

**Self Assessment & Review**

# **Gynecology**

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Self Assessment & Review

# Gynecology

*Ninth Edition*

**SAKSHI ARORA HANS**

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*Dedicated to*

**SAI BABA**

Just sitting here reflecting on where I am and where I started, I could not have done it without you Sai baba... I praise you and love you for all that you have given me... and thank you for another beautiful day... to be able to sing and praise you and glorify you... you are "My Amazing God"



# Preface

Dear Students,

I wish to extend my thanks to all of you for your overwhelming response to all the 8 editions of my book and for making it the bestseller book on the subject. Thanks once again for the innumerable emails you have sent in appreciation of the book; a few of which I have got printed at the end of the book. I apologise to all those who have sent me mails of appreciation but due to paucity of space, I was unable to get them printed.

NEET continued in year 2015, but yes, this time the anxiety of the students for NEET was less. Students looked more settled. The approach of NEET became a little clear. Reading important theory becomes absolutely essential. Whether you do it from a textbook or from subjectwise help-books, that is your choice.

It now gives me immense pleasure to share with you the new edition of the book. Many changes have been done in the book.

Each chapter has been thoroughly revised and updated. All new guidelines have also been incorporated.

## Salient Features of 9th Edition

- i Theory before all the chapters revised and updated. In the theory part, you will get all the information you are required to know as an intern or as an undergraduate student of Gynecology.
- ii Use of a lot of pedagogical features makes learning easy and simple to reproduce during exams:
  - (a) New tables have been added wherever necessary
  - (b) Flowcharts have been used to add simplicity
  - (c) Many new diagrams and real-time photographs have been added, for which I thank **Shri Jitendar P Vij** (Group Chairman), Jaypee Brothers Medical Publishers for allowing me to use photographs and illustrations from eminent Obs. and Gyne. books of Jaypee publication.
- iii. The section of difficult review questions has been merged with the main questions of AI, AIIMS and PGI, because if NEET will be held in the forthcoming years, it is no more important which question was asked in which state and which year; what is important is the *Question* itself. I have incorporated them in the main section so that you do not miss out on any of the important questions.
- iv New pattern questions (more than 200) with their explanations have been incorporated to give a fair idea to the students about how the new pattern would be.
- v. Image-based questions have been included in each chapter to give an idea to the students about this new pattern.
- vi. In the color plates, many new diagrams, HSGs and images of instruments have been included. This section has been created to help not only the undergraduate students for the preparation of their practical exams but also the PG aspirants for the image-based questions.
- vii. For the first time ever, annexures have been added for last-minute revisions.
  1. Lining of female genital tract
  2. Blood supply of genital tract
  3. Lymphatic drainage of female genitalia
  4. pH of vagina at different ages
  5. Some important measurements
  6. Male and female derivatives of embryonic urogenital structures
  7. Origin of female genital tract
  8. Culture media and DOC of various organisms
  9. Clinical features of genital ulcers
  10. Types of hysterectomies and structures removed
  11. Pearl index of contraceptives
- viii. All the references are from Shaw's Gynecology 15th edition, Novak's 15th edition, William's Gynecology 1st and 2nd editions, Jeffcoates' 8th edition, Leon Speroff's 8th edition and Dutta's Gynecology 6th edition.
- ix. Recent solved papers of AIIMS May/November 2015, PGI May 2015 and November 2014, with fully explained, referenced and authenticated answers are included at the end.

I hope all of you will appreciate the changes and accept the book in this new format, like you have done for the previous editions.

Remember there is no substitute to theory books, but hopefully you will find all relevant theory in this user-friendly book of Gynecology. I must admit hereby that despite keeping an eagle's eye for any inaccuracy regarding factual information or typographical errors, some mistakes must have crept in inadvertently. You are requested to communicate these errors and send your valuable suggestions for the improvement of this book. Your suggestions, appreciation and criticism are most welcome.

New Delhi  
June 2016

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# Acknowledgments

*Everything what we are is the outcome of a series of factors and circumstances, in addition to ourselves.*

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- **Shri Jitendar P Vij** (Group Chairman) for being my role model and a father-like figure. I will always remain indebted to him for all that he has done for me.
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Symbols used in the book	Meaning
	Key points
	Previously asked MCQs
	Important concepts
	Definition
	Mnemonic

# Anatomy of the Female Genital Tract

## External Genital Organs (Syn: Vulva, Pudendum)

The vulva includes mons veneris, labia majora, labia minora, clitoris, vestibule and conventionally the perineum (Fig. 1.1).

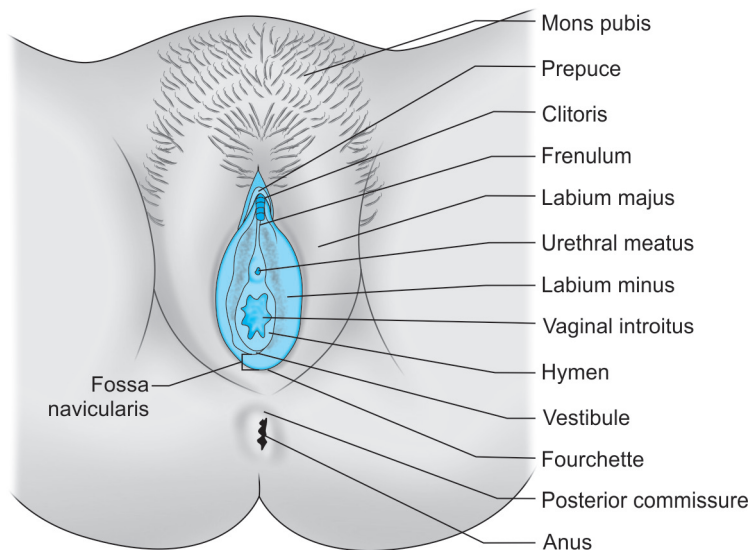


Fig. 1.1: Vulva

- **Mons Pubis (Veneris):** Pad of subcutaneous adipose connective tissue lying in front of the pubis and in the adult female covered by hair.
- **Labia Majora:** Lie on either side; join **posteriorly** to form the **posterior commissure**. Their inner side is hairless. **It is homologous to the scrotum in a male.** The round ligament terminates at its anterior third.
- The labia majora and the mons veneris contain:
  - The hair follicles.
  - The sebaceous glands.
  - Modified sweat glands known as the apocrine glands.
- **Labia Minora:** They are two thick folds of skin, devoid of fat, lying within the labia majora. Anteriorly, they **enclose the clitoris** and unite with each other in front and behind the clitoris to form the **prepuce** and the **frenulum**, respectively. Lower portion of the labia fuses across the midline to form a fold of skin called the **fourchette**. **It is homologous to the ventral aspect of the penis.**
- **Clitoris:** It is a small erectile body (2.5 cm) lying in the anteriormost part of the vulva. **It is homologous to the male penis.** It consists of glans, a body and two crura.
- **Vestibule:** Triangular space bounded anteriorly by the clitoris, posteriorly by the fourchette, and on either side by the labia minora. It has 4 openings, namely (Fig. 1.1):



### Vulva

Collective name for external genitalia and perineum.



The hidradenoma of vulva arises from the apocrine glands of labia majora and mons veneris.



### Development of Vulva

Clitoris develops from genital tubercle.  
 Labia minora → genital folds.  
 Labia majora → genital (labioscrotal) swellings.  
 Vestibule → urogenital sinus.

### Important

#### Vulva

- Blood supply → Internal pudendal artery
- Sensory innervation → Pudendal nerve
- Lymphatic drainage → Inguinal nodes  
(First to superficial inguinal LN (sentinel LN) and then to deep inguinal LN)

1. Urethral opening.
2. Vaginal orifice opening.
3. Bartholin's ducts on either side.
4. Ducts of paraurethral glands, also known as Skene's ducts on the posterior surface of urethra.

#### EXTRA EDGE

- The posterior part of vestibule between fourchette and vaginal opening is called **fossa navicularis**.
- Hymen is thin fold of mucous membrane attached to vaginal orifice all around.
- It is lined by stratified squamous epithelium on both sides.
- The hymen is most commonly torn posterolaterally or posteriorly.
- It is replaced by tags after childbirth, called **carunculae myrtiformes**.

### Internal Genital Organs

The internal genital organs in a female include vagina, uterus, fallopian tubes, and the ovaries.

#### Vagina

- Distensible fibromuscular canal connecting the uterine cavity with the exterior at the vulva.
- Anterior wall = 7.5 cm, posterior wall = 9 cm in length.
- Upper vagina is separated by cervix into anterior, posterior and lateral fornices.
- Deepest fornix = posterior fornix; Shallowest fornix = anterior fornix
- On cut section = It is H-shaped

#### Relations of Vagina

Anterior → Bladder (upper third)  
Urethra (lower two-third)

Posterior → **P** = Pouch of Douglas in the upper 1/3rd  
**A** = Ampulla of rectum in middle 1/3rd  
**P** = Perineal body in lower 1/3rd

Lateral → **Medicos** = Mackenrod's ligament or pelvic cellular tissue  
**Love** = Levator ani muscle  
**Books** = Bulbocavernous muscle  
Vestibular bulb  
Bartholin's glands  
From above downwards

#### The cervix and all 4 fornices are related to:

- Uterine vessels
- Mackenrod's ligament
- Ureter<sup>Q</sup>
- Vagina has inhabitant bacteria called **Doderlein's bacteria** which is a lactobacilli<sup>Q</sup> and converts the glycogen present in vaginal epithelium into lactic acid<sup>Q</sup> under the influence of estrogen.  
Thus, pH of vagina is acidic
  - The pH of vagina in an adult woman is 4–5.5 with an average of 4.5.
  - The pH of vagina varies with age.

#### Important

Posterior wall of vagina is 2.5–3 cm longer than anterior wall.



**Note:** Doderlein's bacilli are present in a newborn female's vagina and then disappear (after 10–14 days) to reappear at puberty and then again disappear after menopause.

Age	Vaginal pH
• In a newborn infant <sup>o</sup>	Between 4–5
• 6 weeks old child <sup>o</sup>	Changes from acidic to alkaline <sup>o</sup> (6–8)
• Puberty <sup>o</sup>	Changes from alkaline to acidic
• Reproductive age group <sup>o</sup>	4–5.5 <sup>o</sup>
• Pregnancy <sup>o</sup>	3.5–4.5 <sup>o</sup>
• During menstruation	6–8
• Menopause	6–8 <sup>o</sup>

**Note:** pH of vagina also varies along its length, being highest in the upper part because of admixture of alkaline cervical mucus.

- Vagina does not have any mucus-secreting glands.<sup>o</sup> Since vagina does not have any glands, vaginal discharge is not derived from vagina.

The components of vaginal secretion are derived from:

- Endocervical glands
- Endometrial glands
- Bartholin's glands
- Vagina does not have any serosal covering except for the area covered by cul de sac posteriorly.<sup>o</sup>
- Apart from Doderlein's bacilli, it contains many other pathogenic organisms including *Cl. welchii*.

### Vaginal Epithelium

Vagina is lined by **stratified squamous epithelium** which is composed of the following types of cells:

- > **Parabasal/basal cells:** Which are predominant when there is no hormonal dominance.<sup>o</sup>
- > **Intermediate cells:** Which are predominant when there is progesterone predominance<sup>o</sup>, i.e. in luteal phase/latter half of menstrual cycle.
- > **Superficial cells:** Which are predominant when there is estrogen predominance, i.e. in follicular phase – first half of menstrual cycle.
  - The intermediate and superficial cells contain glycogen under the influence of estrogen.

**Note:** In newborn females, vagina is lined by transitional epithelium.<sup>o</sup>

### Blood Supply

Is from 3 arteries:

1. **Descending vaginal artery:** Branch of either uterine A or a direct branch of internal iliac A
2. **Internal pudendal artery**
3. **Middle rectal artery**

### Lymphatic Drainage

Upper vagina: Same as cervix (see below)

Middle vagina: Internal iliac lymph nodes

Lower vagina: Superficial inguinal LN

### Nerves

The innervation of vagina contains both sympathetic and parasympathetic fibers ( $S_2$ – $S_4$ ). Only free nerve endings are seen in mucosa. No other type of nerve endings are noted in vagina.



Squamous epithelium is resistant to gonococcal infection hence theoretically gonococcal vaginitis can occur in new born females

**Angle of Anteversion**

Angle between cervix and vagina (Remember V for version)

V for vagina) = 90°

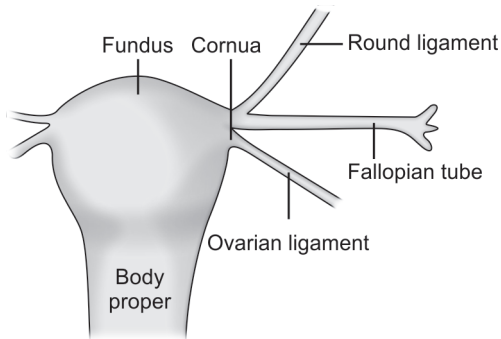
**Angle of Antelexion**

Angle between cervix and uterus = 120°–130°

**Angle which vagina makes with horizontal = 45°**



Middle layer of uterus is called living ligature, since it has fibers in criss-cross manner. Therefore, after the delivery of placenta, uterus contracts and these fibers occlude the blood vessels preventing postpartum hemorrhage (PPH). This is the reason when tone of uterus is lost (atonic uterus), this action cannot take place and PPH occurs.



**Fig. 1.2:** Structures attached at cornua of uterus



**Structures attached at cornua of uterus**

**From anterior to posterior, they are:** R ⇒ F ⇒ O

**From superior to inferior:**

Fallopian tube is the superior-most. Round ligament and ovarian ligament lie inferior to it at the same level.

Hence, **most common cause of failure of ligation**—identification of wrong structure.

## Uterus

- It is **pyriform** in shape
- Weight of nonpregnant uterus in multiparous females = 50–70 gm
- Weight of nonpregnant uterus in multiparous females = 80 gm
- Weight of nonpregnant uterus = 1000 gm
- Length of nonpregnant uterus in nulliparous females = 6 to 8 cm (7.5 cm)
- Length of nonpregnant uterus in multiparous females = 9 to 10 cm
- Length of pregnant uterus = 35 cm
- Capacity of nonpregnant uterus = 10 ml
- Capacity of pregnant uterus = 5000 ml
- Position of uterus: Most common is **anteverted** and **anteflexed**. **Anteflexion** is at the level of the Internal os.
- It consists of: A. body; B. isthmus; C. cervix.

### (A) Body

The wall of body consists of three layers:

1. **Perimetrium:** Serous coat adherent to underlying muscle.
2. **Myometrium:** Consisting of thick bundle of muscle which forms 3 distinct layers during pregnancy:
  - Outer longitudinal.
  - Inner circular.
  - Middle interlacing called living ligature.
3. **Endometrium:** It is the mucous lining of the cavity. As there is no submucous layer, the endometrium is directly attached to the muscle coat. It consists of lamina propria and surface epithelium. **The surface epithelium is a single layer of ciliated columnar epithelium** but cilia are lost once menstruation begins at puberty:

**Note:** For supports of uterus, see chapter on prolapse:

- The body of uterus is further divided into **fundus** and **body proper** (Fig. 1.2).
- Fundus is the part which lies above the opening of the uterine tubes (or fallopian tubes)
- The body proper is triangular and lies between the openings of the tube at the cornua and isthmus
- The site of uterus at which the fallopian tube opens in the uterus is called **cornua**.
- The structures attached at the cornua are (Fig. 1.2):
  1. Round ligament (R)
  2. Fallopian tube (F)
  3. Ovarian ligament (O)

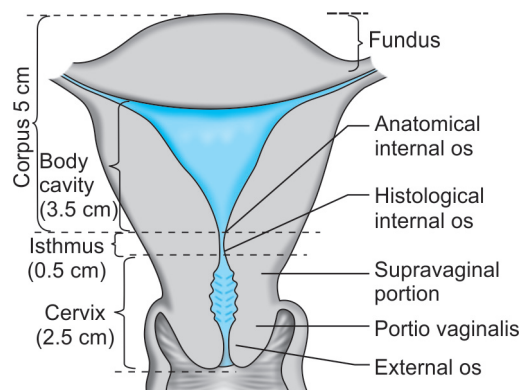
### (B) Isthmus

- Constricted (0.5 cm) part of uterus situated between body of uterus and cervix.
- It extends from anatomical internal os above to the histological os below (Fig. 1.3).
- Isthmus forms the lower uterine segment (LUS) after the 12th week of pregnancy (in the second trimester).
- It is best formed in late pregnancy.
- At term, LUS is formed by isthmus–70% and cervix–30%
- At cesarean, LUS can be identified by a loose fold of peritoneum (utero-vesical fold)



**(C) Cervix**

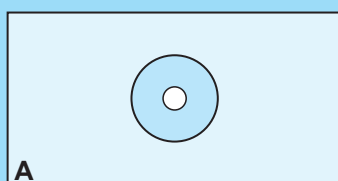
- It is the lowermost part of the uterus extending from the histological internal os to the external os
- It is cylindrical in shape measuring 2.5 cm in length and **diameter**.
- The cervix is divided into a supravaginal part (**Endocervix**) – the part lying above the vagina and a vaginal part (**Portio vaginalis** or **exocervix**) which lies within the vagina, each measuring 1.25 cm.
- **Endocervix** is lined by single layer of tall columnar epithelium<sup>Q</sup> and has complex racemose glands secreting alkaline mucus (pH 7.8)<sup>Q</sup> **Portio vaginalis** or **exocervix** is lined by nonkeratinized stratified squamous epithelium.<sup>Q</sup> The place where columnar epithelium gradually changes to squamous epithelium is called **squamocolumnar junction/transformation zone**.



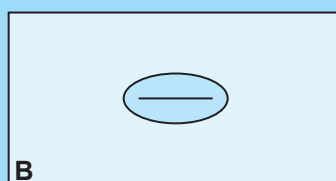
**Fig. 1.3:** Coronal section showing different parts of uterus

**External os (Figs. 1.4A and B)**

Where cervix opens into vagina

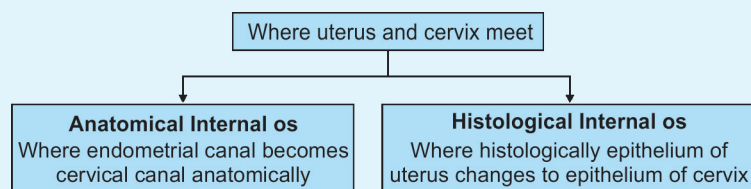


Pinpoint/circular in nulliparous females



Transverse slit-like in multiparous females

**Figs. 1.4A and B:** External os (A) Pinpoint; (B) Transverse slit-like

**Internal os****Significance of internal os**

- Area between anatomical and histological internal os is called **isthmus**.
- At the level of internal os, uterine artery moves upwards.
- Peritoneum is reflected at this level on to the bladder. This is the point of identification of internal os during lower segment cesarean sections (LSCS).
- Uterosacral ligaments lie at this level and Mackenrodt's ligament lies below this level.

**Cervical Mucus**

pH = 7.8 (Alkaline).

**Characteristics of cervical mucus:**

Shape of cervical canal is fuseform or spindle-shaped on cut-section. The anterior and posterior walls are opposed to each other and show mucosal folds, which resemble branches of tree called Arbor vitae.

**Blood Supply A:** Uterus the blood supply of uterus is from the uterine artery (branch of anterior division of internal iliac artery) and ovarian artery



M/c site for cancer cervix/  
CIN is transformation zone.



In erect posture, the internal os lies on the upper border of the symphysis pubis and the external os lies at the level of ischial spines.



Transverse vaginal septum mostly corresponds to External os.



Age	Corpus/ Cervix ratio
Before puberty	1:2
At puberty	2:1
In adults/ Reproductive age	3:1 or 4:1
After menopause	Whole of uterus and cervix atrophy

**B) Cervix:** is from descending cervical artery (branch of uterine artery)

### Lymphatic Drainage

#### A) Uterus:

Fundus: Drains into para-aortic/lateral aortic lymph nodes.

Body: Drains into external iliac lymph nodes

Cornua: Drains into superficial inguinal nodes along with round ligament

#### B) Cervix:



I–Internal iliac lymph nodes  
H–Hypogastric lymph nodes  
O–Obturator lymph nodes  
P–Presacral/paracervical lymph nodes  
E–External iliac lymph nodes  
Mnemonic: **IHOPE**

#### Remember:

- MC lymph node involved in Ca cervix – Obturator LN
- 1st lymph node involved in Ca cervix – Paracevical LN (Ureteric LN)
- Ca Cervix does not involve superficial inguinal LN.

#### Sensory supply:

Uterus: T10 to L1

Cervix: S2 to S4

### Fallopian Tube

Important facts about fallopian tube:

- **Length** = 4 inches or 10–12 cm.
- Parts are:
  - **Interstitial (Intramural):** 1.25 cm long and 1 mm diameter (narrowest part<sup>Q</sup>). It has no longitudinal muscles, only circular muscles are present and acts as anatomical sphincter<sup>Q</sup>.
  - **Isthmus:** 2.5 cm long and 2 mm in diameter<sup>Q</sup> (second narrowest part<sup>Q</sup>); acts as physiologic sphincter.
  - **Ampulla:** Widest<sup>Q</sup> and longest part<sup>Q</sup> (5 cm) and fertilization occurs here<sup>Q</sup>
  - **Fimbria/infundibulum<sup>Q</sup>:** 1.25 cm long with a maximum diameter of 6 mm
- **Histologically:** Fallopian tube is lined by ciliated columnar epithelium with a unique type of cell called **Peg cell<sup>Q</sup>** whose function is not known<sup>Q</sup>. It also has secretory cells whose secretions are rich in pyruvate. Early conceptus derives its nutrition from pyruvate.

**Blood supply:** Medial: 2/3rd by uterine artery

Lateral: 1/3rd by ovarian artery

#### Lymphatic drainage:

- Lateral part along with ovarian lymphatic drains into lateral aortic LN.
- Medial part along with cornua drains into superficial inguinal LN.

### Bartholin's Glands

- **Bartholin's Glands** are homologous to Cowper's gland<sup>Q</sup>/bulbourethral glands in males.
- They are 2 in number and of racemose type<sup>Q</sup>
- Lie in the superficial perineal pouch embedded in the posterior part of vestibular bulb.
- Glands are oval in shape and are of size of a pea<sup>Q</sup>
- They are impalpable unless enlarged.
- The acini is lined by single layer of low columnar or cuboidal cells<sup>Q</sup>



#### 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 tubectomy = isthmus.
- Best prognosis for reversibility/recanalization of tube is isthmo-isthmic part of tube.



**Bartholin's cyst** – formed when Bartholin's duct is blocked.

- M/c cyst of vulva.
- M/c cause = gonococcal infection.
- M/c site = fluctuant, non-tender, swelling present on inner side of junction of anterior 2/3rd with posterior 1/3rd of the labium majora.
- TOC = Marsupialization
- **Bartholin abscess.**
- Management = Incision and drainage.

- Bartholin's duct is 2 cm long<sup>Q</sup> and opens into the vestibule, outside the hymen at the **junction of the anterior 2/3rd and posterior 1/3rd in the groove between the hymen and labium minora**.<sup>Q</sup>
- Duct is lined by multilayered columnar epithelium<sup>Q</sup> (not by transitional epithelium as is usually stated).<sup>Q</sup>
- Function of the gland is to produce abundant alkaline mucus during sexual excitement.

### Skene's Tubules

Skene's tubules are the paraurethral glands equivalent to **prostate in males**. Both Bartholin's glands and Skene's tubules arise as downgrowths of urogenital sinus.

### Ovary

- Measures 3 × 2 × 1 cm.
- They are intraperitoneal structures lying in the **ovarian fossa of Waldeyer** on the lateral pelvic wall.
- Ovary is formed at T10 and then descends down in the pelvis with the help of **Gubernaculum**. Uterus **divides the Gubernaculum into ovarian ligament and round ligament**.
- The ovary is attached to the posterior layer of the broad ligament by the mesovarium, to the lateral pelvic wall by infundibulopelvic ligament and to the uterus by the ovarian ligament.
- The ovarian fossa is related **posteriorly to ureter and internal iliac vessels and laterally to the peritoneum separating the obturator vessels and nerve** medially to ovarian ligament.
- **The ovary is covered by a single layer of cubical cell known as germinal epithelium** of Waldeyer.
- **Blood supply** – Ovarian artery – Branch of abdominal aorta at L<sub>2</sub> level
- **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

### Lining of Female Genital Tract

Organ/Structure	Epithelial lining
• Bartholin's gland	Single layer of low columnar cell
• Bartholin's duct ( <i>Jeffcoate 7/e, p 24</i> )	Multilayered columnar cells (Not transitional)
• Adult vagina	Stratified squamous epithelium
• Newborn vagina	Transitional epithelium
• Uterus	Columnar epithelium
• Cervix (endocervix, cervical canal)	High columnar epithelium
• Ectocervix	Squamous epithelium
• Fallopian tube	Ciliated columnar epithelium

### Blood Supply of Genital Tract

#### Ovarian Artery

- Arises from aorta below the renal artery
- Branches in pelvis other than the ovary are:
  - Branch to ureter
  - Uterine tube



#### Ligaments in relation to ovary:

- **Ovarian ligament**— connects ovary to uterus
- **Infundibulopelvic ligament** (suspensory ligament of ovary)
- It has ovarian nerves and vessels
- **Mesovarium**—It connects ovary with broad ligament posteriorly



#### Lining epithelium of the organ is important because

- M/C histological type of cancer depends on lining epithelium, e.g. M/C variety of fallopian tube cancer is adenocarcinoma as tube is lined by columnar epithelium.
- M/C variety of uterine cancer is adenocarcinoma of the uterus (lining epithelium columnar).
- M/C variety of vaginal cancer is squamous cell carcinoma (lining epithelium is squamous cell).
- In cervix, endocervix is lined by columnar epithelium and exocervix by squamous epithelium. Hence, in all females, there is an area in cervix where one epithelium changes into other, this is called transformation zone. Since here one type of epithelium is changing into other type, it is the M/C site for cancer cervix.
- M/C variety of cancer cervix is squamous cell cancer.
- Now since endocervix is lined by columnar epithelium, adenocarcinoma can also occur in cervix. The M/C site for adenocarcinoma of cervix is endocervix.

- Round ligament
- Uterine anastomosis.

**Note:** In the abdomen, just at its origin, it gives branch to ureter.

- Ovarian vein drains into inferior vena cava on right side and left renal vein on left side.

### Internal Iliac Artery

**It is the main feeding vessel of the pelvis and pelvic organs.** It divides into anterior and posterior divisions.

**Note:** Only the anterior division supplies the pelvic viscera.

### Branches of the Internal Iliac Artery

	Anterior division	Posterior division
Visceral branches	Superior vesical Obliterated umbilical Inferior vesical Middle rectal Uterine	Nil
Parietal branches	Vaginal  Obturator Inferior gluteal Internal pudendal	Iliolumbar Sacral Superior gluteal

### Uterine Artery

- As a terminal branch of anterior division of internal iliac artery, uterine artery runs downwards and medially to cross the ureter near the cervix (2 cm lateral to cervix). It then ascends along the lateral border of the uterus in a tortuous course giving branches to both uterine surfaces.
- 2 cm lateral to cervix, where it crosses the ureter, is called water under bridge (bride-artery, water-urine in ureter). **This is the most common site of ureteric injury during hysterectomy followed by pelvic brim.**



### Branches of uterine artery to uterus:

- U = Uterine artery
- A = Arcuate artery—supplies outer 1/3rd of myometrium
- R = Radial artery—supplies inner 2/3rd of myometrium
- B = Basal artery—supplies basal endometrium
- S = Spiral artery—supplies superficial endometrium

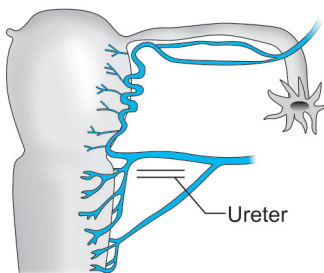
### Pelvic Ureter

- It extends from its crossing over the pelvic brim up to its opening into the bladder.
- Measures 13–15 cm in length and has a diameter of 5 mm.
- The ureter enters the pelvis in front of the bifurcation of the common iliac artery anterior to the sacroiliac joint. As it courses downwards, it lies anterior to the internal iliac artery medial to the obturator nerves and vessels and forms the posterior boundary of ovarian fossa.
- On reaching the ischial spine, it lies over the pelvic floor and as it courses forwards and medially on the base of the broad ligament, it is crossed by the uterine artery anteriorly (Fig. 1.5).
- Soon, it enters into the ureteric tunnel and lies close to the supravaginal part of the cervix, about 1.5 cm lateral to it.



**Int iliac artery** also called as **hypogastric artery** and can be ligated in severe uncontrollable PPH to save the life of the patient.

**Site of ligation:** 2.5–3 cm distal to bifurcation of the common iliac artery to preserve the posterior division of the artery and thereby preserving blood supply to lower limb. The dissection should be done laterally to medially to avoid damaging the hypogastric vein.



**Fig. 1.5:** Water under bridge

- After traversing a short distance on the anterior fornix of the vagina, it enters into the wall of the bladder obliquely and opens into the base of the trigone.
- In the pelvic portion, the ureter is comparatively constricted:
  - Where it crosses the pelvic brim.
  - Where crossed by the uterine artery.
  - In the intravesical part.
- **Blood supply** of the ureter is from nearly all the visceral branches of the anterior division of the internal iliac artery (uterine, vaginal, vesical, middle rectal, and superior gluteal). The venous drainage corresponds to the arteries.
- The **lymphatics** from the lower part drain into the external and internal iliac lymph nodes and the upper part into the lumbar lymph nodes.
- **Nerve supply:** Sympathetic supply is from the hypogastric and pelvic plexus; parasympathetic from the sacral plexus.

### Pelvic Floor (Syn: Pelvic Diaphragm)

Pelvic floor is a muscular partition which separates the pelvic cavity from the anatomical perineum. It consists of the two levator ani muscles composed of pubococcygeus, iliococcygeus, and coccygeus muscle.

#### Levator Ani Muscle (Fig. 1.6)

- **Origin:** It arises from the back of the pubic rami, from the condensed fascia covering the obturator internus (white line) and from the inner surface of the ischial spine.
- **Insertion:** The fibres of pubococcygeus arch backwards and medially. The anterior fibres pass across the sides of the vagina to end in the perineal body. They form the pubovaginalis muscle. The intermediate fibres pass across the sides of the rectum and become continuous with those of the opposite side behind the anorectal junction. They form the puborectalis. They merge with the internal and external sphincters of the anal canal to form the anorectal ring. The most posterior fibres are attached to the coccyx, and to a fibrous band called the anococcygeal ligament.
- **Coccygeus:** It is triangular in shape. It arises from apex of ischial spine and sacrospinous ligament and is inserted to the sacrum and coccyx.

### Perineum

As seen on the surface of the body, the perineum is the region where the external genitalia and the anus are located. Anatomically, the perineum is bounded above by the inferior surface of the pelvic floor, below by the skin between the buttocks and thighs. Laterally, it is bounded by the ischiopubic rami, ischial tuberosities and sacrotuberous ligaments and posteriorly, by the coccyx.

Perineum is rhomboid in shape, and can be divided into anterior and posterior triangular areas. These are the urogenital triangle placed anteriorly, and the anal triangle placed posteriorly (Fig. 1.6).

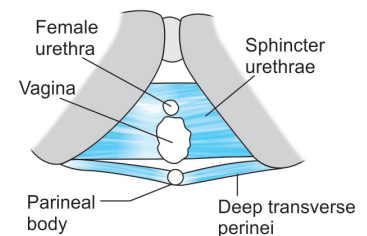
#### Urogenital Triangle

- The urogenital triangle is placed between the two ischiopubic rami.
- Stretching transversely across the rami, there are three membranes between which are enclosed two spaces as shown in Figure 1.7. From above downwards, the membranes are as follows:
  - Part of the pelvic fascia, constitutes the **superior fascia of the urogenital diaphragm**.



#### The ureter is recognized by the following features during surgery:

- i. Pale glistening appearance.
- ii. Longitudinal vessels on the surface.
- iii. Peristalsis.

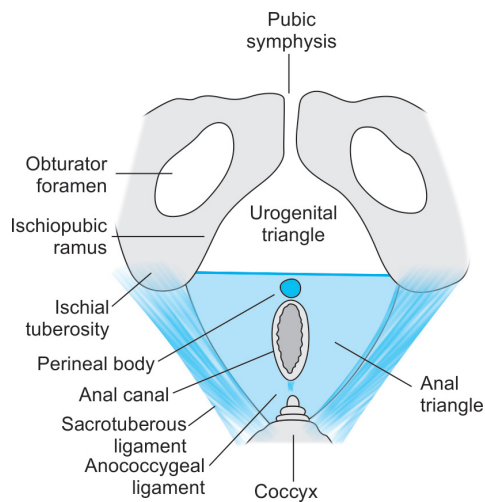


**Fig. 1.6:** Levator ani muscles viewed from above



#### Relations of superior surface of pelvic diaphragm

Ureter lies on the floor in relation to the lateral vaginal fornix. The uterine artery lies above and the vaginal artery lies below it.



**Fig. 1.7:** Boundaries of the perineum

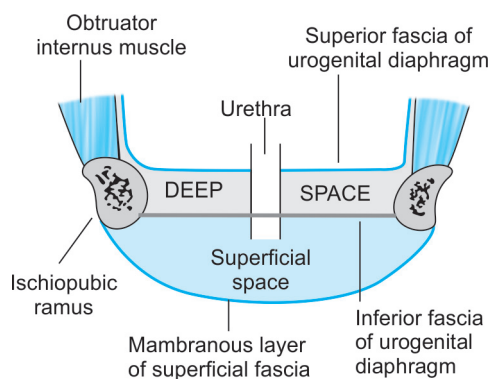
- The second membrane is the **inferior fascia of the urogenital diaphragm**. It is thick and is also called the perineal membrane.
- The most superficial membrane is **the membranous layer of superficial fascia**.
- Between the upper and middle membranes, there is the **deep perineal space (or pouch)**. The deep perineal has pouch the following muscles—deep transverse perinei (paired) and sphincter urethrae membranaceae (Fig. 1.8).
- Between the middle and lower membranes, there is the **superficial perineal space (or pouch)**. The superficial perineal pouch has superficial transverse perinei (paired), bulbocavernosus covering the bulb of the vestibule, ischiocavernosus (paired) covering the crura of the clitoris and the Bartholin's gland (paired).
- Posteriorly, all the three membranes are attached to the perineal body and to each other thus closing the superficial and deep perineal spaces behind.

### Perineal Body

The perineal body (or central tendon of the perineum) is a fibromuscular body placed in the median plane at the junction of the anal and urogenital triangles.

It is pyramidal in shape and has all the 3 layers of muscles, i.e.

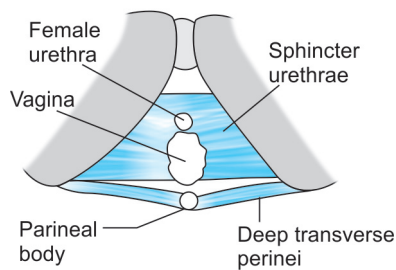
- Levator ani
- Deep transverse perinei
- Superficial muscles except Ischiocavernosus
- Fibres of external anal sphincter.



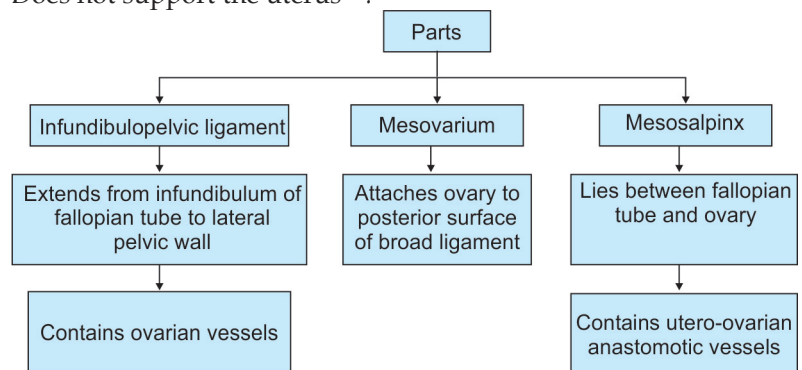
**Fig. 1.8:** Schematic coronal section through urogenital triangle to show formation of superficial and deep perineal spaces

### Broad Ligament

- It is a double fold of peritoneum extending from side of uterus to lateral pelvic wall.
- Does not support the uterus<sup>QQ</sup>.



**Fig. 1.9:** Muscles present in deep perineal space (as seen in the female)



### Pelvic Cellular Tissue

- The pelvic cellular tissue condenses at many plaes and gives rise to
  - **Uterosacral ligament** that extends from  $S_2$ ,  $S_3$ , and  $S_4$  to the posterior and lateral part of supravaginal cervix.
  - **Cardinal liagments/Mackenrodts ligaments/transverse cervical ligaments** that extends in fan-shaped manner from pelvic wall and inserted into the lateral supravaginal cervix.

- **Pubocervical ligament** extend from anterolateral aspect of cervix to the back of pubic bone lateral to pubic symphysis.

**Importance**

- Support the pelvic organs.
- Form a protective sheath for blood vessels and ureter.

**Round Ligament**

Paired ligaments (10–12 cm). One end is attached at the cornu of the uterus and other end terminates in the anterior third of the labium majus. It develops from gubernaculum.

## FIGURE BASED QUESTIONS

- F1.** Identify the structure 'X' shown in figure F1:
- |                     |                   |
|---------------------|-------------------|
| a. Fallopian tube   | b. Round ligament |
| c. Ovarian ligament | d. Broad ligament |

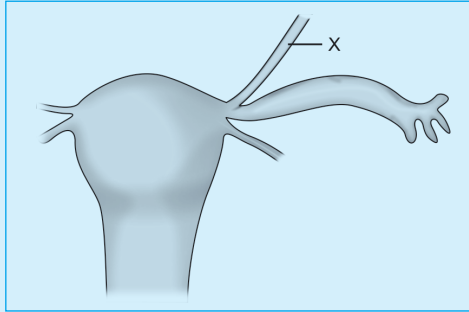


Fig. F1

- F2.** Identify the structure 'X' marked on the figure F1:
- |                         |               |
|-------------------------|---------------|
| a. Fossa navicularis    | b. Fourchette |
| c. Posterior commissure | d. Vestibule  |



Fig. F2

## QUESTIONS

1. All of the following pelvic structures support the vagina, except: [AIIMS May 04]
  - a. Perineal body
  - b. Pelvic diaphragm
  - c. Levator ani muscle
  - d. Infundibulopelvic ligament
2. All are related to lateral vaginal fornix except: [JIPMER 90]
  - a. Ureters
  - b. Mackenrod's
  - c. Inferior vesical artery
  - d. Uterine artery
3. The pH of vagina in adults is: [Delhi 98, DNB 00 95]
  - a. 3.5 - 4.5
  - b. 4.5 - 5.5
  - c. 5.5 - 6.5
  - d. 6.5 - 7.5
4. Protective bacterium in normal vagina is: [J and K 01]
  - a. Peptostreptococcus
  - b. Lactobacillus
  - c. Gardenella vaginalis
  - d. E. coli
5. The main source of physiological secretion found in the vagina is: [AIIMS 98]
  - a. Bartholin's glands
  - b. Gartner's duct
  - c. Vagina
  - d. Cervix
6. With reference to vagina which of the following statement is not correct: [UPSC 07]
  - a. It has mucus secreting gland
  - b. It is supplied by uterine artery
  - c. It is lined by stratified squamous epithelium
  - d. Its posterior wall is covered by peritoneum
7. Which of the following about lymphatics of vulva is true: [AI 98]
  - a. Do not cross the labiocrural fold
  - b. Traverse labia from medial to lateral
  - c. Drain directly into deep femoral glands
  - d. Do not freely communicate with each other
8. Uterine-cervix ratio upto 10 years of age: [PGI 89]
  - a. 3:2
  - b. 2:1
  - c. 3:1
  - d. 1:2
9. The epithelial lining of cervical canal is: [TN 90]
  - a. Low columnar
  - b. High columnar
  - c. Stratified squamous
  - d. Ciliated columnar
10. Nabothian follicles occur in: [TN 91]
  - a. Erosion of cervix
  - b. Ca endometrium
  - c. Ca cervix
  - d. Ca vagina
11. Bartholin's duct opens into: [DNB 99]
  - a. Labia majora and minora
  - b. A groove between labia minora and hymen
  - c. The lower vagina
  - d. The upper vagina
12. A woman presents with a fluctuant non tender swelling at the introitus. The best treatment is: [AI 08]
  - a. Marsupialization
  - b. Incision and drainage
  - c. Surgical resection
  - d. Aspiration
13. Bartholin's cyst is caused by: [DNB 04]
  - a. Candida
  - b. Anaerobes
  - c. Gonococcus
  - d. Trichomonas
14. Narrowest part of fallopian tube is: [Delhi 93]
  - a. Interstitial portion
  - b. Isthmus
  - c. Infundibulum
  - d. Ampulla
15. 'Peg cells' are seen in: [DNB 00]
  - a. Vagina
  - b. Vulva
  - c. Ovary
  - d. Tubes
16. The length of fallopian tube is: [DNB 95]
  - a. 8 - 10 cm
  - b. 10 - 12 cm
  - c. 15 - 18 cm
  - d. 18 - 20 cm
17. Uterine artery is a branch of: [DNB 00, 95]
  - a. Aorta
  - b. Common iliac
  - c. Internal iliac
  - d. External iliac
18. Vaginal epithelium is derived from: [AIIMS Nov 13]
  - a. Endoderm of urogenital sinus
  - b. Mesoderm of urogenital sinus
  - c. Endoderm of genital ridge
  - d. Mesoderm of genital ridge
19. Anatomical sphincter of fallopian tubes? [AIIMS Nov 13]
  - a. Ampulla
  - b. Isthmus
  - c. Intramural
  - d. Infundibulum



## NEW PATTERN QUESTIONS

20. With regards to labia majora all are correct except:
- Is homologous to scrotum in males
  - Is supplied by branches of internal and external pudendal arteries
  - Drains into superficial inguinal lymph nodes
  - The broad ligament terminates at its anterior end
21. With regards to vagina all are correct except
- Makes an angle of 45° with the horizontal in erect posture
  - Looks like letter 'H' on cross section
  - Vaginal axis lies parallel to the uterus and at right angles to the plane axis of inlet
  - Is lined by stratified squamous epithelium
22. Vaginal defence is lost:
- Within 10 days of birth
  - After 10 days of birth
  - During pregnancy
  - At puberty
23. Ovary is:
- Is attached to the posterior layer of the broad ligament by mesovarium
  - Has hilus cells in the cortex
  - Ovarian veins drain into inferior vena cava
  - Is connected to the uterus by infundibulopelvic ligament
24. The fallopian tube:
- Is lined entirely by ciliated columnar epithelium
  - Has a submucous layer
  - Undergoes shedding during menstrual cycle
  - Surrounded by peritoneum on all sides except along the line of attachment of mesosalpinx
25. All are true about the round ligament except:
- Measures 12 cm in length
  - Is homologous to the gubernaculum testes
  - Lies anterior to the obturator artery along its course
  - Contains smooth muscles
26. All of the following are true with respect to ligation of internal iliac artery except:
- For hemostasis, anterior division is to be ligated
  - Collateral circulation is established later between middle sacral and lateral sacral arteries
  - Bleeding is always controlled with it
  - The artery should be ligated and not transected
27. With regards to the nerve supply of pelvis all are correct except
- The sensory component of pudendal nerve supplies the skin of vulva, clitoris, perineum and lower vagina
  - The motor component of pudendal nerve supplies all the muscles of pelvic floor
  - The anterior half of the vulva is supplied by ilio-inguinal and genitofemoral nerves
  - The posterior half of vulva is supplied by ilioinguinal nerve only
28. The triangular area bounded by clitoris, fourchette and labia minora is:
- Fossa navicularis
  - Fourchette
  - Vestibule
  - Vulva
29. Fourchette is where:
- Both labia minora meet posteriorly
  - Both labia minora meet anteriorly
  - Labia minora and majora meet
  - Distance between vulva and labia minora
30. Glands of Littre are homologous to:
- Bartholin gland
  - Cowper's gland
  - Skene glands
  - Glands on labia
31. For hormonal study, sample should be taken from which wall of vagina:
- Anterior
  - Posterior
  - Lateral
  - Any wall
32. Theoretically, Gonococcal vaginitis can be seen:
- In puberty
  - In newborn females
  - In reproductive age females
  - Sex workers
33. Cervix: corpus ratio before puberty is:
- 1:2
  - 2:1
  - 1:3
  - 3:1
34. Which ligament carries ovarian A in lateral wall:
- Ovarian ligament
  - Suspensory ligament of ovary
  - Broad ligament
  - Round ligament
35. M/C site of ureteric injury during hysterectomy:
- Pelvic brim
  - Where it is crossed by uterine artery.
  - Where it enters the bladder
  - Where it is over obturator vessels

## ANSWERS TO FIGURE BASED QUESTIONS

### F1. Ans. is b, i.e. Round ligament

At the cornua structures attached from anterior are to posterior

- Round ligament (R)
- Fallopian tube (F)
- Ovarian ligament (O)

The structure marked 'x' is the anteriormost i.e. it is round ligament.

### F2. Ans. is a, i.e. Fossa navicularis

The structure marked is the distance between fourchette (place where posterior end of labia minora join) and hymen i.e. it is fossa navicularis.

## ANSWERS

### 1. Ans. is d, i.e. Infundibulopelvic ligament

*Ref. Jeffcoate 7<sup>th</sup>/ed p 46; CGDT 10<sup>th</sup>/ed p 49*

- Friends our question is related to the supports of vagina. Before going into its details lets have a second look at the options. All the options given in the question are somehow related to vagina, therefore may have a role in supporting vagina except the infundibulopelvic ligaments.
- *Infundibulopelvic ligament attach the ovary to the lateral pelvic wall and supporta the ovary, but has no connection to the vagina or uterus, therefore does not support either structures.*

So, by exclusion, our answer is infundibulopelvic ligament.

Now, coming on to the details of supports of vagina.

#### Vagina is supported in the lower part by:

- Bulbocavernosus muscle (at the level of introitus).
  - Urogenital diaphragm.
  - Perineal muscles.
  - Levator ani muscles (known as pelvic diaphragm) support the lower 1/3rd of vagina.
- In its upper part: vagina is supported by: Cardinal ligament (also called as transverse cervical ligament).  
The anterior wall of vagina, urethra and bladder base are supported by: Pubocervical fascia.  
The posterior wall of vagina is supported by: Perineal body.

### 2. Ans. is c, i.e. Inferior vesical artery

*Ref. Shaw 15<sup>th</sup>/ed p 5*

The cervix and all 4 fornices are related to

- Uterine Vessels<sup>Q</sup>
- Mackenrodt's ligament<sup>Q</sup>
- Ureter<sup>Q</sup>

Posteriorly surrounding the pouch of douglas lie the uterosacral ligaments.<sup>Q</sup>

### 3. Ans. is b, i.e. 4.5–5.5

### 4. Ans. is b, i.e. Lactobacillus

*Ref. Jeffcoate 7<sup>th</sup>/ed pp 27-28; Dutta Gynae 5<sup>th</sup>/ed p 7*

Vagina has inhabitant bacteria called as Doderleins bacteria which is a lactobaccilli, and converts the glycogen present in vaginal epithelium into lactic acid.

Thus, pH of vagina is acidic

- The pH of vagina in an adult woman is 4 - 5.5 with an average of 4.5.
- **The pH of vagina varies with age – for further details see preceeding text.**

### 5. Ans. is d, i.e. Cervix

*Ref. Shaw 15<sup>th</sup>/ed p 128; Dutta Gynae 5<sup>th</sup>/ed p 6*

Vagina is lined by a mucous coat which is lined by stratified squamous epithelium without any secreting glands. So, whatever secretions are present in the vagina comes from other structures.

**The components of vaginal secretion are from :**

- *The sweat and sebaceous glands of the vulva and the specialized racemose glands of Bartholin's.* (The characteristic odor of the vaginal secretion is provided by the apocrine glands of the vulva).
- *The transudate of the vaginal epithelium and the desquamated cells of the cornified layer.* (This is strongly acidic).
- *The mucous secretion of the endocervical glands (which is alkaline).*
- *The endometrial glandular secretion.*

6. **Ans. is a, i.e. It has mucus secreting glands**Ref. Shaw 15<sup>th</sup>/ed pp 4, 20, 18 for blood supply**Lets analyse each option separately:****Option a:** It has mucus secreting glands – incorrect as*No glands open into vagina<sup>Q</sup> and vaginal secretion is mainly derived from mucous discharge of cervix and partly from transudate through vaginal epithelium.<sup>Q</sup>*

- The vaginal mucosa is lined by stratified squamous epithelium.<sup>Q</sup>
- In newborn, the epithelium is transitional in nature and cornified cells are scanty until puberty and this is the reason why gonococcal vaginitis can occur in newborns.

**Option b:** Supplied by uterine artery – correct as vagina is supplied by vaginal artery which arises either from uterine artery or can sometimes be a direct branch of internal iliac artery.**Option c:** It is lined by stratified squamous epithelium – correct.**Option d:** Posterior wall is covered by peritoneum.*“There is no serosal covering (on vagina) except for the area covered by cul de sac and we all know that cul de sac is related to posterior wall of vagina”.*  
– Shiela Balakrishnan, 1<sup>st</sup>/ed p 57. **Ans. is b, i.e. Traverse labia from medial to lateral**Ref. Dutta Gynae 5<sup>th</sup>/ed pp 29-30; CGDT 10<sup>th</sup>/ed p 18**Special features of vulval lymphatics are as follows:**

- The lymphatics of each side freely communicate with each other.
- The lymphatics hardly cross beyond labiocrural fold.
- Vulval lymphatics also anastomose with lymphatics of lower 1/3<sup>rd</sup> of vagina and drain into external iliac nodes.
- Superficial lymph nodes are the primary lymph nodes that act as sentinel glands of vulva. Deep inguinal nodes are secondarily involved. It is unusual to find pelvic glands without metastasis in inguinal nodes.

*“From the upper 2/3<sup>rd</sup> of the left and right labia majora superficial lymphatics pass towards the symphysis and turn laterally to joint the medial superficial inguinal nodes.”*– CGDT 10<sup>th</sup>/ed p 18

Hence, they traverse labia from medial to lateral side.

8. **Ans. is d, i.e. 1:2**Ref. Shaw 15<sup>th</sup>/ed p 8

The relationship of the length of the cervix and that of the body of uterus varies with age.

Age	Uterus to cervix ratio (Corpus / Cervix ratio)
• Before puberty	1:2
• At puberty	2:1
• In adults/Reproductive age	3:1 or 4:1
• After menopause	Whole of uterus and cervix atrophy

9. **Ans. is b, i.e. High columnar**Ref. Shaw 15<sup>th</sup>/ed p 7

Read the text for explanation.

10. **Ans. is a, i.e. Erosion of cervix**Ref. Shaw 15<sup>th</sup>/ed p 325; Dutta Gynae 5<sup>th</sup>/ed p 259**Cervical erosion:** Condition where squamous epithelium of ectocervix is replaced by columnar epithelium which is continuous with endocervix. It occurs when estrogen levels are high as in pregnancy and use of oral contraceptives (ocp's).

- As a result of healing of an erosion, the mouth of cervical gland is blocked. The blocked gland becomes distended with secretion and forms small cysts which can be seen with naked eye and so called *Nabothian cyst*.

11. **Ans. is b, i.e. A groove between labia minora and hymen**Ref. Dutta Gynae 5<sup>th</sup>/ed p 2; Jeffcoate 7<sup>th</sup>/ed p 24

- Bartholin's glands are pea sized oval glands in females homologous to Cowper's Gland in male.<sup>Q</sup> / *bulbo urethral glands in males.*
- The ducts of bartholin gland is 2 cm long<sup>Q</sup> and opens into the vestibule outside the hymen at the junction of the anterior 2/3<sup>rd</sup> and posterior 1/3<sup>rd</sup> in the groove between the hymen and labium minora.<sup>Q</sup>
- Duct as well gland is lined by multilayered columnar epithelium<sup>Q</sup> (Not by transitional epithelium as is usually stated).<sup>Q</sup>
- Function of the gland is to produce abundant alkaline mucus during sexual excitement.

12. **Ans. is a, i.e. Marsupialization**13. **Ans. is c, i.e. Gonococcus**Ref. Jeffcoates 7<sup>th</sup>/ed pp 450-1; William Gynae 1<sup>st</sup>/ed p 96

Fluctuant non-tender swelling at the introitus suggests a diagnosis of bartholins cyst.

**Bartholins cyst:**

- It is the most common cyst of vulva.
- Bartholins' cyst are produced from accumulation of secretions of Bartholins gland.
- The cyst may develops either in the duct (more common) or in the gland
- Etiology: Cyst formation occurs due to the obstruction of the main duct or opening of an acinus.
- The cause of obstruction is usually fibrosis which follows either infection or trauma.
- It was formerly believed that the infection was invariably gonococcal but almost any orgnaism can be responsible.
- Left Bartholins' gland is more often affected than the right.

**Presentation:**

- Usually presents as a unilateral swelling that bulges across the vaginal introitus.
- Size of the cyst rarely exceeds hen's egg.
- Swelling is present characteristically on the inner side of the junction of the anterior 2/3<sup>rd</sup> with posterior 1/3<sup>rd</sup> of the labium majus.
- The swelling is fluctuant and usually non tender
- Patient may present with discomfort, dyspareunia, or infection.

**Treatment of choice is Marsupialization:** It is preferred over traditional excision operations.

14. **Ans. is a, i.e. Interstitial portion**

15. **Ans. is d, i.e. Tube**

*Ref. Shaw 15<sup>th</sup>/ed p 11*

16. **Ans. is b, i.e. 10–12 cm**

*Ref. Shaw 15<sup>th</sup>/ed p 11*

See the text for explanation

17. **Ans. is c, i.e. Internal iliac artery**

*Ref. Shaw 14<sup>th</sup>/ed p 17*

Uterine artery is a branch of anterior division of internal iliac artery.

In cases of uncontrollable PPH – uterine artery or anterior division of internal iliac artery can be performed to stop further blood loss.

18. **Ans. is a, i.e. Endoderm of urogenital sinus**

*Ref. Shaw's textbook of gynecology 15<sup>th</sup>/ed p 91; Dutta Gynae 6<sup>th</sup>/ed p35*

Development of vagina is composite, partly from the mullerian ducts (paramesonephric ducts) and partly from the urogenital sinus.

Part of vagina	Development
Upper 3/5ths	Mullerian ducts
Lower 1/5th	Urogenital sinus
Hymen	Junction of mullerian ducts and urogenital sinus
Epithelium of the vagina and portio vaginalis part of cervix	Endoderm of urogenital sinus
Fibromuscular layer of vagina	Mesoderm of fused caudal part of mullerian ducts
Vaginal introitus	Ectoderm of genital folds

19. **Ans. is c, i.e. Intramural part**

*Ref. John Hopkins manual of human functional anatomy p 144*



Anatomical sphincter of fallopian tube is intramural part  
Physiological sphincter: is Isthmus part

20. **Ans. is d, i.e. The broad ligament terminates at its anterior end**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 1*

All options are correct with respect to labia except: Option d because it is round ligament and not broad ligament which terminates at its anterior end.

21. **Ans. is c, i.e. Vaginal axis lies parallel to the uterus and at right angles to the plane axis of inlet**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 4,5*

The canal is directed upwards and backwards forming an angle of 45° with the horizontal in erect posture. **The long axis of the vagina almost lies parallel to the plane of the pelvic inlet and at right angles to that of the uterus (not vice versa).** Vagina has got an anterior, a posterior, and two lateral walls. The anterior and posterior walls are apposed together but the lateral walls are comparatively stiffer especially at its middle, as such it looks 'H' shaped on transverse section.

22. **Ans. is b, i.e. After 10 days of birth**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 5*

Vaginal defence is lost at 10 days after birth. The maternal estrogen circulating the newborn maintains the vaginal defence for 10 days. Thereafter it is lost upto pre-puberty and after menopause. High level of circulating estrogen increase the vaginal defence during puberty, pregnancy and in premenstrual phase.

23. **Ans. is a, i.e. Is attached to the posterior layer of the broad ligament by mesovarium** *Ref. Dutta Gynae 6<sup>th</sup>/ed p 11,12*  
Ovary measures about 3 cm in length, 2 cm in breadth and 1 cm in thickness. The ovaries are intraperitoneal structures. In nulliparae, the ovary lies in the ovarian fossa on the lateral pelvic wall. The ovary is attached to the posterior layer of the broad ligament by the mesovarium, to the lateral pelvic wall by infundibulopelvic ligament and to the uterus by the ovarian ligament.

The substance of the gland consists of outer cortex and inner medulla.

**Medulla:** It consists of loose connective tissues. There are small collection of cells called "hilus cells" which are homologous to the interstitial cells of the testes.

**Arterial supply** is from the ovarian artery.

**Venous drainage** is through pampiniform plexus, to form the ovarian veins which drain into inferior vena cava on the right side and left renal vein on the left side.

Sympathetic supply comes down along the ovarian artery from T<sub>10</sub> segment. Ovaries are sensitive to manual squeezing.

24. **Ans. is d, i.e. Surrounded by peritoneum on all sides except along the line of attachment of mesosalpinx**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 11*

**Structure of fallopian Tube**— It consists of 3 layers:

1. **Serous:** Consists of peritoneum on all sides except along the line of attachment of mesosalpinx (i.e. option d is correct).
2. **Muscular:** Arranged in two layers—outer longitudinal and inner circular.
3. **Mucous membrane** is thrown into longitudinal folds. It is lined by **columnar epithelium**, partly ciliated, others secretory nonciliated and 'Peg cells'. **There is no submucous layer nor any glands.** Changes occur in the tubal epithelium during menstrual cycle but are less pronounced **and there is no shedding during menstrual cycle** (option c is incorrect).

**Note:** The uterine tubes (fallopian tubes) are 10 cm in length. They are situated in the medial three-fourth of the upper free margin of the broad ligaments. Each tube has got two openings, one communicating with the lateral angle of the uterine cavity, called uterine opening and measures 1 mm in diameter, the other is on the lateral end of the tube, called pelvic opening or abdominal ostium and measures about 2 mm in diameter. The abdominal ostium is surrounded by a number of radiating fimbriae, one of these is longer than the rest and is attached to the outer pole of the ovary called **ovarian fimbria**.

25. **Ans. is d, i.e. Contains striated muscles**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 23,24*

**Round ligaments:** These are paired, one on each side. Each measures about 10–12 cm. It is attached at the cornu of the uterus below and in front of the fallopian tube. It courses beneath the anterior leaf of the broad ligament to reach the internal abdominal ring. After traversing through the inguinal canal, it fuses with the subcutaneous tissue of the anterior third of the labium majus. During its **course, it runs anterior to obturator artery and lateral to the inferior epigastric artery.** It contains **plain muscles and connective tissue.** It is hypertrophied during pregnancy and in association with fibroid. It corresponds developmentally to the **gubernaculum testis and is morphologically continuous with the ovarian ligament.** The blood supply is from the utero-ovarian anastomotic vessels. The lymphatics from the body of the uterus pass along it to reach the inguinal group of nodes. While it is not related to maintain the uterus in anteverted position, but its shortening by operation is utilized to make the uterus anteverted.

**Embryologically, it corresponds with gubernaculum testis.** In the fetus, there is a tubular process of peritoneum continuing with the round ligament into the inguinal region. This process is called **canal of Nuck. It is analogous to the processus vaginalis which precedes to descent of the testis.**

26. **Ans. is c, i.e. Bleeding is always controlled with it**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 33*

Only the **anterior division of internal iliac artery** supplies the pelvic viscera and **hence should be ligated for controlling** severe PPH. **The artery should not be transected.** Hemostasis is effective due to temporary lowering of pulse pressure by 85%. On ligation of internal iliac artery → **collateral circulation develops between systemic arteries and internal iliac artery.**

Ligation of internal iliac artery and development of collateral circulation		
Systemic artery		Internal iliac artery
Lumbar (aorta) →	with	← Iliolumbar
Middle sacral (aorta) →	with	← Lateral sacral
Superior rectal (inferior mesenteric) →	with	← Middle rectal
Ovarian (aorta) →	with	← Uterine

**Bleeding doesnot always stop after ligation due to presence of aberrant vessels or it could be venous bleeding.**

27. **Ans. is d, i.e. The posterior half of vulva is supplied by ilioinguinal nerve only** *Ref. Dutta Gynae 6<sup>th</sup>/ed pp 31,32*  
Both the motor and sensory part of the somatic supply to the pelvic organs are through:

- Pudendal nerve—S<sub>2</sub>, S<sub>3</sub>, S<sub>4</sub>.
- Ilio-inguinal nerve—L<sub>1</sub>, L<sub>2</sub>.
- Genital branch of genitofemoral nerve—L<sub>1</sub>, L<sub>2</sub>.
- Posterior cutaneous nerve of thigh.

**Pudendal nerve**

The sensory component **supplies the skin of the vulva**, external urethral meatus, clitoris, perineum and lower vagina. The **motor fibers supply all the voluntary muscles of the perineal body**, levator ani and sphincter ani externus. Levator ani, in addition, receives direct supply from S<sub>3</sub> and S<sub>4</sub> roots.

While the anterior half of vulval skin is supplied by the ilioinguinal and genital branch of genitofemoral nerves, **the posterior part of the vulva, including the perineum is supplied by the posterior cutaneous nerve of thigh.**

28. **Ans. is c, i.e. Vestibule** *Ref. COGDT 11/e, page 26*

Vestibule is the triangular area bounded anteriorly by the clitoris, posteriorly by Fourchette and on either side by labia minora.

29. **Ans. is a, i.e. Both labia minora meet posteriorly** *Ref. COGDT 11/E, page 24*

Remember: Mnemonic FFP: from anterior to posterior  
F = Fossa Navicular is: Distance between hymen and fourchette  
F = Fourchette—Posteriorly where labia minora meet  
P = Posterior Commissure—Posteriorly where labia majora meet

30. **Ans. is d, i.e. Glands of labia** *Ref. COGDT 11/e, page 24*

The glands of labia minora are homologous to the glands of Littre (glandulae preputiales) of the penile portion of the male urethra

31. **Ans. is c, i.e. Lateral wall**

Vaginal study gives a fair idea about the hormonal status and, in turn, about ovulation/ovarian cycle.

For hormonal study, sample should be taken from: Lateral wall  
For cytological study (Papsmear), sample should be taken from: Posterior wall

32. **Ans. is b, i.e. Newborn females**

Squamous epithelium is resistant to Gonococcal infection, since in all females, vagina is lined by stratified squamous epithelium. Hence, gonococcal vaginitis does not occur.

In newborn females, vagina is lined by transitional epithelium. Therefore, theoretically speaking, gonococcal vaginitis can occur in newborn females.

33. **Ans. is b, i.e. 2:1** *Ref. Shaw, 15/e, page 8*

Read the text for explanation.

34. **Ans. is b, i.e. Suspensory ligament of ovary** *Ref. COGDT 11/e, Page 36*

The suspensory ligament of ovary (infundibulopelvic ligament) contains the ovarian artery, veins and nerves.

35. **Ans. is b, i.e. Where it is crossed by uterine artery**

Site of ureteric injury during hysterectomy

1st M/C= where it is crossed by uterine artery

2nd M/C= Near pelvic brim

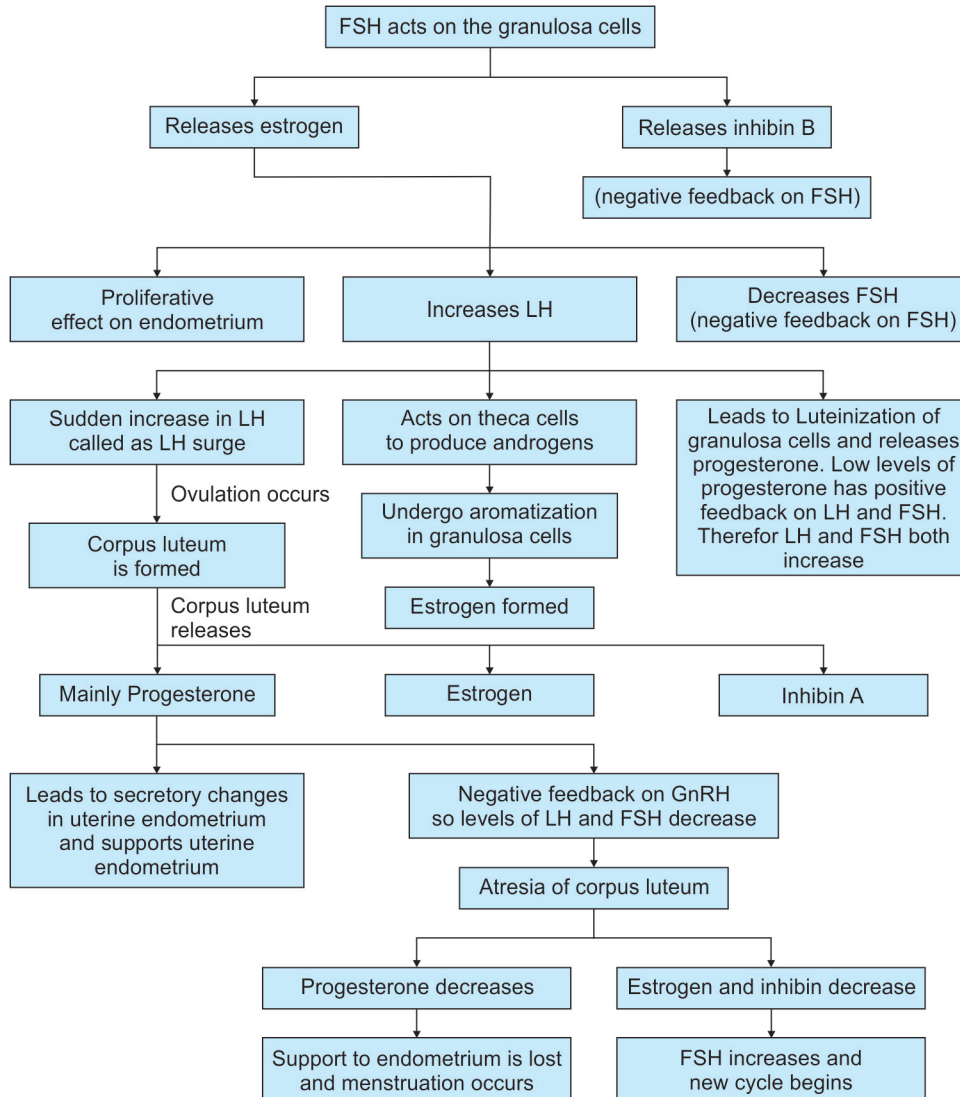
# CHAPTER

# 2

# Reproductive Physiology and Hormones in Females

## Ovarian Cycle

- Ovarian cycle begins with hormone follicular stimulations hormone (FSH).
- Primary oocytes in intrauterine life get surrounded by follicular cells and are called as **primordial follicle**. (Measurement 0.03–0.05 mm).
- Under the influence of FSH, the follicular cells of the dominant primordial follicle differentiate into an outer layer of cells called as **theca cells** and an inner layer called as **granulosa cells**.



Ovarian cycle can be divided into:

- Early follicular phase
- Late follicular phase
- Ovulatory phase
- Luteal phase

As early as 5–7 days, dominant follicle is selected. The rest of the follicles become atretic by Day 8

The two-cell theory of steroidogenesis suggests that FSH acts on granulosa cells to produce estrogen, and LH acts on theca cells to produce androgens.

With LH peak at the time of ovulation, there is a precipitous fall in estrogen as steroidogenesis now shifts to progesterone. This dramatic decrease in estrogen can sometimes result in midcycle spotting in some women which is a form of estrogen withdrawal bleeding.

Corpus luteum–

- In non-pregnant state it is maintained by hormone LH
- Life span = 10–12 days
- Maximum activity occurs 8 days after ovulation, i.e. day 22 of menstrual cycle.
- In pregnant state, corpus luteum is maintained by hormone hCG.
- Life span in pregnant state ≈ 10 weeks.



The basic prerequisite in ovulatory cycle is fluctuating levels of  $E_2$ . If for any reason, the  $E_2$  levels become static, anovulation is a rule (as in PCOS)

## Ovulation

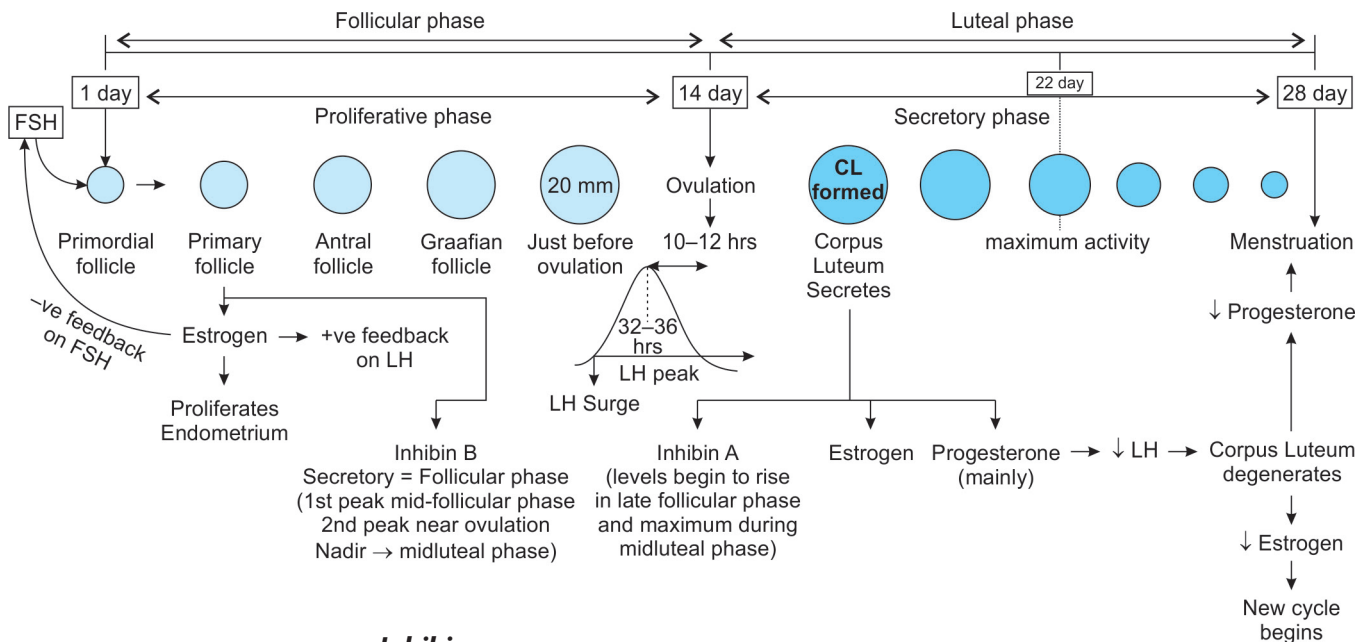
### Important Points:

- There is induction of LH receptors in the dominant follicle.
- There is shift of dominant follicular control from FSH to LH since the midfollicular phase.
- LH in the late follicular phase causes follicular atresia other than the dominant follicle.
- Peak level of estradiol is 100 pg/follicle (200 pg/ml) seen on D10–D11. LH surge occurs after estradiol peak is sustained for 48 hours.
- Ovulation occurs 32–36 hours after luteinizing hormone (LH) surge or 10–12 hours after LH peak, i.e. 75 ng/mL of LH.
- Just before ovulation size of graafian follicle is 20 mm.
- At ovulation, there is completion of metaphase of 1<sup>st</sup> meiotic division and there is extrusion of 1<sup>st</sup> polar body.
- Ovulation occurs 14 days before the first day of succeeding cycle. Therefore, in a 26 day cycle ovulation will occur 14 days prior to 26<sup>th</sup> day, i.e.  $26 - 14 = 12^{\text{th}}$  day.

**Therefore, Day of ovulation = Length of menstrual cycle - 14**

- 1<sup>st</sup> sign of ovulation on endometrial biopsy is basal vacuolation.

### Line diagram showing Ovarian and Menstrual Cycle



Approximate time interval of events in menstrual cycle prior to ovulation

Events	Hours
Estradiol rise	83
Onset of LH surge	34–36
Estradiol peak	24–36
LH peak	10–12
Progesterone rise	8

## Inhibin

- Consists of 2 dissimilar peptides (called as  $\alpha$ - and  $\beta$ - subunits). There are 2 forms of inhibin viz. inhibin A and inhibin B.
- In both of them  $\alpha$ - subunit is identical, whereas  $\beta$ - subunit is specific.
- FSH stimulates the secretion of inhibin from granulosa cells of ovarian follicle and in turn, is suppressed by inhibin.
- Inhibin B is the form of inhibin predominantly secreted by granulosa cells in follicular phase of the cycle.
- Inhibin B reaches a peak in midfollicular phase and then decreases in the late follicular phase to reach a nadir in midluteal phase. A small peak is seen a day after ovulation.
- Inhibin A is mainly active in luteal phase and its release is under the control of LH. Levels of inhibin A rise in late follicular phase to reach a peak at midluteal phase.



## During pregnancy

- Placenta produces mainly inhibin A - the levels of inhibin A are high during pregnancy at 8 weeks of gestation, third trimester, and at term.
- Maternal levels of inhibin B are very low during pregnancy.

## Activin

It is derived from granulosa cells and released by pituitary in early follicular phase and augments FSH secretion and action.

## Menstruation

Feature	Menstrual Phase	Proliferative Phase	Secretory Phase
Thickness of stratum functionale	Absent	Thin to thick	Thickest
Appearance of endometrial glands	Portions of glands in stratum basale	Straight	Highly coiled
Degree of coiling of coiled arteries	Absent	Less coiled	Highly coiled
Predominant gonadotropin	Falling LH, rising FSH	FSH	LH
Predominant ovarian hormone	Transition from progesterone to estrogen	Estrogen	Progesterone
Days of idealized 28-day cycle	1–5	5–14	14–28
Viscosity of cervical secretions	Difficult to determine	Thinnest at day 14	Increasing viscosity

### Also Know

In the follicular phase as LH increases → it leads to luteinization of the granulosa cells, resulting in progesterone production. At low levels progesterone does not have negative but positive feedback on LH and EH.

Thus, levels of FSH also rise just before ovulation called as FSH surge.

## Endometrium

Superficial layer (2/3 <sup>rd</sup> )	Deep layer (1/3 <sup>rd</sup> )
It consists of stratum compactum and stratum spongiosum	It consists of Stratum Basalis
These layers are supplied by spiral arteries which undergo vasoconstriction during secretory phase	It is supplied by basilar arteries
This causes necrosis or sloughing of these layers at the time of menstruation	During secretory phase these basilar arteries remain straight, so the blood supply of stratum basale remains intact. <i>Therefore, this layer is not shed during menstruation and during secretory phase it causes regeneration of whole endometrium</i>

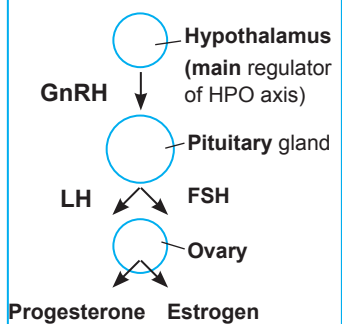


Stratum Basalis is responsible for regeneration of endometrium during next menstrual cycle.

## Hormones

Hypothalamic-pituitary-ovarian (HPO) axis is not developed before puberty. It becomes sensitive around 8–12 years and is fully established by 13–14 years. Initially due to release of GnRH → only LH is released from pituitary, later as the axis matures both LH and FSH are released. That is why initial few cycles are anovulatory.

### Hormonal control of ovarian/ menstrual cycle



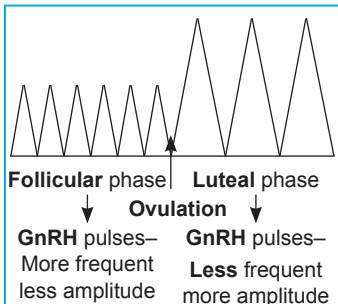


Schally and Guillemin were the first to discover GnRH

1st hormone which after GnRH secretion at rises puberty -LH



Nafarelin and busarelin can be administered by nasal route.



GnRH agonists stimulate gonadotropin secretion when given in a pulsatile manner whereas inhibit the release on continued administration.



Long-term use of GnRH can result in menopausal symptoms and osteoporosis. Hence, GnRH therapy is not recommended for more than 6 months.

### Natural

- Secreted in a pulsatile manner at different times of menstrual cycle
- Initially secreted only at night

### Synthetic

Initially, there is a supraphysiological release of FSH and LH from pituitary (flare) followed by decrease in the synthesis and release of both FSH and LH.

- When given in pulsatile manner they stimulate gonadotropin secretion.

#### Preparations of GnRH

- Buserelin
- Nafarelin
- Goserelein
- Historelin
- Leuprorelin
- Triptorelin

## Peptide Hormones – GnRH



### A - F and HIP.

- A** = Adenomyosis
- B** = Irritable bowel syndrome (under Trial)
- C** = Ca Breast (Tamoxifen + GnRH agonist give good result)
- D** = Dysfunctional uterine bleeding
- E** = Endometriosis
- F** = Fibromyoma uterus
- H** = Hirsutism
- I** = Infertility
- P** = Precocious puberty.

GnRH is the controlling factor for gonadotropin release (LH and FSH).

### Indications for using Synthetic GnRH

**In females:** (In all those conditions where there is increased estrogen, GnRH analogues are useful).

**In males:**

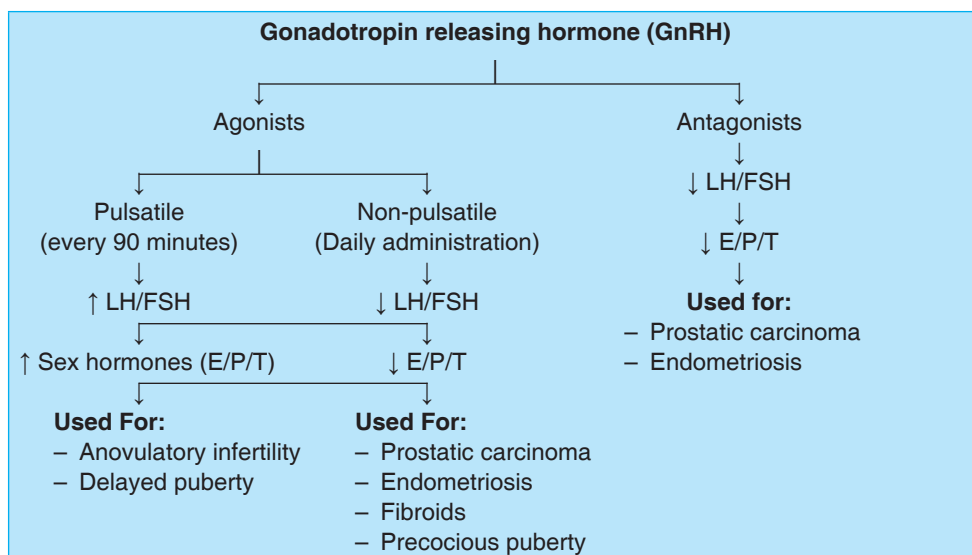
- **Cryptorchidism:** short-term intranasal nafarelin is used.
- **Carcinoma prostate:** GnRH agonist are as effective as orchidectomy in Ca prostate but if there are neurological symptoms or life-threatening metastatic disease - androgens should first be started followed by GnRH agonist.
- **BPH:** Daily administration of leuprorelin or nafarelin decreases obstructive urinary symptoms in 1–6 months time.

### Adverse Effects of GnRH

- Local allergic reaction may occur at injection site.
- They cause menopause like symptoms – hot flushes, vaginal dryness, headache, joint and muscle stiffness, depression, osteoporosis, and irregular vaginal bleeding.

**GnRH antagonist:** Acts immediately to stop gonadotropin secretion (without any flare), e.g. Cetrorelix, Ganirelix, Nal-glu.

They have been surpassed by GnRH agonist in clinical practice except for their potential role in contraception. Nal-glu given for 3 weeks inhibits spermatogenesis.<sup>Q</sup>

**Key to Flowchart:**

LH = Luteinizing hormone  
 FSH = Follicle-stimulating hormone  
 E = Estrogen  
 P = Progesterone  
 T = Testosterone

**Natural FSH and LH/Gonadotropins**

- Released from anterior pituitary in a pulsatile manner.
- Produced by basophils
- FSH  $T_{1/2}$  = 3-4 hours
- LH  $T_{1/2}$  = 20 minutes
- It has membrane bound cytoplasmic receptors
- FSH receptors are present on granulosa cells in females and sertoli cells in males.
- LH receptors are present on theca cells and granulosa cells in females and leydig cells in males.

**Functions of FSH – Females**

- Promotes gametogenesis in females and spermatogenesis in males
- Production of estrogen

**Functions of LH**

- Ovulation induction
- Formation and maintenance of corpus luteum in non-pregnant states
- Progesterone production
- Regulation of menstrual cycle

**Synthetic FSH and LH**

- The most commonly used commercial preparation of FSH is human menopausal gonadotropin (HMG 1 ampoule contain 75 U FSH and 75 U LH).
- Recently highly purified FSH (Metrodin-75 IU/amp) has been made available.
- Administered subcutaneously.
- Human chorionic gonadotropin (hCG) has biological action like LH and is available in 1000-5000 ampoules obtained from urine of pregnant woman. Recombinant hCG is now available.

**Prolactin**

- Polypeptide hormone secreted by anterior pituitary gland
- Acts on breast and is responsible for milk secretion<sup>Q</sup>
- Acts on pituitary to reduce secretion of FSH and brings about anovulation.<sup>Q</sup>



Human menopausal gonadotropin (HMG) is obtained from urine of postmenopausal females.

Chances with Gonadotropins:

- Multiple pregnancy - 30%
- OHSS = 15%



**In Prolactinomas** Levels of Prolactin increases and females complain of:

- Galactorrhea
- Amenorrhea (due to ↓ FSH)

**In Sheehan's syndrome**

– There is post partum necrosis of anterior pituitary gland  
 ∴ ↓ FSH → Amenorrhea  
 ↓ LH

↓ Prolactin which leads to failure to lactate baby

**During lactation**

There is ↑ Prolactin which leads to amenorrhea (as prolactin inhibits FSH).

### Oxytocin

- Nonapeptide which has main role in initiation of milk ejection in a lactating women.
- Initiates uterine contraction during labour.
- Half life – 5 minutes.

## Steroid Hormone

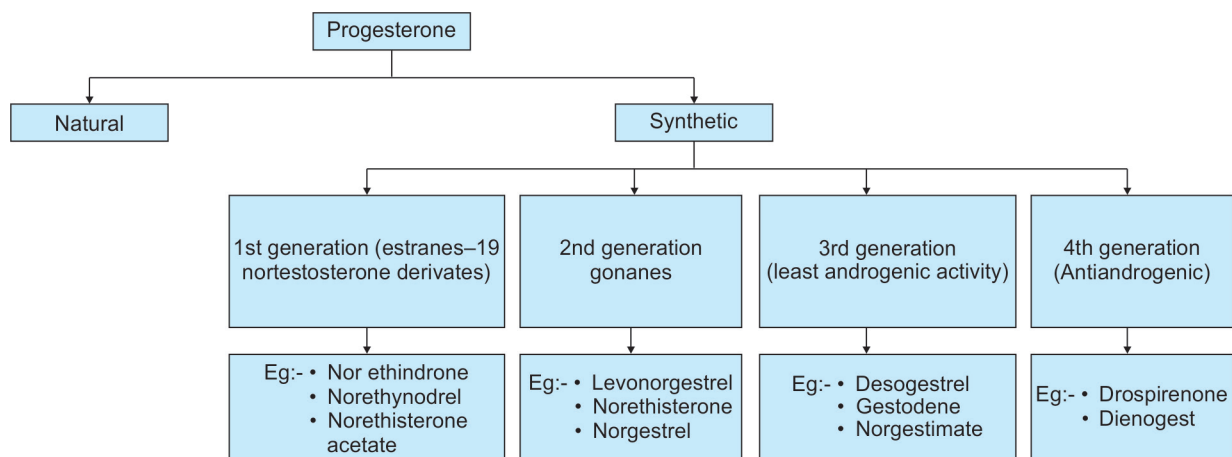
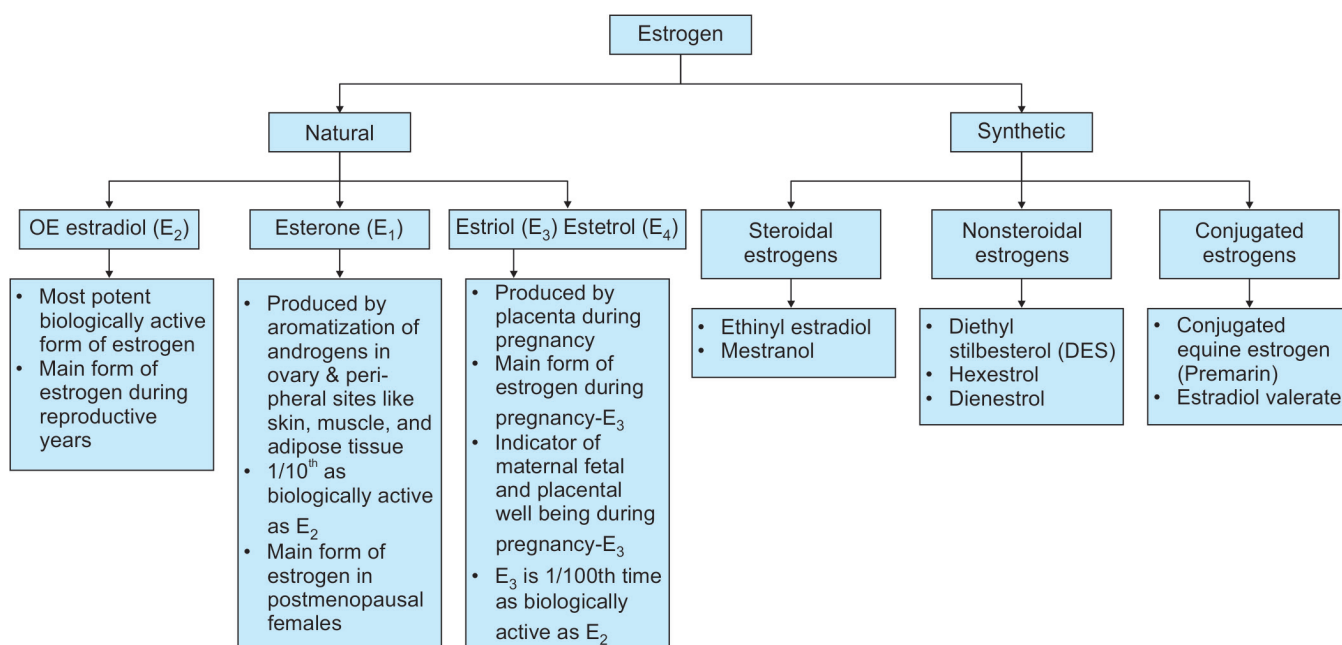
### Estrogen

	Estrogen	Progesterone
Composition	C <sub>18</sub> compounds	Natural progesterone: C <sub>21</sub> compound Synthetic are C <sub>19</sub> steroids similar to androgens. Hence they have androgenic side effects. Remember: As generation increases ⇒ androgenic side effects decrease and effect on lipid profile decreases
Receptor	<ul style="list-style-type: none"> <li>• Intranuclear</li> <li>• Estrogen receptor upregulate progesterone receptor</li> </ul>	Intra cytoplasmic Progesterone receptor down regulate estrogen receptor
Source	<ol style="list-style-type: none"> <li>1. Granulosa cells (E<sub>2</sub>)</li> <li>2. Theca cells (E<sub>1</sub>) (produce androgens which are converted to estrogen by enzyme aromatase in adipose tissue)</li> <li>3. Placenta-(with the help of precursors obtained from fetus) (E<sub>3</sub> and E<sub>4</sub>)</li> <li>4. Corpus luteum (E<sub>2</sub>)</li> </ol>	<ol style="list-style-type: none"> <li>1. Corpus luteum</li> <li>2. Placenta (with the help of maternal LDL)</li> </ol>
State	<ul style="list-style-type: none"> <li>• Mostly present in bound form</li> <li>• Only 1% free</li> <li>• Mostly bound to sex hormone binding globulin (69%) and albumin (30%)</li> </ul>	<ul style="list-style-type: none"> <li>• Mostly present in bound form</li> <li>• Only 2% free</li> <li>• Mostly bound to albumin and cortisol binding globulin</li> </ul>
End product	Glucuronides (sulfonamides)	Pregnanediol
Effect on uterus	<ul style="list-style-type: none"> <li>• Proliferation of endometrium</li> <li>• Growth of uterus in nonpregnant state</li> </ul>	<ul style="list-style-type: none"> <li>• Secretory effect on endometrium</li> <li>• Growth of uterus in pregnancy</li> <li>• Smooth muscle relaxation during pregnancy</li> </ul>
Effect on cervix	Cervical mucus is <ul style="list-style-type: none"> <li>• Copious</li> <li>• Clear and watery</li> <li>• Elastic (can be stretched between fingers-called as <b>spinbarkeit</b>)</li> <li>• Has increased water and electrolyte content, decreased protein content</li> <li>• When dried and seen under microscope, shows a characteristic <b>fern like</b> pattern</li> </ul>	Cervical mucus is <ul style="list-style-type: none"> <li>• Scanty</li> <li>• Thick, tenacious</li> <li>• Loses its stretchability (fractures on stretching, called as <b>'tack'</b>)</li> <li>• Has increased protein content and decreased water and electrolyte</li> <li>• On drying and seeing under microscope it loses its fern like pattern</li> </ul>
Effect on vagina	<ul style="list-style-type: none"> <li>• Superficial cells predominate</li> <li>• High karyopyknotic index</li> </ul>	<ul style="list-style-type: none"> <li>• Intermediate cells predominate</li> <li>• Low karyopyknotic index</li> </ul>
Effect on fallopian tube	Increases motility Decreases secretion	Decreases motility Increases secretion
Effect on salt & water	Retention	Excretion

Contd...

Contd...

	Estrogen	Progesterone
Lipid profile	<ul style="list-style-type: none"> <li>↑ HDL</li> <li>↑ TG</li> <li>↓ LDL</li> <li>(cardio protective)</li> </ul>	<ul style="list-style-type: none"> <li>↓ HDL</li> <li>↓ TG</li> <li>↑ LDL</li> </ul>
Least	Ductular development	Glandular development
Effects on LH & FSH	<ul style="list-style-type: none"> <li>• At low conc → inhibits LH</li> <li>• High conc: positive feedback on LH called as LH surge</li> <li>• Inhibits GnRH</li> </ul>	<ul style="list-style-type: none"> <li>• At low conc: positive feedback on LH and FSH</li> <li>• At high concentration negative feedback on LH</li> <li>• Inhibits GnRH</li> </ul>
Other effects	<ul style="list-style-type: none"> <li>• Closure of epiphysis</li> <li>• Procoagulant inhibits fibrinolysis</li> </ul>	<ul style="list-style-type: none"> <li>• Thermogenic-raises</li> <li>• Basal body temperature by 0.2–0.5°C</li> </ul>





**Natural estrogens** are ineffective orally due to extensive first pass metabolism. Estrogens undergo enterohepatic circulation that is also responsible for hepatic adverse effects (hepatic adenoma and thromboembolism).



M/c synthetic estrogen used – Ethinyl estradiol.



When estrogen is administered alone, it can lead to endometrial hyperplasia and endometrial cancer. Therefore in reproductive age females, if prolonged use is desired – progesterone (Medroxy progesterone) is added.



### Contraindications to use of estrogen

- History of thromboembolism
- Liver disease
- Severe hypertension
- Heart disease
- Estrogen dependent tumor, e.g. breast adenoma



Tanaproget is a nonsteroidal progestin currently undergoing trials.



Progesterone, unless specially formulated in micronised progesterone, is inactive orally because of high first pass metabolism in liver.

### Indications of Estrogen Therapy

- **Delayed puberty:** If breast development does not start even at 14 years of age then, 10 µg estrogen may be of help.
- **Lactation suppression:** Estrogen suppress lactation effectively (mixogen) but there is a risk of thromboembolism
- **Hostile cervical mucus:** In infertility to improve the quality of cervical mucus and with clomiphene citrate therapy, low dose estrogens are added.
- **DUB and polymenorrhea:**
  - Given for acute bleeding episodes
  - Conjugated equine estrogen in a dose of 10 mg/day. Bleeding stops in 24 hours
  - Combined OCPs can also be given for maintenance therapy
- **Menopausal symptoms:**
  - Short term for hot flushes, sweating, and depression
  - Give topical estrogen cream for senile vaginitis
  - Give long-term for prevention and treatment of osteoporosis
- **OCP's:** Contain estrogen and progesterone
  - Estrogen alone can be used as a post coital pill.
- For treating vulvovaginitis in children
- **Intersex:** In Turner's syndrome or gonadal dysgenesis (46, XY) estrogens are given for the growth of secondary sex characters. In androgen insensitivity syndrome (TFS), estrogen replacement therapy is indicated to prevent regression of breast development after gonadectomy.

