endocervical sampling **should not be performed in pregnant females.**

Done by introducing endocervical curette 1-2 cms into cervical canal.

**Endocervical sampling** : Endocervical curettage or endocervical brushing.

**Endocervical curettage** :

If report comes as adenocarcinoma in situ.

↓  
Rule out pre existing invasive carcinoma.

↓  
Do cone biopsy/ conization

↓  
If no invasive carcinoma



management : **Hysterectomy** (if child bearing is complete)

If woman wishes to concieve :

- Advise risk of carcinoma even if negative excision margins.
- Long term surveillance.
- Timely hysterectomy after family completion.

Colposcopy report comes as CIN 1/CIN 2/ CIN 3.

CIN 1 : Histologically it corresponds to LSIL or HPV changes.

High rate of spontaneous regression : No need of treatment.

mostly regression occurs within 2 years.

If it is done  $\geq 2$  years : Treatment is done.

Treatment : **Cryoablation** ( If criteria are fulfilled).

If criteria is not satisfied : LEEP.

CIN 2/CIN 3 :

Both options : **Cryoablation** and **excisional procedures.**

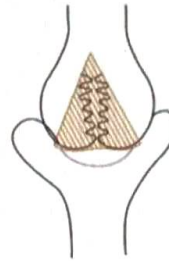
Excisional procedures include :

- LEEP/LLETZ.
- Conization.

Best management : **For any age and parity is LEEP/LLETZ.**

LEEP : Loop electro excisional procedure.

LLETZ : Large Loop excision of transformation zone.



As per WHO : See and treat/ see, triage and treat.

If criteria for ablation fulfilled :

Eligibility criteria for ablative treatment

- There is no suspicion of invasive cancer or glandular disease (i.e. adenocarcinoma or adenocarcinoma in situ, AIS)
- The transformation zone is fully visible, the whole lesion is visible, and it does not extend into the endocervix.
- The lesion is type I transformation zone

If criteria is not fulfilled : LEEP/LLETZ.

## Cryoablation

01:04:31

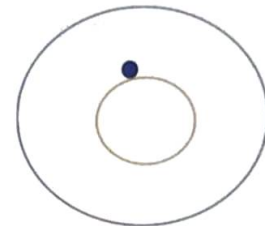
Criteria for cryoablation (as per WHO).

Endocervical curettage should be negative.

CIN should be limited to 2 quadrant of cervix.

Not used for treating :

- CIN 3.
- Female with HIV with CIN.
- After any previous therapy.



After treatment, follow up after 12 months : HPV DNA testing.

In case of positive HPV DNA testing, re treat only with LEEP/LLETZ.

Principle :  $\text{CO}_2/\text{N}_2\text{O}$  at very low temperature leads to crystallisation of intracellular water or cryonecrosis.

When  $\text{N}_2\text{O}$  is used : Temperature  $-65^\circ\text{C}$  is reached.

Cell death occurs at  $-20^\circ\text{C}$ .

OPD procedure.

Procedure : 2 cycles of freeze- thaw.

- Freeze (3mins) → Thaw (5mins) → Freeze (3mins) → Thaw (5mins).

Destroys cervical epithelium : 7 mm distal to probe margin.

Adverse effects :

- Persistent watery discharge.
- No bleeding.

Disadvantages over excisional procedure : **No tissue sample available for HPE.**

## LEEP/LLETZ

01:10:20

- OPD procedure.
- No anaesthesia required.
- Current into wire
- Cut and coagulate at same time.
- Short procedure : 10 minutes.
- No admission needed.
- minimal bleeding.



Tissue removed upto a depth of 10 mm : **Sent for HPE.**

Treatment of choice : CIN 2 & 3 at any age and any parity.

Q1) 55 year old female, complete family diagnosed with CIN 3 on colposcopy : **LEEP/LLETZ.**

Q2) LEEP done female, diagnosed as CIN : LEEP can be done again.

If recurrent : **Hysterectomy.**

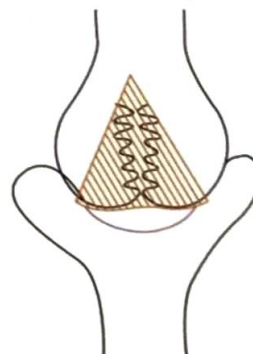
Other than this, hysterectomy is never done in CIN.

## Conization/ Cone biopsy

01:13:55

Sample includes :

- Endocervix.
- Ectocervix.
- Transformation zone.



Advantages :

Sample is obtained from endocervix +  
It tells about invasion too.

Disadvantage :

- OT procedure.
- Decreased anaesthesia.
- Admission needed.
- Risk factor for pre term labor and cervical incompetence.

Indications for cone biopsy :

- If endocervical curettage is positive for adenocarcinoma in situ.
- If suspecting adenocarcinoma in situ.
- Indication for endocervical curettage : Transformation zone is not visible and lesion is extending to cervix.
- If pap smear HSIL, colposcopy normal : Next step endocervical curettage or cone biopsy.

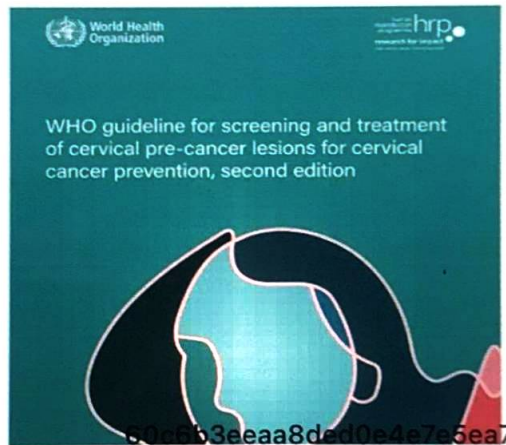
Therapeutic indications :

To treat stage I A<sub>1</sub> of cancer cervix in young females.

**TZ 1 & TZ 2** : Diagnostic procedure after pap smear - Colposcopy.

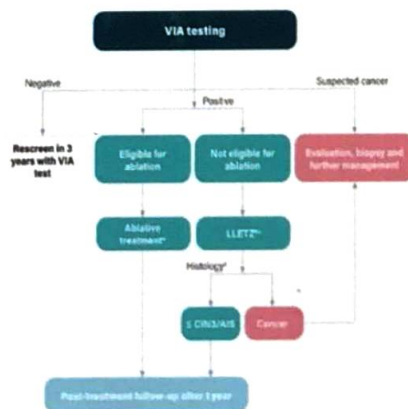
Entire transformation zone is visible.