### Side Effects

- Nausea vomiting.
- Retention of water results in painful breast and weight gain.
- Endometrial carcinoma with unopposed estrogen given for a long time.
- Probably an increased risk of breast carcinoma.
- Thromboembolism and cerebral thrombosis.
- Gall bladder and liver disease.

### ALSO KNOW

Estrogen	Commercial brand	Route of administration
Ethinyl estradiol	Lynoral (.01 mg EE)	Oral
Ethinyl estradiol	Mixogen (EE 4.4 mg + Methyl testosterone 3.6 mg)	Oral/injectable
Ethinyl estradiol	Orgalutin (EE 0.5 mg + lynoetenol 2.5 mg)	Oral
Estradiol succinate	Evalon	Oral

### Uses of Progesterone

- **Progesterone challenge test:** Details in chapter on amenorrhea.
- **Contraception:** Progesterone alone is used as mini pill. DMPA, NET EN, implants, vaginal ring, LNG IUCD are also available.
- **DUB:** To stop acute bleeding episode Norethisterone 5 mg TDS is effective. Can also be used for regulation of menstrual cycle by giving either from day 5 to 25 or day 15 to 25.
- **Dysmenorrhea and Premenstrual tension:** Dydrogesterone from 5<sup>th</sup> day for 20 days relieves dysmenorrhea. Ovulation is not suppressed.

- **Postponement of menstruation:** 5 mg NE TDS for 3 days before the expected period and continued till the need for postponement. Bleeding occurs 48 – 72 hours after withdrawal.
- **Luteal phase defect:** Daily I.M. injection of 12.5 mg progesterone, oral micronized progesterone, or vaginal suppositories can be given.
- **Endometriosis:** Progesterone induces a hyperprogestogenic, hypoestrogenic state, thus causing atrophy of ectopic endometrial tissue. The drugs used are MPA, dydrogesterone, or NE.
- **Endometrial hyperplasia and endometrial carcinoma:** Role depends on number of steroid receptor on tumor which is maximum in well-differentiated grade I endometrial carcinoma. These cases are suitable for progesterone therapy.  $17\alpha$  hydroxy progesterone caproate 1000 mg IM daily for 1 week and then weekly or MPA 400 mg, IM weekly for 3 months and then every 2 weeks.
- **Hormone replacement therapy (HRT):** Progestins are combined with estrogen as an HRT for post menopausal woman where uterus is present. Can be used cyclically or continuously.

### Selective Estrogen-Receptor Modulators (SERMs)

These are the agents that act as estrogen agonists in some tissues and antagonists in other tissues. *Agonistic action is beneficial in tissues like bone (decreased resorption) and blood (better lipid profile) whereas it is deleterious in endometrium, breast (increased risk of carcinoma) and liver (predisposition to thromboembolism).*

- SERMs are targeted to provide beneficial effect of estrogen as well as to antagonize its adverse effects. **Clomiphene, tamoxifen, droloxifene, toremifene, fulvestrant, raloxifene and ormeloxifene** are now classified as SERMs.
- In humans **clomiphene** has *estrogen antagonistic action in hypothalamus* (reduces feedback inhibition of GnRH secretion). It is used for the treatment of **anovulatory infertility** by increasing GnRH release. Major adverse effect is *hyperstimulation syndrome (polycystic ovarian disease) and multiple pregnancy*.
- **Tamoxifen, doloxifene and toremifene** possess estrogen antagonistic activity in the breast and blood whereas agonistic activity in bone, uterus and liver. Their major indication is in the treatment of **breast carcinoma**. *These have beneficial effect on bone and lipid profile but increase the risk of endometrial carcinoma and thromboembolism.*
- **Raloxifene** is used for **osteoporosis**. It also possesses beneficial effects on lipid profile, breast and endometrium. *Major adverse effect is increased predisposition to thromboembolism.*
- **Centchroman (ormeloxifene)** is used as a **non hormonal oral contraceptive (Saheli)**. It is also approved for the treatment of DUB.
- **Fulvestrant** is the first FDA approved agent in the new class of drugs that are called **selective estrogen-receptor downregulators (SERDs)**. These have an *improved safety profile, faster onset, and longer duration of action than the SERMs* due to their pure ER antagonist activity. It was approved for postmenopausal women with **hormone receptor-positive metastatic breast cancer that has progressed despite antiestrogen therapy**.

### Clomiphene Citrate

- Was first used in gynecology in 1956
- It is non steroidal triphenylethylene compound related to diethylstilbestrol (DES).
- It is an isomer of cis and trans form. Enclomiphene is more potent isomer and anti estrogenic whereas zuclomiphene is weak antiestrogenic

**Ospemifene** is a new SERM indicated for dyspareunia due to menopause

- **Tamoxifen** has Beneficial effect on:
  - Bone ( $\downarrow$  resorption)
  - Breast ( $\downarrow$  carcinoma)
  - Blood ( $\uparrow$  HDL &  $\downarrow$  LDL)
- **Fulvestrant** is a selective estrogen-receptor down-regulator (SERD). It has improved safety profile, faster onset, and longer duration of action than the SERMs due to its pure ER antagonist activity.

Clomiphene binds and blocks estrogen receptors in hypothalamus (i.e. antiestrogen)

↓  
Decrease in estrogen negative feedback  
↓  
Increase GnRH pulses  
↓  
 $\uparrow$  in FSH and LH  
↓  
 $\uparrow$  folliculogenesis & ovulation

**Prerequisite:** A functional hypothalamic pituitary ovarian axis is required for appropriate clomiphene citrate activity. It is the agent of choice for treating anovulation in women with oligomenorrhea or amenorrhea having sufficient ovarian function to maintain estrogen at serum level of 40 pg/mL.

The required dose of clomiphene is correlated to body weight as their is significant association between its treatment failure and BMI  $\geq 27$  kg/m<sup>2</sup>



#### Side effects of clomiphene:

- Multiple pregnancy (6–8%) < 10%
- Ovarian cysts
- Ovarian hyperstimulation syndrome (<1%)

#### Antiestrogenic side effects

- Hotflashes, osteoporosis
- Longterm use-ovarian malignancy

**Note:** No congenital malformation seen

- Most common effect hot flushes and ovarian cyst formation.



- Clomiphene citrate is the drug of choice for postpill amenorrhea
- hCG acts as an ovulation trigger when using clomiphene for anovulation since hCG is functionally and structurally similar to LH.



**Letrozole:** for ovulation induction

- Pregnancy rates similar to clomiphene
- Multiple pregnancy rates: less
- NO congenital malformation seen in fetus.

- It binds to estrogen receptors in the hypothalamus, so the negative feedback of estrogen on FSH is prevented resulting in increased pulsatile GnRH frequency and rise in FSH and LH.
- The antiestrogenic effects of Clomiphene are seen on cervix and endometrium.

#### Indications

- Anovulation, PCOS.
- Anovulatory DUB with infertility.
- Amenorrhea and anovulation following the use of OCP's (Post pill amenorrhea).
- In vitro fertilisation, GIFT technique and assisted reproduction technique.
- Male infertility (Role doubtful).

#### Schedule of Administration in Case of Amenorrhea

- Given orally from 2<sup>nd</sup> or 3<sup>rd</sup> of menstruation in dose of 50 mg daily for 5 days.
- Maxm dose = 100 mg 1 day
- MAXm duration = 12 months on 12 days practically given only for 6 months.
- Monitoring of follicle is done by serial USG (follicular monitoring) or home urine LH kits.
- When the dominant follicle is 20 mm, hCG 5000 IU is given by IM route (hCG acts as an ovulation trigger as functionally hCG is similar to LH).
- Coitus is advised 32–36 hours after hCG (since hCG is similar to LH so ovulation occurs 32–36 hours after LH surge).

#### Result

80% ovulate but 30–40% conceive because of antiestrogenic effect of clomiphene in cervical mucus leading to thick cervical mucus. Multiple pregnancy chances with clomiphene are 10%.

#### Contraindications

- Cystic ovaries.
- Chronic liver disease.
- Scotoma.
- Hypogonadotropic and hypoestrogenic states.

#### Aromatase Inhibitors

- Androgens are converted to estrogen in the peripheral tissue in females with the help of an enzyme, aromatase. The drugs inhibiting this enzyme will *decrease the formation of estrogen*.
- Aromatase inhibitors are divided into first and second generation compounds. **First generation drugs include aminoglutethimide and second generation agents are letrozole, anastrozole, fadrozole, formestane, vorozole and exemestane.**
- Aromatase inhibitors are useful in all those conditions where there is hyperestrogenemia like fibroids, endometriosis and breast cancer.
- It is also used for ovulation induction. Principle is same like clomiphene.
- Common side effects of these drugs include bone pain, hot flushes and thromboembolism.

#### Antiprogestrone

##### Mifepristone RU 486

- Derivative of 19 nortestosterone.
- Competitive antagonist of progesterone and glucocorticoid receptors.



- Binds to progesterone receptors and nullifies the effects of endogenous progesterone.
- There is release of prostaglandins from the endometrium and early termination of pregnancy.
- 85% drug is absorbed after oral therapy, peak is reached in 1–2 hours. Half life is 24 hours and excreted in bile and feces.
- In the absence of progesterone, it acts as weakly progesteric.

### Uses of Mifepristone

- As postcoital pill (600 mg given within 72 hours of unprotected sex).
- To induce abortion upto 7 weeks of amenorrhea along with misoprostol (medical abortion).
- Ripening of cervix prior to prostaglandin induction of mid-trimester abortion.
- Management of ectopic pregnancy.
- Cushing's syndrome: because of its antiglucocorticoid action.
- Medical management of uterine fibroid.
- As an emergency contraceptive (single dose of 10 mg is taken on 27th day of cycle irrespective of day and number of times intercourse)

### Side Effects

- Headache.
- GI upset.
- Adrenal failure.
- Teratogenicity (If medical methods of abortion fails with RU - 486, pregnancy should be terminated any how).

## Androgens in the Female

Circulating androgens found in the blood of premenopausal women include dehydroepiandrosterone (DHEA), DHEA sulfate (DHEA-S), androstenedione, and testosterone. Androgens are produced by the adrenal glands, the ovary, and from peripheral conversion of estrogen (with the help of enzyme aromatase).

### Androstenedione

- Produced in equal amounts by the adrenal glands (50%) and the ovaries (50%)
- Majority of androstenedione is converted to testosterone
- Normal serum concentration ranges from 60 to 300 ng/dL
- Mostly bound to Albumin and sex hormone binding 1.1 free in females (2% in globular males)
- **Receptors:** Intra cytoplasmic
- **Endproduct** oxosteroid (keto steroid)

### Testosterone

- Second most potent androgenic hormone.<sup>Q</sup> (first being DHT)
- In women, nearly 25% of testosterone is secreted from the ovaries and 25% is from the adrenal glands. The remaining one-half is produced from peripheral conversion of androstenedione to testosterone in the skin, muscle kidneys, liver, and adipose tissue.
- Normal circulating concentrations range from 20 to 80 ng/dL.
- Mostly bound to Albumin and sex hormone binding globulin.
- 1% free in females (2% in males)
- Receptors—Intra cytoplasmic
- Endproduct—Oxosteroid (steroid)



#### Selective Progesterone Receptor Modulator (SPRM)

Asoprisnil is an investigational SPRM, tested for treatment of progesterone sensitive myomata. Clinical trials were discontinued due to endometrial changes in patients.



Moebius syndrome occurs due to the use of misoprostol and not mifepristone during pregnancy.



Ovary :- M/C androgens secreted Androstenedione > DHEA > Testosterone  
Androstenedione is formed by theca cell of ovary



Measurement of DHEA-S is used to assess adrenal function

S

SHBG is synthesized in liver. Inhibits its Testosterone synthesis. Estrogen promotes its - low levels of SHBG are marker of a insulin receptor.

### DHEA and DHEA-S

- Androgen precursors, much less potent than testosterone and produced predominantly by the adrenal glands (DHEA-S is produced only by adrenal).
- DHEA is metabolized quickly, thus measurement of its serum concentration does not reflect adrenal gland activity. **DHEA-S has a much longer half-life than DHEA, and measurement of its serum level is used to assess adrenal function.**<sup>Q</sup>

### Dihydrotestosterone (DHT)

- Testosterone is converted to dihydrotestosterone (DHT) by 5-alpha-reductase, an enzyme found in many androgen-sensitive tissues.
- Very potent androgen primarily responsible for the androgenic effects on hair follicles.
- 3 $\alpha$  androstanediol glucuronide (3 $\alpha$ -AG) is an important metabolite of DHT.

### Danazol

- It is a 17 $\alpha$  ethinyl testosterone derivative.
- It is a compound with weak androgenic, progestational and antigonadotropic activity.

Danazol should not be used in young females because of its virilising side effects.

Antigonadotropic agent	Androgenic
<p>Acts on HPO axis and decreases frequency of GnRH pulses</p> <p style="text-align: center;">↓</p> <p>↓ LH surge ↓ FSH surge (no change in basal gonadotropin levels)</p> <p style="text-align: center;">↓</p> <p>↓ estrogen (endometrial atrophy)</p> <p style="text-align: center;">↓</p> <p>Pseudomenopause like state</p>	<p>As it decreases synthesis of sex hormone binding globulin hence level of free testosterone increases and thus it has virilising side effects</p>

- It acts directly on ovaries and inhibits steroidogenesis.

### Danazol is used in

In females		In males
<p><b>Uterus :</b></p> <ul style="list-style-type: none"> <li>• Endometriosis (as it causes endometrial atrophy)</li> <li>• DUB in old females</li> <li>• Fibromyoma (to ↓ its size and vascularity)</li> <li>• Infertility</li> </ul>	<p><b>In Breast for :</b></p> <ul style="list-style-type: none"> <li>• Cyclical mastalgia</li> <li>• Fibrocystic breast disease</li> </ul>	<ul style="list-style-type: none"> <li>• Precocious puberty</li> <li>• Gynecomastia</li> <li>• Improves libido</li> </ul>

#### Also Know

Gestrinone has actions and uses similar to danazol but has longer t $\frac{1}{2}$ , so is used in biweekly doses. Its side effects are milder to danazol and thus it is preferred over danazol.

### Other use

In hereditary angioneurotic edema.

### Side Effects

It has androgenic side effects like acne, hirsutism<sup>Q</sup>, deepening of voice (irreversible), Oily skin weight gain, etc.

- Teratogenic in early pregnancy (causing masculinization of female fetus), therefore it should not be used in young females.

- *Danazol should not be given for more than 6–9 months at a time because of its antiestrogenic action and virilizing effects.*<sup>Q</sup>

### Contraindications

- Liver disease
- Carcinoma prostrate

### Antiandrogens

Drugs in this group can act by **inhibiting the synthesis, activation or action of androgens**.

- **Steroid synthesis inhibitors: Ketoconazole** inhibits the synthesis of adrenal and gonadal hormones but its usefulness in the treatment of prostatic carcinoma is limited by serious toxicity on prolonged use. It can cause **gynaecomastia** due to increase in estradiol: testosterone ratio. **Abiraterone** is an **orally active prodrug** that acts by inhibiting 17- $\alpha$ -hydroxylase and 17, 20-lyase.
- **5- $\alpha$  reductase inhibitors:** Most of the actions of testosterone are mediated by its conversion to DHT by 5- $\alpha$  reductase. Important amongst these are growth of prostate, male pattern baldness and hirsutism in females. **Finasteride and dutasteride** are 5- $\alpha$  reductase inhibitors useful in the *treatment of BPH, male pattern baldness and hirsutism* by reducing the production of DHT.
- **Androgen receptor inhibitors: Cyproterone and cyproterone acetate** act as antagonists of androgen receptors. Latter compound has marked progestational activity that inhibits feedback enhancement of LH and FSH. These drugs are useful in the **treatment of hirsutism** and as a component of **contraceptive pills**. **Flutamide, bicalutamide and nilutamide** are other antiandrogens that act by same mechanism. These are useful for the *treatment of prostatic carcinoma*. *Flutamide can cause gynaecomastia and reversible liver damage*. These drugs can also be combined with GnRH agonists (like leuprolide) to reduce the initial flare up reaction.
- **Spirolactone:** It is an aldosterone antagonist that also competes with DHT for its receptor. It can be used for the *treatment of hirsutism*.

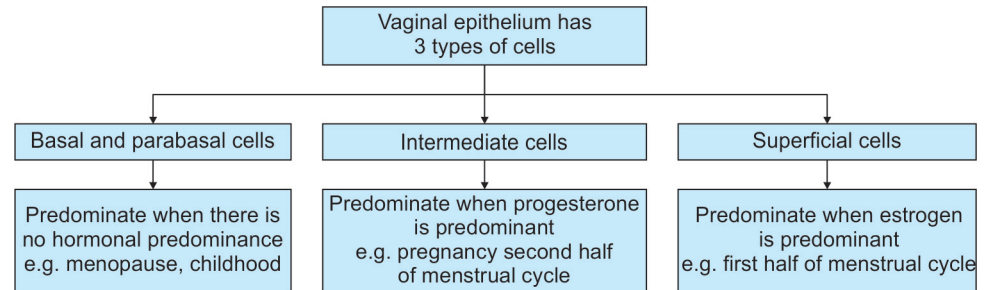


Diane 35 or Ginette has EE 35 mg & cyproterone acetate 2 mg. It is the DOC in teenagers with irregular periods & hirsutism.

### Important Points

- LH surge 32–36 hrs → ovulation
- LH peak 10–12 hrs → ovulation
- What initiates LH surge :- estradiol-levels 200 pg/ml for 48 hours initiates LH surge.
- LH leads to luteinization of granulosa cells and progesterone is released by granulosa cells. Therefore progesterone synthesis begins 36 hours before ovulation.
- Hormone responsible for resumption of meiosis - LH
- When in Meiosis I resumed - 36 hours before ovulation (because of LH surge)
- Just before ovulation LH and FSH both increase - LH surge is initiated by estrogen. At low levels-progesterone has positive feedback on LH & FSH, so-FSH also rises. Remember: LH surge is initiated by estrogen but for maintenance of LH surge both estrogen and progesterone required.
- Minimum levels of LH & FSH are seen in Luteal phase (as high conc of progesterone → has -ve feedback on LH & FSH)
- After ovulation, the ruptured Graafian follicle becomes corpus luteum.
- The yellowish color is due to lipid and pigment carotene. Regression starts on day 22–23 of infertile cycle.
- Progesterone attains its highest peak about 8 days after the LH peak like day when corpus luteum has maximum function.
- **Luteal-Placental shift** is the turnover of function from corpus luteum of pregnancy to placenta. This transition period continues from seven weeks to ten weeks.

- **Luteal-Follicular shift** is the period that extends from the demise of corpus luteum to the selection of a new dominant follicle for the next cycle. It is due to fall in the levels of estradiol, progesterone and inhibin. There is simultaneous rise in the levels of GnRH and FSH.



- The ovarian hormones estrogen and progesterone thus influence vagina.
- The exfoliated cells in vagina reflect the prevailing hormone system at that time.

Note: For hormonal study – smear should be taken from lateral wall of upper third of vagina<sup>Q</sup>.

#### ➤ **Maturation Index:**

- It is the relative percentage of parabasal, intermediate and superficial cells per 100 cells counted.
- It is expressed in 3 numbers, a/b/c.  
'a' represents number of parabasal cells per 100 cells counted.  
'b' represents number of intermediate cells per 100 cells counted.  
'c' represents number of superficial cells per 100 cells counted.
- It indirectly reflects the endocrine status of the cervix.
- **Maturation index from birth to menopause:**

	M.I	Smear features	Inference
At birth	0/95/5	—	Combined effect of circulating maternal hormones: oestrogen, progesterone & corticoids.
Childhood	80/20/0	—	MI shifting to left because of diminished steroid hormones.
<b>Reproductive period :</b> Preovulatory	0/40/60	Smear clear, cells are discrete	Oestrogen ++
Mid secretory	0/70/30	Smear dirty, cells in clusters	Oestrogen + Progesterone ++
During pregnancy	0/95/5	Marked folding of the intermediate cells : 'navicular cells'	Oestrogen ++ Progesterone ++ Corticosteroids +
Postpartum	100/0/0	—	Parabasal maturation
Postmenopausal	100/0/0	—	Lack of oestrogen.

#### **Important facts:**

- The intermediate and superficial cells contain glycogen under the influence of oestrogen and therefore vagina stains deep brown in colour after painting with iodine solution (called as Positive schillers test).<sup>Q</sup>
- The glycogen content is highest in vaginal fornix and lowest in lower one third of vagina.
- Estrogen dominant smears appear clear and show discrete cornified polygonal eosinophilic cells.
- Progesterone dominated smears are dirty as intermediate cells predominate.
- **Cornification index/karyopyknotic index:** It is the ratio of cornified cells (mature squamous cells) per 100 cells counted since epithelial cells are cornified under the influence of hormone estrogen, so cornification index indicates estrogenic effect.

## QUESTIONS

### Ovarian cycle

- Which of the following is seen in the ovulatory phase?  
(AIIMS May 11)
  - Stimulation of continuation of reduction division of oocytes
  - Inhibin A is increased
  - FSH increases steroid synthesis in granulosa cells
  - Activin causes FSH to act on granulosa cells
- In ovarian cycle increased levels of LH are due to:  
(AIIMS May 11)
  - Increased Progesterone
  - Increased Estrogen
  - Increased FSH
  - Increased Androgens
- In 40 days of menstrual cycle the ovulation occurs at:  
[UP 03]
 

a. 14 <sup>th</sup> day	b. 20 <sup>th</sup> day
c. 26 <sup>th</sup> day	d. 30 <sup>th</sup> day
- The ovarian cycle is initiated by:  
[DNB 96]
 

a. FSH	b. Estrogen
c. LH	d. Progesterone
- The corpus luteum secretes:  
[DNB 04]
 

a. Estrogens	b. Progesterone
c. Both	d. None
- Apoptosis can occur by change in hormone levels in the ovarian cycle. When there is no fertilization of the ovum, the endometrial cells die because:  
[AIIMS Nov 03]
  - The involution of corpus luteum causes estradiol and progesterone levels to fall dramatically
  - LH levels rise after ovulation
  - Estradiol levels are not involved in the LH surge phenomenon
  - Estradiol inhibits the induction of the progesterone receptor in the endometrium
- Corpus luteum functions maximally without an implantation for ..... days:  
[PGI June 00]
 

a. 9	b. 12
c. 6	d. 15
- Maximum function of corpus luteum occurs:
  - At ovulation
  - Before ovulation
  - 3 days after ovulation
  - 8–9 days after ovulation
- In a study it is observed that the right ovary ovulates more than the left, all are possible explanations for the cause except:  
[AIIMS Nov 2010, AIIMS Nov 2012]
  - Anatomical asymmetry
  - Difference in blood supply to both sides

- Right handedness is more common in population
  - Some embryological basis
- Ovulation occurs  
[AIIMS May 2013]
    - Before LH surge
    - After biphasic rise in body temperature
    - After ripening of follicle by FSH
    - Before estrogen peak
  - True about timing of LH surge:  
[PGI May 2013]
    - Occur 12 hour before ovulation
    - Occur 24 hour before ovulation
    - Occur 12 hour after ovulation
    - Occur 24 hour after ovulation
    - Occur at time of ovulation
  - Which of the following is not related with menstrual cycle?  
[AI 2011]
 

a. Hormonal changes	b. Vaginal cytology
c. Estrous cycle	d. Endometrial sampling

### Hormones – Estrogen/Progesterone

- Naturally occurring estrogens are:  
[PGI Dec 08]
 

a. Estrone	b. Estradiol
c. Estriol	d. Diethylstilbestrol
e. Pregnanediol	
- The production of cervical mucus is stimulated by:  
[AIIMS Nov 02]
 

a. Progesterone	b. Estradiol
c. Estriol	d. Pregnenolone
- Ferning of cervical mucus depends on:  
[DNB 96]
 

a. Estrogen	b. Progesterone
c. LH	d. FSH
- In an infertile woman, endometrial biopsy reveals proliferative changes. Which hormone should be preferred?  
[AI 01]
 

a. MDPA	b. Desogestrel
c. Norethisterone	d. None of the above
- End product of progesterone metabolism found in urine is:  
[AIIMS May 2013]
  - Pregnenolone
  - 17-OH pregnanelone excreted in urine
  - Pregnanediol
  - Pregnanetriol

### Clomiphene

- Clomiphene citrate is:  
[AP 97]
 

a. Antiandrogen	b. Synthetic steroid
c. Antiestrogen	d. GnRH analogue
- Clomiphene citrate is indicated in:  
[AI 98]
  - Stein–Leventhal syndrome
  - Ovarian cyst
  - Asherman's syndrome
  - Carcinoma endometrium

20. True about Clomiphene citrate : [PGI June 07]  
 a. Commonly causes hyperstimulation syndrome  
 b. Used for ovulation induction  
 c. Multiple pregnancies seen in 3–8% cases
21. True about clomiphene citrate is: [AIIMS May 09/May 10]  
 a. Enclomiphene has antiestrogenic affect  
 b. Chance of pregnancy is three fold as compared to placebo  
 c. Risk of multiple pregnancy is 2–4%  
 d. It can also be used for male infertility with oligozoospermia
22. Side effect of clomiphene citrate includes all except: [AIIMS Nov 07]  
 a. Multiple pregnancy  
 b. Increase risk of ovarian cancer  
 c. Multiple polycystic ovary  
 d. Teratogenic effect on offspring
23. A patient treated for infertility with clomiphene citrate presents with sudden onset of abdominal pain and distension with ascites, the probable cause is:  
 a. Uterine rupture  
 b. Ectopic pregnancy rupture  
 c. Multifetal pregnancy  
 d. Hyperstimulation syndrome

### GnRH

24. GnRH analogue may be given in all of the following except: [AI 99]  
 a. Prostate Ca  
 b. Endometrial Ca  
 c. Fibromyoma – uterus  
 d. Precocious puberty
25. GnRH analogues are useful in all except : [AP 97]  
 a. Endometriosis      b. Hyperprolactinemia  
 c. Precocious puberty      d. Menstrual disturbances

### Danazol

26. Danazol is used in the treatment of: [AIIMS May 02]  
 a. Cyclical mastalgia  
 b. Breast cyst  
 c. Noncyclical mastalgia  
 d. Epithelial changes in breast
27. Danazol is used in all except : [JIPMER 91]  
 a. Hirsutism  
 b. Endometriosis  
 c. Dysfunctional uterine bleeding  
 d. Fibroid

### Mifepristone

28. Which of the following statements are true about mifepristone? [PGI Dec 01]  
 a. Also called RU – 486  
 b. It is a 19 – norsteroid  
 c. Acts on receptors  
 d. Given only intravenously  
 e. Used for menstrual regulation

### Inhibin/Relaxin

29. Following are the features of inhibin except: [Karnataka 06]  
 a. Non steroidal water soluble protein  
 b. Secreted by Graafian follicle  
 c. Stimulates FSH secretion  
 d. Increased secretion of inhibin occurs in polycystic ovarian disease
30. The probable source of relaxin is: [JIPMER 91; DNB 98]  
 a. Ovary      b. Adrenal cortex  
 c. Liver      d. Bartholin's gland  
 e. Anterior pituitary

### NEW PATTERN QUESTIONS

31. All are true regarding folliculogenesis and ovulation except:  
 a. Follicular development and differentiation takes about 85 days  
 b. AMH supports monofollicular development  
 c. First phase of follicular growth is gonadotropin insensitive  
 d. Elevated and static level of estradiol is essential for ovulation.
32. The following are related to granulosa cells except:  
 a. It has got no blood supply  
 b. In the first half of the cycle, it has no steroidogenic function  
 c. Granulosa cells produce activin and inhibin  
 d. Estrogen stimulates the proliferation of granulosa cells
33. The following are related to corpus luteum except:  
 a. Luteinised granulosa cells produce progesterone  
 b. Estrogen continues to be produced by the luteinised theca cells  
 c. Luteolysis is due to estrogen, PGF<sub>2</sub>α and endothelin  
 d. The peak steroid production is between 23 and 25th day
34. Granulosa cells produces estrogen with the help of the enzyme:  
 a. Alkaline phosphatase  
 b. Aromatase  
 c. Acid phosphatase  
 d. Glucuronidase
35. Peak level of plasma progesterone in the luteal phase:  
 a. 5 ng/ml      b. 10 ng/ml  
 c. 15 ng/ml      d. 30 ng/ml
36. The earliest morphological evidence of ovulation on endometrial biopsy is:  
 a. Pseudostratification  
 b. Basal vacuolation  
 c. Decrease in glycogen content  
 d. Predecidual reaction
37. The most serious complication of clomiphene therapy for induction of ovulation is:  
 a. Bone marrow depression  
 b. Hyperstimulation syndrome

- c. Secondary amenorrhea
  - d. Multiple pregnancy
38. Major sources of androgen in females are all *except*:
- a. Adrenals
  - b. Ovaries
  - c. Peripheral conversion to androgen precursors in the liver, gastro-intestinal tract and adipose tissue
  - d. Corpus luteum
39. The side effect of clomiphene because of which its use should be immediately stopped:
- a. Hotflashes
  - b. Multiple pregnancy
  - c. Teratogenicity
  - d. Visual symptoms
40. Vaginal smear in old lady shows:
- a. Atrophic cells on smear
  - b. Basal and parabasal cells
  - c. Superficial cells
  - d. Few intermediate cells seen
41. The maturation index on vaginal cytology is a diagnostic method for evaluating the:
- a. Adequacy of cytotoxic drug therapy
  - b. Gender of an anatomically abnormal child
  - c. Malignant change at squamocolumnar junction of cervix
  - d. Endocrine status of cervix
42. Vaginal cytology for hormonal change is best taken from:
- a. Posterior wall
  - b. Anterior wall
  - c. Lateral wall
  - d. Any wall
43. Cornification index or eosinophilic index indicates:
- a. Progesterone effect
  - b. Estrogenic effect
  - c. Effect of LH
  - d. All of the above

## ANSWERS

## Ovarian Cycle

## 1. Ans. is a, i.e. Stimulation of continuation of reduction division of oocytes

Ref. Leon Speroff 8<sup>th</sup>/ed pp 213,223,226,229; Jeffcoate 7<sup>th</sup>/ed pp 60-63

Lets analyse each option – In ovulatory phase.

**Option a:** Stimulation of continuation of reduction division of oocytes – correct

During oogenesis the primary oocyte is arrested in prophase of meiosis 1. Just before ovulation, the LH surge initiates the continuation of meiosis, forming secondary oocyte and 1<sup>st</sup> polar body.

*“The LH surge initiates the resumption of meiosis in the oocyte (meiosis is not completed until after the sperm has entered and second polar body is released.”*

– Leon speroff 8<sup>th</sup>/ed p 229

**Option b:** Inhibin A is increased in ovulatory phase – incorrect

Levels of inhibin A are increased and reach peak in midluteal phase, not in ovulatory phase.

**Option c:** FSH increases steroid synthesis in granulosa cells –

FSH acts on the granulosa cells to produce estrogen mainly in the follicular phase and not in ovulatory phase.

**Option d:** Activin causes FSH to act on the granulosa cells –

As discussed, activin does augment the action of FSH on granulosa cells but during early follicular phase and not during ovulatory phase.

*“In the granulosa of the early follicular phase, activin augments FSH activities: FSH receptor expression, aromatization, inhibin/activin production, and LH receptor expression. In the theca, activin suppresses androgen production, allowing the emergence of an estrogen microenvironment.”*

– Leon speroff 8<sup>th</sup>/ed p 226.

## 2. Ans. is b i.e. Increased estrogen

Ref. Shiela Balakrishman TB of gynae p 34

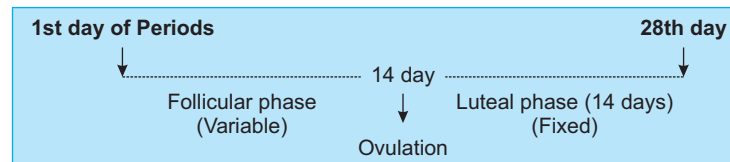
As discussed in the preceding text – Estrogen has a positive feedback on LH near ovulation and therefore levels of LH are suddenly increased resulting in LH surge.

*“With dramatic increase in estradiol, however there is a change in the LH feedback. There is initial suppression of LH with low levels of oestradiols. It switches to positive feedback when estradiol levels reach 200 pg/ml. These high estrogen levels also increase the production of more bioactive form of FSH and LH. This causes the dramatic bioovulatory LH surge causing 10 fold increase in LH.”*

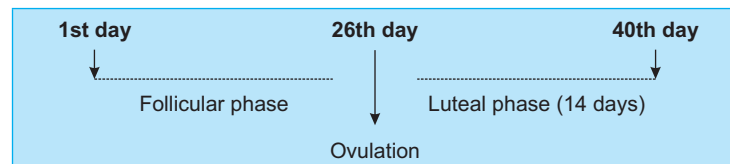
– Shiela Balakrishman 1<sup>st</sup>/ed, p 34

3. Ans. is c, i.e. 26<sup>th</sup> day

Ref. Shaw 15<sup>th</sup>/ed p 30



- Ovulation is estimated to occur 14 days before the first day of succeeding cycle and this interval is fixed.
- In case of irregular cycles, it is the follicular phase which varies, but the luteal phase remains more or less constant at 14 days, therefore day of ovulation can be estimated by counting 14 days backward.
- As in the question the cycle is of 40 days, ovulation will occur 14 days prior to next menstruation i.e. (40-14) = 26 day



**Remember = Day of ovulation = Length of Menstrual cycle – 14**

## 4. Ans. is a i.e. FSH

Ref shaw 14<sup>th</sup>/ed p 41, Dutta Gynae 5<sup>th</sup>/ed p 82

As discussed in text –

Ovarian cycle is initiated by FSH

**Remember:** Following questions werl asked previously on FSH

## FSH

- It is the hormone which initiates ovarian cycle
- In menopausal females- Since primordial follicles are decreased so levels of estrogen is decreased, so negative feedback on FSH is decreased, hence levels of FSH are increased and increased FSH levels are a sine qua non of menopause.

Contd...



Contd...

FSH
iii. Human menopausal gonadotropin (HMG) is FSH and LH obtained from the urine of postmenopausal females
iv. FSH levels can help in differentiating the causes of male infertility viz In pretesticular cause of male infertility = FSH decreases In testicular cause = FSH levels increase In posttesticular cause = FSH is normal
v. Best test for ovarian reserve = FSH

5. Ans. is c, i.e. Both

Ref. Dutta Gynae 5<sup>th</sup>/ed p 85

6. Ans. is a, i.e. The involution of corpus luteum causes estradiol and progesterone levels to fall dramatically

Ref. Jeffcoates 7<sup>th</sup>/ed pp 83-84; Leon speroff 7<sup>th</sup>/ed pp 121-122

7. Ans. is a, i.e. 9 days

Ref. Leon speroff 8<sup>th</sup>/ed p 236

8. Ans. is d, i.e. 8-9 days after ovulation

Ref. Shaw 14<sup>th</sup>/ed p 28

**Corpus luteum:** After ovulation, the ruptured Graafian follicle develops into corpus luteum.

- Corpus luteum reaches its maximum maturity by 22<sup>nd</sup> day of cycle (Size = 2 cms or more), ovulation occurs on day 14, i.e. 8<sup>th</sup> days after ovulation corpus luteum reaches its maximum maturity.
- Colour of corpus luteum in early stages is greyish yellow<sup>Q</sup> due to presence of lipids and later is distinctive yellow due to pigment carotene.<sup>Q</sup>
- Corpus luteum secretes:
  - a. Progesterone (mainly)
  - b. estrogen
  - c. Inhibin
  - d. Relaxin - secreted by corpus luteum of pregnancy
- In non-pregnant states activity of corpus luteum is maintained by hormone LH whereas in pregnant states by hormone hCG.<sup>Q</sup>
- The corpus luteum rapidly declines 9-11 days after ovulation and starts forming corpus albicans if pregnancy does not occur
- In the first half of the secretory phase, acid phosphatase and potent lytic enzymes are confined to lysosomes. Their release is inhibited by progesterone stabilization of the lysosomal membranes. With the involution of corpus luteum levels of estrogen and progesterone fall, the lysosomal membranes are not maintained and enzymes are released which cause apoptosis of the endometrial cells.
- *"The withdrawal of estrogen and progesterone initiates important endometrial events, vasoconstriction, the process of apoptosis, tissue loss and finally menstruation."*  
- Leon Speroff 7<sup>th</sup>/ed p 121
- If pregnancy occurs, hCG similar to LH stimulates corpus luteum to secrete progesterone. It's growth reaches a peak at 8<sup>th</sup> week of gestation and it remains functionally active till 10-12 weeks of gestation, whereby the placenta takes over its function of producing progesterone.

9. Ans. is c, i.e., Right handedness is more common in population

Ref. humrep.oxfordjournal.org/content/12/8/1730.full.pdf

- In the primate it is suggested that ovulations occur with equal frequency in the left and right ovary.
- In the humans there is some controversy about the frequency of ovulation on each side.
- It is believed that in normally menstruating women ovulation was significantly higher in right ovary.
- It is believed that right sided predominance was either **genetically determined** or due to **difference in the vasculature of the ovaries**.
- **The anatomical asymmetry** between the left and right side are also thought to be the reason.
- The left ovarian vein drains to the left renal vein and the right ovarian vein to the inferior vena cava.
- The left renal vein is thought to be under high pressure than the right and therefore drain slower. Because the left ovary drains slower, the collapsed follicle (corpus luteum) takes longer to clean and thereby diminishes the chances that ovulation will occur on that side the following month.
  - No such condition exists on the right side which is why successive right side ovulation is more common.

10. Ans. is c, i.e. After ripening of follicle by FSH

We have discussed ovarian cycle in detail in preceding text.

The question is very simple as ovulation occurs after LH surge and estrogen peak and because of ovulation there is biphasic rise in temperature.

11. Ans is b, i.e. Occur 24 hours before ovulation

Ref. Dutta gynae 6<sup>th</sup>/ed p 93

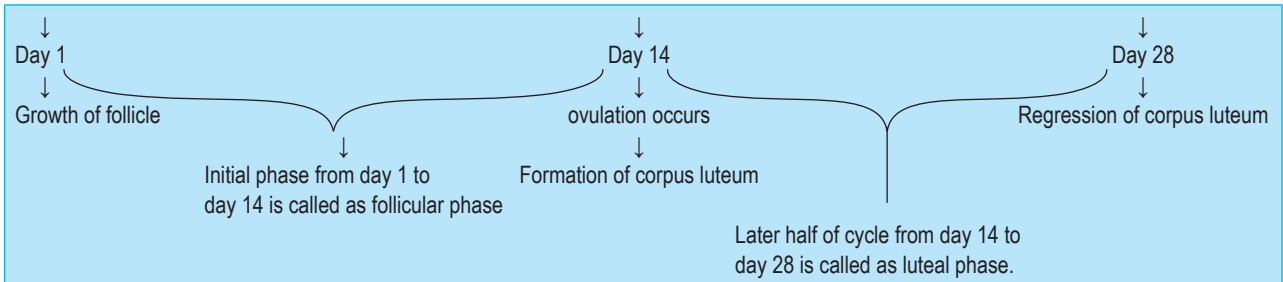
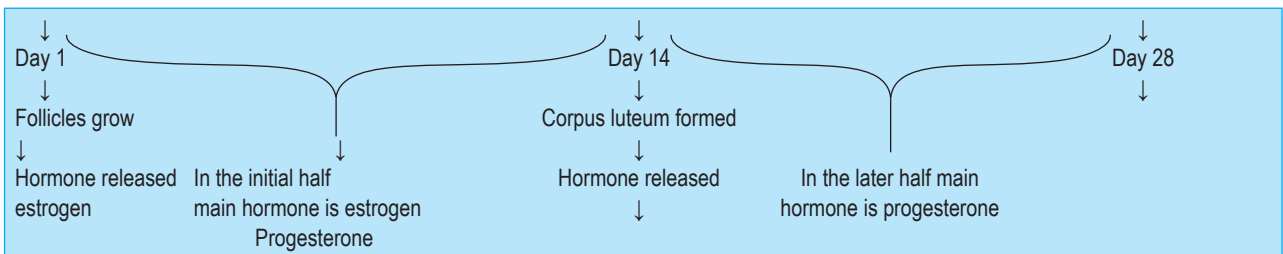
Generally ovulation occurs 32-36 hours after LH surge or 10-12 hours after LH peak, i.e. 75 ng/ml of LH

Some books say LH surge occurs 24-36 hours before ovulation so we are taking 'option b' as correct.

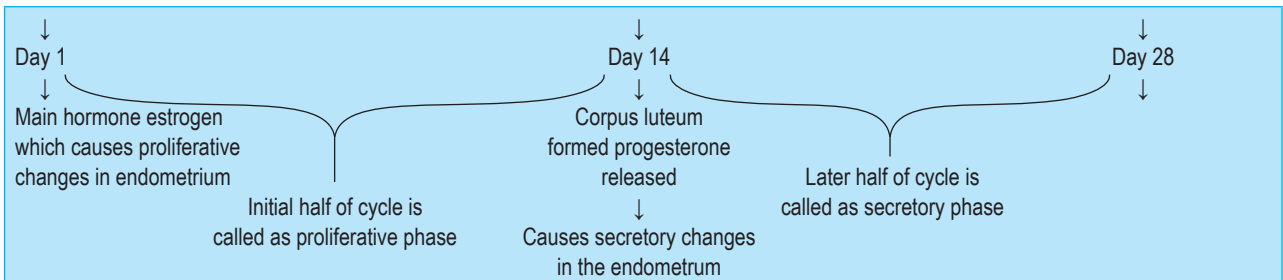
## 12. Ans. is c, i.e. Estrous cycle

Ref. Leon speroff 7<sup>th</sup>/ed pp 116-120**Explanation**

- With these changes in the ovary there are simultaneous changes in the uterine endometrium, i.e. in the menstrual cycle. In a 28 day menstrual cycle.

**Hormonal changes**

Thus, hormonal levels coincide with ovarian cycle.

**Endometrial sampling**

Thus endometrial sampling reveals whether the endometrium is in proliferative or secretory phase and thus indirectly indicates whether ovulation has occurred or not and so endometrial sampling also coincides with ovarian cycle.

**Vaginal cytology**Dutta Gynae 5<sup>th</sup>/ed p 110

Vaginal squamous epithelium is composed of following types of cells-

<b>Parabasal/ basal cells</b>	Which are predominant when there is no hormonal dominance.
<b>Intermediate cells</b>	Which are predominant when there is progesterone predominance i.e. in luteal phase/later half of menstrual cycle.
<b>Superficial cells</b>	Which are predominate when there is estrogen predominance i.e. in follicular phase first half of menstrual cycle. Vaginal cytology gives a fair idea about the hormonal status and in turn about ovulation/ ovarian cycle.

**Cervical changes**

Cyclical changes occur in the cervix in response to the changes in estrogen and progesterone.

Under the influence of estrogen cervical mucus is thin, profuse, watery, more alkaline, promoting the ascent of sperms. The cervical mucus is thinnest at the time of ovulation and its elasticity increases (spinnbarkeit)

Progesterone makes cervical mucus scanty, thick, viscous and it loses its stretching ability (Tack). So cervical changes also correspond to the ovarian cycle.

## Hormones – Estrogen/Progesterone

13. **Ans. is a, b and c, i.e. Estrone, Estradiol and Estriol**

Ref. Shaw 15<sup>th</sup>/ed p 42; Jeffcoate 7<sup>th</sup>/ed pp 67; KDT 6<sup>th</sup>/ed p 297

### Estrogens :

- Natural estrogens are C18 steroids
- Main Source – Theca and granulosa cells of graafian follicle and corpus luteum.
- Secondary source – Adrenal cortex

### Naturally occurring estrogen

*Estradiol – Main estrogen during reproductive years.*

*Esterone (Produced by peripheral aromatization of androstenedione) – Main estrogen after menopause*

*Estriol (main source is placenta) – Main estrogen during pregnancy. It is a marker of fetomaternal-placental well being.*

14. **Ans. is b, i.e. Estradiol**

Ref. Shaw 15<sup>th</sup>/ed pp 42-43,216

15. **Ans is a, i.e. Estrogen**

Estrogen is responsible for the secretion of cervical mucus and progesterone is responsible for making it thick and viscid. Under the influence of estrogen cervical mucus is copious, watery elastic (can be stretched) and when dried it shows a characteristic fern pattern. Under the influence of progesterone cervical mucus is thick, scaly, loses its stretchability and an drying doesnot show fern like pattern.

In Q 14

- Now we have to choose between option b and c as both estradiol and estriol are derivatives of estrogen.
- I have mentioned earlier that estradiol is the more potent form of estrogen, in fact it is the most potent estrogen and estriol the least. So obviously estradiol will be responsible for most of the physiological action of estrogen and is therefore the option of choice.

16. **Ans. is a, i.e MDPA**

Ref. KDT 6<sup>th</sup>/ed p 307

In the question, the infertile woman's endometrial biopsy shows proliferative changes. Endometrial biopsy for infertility is taken on D 25 of cycle with the aim to rule out anovulation. Normally on these days, endometrial biopsy should show secretory changes (as ovulation occurs on D-14 and subsequently there is an increase in progesterone levels in body). But in case of anovulation, endometrial biopsy shows proliferative changes.

The hormone which should be administered here is obviously progesterone, but that derivative of progesterone which has a weak antioovulatory effect so that it would not further inhibit ovulation.

### Synthetic progesterones :

Progesterone derivatives	19 Nortestosterone derivatives
have weak antioovulatory actions. except chlormadinone acetate e.g. : MDPA, Megestrol, Dydrogesterone, Hydroxy progesterone caproate, Nomegestrol	Have strong antioovulatory actions e.g. Desogestrel, Norgestimate, Gestodene, Norethindrone, Norethisterone Norgesterel

So, according to this our answer is Medroxy Progesterone Acetate (MDPA).

Besides the above reasoning – another reason for using medroxy progesterone acetate is that it can be given intramuscularly.

*"In treatment of LPD (Luteal phase defect) – Intramuscular progesterone in oil produces higher plasma concentration, which sustained for longer period. Hence the intramuscular route of progesterone administration is considered the "gold standard." – Advanced infertility management by Mehroohansotia*

Since, medroxy progesterone acetate can be given intramuscularly so it is the preferred agent.

17. **Ans. is c, i.e. Pregnanediol**

Ref. Dutta Gyane 6<sup>th</sup>/ed p 75

See the text for explanation.

## Clomiphene

18. **Ans. is c, i.e. Antiestrogen**

Ref. Shaw 15<sup>th</sup>/ed p 314

Clomiphene is an antiestrogen.

Category	Drug
Antiestrogen/SERM	Clomiphene, Tamoxifen
Antiprogestrone	Mifepristone
Testosterone (Androgen derivative)	Danazol, Gestrinone
Antiandrogen	Cyproterone acetate, Spironolactone, Flutamide, Finasteride

19. Ans. is a, i.e. Stein-leventhal Syndrome

Ref. Shaw 15<sup>th</sup>/ed p 314

20. Ans. is a, b and c, i.e. All are correct options

Ref. Shaw 15<sup>th</sup>/ed p 314

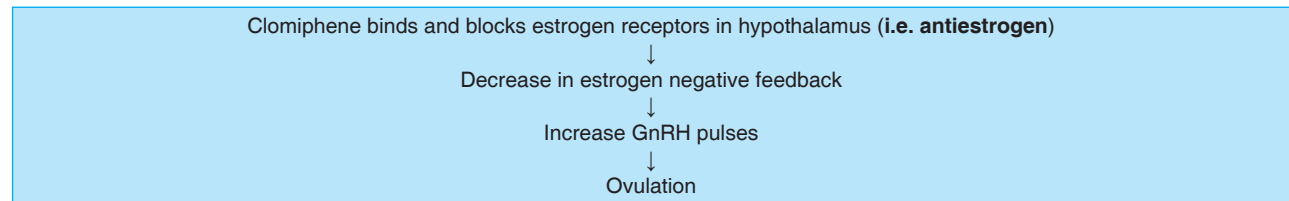
21. Ans is a, i.e. Enclomiphene has antiestrogenic effect.

Ref. Novak 15<sup>th</sup>/ed pp 1153-1154; Shaw 15<sup>th</sup>/ed p 314; Jeffcoates 7<sup>th</sup>/ed pp 104-105;  
Ref. Leon speroff 8<sup>th</sup>/ed, pp 1294-1295,1281

Lets quickly revise –

#### Clomiphene citrate :

- Clomiphene citrate is the first line intervention for medical induction of ovulation in almost all circumstances, clomiphene acts purely as an antagonist or antiestrogen.



Thus clomiphene is used for anovulation and is the DOC for PCOD patients.

Clomiphene is a racemic mixture of zuclomiphene enclomiphene. Hence, all actions of clomiphene will be the actions of both these isomers.

#### Indications :

- Anovulatory infertility in case of PCOS (Stein-Leventhal syndrome), Chiari frommel syndrome.
- Amenorrhea and anovulation following the use of OCP's (Post pill amenorrhea).
- In vitro fertilization, GIFT technique and Assisted Reproduction Technique.

*"It is the usual first choice for ovulation induction in most patients because of relative safety, efficacy, route of administration and relative low cost".*

– Novak 14<sup>th</sup>/ed p 64

**Results :** 80–85% treated women ovulate and 40-50% conceive after the use of Clomiphene.

Novak 14<sup>th</sup>/ed p 1064; Shaw 14<sup>th</sup>/ed p 284

#### Side effects :

##### Clomiphene and multiple pregnancy

*"Multiple ovulation and multiple pregnancy in (case of clomiphene) is 10%" .... Shaw 15<sup>th</sup>/ed p 314.*

*"Multi follicular development is relatively common and the overall risk of multiple pregnancy is increased approximately 7-10%"*

– Leon speroff 8<sup>th</sup>/ed p 1302

Novak 14<sup>th</sup>/ed, p 1064 says – *"Incidence of multiple pregnancies ranges from 6.25 to 12.3%."*

Jeffcoates 7<sup>th</sup>/ed, p 105 says –

*"Pregnancy occurs in 40 - 50% of women following treatment and even though the dosage is carefully monitored, 5-10% of the conceptions are multiple."*

Clomiphene for the management of oligospermia in males with idiopathic male infertility.

– Leon speroff 8<sup>th</sup>/ed p 1281

- Most infertile men are eugonadotropic, normally virilized, and otherwise normal, but have low sperm density. Empiric treatment with either clomiphene citrate or tamoxifen is commonly offered to stimulate increased pituitary gonadotropin secretion and spermatogenesis in men with idiopathic subfertility. Whereas treatment appears to benefit some men, there is no reliable method for identifying those who might respond. Overall antiestrogenic treatment is not effective.

*"A randomized clinical trial conducted by WHO involving nearly 200 men and over 1300 couple months of observation found no differences among men treated with clomiphene or placebo. Moreover a meta analysis including 10 randomized trials involving over 700 men concluded that evidence is inefficient to indicate that anti estrogen treatment improves semen quality or male fertility."*

– Leon speroff 8<sup>th</sup>/ed p 1281

From the above lines it is clear - It has shown to increase fertility in oligospermic males in randomized controlled trials is incorrect.

22. Ans. is d, i.e. Teratogenic effect on offsprings

Ref. Jeffcoates 7<sup>th</sup>/ed p 105; Leon Speroff 7<sup>th</sup>/ed p 1182

**Side effects of clomiphene:**

Ref. Textbook Gynecology Show 4<sup>th</sup>/ed p 281

- Increased risk of multiple pregnancy
- Hot flushes
- Nausea, vomiting
- Headache
- Visual disturbances like scotoma
- Ovarian hyperstimulation syndrome

- Increase chances of enlargement, pain, cystic changes, haemorrhage and multiple ovulation in the ovaries.
- Increase risk of ovarian cancer
- Increase rate of abortion
- Alopecia (rare) and galactorrhoea (rare).

*"There is no substantial evidence that clomiphene treatment increases the overall risk of birth defects or any one anomaly in particular"*

— Leon Speroff 7<sup>th</sup>/ed, p 1182

*There is no evidence to indicate that cc treatment is associated with a higher incidence of congenital abnormalities*

## GnRH

23. **Ans. is d, i.e. Hyperstimulation syndrome**

Read the text for explanation.

24. **Ans. is b, i.e. Endometrial Ca**

Ref. Jeffcoate 7<sup>th</sup>/ed p 652

25. **Ans. is b, i.e. Hyperprolactinemia**

Ref. Shaw 15<sup>th</sup>/ed pp 319-320,653

Read the text for explanation.

## Danazol

26. **Ans. is a, i.e. Cyclical mastalgia**

Ref. Shaw 15<sup>th</sup>/ed p 313; KDT 5<sup>th</sup>/ed p 271

27. **Ans. is a, i.e. Hirsutism**

Ref. Shaw 15<sup>th</sup>/ed p 313

Read the text for explanation.

## Mifepristone

28. **Ans. is a, b, c and e, i.e. Also called RU – 486; It is a 19 Norsteroid; Acts on receptors; Used for menstrual regulation**

Ref. Shaw 15<sup>th</sup>/ed pp 237,246,317

RU 486 (Mifepristone) is a 19 Norsteroid synthetic derivative of progesterone. It has affinity for progesterone receptors and therefore blocks its actions.

**Route of administration :** Oral

**Uses :**

- As post coital pill (600 mg given within 72 hours of unprotected sex).
- To induce abortion upto 7 weeks of amenorrhea along with misoprostol (medical abortion).
- Ripening of cervix prior to prostaglandin induction of mid trimester abortion.
- Management of ectopic pregnancy.
- Cushing's syndrome : because of its antiglucocorticoid action.
- Medical management of uterine fibroid.

**Side effects :**

- Headache
- GI upset
- Adrenal failure
- Teratogenicity (If medical methods of abortion fails with RU – 486, pregnancy should be terminated any how).

## Inhibin/Relaxin

29. **Ans. is c, i.e. Stimulates FSH secretion**

Ref. Shaw 15<sup>th</sup>/ed p 45; Dutta Gynae 5<sup>th</sup>/ed p 72; Leon Speroff 7<sup>th</sup>/ed p 197, 8<sup>th</sup>/ed pp 212,213,172

**Inhibin:**

- Inhibin is a non-steroidal water soluble protein.<sup>Q</sup>
- It is secreted by Graffian follicle.<sup>Q</sup>
- It is of two types - Inhibin A and B. In the early and midfollicular phase Inhibin B is the predominant form secreted whereas Inhibin A begins to rise in late follicular phase to reach a peak in mid luteal phase.

Inhibin suppresses FSH secretion and not LH

- In PCOS inhibin secretion increases.<sup>Q</sup>

30. **Ans. is a, i.e. Ovary**

Ref. Clinical Gynecology Endocrinology and Infertility by Leon Speroff 7<sup>th</sup>/ed pp 284-285, 8<sup>th</sup>/ed p 299; Shaw 15<sup>th</sup>/ed p 45

- Relaxin is a peptide hormone.<sup>Q</sup> It is produced by the ovary<sup>Q</sup> to be specific by the corpus luteum of pregnancy<sup>Q</sup> If corpus luteum is in options, it should be the answer of choice. It has also been identified in :
  - placenta<sup>Q</sup>
  - decidua<sup>Q</sup>
  - chorion<sup>Q</sup>
- It is not detected in men<sup>Q</sup> and non pregnant women.<sup>Q</sup>
- Levels of Relaxin rise during 1st trimester when corpus luteum is dominant and declines in the second trimester. This suggests a role in maintaining early pregnancy.<sup>Q</sup>
- In animals, relaxin softens the cervix, inhibits uterine contractions and relaxes pubic symphysis.<sup>Q</sup>
- It has no effect on prolactin secretion but enhances growth hormone secretion by the pituitary.<sup>Q</sup>

31. **Ans. is d, i.e. Elevated and static level of estradiol is essential for ovulation** *Ref. Dutta Gynae 6<sup>th</sup>/ed p 84–87*

“The cohort of the growing follicles undergoes a process of development and differentiation which takes about 85 days and is spread over 3 ovarian cycles.

It is not clear as to how many and which of the primordial follicles amidst several thousands are recruited for a particular cycle. It is presumed that about 20 antral follicles (about 5–10 per ovary) proceed to develop in each cycle.

The initial recruitment and growth of primordial follicles are not under the control of any hormone. After a certain stage (2–5 mm in size) the growth and differentiation of primordial follicles are under the control of FSH. **Unless the follicles are rescued by FSH at this stage, they undergo atresia**”. Dutta gynae 6/e p 84-87

Thus it is clear option a and c both are correct.

**Remember:** For initial 60 days: Follicles are gonadotropin resistant and for later 20 days they are gonadotropin sensitive

#### Role of AMH (anti mullerian hormone)

AMH inhibits initial recruitment of primordial follicles into the pool of growing follicles. It also decreases responsiveness of follicles to FSH. AMH plays an important role for monofollicular development and ovulation.

#### The probable mechanisms for monofollicular development and ovulation

1. All the primordial follicles that reach the preantral stage, produce AMH.
2. AMH inhibits further growth of primordial follicles by decreasing the responsiveness of follicles to FSH.
3. The growth of dominant follicle is uninhibited as the dominant follicle has maximum number of FSH receptors, and it produces less AMH.

Coming to option 'd'

As discussed in the preceding text:

The basic prerequisite in ovulatory cycle is fluctuating levels of E<sub>2</sub>. If for any reason the E<sub>2</sub> levels become static, anovulation is a rule (as in PCOS). Thus option d is incorrect.

32. **Ans. is b, i.e. In the first half of the cycle, it has no steroidogenic function** *Ref. Dutta Gynae 6<sup>th</sup>/ed p 85*

As discussed in the text; primordial follicle has granulosa cells and theca cells.

In the Dominant follicle, there is marked enlargement of granulosa cells with lipid inclusion under the influence of FSH and estrogen. (i.e. option d is correct)

Granulosa cells produce estrogen and inhibin B in the first half of the menstrual cycle. (So option b is incorrect). The granulosa cells do not have a blood supply. The granulosa cells layer become vascularised only after ovulation with the formation of corpus luteum. *Ref. Shiela Balakrishnan TB of Gynae 1<sup>st</sup>/ed p 35*

33. **Ans. is d, i.e. the peak steroid production is between 23–25th day.** *Ref. Dutta Gynae 6<sup>th</sup>/ed p 72, 73*

**In corpus luteum:** The granulosa cells whose basic role in the follicular phase was aromatisation of androgens to estrogens, undergo a change in role and become predominantly progesterone synthesising cells (option a correct). Although they continue to aromatase estrogen produced by theca cells.

The theca cells continue to produce androgens which are peripherally converted to become estrogen (option b is correct).

The size of and activity of corpus luteum reaches peak by 7th–8th day post ovulation (i.e. 14 + 8 = 22nd Day of menstrual cycle), this also correlates with peak luteal phase estrogen and progesterone (i.e. option d is in correct it should 20–22 days and not 23–25th day).

Corpus luteum has a life span of 12–14 days, on day 22–23 of cycle, regression begins. The cause of degeneration is prostaglandin F<sub>2α</sub>, estrogen and endothelin.

34. **Ans. is b i.e. Aromatase** *Ref. Dutta Gynae 6<sup>th</sup>/ed p 72*

Estrogen produced by theca cells is converted to androgens in granulosa cells with the help of enzyme aromatase.

35. **Ans. is c, i.e. 15 ng/ml** *Ref. Dutta Gynae 6<sup>th</sup>/ed p 75*

“Serum value of progesterone is less than 1ng/ml in follicular phase and 5–15 ng/ml mid luteal phase.”

*Dutta Gynae 6<sup>th</sup>/ed p 75*

Daily production, serum values and urinary excretion of hormones

Hormones	Follicular phase	At ovulation	Luteal phase
<i>Daily production</i>			
Estradiol (µg)	50	150–300	100
Progesterone (mg)	2–3		20–30
<i>Serum values</i>			
Estradiol (pg/mL)	50	300–600	150–200
Progesterone (ng/mL)	< 1		> 5
FSH (mIU/mL)	10	15–20	10
LH (mIU/mL)	5	60	5
<i>Daily excretion</i>			
Total estrogen (µg)	10–25	35–100	25–75
Pregnanediol (mg)	< 1		3–6

## 36. Ans. is b, i.e. Basal vacuolation

Ref. Leon speroff 7<sup>th</sup>/ed pp 120,190; Dutta Gynae 6<sup>th</sup>/ed p 91

Endometrial biopsy was used in the past to find out whether the female has ovulated or not. Nowadays USG follicular monitoring is being done

**Subnuclear basal vacuolation** is characterized by glandular growth and presence of vacuoles due to secretion of glycogen between nuclei and basement membrane. It is due to the effect of progesterone. **Basal vacuolization is the earliest evidence of ovulation (36–48 hours after ovulation) and persists until about 21<sup>st</sup> day of the cycle.**

Pseudostratification of nuclei is characteristic of proliferation phase but persists until active progesterone secretion begins. Hence, it is noted until 18<sup>th</sup> – 19<sup>th</sup> day of the menstrual cycle.

Predecidual reaction is first evident on day 23 of the menstrual cycle.

## 37. Ans. is b, i.e. Hyperstimulation syndrome Ref. Shaw 15/e p 315

Ref. Shaw 4/e d p 315

Ovarian hyperstimulation syndrome is the most dreaded complication of Clomiphene (discussed in detail in chapter 9 on infertility).

## 38. Ans. is d, i.e. Corpus luteum

Read the preceding text for explanation.

## 39. Ans. is d, i.e. Visual symptoms:-

**Remember:- for clomiphene**

- M/C side effect of clomiphene- Menopausal symptom
  - Ovarian cyst formation
- Side effect for which its use - Should be immediately stopped - visual symptoms
- Most dreaded side effect - OHSS
- Chances of OHSS = <1%
- Chances of multiple pregnancy - <10% (6–8%)
- Maximum dose = 100 mg
- Maximum duration of use = 12 months.

## 40. Ans. is b, i.e. Based found parabasal cells

## 41. Ans. is d, i.e. Endocrine status of cervix.

## 42. Ans. is c, i.e. Lateral wall of vagina

Ref: Dutta Gynae 5<sup>th</sup>/ed p 110

Read the text for explanation.

## 43. Ans. is b, i.e. Estrogenic effect

Ref. Taber's Dictionary 19<sup>th</sup>/ed p 714

**Estrous:** It is cyclical period of sexual activity in non human female mammals, marked by congestion of and secretion by the uterine mucosa, proliferation of vaginal epithelium, swelling of the vulva, ovulation, and acceptance of the male by the female. During estrus, the animal is said to be "in heat".

**Also Know:**

**Estrus cycle** - The sequence from the beginning of one estrus period to the beginning of the next.

- It includes :
- Proestrus
  - Estrus
  - Metestrus followed by
  - Diestrus (period of quiescence).

# CHAPTER

# 3

## Menopause and HRT



### Menopause is-

Permanent cessation of menses dated by the last menstrual period followed by 12 months of amenorrhea

### Perimenopause

Period of time surrounding menopause (2-8 years preceding + 1 year after last menses) characterized by fluctuating hormone levels irregular menstrual cycle and symptom asset



### Diagnostic criteria of menopause-

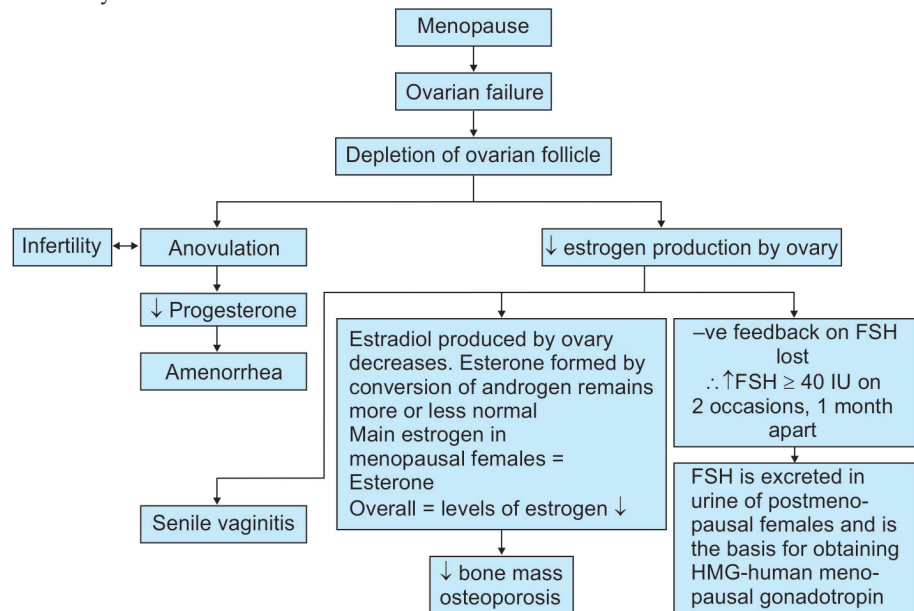
- Cessation of menstruation
- Appearance of menopausal symptoms 'hot flushes'
- Vaginal cytology 100/0/0
- Serum estradiol <20 pg/mL
- Serum FSH and LH >40 mIU/mL



It is the hormone which initiates ovarian cycle

- In menopausal females- Since primordial follicles are decreased so levels of estrogen is decreased, so negative feedback on FSH is decreased, hence levels of FSH are increased
- Human menopausal gonadotropin (hmg)- is FSH and LH obtained from the urine of postmenopausal females
- FSH levels can help in differentiating the causes of male infertility viz. In pretesticular cause of male infertility = FSH ↓  
In testicular cause = FSH ↑  
In post testicular cause = FSH is normal
- Best test for ovarian reserve = FSH

The average age of menopause is 51 years with a normal range of 43-57 years. In India = 47 years.



### Menopausal Symptoms and Treatment

Menopausal symptom	Description	Treatment
<b>Vasomotor symptoms:</b> Hot flushes, night sweat M/C symptom of menopause	Hot flushes are the <b>hallmark of menopause</b> . It is a recurrent transient period of flushing, sweating, and a sensation of heat often accompanied by palpitations, anxiety, sometimes followed by chills. The episodes last for 1-3 minutes & recur 5-10 times/day Cause: Estrogen withdrawal. Coincides with LH surge	<b>Hormone therapy</b> <ul style="list-style-type: none"> <li>• Estrogen therapy<sup>o</sup> (<i>most effective</i>). It should be given as a short-term therapy in minimum possible doses to women whose uterus is removed.</li> <li>• Combined estrogen and progestin therapy<sup>o</sup> is uterus is intact</li> <li>• Progestin therapy<sup>o</sup> (to be given in those women in whom estrogen is contraindicated)</li> <li>• Tibolone<sup>o</sup> (it is STEAR-selective tissue estrogen activity regulator, which has estrogenic, progestogenic, and androgenic properties)</li> </ul> <b>Non-hormonal prescription medicines: (not approved by FDA)</b> <ul style="list-style-type: none"> <li>• Clonidine<sup>o</sup></li> <li>• Selective serotonin reuptake inhibitor: <i>paroxetine, fluoxetine</i></li> <li>• Serotonin and nor epinephrine<sup>o</sup> reuptake inhibitor: <i>venlafaxine<sup>o</sup></i></li> </ul>

Contd...



Contd...

Menopausal symptom	Description	Treatment
		<ul style="list-style-type: none"> <li>Dopamine antagonist : <i>Verapride</i><sup>o</sup></li> <li><i>Gabapentin</i><sup>o</sup></li> <li>Bellergal (combination of ergotamines, phenobarbital and belladonna, approved for the treatment of migraine).<sup>o</sup></li> <li>Mirtazapine</li> <li>Trazodone</li> </ul>
		<b>Non-prescription medicines :</b> <ul style="list-style-type: none"> <li>Isoflavones (100 mg/day)<sup>o</sup></li> <li>Soy products (60 g/d)<sup>o</sup></li> <li>Vitamin E (800 IU/day)<sup>o</sup></li> </ul>
Osteoporosis	<ul style="list-style-type: none"> <li>It is the single most important health hazard associated with menopause</li> <li>Osteoporosis is loss of bone strength resulting in an increased risk of fracture</li> <li>Diagnosis is made by determining bone mineral density (BMD) by dual energy X-ray absorptio metry (DEXA)</li> <li>BMD is best measured at hip is predictive of hip fracture and fracture at other sites</li> </ul> <p>M/c sites of fracture in osteoporotic women</p> <ul style="list-style-type: none"> <li>Lumbar vertebrae</li> <li>Wrist (distal radius)</li> <li>Hip (femoral neck)</li> </ul>	<b>Hormone therapy</b> <ul style="list-style-type: none"> <li>Combined estrogen &amp; progestin therapy (if uterus is intact)</li> <li>Only estrogen (if female is hysterectomised)</li> <li>Tibolone (STEAR)</li> <li>Raloxifene (SERM)</li> </ul> <b>Non hormonal</b> <ul style="list-style-type: none"> <li><b>Bisphosphonates like Alendronates risedronate. It is the first line of treatment for osteoporosis</b></li> <li>Calcium</li> <li>Calcitonin</li> <li>Vitamin D</li> <li>Slow releasing sodium fluoride</li> </ul>
Senile vaginitis	Dry vagina due to decreased estrogen	Topical estrogen application



85% of women experience hot flushes

- Norepinephrine & serotonin are the neurotransmitters which trigger hot flushes
- Main indication for prescribing HRT: is Hot flushes

## Osteoporosis

Prevention	Treatment
<ul style="list-style-type: none"> <li>Calcium 1200 mg/day</li> <li>Vitamin D, 800-1000 IU/day</li> <li>Regular weight bearing, muscle strengthening exercise</li> <li>Smoking cessation</li> <li>Moderate alcohol consumption</li> </ul>	<p>Treatment is given to all women <math>\geq 50</math> years old with any of the following:</p> <ul style="list-style-type: none"> <li>Vertebral or hip fracture</li> <li>T score <math>\leq -2.5</math> at the femoral neck or spine</li> <li>T score between <math>-1.0</math> and <math>-2.5</math> at the femoral neck or spine &amp; 10-year hip fracture risk <math>\geq 3\%</math></li> <li>Ten-year major osteoporosis related fracture probability <math>\geq 20\%</math></li> </ul>

- Screening for osteoporosis should be offered to any postmenopausal patient who presents with a fracture.
- Other candidates for bone mineral density determination are women older than age of 65.



**T scores:** Deviation above or below the comparison mean BMD\* of women aged 20-29 yrs.

**Z scores:** It corresponds to the same measurements using women of same age as the reference

**Normal bone T scores:**  $> -1.0$   
 Osteopenia – T scores between  $-1$  and  $-2.5$   
 Osteoporosis – T scores at or below  $-2.5$

When bone mass decrease by one standard deviation, the risk of fracture doubles

\*BMD = Bone mineral density

- The US Preventive Services Task Force recommends screening at the age of 60 for women who have risk factors for osteoporosis.
- The strongest risk factors for osteoporosis are –
  - low body weight (< 70 kg or BMI < 21)
  - older age
  - women not taking estrogen

## Drugs Useful for the Treatment of Osteoporosis

### Bisphosphonates

- These agents are used for the treatment of osteoporosis due to their *inhibitory effect on osteoclast mediated bone resorption*. These drugs accelerate apoptosis of osteoclasts and also suppress differentiation of osteoclast precursors to mature osteoclasts (by inhibiting IL-6).
- Drugs in the group include **first generation** agents (least potent) like *medronate, clodronate and etidronate*, **second generation** drugs like **alendronate, ibandronate and pamidronate** and **third generation compounds like risedronate and zoledronate (most potent)**.
- Bisphosphonates – they are the first line treatment for osteoporosis.
- Bisphosphonates – side effects are heart burn, esophageal irritation, esophagitis, and diarrhea.
- Patient should take each dose after an overnight fast, while sitting in the upright position and should follow by drinking a glass of water and should remain upright and not eat for 30 minutes after administration.
- Main contraindications of bisphosphonates are renal dysfunction, esophageal motility disorders and peptic ulcer.
- **Zoledronate** infusion of 5 mg **once yearly** has been approved for treatment of osteoporosis.
- Bisphosphonates are the first line drugs used for management of osteoporosis.



Distinctive toxicity of bisphosphonates is **esophageal irritation** that can lead to ulceration as well

### Raloxifene

#### ALSO KNOW

- Raloxifene is a *Selective Estrogen Receptor Modulator (SERM)*<sup>Q</sup>.
- SERM are compounds that act as both estrogen agonist and antagonists depending on the tissue.
- Raloxifene exercises estrogen-like action on both bones and lipids and estrogen antagonist on breast or endometrium.
- R reduces the risk of fracture by 50%, specially in vertebra by increasing bone mineral density by 2–3%.
- It causes 10% reduction in total and low density lipoprotein and raises HDL.
- It does not raise the level of triglycerides.
- Cardioprotective in long term.
- It does not have a proliferative effect on endometrium, so raloxifene is not associated with an increase in the risk of uterine cancer.



Hot flushes are a side effect of raloxifene therapy, hence raloxifene cannot be used to treat it.

### Side Effects

Hot flushes (so it cannot be used in managing hot flushes), cramps, increased incidence of retinopathy, and venous thrombosis.<sup>Q</sup>

### Contraindications

- Venous thrombosis
- It should not be given with estrogen

- Hepatic dysfunction
- Stop the drug 72 hours before surgery
- Not to be given with drugs such as indomethacin, naproxen, ibuprofen, and diazepam.

### Teriparatide

- It is **recombinant PTH**. It has been noted that PTH in low and pulsatile dose stimulates bone formation whereas in excess it causes resorption of bones.
- Teriparatide and strontium ranelate can stimulate osteoblast whereas most other agents used for osteoporosis act by inhibiting osteoclast.

### Denosumab

- Osteoclasts express a receptor called **receptor for activated nuclear factor k B (RANK)** on its surface. When this receptor is stimulated by RANK ligand, bone resorption results due to activation of osteoclasts. Denosumab is monoclonal antibody against this ligand and is useful for the treatment of osteoporosis.

### Strontium Ranelate

- It has a novel mechanism of action as it inhibits bone resorption as well as stimulates bone formation. Strontium is incorporated into hydroxyapatite, replacium. Small increased risk of venous thrombosis, seizures are abnormal cognition have been seen with them.



Strontium ranelate inhibits bone resorption as well as stimulates bone formation.

## Hormone Replacement Therapy (HRT)

### Components

#### Estrogen

- Oral or transdermal
- Transdermal preferred for women with hypertriglyceridemia or impaired hepatic function
- Given alone in women who have undergone hysterectomy

#### Progestin

- Given in conjunction with estrogen for women with an intact uterus to decrease the risk of endometrial cancer.



### Indications of HRT:

- Relief of menopausal symptoms
- Prevention of osteoporosis
- To maintain quality of life in menopausal females.

### Side Effects of HRT

- Abnormal uterine bleeding
- Mastodynia
- Edema, bloating, heartburn, and nausea
- Mood changes (due to progesterone component)



Risk of coronary heart disease does not decrease by giving HRT but rather risk increases after giving HRT.

### Women's Health Initiative (WHI)

- The study investigated health risks and benefits of hormone therapy in healthy postmenopausal women aged 50–79 old.
- In the study
  - Continuous combined HRT (CEE 0.625 mg + MPA 2.5 mg OD) was given to 16,608 women with an intact uterus
    - » Originally designed to run for 8.5 years but stopped early after 5.2 years (July 2002) because the evidence for harm (breast cancer, CHD, stroke, pulmonary embolism) outweighed benefit (fracture reduction and colon cancer reduction)



### Special groups of woman who require HRT:

- Premature ovarian failure
- Gonadal dysgenesis
- Surgical or radiation menopause



Coronary artery disease (CAD/CHD) is the leading cause of death among post-menopausal women.



#### Absolute contraindications to HRT – ABCD

A = **A**cute liver disease or current gallbladder disease  
 B = Undiagnosed vaginal **B**leeding  
 C = **C**ancer (breast/uterine)  
 D = **D**VT (thrombo-embolic disease) or its history



DOC to treat decreased libido in menopausal females is testosterone/androgens.

- Estrogen-alone (CEE 0.625 mg) was given to 10,739 women with a previous hysterectomy
  - » This arm was also stopped early (February 2004 instead of March 2005) because of increased stroke risk and no heart disease benefit. The women taking only estrogen did not show an increased risk of breast cancer.

### Potential Benefits and Harms of HRT *Harrison 18<sup>th</sup>/ed p 259*

Benefits	Uncertain risks	Definite risk
<ul style="list-style-type: none"> <li>• Hip fracture</li> <li>• Wrist fracture</li> <li>• Vertebral fracture (i.e. osteoporosis)</li> <li>• Symptoms of menopause</li> </ul>	<ul style="list-style-type: none"> <li>• Thromboembolic events (use of <i>E+P not with E alone</i>)</li> <li>• Dementia</li> <li>• Endometrial cancer (use of <i>E alone</i>)</li> </ul>	<ul style="list-style-type: none"> <li>• Coronary heart disease<sup>o</sup></li> <li>• Breast cancer (use of <i>E+P not with E alone</i>)</li> <li>• Stroke<sup>o</sup></li> <li>• Ovarian cancer (E+P)</li> <li>• Cholecystitis</li> </ul>
<b>Uncertain benefits</b> <ul style="list-style-type: none"> <li>• colorectal cancer</li> <li>• diabetes mellitus</li> </ul>		

#### LAST MINUTE REVISION

- Increase in FSH is the *sine quio non* for menopause
- M/c symptoms of menopause – Hot flushes
- DOC for hot flushes – Estrogen (oral/transdermal) in lowest possible doses for shortest possible time
- If uterus of female is intact, give estrogen + progesterone
- Side effect of raloxifene is hot flushes. Raloxifene cannot be used to treat hot flushes.
- Most important health hazard associated with menopause = Osteoporosis.
- First line of management of osteoporosis – Bisphosphonates females.
- DOC for senile vaginitis – Estrogen cream
- DOC for decreased libido in postmenopausal females – Testosterone
- Coronary artery disease is the main cause of death in postmenopausal females. HRT does not decrease its incidence.
- **Premature menopause:** If menopause occurs at or below the age of 40, it is premature menopause.
- **Delayed menopause:** If menopause fails to occur even beyond 55 years, it is called delayed menopause.

## QUESTIONS

1. HRT is helpful in all of the following except:  
(AIIMS Nov 06, AIIMS May 2013)
  - a. Vaginal atrophy
  - b. Flushing
  - c. Osteoporosis
  - d. Coronary heart disease
2. Hormone replacement therapy (HRT) is indicated in:  
(PGI Nov 2012)
  - a. Cardiovascular disease
  - b. Osteoporosis
  - c. Hot flushes
  - d. Atrophic vaginitis
3. Estrogen replacement for postmenopausal symptoms causes an increase in:  
(AIIMS May 02)
  - a. LDL
  - b. Cholesterol
  - c. VLDL
  - d. Triglycerides
4. Estrogen administration in a menopausal woman increases the:  
(AIIMS May 06)
  - a. Gonadotropin secretion
  - b. LDL - cholesterol
  - c. Bone mass
  - d. Muscle mass
5. True regarding postmenopausal osteoporosis is:  
(PGI May 00)
  - a. Decreased vitamin D
  - b. Decreased serum calcium
  - c. Normal serum chemistries
  - d. Decreased vitamin C
  - e. Amenorrhea
6. Non-hormonal drug to prevent post menopausal osteoporosis is:  
(Delhi 99)
  - a. Alendronate
  - b. Estrogen
  - c. Raloxifene
  - d. Parathyroid
7. All of the following are the advantages of using Raloxifene over estrogen in postmenopausal women except:  
(AI 04)
  - a. Reduces fracture rates
  - b. Avoids endometrial hyperplasia
  - c. Reduces the incidence of venous thrombosis
  - d. No increase in incidence of breast carcinoma
8. A 48-year-old female suffering from severe menorrhagia (DUB) underwent hysterectomy. She wishes to take hormone replacement therapy. Physical examination and breast are normal but X-ray shows osteoporosis. The treatment of choice is:  
(AIIMS May 01)
  - a. Progesterone
  - b. Estrogen and progesterone
  - c. Estrogen
  - d. None
9. Basanti devi, 45 years old women presents with hot flushes after stopping of menstruation. 'Hot Flush' can be relieved by administration of following agents:  
(AI 02)
  - a. Ethinyl estradiol
  - b. Testosterone
  - c. Fluoxymesteron
  - d. Danazol
10. All of the following appear to decrease hot flushes in menopausal women except:  
(AI 05)
  - a. Androgens
  - b. Raloxifene
  - c. Isoflavones
  - d. Tibolone
11. Absolute contraindication of hormone replacement therapy is:  
(AIIMS Dec 98)
  - a. Thrombosis
  - b. Fibrocystic disease
  - c. Fibroadenoma
  - d. Hemorrhage

### NEW PATTERN QUESTION

12. The cut-off point of serum estrogen level for the diagnosis of ovarian failure:
  - a. 10 pg/mL
  - b. 20 pg/mL
  - c. 30 pg/mL
  - d. 40 pg/mL

## ANSWERS

1. **Ans. is d, i.e. Coronary heart disease**

2. **Ans. is b, c and d, i.e. Osteoporosis; Hot flushes; and Atrophic vaginitis**

*Ref. Harsison 16<sup>th</sup>/ed p 30, 18<sup>th</sup>/ed p 3043; Williams Gynae. 1<sup>st</sup>/ed p 494; Jeffcoate 6<sup>th</sup>/ed pp 105-106*

- Friends, *Harrison 16<sup>th</sup>/ed p 30* breaks a popular myth of using HRT for prevention of coronary. Heart disease. Until recently, it was believed that the sex specific effect of gonadal steroids on CVS and lipid metabolism accounted for the different rates of coronary heart disease (CHD) in women as compared to men.
- Estrogen increases HDL and decreases LDL whereas androgens have the opposite effect and this was further supported by the increase in incidence of CHD after menopause.
- These findings led to the widespread use of HRT for primary and secondary prevention of CHD.

But recent trials have shown an increase in the incidence of CHD in women placed on HRT as compared to those not on HRT. – Harrison 16<sup>th</sup>/ed p 30

This fact is supported by *Williams Gynae. 1<sup>st</sup>/ed p 494* which says –

*“In the many reviews and discussions following WHI (Women Health Initiative), most clinicians agree that Hormone Therapy is associated with an increased risk of CHD in older menopausal women and an increased risk of breast cancer, stroke, venous thromboembolism and cholecystitis.”*

*“The WHI randomized controlled trial of combination hormone therapy versus placebo shoed that hormone therapy didnot prevent heart disease in healthy women, but instead it increased the risk of cardiovascular events in older women”* – Novak 15<sup>th</sup>/ed p 1242

3. **Ans. is d, i.e Triglycerides**

*Ref. KDT 6<sup>th</sup>/ed p 299*

**Estrogen causes:**

- ↓ Plasma LDL
- ↓ Cholesterol
- Plasma HDL ↑
- Triglycerides ↑
- There is increased HDL = LDL ratio, this is probably responsible for rarity of atherosclerosis in premenopausal women.
- It also increases blood coagulability by inducing formation of clotting factors
- Estrogen increases lithogenecity of bile.

**Progesterone causes:**

- Plasma LDL ↑
- ↓ HDL

4. **Ans. is c, i.e Bone mass**

*Ref. Harrison 18<sup>th</sup>/ed p 3041; Novak 13<sup>th</sup>/ed p 1124; KDT 6<sup>th</sup>/ed p 298*

Before seeing any reference for the question let's rule out some options.

- Estrogen administration will exert a negative feedback on gonadotropin secretion and decreases gonadotropin secretion rather than increasing it (**Option 'a' ruled out**).

As I have already discussed in previous question, estrogen decreases LDL and not increases it (**ruling out Option 'b'**).

Now we are left with 2 options, Option 'c', i.e. Bone mass and Option 'd', i.e. Muscle mass.

- Estrogen given as hormone replacement therapy is most beneficial in preventing osteoporosis, i.e. it must be increasing bone mass.

So, Option 'c' is correct.

Now have a look what texts have to say :

*“Estrogen helps to maintain bone mass and skeletal integrity thereby protecting against osteoporosis.”*

*– Novak 13<sup>th</sup>/ed p 1124*

*“Estrogen is important in maintaining bone mass primarily by retarding bone resorption.”*

*– KDT 6<sup>th</sup>/ed p 298*

**Effect of estrogen on bones:**

- Estrogen causes increased osteoblastic activity in the bones.
- It is important in **maintaining bone mass** primarily by **retarding bone resorption**. The major action of estrogen is directed at reducing the maturation and activity of osteoclasts, by modifying regulatory cytokine signals from **osteoblasts**.
- The action of estrogen and progesterone result in increased expression of bone matrix proteins such as **osteonectin, osteocalcin, collagen, and alkaline phosphatase**.

5. **Ans. is a, and b, i.e. Decreased vitamin D; and Decreased serum calcium**

*Ref. Gynae for PG's by Bijoy Sree Sen Gupta 2<sup>nd</sup>/ed p 296*

- During perimenopausal and postmenopausal period there is decrease in bone mass called as osteoporosis.
- Main cause of osteoporosis in perimenopausal and postmenopausal period is decreased estrogen.

**Other causes of decreased bone mass are:**

- Decreased calcium absorption
- Decrease in conversion of 25-hydroxy D3 to 1,25-dihydroxy D3, as a result of age-related decrease in hydroxylase activity.

6. **Ans. is a, i.e. Alendronate** Ref. Novak 14<sup>th</sup>/ed p 1130  
*Alenderonate, etidronate, pamidronate, and Ibandronate are bisphosphonates which inhibit bone resorption, and are very effective for both osteoporosis prevention and treatment.*

**Uses:**

- First line drugs for treating postmenopausal osteoporosis
- Paget's disease
- Osteolytic bone metastasis.

**Caution:** Patient should be instructed to take these drugs on an empty stomach with a large glass of water and then to remain upright for atleast 30 minutes as its major side effect is GI upset.

**Route of administration:** Oral or IV infusion

**Now lets have a look at other options:**

- *Raloxifene:* It is a selective estrogen receptor modulator which is also useful in management of osteoporosis but it is a hormonal preparation.
- *Parathyroid hormone:* It is a novel therapy for osteoporosis. Unlike most of the treatments for osteoporosis that inhibit bone resorption, parathyroid hormone stimulates new bone formation. It is given by daily subcutaneous injection.

**Also Know:****Other non-hormonal drugs used for treatment of osteoporosis:**

- Calcium
- Vitamin D
- Calcitonin
- Slow releasing sodium fluoride.

7. **Ans. is c, i.e. Reduces the incidence of venous thrombosis** Ref. Shaw 15<sup>th</sup>/ed p 69  
 Raloxifene increases the incidence of venous thrombosis rather than decreasing it.  
 It does not have a proliferative effect on endometrium, so it is not associated with an increase in the risk of uterine cancer.

**Role of raloxifene in breast cancer.**

*"The SERM tamoxifen is an estrogen antagonist in the breast that is used in the treatment of estrogen-receptor positive breast cancer. Raloxifene also may reduce the risk of breast cancer. Postmenopausal women receiving raloxifene as part of a large osteoporosis treatment trial, experienced a 76% reduction in the risk of invasive breast cancer compared with placebo-treated women."*

– Novak 14<sup>th</sup>/ed p 1333

8. **Ans. is c, i.e. Estrogen** Ref. Jeffcoate 7<sup>th</sup>/ed p 95 onwards; Williams Gynae 1<sup>st</sup>/ed pp 495, 499-500
- The female underwent hysterectomy, i.e. surgical menopause at the age of 48 years and her X-ray shows osteoporosis – hence HRT can be advised.
  - Both estrogen alone or estrogen + progesterone can be used for treating osteoporosis.  
 The choice depends on whether uterus is present or not (i.e. patient is hysterectomised or not).  
 We have already discussed the agents used for treating osteoporosis and as I have mentioned earlier bisphosphonates are the first line of treatment for osteoporosis (Ref: John Hopkin's Manual of Obs and Gynae 4/e,p 513) but it is not given in the options.

*"For women with a uterus, a progestin should be combined with an estrogen, to lower the risk of endometrial cancer."*

– William Gynae 1<sup>st</sup>/ed p 495; According to Jeffcoate 7<sup>th</sup>/ed p 96

*All women who have intact uterus or even those who underwent hysterectomy for endometrial Cancer (Stage I), endometrioid ovarian tumors or endometriosis or those with severe osteoporosis should receive combined estrogen - progesterone therapy or be considered for selective estrogen receptor modulator therapy (SERM therapy).*

In the question the patient has undergone hysterectomy therefore we can use only estrogen.

9. **Ans. is a, i.e. Ethinyl estradiol** Ref. Shaw 15<sup>th</sup>/ed p 67; Novak 14<sup>th</sup>/ed p 1326; Williams Gynae 1<sup>st</sup>/ed p 495  
 10. **Ans. is b, i.e. Raloxifene** Ref. Jeffcoates 7<sup>th</sup>/ed p 98

*Raloxifene is a SERM. It does not decrease hot flushes and leg cramps, rather increases them.*

11. **Ans. is a, i.e. Thrombosis** Ref. Novak 15<sup>th</sup>/ed p 1245; John hopkins manual of obs and gynae 4<sup>th</sup>/ed p 510

**M**

- A = Active liver disease
- B = Undiagnosed vaginal bleeding
- C = Cancers → endometrial/breast
- D = DVT

12. **Ans. is b, i.e. 20 pg/mL** Ref. Dutta Gynae 6<sup>th</sup>/ed pp 57, 65  
 Diagnosis of menopause or ovarian failure is made from classical symptom of hot flush (50%) confirmed by elevated FSH levels to more than 40 IU/mL and serum estradiol < 20 pg/mL.

**Hyperandrogenism:** It is characterised by an abnormally elevated serum concentration of androgen or physical findings consistent with androgen excess. Androgenic hormones in female can stimulate abnormal terminal hair growth i.e. hirsutism.



- M/C cause of hirsutism in a young female is idiopathic
- M/c pathological cause of hirsutism in young female – PCOS
- M/c cause of rapid onset hirsutism in a young female: Testosterone producing tumor.

Hirsutism	Virilization	Hypertrichosis
<ul style="list-style-type: none"> <li>• Excessive growth of androgen dependant sexual hair or male distribution of hair in females.</li> </ul>	<ul style="list-style-type: none"> <li>• It is characterized by more extensive androgen induced changes than hirsutism alone, like acne, increased oily skin, temporal balding, clitoromegaly, deepening of voice, development of male muscular pattern and body habitus with atrophy of breasts.</li> </ul>	<ul style="list-style-type: none"> <li>• Excessive growth of nonsexual hair, i.e. lanugo hair</li> </ul>
<ul style="list-style-type: none"> <li>• Hair are coarse, dark and terminal hair</li> </ul>		<ul style="list-style-type: none"> <li>• Hair are soft and lightly pigmented</li> </ul>

**Major Causes of Hyperandrogenism**

- PCOS
- Late Onset Congenital Adrenal Hyperplasia (CAH)
- Tumors of ovary and adrenal gland
- Cushing’s syndrome
- Idiopathic or drug induced process

**Note:** Hyperprolactinemia can be associated with hyperandrogenism as it is likely that prolactin receptors are located on adrenal glands. When prolactin binds to these adrenal receptors, it stimulates the release of DHEAS.

**Late-Onset or “Nonclassical” Congenital Adrenal Hyperplasia**

- Excess androgen production is a common feature shared by most forms of CAH.
- Unlike typical CAH, symptoms of late-onset CAH are not evident until late childhood or adolescence.
- It is an autosomal recessive disorder with an enzyme defect.
- The most common adrenal enzyme defect is 21-hydroxylase (21-OH) deficiency.