**TZ 3** : Diagnostic procedure after pap smear - Conization.  
Not visible entirely.



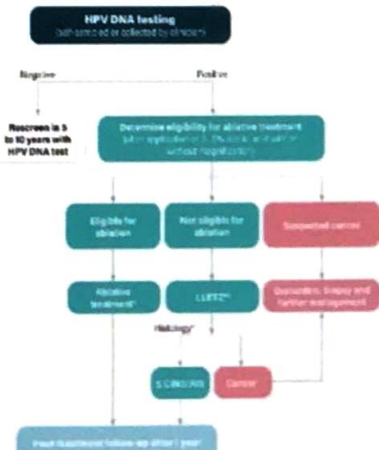
**ALGORITHM 1. PRIMARY VIA SCREENING (SCREEN-AND-TREAT APPROACH)**

For both the general population of women and women living with HIV



**ALGORITHM 2. PRIMARY HPV DNA TEST SCREENING (SCREEN-AND-TREAT APPROACH)**

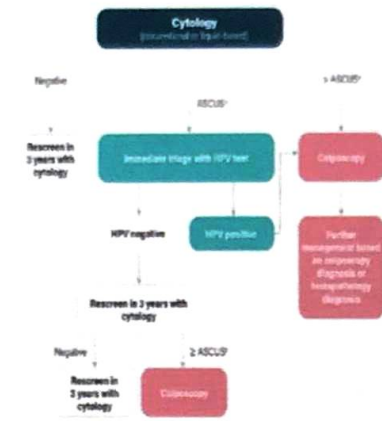
For the general population of women



Active space

**ALGORITHM 3. PRIMARY CYTOLOGY SCREENING AND COLPOSCOPY TRIAGE (SCREEN, TRIAGE AND TREAT APPROACH)**

For both the general population of women and women living with HIV



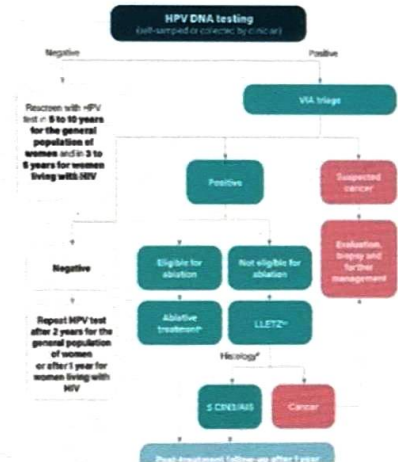
**ALGORITHM 4. HPV DNA SCREENING AND HPV16/18 TRIAGE (SCREEN, TRIAGE AND TREAT APPROACH)**

For both the general population of women and women living with HIV



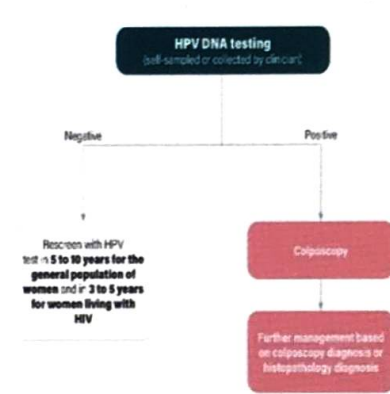
**ALGORITHM 5. PRIMARY HPV DNA SCREENING AND VIA TRIAGE (SCREEN, TRIAGE AND TREAT APPROACH)**

For both the general population of women and women living with HIV



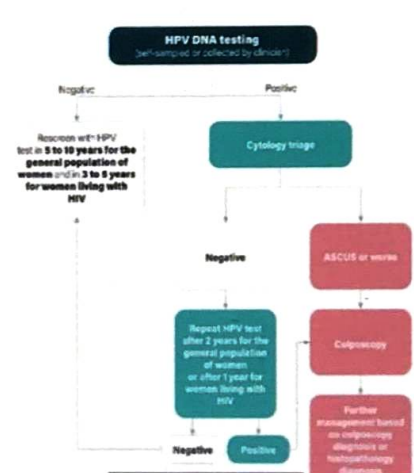
**COLPOSCOPY TRIAGE (SCREEN, TRIAGE AND TREAT APPROACH)**

For both the general population of women and women living with HIV

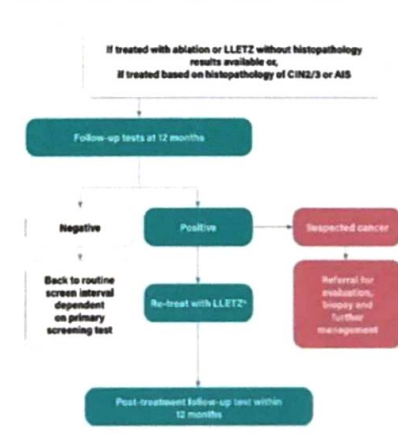


**ALGORITHM 7. PRIMARY HPV SCREENING AND CYTOLOGY TRIAGE FOLLOWED BY COLPOSCOPY (SCREEN, TRIAGE AND TREAT APPROACH)**

For both the general population of women and women living with HIV



**FOLLOW-UP TESTS AT 12 MONTHS POST-TREATMENT FOR THE GENERAL POPULATION OF WOMEN**



Active space



## CANCER CERVIX

### Relevant Anatomical facts

00:00:40

MC site for cancer cervix : Transformation zone > squamo-columnar junction.

MC variety of cancer cervix : Squamous cell carcinoma.

(Any - Keratinising or non Keratinising type) ~70%.

2<sup>nd</sup> MC variety of cancer cervix : Adenocarcinoma. (25%)

Lymphatic drainage of cervix :

Sentinel / 1<sup>st</sup> lymph node involved in carcinoma cervix :

Paracervical LN > Parametrial LN

↓ drains into

Obturator LN

↓

Internal iliac, External iliac, Common iliac

↓

Para aortic LN.

Applied aspects :

In radical hysterectomy for Ca Cx :

Paracervical and Parametrial LN are removed, along with Pelvic Lymphadenectomy, paraaortic and Rectal Lymph node dissection. (As lymphatic channels from posterior cervix drain via uterosacral ligaments into rectal LN).

Cervix doesn't drain into superficial inguinal LN.

In case of involvement of superficial inguinal LN, it is considered Stage IV B (distant metastasis has occurred).

Thus superficial inguinal lymph nodes are not included in pelvic radiotherapy for carcinoma cervix.

In clinical staging of Ca Cx : Lymph vascular space is not involved. In case of invasion it is a poor prognostic marker.

## Clinical presentation of Cancer cervix

00:08:18

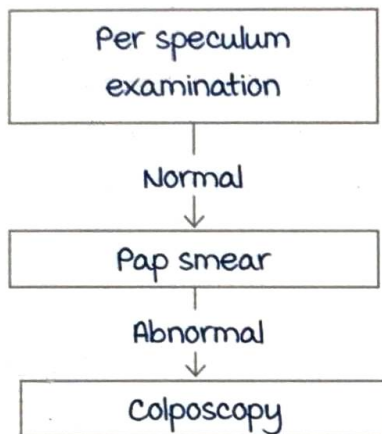
most common presentation of cancer cervix : **Irregular vaginal bleeding** > post coital bleeding (contact bleeding).

most specific symptom : **Post coital bleeding**.

Case scenarios :

1. Female of reproductive age group comes with C/o post coital bleeding :

Next step in management :



To rule out local causes like :

- Polyp.
- Cervicitis.
- Ectropion.

2. Female of reproductive age with **post coital bleeding and visible growth** is seen on cervix :  
Initial management : **Punch biopsy**.

3. Female of reproductive age with post coital bleeding and abnormal looking cervix :  
Initial management : **Punch biopsy + Endocervical curettage**

**Abnormal looking cervix :**

- Barrel shaped cervix.
- Thick, indurated cervix.
- Firm cervix.

On Physical examination :

- Cervix may appear normal.
- Growth might be exophytic/endophytic.
- In case of Adeno Ca : Palpable barrel shaped cervix or Cervical ulcer or necrotic ulcer might be present.

most common age group for Ca Cx : Younger age groups.

Since HPV association is the MC risk factor.  
median age for diagnosis being 50yrs.

Ca Cx is the 4<sup>th</sup> MC cancer in females worldwide.  
most common being : Breast > Colorectal > Lung > Ca Cx.

most common route of spread : Lymphatic.  
most common site of Hematogenous spread : Lungs > Ovary  
> Liver > Bone.

Though involvement of ovaries in cancer cervix is Rare.  
Thus hysterectomy for cancer cervix in young females : No  
need of removal of ovaries.

Oophorectomy is not done.

most important prognostic factor in cancer cervix : Stage >  
Lymph node involvement.

### Investigations for Cancer cervix

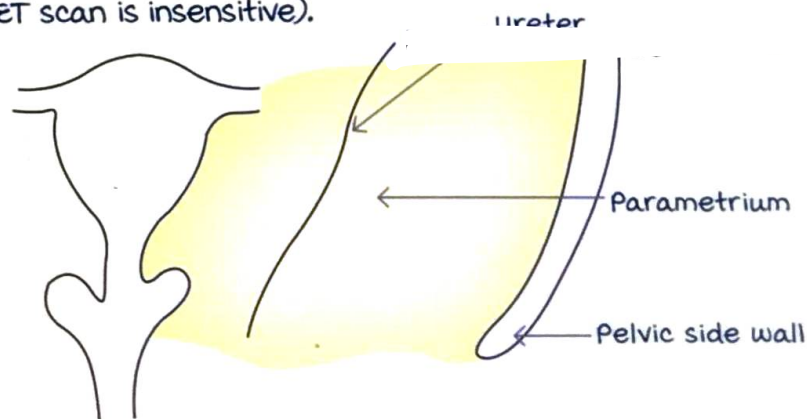
00:19:20

1. Lab tests : CBC, urine analysis, LFT, KFT.
  2. Radiology : Chest xray, IVP, CT, PET scan, MRI.
  3. Procedural : Cystoscopy, Proctoscopy.
- MRI is preferred over CT for assessing :

- Tumour size.
- Tumour extension.
- Parametrial involvement.

While CT is useful for assessing : LN involvement & distant metastasis.

Best test for LN involvement : PET Scan (But if LN < 5mm, PET scan is insensitive).



(Parametrium : All ligaments that surround uterus)

## FIGO staging of cancer cervix

00:23:00

Staging of cancer cervix :

Stage	Description	management
Stage IA : • IA1. • IA2.  Stage IB: • IB1. • IB2. • IB3.	I : Cancer is limited to cervix. Extension to corpus is disregarded. A : micro invasive (<5 mm deep). AI : < 3 mm deep. A2 : 3-4 mm deep.  macro invasive ( $\geq 5$ mm deep). Size of Tumor < 2 cm. Size of Tumor $\geq 2$ cm. Size of Tumor $\geq 4$ cm. $\longrightarrow$	Surgery is the preferred option, except if size of tumor is $\geq 4$ cm.          Chemo radiation.
Stage II :  IIA : • IIA1. • IIA2.  IIB.	Cancer spreads to upper 2/3 <sup>rd</sup> of vagina. Parametrium not involved. Size of Tumor < 4 cm. Size of Tumor $\geq 4$ cm. $\longrightarrow$  Parametrium involved. $\longrightarrow$	Surgery. Chemoradiation.  Chemoradiation.
Stage III :  IIIA. IIIB.  IIIC: • IIIC1. • IIIC2.	Cancer involved lower 1/3 <sup>rd</sup> of vagina. Pelvic side wall not involved. Pelvic side wall involved / Hydroureter/ Hydronephrosis. Lymph nodes involved. Pelvic lymph nodes. Para aortic lymph nodes.	Chemoradiation.
Stage IV: IVA.  IVB.	metastasis : Regional metastasis : Bladder/ bowel. Distant metastasis or Superficial inguinal lymph node involvement.	Palliative care : Chemoradiation.

MC cause of death in Ca Cx : **uremia/ renal failure.**

2<sup>nd</sup> most common cause of death : **Hemorrhage/ Bleeding.**

**Bullous edema** of bladder (on cystoscopy) :

- This is a sign of **lymphatic obstruction.**
- Not due to cancer involving bladder.

**Stage 0 : Ca insitu or CIN 3.**

Active space

## Management of cancer cervix

00:36:04

Basic principles of management for Ca Cx :

1. Surgery :

- Can be done in early stages of Ca Cx till : **Stage IIAa**.
- Cannot be done if size of tumor  $\geq 4$  cm.
- Treatment of choice for : IA1, IA2, IB1, IB2, IIA1.
- Cannot be done for IB3, IIAa.

2. Radiotherapy :

- Can be done in **all stages**.
- Preferred in later stages : **From stage IIAa onwards**  
 $\&$  in all those stages ~~where surgery cannot be done.~~
- Treatment of choice for : IB, III, IV, IB3, IIAa.
- Side effect :
  - **Ovarian failure**. (Ovaries are the most radio sensitive organ).
  - Fibrosis of vagina.

3. Chemo radiation :

- Before radiotherapy, **Cisplatin** is given to increase sensitivity to radiotherapy.
- Cisplatin is used as a **radiosensitizer**.
- Hence radiotherapy is preferably called as chemoradiation.
- Instead of cisplatin, **5 FU** can be given.

Q. For stage IB, treatment of choice :

- RT.
- CT.
- Surgery.
- Chemoradiation.**

Q. For stage IIB, treatment of choice :

- RT.
- CT.
- Surgery.
- Surgery + RT.**

## Surgical management of cancer cervix

00:41:43

Stage	Surgery		Lymph node dissection
	Young	Old	
Stage IA1	Conization / cone biopsy.	Type 1 hysterectomy : TAH +BSO.	Not needed.
Stage IA1 with LVSI or Stage IA2	Radical trachelectomy.	Type 2 : Wertheim / modified radical hysterectomy, Type 2 or Type 3 radical hysterectomy.	Pelvic + para-aortic lymph node dissection.
Stage IB1	Radical trachelectomy.	Type 3 radical hysterectomy.	
Stage IB2	Type 3 hysterectomy.	Type 3 hysterectomy.	
Stage IIA1	Type 3 hysterectomy.		

## Radical trachelectomy :

- Removal of cervix with entire parametrium.
- uterine artery ligated.
- uterus stitched to vagina with absorbable sutures.
- Cervical cerclage done with permanent sutures.
- Can be done vaginally or abdominally.
- Prerequisite for vaginal trachelectomy :  
Size of tumor < 2cm.
- Abdominal trachelectomy can be done for tumour size ≥ 2cms.
- If female becomes pregnant after trachelectomy :  
delivery by C-section.

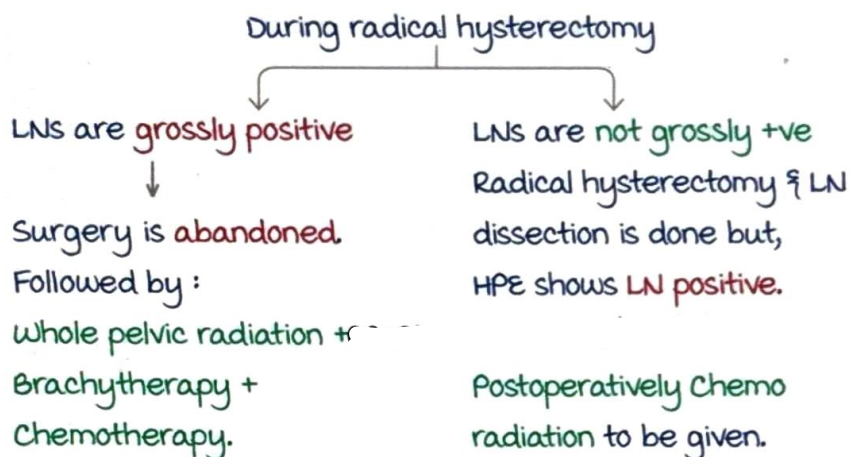
Pelvic lymphadenectomy can lead to complications like **lymphocyst** and **lymphedema**.

In females with Ca Cx, **sentinel lymph node biopsy (SLNB)** can be done alternatively to assess **lymphatic** spread.

For biopsy, inject a blue colored dye or **technetium radioactive tracer** preoperatively into cervix.

SLNB is useful when, Tumour size < 2cms &

In early stages of disease.