**Diagnosis**

- **Screening test for CAH:** Measure the basal levels of 17-OHP in the morning. Levels of 17-OHP should be >200 ng/dL.
- If levels are > 800 ng/dL. They are virtually diagnostic of CAH.
- **Confirmatory test:** Patients with late-onset hyperplasia have 17-OHP levels >1,500 ng/dL in response to a 250-µg ACTH stimulation challenge.
- Patients should be tested for 21-hydroxylase deficiency (CYP21A2 deficiency) especially when they present with symptoms of hyperandrogenism at a young



- DHEA-S > 700 ng/dL is consistent with abnormal adrenal function.
- 17 alpha hydroxy progesterone Normal range = 100 – 300 ng/dL
  - Prolactin = Normal range is 1 to 20 ng/mL

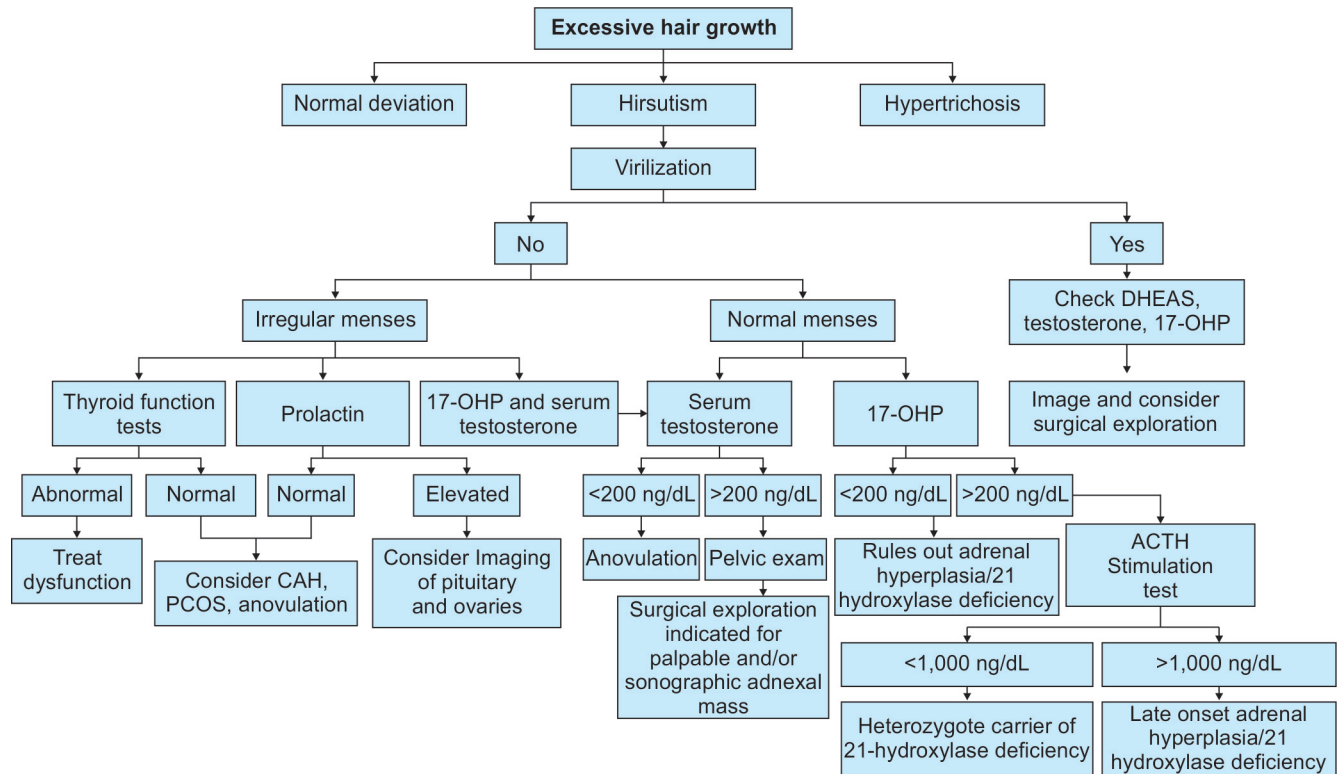


In patients with late onset congenital adrenal hyperplasia :

- No genital ambiguity at birth
- They present with androgen excess at puberty in the form of premature pubarche, acne and hirsutism.



## Algorithm for differential diagnosis of Hirsutism



age or if they have a known family history of CAH. Women of Hispanic or Eastern European Jewish descent should also be tested, as the prevalence of this disorder among these populations is greater than in the general population.

### Treatment

- **Glucocorticoids:** Restore ovulation, by reducing circulating androgen levels.

### Androgen-Producing Ovarian or Adrenal Tumors

- Tumors of the ovary or adrenal gland that secrete androgens are rare.
- The presence of an **androgen-producing tumor** is suspected on the basis of clinical findings.
- Palpation of an adnexal mass in a patient with symptoms of hyperandrogenism or rapid onset of virilization even in the presence of normal testosterone levels should prompt a workup for a pelvic tumor.

### Idiopathic Hirsutism

It is presence of hirsutism in absence of hyperandrogenism, i.e. androgen levels are normal.

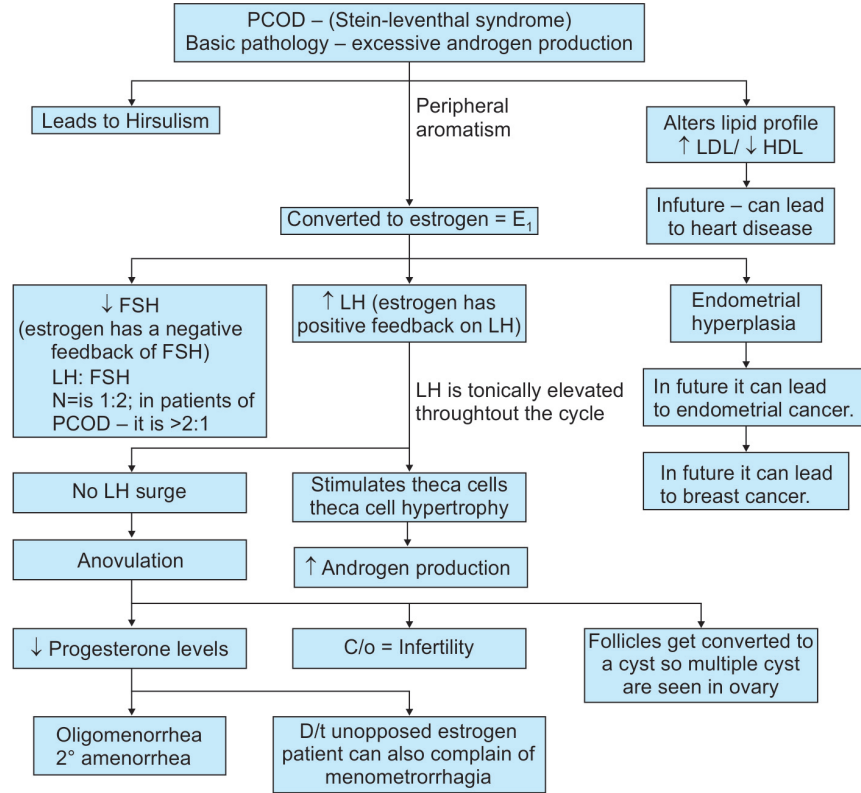
#### In a Nutshell

- 17-OHP - >200 ng/dl may be CAH  
> 800 ng/dl-confirmed CAH
- Testosterone- > 200 ng/dl - ovarian tumor
- DHEAS = > 1000 µg/dl - adrenal tumor

- Testosterone levels exceeding 200 ng/dL and DHEA-S levels > 1,000 µg/dL are concerning for the presence of an ovarian or adrenal androgen-producing tumor.
- TVS identifies almost all solid mass lesions.

## Polycystic Ovary Syndrome (PCOD)

- PCOS/PCOD is a syndrome manifested by amenorrhea hirsutism, obesity and enlarged ovaries.



BMI (kg/m <sup>2</sup> )	Category
< 19	Underweight
19.1-24.9	Normal
25-29.9	Overweight
30-34.9	Obese
> 35	Morbidly obese

Insulin resistance is the hallmark in pathophysiology of PCOS. Increased insulin secretion stimulates increased ovarian androgen production and inhibits serum hepatic SHBG production.

Insulin resistance –

$$\frac{\text{Sr. fasting blood sugar}}{\text{Sr. fasting insulin}} < 4.5$$

Fasting serum insulin – > 25m IU/ml

### Besides this – patients of PCOD/PCOS are:

- Obese–obesity is defined as BMI  $\geq 30$  ng/m<sup>2</sup>
- In PCOS: **Waist to hip ratio** is also measured. Waist measurement is the – smallest circumference between rib cage and iliac crest.
- Hip measurement is the largest circumference between waist and thighs.

Waist: Hip	
$\geq 0.85$	Android obesity
< 0.75	Gynaecoid obesity

- In PCOS patients-there is hyperinsulinemia which is associated with android obesity.
- Insulin resistance also leads to hyperpigmented velvety patches of skin in nape of neck/ axilla/ below breast or thigh called as acanthosis nigricans and in future patients can develop diabetes.

### ➤ HAIRAN Syndrome:

H } Hyperandrogenism  
A }  
I } Insulin resistance  
R }  
A } Acanthosis nigricans  
N }

## In future patients of PCOD can also develop, metabolic X syndrome

### Diagnostic Criteria

**Rotterdam criteria (2003).** Any two of the following three should be present to diagnose a patient with PCOD. *(Novak 15<sup>th</sup>/ed p 1076)*

- Ovulatory dysfunction such as oligomenorrhea or amenorrhea
- Clinical (hirsutism/acne/alopecia) or biochemical evidence of hyperandrogenism i.e. S. testosterone between 70-150 ng/dl (levels >200 indicate testosterone secreting ovarian tumor not PCOS)
- Polycystic ovarian morphology on USG scan defined as presence of 12 or more cysts (2-9mm) in size in any one ovary or both ovaries with enlarged ovaries (>10ml) and other criterias being excluded (like cushing disease, adrenal hyperplasia)

### Hormonal changes in PCOS

Hormones Increased	Hormones Decreased
<ul style="list-style-type: none"> <li>• Androgens<sup>o</sup> (Testosterone, Androstenedione DHEAS)</li> <li>• Luteinizing hormone<sup>o</sup> (LH &gt; 10 IUI ml)</li> <li>• Estrogen (Estrone &gt; Oestradiol)</li> <li>• Total Free Estrogen</li> <li>• Insulin (&gt; 10 m IU / L due to insulin resistance)</li> <li>• Prolactin (in some patients)</li> <li>• LDL/cholesterol and triglycerides</li> </ul>	<ul style="list-style-type: none"> <li>• Follicle stimulating hormone (FSH)</li> <li>• Progesterone (due to anovulation)</li> <li>• Sex hormone binding Globulin</li> <li>• HDL &amp; Apoprotein A-I</li> </ul>

### Management of PCOD

Depends on the complain of the patient

Complaint	Management
Irregular periods	OCP's
Obesity	Life style modifications
Insulin resistance	Metformin (Can be used in pregnancy also)
Hirsutism/ acne	OCP's with cyproterone acetate

### Management of Infertility due to PCOD

- In PCOD – the basic cause of infertility is anovulation
- It is easily reversible and treatable using ovulation inducing drugs
- First advise weight loss (In 5-10% cases-weight loss will cause resumption of ovulation)

#### 1<sup>st</sup> line drugs-SERM'S

- Clomiphene citrate–DOC for ovulation induction in PCOS patients
- Tamoxifen-given to patients who cannot tolerate clomiphene.
- Raloxifene-Not used for ovulation induction

#### 2<sup>nd</sup> line agents

- Gonadotropins:
- LH/FSH injection

#### Insulin Sensitizers

- M/C used drug: Metformin
- Metformin is added when clomiphene citrate is not showing any effect and patient is obese
- It well help the patient to lose weight
- M/C side effect-GI upset
- Most dangerous side effects-Lactic acidosis
- Metformin is safe during pregnancy

### Long term consequences of PCOS/ Anovulation

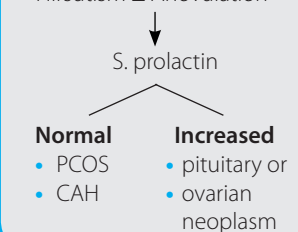
- ↑ risk of cardiovascular disease
- ↑ risk of diabetes (Type 2)
- ↑ risk of endometrial cancer
- ↑ risk of breast Ca
- ↑ use of Ovarian Ca
- ↑ risk of depression & mood disorder
- ↑ risk of metabolic X syndrome.
- ↑ risk of sleep apnea syndrome
- ↑ risk of non-alcoholic steatohepatitis

### Metabolic X syndrome :

Any 3 of following 5 should be present–

- Abdominal obesity (waist circumference > 88 cm or 35 inches)
- Triglyceride > 150 mg/dl
- HDL- cholesterol < 50 mg/dl
- BP > 130/85 mm of hg
- Fasting blood sugar of 110 – 126 mg/dl and 2 hour 140 – 199 mg/dl

### Hirsutism ± Anovulation



**Important concept:**

Q. Can a thin patient have PCOS

Ans. yes (only 30% patients are obese in PCOS pts)

Q. LH/FSH is useful in making a diagnosis

Ans. No

Q. Can ovaries be (space) normal in PLOS

Ans. Yes



Short term consequences of PCOS-

- Hirsutism
- Irregular cycles
- Infertility

**3<sup>rd</sup> line agents: GnRH agonist**

- Luprolide
- Goserelin given in pulsatile manner
- Nafarelin

**Surgery for PCOS**

It is reserved for cases not responding to medical therapy

**Laparoscopic Ovarian Drilling (LOD) or Laparoscopic Electrocoagulation of Ovarian Surface (LEOS)**

- Monopolar current or Laser is passed within the ovary to destroy the ovarian theca when very high doses of gonadotropins are required for ovulation.
- **Advantages:** no risk of Ovarian hyperstimulation syndrome and multiple pregnancy
- **Disadvantages:** if excessive ovarian tissue is damaged, it can lead to premature ovarian failure.

**Hirsutism****Causes of Hirsutism:**

Hirsutism is associated with excess androgen production (either from ovaries or adrenals), so any cause which increases androgens causes hirsutism.

- Most of the testosterone is bound to sex hormone binding globulin (SHBG) and is considered biologically inactive.
- Testosterone which is not bound to SHBG is considered biologically active, therefore any factor which decreases SHBG; cause increase in free testosterone and therefore causes hirsutism.

Factors	
<b>Increase SHBG</b> (Therefore, ↓ free Testosterone) <ul style="list-style-type: none"> <li>• High estrogens like in OCP's</li> <li>• Pregnancy</li> <li>• Liver cirrhosis</li> <li>• Elevated Thyroid Hormone</li> </ul>	<b>Decrease SHBG</b> (Therefore, ↑ free Testosterone) <ul style="list-style-type: none"> <li>• PCOD<sup>o</sup></li> <li>• Adrenal hyperplasia<sup>o</sup></li> <li>• Cushing syndrome<sup>o</sup></li> <li>• Growth hormone<sup>o</sup></li> <li>• Insulin<sup>o</sup></li> <li>• Prolactin<sup>o</sup></li> <li>• ↑ in Androgens itself<sup>o</sup></li> </ul>

Causes of Hirsutism			
<b>Ovary Related</b> <ul style="list-style-type: none"> <li>• PCOD (M/C)<sup>o</sup></li> <li>• Masculinizing tumors of ovary<sup>o</sup></li> <li>• Theca lutein cyst<sup>o</sup></li> <li>• Luteoma of pregnancy<sup>o</sup></li> </ul>	<b>Adrenal Related</b> <ul style="list-style-type: none"> <li>• Congenital adrenal<sup>o</sup> hyperplasia</li> <li>• Adrenal tumor<sup>o</sup></li> <li>• Cushing syndrome<sup>o</sup></li> </ul>	<b>Medications</b>	<b>Others</b> <ul style="list-style-type: none"> <li>• Acromegaly<sup>o</sup></li> <li>• Hyperprolactinemia<sup>o</sup></li> <li>• Hypothyroidism<sup>o</sup></li> </ul>

**Medications that may cause hirsutism and / or hypertrichosis :**

Hirsutism	Hypertrichosis
<ul style="list-style-type: none"> <li>– Anabolic steroids</li> <li>– Danazol</li> <li>– Metoclopramide</li> <li>– Methyl dopa</li> <li>– Phenothiazines</li> <li>– Progestins</li> <li>– Reserpine</li> <li>– Testosterone</li> </ul>	<ul style="list-style-type: none"> <li>– Cyclosporine</li> <li>– Diazoxide</li> <li>– Hydro cortisone</li> <li>– Minoxidil</li> <li>– Pencillamine</li> <li>– Phenytoin</li> <li>– Psoralens</li> <li>– Streptomycin</li> </ul>

### Medical Management of Hirsutism:

Hormone profile	Drugs
Elevated Testosterone (Ovary source)	Combined contraceptives (COCs containing drospirenone or desogestral or cyproterone acetate dianette)
Normal T and DHEA-S 3 $\alpha$ -AG $\uparrow$ (idiopathic)	Anti-androgens
DHEA-S $\uparrow$ , normal T	Dexamethasone

### Galactorrhea

- **Galactorrhea is the secretion of a milky fluid which is inappropriate (unrelated to child birth).** The secretion contains fat globules when examined under microscope and is confirmatory for milk.
  - Prolactin (PRL) is the most important hormone involved in the **pathophysiology of amenorrhea and/or galactorrhea**. Prolactin is under tonic hypothalamic inhibitory control of prolactin inhibitory factor (PIF).
  - Prolactin inhibits GnRH pulse secretion. So gonadotropin levels are suppressed. Hyperprolactinemia inhibits ovarian steroidogenesis. Thus, it results in hypogonadotropic hypogonadism, oligomenorrhea, amenorrhea, anovulation and many other clinical effects of hypoestrogenism.
  - PRL levels should be estimated in all women with galactorrhea, oligomenorrhea or amenorrhea. TSH level should also be measured to rule out primary hypothyroidism.
  - Prolactinoma is present in about 50 percent of women with hyperprolactinemia. Serum prolactin level when raised on repeat assay beyond 20 ng/mL, suggests evaluation of sella turcica. Level beyond 100 ng/mL is associated with high incidence of prolactinoma. Most of the prolactinomas are microadenomas. **About 33 percent of women with high prolactin levels, have galactorrhea.** However, galactorrhea can be seen in women with normal serum prolactin.
  - Bromocriptine was the drug used for galactorrhea. Cabergoline is more effective and well tolerated as compared to bromocriptine and has become the DOC for treating hyperprolactinemia.
- Note:** Pregnancy following bromocriptine has teratogenic effect on the offspring. There is no increased incidence of multiple pregnancy.



In patients presenting with galactorrhea, amenorrhea and visual symptoms or headache always measure prolactin levels to rule out prolactinoma.

## FIGURE BASED QUESTION

**F1.** Figure F1 shows a 22-year female complaining of irregular cycles, weight gain and discoloration of neck. USG revealed multiple cysts in both the ovaries. The metabolic abnormalities which need to be ruled out in this patient are:

- a. Hyper insulinism
- b. Hyper androgenism
- c. Diabetes mellitus
- d. Diabetes insipidus



**Fig. F1**

## QUESTIONS

1. Which of the following statements is incorrect regarding polycystic ovarian disease? (AI 06)
  - a. Elevated LH hormone
  - b. Can cause infertility
  - c. May be associated with abnormal glucose tolerance test
  - d. Results in postdated pregnancy
2. The following hormone is raised in polycystic ovarian syndrome: (AI 06)
  - a. 17 - OH progesterone
  - b. Follicular stimulating hormone
  - c. Luteinizing hormone
  - d. Thyroid stimulating hormone
3. PCOD- Hormonal Status: (PGI Dec 08)
  - a. LH decreased
  - b. LH increased, FSH normal to low
  - c. FSH increased
  - d. 17 OH progesterone normal
  - e. Testosterone increased
4. True about PCOD: (PGI June 09)
 

a. ↑ LH & ↓ FSH	b. ↑ FSH & ↓ LH
c. ↑ LH & ↓ FSH	d. Hyperinsulinemia
e. ↑ TSH	
5. Which of the following is the most likely diagnosis in a 27-year-old obese woman presenting with Oligomenorrhea, infertility and hirsutism? (AI 04)
  - a. Polycystic ovaries
  - b. Endometriosis
  - c. Pelvic inflammatory disease
  - d. Turner's syndrome
6. In PCOD symptoms and signs seen are: (PGI June 07)
  - a. Amenorrhoea
  - b. Alopecia
  - c. Theca cell hyperplasia
  - d. Hyperandrogenism
  - e. Anovulation
7. A 28-year-old lady, Rani, is suspected to have polycystic ovarian disease. Sample for testing LH & FSH are best taken on the following days of menstrual cycle: (AI 02)
  - a. 1-4
  - b. 8-10
  - c. 13-15
  - d. 24-26
8. True about Stein-Leventhal syndrome is/are: (PGI June 03)
  - a. Oligomenorrhoea and amenorrhoea
  - b. Seen in postmenopausal women
  - c. Innumerate cysts in ovary
  - d. BRCA - 1 is associated
  - e. Theca cell hypertrophy
9. PCOD which of the following is seen: (PGI Dec 02)
  - a. Hirsutism
  - b. Secondary amenorrhoea
  - c. Streak ovaries
  - d. ↑ FSH / LH
  - e. Oestrogen (E2)
10. In Polycystic ovarian diseases, all of the following are seen *except*: (PGI Dec 01)
  - a. Endometrial carcinoma
  - b. Increased FSH
  - c. Streak ovaries
  - d. Insulin resistance
  - e. Hirsutism
11. All are true about polycystic ovarian disease except: (AIIMS Nov 08)
  - a. Persistently elevated LH
  - b. Increased LH/FSH ratio
  - c. Increased Dheas
  - d. Increased prolactin
12. The first step in the management of hirsutism due to Stein-Leventhal syndrome is: (PGI June 99)
  - a. OCP
  - b. HMG
  - c. Spironolactone
  - d. Bromocriptine
13. Treatment of Hirsutism in PCOD, drugs used are: (PGI Dec 08)
  - a. Menopausal Gonadotropin
  - b. GnRH
  - c. Spironolactone
  - d. Hcg
14. A hirsute lady with PCOD treatment is: (Kolkata 2009)
  - a. Ethinyl estradiol + Levonorgestrel
  - b. Ethinyl estradiol + Desogestrel
  - c. Levonorgestrel
  - d. None
15. Most common cause of hirsutism: (AIIMS Dec 97)
  - a. Polycystic ovary disease
  - b. Arrhenoblastoma
  - c. Cushing syndrome
  - d. Congenital adrenal hyperplasia
16. Most common cause of hirsutism in a teenage girl: (AIIMS June 97)
  - a. Ovarian disease
  - b. Pheochromocytoma
  - c. Obesity
  - d. Adrenogenital syndrome
17. A 16-year-old girl presents with rapid onset hirsutism and amenorrhoea. Best investigation is: (AIIMS June)
  - a. Testosterone estimation
  - b. Dihydroepiandrosterone

- c. Adrenocorticoids  
d. LH and FSH estimation
18. Kali Rani, a 20-year-old girl presents with history of rapidly developing hirsutism and amenorrhea. To establish the diagnosis you would like to proceed with which of the following tests in blood: (AI 02)  
a. 17 - OH progesterone    b. DHEA  
c. Testosterone            d. LH: FSH ratio
19. A 22-year-old woman comes for treatment of hirsutism. She is obese and has facial acne and hirsutism on her face. Serum LH level is 36 mIU/mL and FSH is 9 mIU/mL. Androstenedione and testosterone levels are mildly elevated, but serum DHEAS is normal. The patient does not wish to conceive at this time. Which of the following is the most appropriate treatment of her condition?  
a. Oral contraceptives pills (All India 2002)  
b. Corticosteroids  
c. GnRH analog  
d. Wedge resection of ovary
20. Persistent anovulation not treated leads to all *except*:  
a. Hirsutism (PGI June 99)  
b. Ovarian carcinoma  
c. Endometrial carcinoma  
d. Increased risk of CVS disease
21. A 20-year average weight female presented with oligomenorrhea and abnormal facial hair growth along with high serum free testosterone level. On USG the ovaries are normal. The diagnosis:  
(AIIMS Nov 2010, AIIMS Nov 2012)  
a. Idiopathic hirsutism  
b. PCOD  
c. Testosterone secreting tumor  
d. Adrenal hyperplasia
22. All of the following are associated with polycystic ovarian syndrome *except*: (AI 2010)  
a. Ovarian carcinoma    b. Endometrial carcinoma  
c. Insulin resistance      d. Osteoporosis
23. True about PCOS: (PGI May 2010)  
a. High FSH/LH ratio  
b. Unilateral large ovarian cyst  
c. Hirsutism  
d. Increased risk of diabetes mellitus  
e. OCP is given for treatment
24. In PCOD, which of the following drugs is not used for infertility? (AIIMS Nov 2013)  
a. Spironolactone        b. Tamoxifen  
c. Clomiphene            d. OC pill

## NEW PATTERN QUESTIONS

25. The biochemical changes in established cases of Stein-Leventhal syndrome are as mentioned *except*:  
a. Marked elevation of LH in contrast to FSH  
b. Insulin resistance  
c. Elevation of plasma testosterone  
d. Elevation in the level of sex hormone binding globulin (SHBG) level
26. As regard the PCOS and hyperinsulinaemia:  
a. Hyperinsulinaemia is observed in about 40% to 80% of women with PCOS  
b. Hyperinsulinaemia stimulates hepatic synthesis of SHBG  
c. Metformin causes hypoglycaemia in normoglycaemic women  
d. Metformin has many other health benefits
27. The following are related to bromocriptine therapy *except*:  
a. It is used to inhibit inappropriate lactation with secondary amenorrhoea  
b. It is specific in suppressing only the prolactin secretion  
c. If pregnancy occurs, there is increased incidence of multiple pregnancy  
d. Its teratogenic effect on the fetus is inconclusive
28. According to Ferriman Gallwey scoring system—hirsutism is diagnosed when score is more than:  
a. 8                                b. 12  
c. 16                              d. 20
29. A 24-year-old comes with a chief complaint of hair growth all over body. She reports that her menses began at the age of 13 years and has always been very irregular. She also complains of acne. On physical examination there is hair around the nipples, chin and upper lip. There is no galactorrhea, thyromegaly, or temporal balding on examination. Pelvic examination is normal, and there is not evidence of clitoromegaly. All of the following should be included in the differential diagnosis based on the patient's history and physical examination, *except*:  
a. Idiopathic hirsutism  
b. Stein-Leventhal syndrome  
c. Late-onset congenital adrenal hyperplasia  
d. Sertoli-Leydig cell tumor
30. BMI of an overweight female is:  
a. 19–24                        b. 25–29  
c. 30–34                        d. Less than 19

## ANSWERS TO FIGURE BASED QUESTION

### F1. Answer is a; i.e. Hyper insulinism

The condition shown in the image is acanthosis nigricans seen in cases of insulin resistance. This patient is having PCOD/PCOS as suggested by acanthosis nigricans, irregular cycles, weight gain and multiple cyst in the ovary.

All the metabolic abnormalities given in the question are seen in case of PCOD except diabetes insipidus.

## ANSWERS

### 1. Ans. is d, i.e. Results in postdated pregnancy

*Ref. Dutta Gynae 4<sup>th</sup>/ed p 421-425; Shaw 15<sup>th</sup>/ed p 369-371; Williams Gynae 1<sup>st</sup>/ed p 383 onwards*

As discussed in the preceding text PCOD

- Leads to increase in LH (option a correct)
- Associated with glucose intolerance (due to insulin resistance).
- Can cause infertility.
- Postdated pregnancy is not a complication of PCOD/PCOS.

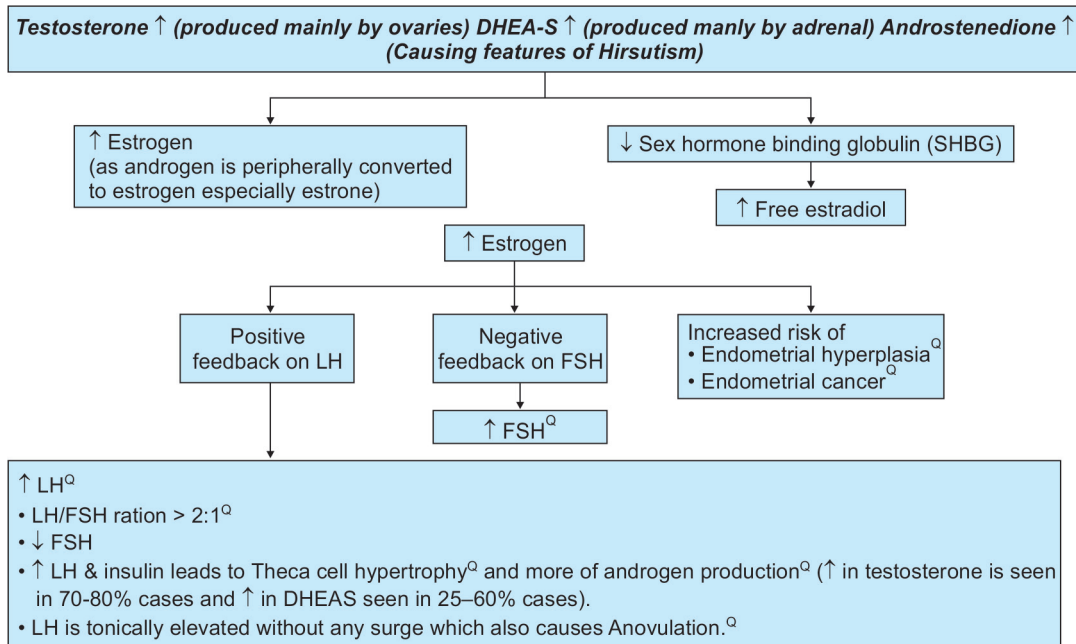
### 2. Ans. is c, i.e. Luteinizing hormone

### 3. Ans. is b, and e, i.e. LH increased, FSH normal to low and Testosterone increased

### 4. Ans. is a, and d, i.e. ↑ LH & ↓ FSH and Hyperinsulinemia

*Ref. Shaw 15<sup>th</sup>/ed p 370; Dutta Gynae 5<sup>th</sup>/ed p 440-441; Williams Gynae 1<sup>st</sup>/ed p 384-386*

#### Lab Abnormalities



- Ratio of LH/FSH in PCOS is > 2:1
- Ratio of Fasting Glucose: Fasting insulin in PCOS < 4.5

### 5. Ans. is a, i.e. Polycystic ovary

*Ref. Shaw 15<sup>th</sup>/ed p 371; Novak 14<sup>th</sup>/ed p 1076*

*A young woman presenting in the third decade with obesity, oligomenorrhea, infertility and hirsutism leaves no doubt for the diagnosis of PCOS.*

According to Rotterdam criteria → PCOD is diagnosed if any 2 of the following criteria are being fulfilled:

- i. Ovulatory dysfunction such as oligomenorrhea or hyperandrogenism.
- ii. Clinical or biochemical evidence of hyperandrogenism.
- iii. USG criteria

Since this female, has oligomenorrhea and hirsutism, so 2 of the criteria are being fulfilled.

### 6. Ans. is a, b, c, d and e, i.e. All are correct options

*Ref. Shaw 15<sup>th</sup>/ed p 369-371; Williams Gynae 1<sup>st</sup>/ed p 386*

In a patient of PCOD, amenorrhea, hyperandrogenism, anovulation and theca cell hyperplasia will be seen as discussed in the preceding text.



**Hyperandrogenism:** It is manifested clinically by:

- **Hirsutism** (i.e. presence of coarse, dark terminal hair distributed in male pattern).
- **Acne** (Acne that is persistent or is late in onset) and/or<sup>Q</sup>
- **Androgenic alopecia.**<sup>Q</sup>

Therefore alopecia can also be seen in PCOD patient

**Note:** In contrast signs of virilization such as increased muscle mass, deepening of the voice and clitoromegaly are not typical of PCOS. Virilization reflects much higher androgen levels and should prompt investigation for an androgen producing tumor of ovary or the adrenal gland.<sup>Q</sup>

7. Ans. is a, i.e. 1-4 days

Ref. Jeffcoate 6<sup>th</sup>/ed p 205

**In PCOS:** "Determination of the follicle stimulating hormone (FSH) and luteinizing hormone (LH) levels may help to confirm the diagnosis of polycystic ovaries. These are assayed on the second or third day of the cycle".

– Jeffcoate 6<sup>th</sup>/ed p 205

8. Ans. is a, c and e, i.e. Oligomenorrhoea and amenorrhoea; Innumerate cysts in ovary; and Theca cell hypertrophy

Ref. Shaw 15<sup>th</sup>/ed p 369-371

- There is no doubt that PCOD causes oligomenorrhoea/amenorrhoea, i.e. *option 'a'* is correct.
- PCOS is seen in young females. Most common age affected is 15-25 years<sup>Q</sup>. and not postmenopausal, so *option 'b'* is incorrect.
- *Pathologically* – Ovaries are enlarged (2-5 times the normal size). Tunical albuginea is thickened. There is Theca cell hypertrophy (stromal hyperthecosis) and multiple follicular cysts are localized along the surface of ovary (i.e. *options 'c'* and *'e'* are correct).
- BRCA - 1 is not associated with PCOD.<sup>Q</sup> (i.e. *options 'd'* is incorrect)
- BRCA - 1 gene has been located at the chromosomal locus 17q21; women who inherit a mutated allele of this gene from either parent have an approx. 60-80% lifetime chance of developing *Breast Ca* and about 33% chance of developing *Ovarian Ca*.
- Men who carry a mutant allele of the gene of BRCA-1 have an increased incidence of Prostate Ca, but not usually of Breast Ca.
- BRCA - 2 gene which has been located to chromosome 11, is associated with an increased incidence of Breast Ca in both men and women.

**Also know:**

**Sonographic findings in case of PCOS include :**

- $\geq 12$  small cysts (2 to 9 mm in diameter)
- Increased ovarian volume ( $> 10$  ml).
- Increased amount of stroma relative to the number of follicles.
  - Only one ovary with these findings is sufficient to define PCOS.
  - Other findings like Pearl necklace appearance in which follicles are distributed underneath the capsule in a row and perceived increase in stromal echogenicity have been eliminated as diagnostic criteria.

9. Ans. is a, b, and e, i.e. Hirsutism; Secondary amenorrhoea; and Oestrogen (E2)

Ref. Novak 14<sup>th</sup>/ed p 1078-1079; Williams Gynae 1<sup>st</sup>/ed p 385-386

Friends, here I would like to point out that in *option "e"* it is mentioned oestrogen : which is correct in cases of PCOS but in brackets it is given E2, i.e. oestradiol which is not correct.

Estrogen (in body has 3 forms)	
1. Oestradiol (E <sub>2</sub> ) Predominant estrogen in reproductive age group. Most potent form E <sub>2</sub> >E <sub>1</sub>	2. Oestosterone (E <sub>1</sub> ) Predominant estrogen following menopause It is formed when androgens are converted to estrogen
3. Another form of estrogen is oestriol. Which is a metabolite of oestrogen. It is the predominant form in pregnancy.	

**In PCOS:**

"Patients with PCOS, E<sub>1</sub> levels are increased E<sub>2</sub> is at a follicular phase level." — Novak 14<sup>th</sup>/ed p 1078; 15<sup>th</sup>/ed p 1079

Therefore, in PCOS = E<sub>1</sub> > E<sub>2</sub>, i.e. Reversal of E<sub>2</sub> : E<sub>1</sub> ratio.

"Elevated androstenedione levels contribute to an increase in estrone levels through peripheral conversion."

— Williams Gynae 1<sup>st</sup>/ed p 386

**Warning:** Do not go by what shaws has to say on this issue.

In this question I am taking oestrogen as the interpretation and marking *option "e"* correct.

- Note:**
- Streak ovaries are seen when genetic material is missing either from the long or short arm of X-chromosome or complete X-chromosome is missing as in Turner's syndrome.
  - Streak ovaries are not seen in PCOS patients.

**10. Ans. is b and c, i.e. Increased FSH; and Streak ovaries**

Ref. Shaw 15<sup>th</sup>/ed p 369-371; Jeffcoate 7<sup>th</sup>/ed, p 385-386, 390; Williams Gynae. 1<sup>th</sup>/ed, p 390 for option 'a'

*"In women with PCOS, a threefold increased risk of endometrial cancer has been reported. Endometrial hyperplasia and endometrial cancer are long-term risks of chronic anovulation, and neoplastic changes in the endometrium are felt to arise from chronic unopposed estrogen."*  
-Williams Gynae 1<sup>st</sup>/ed p 390

Rest all options have been explained earlier

**11. Ans. is d, i.e. Increase prolactin**

Ref. Jeffcoate 7<sup>th</sup>/ed p 386; Leon Speroff 7<sup>th</sup>/ed p 472

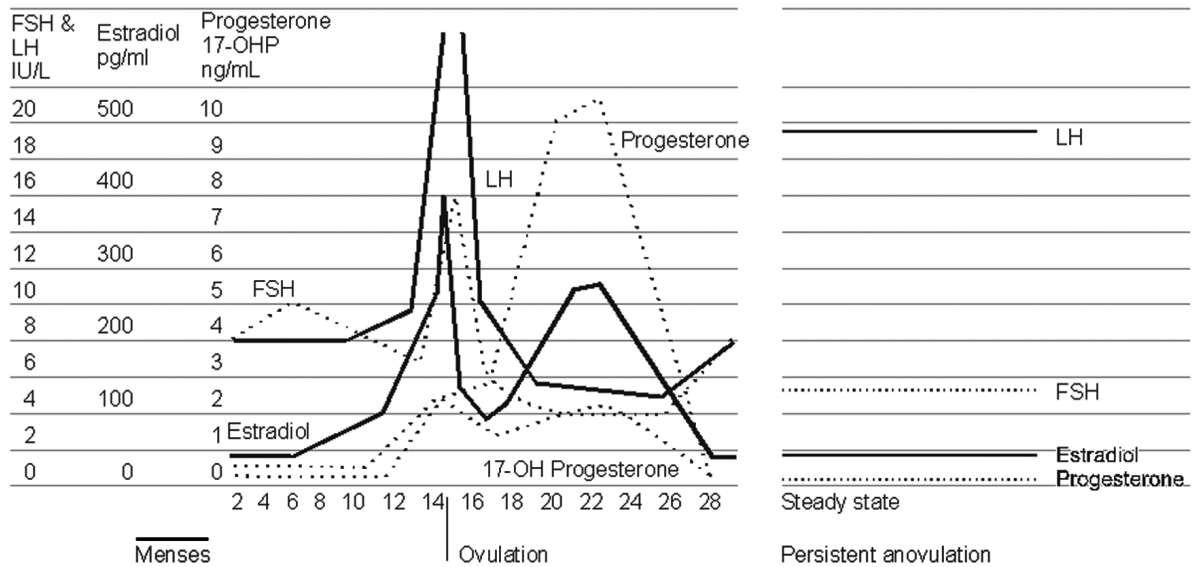
**In patients of PCOS:**

- Alterations in gonadotropin releasing hormone pulsatility leads to preferential production of LH, as compared to FSH. Also estrogen has a positive feedback on LH and negative feedback on FSH which leads to increase in LH and decrease in FSH such that LH/FSH is > 2.1.
- Now the question arises whether this increase in LH is persistent. Most of the books do not state anything clearly except that there is an increase in the LH pulse amplitude and frequency. So I had to look up in Leon Speroff (which is the BAAP of all problems related to endocrinology and infertility in Gynae).

Leon Speroff specifically mentions :

*"In contrast to the characteristic picture of fluctuating hormone levels in the normal cycle, a 'steady state' of Gonadotropins and sex steroids can be depicted in association with persistent anovulation."*  
- Leon Speroff 7<sup>th</sup>/ed p 471

This is depicted clearly in the following graph from Leon Speroff 7<sup>th</sup>/ed p 472.



So now there is no doubt that **option 'a'** is correct.

*"Approximately 70-80% of women with PCOS demonstrate frank elevations in circulating androgens particularly free testosterone, and 25-30% will have elevated levels of adrenal androgen metabolite, DHEAS"*  
- Jeffcoate 7<sup>th</sup>/ed p 386

*"The serum DHEA-S concentration is moderately elevated in over half of the woman with PCOS."*

i.e., **option 'c'** is correct.

*"Prolactin levels are usually normal, although they may be slightly elevated (generally < 40 ng/ml in a small fraction of patients.)"*  
- Jeffcoate 7<sup>th</sup>/ed p 386

According to Williams Gynae 1<sup>st</sup>/ed p 392 - If in a patient of hirsutism with irregular menses (i.e., anovulation) -

Prolactin levels	
<b>Are normal</b>	<b>If elevated</b>
↓	↓
PCOS / congenital adrenal hyperplasia should be considered	Pituitary/ovarian neoplasm should be considered

Thus, increase prolactin levels are not a diagnostic feature of PCOS. So it is the answer of choice.

**12. Ans. is a, i.e. OCP**

**13. Ans. is b and c, i.e. GnRH and Spironolactone**

Ref. Novak 14<sup>th</sup>/ed p 1082-1083; 15<sup>th</sup>/ed p 1085-1089;

Williams Gynae 1<sup>st</sup>/ed p 396-397; Shaw 15<sup>th</sup>/ed p 117-118; John hopkins manual of obs and gynae 4<sup>th</sup>/ed p 491-492

**Medical Treatment of Hirsutism**

Treatment Category	Specific Regimens
Weight loss	
Hormonal suppression	Oral contraceptives Medroxyprogesterone Gonadotropin-releasing hormone analogues Glucocorticoids
Steroidogenic enzyme inhibitors	Ketoconazole
5 $\alpha$ -reductase inhibitors	Finasteride
Antiandrogens	Spirolactone Cyproterone acetate Flutamide Metformin
Insulin sensitizer	Electrolysis
Mechanical	Laser hair removal

**Drug therapy :** If a patient has hirsutism primary goal is lowering androgen levels to halt further conversion of vellus hairs to terminal ones.

**Drugs used are :**

i. OCPs -

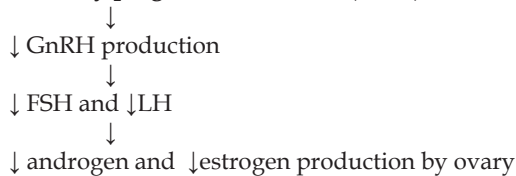
**Basis of using OCPs for hirsutism**

- The progestin component suppresses LH, resulting in decreased ovarian androgen production.
- The estrogen component increases hepatic production of SHBG (sex hormone binding globulin), resulting in decreased free testosterone concentration.
- Circulating androgen levels are reduced.
- Estrogen decreases conversion of testosterone to Dihydrotestosterone in some by inhibition of 5-alpha reductase

*"OCPs are the first line of management of oligomenorrhea caused by PCOS. Progestins decrease total androgen level by reducing the activity of 5-alpha reductase. OCP usage results in an overall decrease in the formation of new androgen dependant hair growth and androgen stimulated acne. All low dose OCP preparations are believed to have similar results. If therapy with OCPs is suboptimal, addition of an antiandrogen, such as spironolactone or finasteride, is recommended."*

- John Hopkins Manual of Obs and Gynae 4<sup>th</sup>/ed p 491-492

ii. Medroxy progesterone acetate: (MPA)



Side effects = amenorrhea, decreased bone mineral density, depression, and fluid retention.

**MPA is not commonly used for hirsutism**

iii. Gonadotropin releasing hormone agonists -

*"GnRH agonists effectively lower Gonadotropin levels over time, and in turn subsequently lower androgen levels. Despite their effectiveness in treating hirsutism, administration of these agents is not a preferred long-term treatment method due to associated bone loss, high cost and menopausal side effects."*

- Williams Gynae 1<sup>st</sup>/ed p 396

iv. Androgen receptor antagonists - like spironolactone, cyproterone acetate and flutamide. These antiandrogens are competitive inhibitors of androgen binding to the androgen receptor.

*"Although these agents are effective in the treatment of hirsutism, they carry a risk of several side effects. Metrorrhagia may frequently develop. In addition, as antiandrogens, these drugs bear a theoretical risk of pseudo hermaphroditism in male fetuses of women using such medication in early pregnancy. None of these antiandrogen agents are approved by the FDA for treatment of hyperandrogenism and thus are used off-label."*

- Williams Gynae 1<sup>st</sup>/ed p 396

*"Spironolactone therapy is initiated if OCP use is not an option for treatment of hirsutism or if results from OCP therapy are suboptimal"*

- John Hopkins manual of obs and gynae 4<sup>th</sup>/ed p 491-492

v. 5- $\alpha$  reductase inhibitor : Conversion of testosterone to dihydrotestosterone can be decreased by 5- $\alpha$  reductase inhibitor, Finasteride. It is modestly effective in treating hirsutism and similar to other antiandrogens the risk of male fetus teratogenicity is present.

So, friends after such a detailed discussion on the management of hirsutism. You can very well understand that the **first line therapy for management of hirsutism are combined oral contraceptive pills.**

**Also know:**

**Other methods of treating hirsutism:**

- **Eflornithine hydrochloride cream:** It is an irreversible inhibitor of ornithine decarboxylase enzyme. This enzyme is necessary for hair follicle cell division and function, and its inhibition results in slower hair growth. It is mainly applied on face in the form of cream. Its main disadvantage is that it does not permanently remove hair.

- **Mechanical methods:**

<b>Depilation methods</b> , i.e. hair removal above the skin surface e.g. – shaving – depilation creams	<b>Epilation methods</b> , i.e. methods which remove the entire hair shaft and root. In includes: Mechanical methods – plucking – waxing – threading	– Thermal destruction using electrolysis or laser
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**Note: While prescribing OCPs in a case of hirsutism:**

Do not prescribe OCPs containing norgestrel and norethindrone acetate as they have androgenic activity. OCPs containing 3rd generation progestins like gestodene, Desogestrel, norgestimate and 4th generation containing drospirenone are the best, as they have minimum androgenic activity.

14. **Ans. is b, i.e. ethinyl estradiol + desogestrol** *Ref. Novak 14<sup>th</sup>/ed p 1083, 15<sup>th</sup>/ed p 1086 KDT Pharma 6<sup>th</sup>/ed p 307*  
As discussed earlier—OCPs decrease adrenal and ovarian androgen production and reduce hair growth in nearly two thirds of hirsute patients. When an OCP is used to treat hirsutism, a balance must be maintained between the decrease in free testosterone levels and the intrinsic androgenicity of the progestin.

**Progesterones with:**

High androgenic bioactivity	Newer progestins with low androgenic bioactivity
<ul style="list-style-type: none"> <li>• Norgestrel</li> <li>• Norethindrone</li> <li>• Norethindrone acetate</li> <li>• Drospirenone</li> </ul>	<ul style="list-style-type: none"> <li>• Desogestrel</li> <li>• Gestodene</li> <li>• Norgestimate</li> </ul>

Thus, newer progestins with minimal androgenic activity are preferred for management of hirsutism in a patient of PCOD/PCOS. (i.e. option b is correct).

15. **Ans. is a, i.e. Polycystic ovary disease (PCOD)** *Ref. CGDT 10<sup>th</sup>/ed p 937; Williams Gynae 1<sup>st</sup>/ed p 387; Leon Speroff 7<sup>th</sup>/ed p 501*  
**Hirsutism** is defined as excessive growth of androgen dependant sexual hair or male distribution of hair in a female.  
*"The most common cause of hirsutism is Polycystic Ovarian Syndrome."* ... CGDT 10<sup>th</sup>/ed p 937  
*"Polycystic ovarian syndrome accounts for 70 - 80% of cases of hirsutism, with idiopathic hirsutism being the second most frequent cause."* - Williams Gynae 1<sup>st</sup>/ed p 387

16. **Ans. is a, i.e. Ovarian disease** *Ref. CGDT 10<sup>th</sup>/ed p 937; Williams Gynae 1<sup>st</sup>/ed p 387*  
*As explained earlier PCOD is the most common cause of hirsutism.*  
PCOD most common affects teenage girls (15–25 years). Therefore, In teenage girls most common cause of hirsutism is PCOD.

17. **Ans. is a, i.e. Testosterone estimation**

18. **Ans. is c, i.e. Testosterone** *Ref. Dutta Gynae 4<sup>th</sup>/ed p 524; Leon Speroff 7<sup>th</sup>/ed p 502-511, 515; Williams Gynae 1<sup>st</sup>/ed p 391*  
*"A variety of ovarian neoplasms, both benign and malignant may produce testosterone and lead to virilization. Specifically, women with an abrupt onset, typically within several months, or sudden worsening of virilizing signs should prompt concern for a hormone producing ovarian or adrenal tumor. Symptoms may include deepening of voice, frontal balding, severe acne or hirsutism or both, increased muscle mass and clitoromegaly. Accordingly, serum testosterone levels may be used to exclude these tumors. Free testosterone levels are more sensitive than total testosterone levels as an indicator of hyperandrogenism. Although improving, current free testosterone assays lack a uniform laboratory standard. For this reason, total testosterone levels remain the best approach for excluding a tumor. Threshold values beyond 200 ng/dl of total testosterone warrant evaluation for an ovarian lesion."* - Williams Gynae 1<sup>st</sup>/ed p 391

So now I do not need to explain that testosterone estimation is the best investigation in case of rapid onset hirsutism and amenorrhea.

Lines of Leon Speroff further support the answer –

*"A serum testosterone concentration greater than 150 mg/dl identifies almost all woman with a potential androgen producing tumor. However, a tumor still should be suspected and excluded in a woman with rapidly progressive hirsutism or signs and symptoms of virilization, even when the serum testosterone concentration is below the threshold value."* - Leon Speroff 8<sup>th</sup>/ed p 520

M/C cause of rapid onset hirsutism in young females = Testosterone producing tumor

DHEA sulphate is produced exclusively by the adrenal gland. Therefore, serum DHEAS levels above 700 mcg/dl are highly sensitive for the presence of an adrenal neoplasm.

Adrenal imaging with abdominal CT or MRI is indicated for any patient with DHEAS levels that exceed this value.

## 19. Ans. is a, i.e. Oral contraceptive pills

This patient is having hirsutism with altered LH: BH ratio. Most probably it is a case of PCOS

1st line management of hirsutism on PCOS is OCP's

## 20. Ans. is b, i.e. Ovarian carcinoma

Ref. *Clinical Gynaecologic Endocrinology & Infertility* by Leon Speroff 7<sup>th</sup>/ed p 484; Novak 1083 15<sup>th</sup>/ed p 1085

Chronic consequences of anovulation. PCOS						
↑ Risk of cardiovascular disease	Infertility (Easily treatable)	↑ risk of diabetes mellitus (Therefore all women with PCOS should be screened with OGTT at the time of presentation and every 2 years after that and those with impaired GTT require annual screening)	hirsutism	↑ risk of endometrial cancer and breast cancer	↑ risk of depression and mood disorders	↑ risk of metabolic X syndrome

As far as ovarian cancer is concerned – Till date we were believing in the theory of incessant ovulation for development of ovarian cancer which says – more a female ovulates, more are the chances of ovarian cancer.

So in patients of PCOS because of anovulation, incidence of ovarian cancer is not increased but because in patients of PCOS, clomiphene is used for ovulation induction therefore ovarian cancer can be seen.

Novaks 15/e, p525 supports this view and says

**“The risk of ovarian cancer is increased two to three-fold in woman with PCOS.”**

– Novak 15<sup>th</sup>/ed p1085

Hence ideally answer to this question should be none but still if you have to opt out, one option it should be ovarian carcinoma

## 21. Ans. is b, i.e. PCOD

Ref. *Leon Speroff 8<sup>th</sup>/ed pp 508, 518, 519, 520; Williams Gynae 1<sup>st</sup>/ed p 383, 384*

In the question patient is presenting with oligomenorrhea, abnormal facial hair growth and high serum free testosterone level.

All these features can be seen in PCOD, Testosterone secreting tumors and adrenal hyperplasia. So lets consider each option separately:

**Option 'a'- Idiopathic hirsutism:** It is defined classically as hirsutism accompanied by normal ovulatory and menstrual function in absence of hyperandrogenemia. Idiopathic hirsutism is ruled out because patient in the question has oligomenorrhea and high serum free testosterone levels.

**Option 'c'- Testosterone secreting tumor-** It is rare condition, which is almost always accompanied by severe or rapidly progressive hirsutism and symptoms or signs of virilisation (deepening of voice, temporal or male pattern baldness, breast atrophy, increased muscle mass and clitoromegaly).

**“The possibility of a tumor is excluded primarily by the clinical history and physical examination. Very few women will require specific evaluation to exclude the diagnosis.”**

Leon Speroff 8<sup>th</sup>/ed p 520

Since other features of virilization are absent and hirsutism is not rapid in onset, so testosterone producing tumor is excluded in this patient.

Another point which goes against - testosterone producing tumor is, ovaries are normal on ultrasound in this patient whereas in case of testosterone producing tumors, solid ovarian mass lesion should be identified in most of the cases.

**“Transvaginal ultrasonography will identify almost all solid ovarian mass lesions, although very small tumors located in the hilar region can escape detection.”**

Leon Speroff 8<sup>th</sup>/ed p 520

**Coming to Option 'd'- Congenital Adrenal Hyperplasia-** Congenital Adrenal Hyperplasia (CAH) is caused by adrenal steroidogenic enzyme defects that result in excessive adrenal androgen production.

M/C cause is 21 hydroxylase enzyme deficiency other rare causes are Defect in 11b hydroxylase, 3b hydroxysteroid dehydrogenase.

Females with classical CAH typically present at birth with ambiguous genitalia and this would rarely be confused with PCOS, but those with non-classical or late onset form of CAH present later, during childhood or early adolescence with precocious puberty or as young adults with signs of hyperandrogenism, very much like those of PCOS.

**“Whereas it is logical to recommend that non-classical CAH be excluded specifically in all women with hyperandrogenism, we believe that specific testing can be safely reserved for those having an early onset of hirsutism (pre or perimenarcheal, including girls with premature adrenarche), women with a family history of the disorder, and those in high risk ethnic groups (Hispanic, mediterranean slavic, Ashkenazi jewish or yupic eskimo heritage). The yield from routine screening is very low as the disorder is uncommon.”**

Leon Speroff 8<sup>th</sup>/ed p 319

**Thus from above discussion-** it is clear that classical congenital adrenal hyperplasia is ruled out completely; non classical hyperplasia may be a possibility but since it is not common in general population but in hispanic, mediterranean, groups, etc. it can be kept in +/- status.

**Option 'b'- PCOD**

A 20 year female presenting with oligomenorrhea and hirsutism- chances of PCOD are high.

According to a the new criteria- **Rotterdam criteria** (2003) adopted for the diagnosis of PCOD.

Any 2 out of the three should be present for diagnosing PCOD

1. Oligoanovulation
2. Clinical and /or biochemical signs of hyperandrogenism
3. Polycystic ovaries on USG

However, because other etiologies like congenital adrenal hyperplasia, androgen secreting tumors and hyperprolactinemia may also lead to oligoovulation or androgen excess, these must be excluded. Thus PCOD is at present a diagnosis of exclusion.

In the question, patient is presenting with oligomenorrhea (anovulation) and increased free serum testosterone levels as well as hirsutism (biochemical and clinical signs of hyperandrogenism), two criteria are being fulfilled and we have also excluded adrogen secreting tumor and congenital adrenal hyperplasia, so PCOD can be diagnosed.

Some of you may argue that ovaries are normal in USG in this patient, whereas in PCOD- multiple cysts ( $\geq 12$  in number, 2-9 mm in diam) are seen in one or both ovaries and ovarian volume is  $\geq 10$  ml.

Read what Leon speroff 8/e, p 514 has to say on this issue-

**"Again, the important point is that PCOS is a functional disorder in which polycystic ovaries result from chronic anovulation. Although present in most women with chronic diagnosis hyper androgenic anovulation, polycystic ovaries donot establish and are not required for diagnosis of PCOS."**

*Leon Speroff 8<sup>th</sup>/ed p 515 and 522*

So it is clear in PCOD- Polycystic ovaries are not required for diagnosis. Another point is that this female is average weight whereas in PCOD- females are obese- so now let us read what leon speroff has to say on this issue:

**"Observations indicate that obesity relates primarily to genetic and environmental factors and is a common but not essential feature of PCOS. Obesity contributes modestly to the risk for developing PCOS and adds to the patho physiology in already affected women by aggravating the degrees of insulin resistance and hyperinsulinemia."** *Leon Speroff 8<sup>th</sup>/ed p 508*

Now this leaves us with no doubt that diagnosis of the patient in the question is PCOD.

- 22. Ans. is d, i.e. Osteoporosis** *Ref. Leon Speroff 7<sup>th</sup>/ed p 470-480, 8<sup>th</sup>/ed p 500-518; Novak 14<sup>th</sup>/ed p 1082, 15<sup>th</sup>/ed p 1085 Relationship between bone mineral density and Insulin resistance in PCOS Journal of Bone mineral metabolism vol 19, Number 4, July 2001, p 257-262*

This was definitely one of the most controversial questions in AIPG 2010. As explained earlier endometrial cancer and insulin resitance are seen in PCOD. Ovarian cancer and osteoporosis both options are incorrect but option 'd': osteoporosis is a better option to mark.

The main theory for development of epithelial ovarian cancer (which accounts for 85-90% of all ovarian CA) is the "Theory of incessant ovulation" which means "more the ovulation, more the risk".

But in PCOS there is anovulation and hence per say it is protective for CA ovary.

But, PCOS patients are infertile and ovulation induction is required for treatment of infertility. Use of ovulation inducing agents like gonadotrophins, clomiphene letrozole, etc. is one of the risk factors for development of ovarian cancer. This is how PCOS can be associated CA ovary.

**"The risk of ovarian cancer is increased two to three fold in woman with PCOS."**

*Novak 15<sup>th</sup>/ed p 1085*

PCOS is protective for osteoporosis because estrogen deficiency and low BMI are risk factors for osteoporosis but incase of PCOS there is:

- Estrogen excess
- Androgen excess
- Insulin resistance and hyperinsulinemia.

All of which are protective for bone mineral loss and osteoporosis.

- 23. Ans. is c, d, and e, i.e. Hirsutism; Increased risk of diabetes mellitus; and OCP is given for treatment**

*Ref. Shaw 15<sup>th</sup>/ed p 369; Novak 14<sup>th</sup>/ed p 1077-1083; 15<sup>th</sup>/ed p 1076-1085, William gynae 1<sup>st</sup>/ed p 383, 384, 385, 387, 395*

PCOS has been discussed in detail, **options 'c'**, i.e. Hirsutism, **option 'd'** = ' increased risk of diabetes mellitus and **option e**, i.e. OCP is given for treatment are correct and do not require any explanation.

In PCOS, LH is raised and FSH is decreased

**Option 'a'**, i.e. high FSH/LH ratio is incorrect

In case of PCOS - multiple  $\geq 12$  cyst (2-9 mm in diameter) are seen in one or both the ovaries, i.e. **option 'b'** unilateral large ovarian cyst is incorrect.

**24. Ans. is a, i.e. Spironolactone** *Ref. Shaw's textbook of gynecology 15<sup>th</sup>/ed p 371; Dutta Gynae 6<sup>th</sup>/ed p 470*  
There is no confusion with regards to the use of clomiphene citrate or Tamoxifen for infertility. The confusion is between OCP's and spironolactone. Spironolactone is not used for treating infertility. OCP's used for sometime, can lead to suppression of gonadotropins and then exogenous gonadotropins can be given.

**25. Ans. is d, i.e. Elevation in the level of sex hormone binding globulin (SHBG) level** *Ref. Dutta Gynae 6<sup>th</sup>/ed p 460*  
In PCOS (stein leventhal syndrome) the levels of SHBG decrease.

**26. Ans. is a and d, i.e. Hyperinsulinemia is observed in about 40% to 80% to of women with PCOS; Metformin has many other health benefits** *Ref. Dutta Gynae 6<sup>th</sup>/ed p 461-2, 470*

Insulin resistance and compensatory hyperinsulinaemia is observed in about 40% of women with normal weight and 80% obese women with PCOS. Hyperinsulinaemia results in decreased hepatic synthesis of SHBG and increased ovarian androgen biosynthesis. Metformin reduces weight, BMI fasting insulin levels, blood pressure and LDL cholesterol. Metformin does not cause hypoglycemia neither in normoglycaemic patients nor with diabetic individuals.

**27. Ans. is c, i.e. If pregnancy occurs, there is increased incidence of multiple pregnancy** *Ref. Leon Speroff 7<sup>th</sup>/ed p 460-470*  
**Bromocriptine:**

- It is a dopamine agonist, used in the management of galactorrhea.
- Peak of Bromocriptine occurs 1-3 hours after oral administration but very little remains in circulation after 14 hours.
- Pregnancy following bromocriptine has got no teratogenic effects on off spring.
- There is no increased incidence of multiple pregnancy.
- **Side effect of bromocriptine:** Giddiness, dizziness and postural hypotension

**Cabergoline:** It is longer acting. A single dose of cabergoline can inhibit prolactin secretion for 7 days. Thus it has become DOC in case of hyperprolactinemia.

A newer dopamine agonist licensed for treatment of hyperprolactinemia is Guinagolide (non ergot dopamine D<sub>2</sub> agonist).

**28. Ans. is a, i.e. 8** *(Ref internet search)*

Ferriman-Gallwey scoring is a scoring method for detecting hirsutism. In the original system—hair growth at 11 sites was noted-

- |                  |                  |
|------------------|------------------|
| 1. Upper lip     | 7. Lower abdomen |
| 2. Chin          | 8. Upper arms    |
| 3. Chest         | 9. Forearms      |
| 4. Upper back    | 10. Thighs       |
| 5. Lower back    | 11. Legs         |
| 6. Upper abdomen |                  |

In the modified method—2 sites were deleted-forearms and legs. Thus in the modified scoring system—hair growth is seen at 9 sites. In each of the nine locations-a score between 0-4 is given depending on growth of terminal hair

Maximum score= 36

In caucasian women a score of 8 or higher is regarded as indicative of androgen excess.

**29. Ans. is d, i.e. Sertoli-Leydig cell tumor** *(Ref: Read below)*

In the question-female is having hair growth all over the body, i.e. hirsutism.

This could be (1) Idiopathic hirsutism

(2) Congenital adrenal hyperplasia of late onset

Since she has irregular menses also:

2 criteria of PCOD are also being fulfilled-so it can be a case of PCOS

This cannot be Sertoli cell Tm as there are no sign of virilization (e.g. clitoromegaly), there is only hirsutism.

**30. Ans. is b, i.e. 25-29** *(Ref: Leon Speroff 7/ed page 470-475, 780)*

BMI (kg/m <sup>2</sup> )	Category
<19	Underweight
19.1-24.9	Normal
25-29.9	Overweight
30-34.9	Obese
> 35	Morbidly obese

# CHAPTER

# 5

# Congenital Malformations



SRY gene is located on short arm of 'Y' chromosome



If Y chromosome/SRY region is present – gonads form testis. If Y chromosome/SRY region is absent – gonads form ovary.



**Note:** For ovarian differentiation – presence of one X chromosome is required whereas presence of both X chromosomes is necessary for normal ovarian function. Thus if only one X chromosome is present it results in streak gonads like in Turners syndrome.



**In females** – external genitalia are formed due to absence of dihydrotestosterone. So if testosterone and dihydrotestosterone is present in intrauterine life in females, it results in male looking genitalia in females, i.e. ambiguous genitalia and this is what happens in case of congenital adrenal hyperplasia.



M/C cause of ambiguous genitalia in females is congenital adrenal hyperplasia.

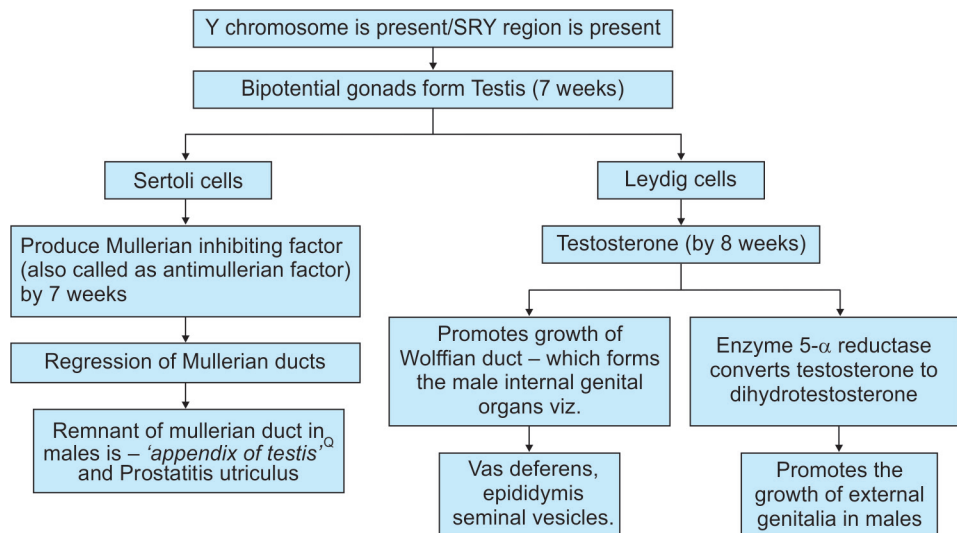
## Embryology Related to Development in Males and Females

The sexual differentiation depends on sex determining region (SRY region) present on short arm of Y-chromosome.

If Y-chromosome is present → gonads which are initially bipotential develop into testes (7 weeks)

If SRY region is absent, i.e. Y chromosome is absent → gonads develop into ovaries (8 weeks)

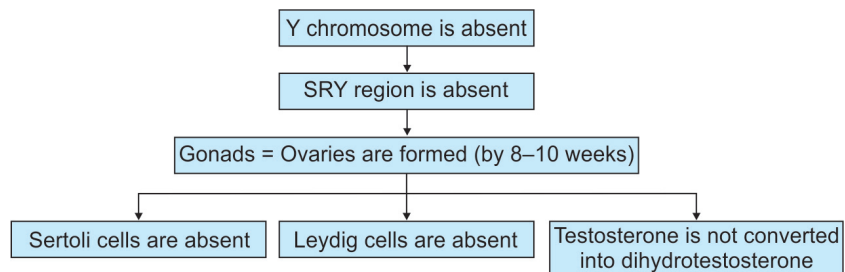
### In Males



### Under the influence of dihydrotestosterone –

- Genital tubercle forms glans penis
- Genital swellings forms scrotum
- Genital folds forms penile urethra
- Male genital development is complete by 14 weeks

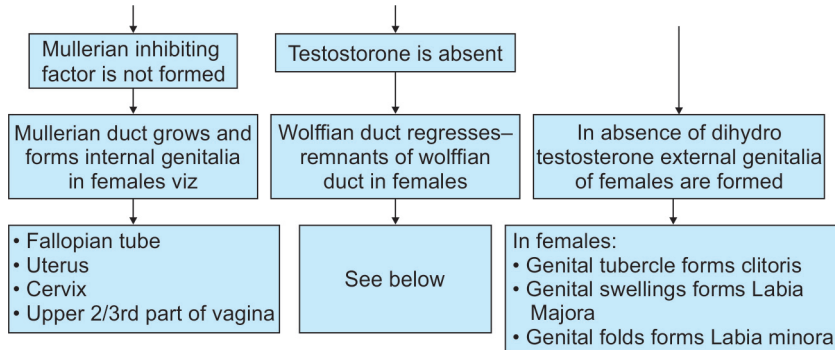
### In Females



Contd...



Contd...

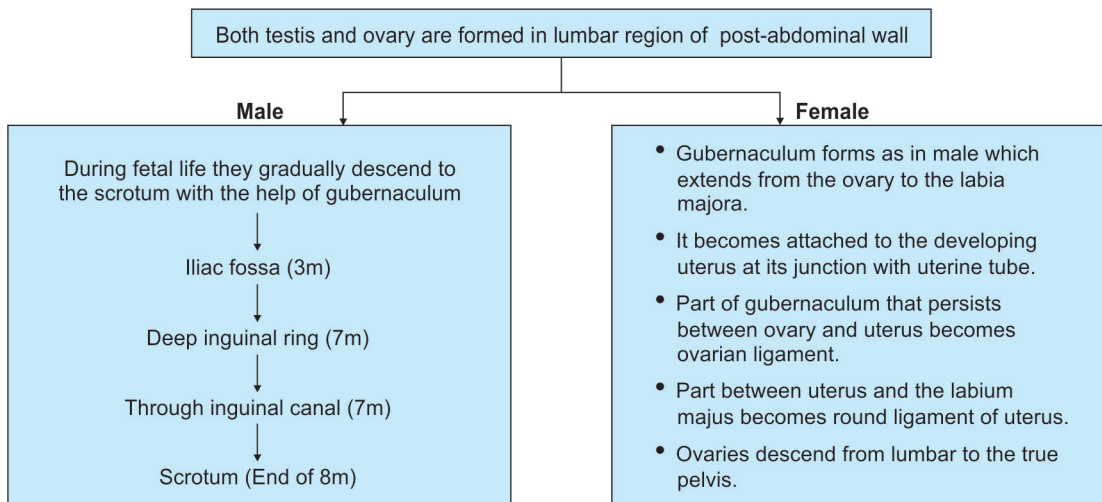


All Remnants are present in lateral part of broad ligament, except Paroophoron which is present in medial part.

#### ➤ Remnants of wolffian duct (mesonephric duct) in females

Part of wolffian duct	Remnant in females
Pronephros	Hydatid of Morgagni or Kobelt tubercle
Mesonephros: • Cranial end • Caudal end	Epo-oophron or Organ of Rosenmuller Para-oophron
WD proper	Gartner's duct

#### Descent of gonads



#### Development of External Genital Organs in Females

- The external genital organs start developing almost simultaneously with the development of the internal genital organs. The site of origin is from the **urogenital sinus**.
- **Clitoris** is developed from the genital tubercle.
- **Labia minora** are developed from the genital folds.
- **Labia majora** are developed from the genital swellings.
- **The Bartholin's glands** are developed as outgrowths from the caudal part of the urogenital sinus and correspond to the bulbourethral glands of male.
- **The vestibule** develops from inferior portion of the pelvic part and whole of the phallic part of the urogenital sinus.
- **Female genital development is complete by 11 weeks.**

## Development of Internal Genital Organs

The major part of the female genital tract develops from the **Mullerian ducts**.

### Development of Mullerian ducts/paramesonephric ducts in females

- In the 5th-6th week of intrauterine life of the embryo mullerian ducts develop as an invagination of intermediate cell mass. Two Mullerian ducts develop, one on either side and grow caudally. They approach each other in the midline after crossing the Wolffian duct and fuse. Fusion begins by 7-8 weeks and is completed by 12 weeks.<sup>Q</sup>
- The cervix can be differentiated from corpus by 10th week.
- Fusion proceeds in below upwards direction.
- Initially when the two Mullerian ducts fuse, an intervening septum is present but later by 5<sup>th</sup> month<sup>Q</sup> of intrauterine life, it also disappears.

### Development of Vagina

Vagina develops from two sources:

- Mainly from the Mullerian duct (forms upper 3/5th part)
- Partly from the urogenital sinus (forms lower 1/5th part) which together form a solid vaginal plate.
  - Canalization of the solid vaginal plate occurs at 20 weeks
  - If this canalization fails to occur it leads to – transverse vaginal septum.
- The mucous membrane of **vagina is derived from endoderm of urogenital sinus<sup>Q</sup>** and muscles from mesoderm of mullerian duct.

### Development of Ovary

- Ovaries are formed because of absence of y chromosome.
- For proper development of ovaries-presence of two X chromosomes is required. This is the reason why- in Turner's syndrome (45X0) ovaries are not developed properly-called as **streak gonads**.
- WNT-4 is the ovary determining gene.
- The ovary is developed from the **genital ridge<sup>Q</sup>**. Genital ridge appears at **5 weeks** of POG.
- The cortex and the covering epithelium are developed from the coelomic epithelium and the medulla from the mesenchyme.
- The germ cells are ectodermal in origin and migrate to the yolk sac (at 2 weeks) and to the genital ridge (3 weeks).
- The estimated number at birth is about 2 million.
- The ovaries descend during seventh to ninth months, and at birth, they are situated at the pelvic brim.

**Note:** The bipotential gonad develops into an ovary about two weeks later than the testicular development.

## Homologous Parts of Genital Tract

	Male development	Female development
Wolffian/mesonephric ducts	Epididymis, vas deferens, and seminal vesicles	Remnant i.e. Gartner duct
Mesonephric tubules	Paradidymis	Epoophoron, and Paroophoron
Mullerian/paramesonephric ducts	Regresses-Remnant is Appendix of testes	Uterus, cervix, tubes, and upper vagina
Urogenital sinus	Urinary bladder, urethra, prostate, prostatic utricle, and bulbourethral glands	Urinary bladder, urethra, paraurethral glands, Bartholin's glands, and lower vagina

Contd...

#### Mullerian Ducts Form

- Both the fallopian tubes
- Uterus
- Cervix
- Upper part of vagina



Ovaries are not formed by Mullerian duct hence in Mullerian agenesis – ovaries/ovulation is normal



- Ovaries are formed by genital ridge



Mullerian duct is also called as Paramesonephric duct. Wolffian duct is also called as mesonephric duct

Contd...

	Male development	Female development
Mullerian tubercle/genital tubercle	Glans of penis	Clitoris
Genital swellings	Scrotum	Labia majora
Urogenital folds	Penis and urethra	Labia minora



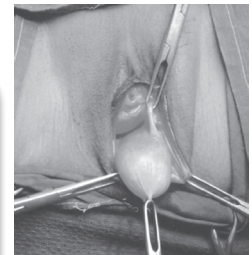
**Fig. 5.1:** Second degree uterine prolapse. Note the rugosities of vaginal mucosa

## Gartner's cyst

### ALSO KNOW

**Gartner's cyst** are cysts of the remnants of Wolffian duct  
Main location = Anterolateral aspect of vagina, hence are often confused with cystocele.

Features of Gartner's cyst	Cystocele
<ul style="list-style-type: none"> <li>&gt; Rugosities of the overlying vaginal mucosa are lost</li> <li>&gt; Vaginal mucosa over it becomes tense and shiny</li> <li>&gt; Margins are well defined</li> <li>&gt; Not reducible</li> <li>&gt; No impulse on coughing</li> </ul>	<ul style="list-style-type: none"> <li>&gt; Rugosities present</li> <li>&gt; Margins not well defined</li> <li>&gt; Reducible</li> <li>&gt; Impulse on coughing present</li> </ul>



**Fig. 5.2:** Gartner's cyst. Note the shiny appearance of mucosa

### ALSO KNOW

#### Anomalies caused by *in utero* exposure to Diethylstilbestrol (DES)

- > Vagina - Vaginal adenosis (M/C anomaly caused by DES)  
Clear cell cancer of vagina
- > Cervix - Cervical hood, collars.  
Increased risk of CIN and adenocarcinoma of cervix
- > Uterus - M/C finding hypoplastic uterus.  
Most characteristic-'T' shaped uterus.
- > Fallopian tubes- Paratubal cysts

**Note:** Renal anomalies are not seen in female fetuses exposed to DES.



*In utero* exposure to DES can lead to a wide range of congenital anomalies **but is never associated with renal malformations**



Urinary bladder develops from upper vesicoureteral part of urogenital sinus except trigone.

## Transverse Vaginal Septum

If there is a disorder in fusion of downgrowing Mullerian duct and upgrowing derivative of urogenital sinus, results in transverse vaginal septum which causes imperforate vagina (or vaginal agenesis).

- > 46% septa are located in upper part.<sup>Q</sup>
- > 40% septa are located in middle part.<sup>Q</sup>
- > 14% septa are located in lower part.<sup>Q</sup>

Transverse vaginal septum can present either in :

### Neonatal Age-group

- > The placental transfer of estrogen results in stimulating the glands of the endocervix which results in formation of mucocolpos, and can present as:
  - o Abdominal tumour.<sup>Q</sup>
  - o Can compress the ureter resulting in hydroureter followed by hydronephrosis.<sup>Q</sup>
  - o Can compress the rectum resulting in obstipation/intestinal obstruction.<sup>Q</sup>



Transverse vaginal septum mostly corresponds to the level of external os (as most of them are located in the upper part).

### At Puberty

- Patient can present with primary amenorrhea (actually called as cryptomenorrhea<sup>Q</sup> as uterus menstruates normally but blood does not come out due to outflow tract obstruction).<sup>Q</sup>
- Secondary sexual characteristics are normal.<sup>Q</sup>
- Due to cryptomenorrhoea, blood gradually collects and distends first the vagina (hematocolpos)<sup>Q</sup>, then cervix, uterus (hematocervix and hematometra) and finally the tube (hematosalpinx)<sup>Q</sup>. All these present as pelvic/abdominal tumor.
- The abdominal tumor can irritate the bladder followed by compression of internal urinary meatus leading to complete retention of urine (This occurs 3–4 years after the onset of hidden menstruation and therefore, patient is generally aged 15–18 years<sup>Q</sup>).
- Patient may complain of monthly cyclic pain (backache/lower abdomen pain).<sup>Q</sup>

### Management

- In case of septa in lower and middle part of vagina- surgical removal of septa vaginally followed by reanastomosis.
- In case of upper septa, abdominal surgery is required.

#### Most common In MD anomalies

- M/C congenital anomaly: Septate > bicornuate
- M/C problem associated with them second trimester recurrent abortions
- M/C anomaly causing abortion: septate uterus
- M/C anomaly associated with infertility: septate uterus



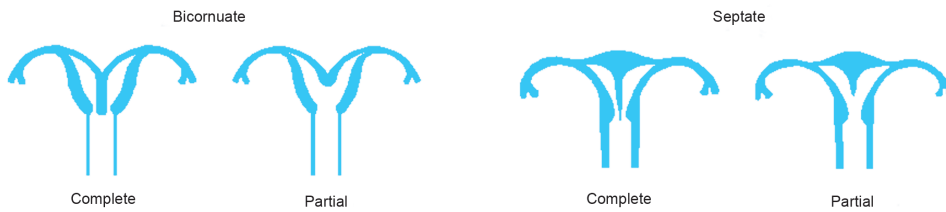
**Fig. 5.3:** Hysterosalpingographic cannula or Leech water son cannula.

### Mullerian Duct Anomalies

Anomaly	Defect	
<b>Uterus Didelphys</b>	It is a condition where there is failure of fusion along the whole length of mullerian duct resulting in 2 vagina, 2 cervix, and 2 uterus <sup>Q</sup>	
<b>Bicornuate uterus</b>	In this condition only the lower part of the ducts fuse leaving the cornua separate, so always there is a single vagina	
<i>a. Uterus bicornis unicollis</i>	Here vagina and cervix are fused, i.e. single vagina, single cervix but 2 uterus. <sup>Q</sup>	
<i>b. Uterus bicornis bicollis</i>	Here vagina is fused but cervix and uterus are not fused, i.e. single vagina, 2 cervix and 2 uterus. <sup>Q</sup>	
<b>Septate / Subseptate uterus</b>	Here the uterus is outwardly normal but contains a complete or incomplete septum which reflects a failure in the breakdown of the walls between the 2 ducts. <sup>Q</sup>	
<b>Arcuate uterus</b>	Here the fundal bulge of uterus does not develop after fusion of the ducts i.e. flat topped uterus. <sup>Q</sup>	
<b>Unicornuate uterus</b>	It does not represent a defect in the fusion of the ducts, rather here one of Mullerian ducts is completely absent and so there is only 1 fallopian tube. Uterus, cervix, and vagina though appear to be normal are only half of the fully developed organ. <sup>Q</sup>	

### Diagnosis

- **HSG:** Hysterosalpingogram (HSG) is mainly preferred in uterine anomalies but it cannot distinguish between a septate and bicornuate uterus. This is because in order to distinguish between the two, uterine fundus should be visible.



In Bicornuate uterus the 2 halves of mullerian duct do not fuse and there is defect in fusion of fundus as well.

In septate uterus a septum passes down from the uterine fundus. The fundus is normal in appearance.

*Note:* Kindly see color plates for HSG appearances of various anomalies

- IOC: MRI followed by 3 dimension USG
- Gold Standard – Laparoscopy

### Management of Bicornuate or Septate Uterus

Presence of uterine malformation per se is not an indication of surgical correction. Unification operation is indicated in otherwise unexplained cases of infertility or if it has lead to  $\geq 3$  abortions.<sup>Q</sup>

### Options Include

- **For bicornuate uterus:** (and if needed for Didelphys uterus)
  - Unification surgery (done either hysteroscopically or by abdominal route-Strassman metroplasty).
- **For septate uterus:**
  - **Earlier:** Jones/Tompkins metroplasty was done.
  - **Nowadays:** **Hysteroscopic resection of septa** is being done after inducing endometrial atrophy by administering GnRH analogue for 2 months.
  - **Main complications:** Uterus perforation and fluid overload.

## Mullerian Agenesis

### KNOW IN DEPTH

Mullerian Agenesis is the complete failure in the development of the mullerian ducts, resulting in absence of the fallopian tubes, uterus, and most of vagina<sup>Q</sup> (as 2/3<sup>rd</sup> of vagina is formed by Mullerian duct).

Karyotype = 46 XX<sup>Q</sup>

Phenotype = Female

### Associated Abnormalities

- Renal anomalies (M/C Renal agenesis followed by horse-shoe shaped kidney)<sup>Q</sup>
- Skeletal abnormalities<sup>Q</sup> (most common - scoliosis).
- Cardiac anomalies.<sup>Q</sup>

When mullerian agenesis is associated with Renal anomalies and skeletal anomalies-it is called Mayer Rokitansky Kuster Hauser syndrome.

### Clinical Features

- Patient present between 15–18 years of age with primary amenorrhoea<sup>Q</sup>.
- Secondary sexual characteristics are normal<sup>Q</sup> as ovaries are normal (because ovaries do not develop from mullerian duct but from genital ridge, so ovulation is also normal) i.e. breast, pubic hair and axillary hair all are normal.

### WHO classification of Mullerian anomalies

Class I	Mullerian agenesis (MRKH syndrome)
Class II	Unicornuate uterus
Class III	Didelphys uterus
Class IV	Bicornuate uterus
Class V	Septate uterus
Class VI	Arcuate uterus
Class VII	DES related abnormalities/T shaped uterus

- Best Reproductive outcome: seen in arcuate uterus > didelphic uterus > bicornuate uterus.
- Worst reproductive outcome serious unicornuate uterus
- Uterine anomaly M/C associated with renal anomalies unicornuate uterus (40%)
- Surgical correction not needed is: Arcuate > didelphys uterus

- P/V = Vagina is felt like a blind pouch and uterus is absent<sup>Q</sup>.
- “Although in MRKH fallopian tube should be absent, typically a part of the distal tube is present (distal 1/3rd present).”  
– William Gynae 1<sup>st</sup>/ed p 416
- Findings are confirmed by USG<sup>Q</sup>.

### Management

- Repair of vaginal agenesis is done either by *frank dilatation* or *vaginoplasty*.
- Vaginoplasty should only be performed when the girl is just married or about to be married<sup>Q</sup>.
- **Surgical management:** Vaginoplasty either by McIndoe reed procedure<sup>Q</sup> or Williams vaginoplasty<sup>Q</sup> or amnion vaginoplasty.
- These females are capable of having their biological child because their ovaries are normal hence - oocyte can be, picked up and with husband semen, IVF can be done Zygotes are then transferred to surrogate mothers uterus.



Ideal time for doing vaginoplasty is either just before or after marriage. Main complication of vaginoplasty – Restenosis and dyspareunia



Frank dilatation should be tried if atleast 1 cm length of vagina is present

### Frank Dilatation

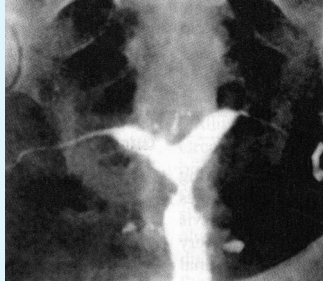
This non-surgical procedure consists of a woman applying gradual pressure with progressively increasing dilators over the mullerian pit for 15 minutes twice a day. An indentation is created by the end of 3 to 6 month. Some have satisfactory intercourse, but in many, vaginal size is inadequate and they need a surgical procedure eventually.

### Differential Diagnosis

- Cryptomenorrhea- Imperforate hymen
- Testicular feminization syndrome.

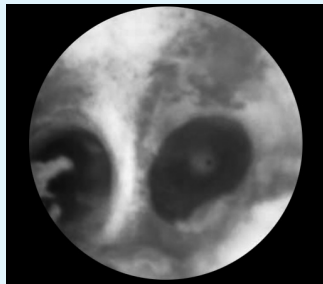
### FIGURE BASED QUESTIONS

- F1.** Identify the condition shown in HSG:- F1 shows
- Septate uterus
  - Bicornuate uterus
  - Didelphys uterus
  - Unicornuate uterus



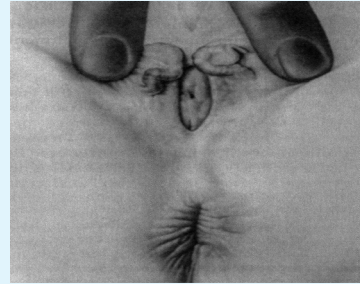
**Fig. F1**

- F2.** Hysteroscopic view shown in figure F2: shows
- Normal uterine cavity
  - Asherman syndrome
  - Septate uterus
  - Uterus perforation



**Fig. F2**

- F3.** Identify the condition shown in Figure F3
- Ambiguous genitalia
  - Bifid clitoric
  - Clitoromegaly
  - Normal genitalia of females



**Fig. F3**

- F4.** Identify the condition shown in HSG:-F4
- Bicornuate uterus
  - Normal uterus
  - Arcuate uterus
  - Septate uterus



**Fig. F4**

### QUESTIONS

- To diagnose uterus didelphys, procedure of choice is:
  - Laparoscopy
  - IVP [AIIMS 92, AI 95]
  - HSG
  - USG
- The most important indication for surgical repair of a bicornuate uterus is: [AIIMS Nov. 05]
  - Infertility
  - Dysmenorrhoea
  - Menorrhagia
  - Habitual abortion
- Vaginal atresia is associated with: [AIIMS June 98]
  - Uterine atresia
  - Exstrophy of bladder
  - Imperforate hymen
  - Ovarian atrophy
- Ideal age for repair of vaginal agenesis is: [AIIMS 92]
  - 6 months
  - 3 years
  - At puberty
  - Before marriage
- Ovary develop from: [PGI June 02]
  - Mullerian duct
  - Genital ridge
  - Genital tubercle
  - Mesonephric duct
  - Sinovaginal bulbs
- Diagnosis of septate uterus done by: [PGI Dec 04]
  - USG
  - Uterine sound
  - Hysteroscopy
  - Hysterosalpingography
  - Laparoscopy
- MC congenital abnormality of uterus is: [PGI Dec 05]
  - Uterus didelphys
  - Arcuate
  - Unicornuate
  - Septate
  - Bicornuate
- Transverse vaginal septum corresponds to: [PGI Dec 04; June 04]
  - External os
  - Vesical neck
  - Bladder base
  - Hymen
  - Above the external meatus
- All of the following are features of mullerian agenesis except: [PGI Dec 04]
  - 46 XX karyotype
  - Normal breast development
  - Absent vagina
  - Ovarian agenesis
- True about MRKH syndrome: [PGI May 2010]
  - Absent uterus
  - Absent ovary
  - Absent vagina
  - XX phenotype
  - XY phenotype
- Characteristic features of Rokitansky Kuster Hauser syndrome are all of the following except: [AI 99; Delhi 05]
  - Absent uterus
  - Absent vagina
  - Anovulation
  - 46 - XX
- Rokitansky Kuster Hauser syndrome is associated with: [AI 01]
  - Ovarian agenesis
  - Absent fallopian tube
  - Vaginal atresia
  - Bicornuate uterus
- In complete mullerian duct aplasia all of the following are likely to be absent except: [AI 07]

- a. Ovaries                      b. Fallopian tubes  
c. Uterus                        d. Vagina
14. Mayer Rokitansky Kuster Hauser syndrome consists of:  
[AIIMS May 09]  
a. Ovaries, uterus fallopian tubes present  
b. Uterus absent, fallopian tube ovaries present  
c. All absent  
d. Uterus present tubes and ovaries absent
15. Which of the following condition does not present with both mullerian and wolffian duct structures?  
a. Antimullerian hormone deficiency [AI 2010]  
b. FSH receptor mutation  
c. Ovotesticular syndrome  
d. Mixed gonadal dysgenesis
16. Vaginal epithelium is derived from: (AIIMS May, Nov 2013)  
a. Endoderm of urogenital sinus  
b. Mesoderm of urogenital sinus  
c. Endoderm of genital ridge  
d. Mesoderm of genital ridge
17. Complete failure of mullerian duct fusion will result in:  
[AI 02; UP 04]  
a. Uterus didelphys            b. Arcuate uterus  
c. Subseptate uterus        d. Bicornuate uterus
18. Bicornuate uterus is due to: [PGI Dec. 98]  
a. Incomplete fusion of uterine cavity  
b. Incomplete fusion of paramesonephric duct  
c. Incomplete fusion of mesonephric duct  
d. Incomplete formation of vagina
- c. Incomplete septum of uterus  
d. Double uterus and double cervix
20. SRY gene is located on:  
a. Short arm of Y chromosome  
b. Long arm of Y chromosome  
c. Short arm of X chromosome  
d. Long arm of X chromosome
21. All of the following structures are homologous *except*:  
a. Labia majora and scrotum  
b. Labia minora and penile urethra  
c. Epoophoron and caudal end of wolffian duct  
d. Clitoris and glans penis
22. All are derivatives of paramesonephric duct *except*:  
a. Appendix of testis        b. Hydatid of morgagni  
c. Uterus                        d. Gartner's duct
23. Diethylstilbesterol causes the following defects *except*:  
a. Renal anomalies        b. Perifimbrial cysts  
c. T shaped uterus        d. Vaginal adenosis
24. Gartner's cyst can be differentiated from cystocele by all *except*:  
a. Not reducible            b. No impulse on coughing  
c. Presence of rugosities of overlying vaginal mucosa  
d. None of above
25. All of the following take part in male genital tract development *except*:  
a. SRY                            b. SOX-9  
c. FGF-9                        d. WNT-4
26. M/C uterine malformation associated with renal anomalies:  
a. Bicornuate                    b. Unicornuate  
c. Septate                        d. Didelphys
27. M/C uterine malformation associated with infertility:  
a. Bicornuate                    b. Unicornuate  
c. Septate                        d. Didelphys

### NEW PATTERN QUESTIONS

19. Unicollis bicornis means:  
a. Two uterine cavity with one cervix  
b. Single vagina with double uterus

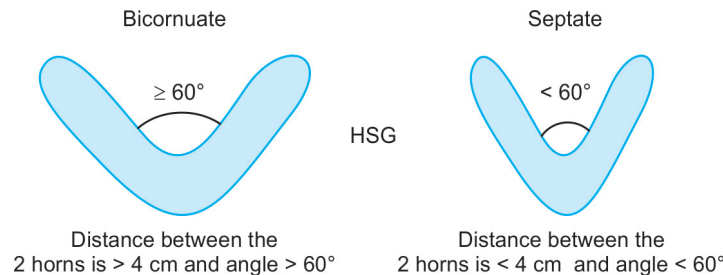


## ANSWERS TO FIGURE BASED QUESTIONS

F1. **Ans. is b, i.e. Bicornuate uterus:**

Ref. *Ieffwates 8/e, p190*

The HSG shown-shows 2 parts of uterus-with single cervix. This could be a case of bicornuate uterus or septate uterus. Although both are difficult to differentiate on HSG-still there are a few ways by which they can be differentiated.



Now as seen in F1:- Angle between the 2 hours is more than  $60^\circ$ , hence it is an HSG of bicormate uterus.

F2. **Ans. is c, i.e. Septate uterus**

The image is a hysteroscopic view of uterine cavity. As seen, the uterine cavity is divided into 2 by a septa, hence it is a hyperoscopic view of septate uterus.

F3. **Ans. is b, i.e. Bifid clitoric**

Ref:- *Ieffcoates 8/e, page 198*

The genital tubercle is formed from two mesodermal bands which grows round from the dorsal aspect of the foetus in the 3<sup>rd</sup> week. These also provide for the musculature of the abdominal wall, musculature of the anterior wall of the bladder and urethra and pubic symphysis. Failure of these bands to develop properly or to fuse result in a **bifid clitoris**, ectopic vesicle, divarication of the foreparts of the labia maiora, absence of hair bearing skin of the pubes and a split pelvis.

F4. **Ans. is c, i.e. Arcuate uterus**

Ref *Ieffcoates 8/e page 186*

Arcuate uterus is a flat topped uterus as seen in the HSG. Here the fundal bulge fails to develop after fusion of the ducts. The fundal myometrium is extremely thin in this case.

## ANSWERS

1. **Ans. is d, i.e. USG**

Ref. *Williams Gynae 1<sup>st</sup>/ed p 417; Leon speroff 8<sup>th</sup>/ed p 147*

IOC for uterine anomalies = MRI or 3D USG

Gold standard is = Laparoscopy

*"Today, vaginal USG, especially three dimensional ultrasound, sonohysterography and MRI are highly accurate. HSG alone can yield inaccurate result due to failure to perfuse both uterine horns on either side of a midline division and cannot reliably distinguish between bicornuate and septate uterus"*

– Leon Speroff 8<sup>th</sup>/ed p 147

2. **Ans. is d, i.e. Habitual abortion**

Ref. *Munrokers Operative Obstetrics 10<sup>th</sup>/ed p 192-193; Jeffcoate 7<sup>th</sup>/ed p 204; Williams Gynae 1<sup>st</sup>/ed p 418*

**Management:** Bicornuate uterus requires surgical treatment only when it causes habitual abortions.<sup>Q</sup>

*"When a bicornuate or septate uterus has caused not less than 3 miscarriages and no pregnancy has resulted in a viable child, surgery may be indicated."*

– Jeffcoate 7<sup>th</sup>/ed p 204

*"Surgical reconstruction of the bicornuate uterus has been advocated in women with multiple spontaneous abortions and in whom no other causative factors are identified."*

– William Gynae 1<sup>st</sup>/ed p 418

**Surgery done is:** Unification surgery (Strassman) where an incision is made over the uterus and the 2 horns are sutured together to form a single cavity.

**After such a surgery:** if woman conceives she should be taken up for elective LSCS at 38 weeks of gestation.<sup>Q</sup> These days hysteroscopic metroplasty is being done.

3. **Ans. is a, i.e. Uterine atresia**

Ref. *Shaw 15<sup>th</sup>/ed p 95; Williams Gynae 1<sup>st</sup>/ed p 416*

Vaginal atresia is associated with uterine atresia and syndrome is called as *Mayer Rokitansky Kuster Hauser syndrome* (for details, see the preceding text).

4. **Ans. is d, i.e. Before marriage**

Ref. Shaw 15<sup>th</sup>/ed p 96

- Repair of vaginal agenesis (seen in testicular feminization syndrome and Mayer Rokitansky-Kuster Hauser syndrome) is done by vaginoplasty.
- Vaginoplasty should only be performed when the girl is just married or about to be married.

**Techniques:**

- Construction of artificial vagina by *Mc Indoe operation* (procedure of choice).
- *Williams vaginoplasty* – creates a pouch out of labia majora dissection.
- Amnionvaginoplasty.

5. **Ans. is b, i.e. Genital ridge**

Ref. Dutta Gynae 5<sup>th</sup>/ed p 38

Male and female derivatives of embryonic urogenital structures.

Part of female genital system	Originates from
Ovary	Genital ridge
Fallopian tubes	Mullerian/paramesonephric duct
Uterus	
Cervix	
Upper part of vagina	Urogenital Sinus
Lower part of vagina	

6. **Ans. is a, b, c and e, i.e. USG; Uterine sound; Hysteroscopy; and Laparoscopy**

Ref. Jeffcoate 7<sup>th</sup>/ed p 203; Williams Gynae 1<sup>st</sup>/ed p 418

Friends here it is first important to understand that septate uterus is confused with bicornuate uterus.

*In septate uterus, after lateral fusion of Mullerian ducts, their is failure of their medial segments to regress which creates a permanent septum within the uterine cavity. The septum passes down from the uterine fundus. The fundus is normal in appearance.*

In bicornuate uterus, the 2 halves of Mullerian duct do not fuse and there is defect in fusion of fundus as well.

So, both these conditions are different.

**Septate uterus can be distinguished:**

**Clinically by:**

- *P/V examination* - Septate vagina and 2 cervix may be felt.
- *By passing a sound.*

**Investigations:**

- **HSG:** HSG is mainly preferred in uterine anomalies but it cannot distinguish between a septate and bicornuate uterus. This is because in order to distinguish between the 2, uterine fundus should be visible.
- **Transvaginal USG:** It is the best method to distinguish between a septate and bicornuate uterus. As it reveals the shape of the fundal contour.   
– Williams Gynae 1<sup>st</sup>/ed p 418
- **Hysteroscopy:** It is both diagnostic and curative.
- **MRI:** Expensive technique but provides the most accurate diagnosis.
- **Sonohysterography** (involves transvaginal ultrasound during or after introduction of sterile saline).  
It can also distinguish between a septate and bicornuate uterus by revealing both the double uterine cavity and the shape of fundal contour.

Laparoscopy and laparotomy (per se) may fail to reveal septate uterus.

– Jeffcoate 7<sup>th</sup>/ed p 203

This is quite obvious as outward appearance of a septate uterus is normal but-

*“When presumptive diagnosis is a septate uterus, laparoscopy is indicated for a definitive diagnosis and before hysteroscopic resection of the septum is initiated.”*

– Williams Gynae 1<sup>st</sup>/ed p 418

It is done to confirm that septate uterus is actually a septate and not a bicornuate uterus.

So, after reading the text from *Williams Gynae*. - I am including laparoscopy also in the correct options.

7. **Ans. most probably d, i.e. Septate**

Ref. CGDT 10<sup>th</sup>/ed, p 550; *Clinical Gynecological endocrinology & Infertility* by Leon Speroff 7<sup>th</sup>/ed p 132

Sorry for this one friends, 2 very reliable textbooks quote different incidences of different malformations.

According to CGDT 10<sup>th</sup>/ed p 550

Leon Speroff 7<sup>th</sup>/ed p 132

Anomaly	Percentage	Anomaly	Percentage
Bicornuate uterus	37%	Septate uterus	35%
Arcuate uterus	15%	Bicornuate uterus	26%
Incomplete septum	13%	Arcuate uterus	18%
Uterus didelphys	11%	Unicornuate uterus	10%
Complete septum	9%	Uterus didelphys	8%
Unicornuate uterus	4%		

8. **Ans. is a, i.e. External os**

Ref. Williams Gynae 1<sup>st</sup>/ed p 413

If there is a disorder in fusion of downgrowing Mullerian duct and upgrowing derivative of urogenital sinus, it results in transverse vaginal septum which causes imperforate vagina (or vaginal agenesis).

In a series reported:

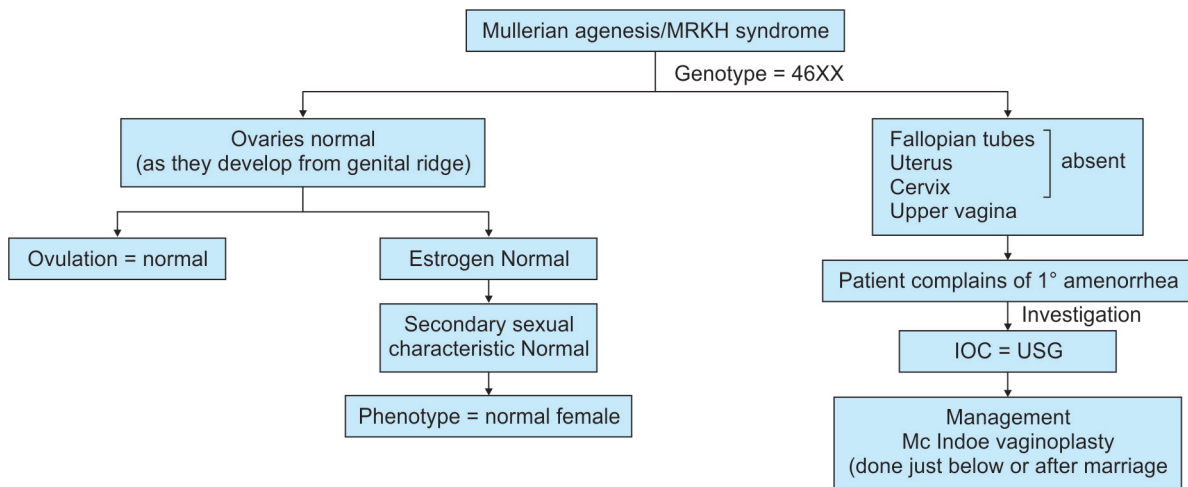
- 46% septa were located in upper part.<sup>Q</sup>
- 40% septa were located in middle part.<sup>Q</sup>
- 14% septa were located in lower part.<sup>Q</sup>

The upper part corresponds to external os, therefore it is the option of choice. For further details on transverse vaginal septum see the preceding text.

9. **Ans. is d, i.e. Ovarian agenesis**

10. **Ans. is a, c and d, i.e. Absent uterus; Absent vagina and XX phenotype**

Ref. Jeffcoate 7<sup>th</sup>/ed p 197-198; Shaw 15<sup>th</sup>/ed p 95-96; COGDT 10<sup>th</sup>/ed p 549; Williams Gynae 1<sup>st</sup>/ed p 416



In question 12 answer is c, i.e. vaginal atresia, I know some of you might be thinking option 'b', i.e. absent fallopian tubes is also correct.

Now to understand why this option is not absolutely correct lets go back to the development of mullerian ducts.

Mullerian ducts grow downward, therefore there will be cases where there will be well formed abdominal ostia associated with hypoplasia or absence of the remainder of the tubes, uterus and vagina or the tubes and uterus may be present and the vagina absent.

The converse is not true as the ducts grow downwards, so vaginal atresia has to be present always in MRKH syndrome.

The answer is further supported by the following lines from William Gynae.

*"Typically, a portion of the distal fallopian tube are present".*

11. **Ans is c, i.e. Anovulation**

12. **Ans is c, i.e. Vaginal atresia**

13. **Ans is a, i.e. Ovaries**

14. **Ans. is b, i.e. Uterus absent, fallopian tube and ovaries present**

Ref. Shaw 15<sup>th</sup>/ed p 95; Jeffcoate 7<sup>th</sup>/ed p 196

Friends here do not get confused - Ovaries are always normal in case of MRKH.

Theoretically uterus, vagina, and tubes are not found in case of MRKH, but some part of tubes (distal 1/3) is always seen practically.

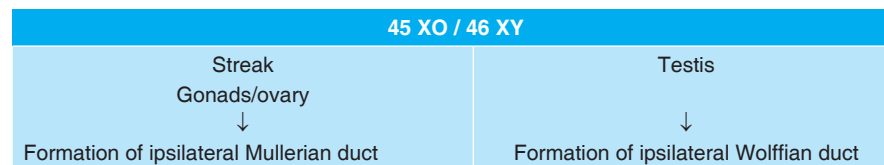
**15. Ans. is b, i.e. FSH receptor mutation**

*Ref. Leon speroff 7<sup>th</sup>/ed pp 344, 348, 8<sup>th</sup>/ed pp 342, 347, 365*

**Antimullerian hormone deficiency = persistent mullerian duct syndrome = uterine hernia syndrome**

- Karyotype is 46 XY
- Since Y chromosome is present gonads are testis, i.e. they are males. In this syndrome, in males – sertoli cells fail to secrete Mullerian inhibiting substance and Mullerian duct is present.
- Since Leyding cell are also present, they secrete testosterone normally, thus Wolffian duct is also present. So in anti-Mullerian hormone deficiency both mullerian and wolffian ducts are present.
- **Ovotestis:** It is seen in true hermaphroditism. Both ovaries and testis are present. There is ambiguity of external genitalia. The internal structures depend on the degree of differentiation of the gonads.
- **Mixed Gonadal dysgenesis** Karyotype = 45XO/46XY.
- In this situation, the gonadal pattern on one side is streak gonad ovary (corresponding to karyotype 45 XO) and a normal testis on the other side (corresponding to karyotype 46 XY)

Mullerian duct and Wolffian duct development correlates with the character of ipsilateral gonad, i.e.



Thus, both Mullerian duct and wolffian ducts are present

**In case of FSH receptor mutation in females**, Mullerian ducts develop normally, the problem is in the binding of FSH to its receptors. The patient presents with primary or early secondary amenorrhea, variable development of secondary sexual characters and high levels of FSH and LH. Thus here only mullerian duct would be present as the karyotype of females is normal i.e. 46(XX). So, answer to our question is FSH receptor mutation.

**16. Ans. is a, i.e. Endoderm of urogenital sinus**

*Ref. Dutta Gyane 6<sup>th</sup>/ed p 37*

**Vagina is developed mainly from the Müllerian ducts and partly from the urogenital sinus.**

Upper three-fifth above the hymen develop from the fused uterovaginal canal of the Müllerian ducts.

- Mucous membrane is developed from the endoderm of the canalized (vaginal plate) sinova-ginal bulb (urogenital sinus).
- The musculature is developed from the mesoderm of the fused caudal vertical part of the Müllerian ducts.
- The hymen is developed from the junction of the Müllerian tubercle (mesodermal) and the urogenital sinus (endodermal).

Lower one-fifth below the hymen is developed entirely from the endoderm of the urogenital sinus.

Vaginal introitus is developed from the ectoderm of the genital folds after rupture of the bilaminar urogenital membrane.

**17. Ans is a, i.e. Uterus didelphys**

**18. Ans is b, i.e. Incomplete fusion of paramesonephric duct**

**19. Ans is a, i.e. Two uterine cavity with cervix**

*Ref. Shaw 14<sup>th</sup>/ed p 85; Jeffcoate 7<sup>th</sup>/ed p 199; Williams Gynae 1<sup>st</sup>/ed p 417*

See the text for explanation.

**20. Ans. is a, i.e. Short arm of Y chromosome**

*Ref. Textbook of Gynae, Shiela Balakrishnan 1<sup>st</sup>/ed p 78*

SRY region, i.e. sex determining region or testicular determining factor is present on short arm of Y chromosome.

**21. Ans. is c, i.e. Epoothoron and caudal end of wolffian duct**

Epoothoron is cranial end of wolffian duct and not caudal.

**22. Ans. is d, i.e. Gartner's duct**

*Ref. Dutta Gynae 5<sup>th</sup>/ed p 38*

Gartner's duct is a remnant of Wolffian duct (mesonephric duct) in females and not paramesonephric duct.

**23. Ans. is a, i.e. Renal anomalies**

*Ref. Jeffcoate 7<sup>th</sup>/ed p 202*

Diethylstilbesterol exposure *in utero* leads to varied anomalies of female genital tract.

But remember simply:

*"Unlike all other congenital uterine malformations, the DES uterus is not associated with an increase in renal anomalies."*

*– Jeffcoate 7<sup>th</sup>/ed p 202*

Even if you don't remember all the anomalies caused by DES, just remember the above line and your MCQ will be solved. For anomalies caused by DES-see the proceeding text.

24. Ans. is c, i.e. Presence of rugosities of overlying vaginal mucos

Ref: Dutta Gynae 6<sup>th</sup>/ed p 210

**Gartner's cyst** – are cysts of the remnants of Wolffian duct.

M/C location = Anterolateral aspect of vagina and hence are often confused with cystocele.

**Features of Gartner's cyst are:**

Upper three-fifth above the hymen develop from the fused uterovaginal canal of the Müllerian ducts.

- Rugosities of the overlying vaginal mucosa are lost.
- Vaginal mucosa over it becomes tense and shiny.
- Margins are well defined.
- Not reducible.
- No impulse on coughing.

25. Ans. is d, i.e. WNT-4

Ref: Langman embryology 12/e, pg. 46-247

Genes for male development

SRY gene	Master Gene for testis development
SOX 9	SRY & SOX 9 induce testis to form FGF-9 (chemotactic factor) FGF-9 causes tubules from mesonepric duct to penetrate gonadal ridge
SF1 (steroidgenens factor)	It stimulates differentiation of sertole or leydig cells

WNT-4 is ovary determining gene. This gene upregulates DAXI-which inhibits the fraction of SOX 9 in females.

26. Ans. is b, i.e. Unicornuate

Ref: Leon speroff 8/e, page 146

*"Approximately 40% of patients with a unicornuate uterus will have a urinary tract anomaly (usually of kidney)*

Leon speroff 8/e, page 146.

27. Ans. is c, i.e. Septate

Ref: Jefferates 8/e, page. 188

*"The only form of malfusion deformity which may lower fertility significantly is a fully septate vagina."*

Jefferates, 8/e, page 188.

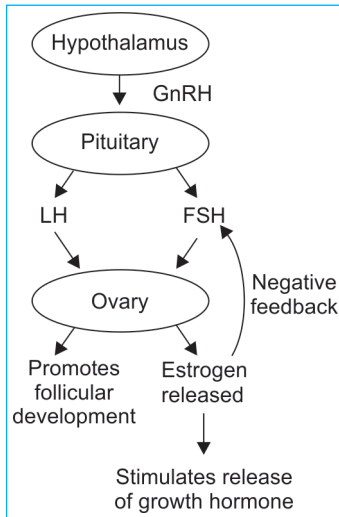
*"Septate anomaly is the anomaly most highly associated with reproductive failure and obstertcial complications including first and second trimester miscarriage, preterm delivery, fetal malpresentation, IUGR and infertility.*

Leon spercoff 8/e, page 1172

# CHAPTER

# 6

## Sexuality and Intersexuality



GH and sex steroids together initiate somatic and sexual growth.

**Estrogen is mainly** responsible for breast growth and increase in height in females.  
**Development of pubic hair and axillary hair in girls also requires androgen secretion.**

**Delayed puberty** is said to occur when there is no breast development by the age of 14 and no menarche by the age of 16.

### Puberty

Normally there is a negative feedback on the hypothalamus in childhood. With the onset of puberty, this negative feedback is removed and there is a significant increase in the amplitude of pulsatile release of GnRH by the hypothalamus leading to puberty.

➤ Age of puberty in girls – 8 to 13.5 years.



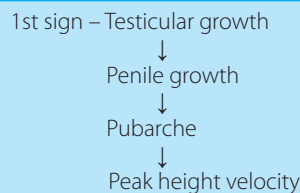
#### Sequence of puberty in girls.

- G = accelerated **g**rowth or growth spurt (1st sign)
- T = **b**reast budding/**T**helarche (1st visible sign of puberty)
- P = Development of **p**ubic hair—Pubarche
- H = Increase in **h**eight/peak growth velocity attained
- Menarche = Menstruation

#### GTPH in males.

- On an average, the entire time taken for puberty is 4.6 years.
- Menarche occurs 2.6 years after onset of puberty.

#### In males – Sequence of puberty



- In girls development of breast and pubic hair occurs in 5 stages as described by tanner, called as **Tanner staging** for breast and pubic hair development.

**Note:** There is no need to know complete Tanner staging, so just remember:

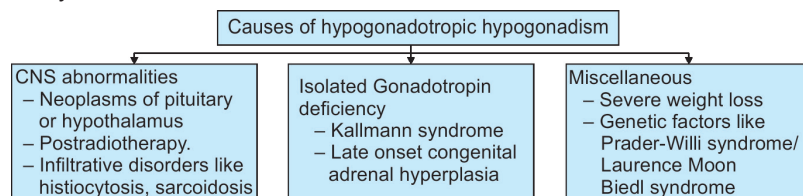
Tanner stages 1 and 2 → refer to initial stage of breast development/less developed breast or pubic hair.  
Tanner stages 4 and 5 — refer to advanced stages of breast and pubic hair development or fully developed breast and pubic hair.

### Delayed Puberty

Delayed puberty is said to occur when there is **no breast development by the age of 14 and no menarche by the age of 16.**

#### Causes of Delayed Puberty

1. **Constitutional delay** (M/c cause of delayed puberty in boys and overall M/c cause of delayed puberty).
2. **Hypogonadotropic hypogonadism:** Defect is at the level of hypothalamus or pituitary. FSH level low < 10 m IU/ml.



DOC for treating **hypogonadotropic** hypogonadism = Oestrogen/(ethinyl estradiol) in order to promote breast development and somatic growth.

3. **Hypergonadotropic Hypogonadism**

- Defect lies at the level of ovary.
- There is sexual infantilism and FSH levels are elevated (as the negative feedback on FSH by estrogen decreases). Levels of FSH > 30 m IU/ml.

**Causes:**

- Turner syndrome (40 XO)
- Pure gonadal dysgenesis 46 XX, 46 XY
- Ovarian failure
  - Infections like mumps or tuberculosis of ovary
  - Iatrogenic (post-surgery/radiotherapy)
  - Sweyer syndrome
  - Primary ovarian failure

M/c cause of primary amenorrhea and delayed puberty in females – Turner Syndrome

**Turner Syndrome**

**Genotype:** *Most common* = 45 XO<sup>Q</sup> (Loss of one X chromosome is due to Non-dysjunction during meiosis<sup>Q</sup>, the X chromosome retained is *maternal in origin*<sup>Q</sup> in most cases).

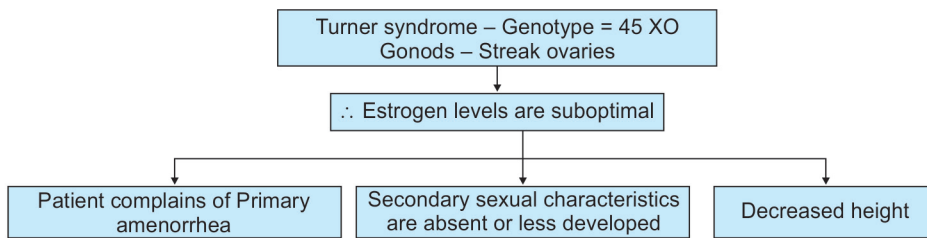
**Mosaics** = 45 XO/46 XX or 45 XO/46 XY

- **Gonads:** *B/L Streak Gonads*.<sup>Q</sup> (since one single X chromosome is present, so ovaries are not properly formed).

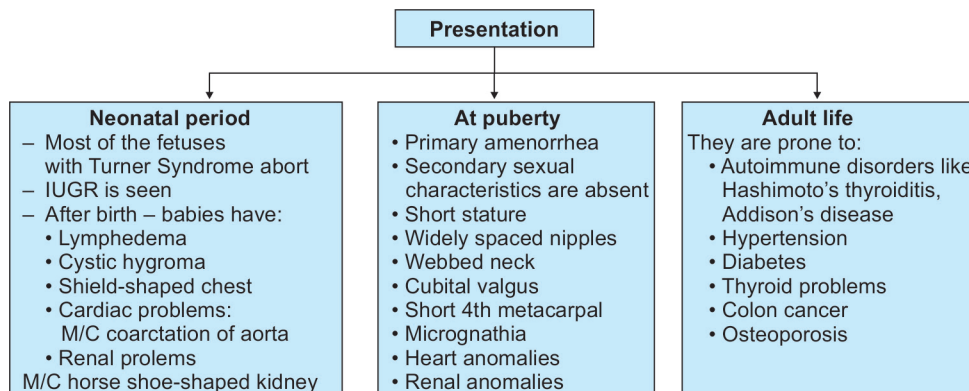
**Kallmann syndrome**  
Also k/a de Morsier syndrome:

- It is a triad of hypogonadism, anosmia and color blindness.
- May be associated with midline defects like cleft lip and palate, cerebellar ataxia and nerve deafness.
- Defect in Kallmann's syndrome is at the level of hypothalamus – (**arcuate nucleus**) which cannot secrete GnRH
- Differentiating feature between Kallmann syndrome and constitutional delay is in constitutional delay, height is short, whereas in Kallmann syndrome, normal height is seen.

Turner syndrome is the most common chromosomal disorder in humans.<sup>Q</sup>



- Since Fallopian Tube/Uterus/Cervix and Vagina develop from mullerian duct, so all these internal genitalia are present but their proper growth requires estrogen stimulation; therefore, they will remain infantile
- Similarly, external genitalia in females are formed due to absence of testosterone (estrogen has no role); so they will be normal.





### Syndromes associated with delayed puberty–

- **Prader-Willi syndrome –**  
An autosomal deletion and imprinting disorder associated with obesity. Emotional instability and delayed puberty due to hypothalamic dysfunction.
- **Laurence-Moon-Biedl syndrome:** Hypothalamic amenorrhea + mental retardation + polydactyly + retinitis pigmentosa.
- **Frohlich syndrome**  
- hypo gonadotropic hypogonadism (delayed puberty) + obesity + genital hypoplasia.
- **Swyer syndrome (46 XY) –** Also leads to delayed puberty. It is caused by mutation or structural abnormality of Y chromosome. Patients have normal to tall stature

**Note:** Intelligence is normal in patients of Turners syndrome  
Management = Estrogen replacement therapy.

Due to the potential risk of endometrial cancer with estrogen therapy, progesterone is given along with estrogen.

### Also know:

#### Male Turner Syndrome – Noonan syndrome:

- Autosomal dominant disorder<sup>o</sup>.
- Streak Gonads<sup>o</sup>.
- 46XY Karyotype<sup>o</sup>.
- Develop autoimmune thyroiditis<sup>o</sup>.
- Somatic defects resemble Turner Syndrome<sup>o</sup>.

#### Exceptions:

- Characteristic cardiac lesion is Pulmonary valve stenosis<sup>o</sup>.
- Mental Retardation present (Absent in Turner)<sup>o</sup>.

### An Overview of Causes of Delayed Puberty

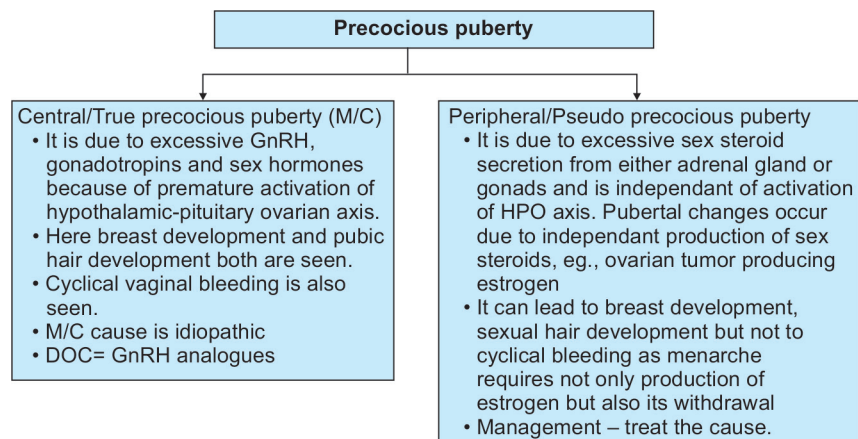
FSH Level	Differential Diagnosis
High > 30 mIU/mL	<ul style="list-style-type: none"> <li>• Gonadal dysgenesis syndromes: Turner syndrome, Swyer syndrome</li> <li>• Primary ovarian failure</li> </ul>
Low < 10 mIU/mL	<ul style="list-style-type: none"> <li>• Constitutional delay</li> <li>• Intracranial neoplasms</li> <li>• Isolated gonadotropin deficiencies</li> <li>• Hormone deficiencies</li> <li>• Kallmann's syndrome</li> <li>• Prader-Willi syndrome</li> <li>• Laurence-Moon-Biedl syndrome</li> <li>• Chronic disease and malnutrition</li> </ul>
Normal	<ul style="list-style-type: none"> <li>• <i>Anatomic deformities</i> result in normal development with primary amenorrhea</li> <li>• Imperforate hymen</li> <li>• Transverse vaginal septum</li> <li>• Mullerian agenesis</li> </ul>



**Precocious puberty** – is onset of menstruation before the age of 10 years or appearance of breast budding before the age of 8 years in females.

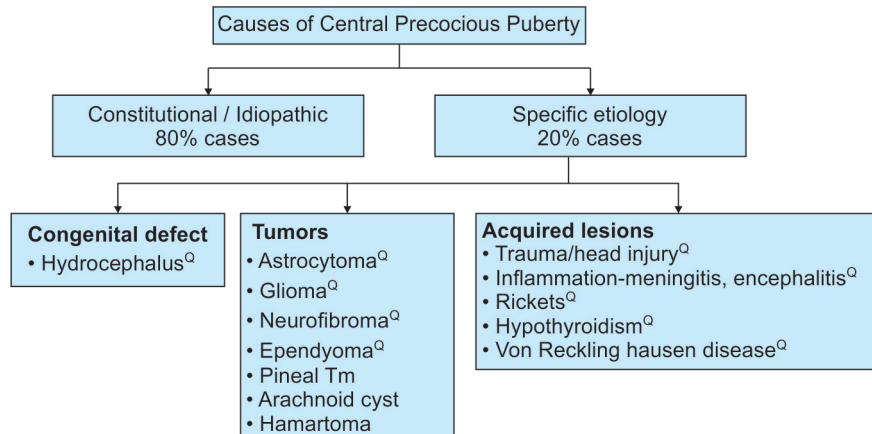
**In males** – if puberty occurs before 9 years — it is precocious.

### Precocious Puberty





### Causes of Central Precocious Puberty



The pathophysiology of central precocious puberty is unclear but most lesions are associated with increased intracranial pressure and are located in the region of hypothalamus.

**?** M/C cause of precocious puberty in females is constitutional/Idiopathic

**Also Know**  
**Causes of Hetrosexual virilizing puberty**  
 i. e virilization/features of masculinization seen at puberty

- PCOS
- Adrenal /ovarian tumor
- Late onset congenital adrenal hyperplasia
- Cushing syndrome – 5- $\alpha$  reductase deficiency

### Causes of Peripheral Precocious Puberty

Here hypothalamic pituitary ovarian axis is intact

#### Isosexual

- A. Ovarian causes
  - Granulosa cell Tm<sup>o</sup>
  - Theca cell Tm<sup>o</sup>
- B. Adrenal cause
  - Feminizing adrenal neoplasia<sup>o</sup> (generally adrenal causes lead to heterosexual puberty)
- C. Ectopic Gonadotropin production
  - Dysgerminoma<sup>o</sup>
  - Choriocarcinoma<sup>o</sup>
  - Hepatoblastoma<sup>o</sup> } Secrete HCG
- D. Exogenous estrogen
  - In the form of OCP's
  - Corticosteroid intake
- E. McCune-Albright syndrome

#### Heterosexual

- Congenital adrenal hyperplasia<sup>o</sup>
- Ovarian/adrenal testosterone<sup>o</sup> secreting tumors<sup>o</sup>:
  - Androblastoma<sup>o</sup>
  - Hilus cell Tm<sup>o</sup>
  - Gynandroblastoma<sup>o</sup>
  - Lipoid cell tumors<sup>o</sup>
- Exogenous androgen<sup>o</sup>

**McCune-Albright Syndrome:**  
 The McCune-Albright syndrome is characterized by the classic triad polyostotic dysplasia of bone, irregular café au lait spots on skin and GnRH-independent sexual precocity

### Ambiguous Genitalia

Males	Females
Ambiguous genitalia is due to androgen insensitivity or decreased androgen levels.	Ambiguous genitalia is due to exposure to an increased androgen levels in intrauterine life.
E.g. • M/c cause: Testicular feminisation syndrome • 5-alpha reductase deficiency • Congenital lipid adrenal hyperplasia.	M/c cause: Congenital adrenal hyperplasia • Cushing's disease • Maternal ovarian androgen secreting tumours • Aromatase deficiency • Maternal drug intake (Testosterone, Danazol)

### True Hermaphroditism<sup>o</sup>

Individuals with this disorder have both ovarian and testicular tissue, most commonly as composite ovotestes but occasionally with an ovary on one side and testis on the other.

## Pseudohermaphroditism<sup>Q</sup>

The genetic sex indicates one sex whereas the external genitalia has characteristics of the other.

### Female Pseudohermaphroditism

Genetic females (gonads ovaries) with masculinized external genitalia manifesting as – clitoral hypertrophy<sup>Q</sup> and some degrees of fusion of urogenital or labioscrotal folds, e.g. as in congenital adrenal hyperplasia.

### Male Pseudohermaphroditism

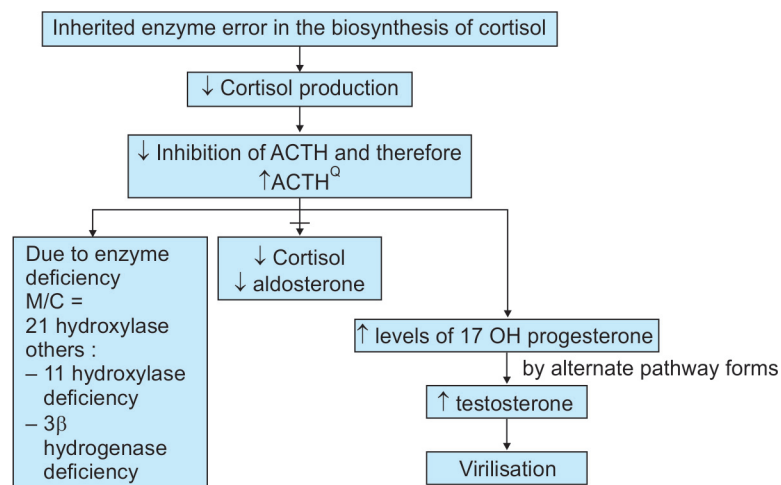
Genetic males (Gonads testis) with feminized external genitalia manifesting as hypospadias, or incomplete fusion of the urogenital or labioscrotal folds, e.g. Testicular feminizing syndrome.

## Congenital Adrenal Hyperplasia (Very Important)

**In a female most common cause of ambiguous sex is congenital adrenal hyperplasia.**

- Infact cases of ambiguity of sex, detected at birth are due to adrenogenital syndrome (congenital adrenal hyperplasia) unless proved otherwise.
- It is an autosomal recessive<sup>Q</sup> disorder (if any couple has had one affected child, subsequent baby has 1 in 4 chance of having the same disability).

### Pathology



Congenital adrenal hyperplasia is the M/c cause of ambiguous genitalia in females.



M/c enzyme deficiency in CAH is 21 hydroxylase deficiency.



Ambiguous genitalia with no palpable gonad and XX karyotype – CAH most likely and parents can be told that child is female.

A point worth nothing is that development of the internal genitalia (i.e mullerian duct and its derivatives) is normal in females with classical CAH because the excess androgen is derived from adrenals and the ovaries are normal so they produce neither antimullerian hormone nor significant amount of androgen.

### Physical Characteristics in Females

- Genotype = 46XX<sup>Q</sup>.
- Gonads = ovaries<sup>Q</sup>.
- Uterus and vagina are present, as mullerian duct develops normally, but remain infantile therefore failure to menstruate<sup>Q</sup>.
- Vulva and introitus are affected. There is clitoromegaly<sup>Q</sup> and the genital folds fuse to form penile urethra rather than labia minora.<sup>Q</sup> Labia majora are fused which appears like scrotum.

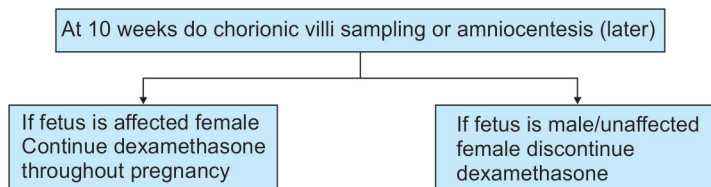
- Heterosexual precocious puberty<sup>Q</sup>: Pubic hair and axillary hair appear and voice deepens by the age of 2-4 years<sup>Q</sup>. (since these characteristics are dependant on androgen).
- Associated metabolic abnormalities (d/t decreased aldosterone): Hyponatremia<sup>Q</sup>, hyperkalemia<sup>Q</sup> and hypotension<sup>Q</sup>.

### Investigation

- **USG**: shows presence of uterus, vagina, fallopian tubes and ovaries<sup>Q</sup>. (Thus, all patients are potentially fertile)
- **Sex chromatin study**: shows positive Barr body<sup>Q</sup>. (Note: whenever a child presents with ambiguous genitalia always do karyotyping)
- Serum 17 hydroxy progesterone is elevated ( $> 800\text{ng/dl}$ )<sup>Q</sup> and serum 17-ketosteroid is elevated.
- Level of serum 17OHP  $< 200\text{ ng/dl}$  virtually rules out the diagnosis of CAH.
- Serum electrolyte studies show salt wasting<sup>Q</sup>.

### Treatment

- Treatment of CAH is aimed at providing sufficient amounts of the deficient hormone, cortisol, to reduce excessive ACTH secretion and to prevent consequences of excessive androgen production.
- DOC is dexamethasone in mothers at risk for having an affected child.
- Dexamethasone should be given to prevent fetal female genital virilisation as dexamethasone is not metabolized by placenta and crosses effectively into fetal circulation.
- Level of serum 17OHP  $< 200\text{ ng/dl}$ , virtually rules out the diagnosis of CAH.
- For maximum benefit-treatment should begin at 4 to 5 weeks of gestation and not later than 8 weeks



- In younger infants the initial dose of dexamethasone is about 25mg/day, and in adults 100mg/day
- In newborn with CAH with defect in electrolyte regulation, it is usually necessary to administer NaCl in amounts of 4-6 gm/day either orally or parenterally in addition to cortisone.

**Besides this:** – Phallus should be removed surgically (*by age of 5 years*).  
– Mc Indoe's vaginoplasty should be done.

### Testicular Feminization Syndrome

- Most common form of male pseudohermaphroditism
- **Genotype** 46XY<sup>Q</sup> so *gonads will be testis*. The testis are intra abdominal<sup>Q</sup>

### Pathology

There is resistance to androgen.



#### Nonclassical or late onset CAH-

There is no genital ambiguity at birth and usual presentation is androgen excess at puberty – Differential diagnoses PCOD



**Note:** Latest recommendations are: Prenatal treatment poses risks like postnatal failure to thrive and psychomotor developmental delay, hence best approach is early prenatal diagnosis by chorionic villi sampling with rapid sex determination (FISH for the X and Y chromosome) and genotyping. Treatment should be given to only those mothers with an affected female child.



Most common form of male pseudohermaphroditism is Testicular Feminisation syndrome



Partial insensitivity to androgens is called as Reifenstein syndrome

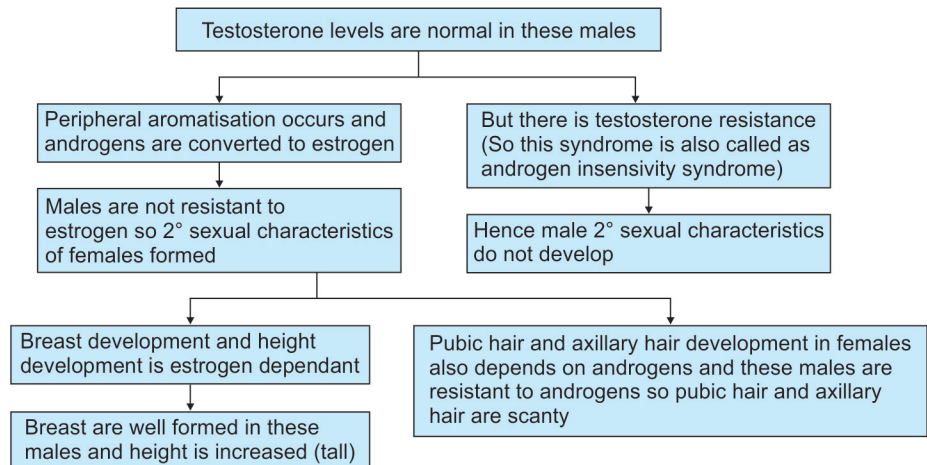


**Testicular Feminization syndrome and Mullerian agenesis are differential diagnosis of each other.**

In both these conditions – a female (phenotypically) presents with:  
 > Primary amenorrhoea  
 > Normal breast development  
 > Absent uterus.  
 The best test to differentiate between them is –  
 Karyotyping/ presence or absence of Barr body.  
 In Mullerian agenesis –  
 Karyotype = 46 XX  
 Barr body = Present  
 In testicular feminization syndrome -  
 Karyotype = 46 XY  
 Barr body = Absent



In Testicular feminizing syndrome patients, uterus is absent and hence no risk of developing endometrial cancer thus with oestrogen no need to add progestin.



- Since mullerian inhibiting factor is 'normal' in these males mullerian duct regresses so uterus, cervix and vagina are not present and obviously they will not menstruate. These males who are being reared up like females, at puberty have proper breast development and are brought with complain of primary amenorrhea.

### Physical Characteristics

- > *The male baby who is reared like a girl grows tall and attractive with normal breast development (Tanner stage 4)*<sup>Q</sup>
- > No uterus (therefore **Primary amenorrhea**)<sup>Q</sup> and a short vagina
- > **Scanty pubic and axillary hair**<sup>Q</sup>
- > Smooth and hairless skin<sup>Q</sup>
- D/D = Mayer Rokitansky Arsky Kuster Hauser-Syndrome (Mullerian agenesis)**
- Lab investigation:** To distinguish it from Mayer Rokitansky Kuster Hauser syndrome do karyotyping.
- > Testosterone levels can be low, normal or high
- > LH level is high due to insensitivity of pituitary and hypothalamus to testosterone.<sup>Q</sup>
- > Gonadal biopsy can confirm the diagnosis.

#### Findings in Gonadal Biopsy:

- o Seminiferous tubules are small and hyalinized.
- o Spermatogenesis is absent.
- o Leydig cells and sertoli cells are normal.

### Management

#### Let them be Females

- > The testis should be removed after puberty<sup>Q</sup> (16-18 years) as they have a high potential for malignant change, specially gonadoblastoma and dysgerminoma.<sup>Q</sup>
- > Bilateral laparoscopic gonadectomy is the preferred procedure for removal of intra-abdominal testes.<sup>Q</sup>
- > Estrogen therapy is desirable to prevent osteoporosis.<sup>Q</sup> since when testis are removed the source of testosterone and in turn estrogens is also gone.
- > Vaginoplasty should be done just before or after marriage.<sup>Q</sup>

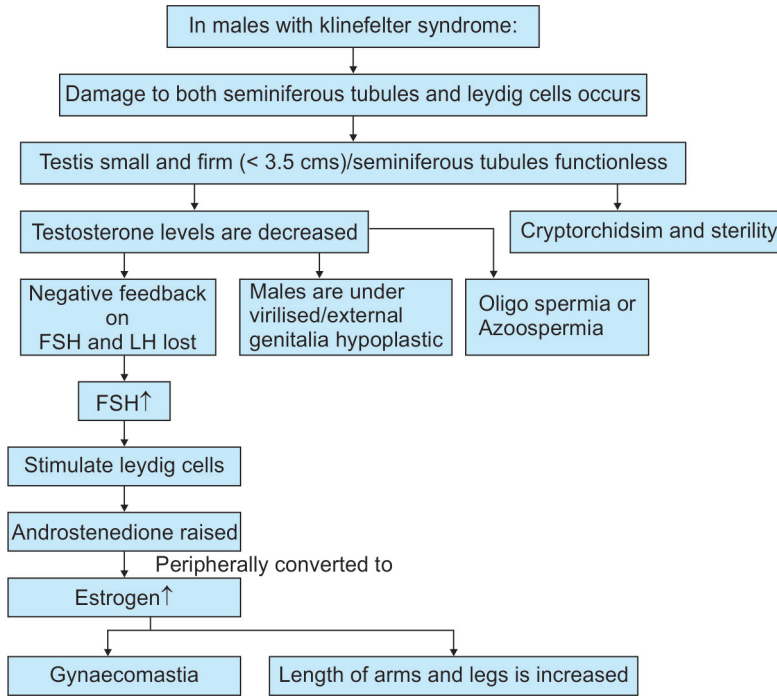
### Klinefelter Syndrome (47XXY)

#### Pathophysiology

- > The classic form of Klinefelter syndrome (47XXY) occurs following meiotic nondisjunction of the sex chromosomes during gametogenesis (40% during spermatogenesis, 60% during oogenesis)

## Clinical Features

- Klinefelter syndrome (KS) is the M/C cause of primary testicular failure affecting 1 in 1000 males



Klinefelter patients are infertile but not impotent.

**In addition to these, men with KS exhibit a number of psychosocial abnormalities like:**

- Lack of insight
- Poor judgement
- Difficulty with complex speech
- Decreased attention span

**In adult life, such males have increased risk of:**

- Pulmonary diseases
- Breast CA
- Mediastinal germ cell tumor
- Varicose legs
- SLE
- Diabetes mellitus
- antisocial mental disorder

## Diagnosis

Testicular biopsy shows hyalinised seminiferous tubules and hyperplastic leydig cells.

Pituitary hormones (FSH, LH) are increased and testosterone levels are reduced

## Management

Give testosterone

## QUESTIONS

1. The sequence of development of puberty in girls is:
  - a. Thelarche, Pubarche, Menarche (AI 00)
  - b. Pubarche, Thelarche, Menarche
  - c. Pubarche, Menarche, Thelarche
  - d. Menarche, Thelarche, Pubarche
2. The first sign of puberty in girls is: (AI 08)
  - a. Breast budding
  - b. Peak height velocity
  - c. Menarche
  - d. Pubic and axillary hair growth
3. Which of the following pubertal events in girls is not estrogen dependant?
  - a. Menstruation
  - b. Vaginal cornification
  - c. Height spurt
  - d. Hair growth
4. Which of the following is responsible for pubertal growth in females? (AIIMS May 2014)
  - a. Decreased level of adrenal androgens at puberty
  - b. High level of estrogen at puberty
  - c. Pulsatile release of GnRH during sleep
  - d. Increased sensitivity of HPO axis to estrogen
5. One of the following forms the basis for sex chromatin testing: (AIIMS May 2014)
  - a. Barr body
  - b. Testosterone receptors
  - c. Hormone levels
  - d. Phenotypic features
6. A 9-year-old girl presents with menarche. History reveals thelarche at the age of 7 years and adrenarche at the age of 8 years- the M/C cause of this condition in girls is:
  - a. Idiopathic
  - b. Gonadal tumor
  - c. McCune Albright syndrome
  - d. Hypothyroidism
7. Medication used in treatment of idiopathic precocious puberty is:
  - a. Exogenous gonadotrophins
  - b. Ethinyl estradiol
  - c. GnRH analogues
  - d. Ethinyl estradiol
8. Gynaecomastia is seen in: (PGI June 07, Dec. 02)
  - a. Secondary syphilis
  - b. Lepromatous leprosy
  - c. HIV
  - d. Klinefelter's syndrome
9. Gynaecomastia is seen in all of the following conditions except: (AI 2012)
  - a. Prolactinoma
  - b. TSH secreting adenoma
  - c. HCG secreting tumor
  - d. estrogen secreting tumor
10. During sexual differentiation in males: (Karnataka 05)
  - a. Leydig cells produce Mullerian Inhibiting Substance
  - b. Primitive Gonads differentiate into testis due to the presence of SRY gene
  - c. Androgen binding protein is responsible for the development of male external Genitalia
  - d. Wolffian duct regresses
11. Most common cause of ambiguous genitalia in a female child is: (AI 2011)
  - a. Placenta steroid sulfatase deficiency
  - b. Fetal aromatase deficiency
  - c. Wnt4 mutation
  - d. Congenital adrenal hyperplasia
12. Most common cause of female pseudohermaphroditism is: (AI 02)
  - a. Virilizing ovarian tumor
  - b. Ovarian dysgenesis
  - c. Exogenous androgen
  - d. Congenital adrenal hyperplasia
13. Female pseudohermaphroditism true is: (PGI Dec 04)
  - a. 46XX chromosomal pattern
  - b. Absent ovary
  - c. Absent uterus
  - d. Presence of testis
  - e. Clitoromegaly
14. The treatment for a case of virilizing adrenal hyperplasia is: (AI 06)
  - a. Estrogens
  - b. Antiandrogens
  - c. ACTH
  - d. Cortisone
15. Best prenatal treatment for CAH is: (AIIMS Nov 2011)
  - a. Dexamethasone
  - b. Betamethasone
  - c. Prednisolone
  - d. Hydrocortisone
16. A newborn with 46XX has external genitalia of male. All the following are the possible causes *except*:
  - a. Placental aromatase deficiency
  - b. Maternal androgen adrenal tumor
  - c. Anti mullerian hormone deficiency
  - d. Wnt 4 mutation
17. C/F of Turner's syndrome: (PGI Dec 06, 09)
  - a. Secondary amenorrhea
  - b. Edema of hands and feet
  - c. XO genotype
  - d. Mental retardation common
  - e. Streak ovaries
18. All are features of Turner's syndrome *except*: (PGI May 2013)
  - a. Karyotype is 46 XO
  - b. Normal breast
  - c. Underdeveloped uterus
  - d. Normal secondary sexual characters
  - e. Primary amenorrhoea

19. A girl presents with primary amenorrhea, short stature, widely spaced nipple. Karyotype of the girl would be: (AIIMS May 2013)
- 45 XO
  - 46 XXY
  - 46 xy
  - 46 xx
20. A 16-year-old girl with 58 inches present with primary amenorrhea and rising FSH. The histological finding most consistent with her conditions is: (AIIMS Nov 2013)
- Low oocyte in ovary
  - Corpus luteum hemorrhage
  - Marfan syndrome
  - Pituitary apoplexy
21. A 17-year-old girl with amenorrhea, atrophied breast, hypoplastic uterus: (AIIMS Nov 09)
- Turner's syndrome
  - Gonadal dysgenesis
  - Androgen insensitivity syndrome
  - Klinefelter's syndrome
22. A 15-year-old female presents with primary amenorrhea. Her breasts are Tanner 4 but she has no axillary or pubic hair. The most likely diagnosis is: (AI 06)
- Turner's syndrome
  - Mullerian agenesis
  - Testicular feminization syndrome
  - Premature ovarian failure
23. Androgen insensitivity syndrome true is: (AIIMS May 08)
- Phenotype may be completely female
  - Predominantly ovarian component in gonads
  - Always in female
  - Testes formed abnormally and receptors are normal
24. Which of the following statement is/are true regarding androgen insensitivity syndrome? (PGI Nov 2012)
- Absent vagina
  - Karyotype is XX
  - Karyotype is XY
  - Pubic hair is normally present
  - Breast development is normal
25. Regarding androgen insensitivity syndrome, which statement is/are true: (PGI May 2013)
- Genotype is 46 XX
  - Scanty pubic hair
  - Well developed female external genitalia
  - Uterus absent
  - Breast development is adequate
26. All are seen in testicular feminization syndrome *except*: (PGI June 99)
- 46XY
  - Primary amenorrhea
  - Short stature
  - Vagina may be present
27. A girl presents with; primary amenorrhea; grade V thelarche, grade II pubarche; no axillary hair; likely diagnosis is: (AI 01)
- Testicular feminisation syndrome
  - Mullerian agenesis
  - Turners syndrome
  - Gonadal dysgenesis
28. All of the following statements about Androgen Insensitivity Syndrome are true *except*: (AI 08)
- Patients have an XY genotype
  - Pubic hair are abundant
  - Short vagina may be present
  - Ovaries are absent
29. 16-year-old female presents with primary amenorrhoea with B/L inguinal hernia. She has normal sexual development with no pubic hair. USG shows no uterus and ovaries and a blind vagina. Diagnosis is: (AIIMS May 07)
- Turner's syndrome
  - Mullerian agenesis
  - STAR syndrome
  - Androgen insensitivity syndrome
30. Among the following which is a feature of testicular feminization syndrome: (PGI June 99)
- XX pattern
  - Commonly reared as male
  - Well formed female internal genitalia
  - High testosterone levels
31. In Testicular Feminization syndrome Gonadectomy is indicated: (UPSC 04)
- As soon as it is diagnosed.
  - At puberty
  - Only when malignancy develops in it
  - When hirsutism is evident
32. Pure gonadal dysgenesis will be diagnosed in the presence of: (AI 03)
- Bilateral streak gonads
  - Bilateral dysgenetic gonads
  - One side streak and other dysgenetic gonads
  - One side streak and other normal looking gonad
33. A 16-year-old female presents with Primary Amenorrhea. Examination shows a Short Blind Vagina, with absent Uterus. The Next Investigation of choice is: (AI 00)
- Karyotyping
  - IVP
  - Gonadotrophin levels
  - Serum Prolactin
34. True about klinefelter syndrome: (PGI May 2010)
- XXY
  - XO
  - Male hypogonadism
  - Female hypogonadism
  - FSH
35. A patient of 47 XXY karyotype presents with features of hypogonadism; likely diagnosis is: (AI 01)
- Turners syndrome
  - Klinefelters syndrome
  - Edwards syndrome
  - Down syndrome
36. A girl has primary amenorrhea with normal ovaries, absent internal genitalia but normal external genitalia. Most probable diagnosis?: (AI 10)
- Mayer-Rokitansky-Kuster-Hauser syndrome
  - Turner's syndrome
  - Noonan's
  - Androgen insensitivity syndrome
37. A 19-year-old patient came with C/o primary amenorrhea. she had well developed breasts and pubic hair. However there was absence of vagina and uterus. Likely diagnosis is: (AIIMS May 2013)
- Turners syndrome
  - Mullerian agenesis
  - Kinefelter's syndrome-XXY
  - Gonadal agenesis

38. Young male presents with delayed puberty with decreased FSH, LH, and testosterone. Which of the following is NOT possible? (AI 2012)
- Kallmann syndrome
  - Klinefelter's syndrome
  - Constitutional delay
  - Dax-1 gene mutation
39. In which of the following conditions do the ovaries function normally? (AIIMS Nov 2011)
- Turner's syndrome
  - Rokitansky-Kuster-Hauser syndrome
  - Androgen insensitivity syndrome
  - Swyer's syndrome
40. A girl with normal stature and minimal or absent pubertal development is seen in: (AIIMS Nov 2014)
- Kallmann syndrome
  - Turner syndrome
  - Testicular feminization syndrome
  - Pure gonadal dysgenesis

### NEW PATTERN QUESTIONS

41. Normal size but non functioning uterus is usually associated with:
- Stenosis of the external os
  - Uterine synechiae
  - Partial agenesis of the vagina
  - Complete absence of vagina
42. Exposure of a female fetus to androgen in early embryogenesis may arrest differentiation of:
- Mullerian ducts
  - Ovary
  - Urogenital sinus
  - Mesonephric ducts
43. Destruction of ovaries prior to 7th week following fertilization results in:
- Pseudohermaphroditism
  - Uterine agenesis
  - Masculinisation
  - None of the above
44. In testicular feminisation syndrome:
- Buccal smear is chromatin positive
  - Normal breast size is observed
  - Menstruation is scanty and infrequent
  - Familial incidence is recognised
45. Precocious puberty may be seen in all of the following conditions *except*:
- Granulosa - cell tumour
  - Head - injury
  - Corticosteroid intake
  - Hyperthyroidism
46. Precocious puberty associated with bony dysplasia and café au lait spots in skin is seen in:
- Frohlich's syndrome
  - Alports syndrome
  - McCune-Albright syndrome
  - Laurence-Moon-Biedl syndrome



## ANSWERS

1. Ans. is a, i.e. Thelarche, Pubarche, Menarche
2. Ans. is a, i.e. Breast budding
3. Ans. is d, i.e. Hair growth

Ref. Williams Gynae 1<sup>st</sup>/ed p 315; Novak 14<sup>th</sup>/ed p 992, 15<sup>th</sup>/ed p 993

In girls the sequence of development of puberty is (Mnemonic: GTPH in males).<sup>Q</sup>

**G** = Growth spurt

**T** = Breast development (Thelarche)<sup>Q</sup>

**P** = Pubic hair development (Pubarche)<sup>Q</sup>

**H** = Height increases; peak growth velocity<sup>Q</sup> attained

**in males** = Menstruation starts (Menarche)<sup>Q</sup>

(Axillary hair develop after menstruation starts)<sup>Q</sup>

- > The main hormone responsible for secondary sexual characteristics in females is estrogen
  - > Estrogen leads to
    - Breast development
    - Growth spurt, i.e. height attained
    - Production of cervical mucus
    - Cornification of vaginal cells
    - Menstruation (menstruation occurs due to withdrawal of progesterone in an oestrogen primed uterus)
  - > Estrogen leads to
  - > As far as hair growth is concerned – in females also the hormone responsible is Androgens(produced by adrenals and ovary)
4. Ans. c, Pulsatile release of GnRH during sleep

Ref. Nelson 19/e p1886; M.Fritz and L. Speroff's 'Clinical Gynecologic Endocrinology and Infertility' 8/e pe p407

**Pulsatile release of GnRH during sleep is responsible for pubertal growth in females.**

*"After a decade of quiescence, pulsatile secretion of GnRH increases and the hypothalamic-pituitary gonadal axis is reactivated (gonadarche), probably in response to metabolic signals from the periphery. FSH and LH levels rise moderately before age 10, followed by a gradual increase in estradiol concentrations, which stimulate breast development (thelarche). The increase in pulsatile gonadotrophin secretion occurs first at night, during sleep, but gradually extends throughout the day."* - M. Fritz and L. Speroff's 'Clinical Gynecologic Endocrinology and Infertility' 8/e pe p407

5. Ans. a. Barr body

Ref. Gamong 24/e p392-393

Barr body forms the basis for sex chromatin testing.

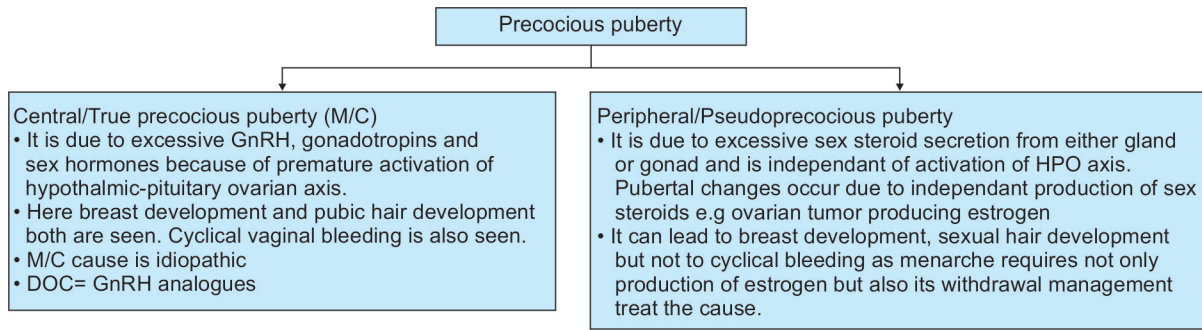
#### Barr Body

When two X chromosomes are present in a cell (as in a normal female) one of them becomes inactivated and condensed on the nuclear membrane and is called the 'Barr body'. This process is termed as X chromosome ionization (inactivation) Presence or absence of Barr bodies helps in ascertaining the sex of an individuals

- Absence of Barr body indicates that the patient has only one X chromosome (eg. Normal male XY or Turner's syndrome (XO))
- Nuclei of cells in females (XX) contain a darkly staining Barr body that is not present in the nuclei of cells in males.
- Barr bodies are most easily seen in a smear of squamous epithelial cells obtained by scraping the buccal mucosa
- Barr bodies react differently to histological stains and are best seen as dark staining bodies with in the nucleus of non dividing interphase cells.

6. Ans. is a, i.e. Idiopathic
7. Ans. is c, i.e. GnRH analogues

Ref. Novaks 15<sup>th</sup>/ed pp 1017, 1020; Textbook of Gynae shielabalakrishnan 1<sup>st</sup>/ed p 67-8



In question no. 4 female has developed both breast and axillary hair and she has cyclical vaginal bleeding, these findings favour central precocious puberty which is most commonly idiopathic.

DOC for managing central precocious puberty is GnRH analogue –(Leuprolide)

Principle → Continuous administration of GnRH agonist, downregulates and desensitizes GnRH receptor of pituitary, decreasing gonadotropin release leading to decreased estrogen production.

*Note:* In these females GnRH should be withdrawn at the age of normal puberty

8. Ans. is b, c and d, i.e. Lepromatous leprosy; HIV; Klinefelter's syndrome

9. Ans is a, i.e. Prolactinoma

Ref. Harrison's 18<sup>th</sup>/ed p 2889, Schwartz 7<sup>th</sup>/ed p 541

Ref. Schwartz 7<sup>th</sup>/ed p 541; Behl 9<sup>th</sup>/ed p 223

*Gynaecomastia implies presence of female type mammary glands in male.*

It can be:

	Physiological		Pathological			
Neonatal period <sup>o</sup>	Adolescence <sup>o</sup>	Senescence <sup>o</sup>	D/t Estrogen <sup>o</sup> excess	D/t decreased androgens <sup>o</sup>	Drugs <sup>o</sup> intake	Systemic <sup>o</sup> diseases
	<ul style="list-style-type: none"> <li>• Occurs b/w 12 and 15 years<sup>o</sup></li> <li>• Unilateral<sup>o</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Occurs b/w 50 and 70 years<sup>o</sup></li> <li>• Bilateral<sup>o</sup></li> </ul>				

**Causes of Gynaecomastia:**

I. *Estrogen excess states:*

A. **Gonadal origin:**

1. True hermaphroditism
2. Gonadal stromal (Nongermlinal) neoplasm of testis:
  - Leydig cell (interstitial)<sup>o</sup>
  - Sertoli cell<sup>o</sup>
  - Granulosa-theca<sup>o</sup>
3. Germ cell tumours:
  - Choriocarcinoma<sup>o</sup>
  - Seminoma, teratoma<sup>o</sup>
  - Embryonal carcinoma<sup>o</sup>

B. **Nontesticular tumours:**

1. Skin-nevus
2. Adrenal cortical Neoplasms<sup>o</sup>
3. Lung carcinoma<sup>o</sup>
4. Hepatocellular carcinoma<sup>o</sup>

C. **Endocrine disorders:**

1. Hypothyroidism<sup>o</sup>
2. Hyperthyroidism<sup>o</sup>

D. **Disease of the liver – Non alcoholic and alcoholic cirrhosis**

E. **Nutrition alteration states:** Starvation (As pituitary adrenal axis is suppressed)

II. *Androgen deficiency states:*

A. **Senescent causes with aging**

**B. Hypoandrogen state (hypogonadism)**1. *Primary testicular failure*

- a. Klienfelter syndrome (XXY)<sup>Q</sup>
- b. Reifenstein syndrome, (XY)<sup>Q</sup>
- c. Rosewater, Gwinup, hamwi familial gynecomastia (XY)
- d. Kallman syndrome<sup>Q</sup>
- e. Kennedy disease with associated gynaecomastia<sup>Q</sup>
- f. Eunuchoidal males (Congenital anorchia)<sup>Q</sup>
- g. Hereditary defects of androgen biosynthesis
- h. ACTH deficiency

2. *Secondary testicular failure:*

- a. Trauma<sup>Q</sup>
- b. Orchitis: due to mumps and leprosy<sup>Q</sup>
- c. Cryptorchidism<sup>Q</sup>
- d. Irradiation<sup>Q</sup>
- e. Hydrocele<sup>Q</sup>
- f. Varicocele<sup>Q</sup>
- g. Spermatocele

**C. Renal failure****III. Drug related conditions that initiate gynaecomastia**

1. Estrogen<sup>Q</sup>
2. Digitalis<sup>Q</sup>
3. Spironolactone<sup>Q</sup>
4. Methyldopa<sup>Q</sup>
5. Captopril<sup>Q</sup>
6. Calcium Channel blocker<sup>Q</sup>
7. Cimetidine (high doses)<sup>Q</sup>
8. Ketoconazole<sup>Q</sup>
9. Tricyclic Antidepressant<sup>Q</sup>
10. Diazepam<sup>Q</sup>

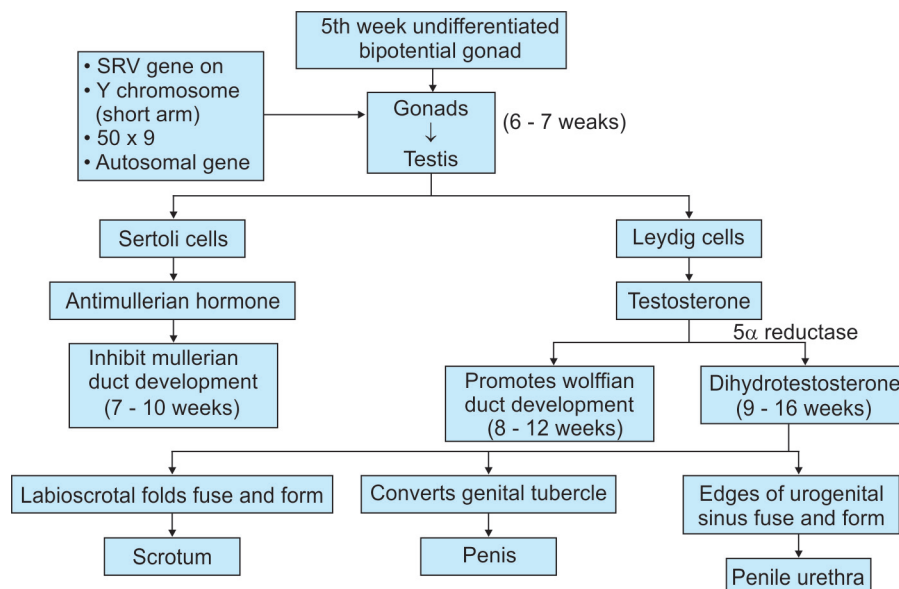
**IV. Systemic disease 'with' idiopathic mechanisms**

- A. Non neoplastic disease of the lung
- B. Trauma (chest wall)
- C. CNS - related causes from anxiety and stress
- D. AIDS (Acquired Immuno Deficiency Syndrome)

**10. Ans. is b, i.e. Primitive Gonads differentiate into testis due to the presence of SRY gene**

*Ref. Dutta Gynae 5<sup>th</sup>/ed p 420, 6<sup>th</sup>/ed p 439; Williams Gynae 1<sup>st</sup>/ed p 403-404; Harrison 17<sup>th</sup>/ed 2339-2340*

As discussed earlier –

**In males**

**In males**—masculinization of external genitals begin at 9–10 weeks and is completed by 12–14 weeks of gestation.

- Thereafter the only change is in the growth and length of penis.
- Since in males, mainly masculinization is due to testosterone/dihydrotestosterone, therefore if it is deficient it will lead to undermasculinization of external genitalia, i.e. males will have small phallus, hypospadias or scrotal defect, i.e. ambiguous genitalia.

**11. Ans. is d, i.e. Congenital adrenal hyperplasia**

*Ref Leon speroff 8<sup>th</sup>/ed p 349; Dutta Gyne 6<sup>th</sup>/ed p 440*

*“CAH due to 21 hydroxylase deficiency is the most frequent cause of sexual ambiguity and the M/C endocrine cause of neonatal death.”*

*Leon speroff 8<sup>th</sup>/ed p 349*

Ambiguity of sex at birth—“Cases of ambiguity of sex detected at birth are due to adrenogenital syndrome unless proved otherwise”.

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 404*

**12. Ans. is d, i.e. Congenital adrenal hyperplasia**

*Ref. Dutta Gynae 4<sup>th</sup>/ed p 404; Williams Gynae 1<sup>st</sup>/ed p 409; Novak 14<sup>th</sup>/ed p 102*

**Most common cause of female Pseudohermaphroditism is Congenital adrenal hyperplasia**

**13. Ans. is a, and e, i.e. 46XX chromosomal pattern; and Clitoromegaly**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 440; William Gynae 1<sup>st</sup>/ed p 409; Shaw 15<sup>th</sup>/ed p 113*

In a female most common cause of ambiguous sex is congenital adrenal hyperplasia.

As discussed in preceding text incase of congenital adrenal hyperplasia:

**Genotype:** 46XX

**Gonads:** Ovary

**Internal genital organs:** Normal (i.e. uterus, vagina)

**External genital organs:** There is clitoromegaly and genital folds fused to form penile urethra rather than labia minora. Labia majora are fused which appears like scrotum

**14. Ans. is d, i.e. Cortisone**

**15. Ans. is a, i. e. Dexamethasone**

*Ref. Shaw 15<sup>th</sup>/ed p 114; CGDT 10<sup>th</sup>/ed p 120; Leon speroff 8<sup>th</sup>/ed p 355*

Treatment of CAH is aimed at providing sufficient amounts of the deficient hormone, cortisol, to reduce excessive ACTH secretion and to prevent consequences of excessive androgen production.

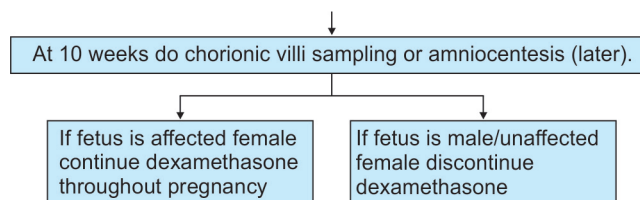
**Thus in patients of CAH:** Hydrocortisone 10–20 mg/m<sup>2</sup> body surface area is given per day.

Once the neonate is stable reconstruction surgery-clitoroplasty (by 5 years) and vaginoplasty are done

**Prenatal Cases:**

DOC is dexamethasone in mothers at risk for having an affected child. Dexamethasone should be given to prevent fetal female genital virilisation as dexamethasone is not metabolized by placenta and crosses effectively into fetal circulation.

For maximum benefit-treatment should begin at 4 to 5 weeks of gestation and not later than 8 weeks



**Note:** Latest recommendations are prenatal treatment poses risks like postnatal failure to thrive and psychomotor developmental delay, hence best approach is early prenatal diagnosis by CVS with rapid sex determination (FISH for the X and Y chromosome) and genotyping and beginning treatment in only those mothers with an affected female child.

**16. Ans. is c, i.e. Anti mullerian hormone deficiency**

*Ref. Leon speroff 7<sup>th</sup>/ed pp 329, 344*

The karyotype of the baby is 46 XX and external genitalia are of male, i.e. it is a case of female pseudohermaphroditism.

Causes of female pseudohermaphroditism are:

- **Congenital adrenal hyperplasia. (M/C cause)**
- **Increased androgens in the mother** which cross the placenta and cause virilization of the external genitalia. Like maternal intake of androgenic drugs, maternal adrenal tumor, etc.
- **Placental aromatase deficiency.** Aromatase enzyme is responsible for conversion of testosterone to estradiol. If this enzyme is deficient there will be excess of testosterone.
- **Wnt4 mutation.** Wnt4 Mullerian aplasia is a disorder that occurs in females and affects their reproductive system. There is abnormal development of the Mullerian duct, and ovarian dysfunction so females have an underdeveloped or absent uterus and may also have abnormalities of other reproductive organs. Women with this condition have primary amenorrhea, normal breast and pubic hair development and higher than normal levels of androgens in their blood. These high levels of androgens cause acne, hirsutism and virilisation. Kidney abnormalities may also be present in some affected individuals.

#### AMH Deficiency/ Uterine Hernia Syndrome/Persistent mullerian duct syndrome

- It is seen in males
- It is an autosomal recessive congenital disorder.

Karyotype = 46 XY

Gonads = testis

Hormone = Testosterone

Thus, external genitalia are normal since levels of testosterone are normal. The problem is there is persistent Mullerian duct so uterus and other mullerian duct derivatives are seen in a male.

Typical features: Include cryptorchidism and the presence of a small, underdeveloped uterus in a male infant or adult.

Here since both mullerian duct and wolffian duct both are seen in males so the tissue are often intertwined, resulting in obstruction or non patency of the vas deference or other parts of the male excretory ducts. This can result in infertility.

The condition can come to attention because of a bulge in the inguinal canal of a male infant due to herniation of the uterus.

There is no ambiguity or malformation of the external genitalia. They look like a normal male.

17. Ans. is b, c and e, i.e. Edema of hands and feet; XO Genotype; and Streak ovaries

18. Ans. is a, b and d, i.e. Karyotype is 46 XO Normal breast, and Normal secondary sexual characters

19. Ans. is a, i.e. 45 XO

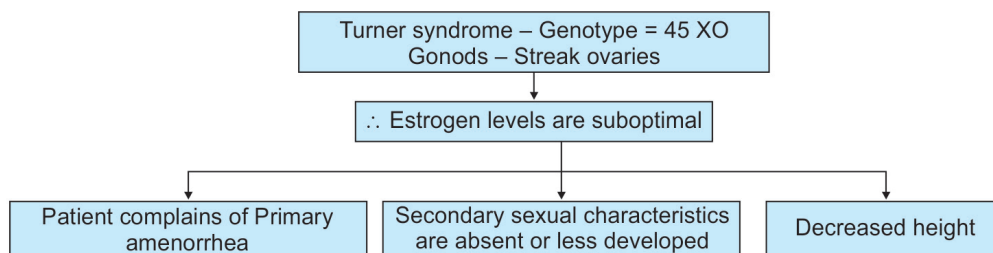
*Ref. Harrison 17<sup>th</sup>/ed p 2341; Jeffcoate 7<sup>th</sup>/ed p 227; Shaw 15<sup>th</sup>/ed p 110-111; Williams Gynae 1<sup>st</sup>/ed p 370*

As discussed in preceding text.

#### TURNERS SYNDROME (also called as *Gonadal Dysgenesis*)

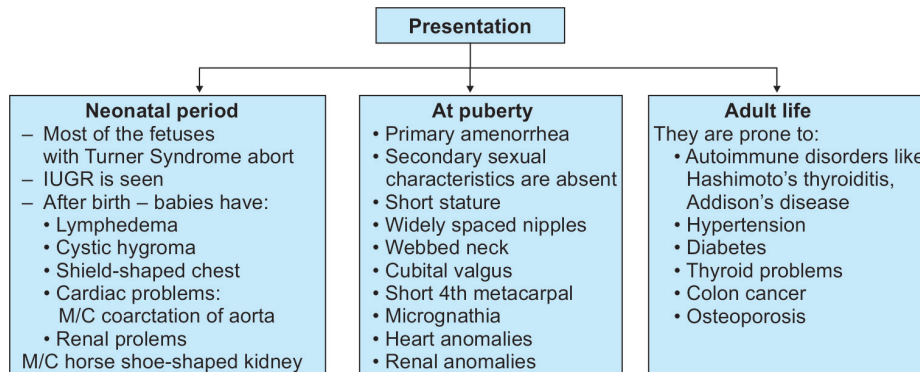
**Karyotype:** Most common = 45 XO<sup>Q</sup>

- **Gonads:** B/L Streak Gonads.<sup>Q</sup> (since one single X chromosome is present so ovaries are not properly formed).



– Since Fallopian Tube/Uterus/Cervix and Vagina develop from mullerian duct, so all these internal genitalia are present but their proper growth requires estrogen stimulation; therefore, they will remain infantile

– Similarly, external genitalia in females are formed due to absence of testosterone (estrogen has no role); so they will be normal.



**20. Ans is a, i.e Low oocyte in ovary**

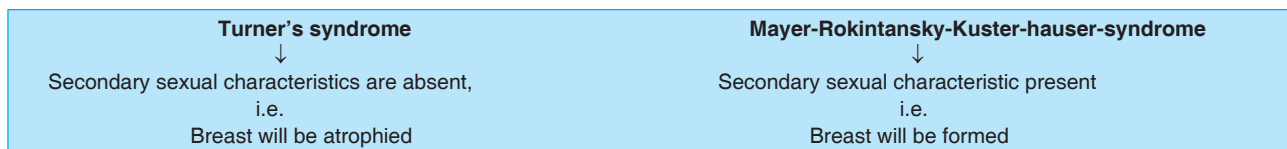
*Ref. Novak's gynecology p 1038*

- A height of 58 inches corresponds to approximately 147 cms. Which is short stature for a female of 16 years. Her FSH levels are rising, i.e., estrogen production is low i.e. there is an ovarian cause for 1° amenorrhea.
- Primary amenorrhea with short stature is seen in Turners syndrome.
- Turner syndrome (45 X) is the most common chromosomal abnormality causing gonadal failure, hence on histological examination their ovary would show low oocyte count.
- After birth, these patients generally grow slowly. Hence they present with short stature. (Height < 150 cms), primary amenorrhea and delayed secondary sexual characteristics.
- They typically have many of the associated stigmata including lymph edema and sometimes large cystic hygromas of neck, webbed neck, coarctation of aorta, horse shoe kidneys.

**21. Ans. is a, i.e. Turner's syndrome**

*Ref. Harrison 17<sup>th</sup>/ed p 23-41; Jeffcoate 7<sup>th</sup>/ed p 227; Shaw 15<sup>th</sup>/ed p 110-111; Williams Gynae 1<sup>st</sup>/ed p 370*

Here the patient is 17 years old and has amenorrhea (i.e. Primary Amenorrhea) with atrophied breast and hypoplastic uterus. Hypoplastic uterus can be seen in case of:



- In Klinefelter syndrome – Gonads are testis and not ovaries. The patient externally resembles a male and not female. Uterus is also absent.
- In pure Gonadal dysgenesis. Uterus and cervix are present but infantile and there is some development of secondary sexual characteristics and a few episodes of bleeding (Leon Speroff 8<sup>th</sup>/ed p1040)
- In Androgen Insensitivity Syndrome – uterus is absent but breast development is normal, so it is also ruled out. Hence – our answer is Turner's syndrome



Swyer syndrome/Pure gonadal dysgenesis - individuals are phenotypically female with sexual infantilism, primary amenorrhea, normal stature, and no chromosomal abnormalities (46 XY). The uterus and cervix are present but, due to hypoestrogenism the gonads are streak. There may be some development of secondary sexual characteristics, as well as a few episodes of uterine bleeding. Swyer syndrome occurs when mutations in the SRY (sex-determining region gene on the Y chromosome) located at Yp11 result in XY females with gonadal dysgenesis. *Ref. Novak's 14<sup>th</sup>/ed p 1040*

**22. Ans. is c, i.e. Testicular feminization syndrome**

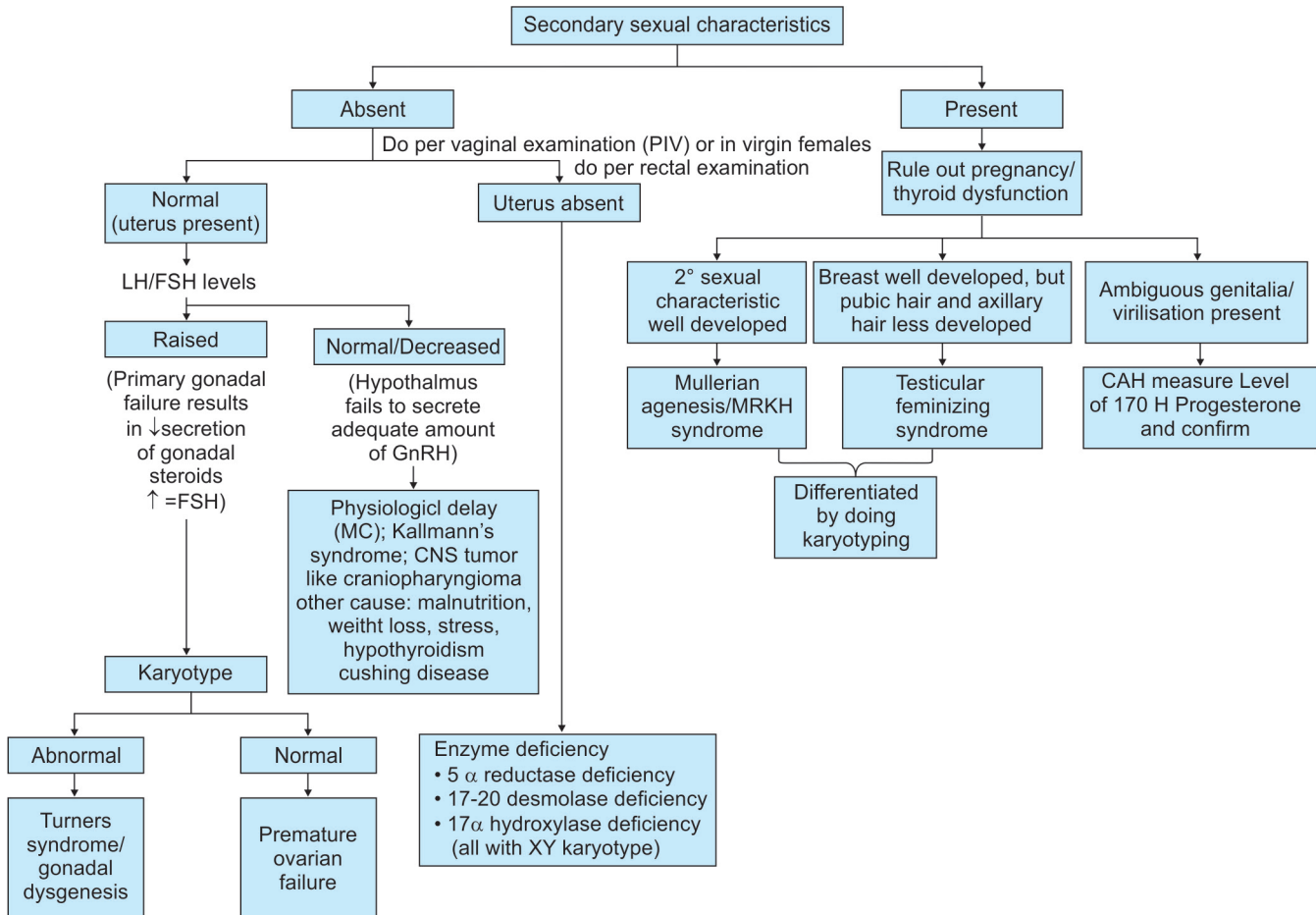
*Ref. Novak 14<sup>th</sup>/ed p 1037-1038*

When a female comes with complaint of primary amenorrhea the first thing to do is see her secondary sexual characteristics:

- *In Turners Syndrome all secondary sexual characteristics are absent where as in the question the female has proper breast development with absent axillary and pubic hair (therefore option 'a' ruled out).*
- *In mullerian agenesis - Patient presents with primary amenorrhea with well developed secondary sexual characteristics (both breast and pubic hair), i.e. option b ruled out.*
- *In option d, i.e. premature ovarian failure - patient will have no secondary sexual characteristic be it breast or pubic hair, i.e. this option is also incorrect.*

- In testicular feminization syndrome as discussed in the preceding text - Genotype is 46 XY, i.e. they are males but with testosterone resistance. Male secondary sexual characteristics do not develop. This testosterone is converted to estrogen and thus these males have well developed breasts (Tanner stage 4 or 5) and since development of pubic and axillary hair is dependant on testosterone, these are not developed or under developed (Tanner stage 1 or 2)

### Remember



23. Ans. is a, i.e. Phenotype may be completely female

Ref. Shaw 15<sup>th</sup>/ed p 111-112; Williams Gynae 1<sup>st</sup>/ed p 410

24. Ans. is a, c and e, i.e. Absent vagina; Karyotype is XY; and Breast development is normal

- Testicular feminization syndrome is the most common form of male intersex
- The individual presents with female phenotype, but genotype is 46XY.
- Gonads are testis and ovary is absent.
- A short blind vagina is usually seen.

The etiology of testicular feminisation involves either –

\_ Williams Gynae 1<sup>st</sup>/ed p 410

- Testicular enzyme defects in the biosynthesis of testosterone
- Peripheral enzyme defect
- Abnormalities in the androgen receptor

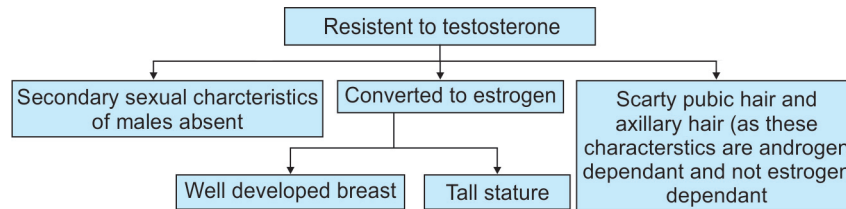
Thus testis are abnormal functionally & not anatomically

25. Ans. is b, d and e, i.e. Scanty pubic hair; Uterus absent; and Breast development is adequate

Ref. Shaw Gynae 15<sup>th</sup>/ed p 111-2; Dutta Gyane 6<sup>th</sup>/ed p 424

**Androgen insensitivity syndrome/Testicular Feminizing syndrome:**

- Genotype: 46 XY
- They are males who are resistant to testosterone
- Internal genitalia and external genitalia of males are present hence (no uterus).



26. Ans. is c, i.e. Short stature  
 27. Ans. is a, i.e. Testicular feminisation syndrome  
 28. Ans. is b, i.e. Pubic hair are abundant  
 29. Ans. is d, i.e. Androgen insensitivity syndrome

Ref. Leon Speroff 7<sup>th</sup>/ed p 330; Shaw 15<sup>th</sup>/ed p 111-112; Novak 14<sup>th</sup>/ed p 1047; Harrison 17<sup>th</sup>/ed p 2344; Williams Gynae 1<sup>st</sup>/ed p 410

All options have been explained in detail in the preceding text, I don't think there is any need to repeat them. Here I want to point out that in these patients testis are intra-abdominal which can present in the form of bilateral inguinal hernia and since the entire testosterone is converted to estrogen hence these patients are tall.

30. Ans. is d, i.e. High testosterone levels Ref. Harrison 17<sup>th</sup>/ed p 2344; Dutta Gynae 6<sup>th</sup>/ed p 443

In Testicular Feminization Syndrome

- Genotype – 46XY
  - Gonads – Testis (intra-abdominal)
  - Phenotype – Female
  - Internal Genitalia – Is of males (except a short vagina may be present)
- They are reared as female.

#### Lab investigation:

- Testosterone levels may be normal/high/low depending on the degree of androgen resistance and the contribution of estradiol to feedback inhibition of the hypothalamus-pituitary axis. \_ Harrison 17<sup>th</sup>/ed p 2344
- “Laboratory evaluation demonstrates elevated LH levels, normal or slightly elevated testosterone levels, and a 46XY Karyotype.” \_ Williams Gynae 1<sup>st</sup>/ed p 410
- LH levels are high (due to insensitivity of pituitary and hypothalamus to testosterone) but FSH levels are Normal.

31. Ans. is b, i.e. At puberty Ref. Novak 14<sup>th</sup>/ed p 1051, 15<sup>th</sup>/ed p 1050

Patients of Testicular Feminization syndrome (Androgen insensitivity) are genotypically males (Karyotype 46XY) but phenotypically females (i.e. male pseudohermaphroditism). Due to the presence of Y chromosome gonads are testis which remain intra-abdominal and have a malignant potential (Most common = Gonadoblastoma, Dysgerminoma). Therefore testis should be removed in such patients. B/L Laparoscopic Gonadectomy is the preferred procedure<sup>Q</sup>. As far as timing of Gonadectomy is concerned-

“In patient with complete androgen insensitivity, the testis should be removed after pubertal development is complete to prevent malignant degeneration.” \_ Novak 14<sup>th</sup>/ed p 1051, 15<sup>th</sup>/ed p 1050

Whereas in cases other than Testicular Feminization syndrome, if patient has XY Karyotype and she develops virilization, the testes should be removed immediately to preserve the female phenotype and to promote female gender identity.

#### Extra Edge:

In case specific age at which Gonads should be removed in Testicular Feminization is asked go for 16-18 years.

\_ Leon Speroff 7<sup>th</sup>/ed p 340

32. Ans. is a, i.e. Bilateral streak gonads Ref. Jeffcoate 7<sup>th</sup>/ed p 226; Williams Gynae 1<sup>st</sup>/ed p 370

In pure gonadal dysgenesis

- Gonads are bilateral ‘streaks’ without any potentiality to produce hormones.
- The vagina, uterus, and tubes are present although infantile.
- The uterus is, however, sensitive to exogenous estrogen.
- As these patients have got no gonads, a female phenotype is expected regardless of the chromosomal complement.
- Karyotype is either 46, XX or 46, XY.
- Sex chromatin is doubtful.

#### Note:

- The genes which protect against the physical malformations of Turner Syndrome are carried on short arms of XX or XY chromosomes<sup>Q</sup> and genes which protect against streak gonads are on the long arms of XX or XY<sup>Q</sup>.



In genotype 46XX / 46XY	
If only short arm of X or Y are missing	If only long arms of X or Y are missing
Physical features of Turner's syndrome	Normal looking female (height is normal or may be increased) with bilateral streak gonads
Seen but gonadal development is normal.	↓ This is pure gonadal dysgenesis. <sup>o</sup>

**Mixed Gonadal dysgenesis<sup>o</sup>:** In this disorder the individual has karyotype of 45XO/46XY and so there is a streak gonad or no gonad on one side (corresponding to 45XO) and a testis on the other side (corresponding to 46XY).

**Also know:** Streak and dysgenetic gonads have a high potential for neoplasia (especially dysgerminoma<sup>o</sup> or gonadoblastoma<sup>o</sup> and Yolk sac tumor<sup>o</sup>) if the owners karyotype contains a Y chromosome.

33. **Ans. is a, i.e. Karyotyping**

Ref. Jeffcoate 7<sup>th</sup>/ed p 198; CGDT 10<sup>th</sup>/ed p 931 Fig. 56-2

A female presenting with absent uterus and short blind vagina:

Friend what are the D/D's which come to your mind.

I can think of only 2: Mullerian dysgenesis and Testicular feminizing syndrome (or male pseudo hermaphroditism).

Presentation	Mullerian Agensis	Androgen Insensitivity
Inheritance pattern	Sporadic	X-linked recessive
Karyotype	46,XX	46,XY
Breast development	Yes	Yes
Axillary and pubic hair	Yes	No
Uterus	No	No
Gonad	Ovary	Testis
Testosterone	Female levels	Male levels
Associated anomalies	Yes	No

So, the best way to differentiate between the two is to do karyotyping or chromatin/barr body test, which comes positive (barr body present) in 46XX and negative (barr body absent) in case of 46XY Genotype.

34. **Ans. is a, c and e, i.e. XXY; Male hypogonadism; and FSH**

35. **Ans. is b, i.e. Klinefelter syndrome**

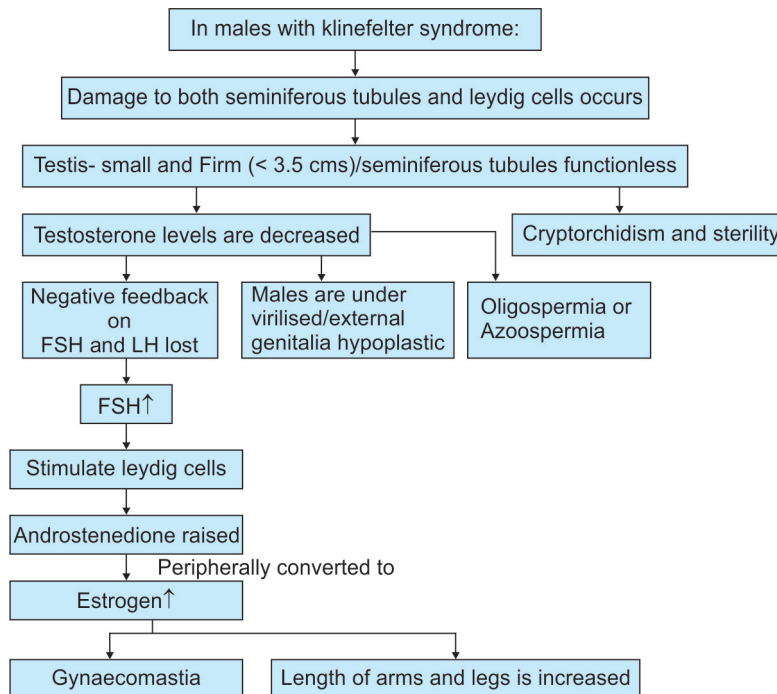
Ref. Leon speroff 8<sup>th</sup>/ed p 1261-1262; Harrison 17<sup>th</sup>/ed p 2340-42

**Klinefelter Syndrome**

**Genotype - 47XXY**

**Clinical features**

- Klinefelter syndrome (KS) is the M/C cause of primary testicular failure, i.e. male hypogonadism affecting 1 in 1000 males



**36. Ans. is a, i.e. Mayer-Rokitansky-Kuster-Hauser syndrome***Ref. Leon Speroff 7<sup>th</sup>/ed p 420-421*

The questions says that the girl has normal ovaries which rules out.

- Turners syndrome where streak gonads are seen
- Noonans syndrome
- Androgen insensitivity syndrome - gonads are testis.

So by exclusion our answer is Mayer-Rokitansky Kuster-Hauser Syndrome.

**Mullerian agenesis or mayer-okintansky-Kuster-hauser syndrome** is a congenital malformation characterized by a failure of the Mullerian ducts to develop, resulting in absent uterus and variable malformations of the vagina, while both ovaries are intact and functioning.

Ovaries are present and function normally so secondary sexual characteristics are normal. External genitalia are also normal as testosterone is absent.

**37. Ans. is b, i.e. Mullerian agenesis***Ref. Shaw 15<sup>th</sup>/ed p 95, 112, 110*

The questions clearly mentions:

- i. Phenotype of the patient is female: This rules out Klinefelter syndrome (47 X XY) as in Klinefelter's syndrome phenotype of the patient resembles a male and not female.
- ii. Presence of well developed breast and pubic hair and absence of uterus and vagina rules out Turners syndrome and gonadal agenesis because in both these conditions gonads (ovary) although present is streak. Hence levels of estrogen are low and so secondary sexual characteristics are not developed or less developed. Here the internal genital organs are present but not well developed due to lack of deficiency of estrogen.

Thus by exclusion our answer is Mullerian agenesis.

Rest all of you know so much about Mullerian agenesis.

**38. Ans. is b, i.e. Klinefelter's syndrome***Ref. Leon Speroff 7<sup>th</sup>/ed p 404-407*

- Decrease in serum follicle-stimulating hormone (FSH), luteinizing hormone (LH), and testosterone indicates that this is a case of hypogonadotropic hypogonadism.
- Hypogonadism resulting from hypothalamic or pituitary defects is called as hypogonadotropic hypogonadism or central hypogonadism. Examples of hypothalamic defects include Kallmann syndrome. Examples of pituitary defects include hypopituitarism. Dax-1 (dosage-sensitive sex reversal, adrenal hypoplasia critical region, on chromosome X, gene 1) is a nuclear receptor protein. Mutations in this gene result in both X-linked congenital adrenal hypoplasia and hypogonadotropic hypogonadism.
- Hypogonadism which results from defects of the gonads is called as primary hypogonadism/hypergonadotropic hypogonadism. Examples include Klinefelter syndrome, mumps, varicocele etc.

In Klinefelter's = Testosterone is decreased, which results in increase in LH and FSH.

**39. Ans. is b, i.e. Rokitansky-Kuster-Hauser syndrome***Ref. Jeffcoates 7<sup>th</sup>/ed p 197-198; Shaw 14<sup>th</sup>/ed p 82; (COGDT 10<sup>th</sup>/ed p 549)*

- Ovaries develop from genital ridge, whereas fallopian tubes, uterus, cervix and upper part of vagina are formed by Mullerian duct.
- In Mullerian agenesis which is also called as Mayer-Rokitansky-Kuster-Hauser syndrome, fallopian tube, uterus, cervix and upper part of vagina are absent and not ovaries.
- Ovaries are normally functioning.

**40. Ans. is a, i.e. Kallman syndrome—Read below**

**Normal stature rules out:**

- Turners syndrome: Short stature

**Absent pubertal development rules out:**

- Testicular feminization syndrome as here breast development is normal but pubic hair and axillary hair are absent so we are left with 2 options:
  - Kallmann syndrome
  - Pure gonadal dysgenesis

In pure gonadal dysgenesis – the ovaries are streak and level of estrogen is low. "The low level of estrogen in these patients results in delayed closure of the epiphysis of the long bones, resulting in long arms and legs relative to the torso. This appearance is termed a eunuchoid habitus"...