## Radiotherapy

00:52:00

Types	Brachytherapy	Teletherapy
	Intracavitary therapy.	External beam radiotherapy (EBRT)
Isotope	Iridium 192.	Cesium
Order	2 <sup>nd</sup> order	1 <sup>st</sup> order (to shrink tumor size)
Source of radiation.	Inside the body at point A. Point A : 2cm above and lateral to external os.	Outside the body.
Dose.	High dose: $\geq 12$ gy/hr Low dose: $< 2$ gy/hr.	50 gy to pelvis (in 25 fractions over 5 weeks).

Lymph nodes included in radiotherapy : All Lymph nodes where cervix drains.

Superficial inguinal lymph nodes are not included in pelvic radiotherapy for carcinoma cervix.

## Management during pregnancy

00:55:12

Diagnosis :

Pap test is recommended for all females  $\geq 21$  yrs of age.



Report : HSIL, AIS or suspected malignancy



Next step : Colposcopy and biopsy (safe) without endocervical curettage.

If pap test indicates malignancy but colposcopy fails to confirm malignancy.



Diagnostic conization may be necessary.  
(Done in 2<sup>nd</sup> trimester)

### management of CIN in pregnancy :

Not LEEP. (As during pregnancy it is associated with high rates of recurrence/ persistent disease).

### management of Stage I & II cancer during pregnancy :

Stage IA1 with no LVSI :

- Deliver vaginally.
- Re-evaluate after 6 weeks.

Other stages :

- Do minimal invasive LN dissection.

Nodes negative :

Wait till fetus is viable.  
Do a classical C-section.  
f/b Radical hysterectomy  
+ LN dissection

Nodes positive :

Cannot wait.  
Do immediate radical hysterectomy with fetus insitu + LN dissection

Classical C-sec avoids risk of cutting through tumour in lower uterine segment which can lead to serious blood loss & tumour spread.



# OVARIAN CANCER : PART 1

## Ovarian cysts

00:00:44

MC cyst in ovary : **Functional ovarian cyst.**

They occur due to hormonal disturbances and are temporary.

They generally resolve spontaneously and do not require specific treatment.

Follicular cyst	Corpus luteal cyst	Theca lutein cyst
MC functional cyst. Cyst : Follicle > 3 cm.	MC to rupture	Due to increased hCG. molar pregnancy Twin pregnancy. Infertility treatment (Clomiphene, hmg).

## Ovarian cancers

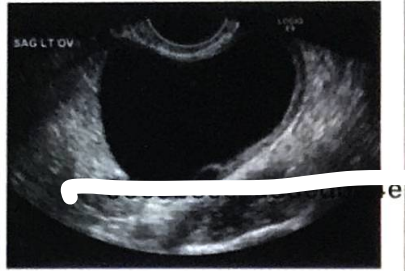
00:03:30

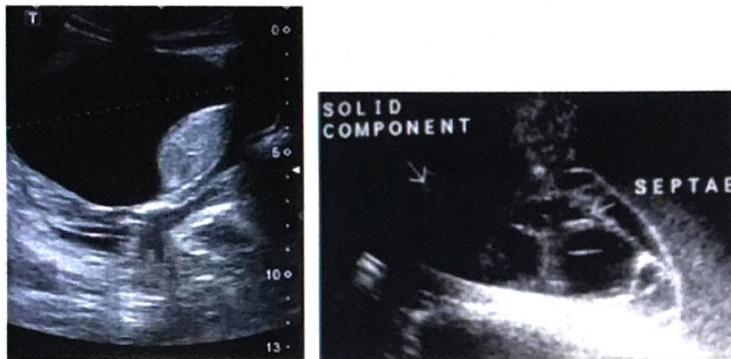
Ovarian cancers are not very common hence screening is not done.

Patient presents with vague symptoms nausea, vomiting etc.

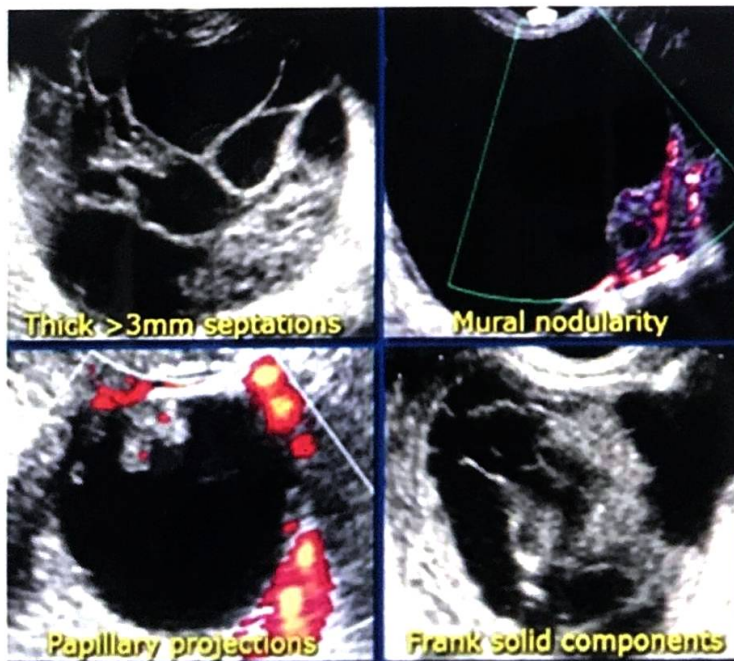
**Adnexal masses** may be benign or malignant (**IOC : TVS**).

Benign adnexal mass	malignant adnexal mass
MC in reproductive age group.	Extremes of age : Pre-pubertal/ menopausal.
Pain present (Inflammation)	No pain initially
Usually, unilateral	Usually, bilateral.
Cystic consistency	Solid consistency.
Tenderness present	Tenderness absent.
Ultrasound features :	Ultrasound features: > 10 cm in size.
	Short history, Rapid progression, associated with weight loss.

<p>Unilateral, anechoic, unilocular, no solid component</p>	<p>Bilateral, variable consistency (solid component), thick septa, papillary outgrowth (excrecences) from septa, high vascularity in septa</p>
	<p>Evidence of ascites, enlarged lymph nodes, matted lymph nodes</p>



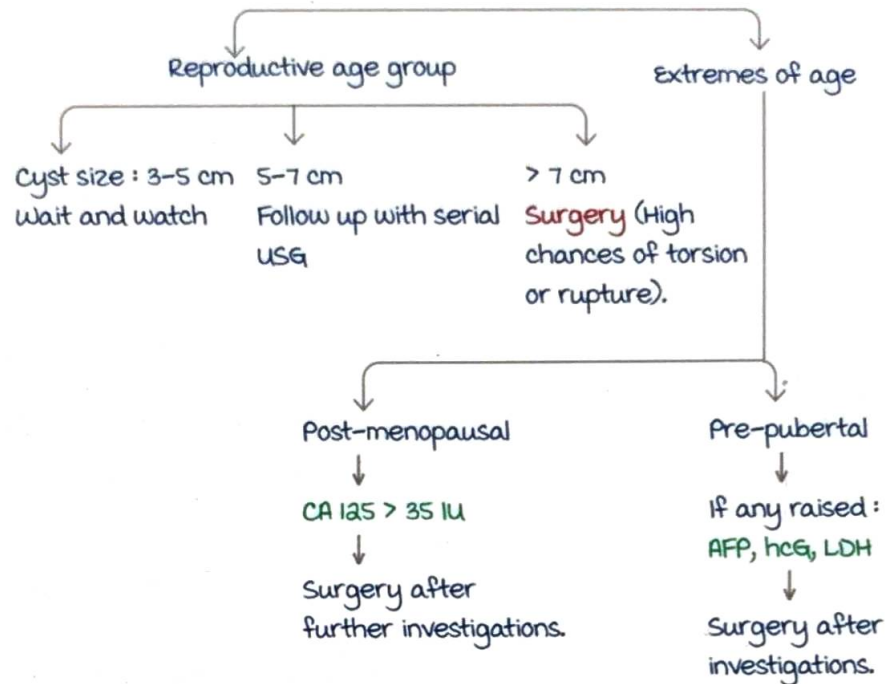
Papillary excrescences



Active space

## Management of ovarian cyst (No features of malignancy)

00:13:53



Percentage of ovarian mass to undergo malignant transformation.