*Williams gynae 2/e, p445*

So we are left with Kallmann syndrome. Kallman patients have a normal complement of GnRH neurons, however these neurons fail to migrate to hypothalamus and remain near the nasal epithelium. As a result locally secreted GnRH is unable to stimulate gonadotropin secretion by anterior pituitary. This results in lack of secondary sexual characteristics height remains unaffected.

**41. Ans. is b, i.e. Uterine synechiae**

Lets have a look at each option:

**Option a:** Stenosis of external os would result in hematometra, i.e. uterus would be large and non functioning (hence ruled out).

**Option c:** Partial agenesis of vagina

...Dutta Gynae 6<sup>th</sup>/ed p 43

In parital agenesis of vagina a segment of vagina may be atretic in the upper-third. It is often associated with hypoplasia or even absence of cervix. Uterus may be normal and functioning or malformed.

**Option d:** Complete absence of vagina is almost always associated with absence of uterus.

Ref. Dutta Gynae 6<sup>th</sup>/ed p 44

Hence by exclusion our answer is b i.e. uterine synechiae (Asherman syndrome)

In Uterine syechiae—the uterus does not function normally due to presence of adhesions size of uterus is normal.

**42. Ans. is c, i.e. Urogenital sinus**

Ref. Read below

This is common sense. We have discussed so many times that in females exposure of androgens in early embryogenesis results in ambiguous external genitalia.

The external genitalia are formed by urogenital sinus (so it is our answer of choice)

**43. Ans. is d, i.e. None of the above**

Ref. Read below

**In females:** If ovaries are destructed prior to 7 weeks then it will lead to decrease in estrogen so secondary sexual characteristics in female will not develop, and she will complain of amenorrhea. Uterus develops from mullerian duct, hence uterus will be present (i.e. option b incorrect) but underdeveloped (infantile) due to lack of estrogen.

Pseudohermaphroditism in females means Gonads are ovaries but external genitalia are of male. External genitalia of male is due to exposure of androgens in females at early stages of development, and not because of absence of ovaries hence both option a and c are incorrect.

**44. Ans. is b and d, i.e. Normal breast size is observed; Familial incidence is recognised**

Ref. Dutta Gynae 6<sup>th</sup>/ed p 443

In testicular feminization syndrome:

Genotype = 46 XY

- Hence borr body is absent i.e. chromatin negative (i.e., option a is incorrect)
- It is inherited as X-linked recessive gene.

(i.e. option d is correct).

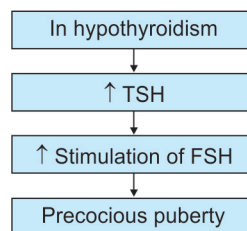
Rest all options you know.

**45. Ans. is d, i.e. Hyperthyroidism**

Ref. Jeffcoate 7<sup>th</sup>/ed p 116-118

- Friend for the details on causes of precocious puberty kindly see the preceeding text.
- Remember hypothyroidism and not hyperthyroidism causes precocious puberty.

**Reason:**



If precocious puberty is associated with delayed bone age it suggests primary hypothyroidism.<sup>Q</sup>

**46. Ans. is c, i.e. McCune-Albright syndrome**

Ref. Novak 15<sup>th</sup>/ed p 1023

Precocious puberty with bony dysplasia and cafe au lait spots points towards incur in McCune-Albright syndrome as the diagnosis.

McCune-Albright Syndrome is characterised by the classic triad of polyostetic fibrous dysplasia of bone, irregular café au lait spots on skin and GnRH independent sexual precocity

- The precocious puberty is the result of secretion of estrogen from functioning ovarian cysts.
- The café au lait spots are usually large, donot cross the midline and have irregular “coast of maine” margins.
- They are located on the same side as the bony lesion

**Laurence-Moon-Biedl syndrome** is hypothalamic amenorrhea+ mental retardation + polydactyl + retinitis pigmentosa.

**Frohlich Syndrome** is hypogonadotropic hypogonadism + obesity + genital hypoplasia

Both these are causes of delayed puberty and not precocious puberty



Theoretically gonococcal vaginitis can occur in newborn females as their vagina is lined by *transitional epithelium*.



M/c site for gonococcal infection in young females is endocervix since endocervix is lined by columnar epithelium and not squamous epithelium. Since endocervix is lined by columnar epithelium and not squamous epithelium.

**Vulvovaginitis**

Vulvar and vaginal inflammation



Most common gynecological problem in prepubertal girls is nonspecific vulvovaginitis

**Vagina – Characteristics**

- In adult females, vagina is lined by stratified squamous epithelium. In newborn females, it is lined by transitional epithelium.
- Squamous epithelium is resistant to gonococcal infection. Thus, gonococcal vaginitis cannot occur in young/adult females.
- Vagina has local inhabitant bacteria called as *Doderlein's bacillus* (lactobacilli) which breaks down the glycogen present in vaginal epithelium into lactic acid resulting in acidic pH (Avg, 4.5; Range, 4–5.5) of vagina. The acidic pH of vagina acts as a barrier for external organisms.

**Physiological Discharge**

- Clear, white, and flocculent odorless discharge
- Smear contains epithelial cells, lactobacilli
- pH ranges from 3.8–4.2
- Increases with increased estrogen stats: pregnancy, OCP, mid-cycle, PCOS, or premenarchal
- If increased in perimenopausal woman, investigate for other effects of excess estrogen (e.g. endometrial cancer).

**Vulvovaginitis****Postmenopausal Vaginitis/Atrophic/Senile Vaginitis**

Vaginitis in postmenopausal females is called as atrophic vaginitis.

**Etiology**

Due to decreased estrogen in postmenopausal females.

**Clinical Features**

- Yellowish or blood stained vaginal discharge
- Discomfort, dryness, soreness in the vulva
- Dyspareunia.

**Investigations**

Diagnosis is usually a visual one – thinning of tissues, erythema, dryness

- Rule out malignancy.

**Treatment**

Local estrogen cream is ideal – (Premarin cream)

- Oral or transdermal hormone replacement therapy (if treatment for systemic symptoms is desired) Infectious Vulvovaginitis

## Infectious Vulvovaginitis

Infectious vulvovaginitis			
	Bacterial vaginosis	Candidiasis	Trichomonas vaginitis
Organism	Alteration of vaginal flora; lactobacilli decrease whereas coccobacilli and Gardnerella increase	Candida albicans > Candida glabrata > Candida tropicalis	Trichomonas vaginalis (flagellated protozoa)
M/C	Most common vaginitis (overall)	M/C vaginitis in: – Pregnancy, diabetes – Immunocompromised – OCP users, steroid users, antibiotic users	–
STD	Not an STD	Mostly not an STD	It is an STD
pH of discharge	> 4.5	< 4.5	5-6
M/C complaint	– Foul smelling dirty white discharge – No inflammation-hence no itching	– Intense pruritis – Curdy white discharge (or cottage cheese like discharge)	– Profuse frothy greenish yellow discharge – Urinary symptoms – Dysuria – Dyspareunia
Signs	–	–	Strawberry vagina or angry looking vagina
IOC	<b>Saline microscopy</b> 'Clue cells', i.e. vaginal epithelial cells to which bacteria are adhered seen	<b>Saline microscopy</b> pseudohyphae seen	<b>Saline microscopy</b> Typical motile flagellated trichomonas seen or motility seen
Gold standard investigation	<b>Gram stain</b> on gram staining <b>Nugent scoring</b> is done-The Nugent score is calculated by assessing the presence of lactobacillus (Gram +ve rods-scored as 0 to 4), Gardnerella vaginalis (scored as 0 to 4) and mobilincus (Gram variable rods-scored as 0-2) A score of $\geq 7$ is consistent with bacterial vaginosis	Culture on sabouraud's medium or Nickerson medium	Culture on—Feinberg-whittington media or Diamond media
Amine test/Whiff test, i.e. 10% KOH added to discharge	Positive, i.e. on adding 10% KOH to discharge, fishy odour or amine like odour obtained.	Negative	Maybe positive/or negative
T/t = Nonpregnant females	Metronidazole (500 mg BD x 7 days) or clindamycin	Azole group of antifungals like fluconazole/miconazole which can be applied topically or given orally (150 mg, single dose)	Metronidazole (2 gm single dose oral)
Pregnancy = DOC	Metronidazole (250 mg TDS x 7 days) To be avoided in first trimester	Topical azole antifungals To be avoided in first trimester	Metronidazole (250 mg TDS x 7 days)
Simultaneous treatment of male partner	Not needed as BV is not an STD	If partner has symptoms then treatment needed	Always done as Trichomonas vaginalis is an STD

### Risk Factors for STIs/ Chlamydia infection

- History of previous STI
- Contact with infected person
- Sexually active individual <25 years of age
- Multiple partners
- New partner in last 3 months
- Not using barrier protection
- Street involvement (homelessness, drug use).
- Low socioeconomic status

**Note:** Amongst all risk factors - age (<25 years) is the strongest risk factor.

80% of women having Chlamydia are asymptomatic; 50% of women having gonococcal infection are asymptomatic.

M/C cause of PID—  
chlamydia

Test of cure for *C. trachomatis* and *N. gonorrhoeae* is not routinely indicated. Repeat testing done 3 weeks after treatment is recommended for pregnant women only.

Gonorrhoea	Chlamydia
<ul style="list-style-type: none"> <li>• 2nd M/C cause of PID</li> </ul>	Most common cause of PID
<ul style="list-style-type: none"> <li>• Caused by Gram negative diplococcus N: Gonorrhoea</li> <li>• Associated with trichomonas or chlamydia infection in 60% cases</li> </ul>	<ul style="list-style-type: none"> <li>• Caused by chlamydia trachomatis (D-K serotype) an obligate intracellular parasite</li> </ul>
<ul style="list-style-type: none"> <li>• M/C route of spread: Ascending infection along with sperms</li> </ul>	<ul style="list-style-type: none"> <li>• Associated with Gonorrhoea infection</li> <li>• M/C route of spread: Ascending infection along with sperms</li> </ul>
<ul style="list-style-type: none"> <li>• M/C site affected: endocervix in young females, the urethra and Bartholin's gland</li> </ul>	<ul style="list-style-type: none"> <li>• M/C site affected—endocervix, urethra and Bartholin's gland: Like Gonococcus—stratified squamous epithelium is resistant to chlamydia also.</li> </ul>
<ul style="list-style-type: none"> <li>• Symptoms: <ul style="list-style-type: none"> <li>– Purulent vaginal discharge</li> <li>– Dysuria and frequency</li> </ul> </li> <li>• No pruritus unless it is associated with trichomonas infection</li> </ul>	<ul style="list-style-type: none"> <li>• Symptoms: It is insidious in onset</li> <li>• Mostly asymptomatic</li> <li>• May present with mucopurulent discharge</li> <li>• Dysuria and frequency of micturition with bacteriuria &lt; 10<sup>5</sup> organisms/ml of urine is pathognomic of chlamydia infection in young sexually active females.</li> </ul>
<ul style="list-style-type: none"> <li>• Diagnosis—Nucleic acid amplification testing (NAAT) of urine or endocervical discharge is done.</li> </ul>	NAAT or PCR
<ul style="list-style-type: none"> <li>• Gold standard—culture in Thayer Martin media.</li> </ul>	<ul style="list-style-type: none"> <li>• Culture in McCoy lines</li> </ul>
<ul style="list-style-type: none"> <li>• Test for cure—Not done routinely.</li> </ul>	<ul style="list-style-type: none"> <li>• Test of cure not done routinely</li> </ul>
<ul style="list-style-type: none"> <li>• DOC: Penicillin (4.8 mega units of procaine penicillin). In areas of resistance—ciprofloxacin (500 mg) and ofloxacin (400 mg).</li> </ul>	<ul style="list-style-type: none"> <li>• DOC: Azithromycin 1 gm single dose or Amoxicillin 500 mg TDS x 7 days</li> </ul>
<p>Sex partners should be treated especially those exposed within 2 weeks prior to outset of symptoms on 4 weeks prior to diagnosis in an asymptomatic patient</p>	
<ul style="list-style-type: none"> <li>• DOC in pregnancy—Injection Ceftriaxone 125 mg single dose or oral cefixime 400 mg, single dose.</li> </ul>	<ul style="list-style-type: none"> <li>• DOC in pregnancy—Azithromycin 1 gm single dose or amoxicillin 500 mg TDS x 7 days</li> </ul>

### Condyloma Acuminata (Genital Warts)

- Most common viral STI
- **Causative agent:** HPV (human papilloma virus)
- >200 subtypes of which more than are genital subtypes
- HPV types 6 and 11 are classically associated with anogenital warts/condylomata acuminata
- HPV types of 16 and 18 are the most oncogenic (classically associated with CIN and Ca cervix)
- Anatomical distribution of anogenital HPV infection is: cervix 70%, vulva 25%, vagina 10% and anus 20%.

### Clinical Features

- Soft, multiple warts on any dermal or mucosal surface. Mostly seen in the posterior introitus, the labia majora and minora.
- Genital warts can be diagnosed by gross inspection and colposcopic examination may help to rule out other cervical/vaginal lesions.

**Treatment**

- **Patient applied –**
  - Podofilox 0.5% solution or gel (Pregnancy category C)
  - Imiquimod 5% cream (Pregnancy category C).
- **Provider administered –**
  - Cryotherapy with liquid nitrogen (safe in pregnancy)
  - Podophyllin resin in tincture of benzoin (pregnancy category C)
  - Trichloroacetic acid (TCA) or bichloroacetic acid weekly (80–90%) (safe in pregnancy)
  - Surgical removal/laser
  - Intralesional interferon (not approved by FDA).

**Prevention**

- HPV types 6, 11, 16 and 18 are preventable with Gardasil (quadrivalent HPV recombinant) vaccine. Details of vaccine given in chapter on Cancer Cervix – 14B.

**Genital Ulcers**

The M/c causes of genital ulcers in young, sexual active women are:

- Herpes simplex virus (HSV)
- *Treponema pallidum* (syphilis)
- *Haemophilus ducreyi* (chancroid).

**Herpes Simplex Virus****SUPERFICIAL KNOWLEDGE**

- Etiology – 90% cases are due to HSV-2; 10% cases are due to HSV-1
- Classically
  - HSV-1 – causes disease above the belt (i.e. oral lesions)
  - HSV-2 – causes disease below the belt (i.e. genital lesion)
- Lesion first appears as erythematous plaque which later forms vesicles and then small ulcers with an erythematous halo and yellow base. Ulcers are extremely tender and inguinal lymph nodes are enlarged
- DOC – Acyclovir (200 mg 5 times a day × 5 days)
- Gold standard for diagnosis – Tissue culture (William's Gynecology 2nd ed., p. 77).

**Syphilis**

- **Etiologic agent** – *Treponema pallidum*
- **Primary syphilis** presents as a hard, painless, solitary chancre on the vulva, vagina or cervix, although non-genital lesions may also be present. Non-tender inguinal lymphadenopathy is present. Primary chancre resolves spontaneously within 2–6 weeks
- DOC – Benzathine penicillin.

**Molluscum Contagiosum**

- Caused by Pox virus
  - M/c in developing countries
  - M/c route of spread = Skin contact (sexual/non sexual)
  - Characteristic lesion = Multiple dome-shaped papules with central umbilication
  - Diagnosis = By gross inspection
  - Management = Self-limiting condition
- If required – cryofreezing/curettage of core material should be done

Note: For clinical features of genital ulcers see Annexure 7.



Gonococcus chlamydia

Gonococcus is the M/c cause of acute cervicitis and acute salpingitis in young females

> M/C PID = Chlamydia

**Genital Warts During Pregnancy**

- Condylomata tend to get larger in pregnancy and should be treated early (consider excision)
- Cesarean section as done only if obstruction of birth canal or risk of extensive bleeding
- Do not use imiquimod, podophyllin, or podofilox
- Vertical transmission can occur during pregnancy leading to juvenile laryngeal papillomatosis in the neonate



HPV cannot be prevented by using condoms.



M/c cause of genital ulcers is herpes.

### Manifestations of syphilis in genital tract-

Stage of syphilis	Lesion seen
Primary	Chancre/ulcer
Secondary	Condyloma lata-coarse flat topped moist necrotic lesion
Tertiary syphilis	Gumma-punched ulcer with rolled out margins.

Tubes are not affected in 1° syphilis and infertility does not occur in syphilis.

Infection or inflammation of the upper genital tract involving fallopian tube, ovaries and uterus

Cervicitis and vaginitis are not included in PID

Genital TB is the only PID which does not spread sexually so PID in virgin females is always due to tuberculosis.

## Pelvic Inflammatory Disease (PID)

### KNOW IN-DEPTH

#### Organisms Causing PID

Primary	Secondary
Chlamydia (M/C)	<i>E. coli</i>
Gonococci	Group B <i>Streptococcus</i>
Mycoplasma	<i>Klebsiella</i>
	Anaerobes

#### Syndromic Approach

These days focus has shifted on syndromic approach for diagnosis of PID. This involves treatment based on signs and symptoms rather than laboratory tests.

The current CDC recommendations are that empirical treatment of PID should be initiated in sexually active young females and other females at risk for STD if they experience pelvic or lower abdomen pain, if no other cause can be identified and if one or more of the minimum criteria specified below are present on pelvic examination.

#### CDC 2006 Criteria for the Diagnosis of PID

##### Minimum Criteria

- Lower abdominal tenderness or
- Adnexal tenderness
- Cervical motion tenderness.

##### Additional Criteria

- Oral temperature more than 38.3°C (101°F)
- Abnormal cervical or vaginal mucopurulent discharge
- Presence of abundant WBC on saline mount of vaginal secretions
- ESR > 15 mm/hours
- Elevated C-reactive protein
- Laboratory documentation of cervical infection with *Neisseria gonorrhoeae* or *Chlamydia trachomatis*.

##### Definitive Criteria

- Histopathological evidence of endometritis on endometrial biopsy
- Tubo-ovarian abscess on sonography or other radiologic tests
- Laparoscopic abnormalities consistent with PID.

##### Indications of Inpatient treatment CDC-2006

- Surgical emergencies like appendicitis cannot be ruled out
- Patient is pregnant
- Patient is HIV positive
- Patient does not respond to oral antibiotics (within 72 hours)
- Patient is unable to follow or tolerate an outpatient oral regimen
- Patient has severe illness, nausea and vomiting or high fever
- Patient has tubo-ovarian abscess



## CDC Guidelines for treatment of PID

Dutta Gynae 6<sup>th</sup>/ed p 128

Outpatient Treatment	Inpatient Treatment
<ul style="list-style-type: none"> <li>• Patient should have oral therapy for 14 days</li> <li>• Regimen A               <ul style="list-style-type: none"> <li>– Levofloxacin 500 mg (or ofloxacin 400 mg BD) PO once daily with or without</li> <li>– Metronidazole 500 mg PO BID</li> </ul> </li> <li>• Regimen B               <ul style="list-style-type: none"> <li>– Ceftriaxone 250 mg IM single dose PLUS</li> <li>– Doxycycline 100 mg PO BID with or without</li> <li>– Metronidazole 500 mg PO BID for 14 days</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Regimen A               <ul style="list-style-type: none"> <li>– Cefoxitin/cefotetan 2 g IV every 6 hours for 2–4 days PLUS</li> <li>– Doxycycline 100 mg PO for 14 days</li> </ul> </li> <li>• Regimen B               <ul style="list-style-type: none"> <li>– Clindamycin 900 mg IV every 8 hours PLUS</li> <li>– Gentamicin 2 mg/kg IV (loading dose), followed by 1.5 mg/kg IV (maintenance dose) every 8 hours</li> </ul> </li> <li>• Alternative Regimen               <ul style="list-style-type: none"> <li>– Levofloxacin 500 mg IV once daily with or without</li> <li>– Metronidazole 500 mg IV every 8 hours</li> </ul> </li> </ul>
Broad spectrum antibiotic coverage (cefotaxime/cefotetan) is indicated as most PIDs are polymicrobial (Gram-negative and positive aerobes as well as anaerobic rods and cocci)	Regimen B is preferred for cases with pelvic abscess as it has anaerobic coverage. Alternative regimen is dosed once a day.

## Treatment in a Woman with an Intrauterine Device

**Grade B Recommendation, RCOG 2003**

An intrauterine device (IUD) may be kept in site in mild PID, but should be removed in severe disease. IUD increases the risk of development of PID only in the first few weeks after insertion.

**Surgical Treatment (Grade B Recommendation RCOG 2003)**

Surgical treatment is considered in severe cases or where there is clear evidence of a pelvic abscess. Help of laparoscopy or laparotomy may be taken for adhesiolysis or drainage of pelvic abscess. USG guided aspiration of pelvic abscess is less invasive and equally effective.

## PID in Women with HIV

Contrary to the previous belief that HIV infected women get more severe PID, recent studies show that there may be minor differences and they respond equally well as of the women who are not infected with HIV.

## PID in Postmenopausal Women

Pelvic inflammatory disease is a rare entity in this age group. Extragenital pathology in addition to genital tract malignancy must be considered in these patients. Direct extension of infectious processes from adjacent intra-abdominal viscera is more likely to be associated with PID in older women. Forgotten IUD may be associated with a serious genital tract infection. Postmenopausal women are less likely to harbor a sexually transmitted organism than the premenopausal counterpart. In most reported cases the organisms frequently encountered were *Escherichia coli* (76%) and *Klebsiella* (43%). Other isolated bacteria included *Pseudomonas* (14%) and *Staphylococcus aureus* (< 5%). Broad spectrum antimicrobial therapy should be started and appropriate imaging studies obtained. Surgical intervention should be considered if there is no clinical improvement within 48 hours. Aggressive treatment in these seriously ill patients may lead to decrease in mortality and morbidity in this disease.



M/c route of spread of PID  
– Ascending infection along with sperms

- All PIDs are sexually transmitted except TB



Fitz Hugh Curtis syndrome is development of perihepatic adhesions which leads to right upper quadrant pain. It is seen in PID due to Chlamydia and *N. gonorrhoea*



- IOC for diagnosis of PID – Laparoscopy
- Surest sign of salpingitis is pus extruding from fimbrial end of tube.
- **Violin string like adhesions** in the pelvis and around liver suggests chlamydial infection.

**Laparoscopic findings and severity of PID:**

- **Mild:** Tubes: edema, erythema, no purulent exudates and mobile.
- **Mod:** Purulent exudates from the fimbrial ends, tubes not freely movable.
- **Severe:** Pyosalpinx, inflammatory complex, abscess.

### Sequelae of PID

1. Infertility – seen in 6–60% patients
2. Ectopic pregnancy
3. Chronic pelvic pain, dyspareunia
4. Fitz-high-Curtis syndrome

### Genital Tuberculosis

#### KNOW IN-DEPTH

- Genital tuberculosis is almost always a secondary infection, with M/c primary sites being (in that order) lungs > lymph nodes > abdomen
- Route of spread – Hematogenous
- M/c site is B/L Fallopian tubes (In Fallopian tubes – M/c affected part = Ampulla and M/c encountered pathology is endosalpingitis)
- M/c age group = 20–30 years (28 years specifically)
- M/c symptom = Infertility
- If patient conceives spontaneously, ectopic pregnancy is the most likely outcome.
- IInd M/c site of involvement: uterus
- Cornu of the uterus is most commonly affected as it is in continuation with the fallopian tube and infection descends from the tubes
- Uterine TB can manifest in the form of
  - Asherman's syndrome – i.e. destruction of the endometrial lining of uterine cavity with the formation of intrauterine synechiae or adhesions
  - Pyometra – i.e. pus-filled uterine cavity.

Sites of Genital TB	% involvement
Tubes	90–100%
Uterus	50–60%
Ovaries	20–30%
Vagina and Vulva	1–2%



Infertility results from tubal as well as endometrial disease. The tubes may be patent on HSG but there is functional loss.

#### ➤ Menstrual problems occurring in TB patients:

M/C menstrual complain oligomenorrhea/Amenorrhea 1st menstrual complain – Menorrhagia (due to Endometritis in acute phase)  
 Pelvic examination – M/C finding = Normal pelvic examination  
 2nd M/C finding – tenderness present  
 M/C finding in genital TB in adolescent girls – B/L Adnexal mass



- What % of TB patients are infertile – 70%
- What % of infertile patients have TB = worldwide = 10%  
India = 17%

### Hysterosalpingography in TB

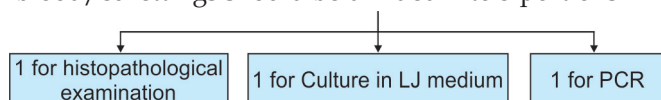
HSG is contraindicated in patients of genital TB as it can lead to reactivation or spreading of disease. But, if unknowingly HSG is done in patients of TB, typical/characteristic findings seen are:

- Lead pipe appearance of tube
- Beaded appearance of tube
- Hydrosalpinx
- Cornual block
- Intravasation of dye
- Golf club stick like appearance of tube

- Tobacco pouch appearance of the fimbrial end of tube
- Uterus – honeycomb appearance due to Asherman syndrome

### Diagnosis

- **Endometrial biopsy:** Best time = 1–2 days before or 12 hours after onset of menses. In unmarried girls – menstrual blood can be collected within 12 hours of onset of menstruation.
- PCR done on endometrium or menstrual blood is more sensitive than microscopy and bacteriological culture.
- Menstrual blood/curettings should be divided into 3 portions



### Treatment

- Genital tuberculosis falls in category 1. The treatment is for 6 months
- 4-drug AKT (isoniazid, ethambutol, pyrazinamide, and rifampicin) is given for 2 months, and 2 drugs (INH and rifampicin) are given for remaining 4 months
- Surgery for restoration of fertility (corrective tuboplasty) is contraindicated in genital TB
- IVF after completion of AKT is the treatment for infertility.

**Note:** The text of this chapter has been referenced and updated from current diagnosis and treatment sexually transmitted infection international edition.

### Most Common

- M/c cause of genital ulcers – Herpes
- M/c vaginitis in pregnant women – Candidiasis
- M/c vaginitis in young females – Trichomonas vaginitis
- M/c organism causing candidiasis – *Candida albicans*
- M/c cause of acute cervicitis and acute salpingitis – Gonorrhoea
- M/c site for asymptomatic Gonorrhoea in young females – Endocervix
- M/c cause of PID in virgin females – Tuberculosis
- Strawberry vagina seen in Trichomonas vaginitis
- Curdy white discharge/cottage cheese like discharge – Candidiasis
- Whiff test positive/clue cells/Amsel's criteria – Bacterial vaginosis
- Genital warts caused by HPV 6 and 11 (Condyloma acuminata)
- Chancroid caused by *Haemophilus ducreyi*
- IOC for PID – Laparoscopy
- IOC for Chlamydia – NAAT > Polymerase chain reaction.

### Important Percentages

- 50% of patients of gonorrhoea are asymptomatic.
- 80% of patients of *Chlamydia* are asymptomatic.
- After treatment of Genital TB of the patients who conceive 50% have tubal pregnancy. 20–30% abort and 2% have live birth.

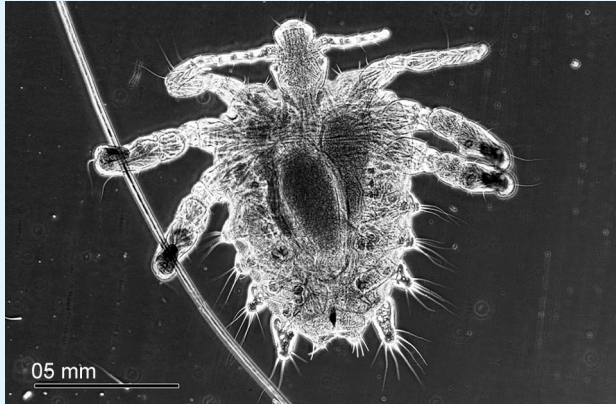


### Asherman syndrome

- M/c cause – dilatation and curettage done in post-partum period followed by D&C done for missed abortion
- Presentation:
  - Hypomenorrhea
  - Amenorrhea
  - Infertility
- IOC – hysteroscopy as it is diagnostic and therapeutic.
- Hysterosalpingography shows honey comb appearance
- Management – Hysteroscopic adhesiolysis followed by insertion of Cu T to prevent adhesion formation and a combination of estrogen & progesterone given to rebuild endometrium.

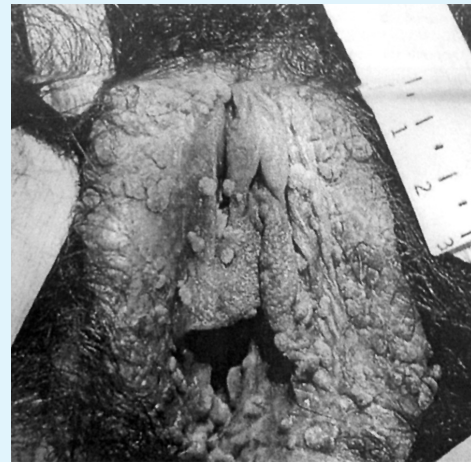
## FIGURE BASED QUESTIONS

- F1.** Figure 6 shows phthirus pubis. The pathogen was seen in pubic hair of a pregnant female complaining of genital itching. DOC for pubic lice in pregnant females is:
- Premetharin cream 1%
  - Malathion 0.5%
  - Overnectin
  - Petroleum jelly



**Fig. F1**

- F2.** Identify the lesion in the figure. All of the following drugs can be used in this condition except:
- Imiquimod
  - Podophyllin
  - Methotrexate
  - Trichloroacetic acid



**Fig. F2**

## QUESTIONS

- Which of the following is not sexually transmitted? (AIIMS June 00)
  - Echinococcus
  - Candida
  - Molluscum contagiosum
  - Group B. Streptococcus
- A patient with discharge per vagina was evaluated and on endocervical biopsy Chlamydia was found. Treatment to be given in this case is: (AIIMS June 00)
  - Azithromycin and contact tracing
  - Metronidazole only
  - Doxycycline and metronidazole
  - Azithromycin
- Strawberry vagina is seen in: (AIIMS June 98)
  - Candida albicans
  - H. vaginalis
  - Syphilis
  - Trichomonas vaginalis
- All are risk factors for vaginal candidiasis except: (AIIMS Nov 10)
  - HIV
  - Hypertension
  - Pregnancy
  - Diabetes mellitus
- Clue cells are seen in: (AIIMS May 08)
 

a. Bacterial vaginosis	b. Candidiasis
c. Trichomoniasis	d. Gonorrhoea
- A 40-year-old woman presented to the gynecologist with complaints of profuse vaginal discharge. There was no discharge from the cervix on the speculum examination.

The diagnosis of bacterial vaginosis was made based upon all of the following findings on microscopy except: (AIIMS 06)

- Abundance of gram variable coccobacilli
  - Absence of lactobacilli
  - Abundance of polymorphs
  - Present of clue cells
- In hysterosalpingography, fallopian tubes are seen beaded in appearance with clubbing of fimbrial end and ampulla. Most likely cause is: (AIIMS June 00)
    - Tuberculosis
    - Candidiasis
    - Chlamydia
    - Gonococcus
  - A lady approaches a physician for contraceptive advice. On examination, there were two symmetrical ulcers on vulva, which were well-defined with firm base. Which of the following is the most likely cause? (AIIMS Nov 00)
 

a. Chancre	b. Herpes
c. Syphilis	d. Malignancy
  - A 25-year-old female with history of multiple contacts presenting with growth on vulva, the probable diagnosis is: (AIIMS June 98)
    - Condyloma accuminata
    - Verruca plana
    - Verruca vulgaris
    - Condyloma lata

10. A young lady presents to your office with complain of copious vaginal discharge, but there is no cervical discharge on per speculum examination. Which of the following should be given for the management?  
 a. Metronidazole and fluconazole (AIIMS Nov 2012)  
 b. Metronidazole and azithromycin  
 c. Metronidazole and doxycycline  
 d. Fluconazole only
11. Cervicitis is caused by: (PGI June 03)  
 a. Pseudomonas  
 b. Staphylococcus  
 c. Chlamydia  
 d. Trichomonas  
 e. N. gonorrhoea
12. Minimum criteria to diagnose PID include(s):  
 a. Lower abdominal pain (PGI May 2013)  
 b. Fever  
 c. Cervical motion tenderness  
 d. Adnexal tenderness  
 e. Leucocytosis
13. Acute PID is treated by: (PGI June 03)  
 a. IV antibiotics (broad spectrum)  
 b. Drainage of TO mass  
 c. Abdominal hysterectomy  
 d. Laparoscopic exploration
14. Nongonococcal urethritis is caused by: (PGI Dec 99)  
 a. Chlamydia  
 b. LGV  
 c. Syphilis  
 d. Gardnerella vaginalis
15. Gonorrhoea – which is not a presenting feature?  
 a. Discharge (PGI Dec 08)  
 b. Acute febrile episodes  
 c. Hematuria  
 d. Reddened lips of vulva and vagina
16. Which of the following statements about clinical features in a female suffering from Gonorrhoea is correct?  
 a. 50% patients are asymptomatic  
 b. Excessive vaginal discharge is seen  
 c. Vaginal discharge is purulent  
 d. Features of perihepatitis present  
 e. All of the above statements are correct
17. True about Trichomonas vaginalis: (PGI June 05)  
 a. Flagellated parasite  
 b. Fungal infection  
 c. Curdy white discharge  
 d. Pruritus  
 e. Sexually transmitted disease
18. Trichomonas – which of the following true is?  
 a. Foul smelling vaginal discharge (PGI June 08)  
 b. Vaginal pH is 4  
 c. Strawberry vagina  
 d. Infertility  
 e. Abortion
19. True about bacterial vaginosis: (PGI June 05)  
 a. Itching  
 b. Gray discharge  
 c. Clue cells found  
 d. Fishy odor discharge  
 e. Caused by *Gardnerella vaginalis*
20. True about bacterial vaginosis: (PGI Dec 04)  
 a. Intense pruritis  
 b. Gray and white discharge  
 c. Associated with vaginal pH  
 d. Commonly associated with intensive mucosal inflammation  
 e. Oral metronidazole is the drug of choice
21. Not true about bacterial vaginosis: (PGI Nov 2012)  
 a. Clue cells present  
 b. With KOH gives amine smell  
 c. pH < 4.5  
 d. Yellow green discharge  
 e. Whiff test positive
22. In a patient with pelvic inflammatory disease due to tuberculosis, which of the following statements is true?  
 (PGI Dec 01)  
 a. Mycobacterium can be grown from menstrual blood  
 b. Associated with infertility  
 c. Ectopic pregnancy is common  
 d. Dysmenorrhea is a common presentation
23. All are clinical features of PID except:  
 a. Temp > 38°C  
 b. WBC count of 15,000  
 c. ESR – 10 mm/hour  
 d. Tenderness on movement of cervix
24. During laparoscopy, the preferred site for obtaining cultures in a patient with acute PID is:  
 a. Endocervix  
 b. Endometrium  
 c. Pouch of Douglas  
 d. Fallopian tubes
25. Asymptomatic carriage of gonococcal infection in female is commonly seen in:  
 (AI 97)  
 a. Endocervix                      b. Vagina  
 c. Urethra                            d. Fornix
26. Gonococcal vaginitis occurs in: (TN 2007)  
 a. Adults                              b. Children  
 c. Infants                             d. Adolescents
27. Which of the following cannot be detected by wet film?  
 (Delhi 08)  
 a. Candida                            b. Trichomonas  
 c. Chlamydia                        d. Bacterial vaginosis
28. The most sensitive method for detecting cervical chlamydia trachomatis infection is:  
 (AI 04)  
 a. Direct fluorescent antibody test  
 b. Enzyme immunoassay  
 c. Polymerase chain reaction  
 d. Culture on irradiated McConkey cells

29. 45-year-old female complains of lower abdominal pain and vaginal discharge. On examination, there is cervicitis along with a mucopurulent cervical discharge. The Gram smear of the discharge shows presence of abundant pus cells, but no bacteria. The best approach to isolate the possible causative agent would be: (AI 05)
- Culture on chocolate agar supplemented with hemin
  - Culture on McCoy cells
  - Culture on a bilayer human blood agar
  - Culture on Vero cell lines
30. Drug of choice for Chlamydia in pregnancy: (AI 10)
- Doxycycline
  - Tetracycline
  - Erythromycin
  - Penicillin
31. A woman presents with a thick curdy-white vaginal discharge. The best treatment for her is: (AI 00)
- Miconazole
  - Metronidazole
  - Nystatin
  - Doxycycline
32. Creamy fishy odor is caused by: (AI 09)
- Trichomonas
  - Gardnerella
  - Candida
  - Chlamydia
33. A lady presented with creamy white vaginal discharge with fishy odor, drug of choice is: (AIIMS May 09)
- Doxycycline
  - Ofloxacin
  - Metronidazole
  - Clindamycin
34. Most common site for genital tuberculosis is: (AI 98)
- Ovary
  - Uterus
  - Cervix
  - Fallopian tube
35. Most common route of transmission of endometrial tuberculosis is: (AIIMS June 98)
- Direct local spread
  - Lymphatic spread
  - Retrograde spread
  - Hematogenous
36. The most common cause of tubal block in India is: (AI 06)
- Gonorrhoea infection
  - Chlamydia infection
  - Tuberculosis
  - Bacterial vaginosis
37. Salpingitis/Endosalpingitis is best confirmed by: (AI 08)
- Hysteroscopy and laparoscopy
  - X-ray
  - Hysterosalpingography
  - Sonosalpingography
38. A 19-year-old girl with painless ulcer in labia majora with everted margins: (AIIMS May 2013)
- Treponema pallidum
  - Chlamydia
  - Gonorrhoea
  - Herpes genital ulcer disease

## NEW PATTERN QUESTIONS

39. Which of the following is true with regards to genital tuberculosis?
- Ovarian involvement can occur without tubal affection
  - Infertility is mainly due to anovulation
  - Acid fast bacilli is identified in 100% cases of tubercular endometritis
  - A negative Mantoux test reasonably excludes tuberculosis
40. The following statements are related to tubercular salpingitis except:
- The abdominal ostium may be patent with eversion of fimbriae
  - The early lesion may be confused with adenocarcinoma on histology
  - Genital tuberculosis is always secondary and the tubes are invariably the primary sites
  - Salpingitis isthmica nodosa is the exclusive pathology to tuberculosis
41. True statement about female genital tuberculosis:
- Genital tract involvement results from lymphatic spread
  - Premenstrual histopathological examination is diagnostic
  - Polymerase chain reaction (PCR) techniques have got higher sensitivity in detection
  - Reproductive outcome following antituberculous chemotherapy is satisfactory
42. The risk factors of acute pelvic inflammatory disease (PID) are the following except:
- Menstruating teenagers who have multiple sex partners
  - IUD users
  - Women with monogamous partner who had vasectomy
  - Previous history of acute PID
43. The following are the primary sites of acute gonococcal infection except:
- Urethra
  - Bartholin's gland
  - Skene's gland (paraurethral glands)
  - Ectocervix
44. Ulceration of the vulva is commonly seen in all except:
- Bacterial vaginosis
  - Syphilis
  - Chancroid
  - Behçet's disease
45. Regarding bacterial vaginosis, all are true except:
- Homogeneous vaginal discharge with pH 5.0 to 6.0
  - Positive KOH – With fishy odour
  - Positive clue cells in 100% of cases
  - It is due to *Gardnerella vaginalis*

**ANSWERS TO FIGURE BASED QUESTIONS**

**F1. Ans. is a, i.e. Premetharin cream 1%**

Ref. *Current Diagnosis and Treatment Sexually Transmitted Diseases*, p227

Pubic lice, a common condition is caused by the crab louse, *Phthirus pubis*.

The pubic louse is 0.8–1.2 mm in length and can be seen with the naked eye.

The louse primarily infests pubic hair but may attach to adjacent hair of the chest, abdomen, legs, and buttocks. Eyelashes may also become infested.

*Phthirus pubis* lives for approximately 2 weeks, during which females produce about 25 ova.

The nits incubate for 1 week, and the nymphs mature to adults over pruritus results from hypersensitivity to louse saliva, it may be 2 or more weeks before symptoms develop following initial infestation.

Bluish-gray macular lesions secondary to deep dermal hemosiderin deposition from the bites of the louse, known as *maculae cerulean*, may be noted in patients with established infestation.

Crab lice and nits may be seen with the naked eye; therefore, the presence of one or both of these forms in the hair is diagnostic.

**Treatment**

- **Permethrin 1% cream rinse** and **pyrethrins with piperonyl butoxide** are the primary agents recommended for the treatment of pubic lice and are the drugs of choice for pregnant or lactating women. These agents should be applied to the affected areas and washed off after 10 minutes.

- **Malathion 0.5% lotion** is in alternative when treatment failure is thought to be secondary to drug resistance. The agent should be applied to the affected area for 8–12 hours and rinsed off.

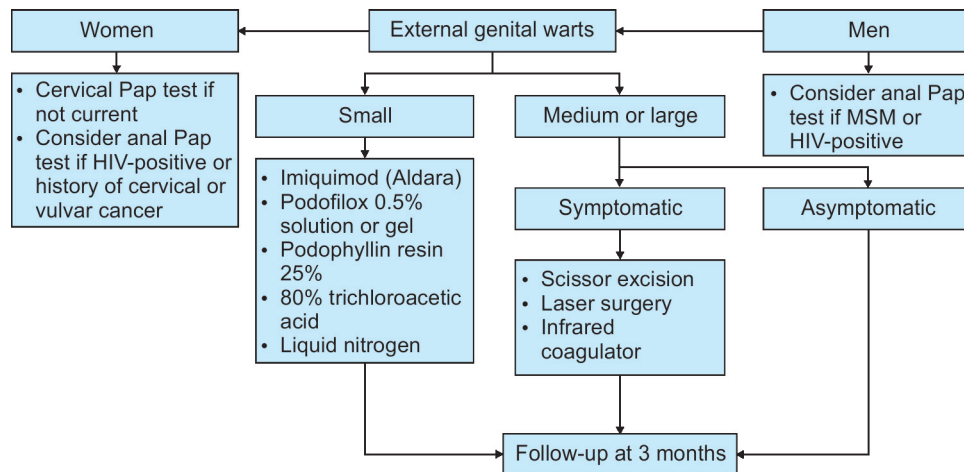
- **Ivermectin** (200 mcg/kg as a single dose, repeated in 2 weeks), provides an oral alternative for therapy.

**Note:** Pubic lice are primarily spread through sexual contact. Therefore, all partners with whom the patient has had sexual contact within the previous 30 days should be evaluated and treated, and sexual contact should be avoided until all partners have successfully completed treatment and are thought to be cured.

**F2. Ans. is c i.e. Methotrexate**

Ref. *Current Diagnosis and Treatment Sexually Transmitted Diseases*, p94, 95

The condition shown in the figure is vulvar warts.



**ANSWERS**

**1. Ans. is a, i.e. Echinococcus**

Ref. *Park 19<sup>th</sup>/ed p 278, 20<sup>th</sup>/ed p 289*

**Classification of sexually transmitted disease**

Bacterial	Viral	Protozoa	Fungal	Ectoparasites
<ul style="list-style-type: none"> <li>• <i>Neisseria gonorrhoea</i></li> <li>• <i>Chlamydia trachomatis</i></li> <li>• <i>Treponema pallidum</i></li> <li>• <i>Haemophilus ducreyi</i></li> <li>• <i>Mycoplasma hominis</i></li> <li>• <i>Ureaplasma urealyticum</i></li> <li>• <i>Calymmatobacterium granulomatis</i></li> <li>• <i>Shigella species</i></li> <li>• Group B streptococcus</li> <li>• Bacterial vaginosis</li> <li>• <i>Campylobacter</i> spp.</li> </ul>	<ul style="list-style-type: none"> <li>• Herpes 1 – 2</li> <li>• Hepatitis B</li> <li>• HPV</li> <li>• HIV</li> <li>• Molluscum contagiosum</li> </ul>	<ul style="list-style-type: none"> <li>• <i>Entamoeba histolytica</i></li> <li>• <i>Giardia</i></li> <li>• <i>Trichomonas</i></li> </ul>	<ul style="list-style-type: none"> <li>• <i>Candida</i></li> </ul>	<ul style="list-style-type: none"> <li>• <i>Phthirus pubis</i></li> <li>• <i>Sarcoptes scabiei</i></li> </ul>

2. **Ans. is a, i.e. Azithromycin and contact tracing**

**Management of Chlamydia**

Uncomplicated chlamydia can be treated with Tetracycline (500 mg 4 times daily), Doxycycline (1000 mg twice daily), Erythromycin (500 mg 4 times daily), Fluoroquinolone -ofloxacin 300 mg twice daily, or Azithromycin -single dose - 1 g

**Advantages of Azithromycin are**

- Single dose regimen - 1 g stat dose (It is as effective as 7 days of doxycycline treatment).
- Better patient compliance.
- Fewer gastrointestinal side effects.

**Disadvantage:**

- High cost of azithromycin.

**Contact tracing:**

- Patients with asymptomatic infection and their sex partners form a major burden of chlamydial infection so, contact tracing should always be done (wherever possible).

*Ref. Harrison 18<sup>th</sup>/ed p 1426; William's Gynae 1<sup>st</sup>/ed p 66;*

*Current diagnosis and treatment of sexually transmitted diseases p 81*

3. **Ans. is d, i.e. Trichomonas vaginalis**

*Ref. Shaw 15<sup>th</sup>/ed p 146; Williams Gynae 1<sup>st</sup>/ed p 64, 65; Jeffcoates 7<sup>th</sup>/ed p 340-342*

Strawberry vagina or angry-looking vagina is seen in case of Trichomonas infection.

4. **Ans. is b, i.e. Hypertension**

*Ref. Shaw 15<sup>th</sup>/ed p 146*

**Risk factors for Candidal (Monilla) Vaginitis**

- Promiscuity
- **Immunosuppression** (like HIV)
- **Pregnancy**
- Steroid therapy
- Following long-term broad spectrum antibiotic therapy
- Oral contraception pills
- **Diabetes mellitus**
- Poor personal hygiene
- Obesity

5. **Ans. is a, i.e. Bacterial vaginosis**

6. **Ans. is c, i.e. Abundance of polymorphs**

*Ref. Shaw 15<sup>th</sup>/ed p 131, 132; CGDT 10<sup>th</sup>/ed p 670; William's Gynae 1<sup>st</sup>/ed pp 51, 63*

*"Clue cells are the most reliable indicator of bacterial vaginosis. The positive predictive value of this test for the presence of BV is 95%."*

*—Williams Gynae 1<sup>st</sup>/ed p 51*

**Microscopy in Bacterial vaginosis shows:**

- Clue cells<sup>o</sup> seen in wet mount
- ↑ number of Gardnerella vaginalis<sup>o</sup>
- ↓ number of lactobacilli<sup>o</sup>
- ↓ leukocytes (conspicuously absent)<sup>o</sup>/polymorphs absent



Clue cells are vaginal epithelial cells to which bacteria are adhered.

7. **Ans. is a, i.e. Tuberculosis**

*Ref. Shaw 15<sup>th</sup>/ed p 157; Dutta Gynae 5<sup>th</sup>/ed p 137-38*

**HSG showing 'Bead-like fallopian tube and clubbing of ampulla are suggestive of genital tuberculosis'.**



**HSG findings in case of tuberculosis:**

- Rigid non-peristaltic pipe like tube called as **lead pipe appearance**.<sup>o</sup>
- **Beading of tube and variation in filling density**.<sup>o</sup>
- Elongated and distended tube with everted fimbriae and patent abdominal ostium called as 'tobacco pouch' appearance.<sup>o</sup>
- Calcification of tube.<sup>o</sup>
- Bilateral cornual block.<sup>o</sup>
- Vascular or lymphatic intravasation of dye.<sup>o</sup>
- Tubal diverticula and/or fluffiness of tubal outline.<sup>o</sup>
- Uterine cavity—irregular outline, honeycomb appearance or presence of uterine synechiae (**Asherman's syndrome**).<sup>o</sup>

**Remember:** In a proven case of genital tuberculosis, HSG is contraindicated as it may spread the infection. So, HSG should not be performed until pelvic tuberculosis is excluded by endometrial study.



## 8. Ans. is a, i.e. Chancere

Ref. Harrison 17<sup>th</sup>/ed p 1040; William's Gynae 1<sup>st</sup>/ed p 58-9  
Current diagnosis and treatment of STD's p 21



**Painless well-defined ulcers with firm base should raise the suspicion of chancere.**

(The lesion in the question is thought to be painless as the lady in the question is not coming because of ulcer, but for contraceptive advice. Presence of ulcer is an incidental finding).

**Chancere** is the primary lesion of primary syphilis.

- It is most commonly found on the labium majus, labium minus, fourchette, clitoris, urethral orifice or cervix but can be found anywhere on the lower genital tract.
- In 10% cases more than one primary lesion is present.
- The first manifestation is a small papule which breaks to form an ulcer.
- Ulcer is firm, painless with raised edges and granulomatous base.
- In fact any sort of discrete relatively painless ulceration on the vulva may be primary syphilitic lesion.
- Inguinal glands enlarge when the primary is on the vulva or lower vagina.
- Lymph nodes are hard, shotty, painless, and do not suppurate.

## 9. Ans. is a, i.e. Condyloma accuminata

Ref. Shaw 15<sup>th</sup>/ed pp 138, 139; Current diagnosis and treatment of sexually transmitted diseases, pp 92-93



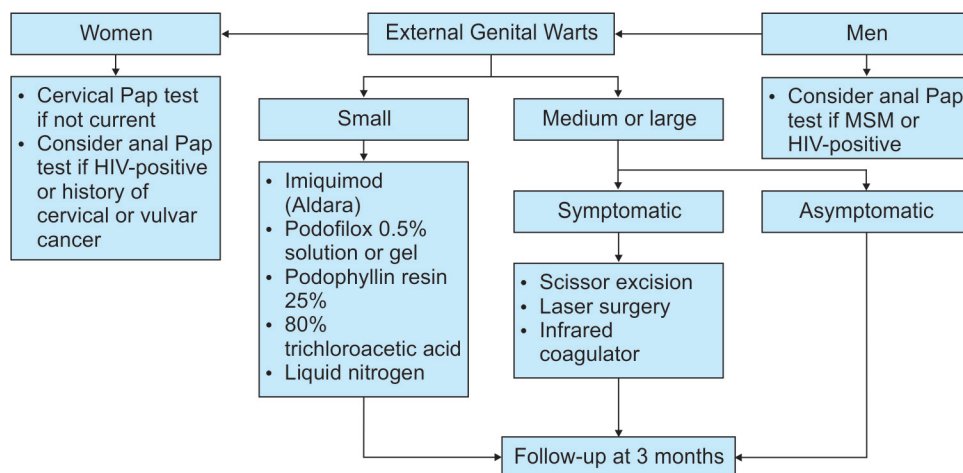
- History of sexual exposure and growths on vulva is consistent with condyloma accuminata.

**Condyloma accuminata:**

- It is a *sexually transmitted disease*<sup>Q</sup> caused by HPV 6<sup>Q</sup>, 16<sup>Q</sup> and 18<sup>Q</sup>
- Warts are seen on the vulval area.<sup>Q</sup>
- Warts are common in the regions affected most directly by coitus<sup>Q</sup> i.e. posterior fourchette<sup>Q</sup> and lateral areas of vulva. These verrucous growths may coalesce to form large cauliflower growths.<sup>Q</sup>
- Condyloma is associated with vulval,<sup>Q</sup> vaginal,<sup>Q</sup> and cervical cancers.<sup>Q</sup>
- Diagnosis is by colposcopy which shows raised patches of aceto-white epithelium with speckled appearance.<sup>Q</sup>

**Management:**

- Young women with flat condylomas may be observed for 6 months, especially if it develops during pregnancy as lesions may disappear spontaneously.
- Treatment options include:
  - Podophyllin<sup>Q</sup>
  - Podofilox<sup>Q</sup>
  - Imiquinod<sup>Q</sup>
 ] *Cannot be used in pregnancy*
- *Trichloroacetic acid*<sup>Q</sup>: Can be applied in the last 4 weeks of pregnancy to avoid cesarean section with large lesions
- *Electrocoagulation/Cryotherapy/Laser therapy*: Can be done in pregnancy but before 32 weeks to avoid post treatment necrosis which may last as long as 4-6 weeks.<sup>Q</sup>



**Lets also rule out other options.**

- **Verrucous plana:**
  - Hands and face are the most common site<sup>Q</sup>, warts are not seen in genital area.
  - It is usually seen in children.<sup>Q</sup>
  - Sometimes, it can also occur in young women, but then face is the most common site involved.<sup>Q</sup>
- **Verruca vulgaris:**
  - Here also the site of warts is different; usually affected areas are exposed parts of the body<sup>Q</sup>, hand<sup>Q</sup>, feet<sup>Q</sup>, nails, arms, and legs, face, and scalp.
- **Condyloma lata:**
  - Is the growth seen on genitalia in secondary syphilis.<sup>Q</sup>
  - The presence of these lesions without any other features of syphilis is very unlikely.

**10. Ans. is a, i.e. Metronidazole and fluconazole**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 176; Internet search-www.naconlinr.org/upload/publication/st*

**Syndromic management of sexually transmitted infections (WHO 1991)**

**Principle:** Treatment of STDs should be initiated at the patient's first visit to a clinic. At the same time the couple is counseled about the importance of condom use and prevention of STD transmission.

Syndromic managements are based on epidemiological studies all over the world. Syndromic diagnosis and laboratory assisted diagnosis have been found similar in terms of accuracy.

**Method:** Management is done by criteria for syndromic diagnosis of PID. These include detection of vaginal discharge abdominal pain, cervical motion tenderness, bilateral adnexal tenderness. Providers are trained up to follow a standardized protocol (flow chart) to treat such a patient. This is particularly suitable in a health care setting of developing countries.

**11. Ans. is b, c and e i.e. Staphylococcus; Chlamydia; and N. gonorrhoea**

*Ref. Dutta Gynae 5<sup>th</sup>/ed p 163*

*Cervicitis refers to infection of the endocervix including the glands and stroma.*

**Organisms causing cervicitis**

- Streptococcus
- Staphylococcus
- Gonococcus
- E. coli
- Chlamydia

Trichomonas, Candida and Herpes simplex virus cause inflammation of the ectocervix (vaginitis) and not of endocervix.

**12. Ans. is a, c and d, i.e. Lower abdominal pain, Cervical motion tenderness and Adnexal tenderness.**

*Ref. Shaw 15<sup>th</sup>/ed 449-50; Dutta's Gynae 6<sup>th</sup>/ed p 130; Johns Hopkins Manual of Gynecology and Obstetrics, The, 3<sup>rd</sup>/ed; William's Gynae 1<sup>st</sup>/ed p 73*

**CDC criteria for Diagnosis of PID has been discussed in detail earlier.**

**13. Ans. is a, b and d, i.e. I/V antibiotics, Drainage of TO mass and Laparoscopic exploration**

*Ref. Textbook of Gynae, Sheila Balakrishnan 1<sup>st</sup>/ed p 217-18; Novak 15<sup>th</sup>/ed p 565-66*

**Management of PID**

- Broad-spectrum antibiotics (oral or IV)
- If tubo-ovarian mass/abscess is present - it should be treated medically but, if there is no response drainage should be done.
- Drainage of a pelvic abscess by colpotomy may occasionally be needed

**Place of surgery in acute PID:** Surgery can range from laparoscopy to laparotomy.

**Indications**

- No response to treatment and worsening of condition
- Ruptured tubo-ovarian abscess
- Drainage of a pelvic abscess
- Doubtful diagnosis

**Other measures**

- Male partners should receive prophylactic treatment for gonococcal and chlamydial infection
- Male partners should be counseled regarding condom use to prevent further exposure
- PID patients and their partners should be counseled regarding HIV and STDs and should be offered confidential HIV testing.
- If an IUCD is present, it must be removed once treatment is commenced.
- Contraceptive counseling must be provided

**14. Ans. is a, i.e. Chlamydia**

*Ref. Harrison 17<sup>th</sup>/ed p 823; Current diagnosis and treatment of STI p 15*

**Non gonococcal urethritis is caused by:**

- *Chlamydia trachomatis* (30 - 40%)
- *Mycoplasma genitalium*

**Rare Cases**

- *Ureoplasma urealyteum*
- *E coli*

- *Ureoplasma urealyticum*
- *Trichomonas vaginalis*
- Herpes simplex virus
- Anaerobic bacteria
- Adenovirus

15. Ans. is a, and d, i.e. Discharge; and Reddened lips of vulva and vagina

16. Ans. is e, i.e. All of the above statements are correct.

Ref. Dutta Gynae 5<sup>th</sup>/ed p 143; CGDT 10<sup>th</sup>/ed p 671; William's gynae 2<sup>nd</sup>/ed pp 86, 87

- Gonorrhoea infection is caused by *Neisseria gonorrhoeae* – a gram-negative diplococci.
- Incubation period = 3–7 days<sup>Q</sup>

#### Clinical features in adults

- 50 percent of patients with Gonorrhoea are asymptomatic<sup>Q</sup>
- Asymptomatic gonorrhoea in females is due to infection of endocervix.<sup>Q</sup>

In symptomatic cases, M/c symptom is usually excessive vaginal discharge, lower abdominal pain, and dysuria.

*"In exceptional cases gonococcal septicemia is described and may be manifested by pyrexia and even vesicular or pustular dermatitis"*

– Jeffcoate's 7<sup>th</sup>/ed p 313

(So I am ruling out option "b" of Q 13, i.e. acute fibrile illness is seen in gonorrhoea)

#### Signs:

- Labia are swollen and look inflamed.<sup>Q</sup>
- Cervicitis with a mucopurulent cervical discharge.
- Bartholin glands are enlarged and tender.<sup>Q</sup>
- On squeezing the ducts: purulent exudate escapes.<sup>Q</sup>

#### Complications-PID, Fitz-Hugh-Curtis syndrome and septicemia.<sup>Q</sup>

**Diagnosis:** Secretions from the urethra, Bartholin's gland and endocervix are collected for Gram staining and culture.<sup>Q</sup>

**Treatment:** Single dose ceftriaxone<sup>Q</sup>/and azithromycin or you can give doxycycline 100 mg twice daily × 7 days for chlamydia

17. Ans. is a, d and e, i.e. Flagellated parasite, Pruritus, and Sexually transmitted disease

Ref. Shaw 15<sup>th</sup>/ed p 146; William's Gynae 1<sup>st</sup>/ed p 64-5; Jeffcoate's 7<sup>th</sup>/ed pp 340-42

As discussed in the preceding text – strawberry vagina or angry looking vagina is seen in *Trichomonas vaginalis*.

#### *Trichomonas vaginalis*

- Is a flagellated protozoa which leads to trichomonas vaginitis.
- Patients complain of profuse frothy creamy/Slightly greenish discharge and pruritis

O/E = Multiple small punctate strawberry spots are seen on vaginal walls and portio vaginalis of cervix called as strawberry vagina.

18. Ans. is a and c, i.e. Foul smelling vaginal discharge; and Strawberry vagina

Ref. John Hopkins Manual of Gynecology and Obstetrics 4<sup>th</sup>/ed p 430; Shaw 15<sup>th</sup>/ed p 145; Novak 14<sup>th</sup>/ed p 544; Leon Speroff 7<sup>th</sup>/ed p 1090

- There is no doubt that trichomonas infection cause foul smelling discharge and strawberry vagina.
- Vaginal pH favoring trichomonas infection is 5–6 (Shaw 14<sup>th</sup>/ed p 131) or 5.5 to 6.5 (Jeffcoate 7<sup>th</sup>/ed p 341).

So option 'b' is incorrect.

*Trichomonas vaginalis* has not been associated with infertility.

Infact Jeffcoates 7<sup>th</sup>/ed p 702 says – *"Clinical observations show that many women with chronic cervicitis and Trichomonas vaginalis conceive repeatedly without difficulty."*

#### Common infections associated with infertility are:

- *Chlamydia trachomatis*
- *N. gonorrhoea*
- *Ureoplasma ureolyticum*

– Shaw 14<sup>th</sup>/ed p 189

#### Infections and Infertility

*"Infections of the female and male genital tracts have been implicated as causes of infertility. Chlamydia infection and gonorrhoea are the major pathogens and should be treated appropriately. Ureoplasma urealyticum and Mycoplasma hominis have also been implicated and if positively identified by culture, they should be treated with oral doxycycline, 100 mg twice daily for 7 days. This has been shown to increase the pregnancy rate in patients with primary infertility."*

– John Hopkin's Manual of Gynecology and Obstetrics 4<sup>th</sup>/ed p 430.

#### Effect of *Trichomonas* on Pregnancy Outcome –

*"Pregnant women with Trichomonas vaginitis are at increased risk for premature rupture of membranes and preterm delivery."*

– Novak 14<sup>th</sup>/ed p 544

**As far as abortions is concerned –**

Organisms which have been associated with sporadic abortions are:

- *Chlamydia trachomatis*
- *Mycoplasma hominis*
- *Listeria monocytogenes*
- Herpes virus
- *Ureoplasma ureolyticum*
- *Toxoplasma gondii*
- *Camphylobacter*
- Cytomegalovirus

– Leon Speroff 7<sup>th</sup>/ed p 1090

19. **Ans. is b, c, d and e, i.e. Gray discharge; Clue cells found; Fishy odor discharge; and Caused by Gardnerella vaginalis**
20. **Ans. is b, c and e, i.e. Gray and white discharge; Associated with vaginal pH; and Oral metronidazole is the drug of choice.**

Ref. Shaw 15<sup>th</sup>/ed p 131-32; CGDT 10<sup>th</sup>/ed p 670; William's Gynae 1<sup>st</sup>/ed p 50, 51

All the following options we have discussed earlier.



**Remember:** Pruritus is not seen in bacterial vaginosis

21. **Ans. is c and d, i.e. pH < 4.5 and Yellow green discharge.** Ref. Shaw 15<sup>th</sup>/ed p 131; Dutta Gynae 6<sup>th</sup>/ed p 152
- Bacterial vaginosis is characterised by homogeneous, greyish white discharge adherent to vaginal wall.

Amsel's diagnostic criteria—bacterial vaginosis can be diagnosed if 3 of the following 4 criteria are present:

- Increased vaginal pH (> 4.5)<sup>o</sup>
- Grayish white homogeneous discharge
- An amine smell with or without potassium hydroxide (positive whiff test)
- **Presence of clue cells<sup>o</sup>.** (> 20% of cells)

**Clue cells** are epithelial cells of the vaginas that get their distinctive stippled appearance by being covered with bacteria. They are a sign of bacterial vaginosis<sup>o</sup>, particularly that caused by *Gardnerella vaginalis*.

**Note:** Yellowish green discharge is seen in case of trichomonas infection and not bacterial vaginosis.

22. **Ans. is a, b and c, i.e. Mycobacterium can be grown from menstrual blood, Associated with infertility, and Ectopic pregnancy is common**

Ref. Shaw 15<sup>th</sup>/ed p 156-58; Jeffcoate 7<sup>th</sup>/ed p 327

Amongst the given option there is no doubt that TB leads to infertility and ectopic pregnancy rather M/C symptom of TB is infertility (i.e. options b and c are correct).

Mycobacterium can be grown from menstrual blood is again correct (i.e. option a). Now coming to option d, i.e. dysmenorrhea is a common presentation.

- **Pain** is uncommon and is a result of subacute PID.
- **"Dysmenorrhea rarely ever occurs"**.

—Jeffcoates 7<sup>th</sup>/ed p 327

23. **Ans. is c, i.e. ESR – 10 mm/hour** Ref. Textbook of Gynae Shiela Balakrishnan 1<sup>st</sup>/ed p 216; Novak 15<sup>th</sup>/ed p 565

- Temp >38°C (100.4° F)
- WBC count >15,000 are all criteria for diagnosing PID
- Tenderness on movement of cervix

ESR ≥ 15 mm/hr is the criteria and not ESR ≥ 10 mm/hr.

For details of the criteria, kindly see the preceding text.

24. **Ans. is d, i.e. Fallopian tubes** Ref. Telinde Operative Gynae 9<sup>th</sup>/ed pp 678, 679; Dutta Gynecology 6<sup>th</sup>/ed p 126  
Dutta Gynae 6<sup>th</sup>/ed pg 130

According to:

For identification of organisms in PID the materials are collected from the following available sources:

- Discharge from urethra or Bartholin's gland
- Cervical canal
- Collected pus from the fallopian tubes during laparoscopy or laparotomy.

The material so collected is subjected to Gram's stain and culture (aerobic/anaerobic). The findings of Gram-negative diplococci is very much suggestive of gonococcal infection.

25. **Ans. is a, i.e. Endocervix**

26. **Ans. is c, i.e. Infants** Ref. Dutta Gynae 5<sup>th</sup>/ed p 143, 6<sup>th</sup>/ed p 147; COGDT 10<sup>th</sup>/ed p 671, 672

There are 2 important points which we should be remembered about gonorrhoea infection.

- Squamous epithelium is resistant to gonococci infection
- Gonorrhoea is an STD (i.e. it is transmitted by ascending infection along with sperms)

Now, since squamous epithelium is resistant to gonococcal infection, in vagina and ectocervix gonococcal infection cannot occur (as both are lined by squamous epithelium). So from there, gonococcal infection will travel along with sperms and reach endo cervix which is lined by columnar epithelium.

∴ M/C site for gonococcal infection in young females is endocervix.

**Others are**

- Bartholin's gland (Bartholin cyst is caused by gonococcal infection)<sup>Q</sup>
- Urethra

**Note:** In newborn females vagina is lined by transitional epithelium so theoretically gonococcal vaginitis can occur in them

**27. Ans. is c, i.e. Chlamydia****28. Ans. is c, i.e. Polymerase chain reaction**

Ref. Shaw 15<sup>th</sup>/ed p 145; Harrison 18<sup>th</sup>/ed p 1426; Dutta Gynae 6<sup>th</sup>/ed p 126

**Chlamydia Infections**

**"Except in highly sophisticated centres, the detection of Cl. trachomatis is difficult by wet film".** Dutta Gynae 6<sup>th</sup>/ed p 126

- "Polymerase and ligase chain reactions are fast highly sensitive and specific (96%) and now considered gold standard in the laboratory diagnosis." Shaw 14<sup>th</sup>/ed p 131; 15<sup>th</sup>/ed p 145

**Note:**

Ref. Harrison 18<sup>th</sup>/ed p 1426

- **The current diagnostic technique of choice for chlamydial infections is NAAT—Nucleic acid amplification tests.**

- **Choice of specimen**—Specimen can be urine or vaginal swabs.
- For screening asymptomatic women—CDC recommends—Self-collected vaginal swabs
- In symptomatic females—cervical swab sample
- In males—urine sample is the specimen of choice

**29. Ans. is b, i.e. Culture on McCoy cells**

Ref. Harrison 18<sup>th</sup>/ed p 1426

Patient is complaining of abdominal pain and vaginal discharge. On examination, cervicitis and mucopurulent discharge is seen—which indicates she is having PID. The presence of pus cells in absence of organism indicates chlamydial infection (most common STD today). It is an intracellular organism that grows only on McCoy or HeLa cell cultures. It cannot be grown on other media and hence, often goes unnoticed, later leading to infertility.

Culture in Mc Coy cells is 100% specific for chlamydia but is inexpensive, technically difficult and takes 3-7 days to obtain the result.

**30. Ans. is d, i.e. Penicillin**

Ref. Williams Obs 23<sup>th</sup>/ed p 124; Harrison 18<sup>th</sup>/ed p 1426

In non pregnant females – DOC for *Chlamydia* = Azithromycin

**Treatment of chlamydia infection during pregnancy**

Regimen	Drug and Dosage
<b>Preferred choice</b>	Azithromycin (1 g) as a single dose Amoxicillin or (500 mg) orally 3 times a day × 7 days

**"Azithromycin is the first-line treatment and has been found to be safe and efficacious in pregnancy."** – Williams Obs 23<sup>rd</sup>/ed p 1241

But since azithromycin is not given in the options, so the next best option is Amoxicillin (penicillin).

Harrison 18<sup>th</sup>/ed p 1426 says– "Although not approved by FDA, for use in pregnancy, azithromycin single dose 1g regimen appears to safe and effective for this purpose. However, amoxicillin can also be given to pregnant women."

**31. Ans is a, i.e. Miconazole**

Ref. Shaw 15<sup>th</sup>/ed pp 146 147; CGDT 10<sup>th</sup>/ed pp 599-601

Thick curdy discharge indicates the causative white organism is candida which is treated by Azole group of antifungals e.g. Fluconazole/Miconazole given orally or applied topically.

**Management of Vulvovaginal Candidiasis in Pregnancy:**

- 1st trimester: Nystatin vaginal tablets
- 2nd trimester: Topical azole antifungal

**Management of Recurrent Vulvovaginal Candidiasis:**

- Recurrent vulvovaginal candidiasis is defined as four or more episodes of vulvovaginal candidiasis in a year. It might be caused by *Candida tropicalis*<sup>Q</sup> or *Candida glabrata*<sup>Q</sup>
- Antibiotic treatment needs to be prolonged (Fluconazole 150 mg weekly x 6 months or ketoconazole/Itraconazole 100 mg daily x 6 months).
- Simultaneous treatment of male partner.<sup>Q</sup>
- Patients on prolonged therapy should have their LFT monitored.

**32. Ans. is b, i.e. Gardnerella****33. Ans. is c, i.e. Metronidazole**

Ref. Shaw 15<sup>th</sup>/ed p 131; CGDT 10<sup>th</sup>/ed p 670; William's Gynae 1<sup>st</sup>/ed p 51

Creamy white discharge with fishy odor is characteristic of bacterial vaginosis (M/C cause Gardnerella)

Drug of choice for management of bacterial vaginosis/Gardnerella vaginitis is—

**Metronidazole:**

**Dose** – 500 mg oral metronidazole is given twice daily for 7 days

Alternatively, metronidazole gel (can be applied once daily for 5 days or clindamycin cream (2%) at bedtime for 5 days.  
**Note:** Treatment of male sexual partner is not required in bacterial vaginosis.<sup>Q</sup>

**In pregnancy:**

- Bacterial vaginosis is associated with preterm birth and premature rupture of membranes.
- Treatment is reserved for symptomatic women who usually complain of fishy odor.
- DOC – Metronidazole (oral) in the 2nd and the 3rd trimester.

Unfortunately, treatment does not reduce preterm birth and routine screening is not recommended.

**34. Ans. is d, i.e. Fallopian tube**

**35. Ans. is d, i.e. Hematogenous**

Ref. Shaw 15<sup>th</sup>/ed p 154

- M/c site involved in genital TB is Fallopian tube.<sup>Q</sup>
- M/c symptom of genital TB is infertility.<sup>Q</sup>

**Reasons for infertility:**

- Tubal blockage<sup>Q</sup>
- Even if tubes are patent infertility is due to loss of tubal function.<sup>Q</sup>
- Tubercular endometritis causes infertility due to uterine scarring resulting in destruction of endometrium<sup>Q</sup>
- Genital tuberculosis is almost always a secondary infection, with primary sites being lungs, lymph nodes, abdomen, etc.
- Hematogenous route is the most common mode of spread from the primary site.

**36. Ans. is c, i.e. Tuberculosis**

Ref. Read Below

Friends, I cannot quote exact reference for this Question but when you read various texts available and my own experience as a Gynecologist. I can bet upon this answer. **Always remember:**

In developing countries like India most common cause of tubal blockage is tuberculosis.

**Note:** Most common cause of tubal blockage in developed countries is *Chlamydia*.

**37. Ans. is a, i.e. Hysteroscopy and laparoscopy** Ref. Shaw 15<sup>th</sup>/ed p 451; William's Gynae 1<sup>st</sup>/ed p 74; Gynecology by Ostrzenski (Lippincott Williams 2001/282); Dutta Gynae 6<sup>th</sup>/ed p 130

Laparoscopy is considered the "gold standard". While it is the most reliable aid to support the clinical diagnosis but it may not be feasible to do in all cases. It is reserved only in those cases in which differential diagnosis includes salpingitis, appendicitis or ectopic pregnancy. Nonresponding pelvic mass needs laparoscopic clarification.

Hysteroscopy may also provide confirmatory evidence for salpingitis.

*"Fallopian tube culture can be obtained laparoscopically and recently the hysteroscopic approach has been introduced. The specimen is obtained during hysteroscopy with a cytobrush."* – Gynecology by Ostrzenski (Lippincott Williams) (2001) / 282

**Also know:**

Since laparoscopy is an invasive procedure for diagnosis of salpingitis/PID, diagnosis should first be made clinically.

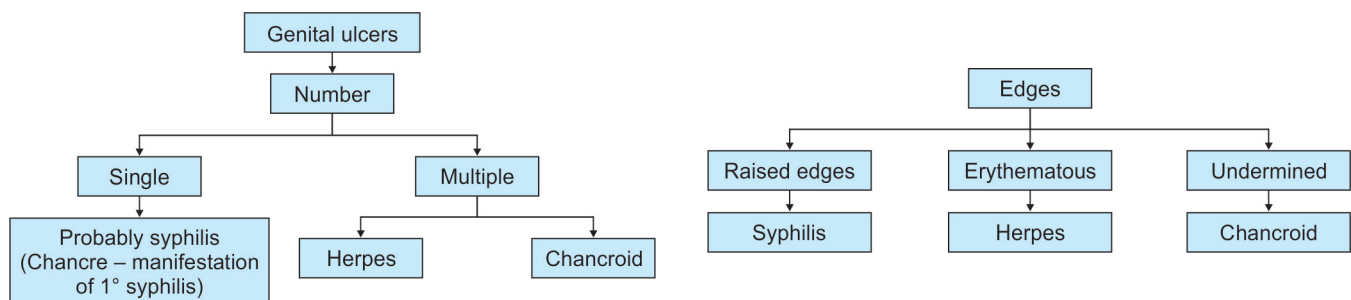
**38. Ans. is a, i.e. Treponema pallidum**

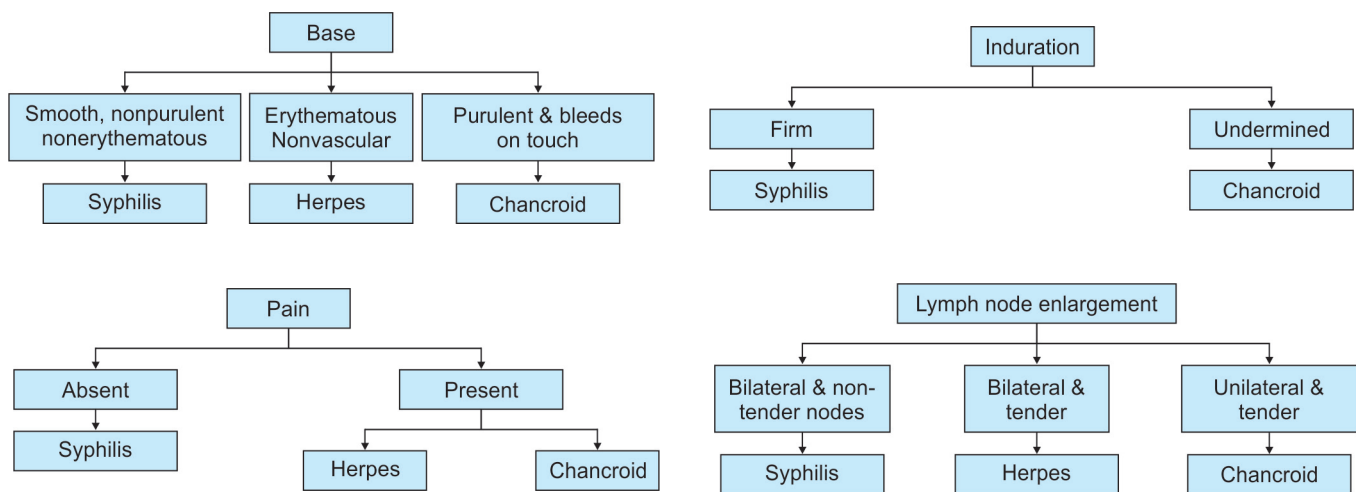
The M/c causes of genital ulcers in young, sexual active women are:

- Herpes simplex virus (HSV)
- Treponema pallidum (syphilis)
- Haemophilus ducreyi (chancroid).

In this case, painless ulcer with everted margin leave no doubt that the cause of the ulcer is syphilis (treponema pallidum).

**Clinical features of genital ulcers**





39. **Ans. is d, i.e. A negative Mantoux test reasonably excludes tuberculosis**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 140*

Let's see each option.

**Option a:** Ovarian involvement can occur without tubal affection incorrect as ovaries do not get involved without tubes being affected

**Option b:** Infertility is mainly due to anovulation incorrect as mainly infertility is due to tubal blockage on adhesions in endometrial cavity

**Option c:** Acid fast bacilli is identified in 1007 cases of TB endometritis incorrect

**Option d:** A negative mantoux test reasonably excludes TB correct

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 140*

40. **Ans. is d, i.e. Salpingitis isthmica nodosa is the exclusive pathology to tuberculosis**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 138*

- In genital TB abdominal ostium may be patent with eversion of fimbrial called as tobacco pouch appearance. Thus option 'a' is correct
- The early lesion may be confused with adenocarcinoma – correct
- Genital TB is always secondary and tubes are invariably the primary sites (i.e. option b is correct i.e. c is correct)
- Salpingitis isthmica nodosa is the exclusive pathology of the tubes incorrect (as it may be seen in endometriosis also)

In some cases of genital TB, nodules are present in the tube first size in the isthmic part near the uterine cornu, it is called as salpingitis isthmica nodosa

**Salpingitis isthmica nodosa** is the nodular thickening of the tube due to proliferation of tubal epithelium within the hypertrophied myosalpinx (muscle layer). Exact aetiology is unknown. It is diagnosed radiologically as a small diverticulum. It is however not specific to tubercular infection only. It is also observed in pelvic endometriosis.

41. **Ans. is c, i.e. PCR techniques have got higher sensitivity in detection**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 140*

Genital tuberculosis is usually secondary to primary infection (lungs, bones, lymph nodes).

It spreads by haematogenous route (not lymphatic route) leading to endosalpingitis.

Caseous granulomatous lesions with giant cells on pathological examination are suggestive of TB but is not diagnostic as it can be seen in fungal infection and sarcoidosis.

PCR is more sensitive (85–95%) than microscopy and bacteriological culture. This method can detect fewer than 10 organisms in clinical specimens compared to 10,000 necessary for smear positivity.

Reproductive outcome even after treatment is poor. Pregnancy rate is about 20%, live birth rate is only 7%. risk of miscarriage and ectopic pregnancy are high.

42. **Ans. is c, i.e. Women with monogamous partner who had vasectomy**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 128*



Women with monogamous partner who had vasectomy is a protective factor for PID and not risk factor

Risk factors of PID	Protective factors of PID
<ul style="list-style-type: none"> <li>• Menstruating teenagers.</li> <li>• Multiple sexual partners.</li> <li>• Absence of contraceptive pill use.</li> <li>• Previous history of acute PID.</li> <li>• IUD users.</li> <li>• Area with high prevalence of sexually transmitted diseases.</li> </ul>	<p><b>Contraceptive practice</b></p> <ul style="list-style-type: none"> <li>• Barrier methods, specially condom, diaphragm with spermicides</li> <li>• Oral steroidal contraceptives have got two preventive aspects. <ul style="list-style-type: none"> <li>– Produce thick mucus plug preventing ascent of sperm and bacterial penetration</li> <li>– Decrease in duration of menstruation, creates a shorter interval of bacterial colonization of the upper tract.</li> </ul> </li> <li>• Monogamy or having a partner who had vasectomy.</li> </ul> <p><b>Others</b></p> <ul style="list-style-type: none"> <li>• Pregnancy</li> <li>• Menopause</li> <li>• Vaccines: Hepatitis B, HPV</li> </ul>

43. **Ans. is d, i.e. Ectocervix**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 147*



Ectocervix is covered by squamous epithelium and squamous epithelium is resistant to Gonococcal infection

Primary genital sites of involvement of gonorrhoea

- Endocervix
- Urethra
- Skene's gland
- Bartholin's gland

44. **Ans. is a, i.e. Bacterial vaginosis**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 262*

#### Vulval ulcers

Vulval ulcers are predominantly due to sexually transmitted diseases. Rarely, it may be due to non-specific causes. Malignant ulcer is also rare. The various etiological factors related to vulval ulcers are given in the below Table.

Table: Ulcers of the Vulva

STD related	Idiopathic	Tuberculosis	Malignancy	Systemic disease related or dermatoses
<ul style="list-style-type: none"> <li>• Syphilis</li> <li>• Herpes genitalis</li> <li>• Chancroid</li> <li>• Granuloma inguinale</li> <li>• Lymphogranuloma venereum</li> </ul>	<ul style="list-style-type: none"> <li>• Behçet's disease</li> <li>• Aphthous ulcers</li> <li>• Lipschutz ulcers</li> </ul>	<ul style="list-style-type: none"> <li>• Tubercular</li> </ul>	<p><b>Primary</b></p> <ul style="list-style-type: none"> <li>• Squamous cell carcinoma</li> <li>• Malignant melanoma</li> <li>• Basal cell carcinoma</li> </ul> <p><b>Secondary</b></p> <ul style="list-style-type: none"> <li>• Leukemia</li> <li>• Choriocarcinoma</li> </ul>	<ul style="list-style-type: none"> <li>• Lupus erythematosus</li> <li>• Crohn's disease</li> <li>• Lichen planus</li> <li>• Lichen sclerosus</li> <li>• Sjogren's syndrome</li> </ul>

**Note: Lipschutz ulcer:** The lesion affects mainly the labia minora and introitus. In acute state, there may be constitutional upset with lymphadenopathy. The causative agent may be Epstein-Barr virus. Treatment is with antiseptic lotions and ointment.

45. **Ans. is c, i.e. Positive clue cells in 100% cases**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 152*

We have discussed BV in detail.

Clue cells are diagnostic but about 40% patients may not have clue cells.



# CHAPTER

# 8

# Urogynecology

## Pelvic Relaxation/Prolapse

### Supports of Uterus

#### Primary Supports

a. Mechanical support	<ul style="list-style-type: none"> <li>• Uterine axis</li> <li>• Angle of anteversion (angle between cervix and vagina)</li> <li>• Angle of antelexion (angle between cervix and uterus)</li> </ul>
b. Muscular or active support	<ul style="list-style-type: none"> <li>• Pelvic diaphragm (formed by levator ani muscle)</li> <li>• Perineal body<sup>o</sup></li> <li>• Urogenital diaphragm (superficial and deep transverse pereneii muscles)</li> </ul>
c. Fibromuscular support	<ul style="list-style-type: none"> <li>• Pubocervical ligament<sup>o</sup></li> <li>• Transverse cervical ligament<sup>o</sup> (cardinal ligament/ Mackenrod's ligament)</li> <li>• Uterosacral ligament<sup>o</sup></li> </ul>

Broad ligament (fold of peritoneum) and round ligaments are secondary supports of uterus and their role as support is doubtful.

### Etiology of Prolapse

Relaxation, weakness, or defect in the cardinal and uterosacral ligaments which normally maintain the uterus in an antelexed position and prevent it from descending through the urogenital diaphragm.

Acquired	Congenital
<ul style="list-style-type: none"> <li>• Menopause</li> <li>• Repeated child birth</li> <li>• Traumatic deliveries</li> <li>• Faulty birth practices</li> <li>• Precipitate labor</li> <li>• Iatrogenic trauma like in case of vaginal hysterectomy, vulvectomy</li> <li>• Increased intra-abdominal pressure like in COPD, constipation, obesity</li> </ul>	<ul style="list-style-type: none"> <li>• Spina bifida occulta</li> <li>• Neurological disorders viz Ehler Danlos syndrome, Marfans syndrome</li> </ul>

### Classification of Prolapse

Vaginal prolapse	Uterine prolapse
<b>A. Anterior vaginal wall:</b> Upper two thirds – cystocele/cytourethrocele Lower one third – urethrocele	<b>Shaw's classification (old classification):</b> 1 <sup>o</sup> – descent of the cervix to the vagina 2 <sup>o</sup> – descent of the cervix to the introitus 3 <sup>o</sup> – descent of the cervix outside the introitus. Procidentia: all of the uterus outside the introitus.



Normally uterus remains in anteverted and antelexed position. **Retroversion is the first step in prolapse.** Therefore, whenever given a case of prolapse – in viva. You can safely say the females uterus is retroverted even without examining.



Broad ligament & round ligament are secondary supports & they donot support the uterus.



#### Pelvic Relaxation/Prolapse

Protrusion of pelvic organs into or out of the vaginal canal. External Os lies at level of ischeal spine and internal Os at upper border of pubic symphysis. Hence any descent of uterus from these levels is a case of prolapse

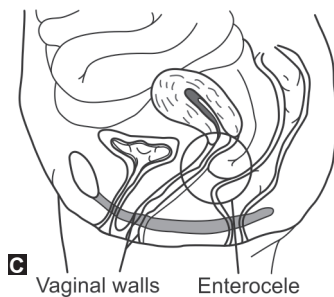
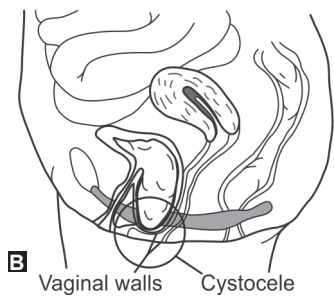
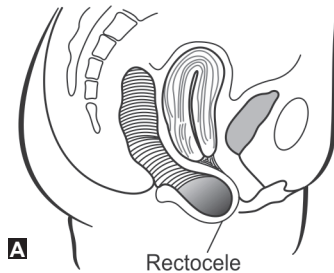


The only **true** hernia of the pelvis is an ENTEROCELE and Rectocele because peritoneum herniates with the small bowel.

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Vaginal prolapse (Fig. 8.1)	Uterine prolapse
<p><b>B. Posterior vaginal wall :</b></p> <ul style="list-style-type: none"> <li>• Upper one third – enterocele (pouch of Douglas herniates)</li> <li>• Middle one third – rectocele.</li> <li>• Lower one third – Lax perineum</li> </ul>	



**Figs 8.1A to C:** Vaginal prolapse  
(A) Rectocele; (B) Cystocele;  
(C) Enterocele

### Newer Classification of Prolapse—POP-Q Classification

More recent grading system of prolapse considers the individual pelvic organ and its distance in relation to the hymen. Pelvic Organ Prolapse (POP) Qualification identifies several points (total 9) within and around the vagina and measures the distance of each **point from the hymen**<sup>Q</sup> while the patient performs valsalva. The points which lies inside vagina is reported as negative number and which lies outside as positive number. Staging is done according to the measurement.

### Staging of Pelvic Organ Prolapse Quantitative System

Stage	Description
0	No descent of pelvic organs
I	Leading edge of the prolapse does not descend below 1 cm. above the hymenal ring (-1)
II	Leading edge of the prolapse extends from 1 cm above to 1 cm below the hymenal ring (between -1 and +1)
III	From 1 cm beyond the hymenal ring but without complete vaginal eversion
IV	Essentially complete eversion of vagina

**Note:** The perineal body is normally at the level of ischial tuberosity. Descent of >2 cm below this level with flattening of the intergluteal sulcus indicates perineal descent.

### Supports of Vagina

**Also know:** De lancey's three level systems of support

Level	Structures included	Defect can lead to
Level I	Cardinal and uterosacral ligament	Uterine prolapse vault
Level II	Paravaginal attachments (pelvic fascia and superior fascia of levator ani)	Anterior and posterior vaginal wall prolapse
Level III	Perineal body, levator ani muscle, urogenital diaphragm (They support distal 1/3 of vagina and introitus)	Anterior and posterior wall prolapse

### Symptoms

- Due to protusion of cervix and uterus into vagina, patient feels something coming down or out.
- Groin/back pain (due to stretching of uterosacral ligaments)<sup>Q</sup>.
- Feeling of heaviness/pressure in pelvis which is
  - Worse with standing and lifting
  - Worse at the end of the day
  - Is relieved by lying down
- Decubitus ulcer – on the most dependant part of cervix or vagina. The ulcer occurs as a **result of venous congestion and circulatory changes** and <sup>Q</sup> not due to friction created by rubbing of the prolapsed parts with the thigh.<sup>Q</sup>



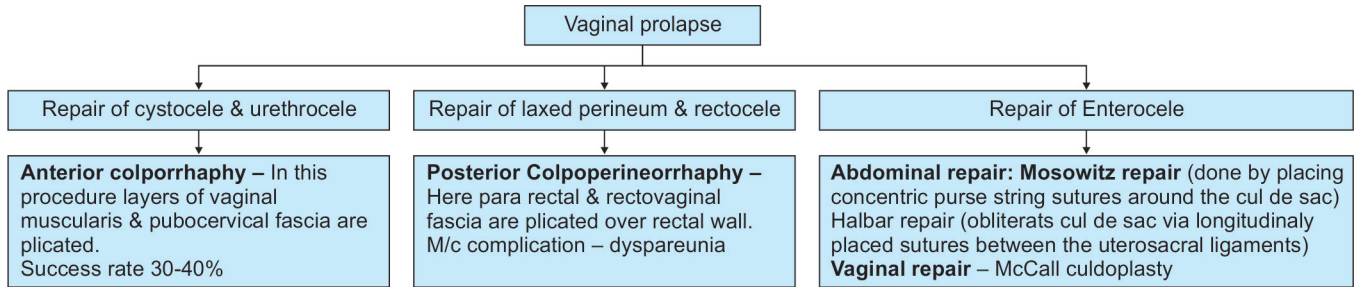
Decubitus ulcer in case of prolapse is due to venous congestion and circulatory changes and not trauma or friction.

- **Treatment of decubitus ulcer:** Reduction of the prolapse part into the vagina and daily packing with glycerine and acriflavine.<sup>Q</sup> Acriflavine is an antiseptic agent while glycerine is a hygroscopic agent.
- Cancer of cervix or vagina is rarely seen<sup>Q</sup>, even in untreated cases of prolapse.

**?** Backache in case of prolapse is due to stretching of uterosacral ligaments.

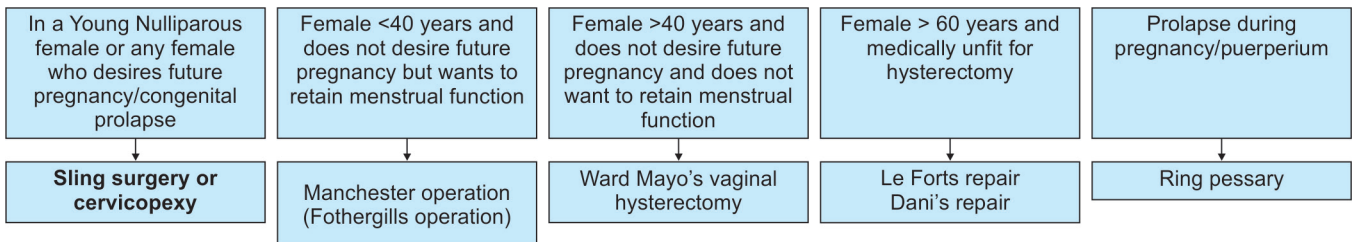
**Management of Prolapse**

**Vaginal Prolapse**



**Uterine Prolapse**

Management depends on age and parity of the female –



**Details of Prolapse Surgeries**

**Abdominal Sling Surgeries**

Purandare Sling/ cervicopexy	Shirodkar Sling	Composite/Virkud Sling
<ul style="list-style-type: none"> <li>• Sling made of fascia lata used</li> <li>• It is type of <b>dynamic/open sling</b> where central part of the sling is fixed anteriorly to the exposed part of <b>isthmus</b> and the two ends of the tape are attached to <b>posterior rectus sheath</b>.</li> <li>• <b>Note:</b> It should be performed only in those females who have a good abdominal tone.</li> <li>• <b>Drawback:</b> It leads to retroversion of uterus, deepening of pouch of Douglas and enterocele formation.</li> </ul>	<ul style="list-style-type: none"> <li>• It is type of <b>static sling</b> which aims at strengthening the uterosacrals. Mersilene tape is attached anteriorly to posterior surface of cervix and posteriorly to anterior longitudinal ligament in front of Sacral promontory.</li> <li>• This surgery has drawback mainly on left side because tape has to pass below the mesentery of sigmoid colon to reach the sacral promontory.</li> </ul>	<ul style="list-style-type: none"> <li>• In this surgery on the Right side - shirodkar sling is performed i.e. tape is attached to sacral promontory and on the Left side purandare sling is performed (as mainly drawback of shirodkar sling is on left side).</li> </ul>

**Also Know**

**Congenital Prolapse**  
 Refers to occurrence of prolapse in a young nulliparous female. Risk factors for congenital prolapse—  
 1. Spina bifida  
 2. Connective tissue disorders like Marfan's syndrome, Ehler Danlos syndrome  
**Note:** There is usually no cystocele in congenital prolapse

**Vault Prolapse**  
 Refers to prolapse of the vaginal stump left behind after performing hysterectomy. Vault is the site where anterior and posterior vaginal walls are sutured. Incidence = 1–10%. It is usually accompanied by enterocele (70%).

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Purandare Sling/ cervicopexy	Shirodkar Sling	Composite/Virkud Sling
	<b>Drawback:</b> <ul style="list-style-type: none"> <li>• Injury to sigmoid colon,</li> <li>• Intestinal obstruction</li> <li>• Injury to ureter</li> <li>• Haemorrhage from mesenteric vessels</li> <li>• Injury to genitofemoral nerve present in psoas muscle.</li> </ul>	



Goal of prolapse surgery is relief of prolapse symptoms-Over correction must be avoided as it has its own complications.



The M/C complication of Purandare cervicopexy is deepening of pouch of Douglas leading to enterocele formation. Enterocele can be prevented after purandare sling surgery by obliterating pouch of Douglas at the time of operation called Moscowitz repair



#### Complications of Shirodkar sling

- Injury to Sigmoid colon (left side)
- Intestinal obstruction
- Injury to ureter
- Injury to mesenteric vessels
- Injury to Genitofemoral nerve



Fothergills repair can lead to cervical incompetence which in turn can lead to 2<sup>nd</sup> trimester abortion and not 1<sup>st</sup> trimester abortion.

### Fothergill's Repair/Manchester Operation

It is suitable for women under 40 years of age, who are desirous of retaining their menstrual function but do not desire future pregnancy.

#### Steps of Fothergill

- Preliminary D and C
- Amputation of cervix
- Strengthening the cervix by suturing cut end of Mackenrodt ligament in front of cervix
- Anterior Colporrhaphy
- Colpoperineorrhaphy.

**Note:** In fothergills surgery, the posterior lip of the amputated cervix is covered by a vaginal flap using **sturmdorff suture** or by **Bonney's method**.

#### Complications

- Cervical amputation leads to:
  - Incompetent os
  - Habitual abortion (second trimester abortion)
  - Preterm deliveries
  - **Premature rupture of membranes (PROM)** – Dutta Obs 6<sup>th</sup>/ed p 317
  - Decreased cervical fertility
- Excessive fibrosis causes stenosis leading to dystocia during labour
- Hematometra (*Very rare*)
- Recurrence of prolapse.

**Note:** Since all these complications of fothergills are mainly due to amputation of cervix-**Shirodkars modification of fothergills operation** (also called as Shirodkars uterosacral ligament advancement surgery), is being done where amputation of cervix is not done, rest all steps are same as fothergills repair.

### Le Forts Repair/Colpocleisis

- In females more than 60 years of age, who have medical complications like previous H/O MI, hypertension and diabetes, vaginal hysterectomy is not possible as the anesthetist will not agree to give anesthesia.
- In such patients, procidentia/3<sup>o</sup> degree prolapse can be managed by Le forts colpocleisis:
- **In Le forts repair/colpocleisis:** The vaginal epithelium is removed followed by suturing of the anterior and posterior walls of denuded vagina, thereby completely obliterating the vagina.
- The procedure is done under local anesthesia.
- Before performing this procedure, PAP smear and pelvic USG should be done to rule out cancers and pelvic pathology.

- **Note:** °Le forts repair cannot be performed in young females because:
  - Their coital function will be hampered
  - Menstrual blood does not get way to come out after Le forts repair so blood will keep on collecting in uterine cavity leading to hematometra.

**Note:** In older females if sexual function is desired partial colpocleisis called as **Goodell Powel Surgery** can be done.

### Management of Vault Prolapse

Patient is fit for abdominal surgery	In obese, elderly patients, not fit for abdominal surgery
<ul style="list-style-type: none"> <li>• <b>Transabdominal sacral colpopexy</b> (Mesh is attached to the vault and sacral promontory).</li> <li>• It is the <b>Gold Standard Surgery for vault prolapse</b></li> </ul>	<b>Transvaginal sacrospinous ligament fixation/ colpopexy</b> can be done. A special instrument: Miya Hook is used for the surgery. Recurrence rate—3%.

### Use of Ring Pessary in Prolapse

Pessaries are of 2 basic varieties:

- Supportive variety, e.g. ring pessary
- Space occupying variety e.g. Gellhorn pessary.

### Indications

- Prolapse during pregnancy.
- In puerperium – to facilitate involution
- Patient unfit or unwilling for surgery
- Women who have undergone at least one previous attempt at surgical intervention without relief
- **Diagnostic:** It may be placed diagnostically to identify which women are at risk for urinary incontinence after prolapse correcting surgery.

### Problems associated with Pessary

- It is never curative and is only palliative
- Can cause vaginitis
- Has to be changed every 3 months
- Forgotten pessary can cause vaginal ulcerations, erosions, and fistula formation.
- May cause dyspareunia
- It does not cure stress incontinence.

### Contraindication of pessary

- Acute genital tract infections
- Adherent retroposition of uterus.

**Note:** For types of pessary – see color plates.

### HOT TOPIC

### Kegel's Exercise

Kegel's exercise are pelvic floor exercises which consists of contracting and relaxing the muscles that form part of the pelvic floor.

The aim of Kegel's exercises is to improve muscle tone by strengthening the pubococcygeus and muscles of the pelvic floor. They are good for treating first degree vaginal prolapse, preventing uterine prolapse, and to aid with child birth in females and for treating prostate pain and swelling resulting from benign prostatic hyperplasia (BPH) and prostatitis in males. These exercises reduce premature ejaculatory occurrences in men as well as increase the size and intensity of erections.



Suspension of the vault by sacro– spinous colpopexy at the time of primary surgery can prevent vault prolapse.



### Management of 3° prolapse in pregnancy

#### In early months of pregnancy

(uptil 18 weeks as after that spontaneous correction occurs)

*If Cervix can be replaced inside the vagina*

- Cervix is to be kept inside the vagina with the help of ring pessary.
- Patients should lie with footend elevated.
- To decrease edema & congestion of the prolapsed mass- gauze soaked with acriflavine & glycerine is to be applied.

*If Cervix is incarcerated & cannot be repositied*

- Termination of pregnancy

#### In late months of pregnancy

Admit the patient at 36 weeks for safe confinement



### Management of prolapse after childbirth

- Perineal exercise
- Ring pessary
- Never do surgery within 6 months<sup>o</sup> of delivery as there is always the possibility of recurrence of prolapse.<sup>o</sup>

Kegel's exercises may be beneficial in treating urinary incontinence in both men and women. The treatment effect might be greater in middle aged women in their 40s and 50s with stress urinary incontinence alone.

### Time for initiating Kegel's exercise in pregnant females

- In 1<sup>st</sup> trimester
- Following vaginal delivery-after 24 hours
- Following cesarean section-after 24 hours

### Limitations of Kiegel's exercises

– Jeffcoates 7<sup>th</sup>/ed p 286

- Kiegel's exercise has a limited effect as it affects mainly voluntary muscles viz bulbocavernous, levator ani, and superficial and deep transverse perineal muscles and not the main fascial supporting tissues



Kegels exercise should begin in pregnancy. In first trimester & following delivery or cesarean after 24 hrs.

### Inversion of Uterus

- It is a condition where the uterus becomes turned inside out; the fundus prolapsing through the cervix
- **Management:** Rectification may be done abdominally (Haultain's operation – after cutting the posterior ring of the cervix) or vaginally (Spinelli's operation – after cutting the anterior ring of the cervix).

### Urinary fistulas

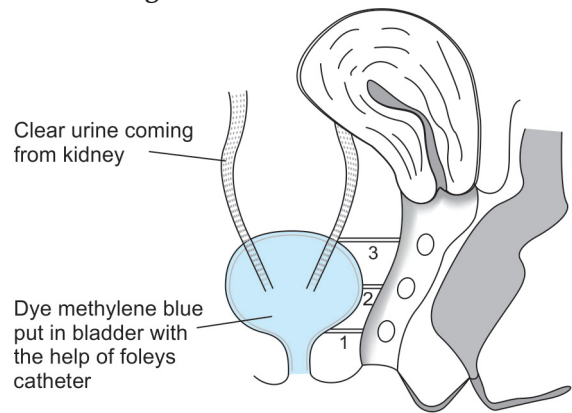
	Vesicovaginal Fistula	Ureterovaginal Fistula	Urethrovaginal Fistula
M/C	VVF is the m/c urinary fistula		
Etiology	In developing countries – Obstructed labor It is due to ischemic necrosis, so develops 3–5days after delivery. In Developed countries – hysterectomy	Hysterectomy Maximum risk is with Wertheims hysterectomy	
Chief Complaint	Continuous dribbling of urine from vagina + no normal urge for urination	Continous dribbling of urine from vagina + normal urge for urination	No continuous leakage but when patient urinates, urine leaks from urethra and vagina.
Methylene blue 3 swab test (Moirs test)	Middle cotton plug is wet with dye and urine (blue in colour)	Uppermost cotton plug is wet with urine but not with dye. Other 2 cotton swabs are dry	Lower most cotton plug is wet with dye, other two are dry.
Investigation of choice	Cystoscopy	Dye test with indigo carmine demonstrates urinary extravasation and identifies the location of injury + Cystoscopy	
Mgt of Choice-Surgery	<b>Technique :</b> Layer technique/ Latzko repair (for post hysterectomy VVF repair) chassar moir technique <b>Time of surgery :</b> If it is due to obstructed labor repair should be done after 3 months. (so that infection and inflammation subside) If it is due to surgery And is recognised within 24 hours- Immediate repair. If recognised later-repair after 10–12 weeks Radiation fistulas are repaired after 12 months	Boari Flap technique  As early as possible	

## Methylene Blue 3 Swab Test

The three swab test helps to differentiate between vesicovaginal, **uretero vaginal** and urethrovaginal fistula.

### Procedure of 3 swab test:

- A red rubber catheter is introduced into the bladder through the urethra.
- 3 cotton swabs are placed in the vagina as follows:
  - One at vault,
  - One at the middle
  - One just above the introitus.
- Methylene blue dye is instilled into the bladder through catheter and swabs are removed for inspection.
  - In case of
    - **Urethrovaginal fistula:** The lower most cotton swab will get wet and will be blue in colour (as evident from Fig. 8.2).
    - **Vesicovaginal fistula:** The middle swab and lower most swab (as urine will drop down) both will be wet with urine and will have blue colour (Fig. 8.2).
    - **In ureterovaginal fistula:** The urine which is being brought by ureters is clear, i.e. does not have any dye. Through the fistula it will reach vagina & uppermost cotton swab will be wet with urine but will not have any colour. (as dye is in bladder and not ureter) (Fig. 8.2).



**Fig. 8.2:** 1. Urethrovaginal fistula  
2. Vesicovaginal fistula  
3. Ureterovaginal fistula

Observation	Interpretation
Upper most swab soaked with urine but unstained with dye	Ureterovaginal fistula <sup>Q</sup>
Upper and lower swab remain dry but the middle swab soaked with dye	Vesicovaginal fistula <sup>Q</sup>
The upper two swab remain dry but lower one soaked with dye	Urethrovaginal fistula <sup>Q</sup>

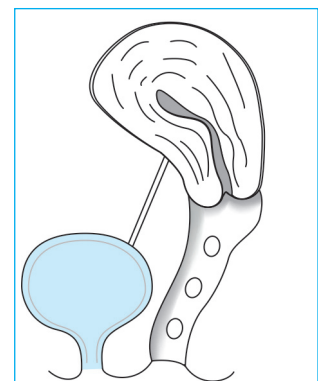
## Most Common in Fistulae

MC urinary fistula	Vesicovaginal <sup>Q</sup>
MC cause of VVF in india	Obstructed labour <sup>Q</sup>
MC cause of Uretero Vaginal Fistula	Injury to ureter after gynecological operation <sup>Q</sup> especially Wertheim' hysterectomy <sup>Q</sup>
MC cause of Vesico Uterine fistula	Cesarean section <sup>Q</sup>
MC cause of Recto Vaginal fistula	Cesarean perineal tear <sup>Q</sup>

### HOT TOPIC

## Menouria

- It is seen in uterovesical fistulae<sup>Q</sup>, i.e. fistula connecting uterus to bladder (Fig. 8.3).
- Usually follows cesarean section<sup>Q</sup>
- The patient complains of hematuria/passage of menstrual discharge via urethra at the time of menstruation. Patient does not have urinary incontinence.<sup>Q</sup>
- As is obvious from from the diagram, the fistula is between bladder and uterus – and the uterus lies at a higher level than bladder, so urine cannot go upwards against gravity, no urine incontinence. Rather at the time of menstruation, blood flows down and
- Mensouria is seen when Uterovesical fistula opens into the uterus above the isthmus.<sup>Q</sup>



**Fig. 8.3:** Uterovesical fistulae



**Sims Triad:** For repair of VVF: **James Sims** described a method for closing very small fistula's called saucerization (where the margins of fistula are closed with interrupted sutures using silver wire without separating bladder from vagina. It is done in **SIMS position** using **SIMS speculum** so called as **SIMS triad**

- The presence of the fistula can be demonstrated by hystero-graphy (but not by cystography) and cystoscopy.<sup>Q</sup>
- Treatment is by abdominal repair.<sup>Q</sup>
- Another important cause of cyclical hematuria is endometriosis<sup>Q</sup> of bladder.



### Micturition cycle

The bladder has two basic functions: storing urine (sympathetic) and, when socially appropriate, evacuating urine (parasympathetic). Bladder filling occurs with relaxation of the detrusor muscle and contraction of the IUS. With bladder filling, afferent activity via baroreceptors triggers the storage reflex to maintain sympathetic tone in the IUS. When the bladder is full, afferent activity in the pelvic nerve stimulates the micturition reflex.

## Urine Incontinence

According to International continence society, **“incontinence”** is defined as the **complaints of any involuntary leakage of urine which is a social and hygienic problem to the patient.**

### Physiology of Micturition

#### Bladder Supply

Sympathetic	Parasympathetic
Via T10 – L 2/ L3 Neurotransmitter – Norepinephrine that acts on 2 types of receptors <ul style="list-style-type: none"> <li>• <math>\alpha</math> receptor – located on urethra (close urethra and <math>\uparrow</math> urine storage and continence)</li> <li>• <math>\beta</math> receptor- located mainly on bladder (<math>\downarrow</math> tone of bladder and urethra and promote storage of urine). (The somatic supply to bladder is mainly by pudendal nerves.)</li> </ul>	Via S2 – S4 Neurotransmitter-acetyl choline that acts via muscarinic receptors in bladder. It promotes bladder emptying: <ul style="list-style-type: none"> <li>• Contracts detrusor muscle</li> <li>• Relaxes urethra</li> </ul>

## Types of Urinary Incontinence

Stress urinary incontinence	Urge urinary incontinence	Mixed incontinence	Functional incontinence	Bypass incontinence
It is involuntary escape of urine when intra abdominal pressure is increased as in sneezing or coughing or laughing.	Involuntary leakage accompanied by or immediately preceded by the urge to void.	Both SUI and urge incontinence together	It is associated with cognitive, psychological or physical impairment that makes it difficult to reach the toilet.	May be caused by urogenital fistula or any congenital abnormality
It is the most common variety of urinary incontinence.	Involuntary detrusor muscle contractions are typically the cause of urge incontinence.		A useful mnemonic for functional incontinence is DIAPERS D = Delirium I = Infection A = Atrophy P = Pharmacological drugs E = Endourinopathy R = Restricted mobility S = Stool impaction	

### Stress Urinary Incontinence (SUI)

- M/C type of urine incontinence in women accounting for 50–70% of cases.



**SUI Can Be Due To**

<b>Bladder Neck Descent</b> (Including urethral hypermobility) (75–80%)	<b>Intrinsic Sphincter Defect</b> (20–25%)
It occurs due to loss of integrity of the fibromuscular tissue that supports the bladder neck & urethra	It is diagnosed when the sphincter mechanism is compromised and fails to close the urethro vesical junction. These patients are severely incontinent.

**Z** Defined as involuntary escape of urine when intra-abdominal pressure is increased as in sneezing or coughing or laughing.

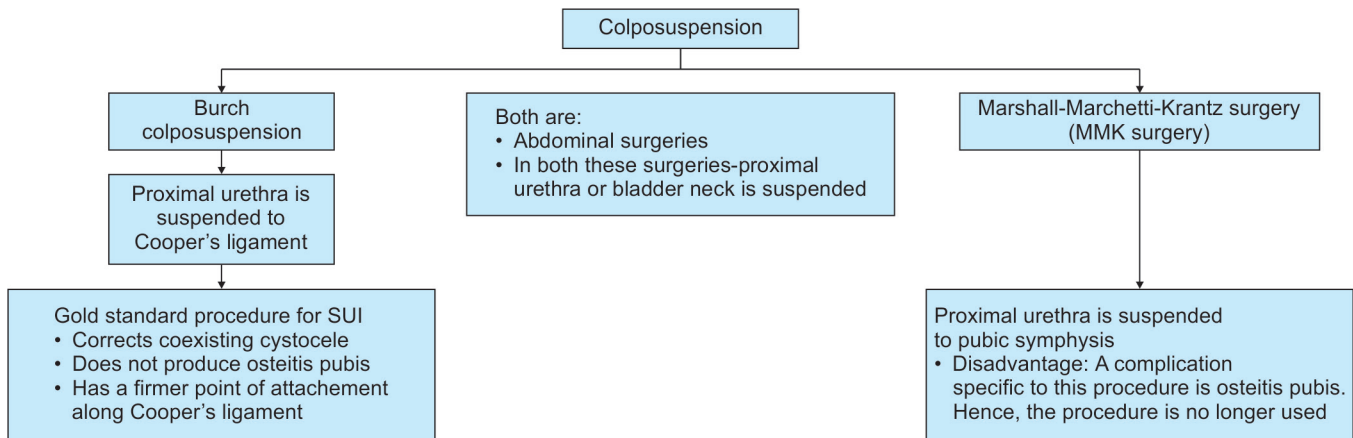
- Risk Factors for UI**
- Gender – UI is more common in women than men
  - Hypoestrogenism
  - Parity – Higher incidence of UI in multiparous females
  - Repeated child birth
  - Underlying medical conditions like diabetes, obesity parkinsonism, and multiple sclerosis
  - Previous pelvic surgery with resultant scar formation
  - Pharmacological agents like diuretics, caffeine, and anticholinergics
  - Chronically increased intra- abdominal pressure as in COPD

**Test for Detecting Stress Incontinence—Which Aim at Evaluating Urethral Support**

- **Bonney’s test:** In this test the patient is asked to insert 2 fingers, in the paraurethral region causing lifting of the bladder neck and then the patient is asked to cough. If SUI gets corrected, then it is due to bladder neck descent. If SUI persists, it is due to sphincter defect.
- **Marchetti test:** is same as Bonney’s test, except that instead of fingers, two Allis forceps are used.
- **Q tip test:** A sterile cotton swab is introduced into the level of bladder neck. Then the patient is asked to strain. Marked upward elevation of cotton tip (>30°) indicates urethra hypermobility. Goniometer is used to measure the urethero – vesicle angle.

**Management**

- **1st line of mgt:** Pelvic floor exercise i.e. Kegel’s exercises.
  - **Definitive management:** Surgical management.
- Earlier concept:**
- For bladder neck descent (urethral hypermobility): Surgery done was colpo-suspension.
  - For intrinsic sphincter defect: Surgery done was pubovaginal sling surgery, e.g. aldrige, McGuire sling.



Current principle: These days – these surgeries have been replaced by minimally invasive synthetic midurethral slings – TVT and TOT.

<b>TVT</b> (Tension-free vaginal table)	<b>TOT</b> (Tension free obturator tape)
<ul style="list-style-type: none"> <li>• Both are vaginal surgeries</li> <li>• Both are day care surgeries</li> <li>• In both surgeries, midurethra is suspended</li> </ul>	

**?** Specific complication of Marshall Marchetti Krantz procedure for treating SUI is Osteitis pubis

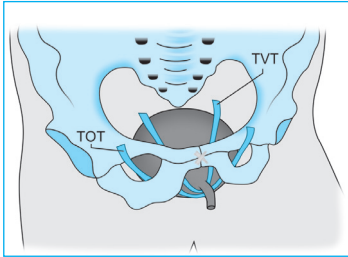


Fig. 8.4 TVT and TOT

## Tension Free Slugs

TVT	TOT
<ul style="list-style-type: none"> <li>Devised by Nelson in 1998</li> </ul>	<ul style="list-style-type: none"> <li>Devised by Delorme in 2001</li> </ul>
<ul style="list-style-type: none"> <li>A mersilene tape is passed vaginally in a U-shaped manner under midurethra to either sides</li> </ul>	<ul style="list-style-type: none"> <li>A multifilament polypropylene tape is passed through obturator foramen</li> </ul>
<ul style="list-style-type: none"> <li>Retropubic space of retzius is entered, chances of bladder injury present</li> </ul>	<ul style="list-style-type: none"> <li>Retropubic space is not entered: ∴ Less complications</li> </ul>
<ul style="list-style-type: none"> <li>Cystoscopy done at the end of procedure</li> </ul>	<ul style="list-style-type: none"> <li>Preferred method</li> </ul>
<ul style="list-style-type: none"> <li>Complications:               <ul style="list-style-type: none"> <li>Injury to bladder</li> <li>Retropubic hematoma</li> <li>Sling erosion</li> <li>Overactive bladder</li> </ul> </li> </ul>	



Although both Burch Colposuspension and TVT/TOT have comparable success rate but if in an MCQ both are given in options and question is asked which is better go for TVT/TOT

## Other Procedures

### Kelly's Plication

This operation was the standard first line of treatment previously. The principle was supposed to be elevation of bladder neck by placating the fascia under the urethra. Cure rates are low, and so it is not recommended nowadays as primary line of treatment but recommended in women who are elderly and medically unfit for prolonged surgery

## Urge Incontinence

- It is more common in older females.
- Characterized by involuntary leakage of urine accompanied by urgency



It is can be mainly due to detrusor overactivity which can be

- Idiopathic (in 90% cases)
- Due to neurogenic causes like:
  - Cerebrovascular accidents
  - Alzheimer's disease
  - Multiple sclerosis
  - Parkinsonism
  - Diabetes
- Cystitis/UTI
- Bladder stones/Cancer
- Urethral obstruction

## Investigations

- Urine culture (to rule out infection)
- Cystourethroscopy (to rule out causes like bladder tumor/calculus)
- **Cystometry:** Main objective is to rule out urge incontinence.



- **Normal values in cystometry:**

- Residual urine less than 50mL
- Residual urine less than 50mL
- First desire to void between 150 and 200 mL
- Capacity of strong desire to void when urine is more than 400 mL
- No detrusor contractions during filling despite provocation
- No leakage on coughing or on any provocation
- Voiding by voluntarily initiated and sustained detrusor contraction
- Flow rate during voiding more than 15 mL/sec with a detrusor pressure less than 15 cm of water during filling and less than 70 cm of water during voiding.



- **Must rule out neurological cause for urge incontinence**

- Multiple sclerosis
- Slipped disc
- Diabetes mellitus

## Management

Urge incontinence is best treated by behavioural therapy and anti-cholinergic drugs (to decrease detrusor contractions).

- **Anti-cholinergic drugs** used are:
  - Tolterodine
  - Hyoscyamine
  - Oxybutynin
  - Dicyclomine

## Mechanical Devices

**Vaginal:** Intriol and continence guard

**Urethral:** Urethral plugs, Reliance 7M urinary control insert, Autocath 100 device, continence control pad.

**Intriol:**

- This pessary consists of silicon rubber flexible bag with two blunt prongs located at one end.
- When placed in vagina, prongs elevate UV angle in a manner like bunch colposuspension.
- Side effects – vaginal abrasions, cystitis.

**Continence guard:** Intravaginal device made of hydrophilic polyurethane foam, when saturated with water increases in size by 30 percent.

**Urethral plug:**

- Made of thermoplastic elastomere
- Invented by Nielson 1990
- Consists of metal plate, soft stalk and either one or two prongs
- Midpoint of proximal sphere is placed at bladder neck while distal sphere is placed at maximal urethral pressure point
- Proximal sphere reduces amount of urine pushed in proximal urethra during increased IAP.

**Autocath 100**

- Consists of a cylinder constructed of surgical steel coated with silver.
- Within cylinder, there is spring loaded plunger which regulates flow of urine.

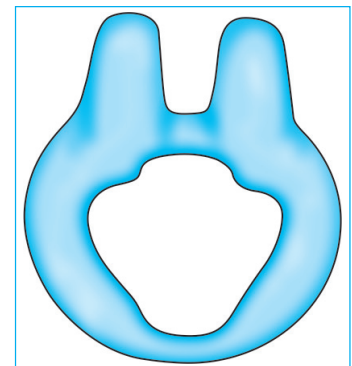


Fig. 8.5: Intriol

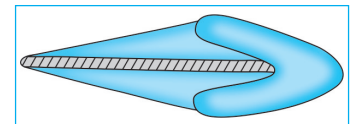
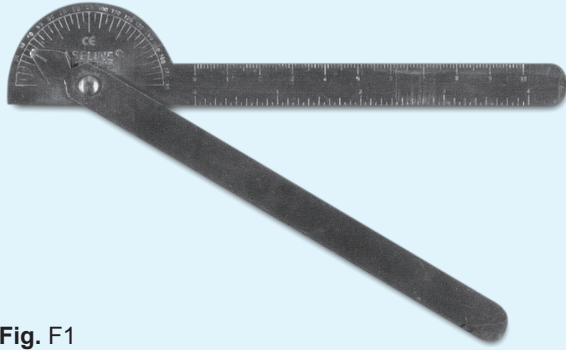


Fig. 8.6: Continence guard

## FIGURE BASED QUESTIONS

- F1.** The instrument used in figure F1 is used to measure:
- Urethrovesical angle
  - Angle of arteflexion
  - Angle of Anteversion
  - Angle of vagina with horizontal



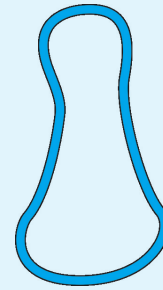
**Fig. F1**

- F2.** The instrument shown in figure F2 is used for:
- Kegel's exercise
  - Retroversion
  - Prolapse
  - Measuring rectal pressure



**Fig. F2**

- F3.** The pessary shown in Figure F3 is used for:
- Prolapse of uterus
  - Stress urinary incontinence
  - Retroversion of uterus
  - Inversion of uterus



**Fig. F3**

## QUESTIONS

- A 30 years old multipara has uterine prolapse, the management of choice is: (AIIMS Nov 99)
  - Fothergill's repair
  - Fothergill's repair with tubal ligation
  - Sling operation
  - Vaginal hysterectomy
- A 28-year-old female P3, has II<sup>nd</sup> degree of utero-vaginal prolapse. The management of choice is:
  - Fothergill's repair (AIIMS Dec 97)
  - Wertheim's hysterectomy
  - Perineal exercises x 3 month
  - Vaginal hysterectomy with vault repair
- A lady with prolapsed uterus after Fothergill's repair will complain of following except: (AIIMS Nov 00)
  - First trimester abortion
  - Cervical dystocia
  - Premature labour
  - Premature rupture of membrane
- Fourteen weeks pregnancy with third degree prolapse. Best management will be: (AIIMS Dec 98)
  - Sling surgery
  - Foot end elevation
  - Ring Pessary
  - No treatment
- Most common cause of vesicovaginal fistula in India is: (AIIMS Nov 02)
  - Gynae surgery
  - Irradiation
  - Obstructed labour
  - Trauma
- Kamla, a 48-years-old lady underwent hysterectomy. On the seventh day, she developed fever, burning micturition and continuous urinary dribbling. She can also pass urine voluntarily. The diagnosis is: (AIIMS May 01)
  - Vesico vaginal fistula
  - Urge incontinence
  - Stress incontinence
  - Uretero-vaginal fistula
- Post partum VVF is best repaired after: (AIIMS 87)
  - 6 weeks
  - 8 weeks
  - 3 months
  - 6 months
- Ureter is identified at operation by: (AIIMS 96)
  - Rich arterial plexus
  - Peristaltic movement
  - Relation to lumbar plexus
  - Accompanied by renal vein
- Version I**  
Most important structure preventing uterine prolapse is: (PGI 88)
  - Round ligament
  - Broad ligament
  - Cardinal ligament
  - Uterosacral ligament
- Version II**  
All of the following are classified as primary supports of uterus except:
  - Transcervical ligament
  - Pubocervical ligament
  - Uterosacral ligament
  - Broad ligament

10. Cause of decubitus ulcer in uterine prolapse is: (PGI Dec 99)  
 a. Friction                      b. Venous congestion  
 c. Intercourse                  d. Trauma
11. Indication of Manchester operation in prolapse: (PGI Dec 03)  
 a. Nulliparous  
 b. Women of < 35 years age  
 c. Patient who wants child bearing function  
 d. Congenital elongation of cervix
12. Most common site of obstetric injury leading to uretero vaginal fistula: (PGI 96)  
 a. Infundibulo pelvic ligament  
 b. Vaginal vault  
 c. Ureteric tunnel  
 d. Below cardinal ligament where uterine artery crosses
13. Treatment of genuine stress incontinence: (PGI Dec 04)  
 a. Anterior colporrhaphy  
 b. Posterior colporrhaphy  
 c. Colposuspension  
 d. Pelvic floor exercise  
 e. Sling operation
14. Cause(s) of retention of urine in reproductive age group: (PGI Dec 00)  
 a. Cervical fibroid  
 b. Retroverted gravid uterus  
 c. Unilateral hydronephrosis  
 d. Severe UTI  
 e. Posterior urethral valve
15. Which is true regarding retroverted uterus: (PGI Dec 01)  
 a. May present congenitally  
 b. Associated with endometriosis  
 c. It is a cause of infertility  
 d. Causes menorrhagia  
 e. Associated with PID
16. Most common genital prolapse is: (AI 02)  
 a. Cystocele                      b. Procidencia  
 c. Rectocele                      d. Enterocoele
17. Birth trauma is a risk factor for: (MAHE 07)  
 a. Prolapse uterus              b. Endometriosis  
 c. PID                              d. Abortions
18. Which of the following is true: (Dellhi 98)  
 a. Pregnancy with prolapse : Pessary treatment  
 b. Uterine prolapse in a nulliparous: Shirodkar sling operation  
 c. Prolapsed pouch of Douglas: Posterior colpoperineorrhaphy  
 d. All of the above
19. A young nulliparous woman has 3rd degree uterovaginal prolapse without any cystocele or rectocele. There is no stress incontinence. Uterocervical length is 3 inches. All other symptoms are normal. The best treatment plan for her will be: (UPSC 00)  
 a. Observation and reassurance till child bearing is over  
 b. Shirodkar's vaginal repair  
 c. Shirodkar's abdominal sling  
 d. Fothergill's operation
20. Shirodkar sling operation may be associated with all complications except:  
 a. Enterocele  
 b. Subacute intestinal obstructions  
 c. Clitoral injury  
 d. Parasthesia over inner aspect.
21. **Version 1**  
 Kegel's exercise should begin:  
 a. immediately after delivery  
 b. 24 hrs after delivery  
 c. 3 weeks after delivery  
 d. 6 weeks after delivery
- Version 2**  
 Kegel's exercise should begin:  
 a. immediately after delivery  
 b. 3 weeks after delivery  
 c. Only after LSCS  
 d. During third trimester of pregnancy
22. A 65-year-old P3+0 female complains of procidencia. She has past history significant of MI and is diabetic and hypertensive. Ideal management of prolapse in the patient is:  
 a. Cervicopexy                  b. Vaginal hysterectomy  
 c. Wait and watch              d. Le forts repair
23. Best management of vault prolapse is:  
 a. Sacral colpopexy  
 b. Sacrospinous ligament fixation  
 c. Le forts repair  
 d. Anterior colporaphy
24. The most appropriate method for collecting urine for culture in case of vesicovaginal fistula is: (AI 04)  
 a. Suprapubic needle aspiration  
 b. Midstream clean catch  
 c. Foley's catheterisation  
 d. Sterile speculum
25. Most useful investigation for VVF is: (AI 10)  
 a. Three swab test              b. Cystoscopy  
 c. Urine culture                  d. IVP
26. Chassar Moir technique is used in: (AMU 05)  
 a. VVF                              b. Stress incontinence  
 c. Urethrocele                  d. Enterocoele
27. In a case of incontinence of urine, dye filled into the urinary bladder does not stain the pad in the vagina, yet the pad is soaked with clear urine. Most likely diagnosis is: (UPSC 00)  
 a. VVF  
 b. Uretero – vaginal fistula  
 c. Urinary stress incontinence  
 d. Urethero – vaginal fistula
28. A case of obstructed labor which was delivered by Cesarean section complains of cyclical passage of menstrual blood in urine. Which is the most likely site of fistula: (AI 04)  
 a. Urethrovaginal              b. Vesico-vaginal  
 c. Vesico-uterine                d. Uretero-uterine

29. Multipara With LSCS, Presents With Cyclical Hematuria, Diagnosis can be: (PGI Dec 08)
- VVF
  - UVF
  - Bladder Endometriosis
  - Ca. Cervix
30. Patient of rectovaginal fistula should be initially treated with: (AI 05)
- Colostomy
  - Primary repair
  - Colporrhaphy
  - Anterior resection
31. The recommended non surgical treatment of stress incontinence is: (AI 09)
- Pelvic Floor Muscle Exercises
  - Bladder Training
  - Electrical stimulation
  - Vaginal cone/weights
32. Kelly's plication operation is done in: (PGI June 05)
- Stress incontinence
  - Vault prolapse
  - Rectal prolapse
  - Uterine prolapse
  - Cervical incontinence
33. Bonney's test demonstrates:
- Stress urinary incontinence
  - Urge incontinence
  - Overflow
  - All of the above
34. **Version I**  
Which of the following surgeries for stress incontinence has highest success rate: (AI 2011)
- Burch colposuspension
  - Pereyra sling
  - Kelly's stitch
  - Tension free vaginal tape (TVT)
- Version II**  
Among the surgeries to correct SUI, the long-term success rate is maximum with: (AI 2002, 2011)
- Burch's colposuspension
  - Stamey's repair
  - Kelly's stitch
  - Aldridge surgery
35. Site of placement of tension free vaginal tapes in stress urinary incontinence: (PGI May 2013)
- At ureterovaginal junction
  - At urethrovaginal junction
  - At upper part of urethra
  - At middle part of urethra
  - At lower part of urethra
36. The disadvantage of Marshall marchetti Krantz procedure compared with other surgical alternatives for treatment of stress urinary incontinence includes?
- Urinary retention
  - Increased incidence of urinary tract infections
  - High failure rate
  - Osteitis pubis
37. A woman treated for infertility, presents with 6 week amenorrhea with urinary retention. The most likely etiology is: (AI 00)
- Retroverted uterus
  - Pelvic hematocoele
  - Impacted Cervical Fibroid
  - Carcinoma Cervix

## NEW PATTERN QUESTIONS

38. Childbirth trauma leading to urine incontinence is seen least in females with:
- Android pelvis
  - Anthropoid pelvis
  - Gynecoid pelvis
  - Platypelloid pelvis
39. Ureterovaginal fistula should best be treated by:
- Ureteroneocystostomy
  - End-to-end anastomosis through an ureteric catheter
  - Implantation into colon
  - Ileal conduit
40. Accidental injury of the ureter during abdominal operation should be managed by all except:
- Deligation
  - End-to-end anastomosis through an ureteric catheter
  - Implantation into the bladder
  - Colonic implantation
41. In anterior colporrhaphy, the best method of suture apposing the vaginal flaps is:
- Interrupted
  - Continuous
  - Interlocking
  - Interrupted mattress
42. Regarding the sling procedure for Urodynamic Stress Incontinence (USI):
- Tension-free vaginal tape (TVT) elevates the bladder neck to a retropubic position
  - TVT is an autologous sling material
  - Intrinsic sphincter deficiency is an indication
  - Success rate of TVT is low than other retropubic procedures
43. Complications of sling procedures (TVT) for USI are all except:
- Injury to bladder and wound haematoma
  - Sling erosion particularly with polytetrafluoroethylene (Goretex)
  - Overactive bladder in about 7% cases
  - Obturator nerve injury is about 10%
44. Urinary symptoms of procidentia:
- Frequency of micturition
  - Retention of urine
  - Stress incontinence
  - All of the above
45. Enterocele formation is a common complication of:
- Suburethral sling surgery
  - TVT
  - Burch colposuspension
  - TOT
46. Baldy webster operation is done in case of:  
In case of:
- Congenital prolapse
  - Retroversion of uterus
  - Inversion of uterus
  - Prolapse in females < 40 yrs of age.
47. In Baden Walker Halfway system of classification of prolapse, the reference point is:
- Hymen
  - Introitus
  - Internal os
  - External os

## ANSWERS TO FIGURE BASED QUESTIONS

**F1. Ans. is a, Urethrovesical angle**

Ref. Novak gynaecology 8/e, page 918

The instrument shown is a goniometer, which is used to measure baseline urethral angle and maximum strain angle of the urethra with a cotton tip swap in place.

**F2. Ans. is a, Kegel's exercise**

Ref. Jeffcoates 8/e, page 883

The instrument shown in F<sub>2</sub> is a kegel perineometer used for pelvic floor exercise–Kegel exercises.

It consists of a vaginal obturator with an air-containing sleeve connected to a manometer which measures the strength of vaginal muscle.

**F3. Ans. is c, Retroversion of uterus**

Ref. Jeffcoates 8/e, page 882–883

The pessary shown in F<sub>3</sub> is Hodge pessary. Hodge pessary is used for treating retroversion. Indications of Hodge Pessary in Retroverted uterus:

1. Mobile retroversion (pessary is of no use in fixed retroversion)
2. Pessary test
3. During pregnancy.

## ANSWERS

**1. Ans. is b, i.e. Fothergill's repair with tubal ligation**Ref. Shaw 15<sup>th</sup>/ed p 339; Jeffocate 7<sup>th</sup>/ed p 289**2. Ans. is a, i.e. Fothergill's repair**Ref. Shaw 15<sup>th</sup>/ed p 339; Jeffocate 7<sup>th</sup>/ed p 289

Fothergill's operation (Manchester Repair) is done in women below 40 years, who want to retain their menstrual function.

In both questions 1 and 2 patient are less than 40 years and multiparous so, Fothergill's repair is the ideal management for them.

Fothergill's repair causes complications of pregnancy like incompetent os, habitual abortion and cervical dystocia therefore in a multipara who have completed their family we can do tubal ligation to prevent pregnancy.

*"If the family is completed, vaginal sterilization is to be done."*

– Dutta Gynae 6<sup>th</sup>/ed p 216

Thus in question 1 answer is fothergill's repair with tubal ligation

**3. Ans. is a, i.e. First trimester abortion**Ref. Shaw 15<sup>th</sup>/ed pp 339-340; Dutta Obs 6<sup>th</sup>/ed pp 169-170, 317

In fothergills repair ceroidical amputation is done which leads to

- Incompetent os
  - Habitual abortion (second trimester abortion and not first trimester, as incompetent os leads to second trimester abortion)
- Preterm deliveries
- Premature rupture of membranes
- Other complications are decreased cervical fertility
- Excessive fibrosis causes stenosis leading to dystocia during labour.
- Hematometra (Very rare)
- Recurrence of prolapse

– Dutta Obs 6<sup>th</sup>/ed p 169-170– Dutta Obs 6<sup>th</sup>/ed p 317

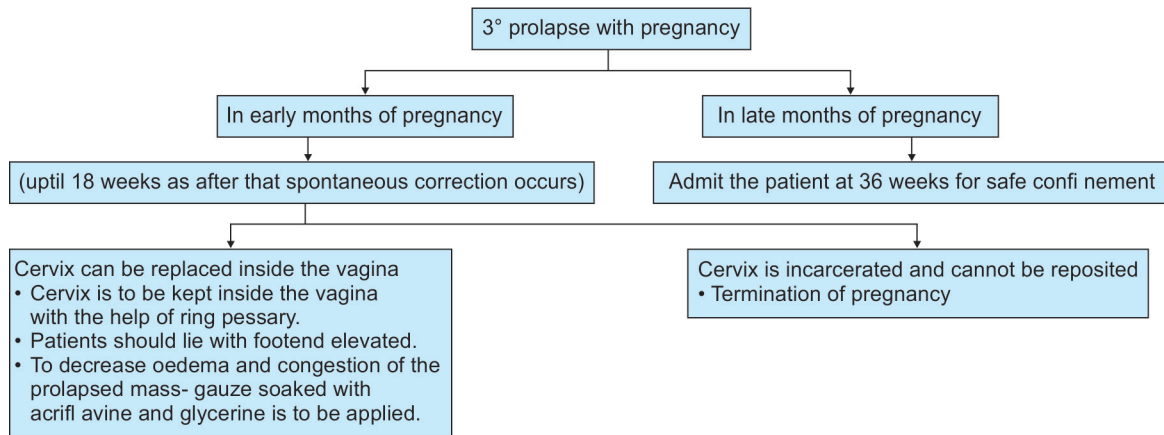
**Note:** Since all these complications of Fothergill's are mainly due to amputation of cervix–**Shirodkar's modification of Fothergills operation** (also called as Shirodkar's uterosacral ligament advancement surgery), is being done where amputation of cervix is not done, rest all steps are same as Fothergills repair.

**4. Ans. is c, i.e. Ring pessary**Ref. Dutta Obs 6<sup>th</sup>/ed p 312-3; Shaw 15<sup>th</sup>/ed p 337-8; Williams Gynae 1<sup>st</sup>/ed p 545-7 (for details of pessaries)**Other indications of Ring pessary:**

- In puerperium – to facilitate involution.
- Patient unfit or unwilling for surgery.
- Women who have undergone atleast one previous attempt at surgical intervention without relief.
- Diagnostic – It may be placed diagnostically to identify which women are at risk for urinary incontinence after prolapse correcting surgery.

**Note:** Pessaries are of two varieties : Supportive pessary eg–Ring pessary

Space occupying pessary eg–Gellhorn pessary.



5. Ans. is c, i.e. Obstructed labour

Ref. Shaw 15<sup>th</sup>/ed p 184; William Gynae 1<sup>st</sup>/ed p 573

*"In developing countries, 90% of genitourinary fistulas arise from obstetric trauma, specifically from prolonged or obstructed labor."*

– William Gynae 1<sup>st</sup>/ed p 573

**Most common Genital Fistula is vesico vaginal fistula and so above statement holds good for VVF also.**

The fistula resulting from pressure during long and difficult labour always involve the trigone of the bladder.<sup>Q</sup>

Whereas – *"In developed countries, iatrogenic injury during pelvic surgery is responsible for 90% of VVF. In industrialised countries, hysterectomy is the most common surgical cause of VVF, accounting for approximately 75% of fistula cases. Laparoscopic hysterectomies were associated with the greatest incidence followed by abdominal and vaginal."*

– Williams Gynae 1<sup>st</sup>/ed p 573

**Extra Edge:**

Most common in fistulae	
MC urinary fistula	Vesicovaginal <sup>Q</sup>
MC cause of VVF in india	Obstructed labour <sup>Q</sup>
MC cause of Uretero Vaginal Fistula	Injury to ureter after gynaecological operation <sup>Q</sup> especially Wertheim' hysterectomy <sup>Q</sup>
MC cause of Vesico Uterine fistula	Cesarean section <sup>Q</sup>
MC cause of Recto Vaginal fistula	Cesarean perineal tear <sup>Q</sup>

6. Ans. is d, i.e. Ureterovaginal fistula

Ref. Jeffcoate 7<sup>th</sup>/ed pp 263, 265

- Continuous dribbling of urine following hysterectomy points towards urinary fistulas as the diagnosis.
- In case of urinary fistulas, if the patient never needs to void as there is continuous dribbling it signifies that the fistula communicates with the bladder. If, there is filling and emptying of bladder along with the fistula, it suggests fistula opening into one ureter i.e. Ureterovaginal fistula.<sup>Q</sup>
- As far as urethral fistula are concerned, they give little trouble because the urethra is normally empty of urine. However during micturition urine passes through the fistula and may then fill the vagina to dribble during body movements for a short time afterwards.
- This patient is developing symptoms on the **seventh day** can be explained by : *"Fistulas resulting from accidental, surgical and obstetrical trauma are produced in two ways. They can be caused by direct injury such as cuts and then they manifest themselves immediately by hematuria and incontinence. Alternatively, if they are the outcome of pressure necrosis or of ischemia, in such a case urinary incontinence, fever and burning micturition develops 7-14 days after the accident."*

– Jeffcoate 7<sup>th</sup>/ed p 263

**Before concluding let's rule out other options as well:**

- In stress incontinence, dribbling of urine occurs only when intrabdominal pressure is raised.
- In urge in continence, the patient has urge to void urine at a moment's notice and she is unable to control her bladder and passes urine instantly.

7. Ans. is c, i.e. 3 months

Ref. Shaw 15<sup>th</sup>/ed p 187; TB of Gynecology Shiela Balakrishnan 335

**Management of VVF is : surgical management:**

**Timing of surgery –**

- Small urinary fistulas sometimes heal spontaneously during the first few weeks.
- However, in a case of established fistula – it is better to wait for about 3 months<sup>Q</sup> for all tissue inflammation to subside. If one attempt fails to heal fistula, second attempt is done after 3 months.<sup>Q</sup>
- In fistulas following surgery, waiting period is 3–6 months.
- In fistulas following radiation : 6 months – 2 years time can be taken before inflammation subsides.



**Techniques of Repair—**

- Layer technique
- Latzko procedure (for fistulas following hysterectomy)
- Chassar Moir technique.<sup>Q</sup>

**Post-operative Management—**

- Continuous bladder drainage for 14 days.<sup>Q</sup>
- Antibiotic coverage.
- No vaginal examination, P/S, intercourse x 3 months.
- Avoid pregnancy for 2 years.
- In pregnancy after repair of vaginal fistula – elective cesarean is done.<sup>Q</sup>

**Extra Edge:**

This question is an old one so here answer will be 3 months but if this question is repeated now remember the following lines from *Williams Gynae. 1<sup>st</sup>/ed 575-576:*

*“Timing of repair:* Traditional teaching recommends delayed repair of fistulas at 3 – 6 months after injury. However, this old dictum is probably no longer applicable. Most agree that unless there is severe infection or acute signs of inflammation, waiting is not necessary. Early surgical intervention of uncomplicated fistulas does not affect closure rates, yet appears to reduce social and psychological patient distress (Balivas, 1995). Fistulas identified within the first 24 – 48 hours postoperatively can be safely repaired immediately with success rates of 90 – 100%.”

**8. Ans. is b, i.e. Peristaltic movement**

Ref. *Stud progress in Obs and Gynae Vol 16 p 306*

**At operation ureter is recognized by:**

1. Its pale glistening appearance
2. By a fine longitudinal plexus of vessels on its surface
3. More particularly by its peristaltic movement
4. By palpation between finger and thumb as a firm cord which, when escapes, gives a characteristic ‘snap’.

Absence of pulsation does not serve to identify a structure as ureter because veins and obliterated umbilical artery are also non pulsatile.

**9. Version 1 Ans. is c and d, i.e. Cardinal ligament; and Uterosacral ligament**

Ref. *Jeffcoate 7<sup>th</sup>/ed p 46*

**Version 2 Ans is d, i.e broad ligament**

Supports of uterus have been discussed in detail earlier

Broad ligament (fold of peritoneum) and round ligaments are **secondary supports** of uterus and their role as support is doubtful.

*“Main support which prevents descent of the uterus is transverse cervical ligament (cardinal ligament) and its posterior extension the uterosacral ligament.”*

– *Jeffcoate 7<sup>th</sup>/ed p 46*

Thus answer to Q9 version 1 is both cardinal ligament and uterosacral ligament.

**10. Ans. is b, i.e. Venous congestion**

Ref. *Jeffcoate 7<sup>th</sup>/ed p 279-280*

*“Ulceration of the prolapsed tissue is often said to be caused by friction with the thighs and clothing. Although this may be partly true, it is notable that the ulcer is nearly always on the most dependant part of the cervix or vagina and not at the sides where friction is greatest. It is to be regarded, therefore more as a result of circulatory and nutritional changes than of trauma.”*

**Treatment of decubitus ulcer:** Reduction of the prolapse into the vagina and daily packing with glycerine and acriflavine. Acryflavin is an antiseptic agent while glycerine is a hygroscopic agent.

**Also know:** Other important points to remember in symptoms of prolapse

- Backache in patents of prolapse is due to the stretching of uterosacral ligaments.
- Genuine stress incontinence is seen in patients of prolapse
- Cancer of cervix or vagina is rarely seen, even in untreated cases of prolapse.

**11. Ans. is b, i.e. Women of < 35 years age**

Ref. *Shaw 15<sup>th</sup>/ed p 339; Principles and Practice of Obs & Gynae for PG’s Pankaj Desai 3<sup>rd</sup>/ed p 559*

**Fothergill’s repair/Manchester operation**

*“It is suitable for women under 40 years who are desirous of retaining their menstrual and reproductive function.”*

– *Shaw 14<sup>th</sup>/ed p 305; 15<sup>th</sup>/ed p 339*

**This means option b and c both are correct. But though this operation was initially advocated for young women desirous of child bearing, now the view has changed –**

*“Cervical amputation may adversely affect subsequent conception (infertility, cervical stenosis) and/or pregnancy outcome (repeated 1<sup>st</sup> trimester abortion, preterm labor, cervical dystocia). For these reasons, this repair is not considered as an operation of the choice in India” (for child bearing function).*

– *Principles and Practice of Obs & Gynae for PG’s Pankaj Desai 3<sup>rd</sup>/ed p 559*

So I am not including **option “c”** in the answer.

In congenital elongation of cervix management is amputation of cervix which is just a part of Fothergill’s repair, it does not require all components of this operation therefore, should not be considered amongst the correct options.

**12. Ans. is d, i.e. Below cardinal ligament where uterine artery crosses**

The crossing of the uterine vessels and ureter is at the level of internal os. Over here the ureter runs below the uterine vessels (water below the bridge) and the distance between the ureter and uterine vessels is only 1.5–2 cm.

**The ureter can get injured at all the sites mentioned in the question but during gynaecological surgeries the commonest site of injury to ureter is where it crosses below the uterine arteries.**

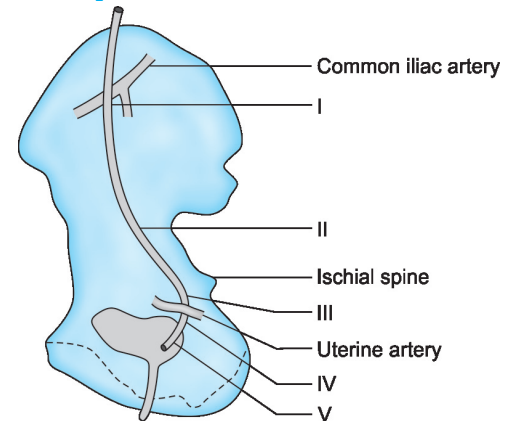
**The next common site of injury is behind the infundibulopelvic ligament at the pelvic brim.**

Close anatomical association between ureter and genital organs may lead to ureteric injury during gynecological surgery.

**Incidence:** 0.5–1% of all pelvic operations.

The sites of ureteric injuries are shown in Figure.

- At or below the pelvic brim (I)
- Along the course of ureter on lateral pelvic wall above the uterosacral ligaments (II)
- In the base of broad ligament where the ureter passes beneath the uterine vessels, about 1.5 cm lateral to cervix at the level of internal orifice (III)
- Beyond the uterine vessels as the ureter passes in the tunnel in Mackenrod's ligament and turns anteriorly and medially to enter the bladder (IV)
- In the intramural portion of bladder (V).



**13. Ans. is a, c, d and e, i.e. anterior colporrhaphy, colposuspension, pelvic floor exercises, and sling operation.**

Ref. Shaw 14<sup>th</sup>/ed p 174; Dutta gynae 5<sup>th</sup>/ed p 387-9; Textbook of Gynae, shielaBalakrishnan 1<sup>st</sup>/ed p 329-330

As explained in preceding text:

- Pelvic floor exercises
- Sling operation
- Colposuspension (Burch) are all done for management of SUI.

As far as anterior colporrhaphy is concerned - Kelly's plication is anterior colporrhaphy along with bladder neck repair, so I have included it in correct option also.

**14. Ans. is a, b, and d, i.e. Cervical fibroid; Retroverted gravid uterus, and Severe UTI**

Ref. Jeffcoate 7<sup>th</sup>/ed p 855; Dutta Gynae 6<sup>th</sup>/ed p 410

**Important gynecological causes of acute retention: –**

Period of life	Associated disorders	Provisional diagnosis
Postmenarchal	<b>Primary amenorrhea</b>	<b>Primary amenorrhea</b>
Childbearing period	Short period of secondary amenorrhea Menorrhagia No menstrual abnormality Irregular bleeding with pain Irregular bleeding with fever	Retroverted gravid uterus Uterine fibroid impacted in POD Impacted ovarian tumor, cervical or broad ligament fibroid Pelvic hematocele Pelvic abscess

Besides the above causes Jeffcoate 6<sup>th</sup>/ed pp 855-858 gives an exhaustive list of other causes of urinary retention- in which urethritis causing spasm of voluntary external urethral sphincter and acute urinary retention is given.

**15. Ans. is b, c, d and e, i.e. Associated with endometriosis; It is a cause of infertility; Causes menorrhagia, and Associated with PID**

Ref. Shaw 15<sup>th</sup>/ed p 345-7; Jeffcoate 7<sup>th</sup>/ed p 295-7

The usual position of the uterus is one of *anteversion* and *anteflexion*, in which the body of the uterus is bent forward at its junction with cervix.

## Retroversion

Retroversion is a condition in which axis of cervix is directed upward and backward (instead of forward).		
Causes		
Developmental		Acquired
<ul style="list-style-type: none"> <li>• Seen in 20% of patients</li> <li>• Retroversion can never be congenital (it is always developmental) malformation as the uterus is without version and flexion at birth.</li> </ul>	<b>Mobile retroversion</b> <ul style="list-style-type: none"> <li>• Prolapse</li> <li>• Puerperium</li> <li>• Fibroid</li> <li>• Ovarian cyst (pushes uterus backward)</li> </ul>	<b>Fixed retroversion</b> <ul style="list-style-type: none"> <li>• <b>PID</b></li> <li>• Pelvic tumors</li> <li>• Chocolate cyst of ovary</li> <li>• <b>Pelvic endometriosis</b></li> </ul>

Contd...

Contd...

**Symptoms:**

- Mobile retroversion is usually symptomless, main disadvantage being increased risk of perforation of the uterus at the time of instrumentation.

**Symptoms which can be seen are:**

- Spasmodic dysmenorrhea<sup>Q</sup>
- Pelvic congestion syndrome causing:
  - Congestive dysmenorrhea
  - Polymenorrhagia
  - Premenstrual low backache
  - Dyspareunia (it is the most specific and genuine complain in case of retroversion)
  - Leucorrhoea

- *Infertility*: as cervix is directed forward away from the seminal pool.

To implicate retroversion as a cause of infertility, it is necessary to perform Sims-Huhner test (postcoital test). Abundant motile sperms are seen in the vaginal pool but their failure to show up in the cervical canal indicates that the cervical canal is away from the seminal pool and is not accessible to the motile sperms. In such a case, retroversion is the cause of infertility. Surgical correction of the retroversion should result in conception.

- *Abortion*: can cause abortion between 10<sup>th</sup> to 14<sup>th</sup> week.

**Treatment:**

- If retroversion is mobile no treatment is required.
- In patient complaining of dyspareunia and backache with retroverted uterus : Hodge pessary may be used to keep uterus in anteverted position.
- **Surgical management:**
  - Modified Gilliams operation
  - Plication of round ligament<sup>Q</sup>
  - Baldy webster operation<sup>Q</sup>

**16. Ans. is a, i.e. Cystocele**Ref. Dutta Gynae 4<sup>th</sup>/ed p 193; Novak 14<sup>th</sup>/ed p 898

Genital prolapse refers to protusion of the pelvic organ into or out of the vaginal wall.

Classification of prolapse:

The answer is further confirmed by following lines from Novak.

*"Data from Women's Health Initiative revealed anterior pelvic organ prolapse in 34.3%, posterior wall prolapse in 18.6% and uterine prolapse in 14.3% of women in the study."*

- Novak 14<sup>th</sup>/ed p 898

Anterior organ prolapse is cystocele

**17. Ans. is a, i.e. Prolapse Uterus**Ref. Shaw 15<sup>th</sup>/ed p 332; Williams Gynae 1<sup>st</sup>/ed p 533

As discussed in the preceding text – birth trauma is an important aetiological factor for prolapse.

**18. Ans. is d, i.e all of the above**Ref. Shaw 14<sup>th</sup>/ed pp 304, 308

**Example:** Already explained in preceding text.

**19. Ans. is c, i.e. Shirodkar's abdominal sling**Ref. shaw 15<sup>th</sup>/ed p 341-2; Text book of Gynae Shiela Balakrishnan 1<sup>st</sup>/ed p 322

- Prolapse in a young nulliparous female is seen in case of congenital prolapse.
- Risk factors for congenital prolapse:
  1. Spina bifida
  2. Connective tissue disorders like Marfans syndrome, Ehler Danlos syndrome
- Cystocele is not seen in congenital prolapse and in congenital prolapse there is infravaginal elongation of cervix (not supravaginal which is usually seen).

**Management of congenital prolapse is:**

Abdominal sling surgeries/cervicopexy Like

- Purandare sling/cervicopexy
- Shirodkar sling Surgeries
- Virkud Sling

Performed through abdominal route

The sling is generally made of mersilene tape

**20. Ans. is a, i.e. Enterocoele**

As discussed in preceding text enterocoele is a long term complication of purandare sling surgery and not of shirodkar's.

**21. Version 1: Ans is b, i.e. 24 hrs after delivery**

**Version 2: Ans is d, i.e. During third trimester of pregnancy**

Ref. internet search

Kegel's exercise are pelvic floor exercises which consists of contracting and relaxing the muscles that form part of the pelvic floor.

The aim of Kegel exercises is to improve muscle tone by strengthening the pubococcygeus muscles of the pelvic floor. Kegel exercises are good for treating vaginal prolapse, preventing uterine prolapse and to aid with child birth in females.

**Kegel's exercises:** Time for initiating Kegel's exercise:

- Pregnancy 1st trimester
- After vaginal delivery after 24 hours
- After cesarean section after 24 hours.

Thus, in version 1-answer to the question is 24 hrs after delivery and in version 2 - answer is 3rd trimester of pregnancy

**Limitations of Kegel's exercises**

– Jeffcoates 7<sup>th</sup>/ed p 286

Kegel's exercise has a limited effect as it affects mainly voluntary muscles viz bulbocavernous, levator ani, and superficial and deep transverse perineal muscles and not the main fascial supporting tissues.

**22. Ans is d, i.e. Le forts repair**

Ref: Dutta Gynae. 5<sup>th</sup>/ed p 197-205; Shaw 15<sup>th</sup>/ed p

In females more than 60 years of age, who have medical complications like, in this patient previous H/O MI, hypertension and diabetes, Vaginal hysterectomy is not possible as the anaesthetist will not agree to give anesthesia.

In such patients procidentia/3° degree prolapse can be managed by Le forts colpocleisis:

**In Le forts repair/colpocleisis:** The vaginal epithelium is removed followed by suturing of the anterior and posterior walls of denuded vagina therapy completely obliterating the vagina.

The procedure is done under local anesthesia.

Before performing this procedure, PAP smear and pelvic USG should be done to rule out cancers and pelvic pathology.

**23. Ans is a, i.e. Sacral colpopexy**

Ref: Telende's 9<sup>th</sup>/ed pp 1003, 1011; Text book of Gynae, Sheila Balakrishnan 1<sup>st</sup>/ed p 321-3

**Vault Prolapse:**

- It is a long complication of hysterectomy and refers to prolapse of the vaginal stump left behind after performing hysterectomy.

Management	
Patient is fit for abdominal surgery ↓	In obese, elderly patients, not fit for abdominal surgery ↓
<ul style="list-style-type: none"> <li>• <b>Trans abdominal sacral colpopexy</b> (Mesh is attached to the vault and sacral promontory).</li> <li>• It is the gold standard surgery for vault prolapse</li> </ul>	Transvaginal sacrospinous ligament fixation/colpopexy can be done.

**24. Ans. is c, i.e. Foley's catheterisation**

Ref. Shaw 15<sup>th</sup>/ed p 185; Dutta Gynae 5<sup>th</sup>/ed p 404

*"Urine culture is mandatory before surgery and infection should be treated. The urine is collected by Catheterization."*

– Shaw 14<sup>th</sup>/ed p 167

In VVF

*"Preoperative collection is best to be done through ureteric catheterization."*

– Dutta 5<sup>th</sup>/ed p 404

So friends undoubtedly ureteric catheterization. (Don't get confused – it is not Foley's catheterization) is the best method for collecting urine for culture in a case of VVF. This option is not given, so, we will have to look for next best option.

- "Urine collected through a sterile vaginal speculum will not serve the purpose because of contamination."  
– Dutta Gynae 5<sup>th</sup>/ed p 405 (Option "d")
- Midstream clean catch sample is also contaminated in vesicovaginal fistulas. (**Option "b"**)
- Supra pubic aspiration done after proper cleansing and draping the patient with full bladder, is easy and next best method of urine collection after ureteric catheterization. But the only prerequisite for this method of collection is 'A full bladder' which cannot be fulfilled in a case of VVF as urine continuously dribbles from the vagina and therefore, bladder is never full. (Ruling out **Option "a"**)

By exclusion our answer is Foley's catheterization, although chances of contamination are present in Foley's catheterization but they can be reduced if proper vaginal douching is done prior to collection of urine.

**25. Ans. is b, i.e. Cystoscopy**

Ref. Principles & Practice of Obs & Gynae Vol. II for PG's 3<sup>rd</sup>/ed by Pankaj Desai, Narendra Malhotra p 613, Telinde 9<sup>th</sup>/ed p 1104

The most useful investigation in case of VVF is cystoscopy as it helps to confirm the size, position and number of fistulas

**26. Ans. is a, i.e. VVF**

Ref. Shaw 15<sup>th</sup>/ed p 186-7; Dutta Gynae 6<sup>th</sup>/ed pp 421, 423

Techniques for repairing VVF:

- Layer Technique
- Latzko procedure (for fistulas following hysterectomy)
- Chassar moir technique

27. **Ans. is b, i.e. Uretero-vaginal fistula**Ref. Dutta Gynae 6<sup>th</sup>/ed p 420; Shaw 15<sup>th</sup>/ed p 186

In the question : In methylene blue swab test, dye filled in the bladder does not stain the pad in vagina but it is soaked with clear urine which means it is a uretero vaginal fistula (for details see preceding text).

Observation	Interpretation
1. Upper most swab soaked with urine but unstained with dye	Ureterovaginal fistula <sup>Q</sup>
2. Upper and lower swab remain dry but the middle swab soaked with dye	Vesicovaginal fistula <sup>Q</sup>
3. The upper two swab remain dry but lower one soaked with dye	Urethrovaginal fistula <sup>Q</sup>

28. **Ans. is c, i.e. Vesico-uterine**Ref. Shaw 15<sup>th</sup>/ed p 188; Jeffcoate 7<sup>th</sup>/ed p 26629. **Ans. is b and c, i.e. UVF, and bladder endometriosis**Ref. Shaw 15<sup>th</sup>/ed p 188

The condition of cyclical passage of menstrual blood in urine is called as **menouria**.

– Jeffcoate 7<sup>th</sup>/ed p 266**Menouria:**

- It is seen in uterovesical fistulae<sup>Q</sup>
- Usually follows cesarean section<sup>Q</sup>
- The patient complains of hematuria/passage of menstrual discharge via urethra at the time of menstruation. Patient does not have urinary incontinence.<sup>Q</sup>
- Mensouria is seen when uterovesical fistula opens into the uterus above the isthmus.<sup>Q</sup>
- The presence of the fistula can be demonstrated by hystero-graphy (but not by cystography) and cystoscopy.<sup>Q</sup>
- Treatment is by abdominal repair.<sup>Q</sup>
- Another Important cause of cyclical hematuria is endometriosis<sup>Q</sup> of bladder.

30. **Ans. is a, i.e. Colostomy**Ref. Novak 14<sup>th</sup>/ed p 704; 15<sup>th</sup>/ed p 711; Sabiston TB of Surgery 17<sup>th</sup>/ed p 1500; Washington Manual of Surgery 3<sup>rd</sup>/ed p 279

**Rectovaginal fistula** is a communication between the epithelium lined<sup>Q</sup> surfaces of the rectum and the vagina.

**Diagnosis:**

- History of passing flatus, stool, mucus or blood per vagina.
- Diagnosis is made usually with:
  - Speculum examination (P/S)
  - Anoscopy/Proctoscopy
  - Methylene blue enema
- **Endoanal ultrasound** can determine the severity of trauma.

**Classification:**

Congenital	Acquired
– Due to congenital abnormalities	– Trauma – Inflammatory bowel disease – Irradiation – Neoplasia – Infection – Other causes

Now lets talk about rectovaginal fistula that results due to obstetric injury:

**Initial treatment:** A small rectovaginal fistula may be managed with conservative medical approach, in hope that decreasing the fecal stream will allow closure of fistula. Large rectovaginal fistula for which there is no hope of spontaneous closure, are best managed by performing initial diverting colostomy.<sup>Q</sup>

Ref. Novak 14<sup>th</sup>/ed p 704; 15<sup>th</sup>/ed p 711

**Definitive treatment:** However, the initial management is either medical conservative approach (small fistula) or a diverting colostomy (large fistula) to allow for the pelvic inflammation to subside, but the definitive treatment is surgical repair.

If even after several months (3–6 months) of conservative approach fistula does not heal, surgical repair is done.

31. **Ans. is a, i.e. Pelvic floor muscle exercises**Ref. Dutta Gynae 5<sup>th</sup>/ed p 586; Novak 14<sup>th</sup>/ed p 875; Williams Gynae 1<sup>st</sup>/ed p 525-6;Textbook of Gynae Sheila Balakrishnan 1<sup>st</sup>/ed p328

**The most recommended non surgical treatment for stress incontinence is pelvic floor muscle exercise.**

“Pelvic floor muscle training should be offered as first line conservative management for stress incontinence.”

– Novak’s 14<sup>th</sup>/ed p 875; Dewhurst 10<sup>th</sup>/ed p 486

“Pelvic floor exercises are the mainstay of conservative therapy for stress incontinence.”

– Urinary incontinence in primary care’ (2000)/73

**32. Ans. is a, i.e. Stress incontinence** *Ref. Shaw 14<sup>th</sup>/ed p 174; Textbook of Gynae Shiela Balakrishnan 1<sup>st</sup>/ed p 330*  
Kelly's plication/Kelley's stitch was the standard first line of treatment for SUI previously but due to low cure rates, it is not being done these days. 5-year failure rate for Kelly's plication is approximately 50%.

**33. Ans. is a, i.e. Stress urinary incontinence** *Ref. Telinde 9<sup>th</sup>/ed p 1035-37*  
Bonney's test is performed in the clinical evaluation of SUI. In the Bonney's test, two fingers are placed in the vagina at the UV junction on either side of the urethra and the bladder neck is elevated.  
On straining or coughing, leakage of urine indicates of positive test. A positive test indicates that the SUI is due to bladder neck descent and urethral hypermobility and can be corrected by bladder neck suspension surgeries.  
A negative test i.e. leakage of urine-means SUI is due to intrinsic urethral sphincteric deficiency and results of performing bladder neck suspension surgery will not be good.  
*Note:* Marchetti test is same as Bonney's test, but two Allis forceps are used instead of fingers.

**34. Version I**

**Ans. is d, i.e. Tension free vaginal taping (TVT)**

Evidence Based Urology' (Wiley Blackwell) 2010/193 'Pelvic Floor Dysfunction. A multidisciplinary Approach' (Springer) 2006/117: Hernia Repair Sequalce (Springer) 2010/440; Assessing and Managing A **cutely** Ill Adult Surgery Patient' (John Wiley and Sons) 2007/182

**Version II**

**Ans. is a, i.e. Burch's colposuspension**

*Ref. Telinde 9<sup>th</sup>/ed pp 1052-6*

As discussed in preceding text SUI is managed basically by performing either of the two surgeries viz-

1. Burch colposuspension
2. Tension free vaginal tapes/tension free obturator tapes.

The rates of success of these two surgeries are comparable, so if either of them is given in options, we will chose it.

So in version II- Answer is Burch colposuspension

*Telinde 9<sup>th</sup>/ed p 1050-6.*

Procedure	Long-term success rate (%)
Burch's colposuspension	89.5
Stamey's repair	85
Kelly's repair	50-60
Aldridge Repair	85

Now suppose both Burch colposuspension and TVT is given (like in version I), then remember-

Tension Free Vaginal Tape (TVT) has emerged as the treatment of choice for genuine stress incontinence in recent years  
Tension Free Vaginal Tape (TVT) is a simple procedure that may be performed under local anesthesia, has a decreased operative and recovery time, and is as effective as 'Burch colposuspension' which was earlier considered the procedure of choice.

*"A number of surgical procedures have been developed to treat genuine stress incontinence and most aim to elevate and support the bladder neck. Burch colposuspension was the procedure of choice, but in recent years this has been superseded by the 'Tension free Vaginal Tape' which is showing comparable results and is less invasive"*

*Ref. Assessing and managing Acutely Ill Adult Surgery Patient' (John Wiley and sonsd) 2007/440*

**35. Ans. is d, i.e. At middle part of urethra**

*Ref. Shaw 15<sup>th</sup>/ed p 193-194; Dutta gynae 6<sup>th</sup>/ed p 404*

Read the text for explanation.

**36. Ans. is d, i.e. Osteitis pubis**

*Ref. Telinde 9<sup>th</sup>/ed pp 1057-8; Textbook of Gynae, Sheila Balakrishnan 1<sup>st</sup>/ed p 329*

Marshall-Marchetti-Krantz (MMK) procedure, involves the attachment of the periurethral tissue to the symphysis pubis. In approximately, 3% of patients undergoing the procedure, osteitis pubis develops.

**37. Ans. is c, i.e. Impacted cervical fibroid**

*Ref. Read below*

The patient in the question:

- Was being treated for infertility.
- Now H/O 6 weeks of amenorrhea.
- Presents with urinary retention.

The first diagnosis which comes in our mind is *retroverted gravid uterus*.

**Points which favour the diagnosis are:** The woman is pregnant and has complain of urinary retention.

*But friends, here it is important to understand that retroverted gravid uterus causes urinary retention at 14-15 weeks of gestation (not 6 weeks).*

*- Jeffcoate 7<sup>th</sup>/ed p 299*

So **Option "a"** is ruled out

**Option "b" Pelvic hematocele**

*"Pelvic hematocele is formed in a patient complaining of 6 weeks amenorrhea in case of ectopic pregnancy."* *- Jeffcoate 6<sup>th</sup>/ed p 212*

Though pelvic hematocoele causes urine retention but then other symptoms (pain) and signs of ectopic pregnancy should be present.

**Option "c" Impacted cervical fibroid**

*"A cervical fibroid impacted in pouch of Douglas can cause retention of urine. The onset of retention is acute and usually occurs immediately before menstruation, when the uterus is further enlarged by congestion or during early pregnancy."*

– Jeffcoate 7<sup>th</sup>/ed p 493

Fibroid is associated with infertility.

Thus, an impacted cervical fibroid can explain all features seen this woman and is our option of choice.

**38. Ans. is a, i.e. Android pelvis**

Ref. Dutta Gynae 6<sup>th</sup>/ed p 399

Childbirth trauma causes damage of the pelvic floor and pubocervical fascia leading to urinary continence. The injury is more common in gynecoid and least in android pelvis.

**39. Ans. is a, i.e. Ureteroneocystostomy**

Ref. Dutta Gynae 6<sup>th</sup>/ed p 427

**Surgeries for ureteric fistula:**

- Bladder flap procedure (modified Boari–Ocker–Blad)
- Ureteroneocystostomy
- Implantation into the bladder

**Note:** End to end anastomosis may lead to stricture formation.

Colonic transplantation results in recurrent pyelonephritis and hyperchloremic acidosis.

**40. Ans. is d, i.e. Colonic implantation**

Ref. Dutta Gynae 6<sup>th</sup>/ed p 427

See previous question

**41. Ans. is a, i.e. Interrupted**

Ref. Dutta Gynae 6<sup>th</sup>/ed p 213

The cut margins of the vagina are repaired by interrupted sutures.

**42. Ans. is c, i.e. Intrinsic sphincter deficiency is an indication.**

Lets see each option-

TVT acts by increasing urethral coaptation, kinking the urethra with the rise in abdominal pressure and not by elevating bladder neck hence option a is incorrect. ;

TVT is made from polypropylene (marlex) or polytetrafluoroethylene (Goretex) and not autologous sling material. Autologous sling material refers to natural sling materials made from rectus fascia or porcine dermis. These are less Antigenic; hence option b is incorrect.

TVT is done in case of intrinsic sphincter deficiency- i.e option c is correct.

Success rate of sling procedure are over 80% i.e option d is incorrect

**43. Ans. is d, i.e. Obturator nerve injury is about 10%**

Ref. Jefferies 8/e, page 803

Complications of TVT are:

- a. Injury to bladder
- b. Retropubic hematoma
- c. Sling erosion
- d. Overactive bladder.

**44. Ans. is d, i.e. All of the above**

Ref. Dutta Gyane 6<sup>th</sup>/ed p 208

All the urinary symptoms given in the options can occur in case of prolapse.

*"Retention of urine may rarely occur."*

Dutta Gyane 6<sup>th</sup>/ed p 208

**45. Ans. is c, i.e. Burch's colposuspension**

Ref. Dutta Gynae 6<sup>th</sup>/ed p 404

Enterocele formation occurs with Burch colposuspension.

**46. Ans. is b, i.e. Retroversion of uterus**

Ref. Jefferies 8/e, page 274.

**Surgeries for Retroversion**

- > Baldy webster operation
- > Modified Gilliam's operation
- > Laparoscopic ventrosuppression

Since round ligament helps to keep uterus in anteverted position in all these surgeries, round ligaments are tightened.

**47. Ans. is a, i.e. Hymen**

(Ref. Jefferies 8/e, page 253)

Bader Walker Halfway's system of grading of prolapse is similar to Shaw's classification but uses the hymen as a reference point.

# CHAPTER

# 9

# Infertility

## Basic investigations done in case of infertile couple—

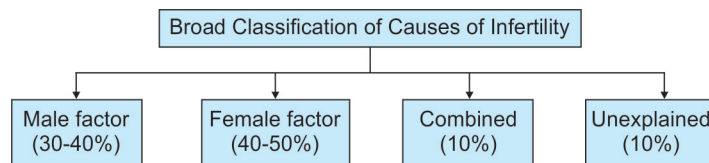
- Semen Analysis (1st investigation)
- Confirmation of ovulation
- Baseline scan
- Assessment of tubal scan

## Hormonal tests to be done in infertile females—

- TSH
- FSH
- 17 hydroxyprogesterone
- Testosterone
- DHEA

## Definitions

- **Infertility:** failure of a couple of reproductive age to conceive after at least 1 year of regular coitus without contraception.
  - **Primary infertility:** Infertility in a woman who has never been pregnant.
  - **Secondary infertility:** Infertility in a woman who has had one or more previous pregnancies.
- **Fecundability:** Probability of achieving pregnancy within one menstrual cycle. For a normal couple, this is approximately 25%.
- **Fecundity:** Ability to achieve a live birth within one menstrual cycle.



## Differential Diagnosis of Infertility

Diagnosis	Percent	Basic Evaluation
Male factors	30	Semen analysis
Tubal/uterine/peritoneal factors	25	HSG, laparoscopy, chromopertubation
Anovulation/ovarian factors	25	BBT chart, midluteal progesterone level, endometrial biopsy, luteinizing hormone testing
Cervical factors	10	Postcoital test
Unexplained infertility	10	All of the above

## Evaluation

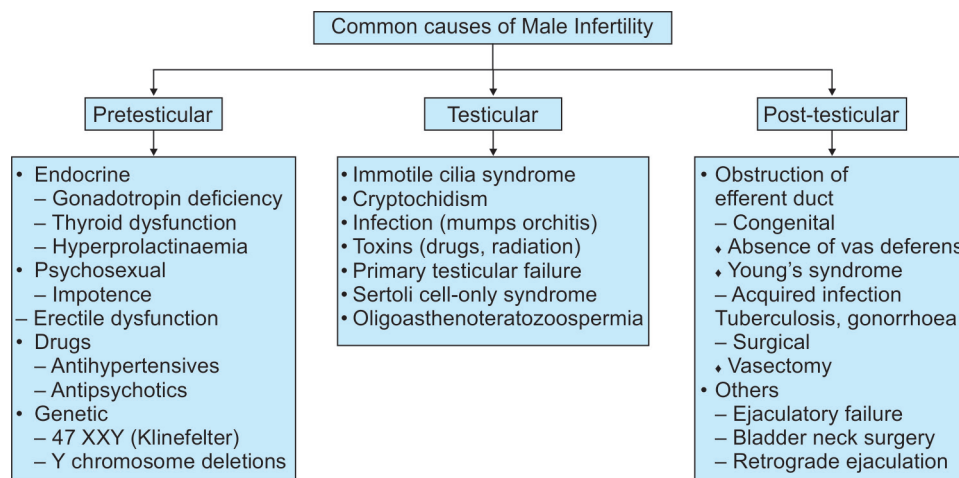
- Evaluation is indicated for women who fail to conceive after one or more years of regular, unprotected intercourse.
- Women over the age of 35 should be evaluated sooner (i.e., after 6 months of regular, unprotected intercourse.)
- No woman should be denied her request for infertility services or counseling, regardless of duration.
- Successful reproduction requires proper structure and function of the entire reproductive axis, including hypothalamus, pituitary gland, ovaries, fallopian tube, uterus, cervix, and vagina.
- **Infertility evaluation** comprises eight major elements:
  - History and physical examination
  - Semen analysis



- Sperm–cervical mucus interaction (postcoital testing (PCT))–for select patients
  - Assessment of ovarian reserve
  - Tests for occurrence of ovulation
  - Evaluation of tubal patency
  - Detection of uterine abnormalities
  - Determination of peritoneal abnormalities
- With proper coordination, the evaluation can be completed within one menstrual cycle. No abnormality or cause of infertility can be identified in 10% to 15% of couples. This group comprises a category known as “unexplained infertility.”

## Male Infertility

### Common Causes



### Semen Analysis

- The semen analysis is the cornerstone of male factor infertility evaluation.
  - Semen sample should be collected after at least 48 to 72 hr abstinence and is best evaluated within 1 hr of ejaculation.
  - Obtained either by masturbation or by sexual intercourse with a silicone condom, because latex condoms are spermicidal.

### Semen Analysis (WHO–2010)

	WHO 2010	WHO 1999
Semen analysis	Minimum (Normal values)	
Volume	≥ 1.5 mL	≥ 2 mL
pH	7.2–7.8	
Viscosity	< 3 (scale 0–4)	
Sperm concentration	15 million/mL	≥ 20 million/mL
Total sperm count	39 million/ ejaculate	≥ 40
Motility	Progressive motility = 32%	≥ 25%
	Total motility ≥ 40	≥ 50%
Morphology	Normal forms 4%	≥ 14
Viability	Living 58%	≥ 75
Leucocytes	Less than 1 million/mL	
Round cells	< 5 million/mL	
Sperm agglutination	< 10% spermatozoa with adherent particles	

### WHO Semen Analysis 1992 guidelines

Parameter	1992 guidelines
Volume	2 ml
Sperm concentration	20 million/ml
Sperm motility or > 25% rapidly progressive	50% progressive
Morphology (Strict Criteria)	> 15% normal forms
WBC	< 1 million/ml
Immuno bead or mixed antiglobulin reaction test	< 10% coated with antibodies

### Extra Edge

- When no motile sperms are observed a **sperm viability** test differentiates viable or non motile sperms from dead sperms.
- Round cells in semen analysis includes epithelial cells, prostate cells, immature sperms (spermatogonia, round spermatids, spermatocytes) and leucocytes. If total round cells is > 5 million/ml it is abnormal. True leukocytospermia means > 1 million leukocytes/ml and requires semen culture for mycoplasma hominis, ureoplasma ureolyticum and Chlamydia.
- Lymphocytes can be distinguished from other cells by immunoperoxide staining “**Endtz Test**”.



To establish the diagnosis of azoospermia, the semen specimen should be centrifuged at high speed (3000 g for 15 minutes and the pellet examined at high magnification (400 x). The absence of sperm should be documented on at least 2 separate occasions)

### Other important values in semen analysis

- pH = > 7.2 (between 7.2–7.8)
- Round cells (including WBC + epithelial cells + immature cells) = < 5 million/ml.
- Sperm agglutination = < 2
- The specimen for semen analysis should be collected after 2 - 3 days of abstinence
- The specimen should be obtained by masturbation failing which it can be obtained by coitus interruptus
- The specimen should be reach the laboratory within an hour of ejaculation

### Semen Analysis Terminology

• Normospermia	– All semen parameters normal
• Oligozoospermia <sup>o</sup> / oligospermia	– Decreased sperm number < 20 million/ml
• Asthenozoospermia <sup>o</sup> / asthenospermia	– Decreased sperm motility <sup>o</sup>
• Teratozoospermia <sup>o</sup>	– Increased abnormal forms of sperm <sup>o</sup>
• Oligoastheno-teratozoospermia	– All sperm variables abnormal <sup>o</sup>
• Azoospermia <sup>o</sup>	– No sperm in semen <sup>o</sup>
• <b>Aspermia</b>	– <b>No ejaculate (ejaculation failure)</b>
• Leucocytospermia <sup>o</sup>	– Increased white cells in semen <sup>o</sup>
• Necrozoospermia <sup>o</sup>	– All sperms non - viable or non-motile <sup>o</sup>

- About 5–15% of infertile men suffer from chromosomal abnormalities. Prevalence is higher (10-15%) in men suffering from azoospermia or severe oligospermia.
- Always do karyotype analysis in men with azoospermia or severe oligo spermia and raised FSH. Klinefelter's syndrome (XXY) is the commonest. Micro deletions of the long arm of Y chromosome can also cause severe seminal abnormalities.

### Klinefelter's Syndrome

- Karyotype is 47, XXY
- Most common genetic anomaly in azoospermic men
- Found in 1:500 to 1:1000 live male births.

### Y-chromosome Microdeletions

- May be found in up to 7% of men with male factor infertility
- While these men may be able to father children via IVF/ICSI, male offspring will inherit the Y-chromosome microdeletion and be infertile.

### Congenital Absence of the Vas Deferens (CAVD)

- Associated with cystic fibrosis gene mutations in the *cystic fibrosis transmembrane conductance regulator* (CFTR) gene
- Partners of men with CAVD must be tested for the CFTR gene mutation before pursuing infertility treatment with retrieved sperm.

### Diagnosis of Male Infertility

In azoospermia the diagnostic test which can distinguish between testicular failure and obstruction of vas deferens is Estimation of FSH levels (see Fig. 9.1).

- A very high FSH would indicate a testicular cause.
- A very low FSH would indicate pretesticular cause.
- A normal FSH would indicate a post-testicular cause.



Men with CAVD suffer with seminal vesicle agenesis. So they have low semen volume, low pH and low fructose levels. Spermatogenesis is normal.

Cause	Lab Test
<b>Pretesticular cause</b> -defect lies at the level of hypothalamus or pituitary, hence GnRH decreases, leading to decrease in LH,FSH and Testosterone.	LH decreased FSH decreased Testicular volume decreased Testosterone decreased
<b>Testicular cause</b> -defect lies at the level of testis hence decreased testosterone, thus negative feedback on FSH is lost-so FSH increases	Testosterone decrease So negative feedback on FSH is lost. Therefore FSH is increased. Testicular volume is decreased.
<b>Post testicular cause</b> LH/FSH/Testosterone all are normal	FSH normal LH normal Testosterone is normal Testicular volume is normal

### Fructose Content in the Seminal Fluid

Its absence suggests congenital absence of seminal vesicle or portion of the ductal system or both.

### Testicular Biopsy

Is done to differentiate primary testicular failure from obstruction as a cause of azoospermia or severe oligospermia. The biopsy material is to be sent in Bouin's solution and not in formal saline. Testicular tissues may be cryopreserved for future use in IVF/ICSI.

### Transrectal Ultrasound (TRUS)

Is done to visualize the seminal vesicles, prostate and ejaculatory ducts obstruction. Indications of TRUS are: (i) Azoospermia or severe oligospermia with a normal testicular volume, (ii) Abnormal digital rectal examination, (iii) Ejaculatory duct abnormality (cysts, dilatation or calcification), (iv) Genital abnormality (hypospadias).

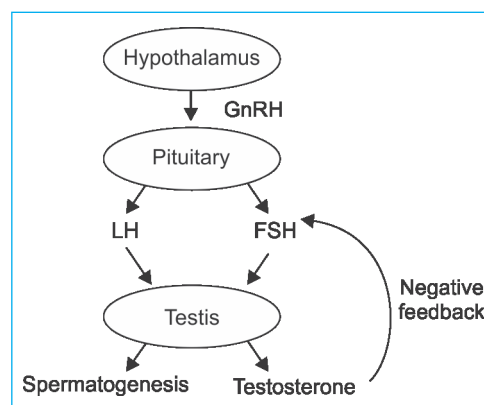


Fig. 9.1: Hypothalamic pituitary testicular axis

### Management Options in Male Infertility

Mild oligospermia = IUI (Intrauterine insemination)

### Severe Oligospermia

- > Hypergonadotropic hypogonadism ( $\uparrow$ FSH &  $\uparrow$ LH) - Testicular biopsy (to check whether sperms are present in testis) is not useful. Donor sperm should be considered.
- > If hormonal levels are normal - Testicular biopsy is done. If sperm is present in biopsy, ICSI is the option following retrieval of sperms by TESE and PESA
- > Men with normal gonadotropin and testosterone level having low volume of ejaculate should be subjected to postejaculatory urine analysis as the patient might be having retrograde ejaculation.

In patients of retrograde ejaculation. Sperms are obtained from post ejaculatory neutralised urine and then IUI/ICSI done.



TESE-Testicular sperm extraction  
PESA-Pretesticular epididymal sperm aspiration  
ICSI-Intracytoplasmic sperm injection  
All details given later.

### Intrauterine Insemination (IUI)

**Intrauterine insemination** is placement of 0.3mL of washed processed and concentrated sperms (devoid of seminal plasma)/semen into the intrauterine cavity by transcervical catheterization.



IUI can be done with patients husbands sperm or donor sperms (in case of azoospermia). In case of donors – frozen sperms are recommended because of the risk of HIV in fresh sample. The sperm donors are screened for HIV, hepatitis, syphilis, etc and then samples are cryo-preserved.



#### Prerequisite for IUI:

- Fallopian tube of the female should be patent so it cannot be used in tubal infertility in females
- It cannot be used in severe oligospermia (Sperm count <5 million/ml.) and azoospermia in males

The purpose of IUI is to bypass endocervical canal and to place increased number of motile sperms close to fallopian tube.

Components of the ejaculate removed in IUI include seminal fluid, excess debris, leukocytes and morphologically abnormal sperms. Best results are achieved when the final specimen contains 10 million total motile sperms.

### Indication

Intrauterine insemination is done in **males** with:

- Severe hypospadias
- Retrograde ejaculation (Immediate postcoital urine is taken and sperms are extracted from it.)
- Neurogenic impotence
- Sexual dysfunction
- Oligospermia
- Asthenospermia
- Low ejaculate volume

**In female infertility** IUI is useful in:

- Cervical infertility–Antisperm antibodies are present in cervix
- Vaginismus (involuntary contraction of perineal muscles during intercourse)
- Unexplained infertility.

### Technique of sperm preparation for IUI (either of the 3)

- Swim down technique
  - Swim up technique
  - Density gradient centrifugation
- ] *Should not be used if sperm count is very low*

### Procedure

Patient is laid in supine position and an insemination catheter is inserted in cervical canal and is advanced slowly in the uterine cavity. 0.5 ml of semen is slowly introduced and patient is then asked to lay supine for 15 minutes.

### Timing for IUI

- In natural and clomiphene stimulated cycles, urinary LH monitoring should be started 3 days before expected ovulation and insemination done on the day after midcycle urinary LH surge or IUI is done on 5 and 7 days after completion of clomiphene.
- If ovulation is triggered by exogenous hCG, IUI is performed 36 hours later.

## ICSI-Intracytoplasmic sperm injection

As the name suggests in this method, the sperm is injected into the cytoplasm of the ova

### Indications

#### In Males

- Oligospermia
- Asthenospermia
- Immune factor (male and female)
- Male factor (impotency, hypospadias)



- Most important parameter for IVF-Motility of sperms.
- Most important parameter for ICSI- Morphology of sperms

### In Females

- Tubal blockage
- Hostile cervical mucus
- Unexplained infertility.

### Technique (Fig. 9.2)

In ICSI the basic steps of oocyte retrieval and embryo transfer are identical to IVF but for fertilization, one sperm is microscopically injected into one oocyte and the resulting embryo then transferred into the uterus.

- Success rate of ICSI following sperm retrieval in obstructive azoospermia is 30–60%.
- Men with obstructive azoospermia need counselling with regard to the transmission of genetic disorder to their offspring.

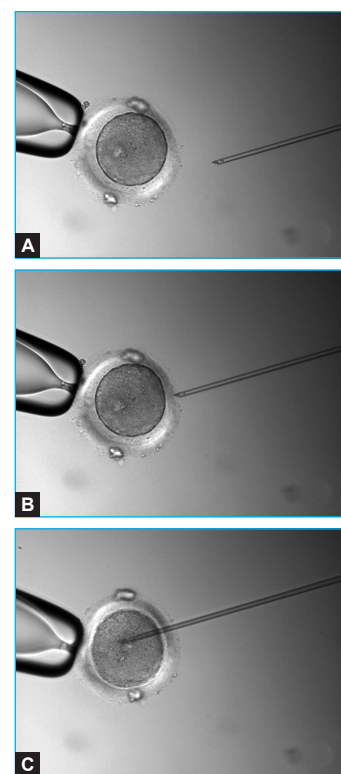
**Drawback** ICSI is associated with higher congenital anomaly risk (4.2%) when compared with conventional IVF (2–3%).<sup>3</sup>

- As discussed ICSI is the management of choice in males with severe oligospermia and azoospermia.
- But then friends if male is azoospermic from where do we get the sperms to do ICSI? Answer is simple - azoospermia means sperms are absent in semen but can still be present the testis. Thus testicular biopsy is done and if sperms are present in testis, they are retrieved by any one of the following methods.

### Methods of Sperm Retrieval in Case of Azoospermia

- Microsurgical Epididymal Sperm aspiration : MESA<sup>Q</sup>
- Percutaneous Epididymal Sperm aspiration : PESA<sup>Q</sup>
- Testicular sperm extraction : TESE<sup>Q</sup>
- Percutaneous Testicular sperm fine needle aspiration : TESA<sup>Q</sup>  
(also called *Fine Needle Aspiration FNA*).
- **The choice of the method depends on:**
  - i. the underlying diagnosis,
  - ii. whether goal of the procedure is diagnostic or therapeutic
  - iii. whether, isolated sperm will be used immediately or cryopreserved.

- |             |  |
|-------------|--|
| <b>TESA</b> | <ul style="list-style-type: none"> <li>• Is a percutaneous method which requires No/Local anesthesia and retrieves sperms from the testis when spermatogenesis is normal as in cases of post-testicular azoospermia (i.e. either there is congenital absence or obstruction of vas deferens/ejaculatory ducts or Retrograde ejaculation).</li> </ul>   |
| <b>MESA</b> | <ul style="list-style-type: none"> <li>• Also indicated in cases of post testicular azoospermia. It is done when one need's to know the nature of obstruction or if surgical correction of the obstruction is to be performed at the same time of sperm recovery. (Done under GA/Regional anesthesia).</li> <li>Another advantage of MESA is that a very large number of sperms are usually retrieved so that cryopreservation and avoidance of repeat surgery may be possible.</li> </ul> |
| <b>PESA</b> | <ul style="list-style-type: none"> <li>• Percutaneous epididymal sperm aspiration can also be used in cases of Post testicular azoosperma but it is a blind procedure. Bleeding, epididymal injury and postsurgical fibrosis can occur.</li> </ul>   |
| <b>TESE</b> | <ul style="list-style-type: none"> <li>• Indicated in men with testicular azoospermia or gonadal failure.</li> </ul>   |



**Fig. 9.2:** Intracytoplasmic sperm injection (ICSI) procedure: (A) The holding (left) and the injecting (right) pipettes are seen. (B) The oolemma is penetrated. (C) The injection pipette has reached nearly the center of the oocyte.



Anovulation is the most easily treatable cause of female infertility.



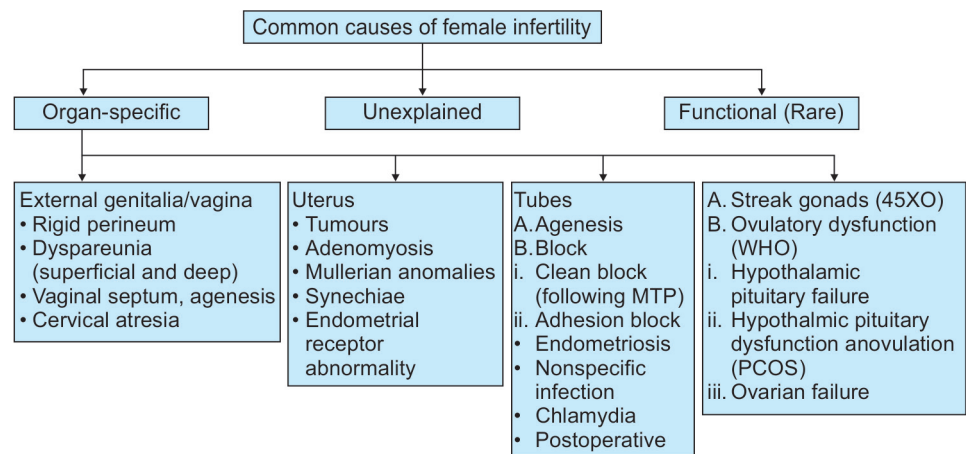
In case of anovulation woman needs to be screened for following underlying pathology leading to anovulation.