Post-menopausal: 30%

Pre-menopausal: 7%

CA 125 levels are not of much use in reproductive age group:

Raised in a number of benign conditions (Fibroid, PID, Cervical TB)

Significant only if very high  $\geq 200$  IU.

## Ovarian cyst in pregnancy

00:20:17

MC benign ovary tumor/ cyst in pregnancy: Dermoid cyst.

MC to undergo torsion: Dermoid cyst (mature cystic teratoma).

MC time for torsion: End of 1<sup>st</sup> trimester or during puerperium.

MC ovarian cancer during pregnancy: Dysgerminoma.

**management:**

Symptomatic (Rupture/ torsion): Removal of cyst irrespective

of gestational age.

Asymptomatic :

1<sup>st</sup> trimester : **wait and watch.**

most often it is corpus luteal cyst which regresses spontaneously.

If removed → Progesterone decreases → Abortion.

2<sup>nd</sup> trimester: If USG shows features of **malignancy** or size

> 10 cm : **Surgery.**

### Risk factors and protective factors related to ovarian cancer

00:25:03

	Proven risk factors	Controversial risk factors
Excessive estrogen	Early menarche Late menopause Obesity Endometriosis	PCOS HRT
Excessive ovulation (Theory of incessant ovulation)	Nulliparity	Infertility and ovulation inducing drugs.
Genetic syndrome	Lynch syndrome BRCA 1 BRCA 2	
Exposure to carcinogens	Asbestos	Talc Smoking (mucinous adenocarcinoma).

Protective factors for ovarian cancer :

Related to estrogen	Related to ovulation	Certain surgeries
Physical exercise	Anovulation : Multiparity <b>OCP</b> (most important) Breast feeding	Hysterectomy. Tubal ligation. Salpingectomy.

### Genetic syndromes related to ovarian cancer

00:33:13

Lynch syndrome :

MC gene : **MLH 1/ MSH 2.**

MC associated cancer : Colorectal cancer.

2<sup>nd</sup> MC associated cancer : Endometrial cancer

(60 - 70%)

Risk of ovarian cancer : 20%.

BRCA 1 gene mutation has maximum risk of ovarian cancer : 40%.

BRCA 2 mutation has 15% risk of ovarian cancer.

5 - 10% ovarian cancers are hereditary.

Hereditary ovarian cancers occur at younger age group : around 50 years.

Sporadic ovarian cancers occur at 60 - 70 years (peak at 60 years).

Best method to prevent ovarian cancer in BRCA 1 mutation :

TAH + BSO after completion of family (Between 35 - 40 years) as they have chance of developing endometrial cancer too.

If 1<sup>st</sup> degree relative has hereditary ovarian cancer/ BRCA -1 mutation :

There is 5% risk of having ovarian cancer.

Annual screening is done : TVS + CA 125 (From 35 - 40 years of age).

If 1<sup>st</sup> degree relative is a case of sporadic ovarian cancer (dies at 65 years of age) : Reassure the patient, no screening needed.

## Types of ovarian cancer

00:41:51

According to WHO classification :

- Epithelial ovarian tumors : most common (90%).
- Germ cell tumors : 2<sup>nd</sup> most common (5-8%).
- Sex cord stromal tumors : 3<sup>rd</sup> most common (3-5%).
- Metastatic tumors.

most common ovarian tumor : serous cystadenoma.

most common ovarian cancer : serous cystadenocarcinoma.

most common ovarian tumor in reproductive age : mature cystic teratoma - dermoid cyst.

most common age for ovarian cancer : 60 years (60-70yrs).

Epithelial ovarian tumors :


- Serous tumors : most common; benign – serous cystadenoma, malignant – serous cyst adenocarcinoma.
- mucinous tumor
- Brenner's tumor.
- Endometrioid tumor.
- Clear cell tumor.

most common age : 60yrs.

mostly bilateral.

Worst prognosis as they have non-specific symptoms like nausea, vomiting, irritable bowel syndrome.

HPE finding : Psammoma body.

Serous tumors	Mucinous tumors
60% cases are benign – serous cystadenoma	80% cases are benign – mucinous cystadenoma
mostly bilateral	mostly unilateral
Associated with BRCA-1, BRCA-2, p53 mutation	Associated with K-RAS mutation
Smoking is not a risk factor	Smoking is a risk factor
malignant counterpart : Serous cystadenocarcinoma Tumor marker : CA-125 HPE : Psammoma bodies	malignant counterpart : mucinous cystadenocarcinoma Tumor marker : CEA, CA 19-9
 <p>Gross : uniloculated cyst filled with clear/serous fluid</p> <p>microscopy : Resembles fallopian tube lining</p>	<p>Gross : multiloculated cyst filled with mucinous material; honey comb appearance.</p> <p>microscopy : Resembles endocervix lining</p> <p>Associated with pseudomyxoma peritonii.</p>

**Pseudomyxoma peritonii :**

most common cause of pseudomyxoma peritonii : appendix CA.

Other causes : mucinous ovarian tumor (metastatic),  
mucocele of appendix.

It has bad prognosis, due to very high recurrence rate.

mutations associated with epithelial cell tumors:

Low grade tumors : K-RAS, PTEN mutations.

high grade tumors : p53 gene mutation.

**Brenner tumor mnemonic (BUST) :**

They are benign tumors.

100% unilateral.

They are solid tumors.

It has lining of Transitional epithelium

HPE finding : Walther cell nest with coffee bean nuclei.

**NOTE :** Ovarian tumors where coffee bean nuclei (central groove present) are seen : Brenner's tumor & granulosa cell tumor.

Endometrioid tumor :

Histologically resembles endometrial glands.

Associated with endometriosis.

Associated with endometrial cancer.

Clear cell tumor :

malignant tumors.

Associated with endometriosis.

Associated with in utero-DES exposure.

HPE finding : Hobnail cells.

- most common ovarian tumor associated with endometriosis : clear cell tumor (best answer); endometrioid tumor (2nd best answer).
- most common ovarian tumor associated with endometrial cancer : endometrioid variety, granulosa cell tumor.

## Germ cell tumors

00:59:55

varieties :

- Teratoma (mature, cystic, benign type : Dermoid cyst; immature : malignant; monoclonal type : Struma ovarii).
- Dysgerminoma.
- Yolk sac tumor (endodermal sinus tumor).
- Embryonal cancer.
- Choriocarcinoma.
- mixed type.

Common points :

most common age : 10 to 30 years.

mostly unilateral.

usually diagnose at early age : have a better prognosis.

**Tumor markers** of germ cell tumors (GCT) :

Teratoma : no tumor marker.

hcg : seen in all GCT except yolk sac tumor.

AFP : seen in all GCT except choriocarcinoma and dysgerminoma.

LHD : seen in all GCT except choriocarcinoma and embryonal tumor.

GCT	Tumor markers
Dysgerminoma (only radiosensitive tumor)	main : LDH. Others : hcg, PLAP Never produces AFP
Yolk sac tumor (endodermal sinus tumor)	main : AFP (alpha fetoprotein) Others : LDH, $\alpha$ -antitrypsin Never produces HCG
Embryonal cancer	main markers : AFP, hcg
Choriocarcinoma	Hcg

**NOTE :**

most common GCT : dermoid cyst (mature cystic teratoma).

most common germ cell cancer : immature cystic teratoma.

2<sup>nd</sup> most common GCT : dysgerminoma.