- Thyroid dysfunction (hypo/hyperthyroidism)
- Hyperprolactinemia
- Weight disorders (excessive weight loss/obesity)
- PCOS
- Pituitary tumor
- Adrenal disease
- Galactorrhea



PCOS is the most common disorder encountered in this category. For details on PCOS see Chapter 13.

## Female Infertility



### Management of Ovulatory Disorders

According to WHO, Ovulatory disorders are grouped into:

**Group I: Hypothalamic-Pituitary failure:** women in this group have hypogonadotropic hypogonadism, low gonadotropin and oestrogen level, normal prolactin and negative progesterone challenge test. Included in this group are: stress related amenorrhoea, Kallmann's syndrome, anorexia nervosa.

Investigations done in these females are

- Serum levels of FSH, LH, GnRH, and serum estradiol are estimated.
- MRI study is done for the detection of central nervous system pathology.

These women are treated with hMG or GnRH. **Note:** Single most important and effective treatment for this group of women with low BMI (<16 kg/M<sup>2</sup>) is to encourage gain weight. Leptin is deficient in such women. Exogenous leptin restores ovulation in these women.

**Group II: Hypothalamic-Pituitary Dysfunction:** Women are normogonadotropic, norm oestrogenic, anovulatory and oligomenorrhoeic. Women with PCOS are in this group. In these women tests for documenting anovulation (discussed below) are done. These women are treated with clomiphene citrate or other ovulation inducing agents.

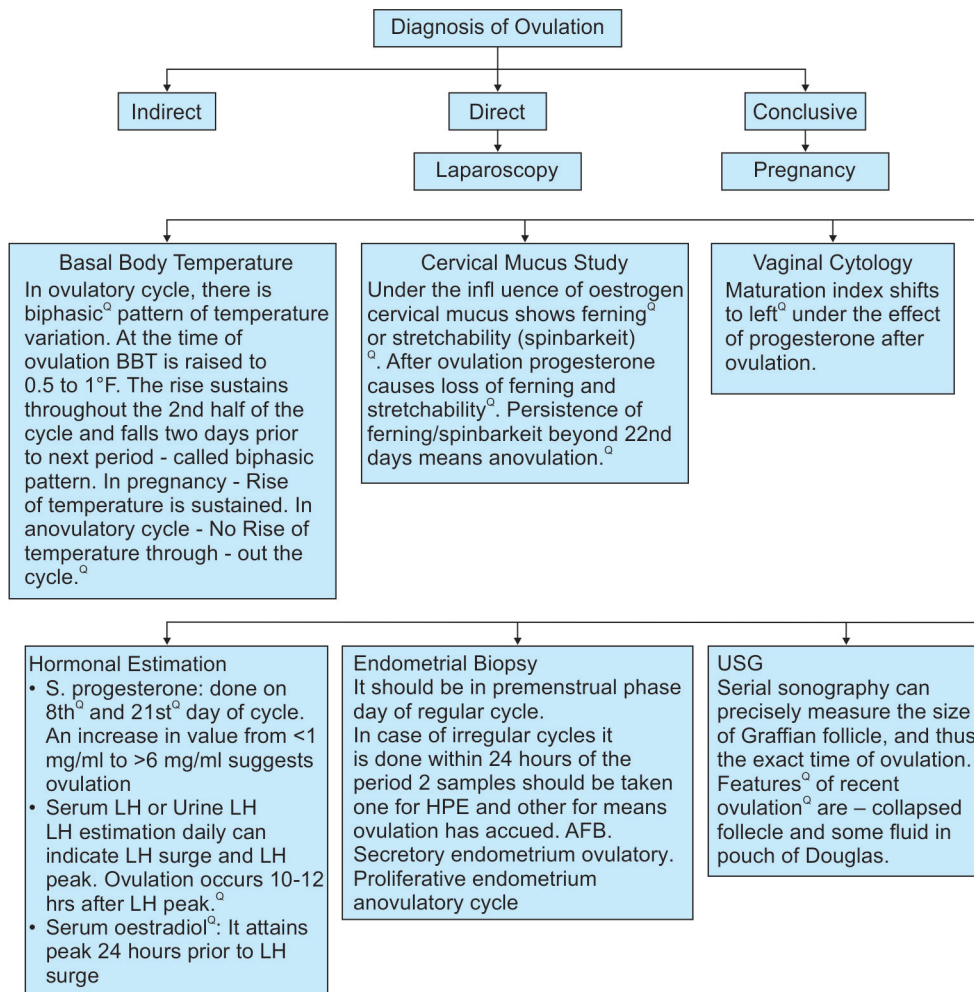
**Group III: Ovarian failure:** Primary ovarian insufficiency (failure) is the cessation of ovarian function prior to the age of 40 years. It is characterized by primary or secondary amenorrhoea with elevated serum gonadotropin levels.

### Causes of premature ovarian insufficiency (failure)

- Abnormal chromosomal pattern (45XO, 47XXX), causing accelerated follicular atresia
- Infections (HIV, Mumps, Tuberculosis)
- Iatrogenic: Radiation, Chemotherapy, Surgery (oophorectomy, excessive ovarian drilling)
- Metabolic: Galactosemia
- Autoimmune disorders (Polyglandular autoimmune syndrome).

In most of these females pregnancy can be achieved by using donor ovum, however 5–10% of women achieve pregnancy and deliver successfully by their own ova depending on the ovarian reserve. This indicates, women should be assessed for ovarian reserve before planning management.

### Tests for Documenting Anovulation



**Management of Anovulation** is by ovulation induction. Ovulation induction aims at the release of one egg per cycle in a woman who has not been ovulating regularly.

### Ovulation Inducing Agents

- > Clomiphene citrate (CC)
- > Letrozole
- > Gonadotropins

**Clomiphene Citrate:** It is a racemic mixture of enclomiphene and zuclomiphene. Enclomiphene is a more potent isomer responsible for its ovulation-inducing action.

- o Dose = 50–250 mg. However, the US FDA-approved maximum dose for clomiphene citrate is 100 mg
- o Clomiphene blocks “Estrogen” receptors → increase FSH from pituitary → growth of follicles
- o Thus it can be used only in patients with intact hypothalamic –pituitary ovarian axis
- o With clomiphene success rate for ovulation is 80% and success rate for pregnancy is 40%

**Letrozole:** It is an aromatase inhibitor which blocks the conversion of testosterone to estrogen, leading to increased FSH from pituitary.

**Gonadotropins:** HMG (Human Menopausal Gonadotropin obtained from the urine of the menopausal women) and recombinant FSH.



M/C used drug for ovulation induction: clomiphene citrate

- Letrozole is now not available in the market due to the associated risk of teratogenicity.



Clomiphene – Risk of multiple pregnancy = 5-10%



hCG is functionally and structurally similar to LH hence giving LH injection creates LH surge like condition.

- Menopausal women have high FSH and LH levels in their blood and urine, and HMG is extracted from urine of menopausal females.

**Note:**

- Recombinant LH is can also be used but is very expensive
- Follicular study is done along with ovulation induction to monitor the growth of follicles and when the dominant follicle is 18–20 mm, ovulation trigger is given to rupture the follicle
- For ovulation trigger, M/C drug used is hCG (derived from the urine of pregnant women or by recombinant technology)
- Ovulation occurs 36 hours after injecting hCG

### Side Effects of Ovulation Induction

- Multiple pregnancies: 5–10% with clomiphene, 15–30% with Gonadotropins
- Ovarian hyperstimulation syndrome (OHSS)
  - It is the most dangerous complication of ovulation induction
  - Risk factors: Young age, low body weight, PCOS patients and past history of OHSS

### Ovarian Reserve

**Ovarian reserve tests** are to assess the quantity as well as the quality of primordial follicles present in the women's ovary. These tests are done to determine how the ovaries will respond to therapy (ovulation induction) in other words it is the assessment of the reproductive potential of the woman.

#### The Tests Done Are:

- 1. Estimation of basal level of serum FSH** on D3 and again on D10 following clomiphene citrate challenge test (CCCT): 100 mg orally each day from D5–D9: values >10 IU/L (more than 2SD) indicates poor ovarian reserve.
- 2. Basal (D3) serum estradiol level** > 70–80 pg/mL, poor ovarian reserve.
- 3. Serum inhibin B (D5):** Reduced inhibin B levels (less than 40 pg/mL) are observed in woman with advanced age.
- 4. Serum antimüllerian Hormone (AMH):** Levels of serum AMH is a good predictor of ovarian stimulation response. Its level also comes with the direct proportion of antral follicle count. Levels of AMH (1ng/mL) declines with age and with poor ovarian reserve. Levels of AMH can be measured any time in the menstrual cycle.

**AMH:** AMH is produced by the granulosa cells of the preantral small follicles. Serum levels of estradiol and inhibin B depend on pituitary FSH feedback mechanism. Level of AMH is not dependent on feedback mechanism. This is one of the reasons for which AMH is being considered as a better predictor of ovarian reserve compared to estradiol and inhibin B. Levels of AMH can be measured at anytime in the menstrual cycle. It therefore understood that AMH is qualitative whereas Antral Follicle Count (AFC) is a quantitative marker of ovarian reserve.

- 5. Antral Follicle Count (AFC)** is done by using TVS in early follicular phase in both the ovaries. AFC reflects the primordial follicular pool in the ovary.
  - AFC more than 6 (2–10 mm size) reflects adequate ovarian follicular reserve.
  - AFC, less than 4, indicates poor ovarian reserve and poor response to ovarian stimulation during IVF.
  - AFC decreases with age.



Best indicator of ovarian reserve is- Serum Day 3 FSH levels.



AFC is a quantitative marker of ovarian reserve.



## Tubal Factors

Tubal factors leading to infertility include endometriosis, pelvic adhesion disease or previous bilateral tubal ligation.

### Tests for Detecting Tubal Potency

#### 1st test/Initial test–Hysterosalpingography (HSG)

- **Hysterosalpingogram (HSG)** assesses uterine and fallopian tube contour and tubal patency. It shows Mullerian anomalies as well as most endometrial polyps, synechiae and submucosal fibroids. It can also determine tubal patency.
  - Performed in the early follicular phase, within 1 week of cessation of menstrual flow, to minimize chances of interrupting a pregnancy.
  - The procedure is performed by injecting a radiopaque dye through the cervix. As more dye is injected, the dye normally passes through the uterine cavity into the fallopian tubes and then spills into the peritoneal cavity.
  - X-ray films are taken under fluoroscopy to evaluate tubal patency.
  - Nonsteroidal anti-inflammatory drugs may be given to prevent cramping.
  - HSG may have therapeutic effects. Several studies have indicated increased pregnancy rates for several months after the procedure.
  - Prophylactic antibiotics (doxycycline, 100 mg orally twice daily for 5 to 7 days) are advisable when the patient has a history of pelvic inflammatory disease or when hydrosalpinges are identified during the study.
- **Saline infusion ultrasonography (Sonohysterography (SHG))**
  - SHG involves transvaginal ultrasound after the introduction of sterile water or saline into the uterine cavity.
  - Useful in assessment of uterine cavity abnormalities such as polyps or submucosal fibroids.
- **Diagnostic laparoscopy/Chromopertubation**
  - This is the most definitive and **gold standard test**.
  - Assesses peritoneal and tubal factors, such as endometriosis and pelvic adhesions and can provide access for simultaneous corrective surgery.
  - Laparoscopy should be scheduled in the follicular phase.
  - Chromopertubation: Dye (usually a dilute solution of indigo carmine) is instilled through the fallopian tubes during laparoscopy to visually document tubal patency.

### Management of Tubal Factor Infertility

- Cornual block **Proximal tubal obstruction** is identified on HSG. Tubal spasm may mimic proximal obstruction, however, and obstruction should be confirmed by laparoscopy. Treatment consists of tubal cannulation by hysteroscopy, If patient does not respond then IVF.
- **Distal tubal disease** or distortion can be seen on HSG and laparoscopy. The success of corrective surgery (neosalpingostomy) depends on the extent of disease. Best is IVF. In mild disease-Fimbrioplasty can be done.
- For patients with a **history of a prior bilateral tubal ligation** who desire fertility, options include microsurgical sterilization reversal as well as IVF.
  - Success of tubal reanastomosis depends on age, type, and location of the sterilization procedure and final lengths of repaired fallopian tubes.
  - IVF may be a better option for these patients who desire only a single additional child.



First test to assess tubal potency – HSG.

- HSG is not the best test because it cannot differentiate between cornual spasm and cornual blockade.
- Obsolete test for tubal patency – Rubins test/CO<sub>2</sub> insufflation test
- Best test – Laparoscopic chromopertubation.



Laparoscopy with chromopertubation is the best investigation for confirming tubal patency and, besides, any pathology can simultaneously be corrected with operative laparoscopy.

As it requires general anaesthesia and admission, so it is not the first line investigation for tubal patency.



- Best management of Tubal Factor infertility is IVF.
- Intra uterine insemination is not useful in case of tubal factor infertility.
- Best treatment of B/L cornual block is cannulation by hysteroscopy



Mnemonic for uses of IVF in females-

- T** = Tubal infertility
- R** = Recanalisation after tubal sterilisation
- O** = Ovarian failure or diminished ovarian reserve (using donor oocytes)
- C** = Females with
  - C**ancers or on
  - C**hemotherapeutic drugs.
- A** = **A**IDS in partner
- R** = **R**isk of transmitting genetic disease to offspring
- S** = **S**urrogate motherhood if patient has no functional uterus.



Fertilisation is documented by the presence of two pronuclei and extrusion of a second polar at 24 hr.

## In vitro Fertilization (IVF)

*IVF was first developed as a means to overcome infertility resulting from irreparable tubal disease as fertilization takes place in fallopian tube.*

Now the spectrum of IVF has broadened and is indicated in number of conditions -

### In Female Infertility

- Tubal pathology resulting from previous infection or advanced stages of endometriosis or in cases with proximal and distal obstruction.<sup>Q</sup>
- In women desiring reversal of tubal sterilization with poor prognosis for recanalization.<sup>Q</sup>
- Ovarian failure and Diminished ovarian reserve: Here IVF is performed using donor oocytes.<sup>Q</sup>
- Women recently diagnosed with a cancer or another medical disorder facing eminent treatment (chemotherapy and radiotherapy) that poses a serious threat to their future fertility. Such women can have cryopreservation of their embryos and later IVF done.<sup>Q</sup>
- Women with normal ovaries but no functional uterus as a result of a congenital anomaly (mullerian agenesis), DES exposure, advanced disease (multiple myeloma, severe intrauterine adhesions) or a previous hysterectomy can be afforded the opportunity to have their own genetic offspring via IVF with transfer of embryos to the uterus of a surrogate.<sup>Q</sup>
- Women who carry genetic risk or disorder which may be expressed in their offspring can be the candidates for IVF with preimplantation genetics to identify and exclude affected embryos.<sup>Q</sup>
- HIV positive serodiscordant couples -use of ICSI or sperm washing techniques has enabled HIV negative women to safely achieve pregnancy using the sperm of their affected male partners.

### In Male Infertility

- When sperm count is < 5 million/ml
  - Repeated IUI failure
  - **Multifactor infertility**<sup>Q</sup>
  - **Unexplained infertility**<sup>Q</sup>
- Since, we have to choose one option: Tubal pathology i.e. *option 'a'* is the best option.<sup>Q</sup>

### Basic Steps of IVF

- Sperms are retrieved from male partner.
- Ovarian stimulation is done with gonadotropins and follicular monitoring is done
- When ova reaches 20 mm in size, injection hCG is given to trigger ovulation.
- Oocytes are then retrieved (ovum pickup) through a 17 gauge needle passed through the vaginal fornix
- For fertilization: 50,000 to 100,000 sperms are put on each oocyte retrieved, in a petridish
- Embryos are kept in incubator for 48-72h
- After fertilisation embryo transfer is done on day 2 or day 3 (48-72h) after oocyte insemination. Note Day 5 blastocyst transfer is becoming more common today due to higher live births compared to cleavage stage (day 3) embryos.
- Generally 3-4 embryos are transferred in the uterine cavity (thus chances of multiple pregnancy are high with IVF), and deposited 1 cm below the fundus (the usual site of implantation).

- Success rate of IVF per cycle is 30–35%
- Excess embryos not used for transfer can be cryopreserved for an unlimited period, with a survival rate of 75%.

### Cervical Factory Infertility

Cervical factor infertility can be due to abnormal or deficient mucus in cases of:

- Infection
- Prior cervical surgery
- Use of antiestrogens (e.g. clomiphene citrate) for ovulation induction
- Presence of Antisperm antibodies

The treatment of cervical factor depends on the cause

- If it is due to chronic cervicitis/infection - Treatment of infection by antibiotics is the cure.
- If is due to decreased mucus volume - Treatment includes short-term supplementation with exogenous estrogen like ethinyl estradiol and use of mucolytic expectorant like guaifenesin. However, their value has not been confirmed.
- If it is due to antisperm antibodies -Investigation done to detect antibodies is post coital test.

### Postcoital Test (Sims or Huhner's Test)

It is designed to assess:

- The quality of cervical mucus.
- Presence and number of motile sperms in the female reproductive tract after coitus.
- Interaction between cervical mucus and sperms.
- It gives an approximate idea of sperm count: (normally 10 – 50 motile sperms are seen per high power field in cervical mucus, if count is < 10 sperms /HPF it indicates the need for complete semen analysis).

**Time of test:**

- It should be performed 1 or 2 days before the anticipated time of ovulation, when maximum estrogen secretion is present.
- For patients with irregular cycles, patients urinary LH surge may be helpful in scheduling the test.

**Method:** The couple is advised to have intercourse and present to the doctor within 2–12 hours of intercourse. The cervical mucus of the female partner is collected and examined under microscope.

- Prerequisites for the test:
- Abstinence of 2 days.<sup>Q</sup>
  - Intercourse to be performed 2 - 12 hours before the test.<sup>Q</sup>
  - No use of lubricant.<sup>Q</sup>

Post coital test is only a screening test for detecting antisperm antibodies.

#### Confirmatory tests for detecting antisperm

- Sperm agglutination test
- MAR (mixed agglutination reaction) Test.
- Immunobead test

### Assessment and Interpretation

Quality of cervical mucus:	Number of motile sperms/HPF:	Motility of sperms:
Preovulatory cervical mucus (under the influence of estrogen) is clear, watery, abundant and stretchable (spin barkeit > 8 – 10 cm) with good tertiary ferning and low cellularity. Characteristic of Progesterone stimulated mucus: – Thick & opaque – Lacks ferning – Breaks (tacks) on stretching	Atleast 15 – 20 motile sperms/HPF should be seen.	<ul style="list-style-type: none"> <li>• Normally sperms show progressive movement and not rotatory of movement. The presence of anti – sperm antibodies in the cervical mucus imparts rotatory on shaking movement to the sperm or renders them completely immolite.</li> </ul>

#### Also Know

#### Tests for studying sperm function

- Sperm Penetration assay
  - Miller kurzrok test<sup>Q</sup>
- tests for studying sperm penetration<sup>Q</sup>

*Hypoosmotic swelling test<sup>Q</sup>:* Test for studying tail function.

*Hemizona Test:* Test for studying the ability of sperm to bind to human zona pellucida.



M/c fibroid leading to abortions and infertility is submucous fibroid.

- Treatment options include:
  - Use of *condom or diaphragm as a barrier method for 3 months*. During this period, the antibodies will disappear and conception may occur then.
  - **Corticosteroids** given to female partner can also help in getting rid of these antibodies.
  - **Intrauterine insemination** at the time of ovulation (most acceptable method for cervical factor infertility) or GIFT (Gamete intrafallopian transfer) are very useful techniques in such cases.

IUI is the best method for treating cervical factor infertility and unexplained infertility. So many clinicians forgo cervical mucus testing and proceed directly to IUI treatment in absence of tubal disease.

### Uterine Factors

Uterine factors, such as submucous leiomyomas, intrauterine synechiae (Asherman's syndrome), and uterine deformities or septa, cause approximately 2% of infertility. The mainstay of treatment for these conditions is surgical correction, frequently via a hysteroscopic approach.

### Luteal Phase Defect

During normal luteal phase when there is adequate progesterone secretion by the corpus luteum, adequate development of secretory endometrium occurs for blastocyst implantation. **Luteal phase defect refers to a condition when production of progesterone is suboptimal by corpus luteum.**

Inadequate progesterone secretion could be due to:

- Inadequate follicular development
- Inadequate FSH or LH secretion
- Hyperprolactinemia

It is an inevitable phenomenon in all ART cycles.

LPD may cause implantation failure and is thought to account for 4% of infertility.

Diagnosis of LPD is not based on uniform criteria:

- Low levels of midluteal serum progesterone (<10 ng/mL)
- Endometrial histology done on 25th–27th day of cycle shows endometrium >2 day out of phase
- A shortened luteal phase <14 days, are considered for the diagnosis.

**Management** – Micronized Progesterone

### Preimplantation Genetic Diagnosis (PGD)

- PGD allows couples with various single-gene disorders and X-linked genetic diseases to avoid transmission of the disorder of offspring.
- Proceeds by biopsy and genetic analysis of one of the following specimens:
  - 1 to 2 blastomeres of a cleavage-stage (days 2 to 3) embryo derived from IVF.
  - Polar body biopsy from a metaphase II oocyte obtained after COH.
  - Trophectoderm tissue from a blastocyst-stage (day 5) embryo.
  - Only unaffected preimplantation embryos would be transferred to the woman's uterus.

## QUESTIONS

### General Infertility

1. In the perspective of the busy life schedule in the modern society, the accepted minimum period of sexual cohabitation resulting in no offspring for a couple to be declared infertile is: *(AIIMS May 05)*
  - a. One year
  - b. One and a half - year
  - c. Two years
  - d. Three years
2. Infertility is seen in: *(PGI Dec 02)*
  - a. Fibroid uterus
  - b. Endometriosis
  - c. Adenomyosis
  - d. PID
3. Common causes of infertility are: *(PGI Dec 00)*
  - a. Chlamydia
  - b. Gonorrhoea
  - c. Mycoplasma
  - d. Pneumococcus
4. Best prognosis in infertile women is seen in/most reversible form of infertility is: *(PGI June 98, Dec 97)*
  - a. Tubal block
  - b. Anovulation
  - c. Oligospermia
  - d. Endometritis
5. TB endometritis causes infertility by: *(PGI Dec 98)*
  - a. Causing anovulation
  - b. Destroying endometrium
  - c. Tubal blockage
  - d. Ciliary dysmotility
6. Kamla, a 30 yrs old lady examined for infertility by hysterosalpingography, reveals 'Bead - like' fallopian tube and clubbing of ampulla. Most likely cause is: *(AI 02)*
  - a. Gonococcus
  - b. Mycoplasma
  - c. Chlamydia
  - d. Mycobacterium tuberculosis
7. The risk of Asherman syndrome is the highest if Dilatation and Curettage (D and C) is done for the following condition: *(AIIMS May 06)*
  - a. Medical termination of pregnancy
  - b. Missed abortion
  - c. Dysfunctional uterine bleeding
  - d. Postpartum haemorrhage
8. What is the cause for luteal phase defect? *(PGI Dec 05)*
  - a. Progesterone is inadequately secreted
  - b. Excess estrogen is secreted
  - c. Excess progesterone is secreted

### Female Infertility: Ovarian Cause

9. Smita is a case of infertility. What is the right time in her menstrual cycle to do endometrial biopsy: *(AIIMS Nov 00)*

- a. 12 - 14 days
  - b. 17 - 19 days
  - c. 20 - 22 days
  - d. 3 - 5 days
10. Fern test is due to: *(SGPGI 05)*
    - a. Presence of NaCl under progesterone effect
    - b. Presence of NaCl under estrogenic effect
    - c. LH/FSH
    - d. Mucus secretion by Glands
  11. Drugs used for ovulation induction are: *(PGI Nov 10)*
    - a. Gn RH
    - b. Clomiphene citrate
    - c. Gonadotropins
    - d. Letrozole
    - e. Danazol
  12. Antihormonal substance used to induce ovulation: *(AI 07)*
    - a. Mifepristone
    - b. Clomiphene citrate
    - c. Tamoxifen
    - d. Raloxifen
  13. A patient treated for infertility with clomiphence citrate presents with sudden onset of abdominal pain and distension with ascites, the probable cause is *(AIIMS May 01)*
    - a. Uterine rupture
    - b. Ectopic pregnancy rupture
    - c. Multifetal pregnancy
    - d. Hyperstimulation syndrome

### Female Infertility: Tubal Cause

14. Fallopian tube dysmotility is seen: *(AIIMS Nov 09, 08)*
  - a. Noonan syndrome
  - b. Turner syndrome
  - c. Kartagener syndrome
  - d. Marfan syndrome
15. Best Investigation to assess tubal patency: *(TN 95)*
  - a. Rubin's test
  - b. HSG
  - c. Laparotomy
  - d. Laparoscopic chromotubation
16. Fallopian tube patency is checked by: *(PGI Dec 02)*
  - a. Hysterosalpingography
  - b. Laparoscopy
  - c. Hysteroscopy
  - d. USG
  - e. CT scan
17. Lady with infertility with bilateral tubal block at cornual best method of management is: *(AIIMS Nov 06)*
  - a. Laparoscopy and hysteroscopy
  - b. Hydrotubation
  - c. IVF
  - d. Tuboplasty

18. An infertile women has bilateral tubal block at cornua diagnosed on hysterosalpingography. Next step in treatment is: (AIIMS Nov 2011)
- IVF
  - Laparoscopy and hysteroscopy
  - Tuboplasty
  - Hydrotubation

### Female Infertility: Cervical Cause

19. Post coital test detects all of the following except: (AIIMS May 01)
- Fallopian tube block
  - Cervical factor abnormality
  - Sperm count
  - Sperm abnormality
20. Postcoital test (PCT) is done for: (PGI June 05)
- Cervical receptivity
  - Sperm motility
  - Absolute sperm count
  - Viable sperm count
  - Endometrial function
21. Cervical hostility is tested by following except: (PGI Dec 97)
- Spinnbarkeit
  - Postcoital test
  - Miller kuzrole test
  - Keller test
22. Postcoital test showing non motile sperms in the cervical smear and Motile sperms from the posterior fornix suggests: (UPSC 97)
- Faulty coital practice
  - Immunological defect
  - Hypospadias
  - Azoospermia
23. Treatment for Cervical infertility can be all except: (Delhi 99)
- Condom for 3 month
  - IUI
  - Gamete Intrafallopian transfer
  - Clomiphene citrate
24. If the life style factor that is causing infertility in a young male is identified. Which of the following life style modification will have no effect (AIIMS Nov 2014)
- Weight gain
  - Less exercise
  - Vegetarian diet
  - Weight loss

### Male Infertility

25. According to WHO criteria, the minimum normal sperm count is: (AIIMS May 03)
- 10 million/ml
  - 20 million/ml
  - 40 million/ml
  - 60 million/ml
26. Which is a not an essential criteria according to WHO for normal semen analysis: (AIIMS Nov 07)
- Sperm count > 20 million/ml
  - Volume > 1 ml
  - Sperm with normal morphology (strict criteria) > 15%
  - Motility > 25% with rapidly progressive motility

27. WHO definition of normal sperm count: (PGI Dec 05)
- 10 million/ml
  - 20 million/ml
  - 40 million/ml
  - 50 million/ml
  - 60 million/ml
28. Aspermia is the term used to describe: (AI 05)
- Absence of semen
  - Absence of sperm in ejaculate
  - Absence of sperm motility
  - Occurrence of abnormal sperm
29. A 25 year old infertile male underwent semen analysis. Results show: sperm count - 15 million/ml; pH - 7.5; volume - 2 ml; no agglutination is seen. Morphology shows 60% normal and 60% motile sperms. Most likely diagnosis is: (AI 02)
- Normospermia
  - Oligospermia
  - Azoospermia
  - Aspermia
30. Which of the following is true about obstructive azoospermia: (AI 09)
- ↑ FSH and ↑ LH
  - Normal FSH and normal LH
  - ↑ LH, Normal FSH
  - ↑ FSH, Normal LH
31. A male with azoospermia. On examination size of testis normal FSH normal testosterone normal. Most probable cause is: (AIIMS Nov 09)
- MAL descended testis
  - Klinefelter's syndrome
  - Kallmann's syndrome
  - VAS obstruction
32. In azoospermia, the diagnostic test which can distinguish between testicular failure and obstruction of Vas deferens is: (UPSC 04)
- Estimation of FSH level
  - Estimation of testosterone level
  - Karyotyping
  - FNAC of testes
33. Semen analysis of a male of an infertile couple. shows absence of spermatozoa but presence of fructose. The most probable diagnosis is:
- Prostatic infection
  - Mumps orchitis
  - Block in efferent duct system
  - All of the above
34. A couple complains of primary infertility inspite of staying together for 4 year and having unprotected intercourse, all tests in wife are normal. Semen analysis shows a volume of 0.8 ml/sperm count is 0, fructose is absent what is done next? (AIIMS Nov 2013)
- Testicular FNAC
  - Ultrasound for obstruction
  - Local palpation of vas
  - Karyotyping

**IUI**

35. Intrauterine insemination means implantation of:  
(PGI June 05)
- Semen
  - Washed semen
  - Million of sperm
  - Fertilized ova

**IVF**

36. In vitro fertilization is indicated in: (AIIMS Dec 97)
- Tubal pathology
  - Uterine dysfunction
  - Ovarian pathology
  - Azoospermia
37. Aspiration of sperms from testes is done in:
- TESA
  - MESA (AI 07)
  - ZIFT
  - GIFT
38. In semen banks, semen is preserved at low temperature using: (JIPMER 81; DNB 90)
- Dry ice
  - Deep freeze
  - Liquid nitrogen
  - Liquid air
39. Which is not an assisted reproduction technique:
- GIFT
  - ZIFT (AI 95)
  - IVF and ET
  - Artificial insemination

**NEW PATTERN QUESTIONS**

40. Ovulation can be diagnosed by all except:
- Measuring day 14 serum progesterone
  - Rise in basal body temperature in the second half of cycle
  - Study of cervical mucus
  - Endometrial histology

41. Indications of intrauterine insemination (IUI) are all except:
- Hostile cervical mucus
  - Unexplained infertility
  - Oligoasthenospermia
  - Luteal Phase defect
42. In which case homologous artificial insemination is used in females:
- Hormonal disturbance
  - Tubal block
  - Cervical factor
  - All of the above
43. Artificial insemination with husband's semen is indicated in all the following situations, except:
- Oligospermia
  - Impotency
  - Antisperm antibodies in the cervical mucous
  - Azoospermia
44. The major contribution to the human seminal fluid is from:
- Testes
  - Seminal vesicles
  - Prostate
  - Bulbourethral and urethral glands
45. Absent fructose content in the seminal fluid suggests:
- Congenital absence of seminal vesicle
  - Partial duct obstruction
  - None
  - Both

## ANSWERS

**1. Ans. is a, i.e. One year**Ref. Shaw 15<sup>th</sup>/ed p 200

*If a couple fails to achieve pregnancy after one year of "unprotected" and regular intercourse, it is an indication to investigate the couple for infertility.*

... Novak 13<sup>th</sup>/ed p 973

- **Infertility:**

- *Primary* : When no previous pregnancies have occurred.
- *Secondary* : When a prior pregnancy although not necessary although not necessary a live birth, has occurred.

**2. Ans. is a, b, c and d, i.e. Fibroid uterus; Endometriosis; Adenomyosis; and PID**Ref. Dutta Gynae 5<sup>th</sup>/ed p 222-223; Novak 15<sup>th</sup>/ed p 1160, 1157; Williams Gynae 1<sup>th</sup>/ed p 427; Jeffcoates 7<sup>th</sup>/ed p 701-703**Common causes of female Infertility are:****a. Decreased ovarian reserve****b. Ovarian Factor**

It is the most easily diagnosed and most treatable cause of infertility<sup>Q</sup>. It includes:

*Anovulation / Dysovulation:*

- Like in case of hypothalamic dysfunction<sup>Q</sup>, Kallmann syndrome
- Hyperprolactinemia (due to drugs, pituitary adenoma<sup>Q</sup>)
- Primary hypothyroidism<sup>Q</sup>
- PCOS<sup>Q</sup>
- Sub clinical adrenal failure
- Diabetes mellitus

*Luteinized unruptured follicle*

*Luteal phase defect*

**c. Tubal Factors:** Partial or complete bilateral tubal obstruction resulting from previous salpingitis/PID. It could be: - Postabortal<sup>Q</sup>

- Gonococcal<sup>Q</sup>
- Chlamydial<sup>Q</sup>
- Tuberculous<sup>Q</sup>

- Tubal inflammation related to endometriosis
- Following Inflammatory bowel disease
- Following surgical trauma

**d. Peritoneal Factors:** - Pelvic adhesions  
- Endometriosis**e. Uterine Factors:**

- Uterine absence, atrophy
- Congenital malformations (Among all congenital uterine abnormalities, septate uterus is the M/C and most highly associated with reproductive failure and obstetrics complications).
- Intrauterine adhesions (Asherman's syndrome)<sup>Q</sup>
- Endometrial polyps
- Leiomyomas (most common with sub mucous variety)<sup>Q</sup>
- Chronic endometritis (TB)<sup>Q</sup>
- Exposure to DES in utero

**f. Cervical Factors:**

- Impenetrable cervical mucus or poorly penetrable cervical mucus due to presence of local sperm antibodies.
- Loss of mucus due to amputation of cervix, cone biopsy or over enthusiastic cervical diathermy.
- Faulty direction of cervix as seen in retroversion or severe prolapse.
- Cervical stenosis.

**g. Others:** Anxiety/apprehension use of contraceptives; anorexia nervosa.

As such adenomyosis is not given as a cause of infertility but if you go through the chapter of adenomyosis: *Jeffcoate 7/e, p 382 says* (In chapter on Adenomyosis): **"The patient may also complain of infertility"**.

So, I am including it in the correct options.



3. **Ans. is a, b and c, i.e. Chlamydia; Gonorrhoea; and Mycoplasma** Ref. Williams Gynae 1<sup>st</sup>/ed p 434; Novak 14<sup>th</sup>/ed p 1227

**PID resulting in salpingitis is an important cause of infertility.**

Infertility from PID can occur due to following organisms:

- a. Chlamydia } ... Williams Gynae 1<sup>st</sup>/ed p 434
  - b. Gonorrhoea } ... Williams Gynae 1<sup>st</sup>/ed p 434
  - c. Tuberculosis } ... Williams Gynae 1<sup>st</sup>/ed p 434
  - d. Mycoplasma (Specifically ureoplasma) ... Novak 14<sup>th</sup>/ed p 1227
- Certain Infections cause Intrauterine synechiae or Asherman syndrome thus leading to infertility like:
- e. Schistosoma

4. **Ans. is b, i.e. Anovulation** Ref. Kistner's Gynecology 6<sup>th</sup>/ed p 279; Novak 14<sup>th</sup>/ed p 1206

**"Disorders of ovulation account for about 30 – 40 % of all cases of female infertility. These disorders are generally among the most easily diagnosed and most treatable causes of infertility."** ... Novak 14<sup>th</sup>/ed p 1206

- In couples with infertility ovulatory disorder have the best prognosis. Relatively poor prognosis is observed in male factor infertility and tubal factor infertility.
- Prognosis can be arranged as below in descending order on the basis of cumulative pregnancy.  
Ovulatory factor > unexplained > Male factors > Endometriosis > Tubal factors.

5. **Ans. is b and c, i.e. Destroying endometrium; and Tubal blockage** Ref. Shaw 15<sup>th</sup>/ed p 154-156; Williams Gynae 1<sup>th</sup>/ed p 423

- Most common site for genital TB is fallopian tube (90% cases).
- Uterus is involved in 70% cases of genital tuberculosis.
- The infection to uterus descends from the tube, i.e. if TB endometritis is present, invariably tubes are involved.
- Most common symptom of Genital TB: Infertility (35 – 60%). Infertility<sup>Q</sup> is either due to blockage of fallopian tube<sup>Q</sup> or due to loss of tubal function even if tubes are patent.<sup>Q</sup>

Tubercular endometritis causes uterine scarring which destroys the endometrium leading to synechia formation (Asherman syndrome) and infertility.

**"In developing countries, genital TB may account for 3% or more of patients with infertility. In these cases tubal damage and endometrial adhesions are the underlying cause."** ... Williams Gynae 1<sup>st</sup>/ed p 423

6. **Ans. is d, i.e. Mycobacterium tuberculosis** Ref. Shaw 15<sup>th</sup>/ed p 157

The following findings on hysterosalpingogram strongly suggest tubercular salpingitis:

- A rigid nonperistaltic pipe like tube, called **lead pipe appearance**<sup>Q</sup>
- **Beading and variation in filling density**<sup>Q</sup>
- **Calcification of the tube**<sup>Q</sup>
- **Cornual block**<sup>Q</sup>
- A jagged fluffiness of the tubal outline<sup>Q</sup>
- Vascular or lymphatic intravasation of the dye<sup>Q</sup>
- Tobacco-pouch appearance seen on naked eye examination.

#### Also Note:

- In a proven case of genital tuberculosis, hysterosalpingography is contraindicated as it may spread the infection.
- In TB Endometritis on HSG: The uterine cavity is shrivelled and obliterated by adhesions giving honeycomb appearance.
- On USG: Incomplete septation of the tubal wall "Cogwheel sign" is a marker for acute disease. Thin wall and beaded string appearance is a marker for chronic disease.

7. **Ans. is d, i.e. Postpartum hemorrhage** Ref. Clinical Gynecologic Endocrinology & Infertility, Leon Speroff 7<sup>th</sup>/ed p. 1045, Net search [www.asherman-syndrome.com](http://www.asherman-syndrome.com)

#### Asherman syndrome

**Asherman syndrome** is the presence of intrauterine adhesions.

**Pathophysiology:** It is the result of scanty or poorly vascularized and dysfunctional endometrium resulting from trauma. Any insult severe enough to remove or destroy endometrium can cause adhesions.

#### Etiology:

Asherman syndrome: **"Generally is the result of an overzealous post partum curettage resulting in intrauterine scarification."** ... Leon Speroff 7<sup>th</sup>/ed p 417

**Most common etiology is:** D and C done for post partum haemorrhage.

#### Other Etiologies:

##### D and C done:

- After previous elective pregnancy termination.<sup>Q</sup>

Contd...

Contd...

- For missed abortion<sup>o</sup>
- For hydatidiform mole<sup>o</sup>
- After cesarean section<sup>o</sup>

**As a postoperative complication of:**

- Abdominal/hysteroscopic myomectomy<sup>o</sup>
- Metroplasty<sup>o</sup>
- Septoplasty<sup>o</sup>
- Uterine artery embolisation for the treatment of uterine fibroids
- Chronic infection-like genital tuberculosis<sup>o</sup> and Schistosomiasis<sup>o</sup> or infection due to IUCD's.

**Symptoms:**

- Menstrual disorders like (hypomenorrhea, amenorrhea, dysmenorrhea).
- Hypomenorrhea is the typical symptom of Asherman syndrome.
- Infertility (it results due to absence of viable endometrium for implantation as well as from obstruction of fallopian tubes).
- Recurrent miscarriage (due to insufficient normal endometrial surface)
- If patients of Asherman syndrome conceive, pregnancy is complicated by preterm labour, placenta accreta, placenta previa and/or PPH.

**Diagnosis:**

- Hysterosalpingography: (X-ray dye test) and saline hysterosalpingogram (fluid ultrasound) demonstrate filling defect.
- Hysteroscopy is both is the method of choice for diagnosis and treatment.<sup>o</sup>

**Treatment:**

- Hysteroscopic lysis of adhesions is the preferred surgical treatment.
- Following surgery some method is used to keep the walls of the uterus apart in the immediate postoperative period to minimize the chances of recurrence. This can be done by the use of balloon catheter or nonmedicated IUCD's.
- Antibiotics are administered prior to the procedure and continued for approximately 10 days after the surgery.
- Postoperative treatment with exogenous estrogens is given to promote rapid reepithelialization and reduce the risk of recurrent adhesion.

**8. Ans. is a, i.e. Progesterone is inadequately secreted**

Ref. Novak 14<sup>th</sup>/ed p 1225, 15<sup>th</sup>/ed p 1161

Read the preceding text for explanation

**9. Ans. is c, i.e. 20 – 22 days**

Ref. Shaw 15<sup>th</sup>/ed p 215; Dutta Gynae 5<sup>th</sup>/ed p 229

Endometrial biopsy should be taken in premenstrual phase 1 – 2 days before the onset of menstruation (Shaw 14<sup>th</sup>/ed p 193-194) or on 21-23 day (Dutta Gynae 5<sup>th</sup>/ed p 229)

**Endometrial Biopsy**

- OPD procedure for hormonal evaluation in case of infertility / DUB/TB.
- Usually performed in pre-menstrual phase from the lateral wall of vagina.
- Interpretation:

Presence of secretory endometrium → Progesterone phase (cycles has been ovulatory)

Presence of proliferative endometrium → Estrogen phase (cycles has been anovulatory)

- *Luteal phase defect can also be diagnosed by endometrial biopsy (which shows a lag of 2 – 3 days between calendar and histological dating of specimen.* Note: For the diagnosis of luteal phase defect endometrial biopsy is done between day 24-26 of the menstrual cycle or 2 to 4 days before anticipated menstruation.
- Endometrial biopsy is contraindicated in suspected malignancy/sepsis.
- 1st sign of ovulation on endometrial biopsy is parabasal vacuolation

## Ideal Time for:

Test	Time	Observation
<b>Tests for Documenting Ovulation</b>		
1. Basal Body Temp	Through out cycle	Biphasic pattern
2. Cervical mucus	Day 12 – 14	Cervical mucus is clear watery, stretchability present, ferning present.
	Day 21 – 23	Cervical mucus is thick, viscid, tack present ferning absent.
3. Vaginal cytology	Day 12 – 14	Estrogen dominated smears – clear, discrete confined, polygonal, superficial cells (predominant cells)
	Day 21 – 23	Progesterone dominated smear –containing dirty, predominantly intermediate (Navicular) cells.
4. Endometrial Biopsy	Day 24 -26	Secretory Endometrium (Confirming ovulation)
5. Serum Progesterone	D8 and D21	D – 8 < 1 ng/ml D – 21 > 6.5 ng/ml
6. Follicular Monitoring	D10 – D14	Follicle is measured by USG.
7. Laparoscopy	Secretory phase	Recent corpus luteum is directly seen

**TESTS FOR TUBAL PATENCY:** (Or for any Tubal Pathology): viz

Insufflation test	}	(Mid follicular phase) Day 6 – Day 11 (not performed later so that if
HSG		Pregnancy has occurred & zygote formed it is not disrupted & not
Sonohysterosalpingography		Earlier when the patient is menstruating as retrograde
Fallopscopy		Menstruation can cause endometriosis)

**TESTS FOR CERVICAL FACTOR:** viz

• Post coital test	}	Done just before ovulation (as cervical mucus is most Receptive for sperm at that time).
• Immunological tests		
• Miller kurzrok test		

## Also know:

- Any radiological investigation in a young/reproductive age woman should be done between Day 1 to Day 10 of the menstrual cycle called as Rule of 10.
- Endometrial Biopsy for diagnosis of TB should be done in late premenstrual phase Q as tubercles are present in superficial layer and shed during menstruation. The tissue obtained is subjected to polymerase chain reaction test instead of culture.

## 10. Ans. is b, i.e. Presence of NaCl under estrogenic effect

Ref. Shaw 15<sup>th</sup>/ed p 215**Fern test is for documenting ovulation.**

**Procedure:** A specimen of cervical mucus is obtained and is spread on a clean glass slide and allowed to dry. It is then viewed under the low power microscope.

**Result and interpretation:** Under the influence of estrogen on Day12-Day 14 cervical mucus shows characteristic pattern of fern formation. *The ferning is due to the presence of sodium chloride in the mucus secreted under estrogen effect.*

After ovulation on Day 21-23, ferning disappears because protein content increases and Sodium chloride decreases under the effect of progesterone.

Disappearance of ferning after ovulation and if previously present is presumptive evidence of corpus luteum activity.

## 11. Ans. is b, c and d, i.e. Clomiphene citrate, Gonadotropins and Letrozole

Ref. Williams Gynae 1<sup>st</sup>/ed p 450-452; Novak, 14<sup>th</sup>/ed p 1210-1213**Most commonly used drugs for ovulation induction:**

1. Clomiphene citrate (CC)
2. Letrozole
3. Gonadotropins

## 12. Ans. is b, i.e. Clomiphene citrate

Ref. Shaw 15<sup>th</sup>/ed p 217; Williams Gynae 1<sup>th</sup>/ed p 450 - 451

## Extra Edge:

Condition	TOC
<ul style="list-style-type: none"> <li>Asherman syndrome</li> <li>Stein-Leventhal syndrome</li> <li>Post pill amenorrhea</li> <li>Ovulation induction in-patient who bleed in response to progestin challenge</li> <li>For ovulation induction in patient with hypoeestrogenemia hypothalamic amenorrhea (Progestin challenge -ve)</li> <li>Ovulation induction in-patient with primary ovarian failure</li> </ul>	hysteroscopic adhesiolysis with IUCD insertion Clomiphene citrate Clomiphene citrate  Clomiphene citrate  HMG (Human menopausal gonadotropin)  Steroid/IVF with donor oocyte

## 13. Ans. is d, i.e. Hyperstimulation syndrome

Ref. Shaw 15<sup>th</sup>/ed p 315; Novak 14<sup>th</sup>/ed p 1225; Recent Advances in Obstetrics & Gynecology no 21 p 123 Onwards; Williams Gynae 1<sup>st</sup>/ed p 452-455

History of clomiphene citrate and presence of ascites, abdominal pain and distension strongly suggest ovarian hyperstimulation syndrome.

## Ovarian Hyperstimulation Syndrome

Ovarian hyperstimulation syndrome (OHSS) is an uncommon, but potentially life threatening, complication of ovarian stimulation by ovulation induction agents like:

- Clomiphene citrate<sup>o</sup>
- FSH/LH (MC)<sup>o</sup>
- GnRH<sup>o</sup>

**Risk factors:** Young patients (Age 35 years), lean and thin patients, PCOS patients, Previous h/o OHSS

**Pathogenesis:** High serum estradiol (> 2500 pg/ml), Pregnancy

There is an increase in vascular permeability - leading to shift of fluid from Intravascular to extravascular space resulting in:

- Increased plasma viscosity<sup>o</sup>
- Increased clotting<sup>o</sup>
- Depletion of Na<sup>+</sup> and albumin<sup>o</sup>
- Third space fluid accumulation manifested by ascites and hydrothorax.<sup>o</sup>

**Clinical features:**

- Related to third space fluid accumulation.
  - Abdominal distension (ascites) leading to abdominal discomfort and respiratory difficulty.
  - Hydrothorax (in severe cases).
- Related to decreased intravascular volume.
  - Decreased urinary output
  - Hypovolemia
  - Finally renal impairment.
- Because of hypercoagulable state patient may present with venous thrombosis.
- Because of excessive ovarian response to stimulation.
  - Size of ovaries increases
  - Ovaries are palpable on P/V
  - If empty follicles are filled with blood, they will be painful and tender.

So, from above discussion it is quite obvious that patient is suffering from OHSS (Friends remember Meigs Syndrome also has same features).

**Now let's see other options:**

- *Multifetal pregnancy:* Clomiphene administration causes multiple pregnancy in about 10% cases. But the symptoms and signs of multiple pregnancy are altogether different from that of the patient.
- *Ectopic pregnancy:* It is not mentioned anywhere that clomiphene administration causes ectopic pregnancy.
- *Uterine rupture:* Clomiphene administration has no effect on uterus.

Contd...

**Extra Edge:** Classification and staging of OHSS –

**Mild OHSS:** enlarged ovaries (5–10 cms)

**Moderate OHSS:** Ovaries > 10 cms, abdominal distension, nausea, vomiting diarrhea

**Severe OHSS:** Ovaries > 12 cms, ascites, hydrothorax & after atoms in blood viscosity.

**Life threatening OHSS:**

- Valuably enlarged ovaries
- WBC > 25,000
- Hematocrit > 55%
- Creature level > 1.6 mph
- Oliguria
- Renal failure
- Tense ascites
- Thromboembolic phenomenon
- ARDS

**Management:** OHSS is managed conservatively.

- Admit the patient (if patients hematocrit is > 0.44, or has abnormal renal or liver function).
- 1st line therapy - correction of hypovolemia.
- Prophylactic heparin to reduce the risk of thromboembolic complications.
- When abdomen is tense and ascites is evident both clinically and on ultrasound, drainage of ascites should be done (paracentesis).

**Surgical intervention has no role in OHSS.**

14. Ans. is c, i.e. Kartagener syndrome

Ref. Leon Speroff 7<sup>th</sup>/ed p 239; www.emedicine.com

- **Primary ciliary dyskinesia (PCD)**, also known as immotile ciliary syndrome or **Kartagener syndrome (KS)**, is a rare autosomal recessive genetic disorder in which there is a congenital absence of dynein arms (a protein structure associated with motility) in all body cilia.
- It can lead to male factor infertility due to diminished sperm motility in males. As far as female infertility is concerned—*patients with kartagener can conceive because motility of the cilia of fallopian tube is distorted and not totally absent.*

15. Ans. is d, i.e. Laparoscopic chromotubation

Ref. Shaw 15<sup>th</sup>/ed p 213; Leon Speroff 7<sup>th</sup>/ed p 1048

16. Ans. is a, b and d, i.e. HSG, Laparoscopy and USG.

The gold standard / best investigation to assess tubal patency is laparoscopic chromotubation.

Laparoscopy enables to look at the external condition of uterus, tubes and pelvis and at the same time the patency of tubes can be seen. Methylene blue/indigo carmine dye is injected through a cannula attached to the cervix to visualize the free spill or absence of spill. It can also demonstrate peritubal adhesions and unsuspected endometriosis.

The greatest advantage of laparoscopy is therapeutic procedure can be performed if adhesions or fimbrial block is recognized in one sitting.

**Also know: Other questions frequently asked on tubal patency tests.**

- *Time for performing tubal patency tests:* Day 6 – Day 10 of cycle<sup>Q</sup>
- No anesthesia is required for tube testing<sup>Q</sup>
- **First test to assess tubal patency is HCG**
- HSG is not the best test because it cannot differentiate between cornual spasm and cornual blockage.
- Obsolete method of testing tubal patency – Rubins test / CO<sub>2</sub> Insufflation test<sup>Q</sup> (in preovulatory phase)
- Best test as discussed is laparoscopic chromopertubation.
- **Other tests are-**

**Sonosalpingography** is a method of assessing tube patency. It was popularized by G.Allahabadia and is also called as **Sion test**. Under USG guidance, a slow and deliberate injection of 200 ml of physiological saline into uterine cavity is accomplished via a foley's catheter, the inflated bulb of which lies above the internal os and prevents leakage. It is possible to visualize the flow of saline along the tube and observe it is coming out as a shower at fimbrial end.

USG shows the presence of free fluid in Pouch of Douglas if tubes are patent.

**Falloscopy:** The interstitial end of the fallopian tubes is visualised by falloscopy.

**Salpingoscopy:** Studies the mucosa of the fallopian tube and helps in deciding whether IVF or tubal microsurgery should be performed.

**Contraindication of tubal Patency tests.**

- HSG should not be performed during and immediately before menstruation and in the post ovulatory period.
- HSG should not be performed after curettage.
- In recently active salpingitis.
- In suspected tuberculosis of genital tract.
- In infection of the lower genital tract.

17. **Ans. is a, i.e. Laparoscopy and hysteroscopy**

Ref. Leon Speroff 8<sup>th</sup>/ed p 1184-1185; Jeffcoates 7<sup>th</sup>/ed p 720; Advanced Infertility Management – Mehroo Hansotia p 10

18. **Ans. b, i.e. Laparoscopy and hysteroscopy**

Ref: Leon speroff 8<sup>th</sup>/ed p 1184-1185

According to KETE Chang, p 367

*"In a case of bilateral cornual occlusion demonstrated by HSG, before performing any surgery, laparoscopy should be done to confirm the obstruction and, to rule out spurious occlusion due to spasm. When obstruction is confirmed on laparoscopy, hysteroscopy is performed and an attempt is made to cannulate the tubes. Hysteroscopy not only confirms the diagnosis of tubal occlusion but often provides direct cannulation of tubes thus sparing the patient of laparotomy or microsurgery."*

Now let us read what Leon Speroff (Clinical Gynaecologic Endocrinology & Infertility 7<sup>th</sup>/ed p 1217 says:

*"IVF is the obvious alternative when surgery is "technically unsuccessful, relatively contraindicated (as in salpingitis isthmica nodosa) or infertility persists for more than 6–12 months post operatively."*

*"Surgical treatment for tubal factor infertility are generally in an era of decline, laparoscopic surgery has replaced simple open procedures and ART has replaced more complicated ones. Tubal surgery remains a legitimate treatment option for women seeking pregnancy after a previous tubal sterilisation, for those with mild distal tubal disease (particularly when they are young) and for some women with proximal tubal occlusion under virtually all other circumstances IVF is the best choice."* Leon speroff 8<sup>th</sup>/ed p 1185

*In Proximal tubal obstruction*

*"In general, success rates achieved with surgery have been extremely poor and IVF represents the best treatment option"*

Leonsperoff 8<sup>th</sup>/ed p 1184

*"Hysteroscopic transcervical cannulation of the tubes has been used in case of proximal tube obstruction. This method has been successful in cases where there is no significant pathology but if there is endosalpingiosis or infection, this method cannot be curative."*

... Jeffcoate 7<sup>th</sup>/ed p 720

**Hysteroscopic cannulation:**

*"Considering the simplicity of the procedure hysteroscopic cannulation should be tried as the first procedure for proximal tubal block. If the procedure is not successful or pregnancy is not achieved IVF is recommended."*

... Advanced Infertility Management – Mehroo Hansotia p 10

From the above discussion it is clear that initial management in a case of B/L cornual block undoubtedly is laparoscopy and hysteroscopy, cannulation. If it fails then only IVF should be done.

**Also know:****Management of unilateral proximal tubal block:**

Hysteroscopic cannulation or microsurgical tubocornual anastomosis (if any periodnema adhesions are also present).

**Management of distal tubal block:**

Best is IVF.

Surgical procedures like fimbrioplasty (lysis of fimbrial adhesions or dilatation of fimbrial stenosis) or neosalpingostomy may be done.

**Management of distal tubal block by hydrosalpinx**

First laparoscopic salpingectomy followed by IVF

**Management of Bipolar tubal obstruction, i.e. both proximal and distal tubal obstruction. Best is IVF**

19. **Ans. is a, i.e. Fallopian tube block**

Shaw 15<sup>th</sup>/ed dp 204

20. **Ans. is a, i.e. Cervical receptivity**

Ref. Shaw 15<sup>th</sup>/ed p 204; Novak 14<sup>th</sup>/ed p 1220; Williams Gynae 1<sup>st</sup>/ed p 439

As discussed in the preceding text –

**Post coital test (Sims or Huhner's test)** is a test for evaluation of the potential role of **Cervical factor in infertility.**

**It is designed to assess:**

- The quality of cervical mucus.
- Presence and number of motile sperms in the female reproductive tract. after coitus.
- Interaction between cervical mucus and sperms.
- It gives an approximate idea of sperm count: (normally 10 – 50 motile sperms are seen per high power field in cervical mucus, if count is < 10 sperms / HPF it indicates the need for complete semen analysis).
- Post coital test gives a very rough idea about sperm count, motility and morphology.

- As far as fallopian tube block is concerned postcoital test has no relation whatsoever with it and we have to select single best answer, therefore in Q. 19 **Option "a"** Fallopian tube block is the answer of choice.

#### Time of test:

- It should be performed 1 or 2 days before the anticipated time of ovulation, when maximum estrogen secretion is present.
- For patients with irregular cycles, patients urinary LH surge may be helpful in scheduling the test.

- Prerequisites for the test:**
- Abstinence of 2 days.<sup>Q</sup>
  - Intercourse to be performed 2-12 hours before the test.<sup>Q</sup>
  - No use of lubricant.<sup>Q</sup>

Assessment and Interpretation		
Quality of cervical mucus:	umber of motile sperms/HPF	Motility of sperms:
Preovulatory cervical mucus (under the influence of estrogen) is clear, watery, abundant and stretchable (spinbarkeit > 8 – 10 cm) with good tertiary ferning and low cellularity. Characteristic of Progesterone stimulated mucus: <ul style="list-style-type: none"> <li>• Thick &amp; opaque</li> <li>• Lacks ferning</li> <li>• Breaks (tacks) on stretching</li> </ul>	Atleast 15 – 20 motile sperms/HPF should be seen.	<ul style="list-style-type: none"> <li>• Normally sperms show progressive movement and not rotatory of movement. he presence of anti – sperm antibodies in the cervical mucus imparts rotatory on shaking movement to the sperm or renders them completely immolite.</li> </ul>

In Q. 20 – I am not including other options because actually-

*"It does not give much information on sperm count, motility and morphology."*

... Novak 14<sup>th</sup>/ed p 1220

#### 21. Ans. is d, i.e. Keller test

Ref. Shaw 15<sup>th</sup>/p 20

Post coital test and miller kurzrok test can detect cervical hostility as noted by rotatory/shaky movement of the sperm in post coital test, or < 3 cm of penetration of cervical mucus in 30 minutes in miller kurzrok test.

**Spinbarkeit is basically a test for assessing ovulation:** At the time of ovulation, the cervical mucus is thin and so profuse that the patient may notice a clear discharge, (called *Normal ovulatory cascade*). This ovulatory mucus has the property of great elasticity and will withstand stretching up to a distance of over 10 cm. This phenomenon is called spinbarkeit, or thread test for oestrogen activity. Under the influence of progesterone after ovulation mucus becomes thick and opaque and breaks on stretching i.e. hostile for sperms

Therefore, indirectly Spinbarkeit test can also detect cervical hostility.

#### 22. Ans. is b, i.e. Immunological defect

Ref. Shaw 15<sup>th</sup>/ed p 204; Jeffcoate 7<sup>th</sup>/ed p 714

Post coital test showing non motile sperms in the cervical smear and motile sperms in the posterior forix suggest that the sperms are normal and motile when they reach forenix. After that in cervix they become inmotile, i.e antisperm antibodies are present in the cervix, i.e imunological defect seen.

#### 23. Ans. is d, i.e. Clomiphene citrate

Ref. Dutta Gyane 5<sup>th</sup>/ed p 241; Williams Gynae 1<sup>st</sup>/ed p 460

**Cervical factor infertility can be due to abnormal or deficient mucus**

... William Gynae 1<sup>st</sup>/ed p 460

- Infection
- Prior cervical surgery
- Use of antiestrogens (e.g. clomiphene citrate) for ovulation induction (so clomiphene is a cause of cervical factor infertility rather than management)
- Sperm antibodies

#### The treatment of cervical factor thus depends on the cause:

- If it is due to chronic cervicitis/infection - Treatment of infection by antibiotics is the cure.
- If is due to decreased mucus volume - Treatment includes short term supplementation with exogenous estrogen like ethinyl estradiol and use of mucolytic expectorant like guaifenesin. However, their value has not been confirmed.
- If it is due to antisperm antibodies. Treatment options include:
  - Use of *condom or diaphragm as a barrier method for 3 months*. During this period, the antibodies will disappear and conception may occur then.
  - **Corticosteroids** given to female partner can also help in getting rid of these antibodies.

- **Intrauterine insemination** at the time of ovulation (most acceptable method for cervical factor infertility) or **GIFT (Gamete intrafallopian transfer)** are very useful techniques in such cases.
- IUI is the best method for treating cervical factor infertility and unexplained infertility. So many clinicians forgo cervical mucus testing and proceed directly to IUI treatment in absence of tubal disease.

24. Ans. c. Vegetarian diet Ref. <http://www.cincinnatiinfertility.com/holistic-treatment/fertility-diet>; <http://www.baby-hopes.com/articles/exercise-fertility.html>

Vegetarian diet will have minimal or no effect on fertility.

**“Weight definitely matters when it comes to fertility. Women who are overweight- or underweight-tend to have a more difficult time conceiving. The same goes for men, but more about that later.”** - <http://www.early-pregnancy-tests.com/weight-fertility.html>

**“Exercise can affect fertility in several ways. Over-exercising is one of the bigger causes of infertility for women. If a woman exercises too much, she is at a risk of losing too much of her body fat. Body fat plays an essential role in the production of estrogen; without enough estrogen, a woman who over-exercises might not ovulate. The technical term for not ovulating is oligomenorrhea, and is a major cause of fertility problems. Women who don't get enough exercise can impact their fertility negatively as well. By not getting enough exercise, a woman runs the risk of becoming overweight or obese. An overweight or obese woman, because she has more fat cells, can actually have too much estrogen. This overproduction of estrogen can negatively impact ovulation and conception. In addition, being overweight puts you at risk for insulin resistance, which can ultimately keep you from ovulating.”**-<http://www.babyhopes.com/articles/exercise-fertility.html>

25. Ans. is b, i.e. 20 million/ml

26. Ans. is b, i.e. Volume > 1 ml  
Normal seminal fluid analysis:

Ref. Novak 14<sup>th</sup>/ed p 1193; 15<sup>th</sup>/ed p 1141; Leon Speroff 7<sup>th</sup>/ed p 1144

Semen analysis - WHO

Parameter	1992 Guidelines	2010 Guidelines
Volume	2 ml	> 1.5 ml
Sperm concentration	20 million/ml	> 15 million/ml
Sperm motility or > 25% rapidly progressive	50% progressive > 15% normal forms	> 32% progressive > 4% normal forms
Morphology (Strict Criteria) WBC	< 1million/ml	< 1million/ml
Immunobead or mixed anti globulin reaction test	< 10% coated with antibodies	< 50%

Note: These questions are based on the older criteria.

27. Ans. is b, i.e. 20 million/ml

Note: This question is based on the older criteria.

Ref. Novak 15<sup>th</sup>/ed p 1141; Leon Speroff 7<sup>th</sup>/ed p 1144

Normal sperm count/ml i.e. sperm concentration is 20 million/ml.

28. Ans. is a, i.e. Absence of semen

Aspermia refers to failure of formation or emission of semen.

The absence of spermatozoa in semen is known as **Azoospermia**.

For other terminologies related to semen analysis – refer preceding text

Ref. Dutta Gynae 4<sup>th</sup>/ed p 218

29. Ans. is b or a, i.e. Oligospermia or Normospermia

The semen analysis of the patient shows:

Ref. Novak 14<sup>th</sup>/ed p 1193; Leon Spiroff 7<sup>th</sup>/ed p 1144

Parameter	1992 Guidelines	2010 Guidelines
• Sperm count is 15 million/ml.	Normal should be at least 20 million/ml	> 15 million/ml
• PH = 7.5	(N = > 7.2)	> 7.2
• Volume = 2 ml	N = at least 2 ml	> 1.5 ml
• Morphology = 60% normal	N = 15% (strict criteria)	> 4 % (strict criteria)
• Motile = 60%	N = > 50% motile	> 32 % motile

Thus based on earlier criteria, this patient is has oligospermia and based on recent criteria he is normospermic.

30. Ans. is b, i.e. Normal FSH and normal LH

31. Ans. is d, i.e. VAS obstruction



32. **Ans. is a, i.e. Estimation of FSH level**Ref. Shaw 13<sup>th</sup>/ed p 203

As discussed in the preceding text: estimation of the levels of FSH can differentiate between pretesticular, testicular and posttesticular causes of male infertility.

Cause	Example	Lab tests
Pretesticular cause	Kallmann syndrome	LH is decreased, FSH is decreased Testosterone decreased Testicular volume decreased
Testicular cause	Varicocele, orchitis, trauma, torsion, klinefelter syndrome	Testosterone decreased so negative feedback on FSH is lost, so FSH is increased. Testicular volume is decreased.
Post testicular cause/ obstructive azoospermia	Obstruction, Kartagener syndrome, Post vasectomy, Congenital B/L absence of vas deferens	FSH is normal LH is normal Testosterone is normal Testicular volume is normal

33. **Ans. is c, i.e. block in the efferent duct system.**Ref: Leon speroff 7<sup>th</sup>/ed p 1135-1140

Condition	Semen Analysis
Prostatic Infection Mumps Orchiditis Block in efferent duct	Sperms will be present, Increased WBC levels-purulent semen Oligo, astheno and teratospermia Azoospermia, presence of fructose, and sperms seen on testicular biopsy system

34. **Ans. is b, i.e. Ultrasound for obstruction**Ref. Reproductive medicine secrets by Peter Chan 1<sup>th</sup>/ed p 33

Absent fructose in semen indicates either there is congenital absence of seminal vesicle or there is obstruction in the ejaculatory duct system.

The best way to detect obstruction is to perform a transrectal ultrasound.

Also know: Role of Transrectal ultrasound in male infertility



**Transrectal ultrasound (TRUS):** is done to visualize the seminal vesicles, prostate and ejaculatory ducts obstruction. Indications of TRUS are: (i) Azoospermia or severe oligospermia with a normal testicular volume, (ii) Abnormal digital rectal examination, (iii) Ejaculatory duct abnormality (cysts, dilatation or calcification), (iv) Genital abnormality (hypospadias).

35. **Ans. is b, i.e. Washed semen**

**Intrauterine insemination** is placement of 0.3mL of washed processed and concentrated sperms (devoid of seminal plasma)/semen into the intrauterine cavity by transcervical catheterization.

36. **Ans. is a, i.e. Tubal pathology** Ref. Shaw 15<sup>th</sup>/ed p 214; Clinical Endocrinology & Infertility by Leon Speroff 7<sup>th</sup>/ed p 1216, John Hopkins manual of obs and gynae 4<sup>th</sup>/ed p 432

**IVF was first developed as a means to overcome infertility resulting from irreparable tubal disease as fertilization takes place in fallopian tube.**

Now the spectrum of IVF has broadened and is indicated in number of conditions -

**In female infertility****Mnemonic for uses of IVF in females-**

- T = Tubal infertility
- R = Recanalisation after tubal sterilisation
- O = Ovarian failure or diminished ovarian reserve (using donor oocytes)
- C = Females with Cancers or on Chemotherapeutic drugs.
- A = AIDS in partner
- R = Risk of transmitting genetic disease to offspring
- S = Surrogate motherhood if patient has no functional uterus.

- **In male infertility:**
  - When sperm count is < 5 million/ml
  - Repeated IUI failure
- **Multifactor infertility**<sup>Q</sup>
- **Unexplained infertility**<sup>Q</sup>

**37. Ans. is a, i.e. TESA**

*Ref. Novak 14<sup>th</sup>/ed p 1201*

Friends, we have studied in detail IVF and IUI but either of them cannot be performed if appropriate methods for sperm recovery are not available in cases of male infertility.

**Sperm retrieval or recovery can be done by:**

- Microsurgical epididymal sperm aspiration : MESA<sup>Q</sup>
- Percutaneous epididymal sperm aspiration : PESA<sup>Q</sup>
- Testicular sperm extraction : TESE<sup>Q</sup>
- Percutaneous testicular sperm fine needle aspiration : TESA<sup>Q</sup>
- **The choice of the method depends on:**
  - The underlying diagnosis,
  - Whether goal of the procedure is diagnostic or therapeutic
  - Whether, isolated sperm will be used immediately or cryopreserved.

For further details refer to the preceding text.

**Note: GIFT: (Gamete Intra Fallopian Transfer) / ZIFT: (Zygote Intra Fallopian Transfer)**

They are alternatives to IVF in which oocytes and sperm (in GIFT) or zygote (in ZIFT) are transferred to fallopian tube instead of uterus via laparoscopy. Once commonly used, as they offered high success rates to women with normal tube anatomy (whereas IVF is mainly used in cases where tubal pathology is present), both procedures are relatively rare now.

**38. Ans. is c, i.e. Liquid nitrogen**

*Ref. Jeffcoate 7<sup>th</sup>/ed p 723*

**Cryopreservation of semen:**

Involves cooling of embryos in the pronucleate stage or early cleavage stage to very low temperature in the presence of cryoprotectants such as:

- I<sub>2</sub> - Propanediol (Iodine)
- Glycerol
- dimethyl sulphoxide (DMSO) with sucrose.
- **They are then stored in liquid nitrogen till required.**<sup>Q</sup>
- Over half the embryos survive thawing process.
- Oocyte preservation has not been successful.
- No adverse effects have been seen in babies born by this technique.

**39. Ans. is d, i.e. Artificial insemination**

*Ref. Novak 14<sup>th</sup>/ed p 1237; Williams Gynae 1<sup>st</sup>/ed p 462*

**All methods of ART, by definition, involve interventions to retrieve oocytes. These techniques includes IVF, ICSI, GIFT, ZIFT, Cryopreserved embryo transfers, and the use of donor oocytes.**

**Different methods of ART**

IVF - ET	In vitro fertilization and embryo transfer
GIFT	Gamete intra fallopian transfer
ZIFT	Zygote intra-fallopian transfer
POST	Peritoneal oocyte and sperm transfer
SUZI	Subzonal insemination
ICSI	Intra-cytoplasmic sperm injection

**40. Ans. is a, i.e. Measuring day 14 serum progesterone**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 240*

Serum progesterone is measured on D8 and D 21 to show the rise and not on D14.

**41. Ans. is d, i.e. Luteal Phase defect**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 250*

**42. Ans. is c, i.e. Cervical factor.**

**43. Ans. is d, i.e. Azoospermia.**

IUI may be either artificial insemination of husbands semen called as **homologous insemination** or artificial insemination of donors semen called as **Heterologous insemination**. Husband's semen is commonly used. The purpose of IUI is to bypass the endocervical canal which is abnormal and to place increased concentration of motile sperm as close to the fallopian tubes.

**Indications of IUI**

- Hostile cervical mucus
- Cervical stenosis
- Oligospermia or asthenospermia
- Immune factor (male and female)
- Male factor – impotency or anatomical defect (hypospadias) but normal ejaculate can be obtained
- Unexplained infertility

In Question 42  $\therefore$  the question says homologous insemination is done in case of: Now obviously if there is cervical factor infertility (i.e. Antisperm antibodies) in female, her husband is absolutely normal & his semen can be used for IUI.

Similarly in Question 43, in option a, b and c homologous insemination can be done but if male is azoospermic, we will have to use donor sperm.

**44. Ans. is b, i.e. Seminal vesicles**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 232*

The seminal vesicle contributes 60% and prostate about 30% of the seminal fluid.

**45. Ans. is d, i.e. Both**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 232-235*

Absent fructose content in the seminal fluid suggests congenital absence of seminal vesicle or portion of the ductal system or both.

# CHAPTER

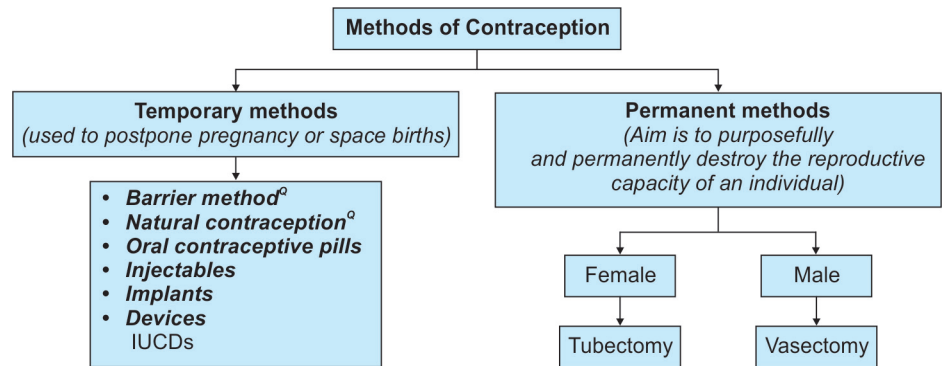
# 10

# Contraception



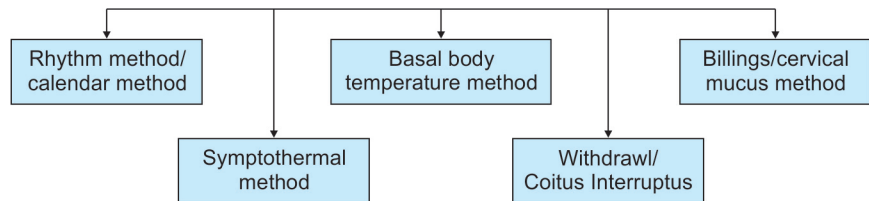
### Characteristic of an Ideal Contraceptive

An ideal is safe, effective, inexpensive, reversible, simple to use, independent of coitus, long lasting and requires minimal medical supervision.



### Natural Family Planning Method

It is the method of planning family without using any drugs or contraceptives.



**Basis:** These methods aim at avoiding sexual intercourse around ovulation. The timing of ovulation can be judged on calendar basis and symptom basis.

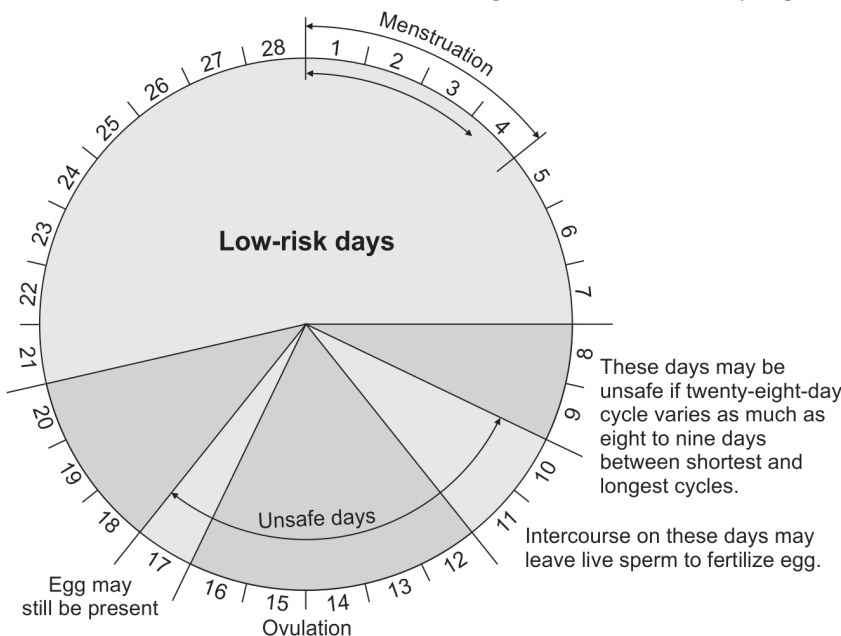


Fig. 10.1: The Calendar (Rhythm) Method

### 1. Rhythm method/calendar method:

It is based on *ogino knaus theory* which states ovulation occurs on day  $14 \pm 2$  in a female with a regular 28 days cycle (i.e. avoid sex between 12<sup>th</sup> and 16<sup>th</sup> day)

But fertilizable span of sperm is 48 - 72 hours and ova is 12 - 24 hours.

Therefore, unsafe period = 8 - 18 day (Failure rate = 25 - 35%)

Failure rate can be reduced if sex is avoided from 7-21 day if (failure rate = 10%)

Thus sex is safe only in the first and last 7 days of a menstrual cycle (park 20/e, p 436) (Fig. 10.1)

### In irregular cycle:

Safe period is = shortest cycle - 18 (gives first day of the fertile period)  
longest cycle - 11 (gives last day of the fertile period).

**Advantage:** Low cost and lack of side effects

**Drawback:** Difficult to predict safe period if cycles are irregular

- Can only be used by educated and responsible couples with a high degree of motivation and cooperation.
- Compulsory abstinence of sexual intercourse for nearly half month called as programmed sex.
- Not applicable during postnatal period.
- High failure rate -9/100 WY.

### Standard Days Method (In India called as Tirumala Method) (Fig. 10.2)

- Developed by Georgetown University's Institute for Reproductive Health.
- It has a simpler rule set and is *more effective than the rhythm* method.
- A product, called *Cyclebeads*, was developed alongside the method to help the user keep track of estimated high and low fertility points during her menstrual cycle.
- The Standard Days Method can only be used by women whose cycles are always between 26 and 32 days in length.

In this system:

- Days 1–7 of a woman's menstrual cycle are considered infertile.
- Days 8–19 are considered fertile.
- From day 20, infertility is considered to resume.
- Failure rate of **2/100 WY**.

### Cervical Mucus Method (Billings Method) (Figs 10.3 and 10.4)

- This method is based on the observation of changes in the characteristics of cervical mucus.
- At the time of ovulation – Cervical mucus is watery, clear (resembling raw eggs white), smooth, slippery and profuse. After ovulation, under the influence of progesterone, the mucus thickens and lessens in quantity.
- It is recommended that women use tissue paper to wipe inside the vagina to assess the quantity and character of mucus.
- Intercourse is considered to be safe during the dry days immediately after the menses and till the mucus is detected. Thereafter the couple must abstain until the fourth day after the peak day.
- To practice this method, the women should be able to distinguish between the different types of mucus. This requires a high degree of motivation.



Fig. 10.2: Standard Day Method



Fig. 10.3: Cervical mucus method

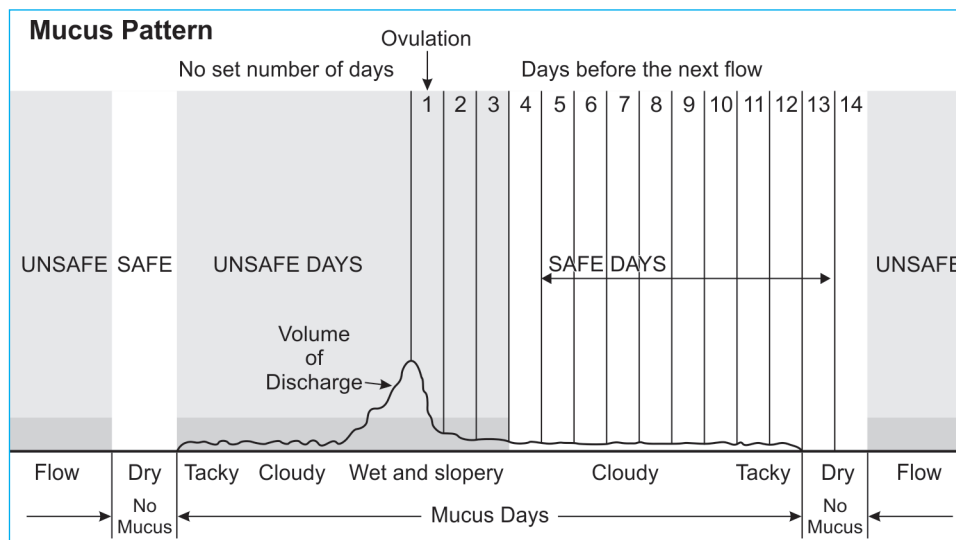


Fig. 10.4: Billings method



Cervical mucus method (Billings method) is based on the principle that under the influence of estrogen, cervical mucus is thin, watery, profuse and elastic (it can be stretched between fingers called Spinnbarkeit). Whereas after ovulation under the influence of progesterone it becomes thick, scanty and loses its elastic nature and breaks on stretching called as Tack.

### Basal Body Temperature Method

A woman's basal body temperature (BBT) drops briefly and then rises half a degree following ovulation, and remains elevated in the secretory phase. Normal BBT is between 96 and 98 degrees, and after ovulation rises to 97 – 98 degrees fahrenheit or rises by 0.2–0.5°C. A rise in temperature that persists for at least 3 days indicates that ovulation has occurred. *The safe period begins from the fourth day (first day being the day of ovulation) to the last day of the next period.* For this method to be effective, a chart of daily temperature reading needs to be kept.

### Symptothermic Method

This method makes use of at least two indicators to identify the fertile period. Usually the cervical mucus method and the BBT methods are combined.

### Withdrawal Method

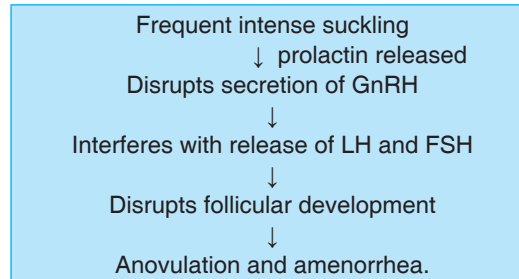
Withdrawal method or coitus interruptus means discharge of semen outside the female genitalia at the time of the intercourse.

### Contraindication

Premature ejaculation

### Lactational Amenorrhea Method (LAM)

#### Basis



The 3 prerequisites for lactational amenorrhea to ensure effective contraception

1. Exclusive breast feeding
2. Baby < 6 months of age
3. There is amenorrhea (menses should not have resumed after delivery)

Failure rate = 5/HWY.

### Recent Advances

Special digital thermometers and use of the ovumeter to note changes in cervical mucus are under experiment. Another device called PERSONA (unipath) consists of dipsticks to detect urinary estrone 3- glucuronide (which indicates the onset of the fertile period) and LH (which indicates ovulation).

### Natural Family Planning Methods are not Suitable for Women

The typical failure rate of natural family planning method is 20 per 100 women in the first year of use but it can be reduced to 1–9% with correct usage and practice.

- > With irregular cycles, cycles shorter than 21 days
- > During adolescence, lactation, and premenopausal
- > Who have had cervical surgery (cautery and conization)
- > With vaginal infection (until cure)
- > Who have sexually transmitted disease (STD) or pelvic inflammatory disease (PID) in the last 3 months
- > Who had abortion recently
- > Noncooperative husbands and couples who have casual sex.

### Pearl Index

- It is expressed in terms of “failure rate per hundred women - years of exposure (HWY)”.
- Failure rate per HWY =  $\frac{\text{Total accidental pregnancies} \times 1200 (12 \times 100)}{\text{No. of patients observed} \times \text{Months of use}}$
- In applying the above formula the following points must be kept in mind:
  - a. The total accidental pregnancies shown in the numerator must include every known conception, whatever its outcome.
  - b. The factor 1200 is the number of months in 100 years.
  - c. The total months of exposure in the denominator is obtained by deducing from the period under review of 10 months for a full term pregnancy and 4 months for an abortion.

**Lets understand this by an example.**

Suppose 100 couples have used a method for a period of 2 years and have resulted in 20 pregnancies, the pearl index is  $\frac{20 \times 1200}{100 \times 24} = 10$

### Pearl Index: WHO category 1 (user independent)

Contraception	Perfect use rate	Typical use
Implants	0.5%	.05%
Sterilization		
Male	0.1%	0.15%
Female	0.5%	0.5%
IUCD		
Mirena	0.2%	0.2%
CuT	0.6%	0.8%

**Pearl index** indicates the effectiveness of a contraceptive or is an index of contraception failure.

### WHO category 2 (user dependent)

Contraception	Perfect use rate	Typical use
OCP's	0.3%	8.7%
Vaginal ring	0.3%	8%
Transdermal path	0.3%	8%
DMPA	0.3%	3%
Diaphragm	20%	20%
<b>Sponge</b>		
Nulliparous	9	16
Parous	26	32
Condom		
Male	2	16
Female	5	21

**Note:** Least failure rate is with perfect use. If in question nothing is mentioned take it as Typical use.

### Barrier Methods

Males	Females
<ul style="list-style-type: none"> <li>• Condoms</li> </ul>	<ul style="list-style-type: none"> <li>• Female condoms (Femshield)</li> <li>• Today contraceptive/vaginal sponge</li> <li>• Vaginal diaphragm/cervical cap</li> </ul>

**Note:** Spermicidal agents like nonoxynol octoxynol and menfegol are added to any of the above barrier methods to increase its effectiveness.

Polyurethane condoms have a longer shelf life and can be used with oil based lubricants (latex condoms get damaged when oil based lubricant is used).

**Also Know****Natural membrane condoms/Lamb skin condoms**

These condoms are usually made from lamb cecum and can have pores upto 1500 nm diameter. These pores do not allow the passage of sperm but are large enough to allow passage of AIDS and hepatitis-B virus.



Female condoms protect against STDs and HIV.

**Female condoms**

FC-1 = Made of polyurethane is not used now  
 FC-2 = Nitrile based female condom, socially marketed free of cost by Govt. of India to female sex workers.  
 FC-3 = Made of latex.

**Male Condoms/French Letters****Types:**

- Latex
- Vylex
- Natural membrane condoms
- Polyurethane
- Polyisoprene

**Directions for Use**

- The condom should be put on by unrolling it over the erect penis after pulling back the foreskin, before there is any contact between the male and female organs. An airfree space should be left by squeezing the tip and holding it up till it is unrolled fully for better collection of semen.
- It should be used only once.
- It should not be inflated for testing.
- Vaseline oils, skin lotions, cold creams, i.e. oil based lubricant should not be used as they increase the chance of rupture. If lubrication is needed, water based lubricant K-Y jelly or spermicidal jelly can be used.
- Soon after discharge, the male should withdraw the penis holding the condom firmly against his body
- To increase the effectiveness, a dose of spermicidal jelly or foam tablet may be used at the same time. In case of breakage, slippage, or defective use, women should report or use emergency contraceptive within 72 hours and a spermicidal agent should be quickly inserted into the vagina.

**Advantages**

- Condoms gives very good protection against STDs. These include syphilis gonorrhoea, trichomoniasis, moniliasis, nongonococcal urethritis, and infection with chlamydia and herpes virus.
- They are the only contraceptives to protect against HIV and against sexually transmitted hepatitis B Virus.
- Condoms reduce the chances of developing cervical dysplasia and cancer cervix (by preventing HPV infection).

**Non-contraceptive Uses**

- After vasectomy to be used till semen analysis confirms azospermia.
- As condoms catheter in males
- After vaginoplasty
- As condom tamponade for managing atonic PPH
- In patients with antisperm antibodies present in cervical mucus.

**Disadvantages**

It can lead to contact dermatitis in female partners.

**Note:** Condoms (Nirodh) are supplied by Govt. of India free of cost at Family planning clinics.

**Female Condom (Reality Condom/Femshield) (Fig. 10.5)**

- Consist of Polyurethane/sac about 15 cm long and 7 cm in diameter with 2 flexible rings.
- The ring at closed end covers the cervix internally like a diaphragm and rug at open end covers the vulva.



- It is pre lubricated with silicon based lubricant (dimethicone)
- The condom is to be inserted like a tampon before intercourse and removed after 8 hours (not later than 24 hours) after intercourse.
- Sexual intercourse takes place within the cavity of the device.
- The advantage of female condom is its use depends on the will of the female partner and does not require male cooperation. It prevents STDS and HIV.

### Occlusive Caps (Vaginal Diaphragm and Cervical Caps) (Figs 10.6 and 7)

- Occlusive caps do not act as sperm proof mechanical barriers like condoms but are used as a means to retain spermicides in contact with cervical os, so spermicides must be used along with these devices.
- After intercourse, the vaginal diaphragm and vault cap should not be removed before 6-8h of the last act and should not be kept for more than 24 h.
- The best time to introduce it is, from a few minutes to 2 h before the sexual act.
- Like condoms, diaphragms and cervical caps prevent the spread of STDs, but AIDS is not prevented by them.

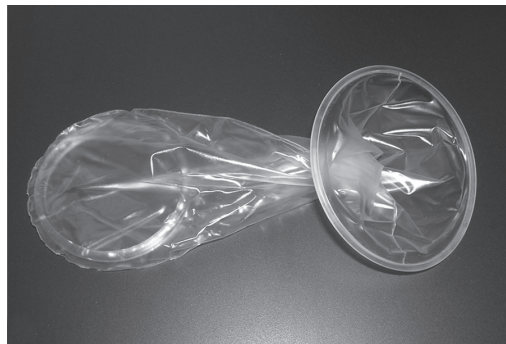


Fig. 10.5: Female condom

### Disadvantages

- Diaphragms increase the chance of UTI and cervical erosion
- They do not protect against HIV
- Rarely, they can produce toxic shock syndrome
- Not suitable for women with uterine prolapse



Fig. 10.6: Vaginal diaphragm



Fig. 10.7: Cervical cap

### Spermicides

- Spermicidal agents are chemical agents which kill the sperms before it enters to the cervical canal. They are available as foam tablets, soluble pessaries, creams, jellies or as films.
- Contents are:
  - Nonoxynol - 9 (N - 9)
  - Menfegol
  - Benzalkonium chloride.
  - Octoxynol
  - Enzyme inhibiting agents
- Failure rate is 20-25 per 100 WY, when used alone. When used in conjunction with a mechanical barrier, they give a reliable contraceptive effect.



#### Contraindications to the use of diaphragm—

- Prolapse, cystocele, rectocele
  - Retroversion
  - Vesico Vaginal Fistula / Rectovaginal Fistula
  - Badly eroded or lacerated cervix
  - Recurrent UTI
- Multiple sex partners is not a contraindication for the use of diaphragms, rather barrier contraceptives protect against STD's so these are a choice in them.



Female condoms protect against STDs and HIV.



The main mechanism by which spermicidal jelly acts is by disruption of cell membrane.

### Recent Advances

Recent evidences indicate spermicides are not effective in preventing cervical gonorrhea, Chlamydia, or HIV infection. In addition, frequent use of spermicides containing N-9 has been associated with an increased risk of HIV transmission.

– CGDT 10<sup>th</sup>/ed p 581

- Advantage 24 is a new contraceptive gel which contains nonoxynol.

### Today/Vaginal Sponge

- It is mushroom shaped polyurethane disposable sponge.
- It contains 1gm of NONOXYNOL - 9 and is provided with a loop for easy removal.
- It is a barrier contraceptive which prevents entry of sperm into the cervical canal and contains a spermicidal agent.
- It should be placed high up in the vagina with concave side covering the cervix.
- It remains effective for 24 hours regardless of the frequency of coitus.
- It is to be used only once.
- It should be left in vagina and removed 6 hrs after sexual intercourse.

### Side Effects

- Allergic reactions
- Vaginal dryness, soreness, or itching
- It can lead to genital lesions which may damage the vaginal mucosa and enhance HIV transmission.

#### Note:

Different books have a different say on role of Today in preventing STD's and toxic shock syndrome. But *Leon Speroff* is the most authentic book for this issue. It says – (*Leon Speroff 7<sup>th</sup>/ed p 1003*)

- There is no risk of toxic shock syndrome, infact nonoxynol 9 retards staphylococcal replication and toxin production.
- It decreases the risk of infection with gonorrhea, Trichomonas, and Chlamydia.



- Main mechanism of action of combined pills is prevention of ovulation.
- Combined pills act by decreasing both LH and FSH
- They do not interfere with placental functioning.
- When taken daily for 3 out of 4 weeks, they provide virtually absolute protection against conception.



#### Compositions Chart

**Mala D** EE = 30 mcg  
LNG = 0.15 mg  
(Available in market @ Rs. 3/- per pkt.)

EE = 30 µg  
**Mala N** Levo  
norgestrel = 0.15 mg  
(Available at Govt. health facilities free of cost). Both of them have 7 tables of ferrous fumarate

**Loette** EE            LNG  
20 mcg      0.1 mg  
EE  
20 mcg

**Femilon** Desogestrel  
0.15 mg

### Oral Contraceptives

#### Mechanism of action

Prevention of ovulation <sup>o</sup>	Prevention of fertilization <sup>o</sup>	Interference with Implantation <sup>o</sup>
<ul style="list-style-type: none"> <li>• Progestin reduces frequency of LH secretory pulses, while estrogen primarily reduces FSH secretion.</li> <li>• Both synergise each other to inhibit midcycle LH surge.</li> <li>• As a result, follicles fail to develop and rupture and ovulation does not occur.</li> </ul>	<ul style="list-style-type: none"> <li>• Thick cervical mucus, hostile to sperms may inhibit fertilization.</li> <li>• Uterine and tubal contractions may be modified to disfavor fertilization.</li> </ul>	<ul style="list-style-type: none"> <li>• Endometrium is rendered either hyperproliferative, hypersecretory, or atrophic and out of phase with fertilization and not suitable for nidation. Thus, even if ovulation and fertilization occur, implantation does not occur normally.</li> </ul>

**OCPs Can Be**

Monophasic	Biphasic	Triphasic
<ul style="list-style-type: none"> <li>Have same estrogen (E) and progesterone (P) in 21 tablets.</li> </ul>	<ul style="list-style-type: none"> <li>First 10 pills have one dosage</li> <li>Next 11 pills have some other E and P dosage</li> </ul>	<ul style="list-style-type: none"> <li>First 7 pills have same dosage (EE - 30 mcg, LNG - 50 mcg)</li> <li>Next 7 have another dosage (EE - 40 mcg, LNG - 75 mcg) and last 7 have yet another dosage (EE - 30 mcg, LNG - 125 mcg)</li> </ul>

**•** Lose dose pills have = Estrogen < 50 mcg (M/C = 35 mcg).

**•** Very low dose < 20 mcg

**•** Minimum effective doses of Estrogen in OCP's = 10 mcg.

**Note:** The last 7 pills (in all types of OCPs with 28 tablets) do not contain any hormone but have 60 mg of elemental iron.