GCT with best prognosis : dysgerminoma.

GCT with worst prognosis : yolk sac tumor.

Active space



GCT which progresses rapidly (presents with acute abdomen)  
: yolk sac tumor.

The only ovarian tumor which is radiosensitive :

Dysgerminoma.

most common ovarian tumor in dysgenetic gonads :

Gonadoblastoma.

most common ovarian cancer in dysgenetic gonads :

Dysgerminoma.

GCT which is 100% unilateral : Yolk sac tumor.

### Dermoid cyst :

Also known as mature cystic teratoma.

It is the most common ovarian tumor in reproductive age.

It is the most common ovarian tumor in pregnancy.

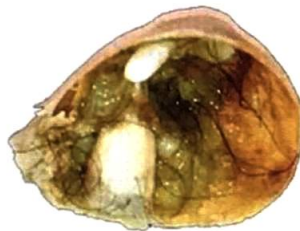
mostly unilateral (bilateral in 10% cases).

It has all 3 components of germ cell layers (most common : ectodermal).

It is mostly benign : but risk of malignancy is 0.2-2%.

most common site for malignancy : Rokitansky protuberance.

most common type of malignancy : squamous cell carcinoma.



Gross specimen of dermoid cyst showing teeth & hair



USG of dermoid cyst showing Rokitansky protuberance

Other USG findings of dermoid cyst :

- **Tip of the iceberg sign** refers to one of the characteristic appearances of an ovarian dermoid cyst. If there are echogenic cyst contents of sebum and hair, they cause marked posterior acoustic attenuation so that only the superficial part of the cyst is seen. Just like an iceberg, you may only be able to see a small piece of the structure, with a much larger piece deeper.
- **Dot-dash appearance** : Due to hair, teeth and sebaceous material (white) rest black.

- m/c to undergo torsion.
- management of dermoid cyst :
- Cystectomy.
  - If female has completed her child bearing :  
oophorectomy.

### Dysgerminoma :

2<sup>nd</sup> most common GCT.

It is unilateral, but bilateral in 15-20% females.

It is the GCT which has the **highest risk of bilaterality.**

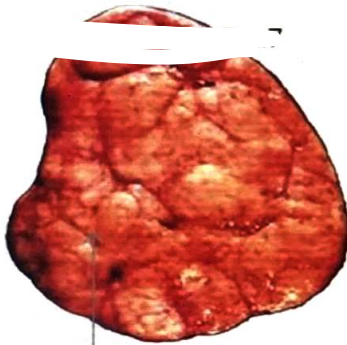
**Best prognosis** (among all GCTs).

It is the most common ovarian cancer in dysgenetic gonads.

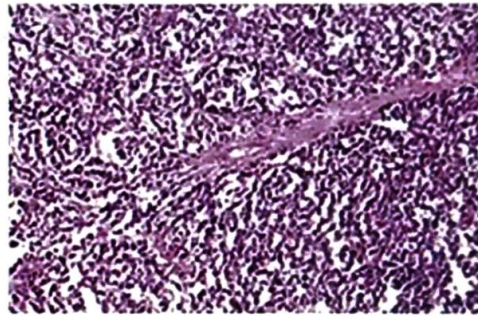
It is the most common ovarian cancer in pregnancy.

It is the only ovarian tumor which is **radiosensitive.**

Tumor markers : **LDH (main marker), PLAP, hcg.**



Gross appearance - fleshy, solid, lobulated, tan in colour



HPE findings : nests of cells  
Separated by fibrous septa;  
Septa infiltrated by lymphocytes.

### Yolk sac tumor :

most malignant GCT.

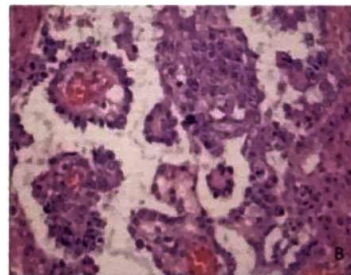
most rapidly progressing tumor.

It can present as acute abdomen.

GCT with worst prognosis.

It is 100% unilateral.

Tumor markers : **AFP (main), LDH,  $\alpha$ 1-AT**



- Q. A 25 year old woman presents to you for routine health checkup. She has had two normal vaginal deliveries and is healthy. She smokes one cigarette per day. She has no gynaecological complaint. Her menstrual period was 3 weeks back. During pelvic examination you notice her left ovary is enlarged. On usg a 5 cms cyst is seen in left ovary. Which of the following is the best recommendation for the patient
- A. Get her CA 125 levels checked
  - B. Get a CT scan done
  - C. Schedule a diagnostic laparoscopy
  - D. Tell her to come for a check up again after 1-2 months.

# OVARIAN CANCER : PART 2

## Introduction

00:00:11

Sex cord tumors	Stromal cell tumors
Estrogen producing : Granulosa cell tumor.  Androgen producing : <ul style="list-style-type: none"> <li>• Sertoli, Leydig cell tumor.</li> <li>• Leydig cell tumor.</li> <li>• Hilus cell tumor : <b>Reinke's crystals</b> seen on HPE.</li> </ul>	<ul style="list-style-type: none"> <li>• Fibroma.</li> <li>• Thecoma.</li> <li>• Fibrothecoma.</li> </ul>

General points :

Can be seen in any age group (m/c : **Perimenopausal** women).

mostly unilateral. Diagnosed at early stage.

Best prognosis among all ovarian tumors :

Sex cord stromal tumors > Germ cell tumors > Epithelial cell Tumors.

## Granulosa cell tumors and Fibroma

00:02:26

Granulosa cell tumors :

Arises from the granulosa cells which produce :

- **Estrogen** : Responsible for all clinical features.
- **Inhibin and Anti-mullerian hormone** : Tumor markers.

Gene : **FOX L-2 gene**.

Presentation :

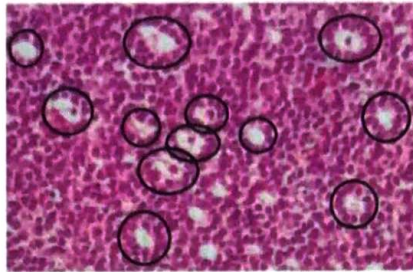
- Excessive bleeding.  
Abnormal uterine bleeding.  
Post menopausal bleeding.  
Precocious puberty.
- Endometrial cancer.  
**Endometrial sampling** should be done for all females with Granulosa tumor.

Active space

Histopathological examination (HPE) : **Call-Exner body.**

Central acidophilic material surrounded by crowded cells appearing like follicles.

Coffee bean nuclei.



**Fibroma**

It is a unilateral, benign and solid tumor.

Histology : **Well differentiated fibroblasts.**

It is associated with **meig syndrome**

meig syndrome	Pseudo meig syndrome
<p>Fibroma/ Thecoma/ Brenner's tumor/ Granulosa cell tumor + Ascites + Pleural effusion.</p> <p>Removal of tumor leads to resolution of ascites and pleural effusion.</p>	<p>Any other ovarian tumor (mucinous cystadenoma) or any other condition (Fibroid). + Ascites + Pleural effusion.</p>

**Metastatic tumors of ovary**

00:09:37

1. Stomach (m/c).
2. GIT
3. Breast cancer.

Krukenberg tumor :

1. Stomach (mc)
2. GIT
3. Breast CA

Retrograde lymphatics

Transcoelomic route

→ Ovary



Active space

Pyloric end of stomach → Retrograde lymphatics → Ovary.

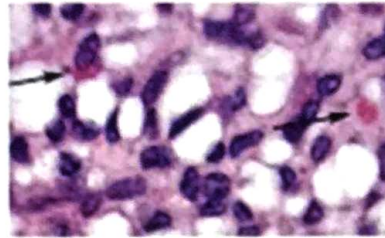
80% cases are bilateral.

There is symmetric enlargement of ovaries.

Shape of ovary retained.

Capsule remains intact.

Waxy consistency, mobile.



HPE :

Signet ring cells :

mucin filled cytoplasm pushes the nucleus to one side.

### FIGO staging of ovarian cancer

00:13:12

Stage I	Limited to ovary IA : One ovary involved. IB : Both ovaries involved. } Intact capsule IC : Capsule ruptured : • IC <sub>1</sub> : Intraoperative rupture. • IC <sub>2</sub> : Preoperative rupture. • IC <sub>3</sub> : malignant ascites.
Stage II	Spreads to other pelvic organs IIA : Fallopian tube or uterus. IIB : Other pelvic organs : Bladder, rectum.
Stage III	Spreads beyond pelvis into abdomen. III <sub>A</sub> : Retroperitoneal lymph nodes involved. } + Extension to III <sub>A</sub> : microscopic involvement above pelvic brim. } liver and spleen III <sub>B</sub> : macroscopic involvement above } capsule or Pelvic brim Size of implant ≤ 2 cm. } surface. III <sub>C</sub> : macroscopic involvement above pelvic brim Size of implant ≥ 2 cm.
Stage IV	Distant metastasis. IVA : malignant pleural effusion. IVB : Liver/ spleen parenchyma involved or Inguinal lymph node involved

Active space

## Surgical staging of Ovarian cancer

00:21:26

Steps :

1. Midline incision.
2. If ascites present : Send sample for cytology,  
If no ascites : Do saline wash and send **saline for cytology.**
3. Inspection and palpation of all abdominal organs.
4. Random peritoneal biopsies.
5. TAH (Type I) + BSO.
6. Infracolic omentectomy. (Not biopsy).
7. Pelvic + Paraaortic lymph node dissection.
8. Closure.

Normally for ovarian cancer : The surgery is **TAH + BSO.**

Exceptions :

1. Conservative : **unilateral salpingo-oophorectomy, No Hysterectomy.**
  - Germ cell tumor.
  - Sex cord tumor in young females.
  - Stage I A of epithelial tumor and family not completed.
2. **Debulking surgery** : Advanced stages (Stage 3, 4).

## Post operative therapy for ovarian cancer

00:27:00

Epithelial cell tumor	Germ cell tumor	Sex cord stromal tumor
Chemotherapy		
<b>6 cycles :</b> IV + Intraperitoneal. Paclitaxel + Carboplatin/ Cisplatin	B : Bleomycin E : Etoposide P : Cisplatin	B : Bleomycin E : Etoposide P : Cisplatin.
All stages <b>except stage I A and I B.</b>	All stages <b>except Dysgerminoma stage I (Best prognosis).</b>	Chemotherapy needed <b>only in stage 3 and 4.</b>

Clinical concept :

Q. For Qs select the ovarian tumor from below that is most likely to be associated with the clinical picture. Each lettered option may be used once, more than once or not at all

- A. Granulosa cell tumor.
- B. Sertoli leydig tumor.
- C. Immature teratoma/dermoid.
- D. Gonadoblastoma.
- E. Krukenberg tumor.

Q. A 26 year old female presents to gynaecology OPD complaining of increased facial hair growth but hair on her head are receding in temporal region. She also has had problems with acne. On physical examination pt has significant amount of coarse hair on chin, face chest. On pelvic examination she has enlarged clitoris and USG shows a 7 cm adnexal mass.

Ans : B. Sertoli leydig tumor.

Q. A 56 year old post menopausal woman presents with complain of vaginal bleeding. Her uterus is slightly enlarged and she has 6 cm adnexal mass. Endometrial biopsy shows adenocarcinoma of endometrium.

Ans : A. Granulosa cell tumor.

Q. A 17 year old woman is referred by her physician for evaluation of primary amenorrhea. On physical examination she has virilisation and during workup it is seen she has sex mosaicism- 45X/ 46XY

Ans : D. Gonadoblastoma.

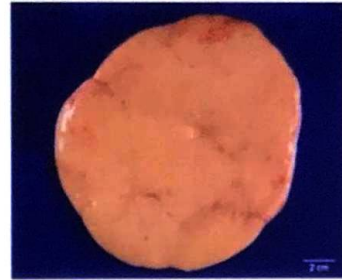
Q. A 67 year old woman is found to have bilateral adnexal mass while undergoing evaluation of her recently diagnosed colon cancer.

Ans : E. Krukenberg tumor.



Q. Which of the following tumor marker is raised in the ovarian tumor shown below

- A. HCG
- B. LDH
- C. AFP
- D. Ca 125



Active space

# VULVAL CANCER

## Relevant anatomy

00:00:48

Lymphatic drainage of vulva :

First lymph nodes to which vulva drains :

Superficial inguinal lymph nodes.



Deep inguinal lymph nodes/ Femoral lymph nodes.

Sentinel lymph node for vulval cancer : Superficial inguinal lymph nodes.

Sentinel lymph node biopsy is done (and more significant) in vulval cancer > cervical cancer.

Dye used : Isosulphan blue dye.

Lymph node dissection in vulval cancer : Inguino femoral lymph node dissection.

Pelvic lymph nodes (iliac group of lymph nodes) are not involved by lymphatics.

If involved, corresponds to metastasis : Stage IV B vulval Ca.

The structures which lie within 2 cm of midline, their lymphatics cross each other.

So vulval cancer within 2 cm of midline (Cancer of clitoris/ Cancer of fourchette/ Cancer of anterior labia minor).



Do bilateral inguino femoral lymph node dissection.  
(because the lymphatics cross each other)

The structures which lie > 2 cm from midline, their lymphatics do not cross.



Do unilateral lymph node dissection.

Active space

## Vulval cancer

00:05:43

Comprises of 4.1% of gynecological cancers.

Lined by stratified squamous epithelium.

most common type : Squamous cell carcinoma.

Second most common type : melanoma.

Other types include :

- Basal cell carcinoma.
- verrucous cancer ( variety of squamous cell carcinoma).

Both are locally invasive & rarely metastasize.

management is radical partial vulvectomy.

Verrucous cancer :

- Radiotherapy is contraindicated as it induces anaplastic transformation & can lead to metastasis.
- Sentinel lymph node biopsy is done. If positive, do lymph node dissection.

Basal cell carcinoma :

- Radical partial vulvectomy + Sentinel lymph node biopsy + Lymph node dissection.

Squamous cell carcinoma :

Age group : 50 to 70 years.

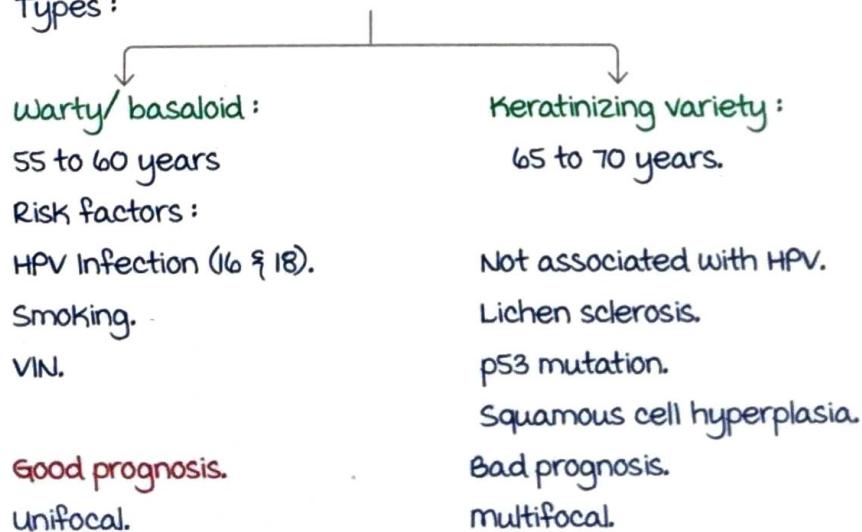
most common symptom : Pruritis.

Common risk factors include :

HIV.

Immuno compromised states.

Types :



MC site for vulval cancer : Labia majora > Labia minora

Additional risk factors :

Extra mammary paget's disease (for adenocarcinoma).

Prognostic factors :

1. Lymph node involvement : most important.

If involved, 5 year survival rate : 50%, if not involved : 80%.

2. Depth of invasion :

If depth < 1 mm → No lymph nodes are involved →

No lymph node dissection needed → Better prognosis.

## Staging of vulval cancer

00:13:28

Both clinical & surgical staging (TNM or FIGO staging) :

FIGO Staging :

Stage	Description	Lymph node involvement
Stage 1 IA IB	Cancer limited to vulva : Size ≤ 2 cm + Depth of invasion ≤ 1 mm. IB Size > 2 cm OR any size with depth of invasion > 1 mm.	No involvement.
Stage 2	Tumor of any size + Involvement of lower 1/3 <sup>rd</sup> of vagina/ Lower 1/3 <sup>rd</sup> of urethra/ lower 1/3 <sup>rd</sup> of anus.	No involvement.
Stage 3 A B C	Tumor of any size + Involvement of lower 1/3 <sup>rd</sup> of vagina/ Lower 1/3 <sup>rd</sup> of urethra/ lower 1/3 <sup>rd</sup> of anus. Bladder mucosa or rectal mucosa involved.	Lymph node involved (inguinofemoral lymph nodes). 1 or 2 lymph nodes < 5 mm in size. ≥ 2 lymph nodes ≥ 5 mm in size/ 3 or more lymph nodes < 5 mm. Extra capsular spread
Stage 4 4A 4B	Tumor invades upper 2/3 <sup>rd</sup> of vagina/ 2/3 <sup>rd</sup> of urethra/ rectum OR fixed to pelvic bone. 4B Distant metastasis.	Fixed or ulcerated inguino femoral lymph node. Pelvic lymph node involved.

Active space

**Anatomy :**

Structures/ compartments seen from pelvis towards perineum :

1. Pelvic floor : Comprised of levator ani muscle which forms pelvic diaphragm.
2. Deep perineal pouch/ urogenital diaphragm :  
Lined by superficial fascia & deep inferior fascia (called as perineal membrane).
3. Superficial perineal pouch :  
Space between perineal membrane & colles fascia.

**Content of deep perineal pouch :**

1. Deep transverse perineii muscle.
2. Compressor urethrae muscle.
3. Urethro vaginalis muscle.
4. Internal pudendal artery.
5. Vein of clitoris.
6. Dorsal nerve.

**Content of superficial perineal pouch :**

1. Bulbospongiosus muscle.
2. Ischiocavernosus muscle.
3. Superficial transverse perineii muscle.
4. Bartholin gland.
5. Vestibular bulb.
6. Clitoris.
7. Pudendal vessels & nerve.

**Management of vulval cancer**

00:23:17

**Stage 1 & 2 :**

- No lymph node involved.
- management : Surgery ( treat both tumor & lymph node).

**Stage 3 :**

Surgery followed by adjuvant radiotherapy.

**Stage 4 :**

Chemoradiation.

### management of tumor :

#### 1. Wide local excision or simple partial vulvectomy :

Excise tumor + 1 cm margin depth up till Colles fascia.  
For management of preinvasive disease & stage IA of vulval carcinoma.

#### 2. Radical partial vulvectomy :

Tumor + 2 cm margin depth up till perineal membrane.  
For management of Stage IB & II.

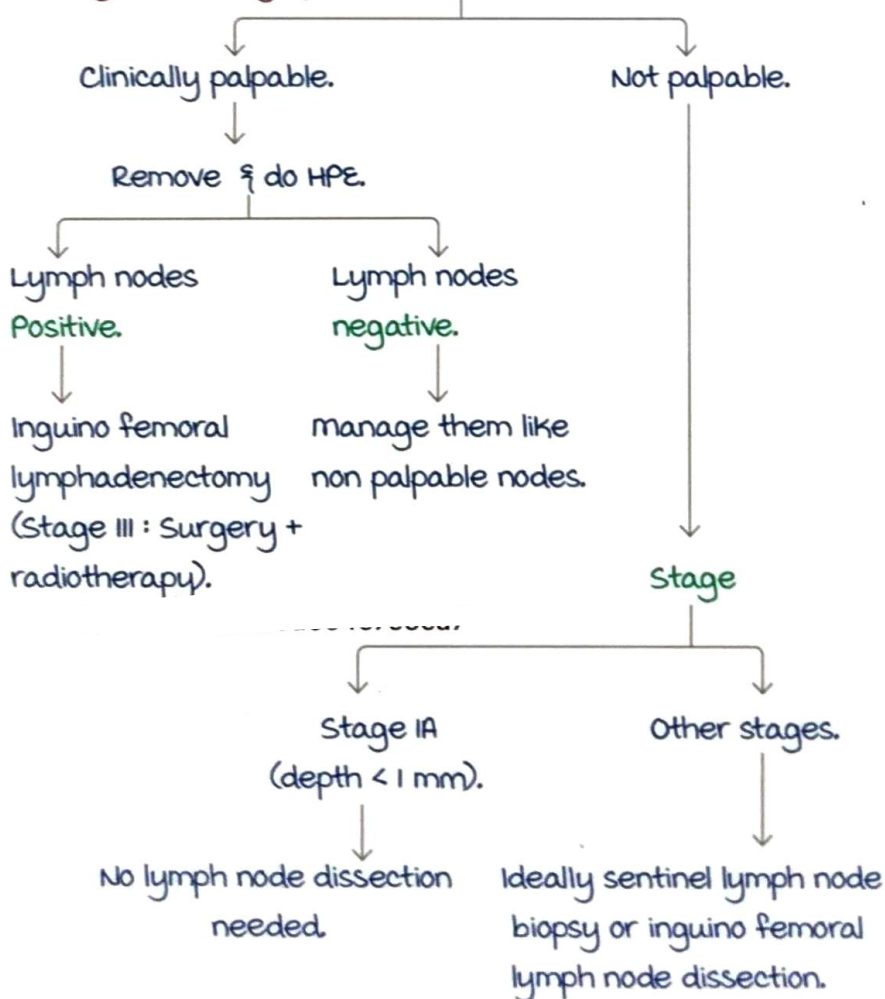
#### 3. Radical total vulvectomy :

Entire vulval tissue up till perineal membrane removed including content of superficial perineal pouch.

For management of :

- Large midline carcinoma.
- Multifocal carcinoma.
- Stage III.

### management of lymph nodes :



### Unilateral or bilateral inguino femoral lymph node dissection :

#### Criteria :

- Size :  $< 2$  cm.
- Location : Laterally located ( $> 2$  cm away from midline).
- Local extension : Absent.

#### Management :

- All criteria present : Unilateral inguino femoral lymph node dissection.
- Any one criteria not present : Bilateral inguino femoral lymph node dissection.

#### MCQ's

Q. All of the following are associated with vulva cancer except

- A. lichen sclerosis.
- B. smoking.
- C. pagets disease.
- D. OCP.

Q. A 76 year old female presented with non healing ulcer on labia majora for 6 months measuring  $2 \times 3$  cm with no palpable lymphadenopathy. Biopsy shows squamous cell carcinoma. management includes?

- A. Radical vulvectomy with unilateral LN dissection.
- B. Radical vulvectomy with bilateral LN dissection.
- C. Simple vulvectomy.
- D. Chemoradiation with resection.