On the basis of amount of estrogen they can be classified as –

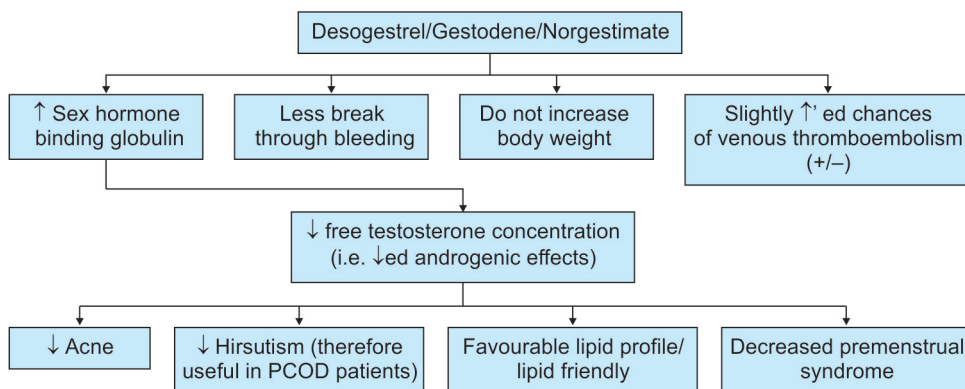
- Standard dose → EE = 0.05 mg (50 mcg)
- Low dose → Less than 50 mcg (30–35 mcg) EE = 0.03 – 0.35 mg (35 mcg)
- Very lose dose → EE = 0.020 mg (20 mcg)

The M/c estrogen used in OCP's is ethinyl estradiol.

**Progesterones in OCPs**

Generation	Progesterone	Comments
1 <sup>st</sup> generation – (Estranes derived from Testosterone)	Norethisterone, Norethindrone, Norethynodrel, lynestrenol	Used in pills with ≥ 50 mcg of EE
2 <sup>nd</sup> generation	Levonorgestrel Norgestrel	Levonorgestrel is the M/c used progesterone in OCPs
3 <sup>rd</sup> generation (Gonanes)	Desogestrel (active from 3-keto DSG), Gestodene, Norgestimate	Benefits given below
4 <sup>th</sup> generation	Drospirenone Dienogest, nomegestrol	Useful in women with hirsutism, acne, and those who have fluid retention after taking OCP and in treating PMS, PMDD

**Benefit of 3<sup>rd</sup> generation Progesterone**



**Tumors and OCPs—**

**Tumors associated with OCP use**

1. Cervical cancer (adeno CA)
2. Hepatic cancer
3. Pituitary adenoma

**OCPs provide protection against**

1. Ovarian tumors/cysts
2. Uterine tumors and fibroid
3. Benign breast disease
4. Colon CA
5. **No Risk** of breast CA and GB cancer

**Non-contraceptive Benefits of OCPs- Oral Contraceptive Pills (OCPs) are beneficial in**

**Cancers/Cysts**

- Uterine cancer (endometrial CA)
- Ovarian cancers<sup>Q</sup>
- Fibroid uterus (Progesterone only pills)
- Ovarian cysts<sup>Q</sup>



#### In OCPs users there is

Increased risk of depression.  
Vit B<sub>12</sub> helps in curing depression after OC use.



Generation of Piles:

**1st generation:** OCP with 50 mcg or more of EE

**2nd generation:** OCP's with EE = 30–35 mcg  
Progesterone-Norgestrel, Norgestimate

e.g. Mala N

Mala D

**3rd generation:** EE = 20–30 mcg progesterone-Desogestrel Gestodene, e.g. Femilon, Loette

**4th generation:** EE = 20–30 mcg progesterone-drospirenone, dinogest, e.g. yasmin (used in PCOS). It has antiminerlocorticoid activity & helps in loose weight. It has drospirenone)

- Diane 35 (It has cyproterone acetate and is useful in acne & hirsutism)



**Failure Rate** of OCPs-0.1

Warning signs of OC Pills complications—

#### ACHES

Severe **A**bdominal pain  
Severe **C**hest pain  
Severe **H**eadache  
**E**yes-blurred vision of brief loss of vision  
**S**harp leg pain

### Benign Disease of Genital Tract

- Benign breast diseases<sup>Q</sup>
- Endometriosis (if used continuously)
- **PID<sup>Q</sup>** (but incidence of chlamydia and candida is ↑)
- Ectopic pregnancy (as it decreases incidence of PID)

**They decrease ovulation thus are helpful in**

- Dysmenorrhea, premenstrual tension, and mittelschmerz syndrome.
- **By decreasing blood loss they are helpful in menorrhagia and polymenorrhea.**
- Acne and hirsutism (especially those containing desogestrel)

### OCPs are also Beneficial in:

– Leon Speroff 7<sup>th</sup>/ed p 914

- Dysfunctional uterine bleedings (DUB)
- Hormone therapy for hypothalamic amenorrhea
- Prevention of menstrual porphyria.

**Note:** OCPs are protective against benign breast diseases but as far as carcinoma breast is concerned, their role is controversial OCPs are being considered in the etiology of Ca breast. The progestogen component of pills is attributable to the Ca breast as the risk is same in users of OCPs 2 progestin only pills.

M/C side effect of OCPs-Break through bleeding

### Contraindications of OCPs

#### Absolute Contraindications-WHO category:

#### KNOW IN-DEPTH



- **Banks** Known or suspected Breast cancer
- **Have Severe** Hypertriglyceridemia/Hypercholesterolemia
- **Various** (Undiagnosed abnormal) Vaginal bleeding
- **Schemes** Smokers over the age of 35 years
- **To** Thrombophlebitis/Thromboembolic disorders, (present H/O, past H/O, family H/O) Cerebral and Cardiac disease
- **Provide** Pregnancy
- **Home** Hypertension (Moderate to severe) (> 160/110 mm of Hg)
- **Loans** Impaired Liver function/infective hepatitis
- **During**-Diabetes mellitus with vascular disease
- **May**-Migraine with aura

### Relative Contraindications

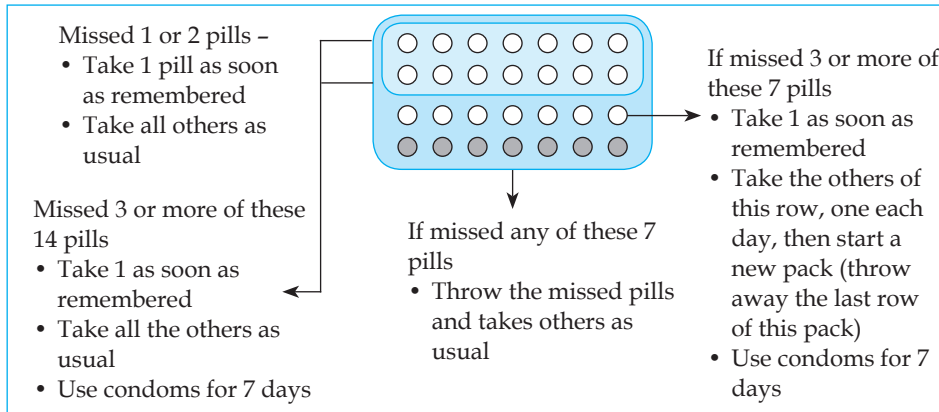
#### KNOW SUPERFICIALY

- Migraine without Aura
- Hypertension (mild)
- Uterine leiomyoma
- Elective surgery (OCP should be stopped 4 weeks before any scheduled surgery)
- Seizure disorders
- Sickle cell disease
- SLE
- Hyperlipidemia
- Diabetes mellitus/Gestational diabetes
- Smoking
- Obstructive jaundice in pregnancy
- Gall bladder disease
- Mitral valve prolapse
- Hepatic disease.

**Important Practical Applications**

- **When to begin a pill –**  
 In menstruating females – Between day 1 – of menstrual cycle (no backup contraceptive required). If she begins after day 5, backup contraceptive should be used for 7 days.
- After Medical Termination of Pregnancy (MTP)/abortion – Can begin immediately (no backup required) after first week abortion and one week after 2nd trimester abortion.
- After delivery: 6 to 8 weeks.

**In the event of missing a pill –**



**OCPs are the contraceptive of choice –**

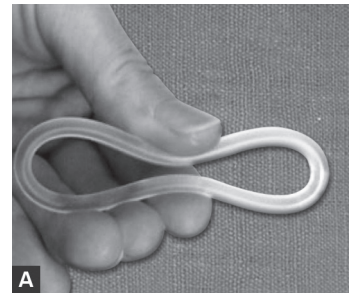
- i. In newly married couples staying together.
- ii. After evacuation of molar pregnancy.
- iii. Women wanting to space their pregnancy.
- iv. Women with family H/O ovarian cancer.

**Note:** OCPs can be used in women with HIV. If the female is on antiretroviral therapy, OCPs can be used as long as their antiretroviral regimen does not contain ritonavir or ritonavir boosted protease inhibitors. Ritonavir reduces the blood levels of contraceptive hormones.

**1.** Ovulation returns within 3 months of withdrawal of the drug in 90% cases

**2.** If OCPs are taken in early pregnancy the risk of congenital malformations is 2–3% same like general population.

- Women who do not smoke have normal BP, no hypertension or diabetes not have increased risk of myocardial infarction if they use low dose OCPs irrespective of age and duration of use of OCPs
- Women <35 yrs, non smokers and non hypertensives do not have increased risk of stroke with OCPs



**Figs. 10.8A and B:** Contraceptive vaginal rings

**Other Rings**

- Silastic vaginal rings (SVR) containing levonorgestrel and releasing 20 mcg of LNG daily.
- Nestorone –150 mcg progesterone + 15 mcg EE<sub>2</sub>

**Other Combined (E + P) Contraceptives**

<p><b>Transdermal patch called as ortho Vera</b></p> <p>P = Norgestimate</p> <p>E = Ethinyl estradiol</p>	<p><b>Vaginal ring called as Nuva ring</b> (Launched in India in November 2009) (Fig. 10.8)</p> <p>P = Etonorgestrel (active metabolite of desogestrel)</p> <p>E = Ethinyl estradiol (Releases 15 µg EE and 120 µg ENG)</p>
<ul style="list-style-type: none"> <li>• Applied weekly to anybody location for 3 weeks followed by 1 week patch free withdrawal bleeding week</li> </ul>	<ul style="list-style-type: none"> <li>• Placed in vagina for 3 weeks and removed for 1 week</li> <li>• Made of diethyl polysiloxane</li> <li>• Can be removed for upto 3 hours daily including during intercourse. If ring is out of vagina for &gt; 3 hours backup method required.</li> </ul>



**Only** POP available in india = **cerazette** (0.075 mg desogestrel)

#### Advantages

- Better compliance
- Avoids first pass hepatic metabolism and maintains a steady hormone level.

#### Disadvantages

- Less effective in obese women (>90 kg)

#### Advantages

- Increased compliance and satisfaction
- Decreases incidence of vaginal yeast and bacterial infections
- All systemic side effects of OCPs are absent

#### Disadvantages

- ↑ Leucorrhea
- Failure rate 0.3%



#### Suited ideally for—

- Lactating women
- Sickle cell anemia (best contraceptive)
- Seizure disorder (raises seizure threshold)



#### Failure rate of POPs

Breast feeding women

- Typical use – 1/HMY
- Perfect use – 0.3/HMY

Nonbreast feeding women

- Typical use – 3-10/HMY
- Perfect use – 0.3/HMY



The biggest drawback of progesterone injections is irregular bleeding. To overcome **this, combined injectables are under trial – Monthly injections.**

#### Cyclofem

DMPA 25 mg + Estradiol cypionate 5 mg

#### Mesigyna and Lunelle

NET EN 50 mg + Estradiol valerate 5 mg

**Marvelon** – Desogestrel 150 mcg + EE 30 mcg

**Femovan** – Gestodene 75 mcg + EE 35 mcg

Anafertin – Dihydroprogesterone 150 mg + testosterone enanthate 5 mg

## Progestin-only Pills (POP)

They contain very low doses of a progestin and no estrogen, and so can be used throughout breastfeeding and by women who cannot use methods with estrogen like in smokers, with past H/O uterine fibroid coendometrium and ovum.

Progestin only pills (POPs) are also called “minipills”, contraceptives.

### Mechanism of Action

- **Thickening cervical mucus:** Main mechanism of action for all progesterone pills.
- **Preventing ovulation:** Main mechanism of action for newer desogestrel containing progesterone pill.

### How to Use

In regular cycles	Amenorrhea	During lactation
<ul style="list-style-type: none"> <li>• Recent WHO recommendations suggest POP should be started <b>within 1st five days of menstrual cycle without need of additional contraception (preferably 1st day).</b></li> </ul>	<ul style="list-style-type: none"> <li>• Start <b>any time after being sure that there is no pregnancy</b> (Additional protection or abstinence from sex being advised for the first 48 hours)</li> </ul>	<ul style="list-style-type: none"> <li>• <i>As per CDC guidelines it can be stated any time after delivery according to WHO it is started after 6 weeks</i></li> </ul>

- Traditional progesterone only pill should be taken every day without break and **at the same time.**<sup>Q</sup>Safety margin (3 hrs). If delay was for > 3 hrs - back method should be used.
- For newer desogestrel containing pill, a **delay of ~12 hours** can be accepted.

### Side Effects

- **Menstrual disturbances:** Most common reason for discontinuation of POP's is irregular bleeding pattern.
- **Other side effects:** Headache, acne, breast pain, nausea, vaginitis, and dysmenorrhea.
- **Carbohydrate metabolism:** At high doses, most progestogens adversely affect carbohydrate metabolism whether given alone or in conjunction with estrogen. **Hence, POP's should not be advised to women with H/O gestational diabetes mellitus.**

## Progestin Only Injectables

- **DMPA** (depot medroxy progesterone acetate): 150 mg IM once in 3 months (13 weeks)

- **NETEN** (Norethindrone enanthate): 200 mg IM once in 2 months (8 weeks)  
With DMPA patient may come up to 4 weeks late and still get an injection.  
With NETO patient may come up to 2 weeks late and still get an injection.  
With either DMPA or NETO, she can come up to 2 weeks early.  
If started 7 days after start of menstrual cycle, backup is required for next 7 days.  
**Note:** DMPA is given in microcrystalline aqueous solution and NETO in castor oil solution.

**Also know: Depo-Sub Q provera 104**, contains 104 mg of DMPA. It is given subcutaneously over the anterior thigh or abdomen. It suppresses ovulation for 3 months as it is absorbed more slowly.

### Side Effects of DMPA

- *Irregular bleeding/poor cycle control*<sup>Q</sup> (Most common side effect) Park 20<sup>th</sup>/ed p 434
- *Occasional phase of amenorrhea*<sup>Q</sup>
- *Weight gain*<sup>Q</sup>
- Prolonged infertility after its use<sup>Q</sup> (Ovulation begins 6 – 12 months after the last injection); therefore, not suitable for women planning pregnancy in near future.
- Decreased bone mass (after prolonged use), so women should be advised to use calcium supplementation.

## Progestin Only Implants

### Subdermal Progesterone Implants Include

Norplant I (Fig. 10.9)	Norplant II/Jadelle	Implanon (Fig. 10.10)
<ul style="list-style-type: none"> <li>• It has 6 rods containing <b>36 mg</b> of Levonorgestrel each</li> <li>• Replaced after 5 years</li> <li>• It is 3 cm long</li> </ul>	<ul style="list-style-type: none"> <li>• It has 2 rods each containing 75 mg of LNG and releases the drug at the same dose as norplant 1</li> </ul>	<ul style="list-style-type: none"> <li>• It has a single rod 4 cms in size containing 68 mg of 3 ketodesogestrel (etonorgestrel). It is 4 cm long</li> <li>• Most popular implant these days.<sup>Q</sup></li> <li>• Replaced after 3 years.<sup>Q</sup></li> <li>• Releases 60 mcg of hormone per day</li> <li>• Doesnot decrease bone mineral density.</li> </ul>

**Note:** Now implanon has been replaced by **Nexplanon** which has same characteristic like implanon.

### Mechanism of Action

Norplant	Implanon
<ul style="list-style-type: none"> <li>• Thickening of cervical mucus<sup>Q</sup></li> <li>• Suppressing the LH surge and causing either anovulatory cycles or luteal insufficiency<sup>Q</sup></li> <li>• Causes endometrial atrophy<sup>Q</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Main mechanism is ovulation inhibition<sup>Q</sup> (Remember - newer progestin only pills containing desogestrel also have ovulation inhibition as their main mechanism).</li> <li>• Rest of the mechanism is same as Norplant</li> </ul>



### Iniection - cyclofem/cyclo-provera

DMPA = 25 mg  
+  
Estradiol cypionate 5 mg  
Administered monthly  
**Mesigyna:**  
Norethindrone = 50 mg  
Enanthate  
+  
Estradiol valerate (5 mg)  
Administered-monthly



Fig. 10.9: Norplant



Fig. 10.10: Implanon



### Extra Edge

Newer implants

#### Single rod implant system:

UNIPLANT

- Contains norgestrel acetate
- Effective for 1 year

#### Biodegradable implant:

CAPRANOR

- Contains Levonorgestrel.
- The capsule (single capsule) begins to disappear after 12 months.



### Return of fertility after removing implants—

- In 40% cases fertility returns by end of 3 months
- In 76% cases fertility by end of 2 years
- In 90% cases fertility by end of 3 years

## Site of insertion

- Implants are inserted subcutaneously on the inner surface of the upper arm using a 10 gauge trocar as an inserter, under local anesthesia.
- The implant should be inserted within day-5 of a menstrual cycle, immediately after abortion and 3 weeks after postpartum.

## Advantages

- Can be used in females with contraindication for the use of estrogen containing contraceptives.
- Can be used immediately postpartum.<sup>Q</sup>
- Can be used by lactating females.<sup>Q</sup>
- Not associated with changes in carbohydrate or lipid metabolism.
- No adverse effect on bone density.

## Disadvantages

- **Failure rate:** 0.1–0.4% with Norplant II
- NO PREGNANCIES have been reported so far with the use of implanon.
- Metrorrhagia and headache are the main reasons for discontinuation of implants by females



### Contraindications (absolute)

**Mnemonic:** GTB library (GTB is Guru Tegh Bahadur Hospital in Delhi).

- |                |   |
|----------------|---|
| <b>G</b>       | – Undiagnosed Genital bleeding                      |
| <b>T</b>       | – Active Thrombophlebitis or Thromboembolic disease |
| <b>B</b>       | – Known or suspected Breast cancer                  |
| <b>Library</b> | – Acute Liver disease                               |
|                | – Benign or malignant Liver Tumours.                |

- Relative contraindications:**
1. Severe acne
  2. Severe vascular or migraine headache
  3. Severe depression

## Intrauterine Contraceptive Devices (IUCDs)

The intrauterine devices are classified as follows –

Generation	Description
<b>First generation IUCDs</b>	These are inert or non-medicated devices. e.g. Lippe's loop.
<b>Second generation IUCDs</b>	It consists of copper or silver containing IUCDs e.g. T Cu-220 C, T Cu 380- Ag, Nova T, Multiload Cu 250/375
<b>Third generation IUCDs</b>	This consists of hormone releasing IUCDs. E.g. Progestasert, Mirena.

## Mechanism of Action of IUCD

Nonmedicated IUCD	Cu containing IUCD	Progestin releasing IUCD
<ul style="list-style-type: none"> <li>• Act as a foreign body in uterus and produce, a sterile inflammatory response and tissue injury of minor degree sufficient enough to be spermicidal. They prevent sperms from reaching the ova and therefore prevent both intra-uterine and ectopic pregnancy</li> <li>• It provokes <b>uterine contractility &amp; increases tubal peristalsis.</b></li> </ul>	<ul style="list-style-type: none"> <li>• Elute copper which bring about enzymatic and metabolic changes in the endometrial tissue &amp; also produce changes in cervical mucus and endometrial secretions.</li> </ul>	<ul style="list-style-type: none"> <li>• They cause decidualization <b>with atrophy of endometrial glands, therefore inhibit implantation</b></li> <li>• Alter cervical Mucus causing inhibition of sperm penetration and capacitation.</li> <li>• In 40% cases ovulation is also inhibited.</li> </ul>



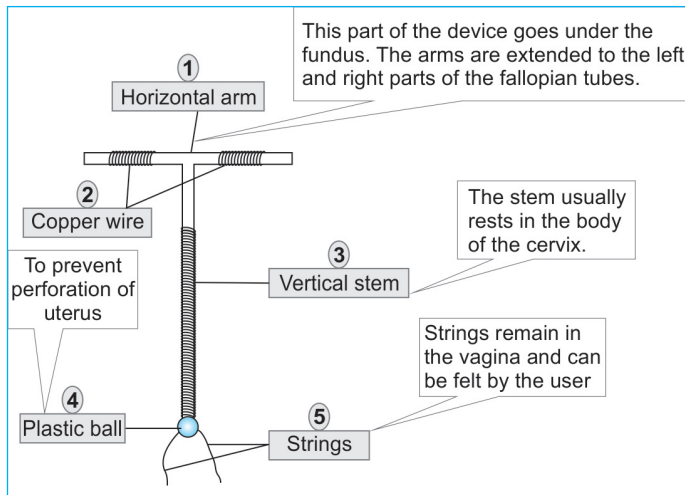


Fig. 10.11: Parts of IUCD

The contraceptive action of all IUCDs is mainly in the uterine cavity. Ovulation is not affected and the IUCD is not an abortifacient. It is currently believed that the mechanism of action for IUCDs is the production of an intrauterine environment that is spermicidal (Fig. 10.11).

### Life Span of IUCD

Most of the IUCDs have an average life span of 3 years.

Exceptions are:

- |   |   |
|---|---|
| • Nova T/Multiload 375/Levonova                           | – 5 years   |
| • CuT 380 A (also known as Paragard)                      | – 10 years – Distributed free of cost                           |
| • Progestasert  | – 1 years   |
| • CuT200 B  | – 4 years, in US and 3 years in India and in European countries |
| • Levonorgestrel containing IUCD can be used for (Mirena) | – 7–10 years, but is approved for 5 years                       |

### IUCD's Description

#### Lippe's Loop

- Double S-shaped device made of polyethylene
- Available in 4 size A, B, C, D
- D is the largest
- Can be left in the uterus as long as desired
- Now not used.
- Method of insertion – Push technique

**CuT 20. (Gyne T)- Copper wire of 200 mm<sup>3</sup> is wound around vertical stem. Earlier, it was M/C used by Indians. Now replaced by CuT 380A.**

**Copper T 380 A/C Paragard.** It is T-shaped, IUD, made of polyethylene with barium sulfate. They have 314 mm<sup>2</sup> copper wire on vertical stem and two 33 mm<sup>2</sup> copper sleeves on each of the two arms (transverse). It is distributed free of cost by Govt. of India. Effective for 10 years. Releases copper @ 50 mcg day. It increases blood loss (80 ml) average. It has been used as an emergency contraceptive.



#### Method of insertion of IUCD—

No touch technique and **withdrawal method.**

- Insertion of Lippes loop by push technique
- Insertion of Multiload
  - **Withdrawal technique without plunger**



**Note:** For more details and illustrations of individual CuT: see the pictorial section at the end of the book



#### Ideal time for insertion of Cu-T

- Within 10 days of start of menstrual cycle. It has the advantage that cervical canal is dilated, uterus is relaxed and chances of pregnancy are remote
- Post-puerperal insertion immediately after delivery (recommended by Govt. of India) or 6 weeks after delivery
- Post-MTP insertion - immediately following a 1<sup>st</sup> trimester pregnancy.



- Previous ectopic pregnancy is not a C/I for IUCD insertion
- M/C infection seen with IUCD use is actinomyces



#### Ideal candidate for Cu-T insertion

- Should have had at least one child
- Are in mutually monogamous relationships; (IUDs do not protect against sexually transmitted diseases)
- Has no history of PID
- Choose not to use hormonal contraceptives.



- Increased menstrual discomfort is the most common medical reason for IUCD removal.
- IUCD's are not contraindicated in HIV infected women.
- Rather in HIV females, contraception of choice is IUCD + Barrier method

### Newer IUCDs

**Cu Safe 300:** has 300 mm<sup>2</sup> of copper in its vertical arm and transverse arm with sharply bent ends that are adapted to the uterine cavity.

- Made from more flexible plastic.
- Smaller than the world's two most popular IUCD's - CuT380A and multiload 375.
- Pregnancy rates are comparable to these two devices.
- Rates of removal for pain and bleeding are reported to be lower.

#### Flexigard/Cu Fix/Gyne Fix:

- It is a frameless IUCD.
- Consists of 6 copper sleeves (330 mm<sup>2</sup> of copper) strung on a propylene thread specially suited for nulliparous and nulligravida females.
- **Fibroplant:** Levonorgestrel containing IUCD being tested for perimenopausal and postmenopausal use.

### Complications of IUCD

- **M/C complication:** Bleeding
- 2<sup>nd</sup> M/C complication- Pain (M/c reason for removal of IUCD)
- Expulsion rate of CuT: 8–10%
- Infection—Doxycycline 200 mg/azithromycin 500 mg should be given 1 hour before insertion to reduce infection. Most typical infection associated with Cu T use is actinomyces.
- **Ectopic pregnancy:** As such it is seen that ectopic pregnancy is 50% less likely in women using IUCD than in women using no contraception. However. If pregnancy occurs chances of ectopic are high.
- **Other complications:** Expulsion of IUCD and uterine perforation (M/c time for perforation is at the time of insertion).

### Absolute Contraindication for IUCD—Category 4 of WHO



Please—puerperal sepsis, pregnancy  
 Don't DUB  
 Try to Gestational trophoblastic disease  
 Put **Current PID/STD** or within the past 3 months puerperal sepsis, known pelvic TB  
 Condom Cancer cervix  
 Cancer endometrium (*Novak 15<sup>th</sup>/ed p 224*)

**Mnemonic:** Please Don't Try to Put Condom

### Relative contraindications of IUCD

— Park 20<sup>th</sup>/ed p 427; Jeffcoate 7<sup>th</sup>/ed pp 798-799; Shaw 14<sup>th</sup>/ed p 205

- Distortions of uterine cavity due to congenital malformations on fibroid<sup>Q</sup>
- Wilsons diseases (CuT)
- Breast CA for mirena

### Progesterone Containing IUCDs

**Mirena:** It contains 52 mg levonorgesterel, eluting 20 µg daily.

**Life span:** 5 years

#### Mode of Action

- Inhibits fertilization
- Thickens cervical mucus

- Inhibits sperm function
- Suppresses endometrium and makes it non-reactive, which prevents implantation
- Ovarian function is not disturbed by Mirena.

### Timing of Insertion

- Within first 7 days of onset of menstruation
- Immediately after first or second trimester termination of pregnancy
- **Post placental IUCD, insertion:** IUCD can be inserted immediately after vaginal delivery or during LSCS before closure of the uterus.

### Non Contraceptive uses of LNG Containing IUCD

- Decrease menstrual blood loss and are used for management of menorrhagia (can be used as an alternative to hysterectomy).
- Significant reduction in dysmenorrhea.<sup>Q</sup>
- Decrease pelvic infection rates.<sup>Q</sup> – Williams Gynae 1<sup>st</sup>/ed p 119
- Can be used in treatment of endometrial hyperplasia, adenomyosis, uterine leiomyomas, and endometriosis.
- Provides the benefits of hormone replacement therapy when used over the transition years of reproduction to perimenopause.

### Drawback

- Irregular bleeding and oligomenorrhea which are common in first 3-4 months of use
- Amenorrhea (seen in 20-50% cases by 1 year of use).
- Not used as an emergency contraceptive

## Emergency Contraception

It can be started up to five days (120 hours) after unprotected intercourse but greatest protection occurs if it is given within 72 hours of unprotected sex. Emergency contraception is also known as emergency birth control, backup birth control, and the morning after pill.

Method of choice/M/C method used = Levonorgestrel 1.5 mg single dose (Tablet = 0.75 mg 2 tablets together)

**Note:** The overall risk of having pregnancy after single unprotected intercourse is 8%.

### Indications

- Breakage or slipping of condom
- Forgot to take OC pills or insert diaphragm or sponge
- Diaphragm slipped out of place
- Miscalculated "safe" days
- Failure to practice coitus interruptus
- Not using any birth control method
- Forced to have unprotected vaginal sex, or were raped.

### Mechanism of Action

- Delay ovulation-Hormonal methods
- Spermicidal-Nonhormonal methods
- Prevents implantation by affecting endometrial lining.
- M/C side effect: Nausea, vomiting
- There are No C/I for emergency contraceptive.

**Note:** E-pills are available free of cost by Govt. of India. It has Levonorgest. One new pill available world wide but not in India is Ella - 30 mg of ulipristal.

### Advantages of 3rd generation IUCD (i.e. hormonal IUCD) over other IUCD's

- High efficacy with low pregnancy rates.
- Longer duration of action
- Low expulsion rates
- Can be given to nursing mothers.

### Drugs used for Emergency Contraception

- Levonorgestrel tablet
- Yuzpe method – OCP's with 50 µg ethinyl estradiol 2 tablets twice 12 hours apart  
OCP's with 30 µg EE – 4 tablets twice 12 hours apart
- Mifepristone (10 mg as soon as possible. Anti-implantation in action)
- Danazol
- Ulipristal (Synthetic Progesterone Receptor Modulator). Delays ovulation. Dose = 30 mg. Single dose to be taken within 5 days.
- IUCD insertion within 5 days of unprotected sex.
- Centchroman 2 tablets (60 mg) twice in 24 hours within 24 hours of intercourse.

**Note:** LNG IUCD and progesterone only pills are not emergency contraceptives



E Pill is available free of cost by Govt. of India as an emergency contraceptive.



Most effective method of emergency contraception CuT> Ulipristal > LNG tablet



- M/C method of post partum sterilization—Minilaparotomy
- M/C method of female sterilization—Laparoscopic sterilization using falope rings



#### Site of Sterilization

Sterilization is done at the junction of proximal and middle third of tube – the loop formed consists mainly of isthmus and part of ampullary region.

- Best chances for reversibility is seen in— Isthmo - isthmic type of anastomosis.



#### Timing for Female Sterilization

Per abdomen

- Post partum – within 48 hours upto 7 days of delivery
- After MTP
- After cesarean section
- Interval sterilization – After a waiting period of 6 weeks after delivery

#### Laparoscopic sterilization

- With 1st trimester MTP
- As interval sterilisation

**Note:** Laparoscopic sterilization should not be performed along with second trimester MTP or in post partum period 6 weeks after delivery, on D5-D11 of cycle avoid any pregnancy.

## Permanent Method of Contraception

### Female Sterilization

- First performed in 1823 in London by Dr J Blundell.
- Female sterilisation is the most commonly used contraceptive method in the world
- Child norm for sterilization in India: 1 child at least 1 year old
- Husband consent is for sterilization atom not necessary.

### Techniques

It can be done laparoscopically (procedure of choice these days) or by mini laparotomy (incision < 3 cms)

### Methods of female sterilization

The basic fundamental principle in female sterilization is breaking the continuity of both fallopian tubes by removing a small segment of both tubes.

### Prerequisites

#### A. Criteria for Eligibility

(Self-declaration by the client should be the basis of this information)

- Patient should be married.
- Female should be below the age of 49 years and above the age of 22 years.
- The couple should have at least one child whose age is above one year unless the sterilization is medically indicated.
- Female or her partners must not have undergone sterilization in the past (not applicable in cases of failure of previous sterilization).
- Clients must be in a sound state of mind so as to understand the full implications of sterilization.
- Mentally ill clients must be certified by a psychiatrist and a statement should be given by the legal guardian/spouse regarding the soundness of the client's state of mind.

### Surgical Techniques

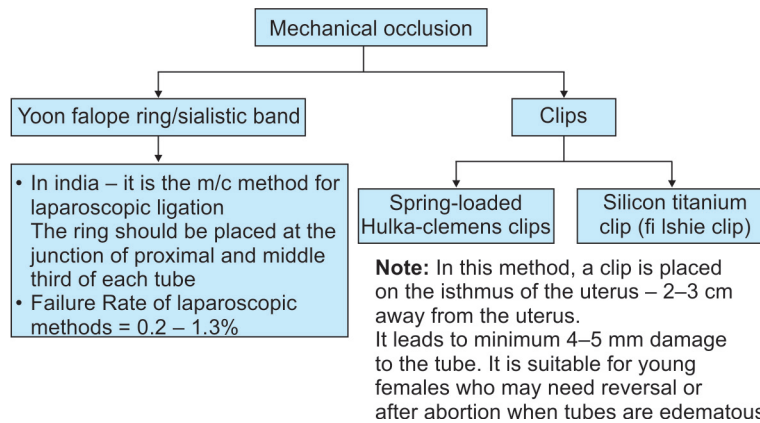
Important points to be kept in mind about surgical techniques are:

- The operating surgeon should identify each fallopian tube clearly by following it up to the fimbrial end.
- The site of the occlusion of the fallopian tube must always be within 2–3 cm from the uterine cornua in the isthmic portion (this will improve the possibility of reversal if required in the future).
- Excision of at least 1 cm of the tube should be done. Use of cautery and crushing of the tube should be avoided.
  - Pomeroy technique**—(Most commonly done laparotomy method). The middle part of tube (3–4 cm away from fundus) is formed into a loop which is tied at the base with catgut and excised. Site of ligation— Isthmus.  
Failure Rate = 1 in 300/400 surgeries
  - Irving method**—Ligating and burying the proximal tubal end in serosa of posterior uterine wall.  
Failure Rate = 1 in 1000 surgeries.
  - Uchida technique**—No Failure Rate in 19000 surgeries
  - Fimbriectomy/kroeners technique**—Very high failure rate 2–3 in 100 surgeries
  - Madlener technique**—High failure rate—0.3–2 in 100 surgeries

- f. **Parkland technique**–Failure Rate 3 in 400 surgeries  
**Note:** Amongst the conventional methods - Uchida followed by Irwing has the least failure rate.

**2. Laparoscopic ligation**

- o Done using laparoscope.
- o It is a safe and effective method.
- o **It should not be done concurrently with 2nd trimester MTPs and in post-partum period.**
- o The patient is laid in lithotomy position and with a help of verses needle (introduced at an angle of 45°) pneumoperitoneum is created.
- o The gas used is CO<sub>2</sub> (M/C)
- o Intraabdominal pressure is maintained between 8-12 mm; max = 15 mm of Hg. The procedure is done on an outpatient basis under sedation and local anaesthesia.
- o The methods of occlusion used during laparoscopy are



- Note:**
- o Clips cause least damage to tube = 4–5 mm
  - o With pomeroy technique damage is 3-4 cm. With Falope ring = damage is 3 cm

**Unipolar cauterization** by laparoscopy although has least failure but is not done as it leads to intestinal burns and has thus been abandoned.

- 3. **Hysteroscopic tubal ligation:** Can be done using cauterization- failure rate 30% or by using sclerosants - failure rate, 15%
- 4. **Essure:** It is a spring-like device which is introduced via females vagina (with the help of a hysteroscope) into the fallopian tube. It blocks the fallopian tube and prevents sperms from reaching the ova. It has an outer coil of Nickel and Titanium and inner coil of stainless steel. It incites tissue reaction. Success rate 99%. Now available in India.

**Method of Female Sterilization and Failure Rates**

Method	Failure Rate
• Pomeroy’s method	0.4% <sup>o</sup>
• Modified pomeroy	0.2%
• Madlener	7%
• Irwing	Very low failure rate
• Uchida	Very low failure rate
• Laparoscopic sterilization	0.2–1.3%
• Hysteroscopic tubal block	
o Cauterization	30%
o Sclerosants	15%

Falope rings introduced by yoon in 1974

**Post-ligation syndrome**  
 Some patients after tubal ligation can experience post ligation syndrome characterized by:

- menstrual irregularities like menorrhagia or irregular periods,
- pelvic pain or congestive dysmenorrhea and
- cystic ovaries.

It is vascular in origin and its incidence can be reduced if the blood vessels adjacent to the mesosalpax are not unduly disturbed.

**Methods with good chances of recanalization**

- Laparoscopic clips (best)
- Laparoscopic - yoon Falope ring/band
- Pomeroy and Uchida methods.
- Lowest with cautery.



Sterility does not occur immediately after vasectomy. Sperms remain in the semen for 15–20 ejaculations, requiring continued contraception for about 3 months. So, the couple is advised to use some form of contraception for the next 3 months or 15–20 ejaculates, generally. Before discontinuing contraceptive method, azoospermia should be confirmed by semen analysis (done either at 16 weeks or at 12 and 16 weeks)



Contraindications of vasectomy–

- Local skin infection
- Varicocele, hernia
- Undescended testis

## Contraindication of Laparoscopic Tubal Ligation

### Absolute contraindications

- Large abdominal mass (uterine or ovarian tumors) needing laparotomy.
- Decompensated heart disease.
- Severe respiratory dysfunction.
- Hiatus hernia.

### Relative contraindications

- Gross obesity with thick abdominal wall and
- Relvic adhesion due to previous pelvic infection or operations. Laparoscopic sterilization should not be done soon after delivery or abortion of more than 12 weeks pregnancy.

## Reversal of Tubal Ligation

- The most important factor affecting successful reversal is length of the remaining tube
- For reversal the minimum length of reconstructed tube should be 4 cms (with ampullary part 2 cms)
- The chances of ectopic pregnancy after reversal are very high

### Results of microsurgical reconstructive surgery after sterilization procedures

Sterilization procedure	Term pregnancy (range %)	Ectopic pregnancy (range %)
Spring-loaded clip	88 (75–100)	2 (0.4)
Ring occlusion (silastic bands)	75 (44–95)	2 (0–4)
Pomeroy ligation	59 (45–70)	2 (0–3)
Electrocoagulation	43 (26–58)	5 (0–9)

**Note:** Most suitable for reversal is clips followed by silastic bands/rings, BUT most commonly used for laparoscopic tubal ligation is silastic band followed by clips

Least suitable for reversal is monopolar cautery followed by bipolar cautery technique.

## Male Sterilization

### Vasectomy

- It is a simple, safe and effective surgical procedure that permanently ends a man's fertility.
- There are two methods by which the vas deferens can be approached *conventional vasectomy* and *noscalpel vasectomy*.
- Vasectomy consists of dividing and excising a part of vas deferens and disrupting the passage of sperms.
- It is done under local anesthesia.
- The first step in the vasectomy is to identify and immobilize the vas through the skin of the scrotum. The second step is to bring the vas into the open.
- Once the vas deferens is brought out into the open it is then occluded using a variety of methods viz:
  - Ligation and excision (most common method used in India)
  - Electrocautery
  - Thermal cautery
  - Clips
  - Open ended vasectomy

### Conventional Vasectomy

- In the conventional incisional method of vasectomy, the surgeon uses a scalpel to make either one midline incision or two incisions in the scrotal skin, each usually 1.2 cm long and one overlying each vas deferens
- The incision is routinely closed with sutures after the vasectomy has been completed
- In general, with conventional vasectomy, only the area around the skin entry site is anesthetized.

### No-scalpel Vasectomy: Introduced in China by Dr Lishuangjiang

- No-scalpel vasectomy (*also known as NSV*) is a unique method of gaining access to vas deferens
- Instead of a scalpel, two specialized instruments – a *ringed clamp* and a *dissecting forceps* (a sharp, curved hemostat) are used
- Because the scrotal skin puncture made with the dissecting forceps is so small, sutures are not needed.

### Advantages of No-scalpel Vasectomy

- A smaller wound than conventional technique
  - Earlier resumption of sexual activity after surgery (because it requires no scrotal incision)
  - Neither conventional nor no-scalpel vasectomy is time-consuming, but it has been reported that the vasectomy procedure time is shorter when skilled providers use the no-scalpel technique
  - Failure Rate = 0.1 – 0.15%
  - Reversibility – Reversal is possible with microsurgery (vasovasotomy) giving 90% return of sperm and 70% pregnancy rate
- Note:** The longer the time interval between vasectomy and reversal, poorer the chances of reversal.

#### Recent advances

- **Gossypol:** It has been discovered in China; an extract from cotton seed. It acts directly on the seminiferous tubules inhibiting spermatogenesis. The side effects are: fatigue, decreased libido and delayed recovery of sperm count. The serious side effects are hypokalemic paralysis and cardiac arrhythmias.

#### Also know

##### Centchroman

- It is a synthetic **NON-STEROIDAL** (ormiloxifene) contraceptive.
- A tablet of 30 mg started on 1<sup>st</sup> day of menstruation and taken twice weekly for (12 weeks or 3 months), and weekly thereafter ( $t_{1/2}$  - 170 hours).
- **Mechanism of action:**
  - It prevents implantation through endometrial changes and does not inhibit ovulation.
  - Increases transport of zygote through the fallopian tube.
  - It accelerates blastocyst formation.
- Developed by CDRI, Lucknow and released in India by 2 trade names Saheli and Centron.
- Exhibits strong antiestrogenic and a weak estrogenic actions peripherally at receptor level.
- It is not teratogenic or carcinogenic, exerts no pharmacological effect on other organs. The only side-effect noted is prolonged cycles and oligomenorrhea in 8% cases. This is due to prolonged proliferative cases.



- M/C method of contraception used by couples, in India-barrier method
- Best method for couples staying for barrier method
- Best method for newly married couples
- Safest method of contraception
- In HIV patients best method barrier - IUCD + barrier method
- Female sterilization
- Most commonly used method in Mini lap - modified polymeria technique
- Most effective method - modified pomenery
- Least effective method - Halka cleps > Biholor country highest risk of ectome pregnancy = category & modeler and modified pomenery
- Least failure rate in Minilap = uchvda > Irving > modified pomenery failure rate in lap contary update country > Ring

- Pregnancy rate is (1-4)/100 WY.
- Return of fertility is within 6 months of stopping the drug.
- The drug can also be used as a post coital pill, given in 60 mg dose within 24 hours of coitus, 2 tablets repeated after 12 hours with a failure rate of 1%.
- Side effects—headache, nausea, vomiting, gain in weight, does not protect against HIV and STD, prolonged cycles (due to prolonged proliferative phase) and oligomenorrhea (in 8% cases). There is some delay in return of fertility.
- **Contraindications:**
  - a. During first 6 months of lactation
  - b. PCOD, hepatic dysfunction, kidney disease, TB, etc

**Non-contraceptive use:**

Because of its potent antiestrogenic activity it is being tried in:

- DUB
- Endometrial hyperplasia
- Endometriosis
- Breast cancer

It is used as emergency contraception also.

**IMPORTANT POINTS**

- M/C method of contraception used by couples in India – Barrier method
- Best method for couples staying far – Barrier method
- Best method for newly married couples – OCPs
- Safest method of contraception – Barrier method
- In HIV patients best method – IUCD+Barrier method
- Female sterilization – Most commonly used method in Minilap Modified Pomeroy technique
- Most effective method – Modified Pomeroy technique
- Least effective method-halka Clips > Bipolar cautery
- Highest risk of ectopic pregnancy > Cautery > Madlener > modified Pomeroy
- Least failure rate in Minilap = Uchida > Irving > Modified Pomeroy
- Least failure rate in laparoscopy: unipolar cautery > Ring.



## FIGURE BASED QUESTIONS

- F1.** Figure F1 shows a transdermal patch used for contraceptive purpose. The patch is not yet available in India. The following statement is incorrect about the patch:
- It contains norelgestromin and ethyl estradiol.
  - A single patch to be used for 3 weeks
  - A single patch to be used for 1 week
  - Compliance is good with the patch



Fig. F1

- F2.** Figure F2 shows a popular method of performing sterilization. Regarding this technique true statements is:
- Is performed with absorbable suture material
  - Is performed using permanent suture
  - Includes crushing the fallopian tube
  - Is irreversible

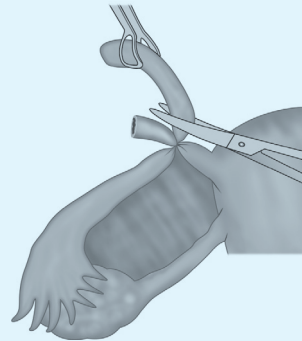


Fig. F2

## QUESTIONS

## General

- Which of the following is correct for the calculation of pearl index: (AIIMS Nov 03)
  - $\frac{\text{No. of accidental pregnancies} \times 1200}{\text{No. of patient observed} \times \text{months of use}}$
  - $\frac{\text{No. of accidental pregnancies} \times 1200}{\text{No. of patient observed} \times 2400}$
  - $\frac{\text{No. of patients observed} \times \text{months of use}}{\text{No. of accidental pregnancies}}$
  - $\frac{\text{No. of patient observed} \times 2400}{\text{No. of accidental pregnancies} \times 1200}$
- Pearl's index indicates: (PGI June 05)
  - Malnutrition
  - Population
  - Contraceptive failure
  - LBW
  - IUGR
- Contraceptive methods with failure rate <5: (Neet Pattern)
  - Copper - T
  - Vaginal sponge
  - Condom
  - OCP
  - Tubectomy
- Reversible methods of contraception are: (PGI June 05)
  - Female sterilization
  - OCP
  - IUCD
  - Barrier
  - Depot injection
- Date of birth of billionth baby is: (Neet Pattern)
  - May 11, 2011
  - May 11, 2000
  - April 11, 2000
  - April 11, 2011

## Natural methods of family planning

- Which natural family planning method is based on ogino knauss theory: (Neet Pattern)
  - BBT method
  - Rhythm method
  - Lactational anorrhea
  - Withdrawl method
- Which of the following statements about calendar method (Rhythm method) is false: (Neet Pattern)
  - Abstinence is needed for only a few days in a month
  - It is associated with no costs
  - Safe period can also be observed using temperature rhythm or mucous method
  - Ectopic pregnancy is a reported complication of calendar method
- Rise in body temperature after ovulation is due to: (Neet Pattern)
  - Estrogen
  - Progesterone
  - LH
  - FSH
- Billing's method of contraception refers to: (UPSC 99)
  - Monitoring BBT
  - Cervical mucus method
  - Rhythm method
  - Coitus interruptus method

## Barrier methods

- Not a barrier contraceptive: (UP 2008)
  - Diaphragm
  - Centchroman
  - Condom
  - Today

11. Which one of the following is not a correct statement regarding the use of condom: (UPSC 07)
- Air should be squeezed out of tip
  - It should be tested by inflating
  - It should be unrolled on erect penis
  - K-Y jelly may be used for lubrication
12. Which one of the following is the most common problem associated with the use of condom: (UPSC 02)
- Increased monilial infection of vagina
  - Premature ejaculation
  - Contact dermatitis
  - Retention of urine
13. All are contraindications of diaphragm except: (UP 05)
- Multiple sex partners
  - Recurrent UTI
  - Uterine prolapse
  - Herpes vaginitis
14. Contraceptive vaginal foam tablet "today" contains:
- Nonoxynol 9
  - Octoxynol 9
  - Menfegol
  - None of the above
15. Spermicidal jelly acts through: (AIIMS Dec 98)
- Acrosomal enzyme
  - Cervical enzyme alteration
  - Glucose uptake inhibition by sperms
  - Disruption of cell membrane
16. Spermicidal agents are: (PGI June 06)
- Nonoxynol
  - Menfegol
  - Progestasert

## OCPs

17. All of the following mechanisms of action of oral contraceptive pills are true, except: (AI 06)
- Inhibition of ovulation
  - Prevention of fertilization
  - Interference with implantation of fertilized ovum
  - Interference with placental functioning

## Composition

### 18. Version I

Amount of estrogen in low dose oral contraceptive pills: (AIIMS Nov 01)

- 30 µg
- 40 µg
- 50 µg
- 20 µg

### Version II

Minimum effective dose of ethinyl estradiol in combination oral pills is: (AIIMS May 04)

- 20 µg
- 35 µg
- 50 µg
- 75 µg

### 19. Low dose OCP's contain:

- Levonorgestrel
- Desogestrel
- Norgestrel
- Norethisterone

20. Third generation oral contraceptive pills containing norgestimate and gestodene along with estrogens:
- Are more lipid friendly
  - Decreases the risk of venous thromboembolism
  - Increase the risk of breakthrough bleeding
  - Are not used for emergency contraception
21. Norgestimate OCP's have the following advantage except:
- Reduces venous thrombosis
  - Is cheaper than standard OCP's
  - Reduces acne and hirsutism
  - Useful in heart disease
22. The progesterone component of OCP acts by:
- Preventing ovulation
  - Inhibiting implantation
  - Bringing about alterations in cervical mucus
  - All of the above
23. Amount of estrogen in Mala D is: (UP 00)
- 30 µg
  - 50 µg
  - 10 µg
  - 80 µg
24. Which of the following OCP's have the least amount of estrogen:
- Mala N
  - Triquilar
  - Femilon
  - Novelon

## Benefits of OCP's

25. Oral contraceptive pills decrease incidence of all of the following conditions except: (AI 99)
- Salpingitis
  - Hepatic adenoma
  - Ovary CA
  - Fibroadenosis
26. Use of OCP's are known to protect against following malignancies except: (AIIMS Nov 02)
- Ovarian carcinoma
  - Endometrial carcinoma
  - Uterine sarcoma
  - Carcinoma cervix
27. Use of oral contraceptives decreases the incidence of all of the following except: (AIIMS May 05)
- Ectopic pregnancy
  - Epithelial ovarian malignancy
  - Hepatic adenoma
  - Pelvic inflammatory disease
28. Non contraceptive use of OCPs are all except: (AI 07)
- Ca endometrium
  - Ca breast
  - Rheumatoid arthritis
  - Endometriosis
29. OCP gives protection against following cancers: (PGI June 06)
- Endometrial
  - Ovary
  - Cervix
  - Breast
  - Liver

## Side Effects of OCPs

30. OCP's cause all except: (AIIMS Dec 98)
- Dysmenorrhea
  - Mastalgia
  - Nausea
  - Chloasma

31. Adverse effects combined OCPs: (PGI Dec 09)  
 a. Liver disorders  
 b. PID  
 c. Weight gain  
 d. Acne  
 e. Endometriosis
32. OCP's intake causes all Except: (AIIMS June 98)  
 a. Decreased risk of ovarian tumour  
 b. Increased risk of fibroadenosis  
 c. Increased risk of liver adenoma  
 d. Increased risk of fibroadenoma
33. The use of combined OCPs is associated with an increased incidence of: (AIIMS Nov 03)  
 a. Bacterial vaginosis  
 b. Chlamydial endocervicitis  
 c. Vaginal warts  
 d. Genital herpes

### Contraindications of OCPs

34. In a young female of reproductive age an absolute contraindication for prescribing OCP's is: (AIIMS May 05)  
 a. Diabetes  
 b. Hypertension  
 c. Obesity  
 d. Impaired liver function
35. Absolute contraindication of OCP's is: (PGI June 02)  
 a. Breast cancer  
 b. Mentally ill  
 c. Migraine  
 d. Fibroid  
 e. Hyperlipidemia
36. Contraindications to OC pills: (PGI June 01)  
 a. Heart disease  
 b. Uterine malformations  
 c. Menorrhagia  
 d. Liver failure  
 e. Epilepsy
37. OCP's are contraindicated in all except: (PGI Dec 99)  
 a. Smoking 35 years  
 b. Coronary occlusion  
 c. Polycystic ovarian disease  
 d. Cerebrovascular disease
38. OCP's intake cause psychiatric symptoms, and abdominal pain. Diagnosis is: (PGI Dec 98)  
 a. Acute intermittent porphyria  
 b. Systemic lupus  
 c. Thrombosis  
 d. Anemia

### Drug Interaction

39. A 20-years old nulliparous women is on oral contraceptives pills. She is currently diagnosed as having pulmonary tuberculosis. Which anti-tubercular drug decreases the effect of OCP: (AIIMS May 01)  
 a. INH  
 b. Pyrazinamide  
 c. Ethambutol  
 d. Rifampicin
40. OCP's efficiency is reduced by simultaneous use of: (PGI Dec 98)  
 a. Rifampicin  
 b. Carbamazepine  
 c. Propranolol  
 d. Tricyclic antidepressants

41. OCPs are C/I in pts receiving: (AIIMS Nov 07)  
 a. Rifampicin  
 b. Ethambutol  
 c. Streptomycin  
 d. Pyrazinamide
42. Hypokalemic paralysis is a side effect of:  
 a. Gossypol  
 b. DMPA  
 c. Testosterone enanthate  
 d. Cyproterone acetate

### Progesterone only Pills/Implants/Injections

43. Newer progestational contraceptives primarily act by: (AIIMS May 03)  
 a. Oviductal motility  
 b. Uterine endometrium  
 c. Cervix  
 d. Inhibiting ovulation
44. True statement about Minipill is: (AI 99)  
 a. Irregular vaginal bleeding may be a side effect  
 b. Used in with combination with oral contraceptive pills  
 c. Cannot be used in lactation  
 d. Prevents ectopic pregnancy
45. DMPA-True: (PGI Dec 09)  
 a. Failure @ 0.3/100 WY  
 b. 150 mg/3 monthly delivered  
 c. Weight gain  
 d. Glucose intolerance occur  
 e. Anemia improves
46. True regarding DMPA including the following except: (AI 09)  
 a. 3% failure rate  
 b. Does not have protective effect on Ca endometrium  
 c. Can be given in seizures  
 d. Useful in treatment of menorrhagia
47. Side effect of depot MPA are all, EXCEPT: (AI 00)  
 a. Weight gain  
 b. Irregular bleeding  
 c. Amenorrhea  
 d. Hepatitis
48. To avoid contraception, DMPA is given: (HP 05)  
 a. Monthly  
 b. 3 Monthly  
 c. 6 Monthly  
 d. Yearly
49. Characteristic problem in females taking nor-ethisterone is: (AI 00)  
 a. Irregular bleeding  
 b. Thromboembolism  
 c. Hirsutism  
 d. Weight gain
50. In a woman on subdermal progesterone implant, the menstrual abnormality seen is: (AIIMS May 01)  
 a. Menorrhagia  
 b. Metrorrhagia  
 c. Polymenorrhagia  
 d. Amenorrhea
51. Mirena is: (AIIMS May 05)  
 a. Used in abortions  
 b. Antiprogestosterone  
 c. Progesterone IUCD  
 d. Hormonal implant

52. Use of Levo-Norgestrel releasing, IUCD is helpful in all of the following conditions except: (AIIMS Nov 02)
- Menorrhagia
  - Dysmenorrhea
  - Premenstrual symptoms
  - Pelvic inflammatory disease
53. Benefits of LNG IUCD: (PGI Dec 09)
- Endometriosis
  - Fibroid uterus
  - PID
  - Contraception
  - Extauterine endometriosis
54. True about Mirena: (PGI Nov 2012)
- Progesterone containing IUCD
  - Contain desogestrol
  - Causes endometrial hyperplasia
  - Decreases menstrual blood flow
55. Which of the following statements is incorrect regarding levonorgestrel releasing intrauterine contraceptive devices: (AI 06)
- There is increased incidence of menorrhagia
  - This system can be used as hormone replacement therapy
  - This method is useful for the treatment of endometrial hyperplasia
  - Irregular uterine bleeding can be a problem initially
56. All of the following mechanisms might account for a reduce-risk of upper genital tract infection in users of progestin – releasing IUDs, except: (AI 06)
- Reduced retrograde menstruation
  - Decreased ovulation
  - Thickened cervical mucus
  - Decidual changes in the endometrium
57. Contraceptive LNG-IUD (levonorgestrel intra-uterine device) has the cumulative pregnancy rate at 5 years of:
- 0.5
  - 1.0
  - 1.5
  - 2.0

## IUCDs

58. Characteristics of an ideal candidate for copper-T insertion include all of the following except: (AIIMS May 05)
- Has born at least one child
  - Is willing to check IUD tail
  - Has a history of ectopic pregnancy
  - Has normal menstrual periods
59. Mechanism by which IUCD does not act: (AIIMS Dec 98)
- Chronic endometrial inflammation
  - Increase the motility of tubes
  - Inducing endometrial atrophy
  - Inhibition of ovulation
60. All IUCD's are changed every 4–5 year except: (AIIMS Dec 97)
- Cu 280
  - Cu 320
  - Multiload devices
  - Progestasert
61. Among of following IUCD's which has life span for 10 years:
- CuT380A
  - CuT200
  - Nova T
  - Multiload
62. Composition of Nova - T: (PGI June 05)
- Copper and silver
  - Copper and aluminium
  - Copper only
  - Copper and selenium
  - Copper and molybdenum
63. A lady with IUCD becomes pregnant with tail of IUCD being seen, next course of action is: (PGI Dec 98)
- MTP
  - Remove the IUCD
  - Continue the pregnancy
  - Remove IUCD and terminate pregnancy
64. An intrauterine pregnancy of approximately 10 weeks gestation is confirmed in a 30 year old, gravida 5, para 4 woman with an IUD in place. The patient expresses a strong desire for the pregnancy to be continued. On examination, the string of the IUD is noted to be protruding from the cervical os. The most appropriate course of action is to:
- Leave the IUD in place without any other treatment
  - Remove the IUD to decrease the risk of malformations
  - Remove the IUD to decrease the risk of infection
  - Terminate the pregnancy because of the high risk of malformations.
65. A 28-year-old P1L1 had Cu T inserted 2 years back, on examination Cu T threads are not seen. USG shows Cu T partly in abdominal cavity. Method of removal is:
- Hysteroscopy
  - No need of removal (wait and watch)
  - IUCD hook
  - Laparoscopy
66. Absolute contraindication for IUCD includes all of the following except: (AI 97)
- Undiagnosed vaginal bleeding
  - Suspected pregnancy
  - Congenital malformation of uterus
  - PID
67. Absolute contraindication of IUCD is: (AIIMS Dec 97)
- Endometriosis
  - Iron deficiency anemia
  - Dysmenorrhea
  - Pelvic tuberculosis
68. Contraindications of IUCD:
- Undiagnosed vaginal bleeding
  - PID
  - Smoking
  - Obesity
  - Diabetes
69. Contraindication of IUCD: (PGI Dec 04)
- Oligomenorrhea
  - PID
  - Uterine malformation
  - Controlled diabetes
  - Previous cesarean section
70. Contraindication of IUCD: (PGI Dec 04)
- Oligomenorrhea
  - PID
  - Uterine malformation
  - Controlled diabetes.
  - Previous ectopic pregnancy

71. The most common complication of IUCD is: (AI 95)  
 a. Ectopic pregnancy    b. Bleeding  
 c. Backache              d. Cervical stenosis

### Emergency Contraception

72. Emergency contraception prevents pregnancy by all of the following mechanisms, except: (AI 06)  
 a. Delaying/inhibiting ovulation  
 b. Inhibiting fertilization  
 c. Preventing implantation of the fertilized egg  
 d. Interrupting an early pregnancy
73. Emergency contraception is required in: (AIIMS Nov 99)  
 a. Partner not willing to use any contraceptive  
 b. In emergency, where sexual intercourse is done in camps in emergency like floods  
 c. Contraception failure  
 d. Unprotected sex
74. Drugs used in emergency contraception are all except: (PGI Dec 06)  
 a. Levonorgestrel              b. Estrogen + progesterone  
 c. Danazol                      d. Mifepristone  
 e. Misoprostol
75. Which is not an emergency contraceptive: (PGI Nov 2012)  
 a. Combined oral pills    b. Estrogen  
 c. Desogestrel              d. Levonorgestrel  
 e. Medoxy progesterone acetate
76. Emergency contraceptive of choice is: (PGI Dec 09)  
 a. OCP                          b. Danazol  
 c. Levonorgestrel            d. Mifepristone
77. Emergency contraceptives are effective if administered within following period after unprotected intercourse: (AIIMS May 04)  
 a. 24 hours                      b. 48 hours  
 c. 72 hours                      d. 120 hours

### Permanent Method

78. Permanent sterilization is all except? (PGI Dec 05)  
 a. Electrocoagulation    b. Vasectomy  
 c. Clipping                    d. Tube ligation  
 e. Medoxy progesterone
79. Which of the following is not an abdominal laparoscopic technique for tubal ligation?  
 a. Pomeroy                      b. Parkland  
 c. Essure                        d. Irving
80. Method of sterilization which is least effective is: (AIIMS Dec 98)  
 a. Pomeroy's technique  
 b. Laparoscopy  
 c. Vaginal fimbriectomy  
 d. Hysteroscopic tubal occlusion

81. Sterilization procedure with maximum chances of reversal is: (AIIMS May 02)  
 a. Pomeroy's tubal ligation  
 b. Irwing's technique  
 c. Laparoscopic tubal ligation with silastic bands  
 d. Laparoscopic tubal ligation with clips
82. During Pomeroy's method of female sterilization, which portion of the tube is ligated? (UPSC 07)  
 a. Isthmus                      b. Ampullary  
 c. Isthmo-ampullary        d. Cornual
83. Sterilization is commonly performed at which site of fallopian tube: (AI 07)  
 a. Ampulla                      b. Infundibulum  
 c. Isthmus                      d. Cornua
84. Best prognosis for reversibility is seen in: (AI 97)  
 a. Isthmo - isthmic type  
 b. Isthmic - ampullary type  
 c. Ampullary - interstitial type  
 d. Ampullary - fimbrial type
85. Which of the following procedure is associated with maximum chance of recanalization during surgery for reversal of tubal ligation:  
 a. Isthmo-isthmic anastomosis  
 b. Isthmo-ampullary anastomosis  
 c. Ampullo-ampullary anastomosis  
 d. Cornual obstruction
86. All of the following are features of post-tubal ligation syndrome except:  
 a. Abnormal menstrual bleeding  
 b. Dysmenorrhea  
 c. Pelvic pain  
 d. Dysperunia
87. Failure rate of vasectomy is:  
 a. 0.2%                          b. 0.1%  
 c. 3%                              d. 10%
88. A couple is advised to use barrier methods after vasectomy till:  
 a. 3 months                      b. No sperms in ejaculate  
 c. Next 15 ejaculations        d. None of the above

### Contraceptive of Choice

89. Which one of the following is the ideal contraceptive for a patient with heart disease: (AI 05)  
 a. IUCD                          b. Depoprovera  
 c. Diaphragm                  d. Oral contraceptive pills
90. Best mode of contraception for a newly married lady with rheumatic heart disease: (AIIMS Nov 99)  
 a. Oral pills                      b. Norplant  
 c. IUCD                          d. Condom
91. PID occurs least common with: (AI 00)  
 a. OCPs                          b. Condom  
 c. IUCD                          d. Diaphragm
92. Ideal contraceptive for newly married couple is: (AIIMS May 2011)  
 a. Barrier method              b. Combined OCP  
 c. IUCD                          d. Progesterone only pill

93. Ideal contraceptive for a couple living in different cities meeting only occasionally: (AIIMS May 2011)
- Barrier method
  - IUCD
  - OCP
  - DMPA
94. Ideal contraceptive for lactating mother is: (AIIMS May 2011)
- Barrier method
  - Combined OCP
  - Lactational amenorrhoea
  - Progesterone only pill
95. Peritoneum is opened in all of the following sterilization procedures except: (AP 97)
- Mini lap
  - Laparoscopy
  - Vasectomy
  - Transvaginal tubectomy
96. Contraceptive to be avoided in epilepsy: (AIIMS May 2011)
- OCP
  - Condom
  - IUCD
  - Mirena

### NEW PATTERN QUESTIONS

97. The following are true related with regards to vasectomy except
- Leads to immediate sterility
  - Failure rate is 0.1%
  - Involves ligation and division of spermatic cord
  - Partner (wife may be given DMPA for 3 months)
98. The following are the contraindications of tubal reconstructive surgery except
- Length of tube <4 cms
  - Patients over 30 years of age
  - Pelvic tuberculosis
  - Reversal done after 5 years of sterilization
99. The intra-abdominal pressure during laparoscopy should be set between:
- 5–8 mm Hg
  - 10–15 mm Hg
  - 20–25 mm Hg
  - 30–35 mm Hg
100. A 30-year-old P<sub>1</sub>L<sub>1</sub> wants contraception for 6 months. She has dhymenorrhoea and is a known case of complicated migraine. On USG, uterus has multiple fibroids. Contraception of choice is:
- Cu T 200
  - OC pills
  - Vaginal diaphragm
  - Tubal sterilization
101. A 28-year-old P<sub>1</sub>L<sub>1</sub> had Cu T inserted 2 years back. O/E-Cu-T threads are not seen. USG shows Cu T partly in abdominal cavity. Method of removal is:
- Hysteroscopy
  - No need removal (wait and watch)
  - IUCD hook
  - Laparoscopy
102. All of the following are contraceptive implants except:
- Norplant
  - Implanon
  - Jadelle
  - Mesigyna
103. Least failure in sterilization occurs with:
- Falope ring
  - Bipolar cautery
  - Unipolar cauterisation
  - Hulka clip
104. All of the following are LARC methods except:
- IUCD
  - DMPA
  - POPs
  - Implanon
105. Preferred method of contraception in family for a female with H/O ovarian cancer:
- POP
  - Cu IUCD
  - OCP
  - Barrier method

## ANSWERS TO FIGURE BASED QUESTIONS

F1. Ans. is c, i.e. A single patch to be used for 1 week

Ref. Textbook of Gynae, Sheila Balakrishnan pg 352

The figure shows transdermal patch-orthoevra.

This is a combination transdermal patch delivering norelgestromin and ethinyl oestradiol and is not yet available in India. The patch has a surface area of 20 cu. cm and delivers a daily dose of 150 µg of norelgestromin and 20 µg of ethinyl estradiol. It can be worn for 7 days. Hence three patches are used for three weeks with a patch-free interval in the fourth week. The contraindications and side effects are similar to the COC. Good cycle control is there. The major advantage compared to the COC is that compliance is better. The disadvantage is patch detachment.

F2. Ans. is b, i.e. Is performed using permanent suture.

Ref. Textbook of Gynae, Sheila Balakrishnan pg 365

**Pomeroy method:** It is a method for performing abdominal sterilization in females. A loop is formed 2 cm lateral to the uterine fundus. Avoiding the blood vessels, a round-bodied needle with 0 chromic catgut is passed through the mesosalpinx. The base of the loop is tied leaving about 2 cm of loop above the tie. Then about 1.5 cm of the loop is removed. The stumps are carefully inspected to ensure haemostasis. The rationale of the procedure is that sine catgut suture is used, there will be prompt absorption of the ligature and subsequent separation of the cut ends. This will reduce the chance of failure. Hence, permanent suture material should not be used.

## ANSWERS

## General

1. Ans. is a, i.e. No. of accidental pregnancies × 1200/No. of patients observed × months of use

2. Ans. is c, i.e. Contraceptive failure

Ref. Dutta Obs. 6<sup>th</sup>/ed pp 531-532

**Pearl index indicates the effectiveness of a contraceptive or is an index of contraception failure.**

- It is expressed in terms of "failure rate per hundred women - years of exposure (HWY)".
- Failure rate per HWY = 
$$\frac{\text{Total accidental pregnancies} \times 1200 (12 \times 100)}{\text{No. of patients observed} \times \text{months of use}}$$
- In applying the above formula the following points must be kept in mind:
  - a. The total accidental pregnancies shown in the numerator must include every known conception, whatever its outcome.
  - b. The factor 1200 is the number of months in 100 years.
  - c. The total months of exposure in the denominator is obtained by deducing from the period under review of 10 months for a full term pregnancy and 4 months for an abortion.

3. Ans. is a, d and e, i.e. Copper-T; OCP, and Tubectomy

Ref. Dutta Gynae 6<sup>th</sup>/ed p 476

See the text for explanation.

4. Ans. is b, c, d and e, i.e. OCP; IUCD; Barrier, and Depot injection

Ref. Dutta Obs 6<sup>th</sup>/ed p 532; Park 20<sup>th</sup>/ed p 424

Methods of contraception (can be classified as)	
<p><b>Temporary methods</b> (used to postpone pregnancy or space births)</p> <ul style="list-style-type: none"> <li>• <b>Barrier method<sup>o</sup></b></li> <li>• <b>Natural contraception<sup>o</sup></b></li> <li>• <b>Oral contraceptive pills</b></li> <li>• <b>Injectables</b></li> <li>• <b>Implants</b></li> <li>• <b>Devices like IUCD's</b> Levonorgestrel IUCD's</li> </ul>	<p><b>Permanent methods</b> (Surgical methods aim is to purposefully and permanently destroy the Reproductive capacity of an individual)</p> <div style="text-align: center;"> <pre> graph TD     A[Permanent method] --&gt; B[In female]     A --&gt; C[In male]     B --&gt; D[Tubectomy]     C --&gt; E[Vasectomy]           </pre> </div>

5. Ans. is b, i.e. May 11, 2000 Ref. internet search

Billionth child was born in India on May 11,2000.

## Natural Methods of Family Planning

6. Ans. is b, i.e. Rhythm Method

7. Ans. a, i.e. Abstinence is needed for only a few days in a month

8. **Ans. is b, i.e. Progesterone**

9. **Ans. is b, i.e. Cervical mucus method**

*Ref. Dutta obs 6<sup>th</sup>/ed p 534, Park 20<sup>th</sup>/ed pp 436, 4437; Textbook of Gynaecology sheila Balakrishnan 1<sup>st</sup>/ed pp 362-363*

Discussed in preceeding text in detail

## Barrier Methods

10. **Ans. is b, i.e. Centchroman**

*Ref. Shaw 15<sup>th</sup>/ed p 222*

### Barrier Methods include-

- Condoms (for male use)
- Diaphragms (for female use) – **Types**
  1. Femshield (female condom)
  2. Today contraceptive/vaginal sponge
  3. Vaginal diaphragm/cervical cap

Besides these spermicidal agents like nonoxynol 9, octoxynol, and menfegol can be added to any of the above barrier contraceptive, to increase its effectiveness.

11. **Ans. is b, i.e. It should be tested by inflating**

*Ref. Practice of Fertility Control S.K. Chaudhari 6<sup>th</sup>/ed p 82; Leon Speroff 7<sup>th</sup>/ed p 998*

12. **Ans. is c, i.e. Contact dermatitis**

*Ref. Shaw 14<sup>th</sup>/ed p 202*

### Directions for use of condom

- The condom should be put on by unrolling it over the erect penis after pulling back the foreskin, before there is any contact between the male and female organs. An airfree space should be left by squeezing the tip and holding it up, till it is unrolled fully for better collection of semen.
- It should be used only once.
- It should not be inflated for testing.
- Vaseline oils, skin lotions, cold creams, should not be used as they increase the chance of rupture. If lubrication is needed, glycerine, K-Y jelly or spermicidal jelly can be used.
- Soon after discharge, the male should withdraw the penis holding the condom firmly against his body
- To increase the effectiveness, a dose of spermicidal jelly or foam tablet may be used at the same time. In case of breakage, slippage, or defective use, women should report or use emergency contraceptive within 72 hours and a spermicidal agent should be quickly inserted into the vagina.

### Advantages of condom

- Condoms gives very good protection against STDs. These includes syphilis gonorrhoea, trichomoniasis, moniliasis, nongonococcal urethritis, and infection with Chlamydia and Herpes virus.
- They are the only contraceptives to protect against HIV and against sexually transmitted hepatitis B Virus.
- Condoms reduce the chances of developing cervical dysplasia and cancer cervix (by preventing HPV infection)

### Disadvantages

It can lead to contact dermatitis in female partners.

Failure rate 12%

13. **Ans. is a, i.e. Multiple sex partners**

*Ref. Shaw 15<sup>th</sup>/ed p 225*

*Occlusive caps (vaginal diaphragm and cervical cap) –*

Occlusive caps donot act as sperm proof mechanical barriers like condoms but are used as a means to retain spermicides in contact with cervical os, so spermicides must be used along with these devices.

### Contraindications to the use of diaphragm

- Prolapse, cystocele, rectocele
- Retroversion
- VVF/RVF
- Badly eroded or lacerated cervix
- Recurrent UTI

Multiple sex partners is not a C/I for the use of diaphragms, rather barrier contraceptives protect against STD's so are contraception of choice in them.

14. **Ans. is a, i.e. Nonoxynol 9**

*Ref. shaw 14<sup>th</sup>/ed p 203*

**TODAY:** It contains 1 gm of NONOX Y NOL-9



## 15. Ans. is d, i.e. Disruption of cell membrane

Ref. Current Concepts in Contraception and Women Health by Jaypee Publication p 32

## 16. Ans. is a and b, i.e. Nonoxynol, and Menfegol Spermicides

Ref. Shaw 15<sup>th</sup>/ed p 224

*"Spermicides are contraceptive chemical agents. They comprise of a chemical capable of destroying sperm, incorporated into an inert base. The commonly used spermicidal agents contain nonionic surfactants which alter sperm surface membrane permeability, causing osmotic changes resulting in killing of sperm. Most of the spermicides contain nonoxynol-9 which is the best for this purpose."*

Ref. Current Concepts in Contraception and Women Health by Jaypee Publication p 32

- Spermicidal agents kill the sperms before it enters to the cervical canal. They are available as foam tablets, soluble pessaries, creams, jellies, or as films.
- Contents are:
 

- Nonoxynol - 9 (N - 9)	- Octoxynol
- Menfegol	- Enzyme inhibiting agents
- Benzalkonium chloride.	
- Failure rate is 20–25 WY 100 woman years when used alone. When used in conjunction with a mechanical barrier, they give a reliable contraceptive effect.

– Jeffcoates 7<sup>th</sup>/ed p 794

**Note:**

- Recent evidences indicate spermicides are not effective in preventing cervical gonorrhoea, Chlamydia or HIV infection. In addition, frequent use of spermicides containing N-9 has been associated with an increased risk of HIV transmission.
- Advantage 24 is a new contraceptive gel which contains nonoxynol.

– CGDT 10<sup>th</sup>/ed p 581

**OCPs**

## 17. Ans. is d, i.e. Interference with placental functioning

Ref. KDT 6<sup>th</sup>/ed pp 314-315

Friends, even if we don't know the mechanisms by which OCP's act, by sheer common sense we know that **"Interference with placental functioning"** is the incorrect option as if placenta is formed it means pregnancy is occurring which in itself is incorrect with regard to OCP's (as OCP's are used to prevent conception).

**The mechanism of action of OCP's has been discussed in detail in text.**

**In brief:**

- Main mechanism of action of combined pills is - prevention of ovulation.
- Combined pills act by decreasing both LH and FSH
- They do not interfere with placental functioning.
- When taken daily for 3 out of 4 weeks, they provide virtually absolute protection against conception.

**Composition**

## 18. Version I

Ans. is a, i.e. 30 µg

Ref. Dutta Obs. 6<sup>th</sup>/ed p 543; Novak 14<sup>th</sup>/ed pp 268, 277

## Version II

Ans. is a, i.e. 20 µg

Ref. Dutta Obs. 6<sup>th</sup>/ed p 542; Shaw 15<sup>th</sup>/ed p 231

Friends, I had a tough time in finding answers to these questions.

*"Low dose pills have estrogen less than 50 mcg."*

– Dutta Obs 6<sup>th</sup>/ed p 543

But it does not specify how much estrogen

*"The low dose OCP (estrogen 30–35 mg EE) reduces the risk for a thromboembolic event when compared with higher dose (50 mg estrogen) OCs."*

– Novak 13<sup>th</sup>/ed p 251, 14<sup>th</sup>/ed p 268

It further says (Novak 14<sup>th</sup>/ed p 277) *"For the average patient, the first choice of preparation for contraceptive purposes is a low estrogen OCP (20–35 µg EE) or a very low estrogen OC (20 µg EE)"*.

So, from here it can be concluded that low dose OCP's are those pills with estrogen < 50 mcg (Normally 35 mcg). Very low dose OCPs are those pills with estrogen ≤ 20 µg EE.

My answer of choice for low dose OCPs is 30 µg.

Newer OCPs like femilon are a type of very low dose OCP's with estrogen = 20–30 or 35 µg of EE

**Version II**

*"Intensive pharmacological research clinical trials conducted to minimise the adverse effects of estrogen without reducing the contraceptive efficacy, resulted in lowering the dose of oestrogen to a minimum of 20 µg or even 15 µg."*

– Dutta Obs 6<sup>th</sup>/ed p 542

Thus, Remember –Low dose OCPs have estrogen = less than 50 mcg (30-35 mcg usually)

Very low dose OCPs have estrogen = 20 mcg

Minimum effective dose of Estrogen = 10 mcg

19. **Ans. is b, i.e. Desogestrel** *Ref. Reffcoate 7<sup>th</sup>/ed p 802, Dutta Gynae 6<sup>th</sup>/ed p 465; SK Chaudhary 7<sup>th</sup>/ed pp 120-130*

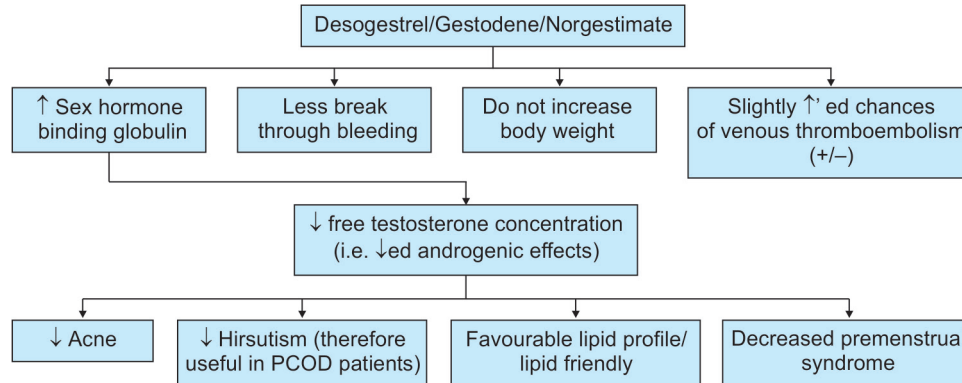
Low dose OCPs on 3rd generation OCP have desogestrel

20. **Ans. is a, i.e. Are more lipid friendly**

21. **Ans. is a, i.e. Reduces venous thrombosis**

*Ref. Lawrence 9<sup>th</sup>/ed pp 723-725*

**Remember**



22. **Ans. is d, i.e. all of the above**

*Ref. SK Chaudhary 7<sup>th</sup>/ed pp 125-126, 14.*

Actions of the progesterone component of combined oral contraceptives:

- Suppresses ovulation by its inhibitory action on the pituitary and the hypothalamus. This is predominantly achieved by estrogens but even by progesterone.
- Causes atrophic changes in the endometrium and prevents nidation even if fertilization occurs.
- Acts on the cervical mucus, making it thick and tenacious and impenetrable by sperms.

The third-generation progestogens have a higher affinity for progesterone receptor and have a role in inhibiting ovulation. The main function of progestogens in combined pills is, to counteract the undesirable effects of estrogen such as endometrial hyperplasia and heavy withdrawal bleeding.

23. **Ans. is a, i.e. 30 µg**

*Ref. Dutta Obs 6<sup>th</sup>/ed p 543*

24. **Ans. is c, i.e. Femilon**

Commercial name	Composition Progestin (mg)	Estrogen (µg)
1. Mala N (Distributed free of cost by govt. of India)	Levo norgestrel 0.15	Ethinyl estradiol 30
2. Mala D	D-levo Norgestrel 0.15	Ethinyl estradiol 30
3. Femilon	Desogestrel 0.15	Ethinyl estradiol 20
4. Loette	Levonorgestrel 0.1 mg	Ethinyl estradiol 20
– Eg's of very low dose OCP'S are femilon and Loette		
– Triphasic/Triquilar		
	Days ----->	
	1.6	7-11
	12-21 day	
Contain	EE 30µg	40µg
	+	30µg
	LNG 50µg	70µg
		125µg

## Benefits of OCPs

25. **Ans. is b, i.e. Hepatic adenoma**

*Ref. Shaw 15<sup>th</sup>/ed pp 231-232; Dutta Obs 6<sup>th</sup>/ed p 545; Harrison 17<sup>th</sup>/ed p 563*

Friends, it is absolutely essential to mug up the benefits, side effects and contraindications of OCPs.

Many questions are framed from these topics.

**Here, I am repeating the list of Non-contraceptive benefits of OCPs:**

**Cancers/cysts**

- Uterine cancer
- Ovarian cancers<sup>Q</sup>
- Fibroid uterus (Progesterone only pills)
- Ovarian cysts<sup>Q</sup>
- Benign breast diseases<sup>Q</sup>

**Benign disease of genital tract**

- Endometriosis (if used conterously)
- **PID (here Salpingitis)**<sup>Q</sup>
- Ectopic pregnancy (as it decreases incidence of PID)

**They decrease ovulation thus, are helpful in**

- Dysmenorrhea, premenstrual tension and Mittleschmerz syndrome.
- **By decreasing blood loss they are helpful in menorrhagia and polymenorrhea.**
- Acne and hirsutism (especially those containing desogesterel)

**OCPs are also beneficial in:**

– Leon Speroff 7<sup>th</sup>/ed p 914

- DUB
- Hormone therapy for hypothalamic amenorrhea
- Prevention of menstrual porphyria.

26. Ans. is d, i.e. Carcinoma cervix

Ref. Dutta Obs 6<sup>th</sup>/ed p 545; Shaw 14<sup>th</sup>/ed p 208; Harrison 17<sup>th</sup>/ed p 563

27. Ans. is c, i.e. Hepatic adenoma

28. Ans. is b, i.e. Ca breast

29. Ans. is a and b, i.e. Endometrial, and Ovary

Friends, in the previous question I have given a list of conditions in which OCP's are beneficial. Here I would like to mention in brief.

OCPs	
Tumors associated	Provides protection
<ul style="list-style-type: none"> <li>• Cervical cancer</li> <li>• Hepatic cancer</li> <li>• Pituitary adenoma</li> <li>• Breast cancer +/-</li> </ul>	<ul style="list-style-type: none"> <li>• Ovarian tumors/cysts</li> <li>• Uterine tumor</li> <li>• Benign breast disease</li> </ul>

OCP's are protective against benign breast diseases, but as far as carcinoma breast is concerned their role is controversial. OCP's are considered in the etiology of Ca breast.

*"The most credible metanalysis of oral contraceptive use suggest that these agents cause little if any increased risk of breast cancer. By contrast, oral contraceptives offer a substantial protective effect against ovarian epithelial tumors and endometrial cancer."* – Harrison

**Side Effects of OCPs**

30. Ans. is a, i.e. Dysmenorrhea

Ref. KDT 6<sup>th</sup>/ed p 315; Jeffcoate 7<sup>th</sup>/ed p 804

31. Ans. is a and c, i.e. Liver disorders, and Weight gain

32. Ans. is b and d, i.e. Increased risk of fibroadenosis, and Increased risk of fibroadenoma

Ref. Dutta Obs 6<sup>th</sup>/ed p 545; Shaw 14<sup>th</sup>/ed p 208

OCP's have antiovlatory effect and by virtue of this property, relieve dysmenorrhea (rather than causing it), premenstrual tension and Mittleschmerz syndrome.

**Side effects of OCPs are:**

Nonserious side effects	Side effects which appear later	Serious side effects
<ul style="list-style-type: none"> <li>• Nausea, vomiting</li> <li>• Headache (Migrane may be precipitated)</li> <li>• Break through bleeding<sup>Q</sup>/spotting<sup>Q</sup>/amenorrhea</li> <li>• Breast discomfort/<b>Mastalgia</b><sup>Q</sup></li> </ul>	<ul style="list-style-type: none"> <li>• <b>Weight gain</b></li> <li>• <b>Chloasma</b></li> <li>• Pruritis vulva</li> <li>• Carbohydrate intolerance</li> <li>• Mood swing</li> <li>• Abdominal distension<sup>Q</sup></li> <li>• Monilial Vaginitis<sup>Q</sup></li> <li>• Corneal edema and irritation</li> </ul>	<ul style="list-style-type: none"> <li>• Leg vein/Pulmonary Thrombosis<sup>Q</sup></li> <li>• Coronary Artery<sup>Q</sup></li> <li>• Cerebral Artery Thrombosis<sup>Q</sup></li> <li>• Hypertension</li> <li>• Increased MI and stroke<sup>Q</sup></li> <li>• Cholestatic Jaundice<sup>Q</sup> and Gall bladder stone<sup>Q</sup></li> </ul>

**Cancers related to OCP use:**

- Carcinoma cervix<sup>Q</sup>
- Hepatic adenoma<sup>Q</sup>
- Pituitary adenoma (+/-)<sup>Q</sup>
- Breast cancer (+/-)<sup>Q</sup>

**Note:**

- OCPs are protective against STDs
- OCPs are protective against PID

*"The risk of hospitalization for PID is reduced by approximately 50–60% but at least 12 months of use are necessary and the protection is limited to current use."*

– Leon Speroff 7<sup>th</sup>/ed p 905

- At present time, no known association exist between oral contraception and viral sexually transmitted infections.

33. **Ans. is b, i.e. Chlamydial endocervicitis** Ref. Novak 14<sup>th</sup>/ed p 275; CGDT 9<sup>th</sup>/ed p 727; Leon Speroff 7<sup>th</sup>/ed pp 904-905  
This is a **tricky question** as some believe **Option "b"** i.e. chlamydial endocervicitis should be the answer while others believe Option "c" i.e. vaginal warts should be concerned. As far as candidial (monilial) vaginitis is concerned, OCP's use increase their incidence.

But for Chlamydial infections: CGDT 9<sup>th</sup>/ed p 727 says:

*"Persons who use barrier contraception are less frequently infected by C. trachomatis than those who use no contraception, and women who use oral contraceptives may have a higher incidence of cervical infection than women not using oral contraceptives".*

**As if replying to CGDT Novak 13<sup>th</sup>/ed p 259; 14<sup>th</sup>/ed p 275 says:**

*"Chlamydial colonization of the cervix appears more likely in OC users than in non users, but despite this, there is a 40–50% reduction in risk for Chlamydial PID"*

I then had to confirm the answer from *Clinical gynaecologic endocrinology and Infertility 7<sup>th</sup>/ed by Leon Speroff* (It is the most authentic and reliable book for all problems related to Endocrinology, Contraception and Infertility)

*"Fifteen of the Seventeen published studies reported a positive association of oral contraception with lower Genital tract infections caused by Chlamydial cervicitis. Because lower genital tract infection are on the rise (now the most prevalent STI in the US) and the rate of hospitalization for PID is also increased, it is worthwhile for both patients and clinicians to be alert for symptoms of cervicitis or salpingitis in women on oral contraceptives who are at high risk of sexually transmitted infections."* – Leon Speroff 7<sup>th</sup>/ed p 905

**As far as HPV infection i.e. Vaginal warts is concerned**

*'The viral sexually transmitted infections (STI's) include HIV, human papilloma virus (HPV), herpes simplex virus (HSV) and hepatitis B (HBV). At the present time, no known associations exist between oral contraception and the viral STI'S'*

– Leon Speroff 7<sup>th</sup>/ed p 904

So, now we can be sure that the answer is Chlamydial endocervicitis.

**Also know:****Infections and Oral contraception:**

Use of OCP is associated with		
Increased risk of infection	Decreased risk of infection	No association with
<ul style="list-style-type: none"> <li>• Candida (Moniliasis)</li> <li>• Chlamydia</li> <li>• Urinary tract infections</li> </ul>	<ul style="list-style-type: none"> <li>• Gonorrhoea<sup>Q</sup></li> <li>• Trichomonas<sup>Q</sup></li> <li>• Bacterial vaginosis</li> </ul>	<ul style="list-style-type: none"> <li>• Viral STI's i.e. HIV<sup>Q</sup>, HPV<sup>Q</sup></li> <li>• Hepatitis B virus</li> <li>• Herpes simplex virus</li> </ul>

**Note:**

- If question says PID and does not specify any organism—Then OCP'S overall not only decrease the incidence of PID but also risk of hospitalisation and severity of the disease is decreased.
- For protection against PID, at least 12 months of continuous use is necessary and this protection is limited only to current users.

**Contraindications of OCPs**

34. **Ans. is d, i.e. Impaired liver function**
35. **Ans. is a, i.e. Breast cancer**
36. **Ans. is a, d and e, i.e. Heart disease; Liver failure, and Epilepsy**
37. **Ans. is c, i.e. Polycystic ovarian disease**

Ref. Leon Speroff 7<sup>th</sup>/ed p 906

**Contraindications of OCPs:**

*Absolute contraindications include:*

- Banks Known or suspected Breast cancer
- Have Severe Hypertriglyceridemia/Hypercholesteremia
- Various (Undiagnosed Abnormal) Vaginal bleeding
- Schemes Smokers over the age of 35 years
- To Thrombophlebitis/Thromboembolic disorders, (present H/O, past H/O, family H/O) Cerebral and Cardiac disease
- Provide Pregnancy
- Home Hypertension (Moderate to severe)
- Loans Markedly Impaired Liver function/infective hepatitis
- During Diabetes mellitus with vascular disease
- May Migraine disease with aura

*For relative contraindications of OCP's: see the preceding text*

Epilepsy is a relative CI for the use of OCP's

38. **Ans. is a, i.e. Acute intermittent Porphyria**

*Ref. Harrison 17<sup>th</sup>/ed p 2439*

Patient taking OCP's and presenting with abdominal pain and psychiatric problem, diagnosis is undoubtedly acute intermittent porphyria as OCP's can precipitate porphyria.

**Some drugs which precipitate porphyria are:**

- Barbiturates
- Meprobamate
- Phenytoin
- Valproic acid
- Griseofulvin
- Synthetic estrogen/progestogen (OCP)
- Alcohol
- Sulfonamide antibiotics
- Gluthemide
- Carbamazepine
- Pyrazolones
- Ergots
- Danazol
- Succinimide

**Drug Interaction**

39. **Ans. is d, i.e. Rifampicin**

40. **Ans. is a and b, i.e. Rifampicin, and Carbamazepine**

41. **Ans. is a, i.e. Rifampicin**

*Ref. KDT 6<sup>th</sup>/ed p 317; Novak 14<sup>th</sup>/ed p 276*

Interactions of OCP's with other Drugs.

**Effect of other drugs on OCP's:**

Drugs reducing the effectiveness of OCP	Drugs which increase the plasma level of steroids of OCP
<ul style="list-style-type: none"> <li>• Rifampicin<sup>o</sup></li> <li>• Carbamazepine<sup>o</sup></li> <li>• Phenytoin</li> <li>• Antifungals like                             <ul style="list-style-type: none"> <li>– Griseofulvin Induce synthesis of cytochrome P450 enzymes in liver.</li> <li>– Ketoconazole</li> <li>– Itraconazole</li> </ul> </li> <li>• Ampicillin Kill gut bacteria and cause hydrolysis of steroid glucuronides in intestine.</li> <li>• Tetracycline</li> </ul>	<ul style="list-style-type: none"> <li>• Ascorbic acid</li> <li>• Acetaminophen</li> </ul>

42. **Ans. is a, i.e. Gossypol**

*Ref. Dutta obs 7<sup>th</sup>/ed p561*

**Gossypol**

- It is a male contraceptive pill which contains–Disequilterpene aldehyd
- Discovered in china from an extract of cottonseed.
- Mechanism of action it inhibits spermatogenesis and decreases epididymal sperm motility.

- Side effect – Hypokalemic paralysis in 1% patients  
Other male hormonal contraceptives:  
Testosterone enanthate injectable  
Testosterone buccalate injectable

### Progesterone only Pills/Implants/Injections

43. Ans. is d, i.e. Inhibiting ovulation Ref. FOGSI Focus-Jan '06 issue-The Modern Pill, Chapter Estrogen Free Pills, p 41;  
Current Concepts in Contraception and Women Health, p 49

FOGSI is Federation of Obstetrics and Gynaecological Societies of India and the highest governing body in Obs and Gynae in India.

Friends, I know this is quite difficult to digest as we have been studying, Progesterone only pills act mainly by causing thickening of cervical mucus.

**But read the question once again:** Here question specifically mentions; “newer progestational pills”.

#### Progesterone only pills

**Mechanism of action of POP's is mainly on cervical mucus –**

*“All Estrogen free pills except the newer desogestrel pill primarily rely on changes in cervical mucus as they do not inhibit ovulation consistently.”*

The cervical mucus effect peaks within 3–4 hours after taking the tablet and lasts for about 22 hours. Hence the next tablet must be taken within 27 hours of the preceding tablet or else the contraceptive benefit of the cervical mucus effect will decrease and finally subside.

- Unlike COC's that almost always prevent ovulation, traditional POP's (progesterone only pills) inhibit ovulation in 40–50% of cycles. *“A randomized double blind study, performed over 13 cycles showed that 75 µg desogestrel daily was sufficient to inhibit ovulation in 97% of cycles. Hence for newer POP's containing desogestrel the primary mode of action is inhibition of ovulation”.*  
FOGSI Focus Jan 06 issue on Modern pill, Chapter Estrogen free pill p 41

**Thus, for newer progestational agents main mechanism of action is by inhibition of ovulation.**

#### Remember

- Traditional POP's are also known as Low-dose progestogen only pills. – Shaw 14<sup>th</sup>/ed p 210
- Main progesterone used are:
  - Norethisterone 350 mcg
  - Norgestrel 75 mcg
  - Levonorgestrel 30 mcg
- Their main mechanism of action (as discussed earlier) is thickening of cervical mucus.<sup>Q</sup>  
They also:
  - Render endometrium unsuitable for implantation
  - Accelerate tubal motility
  - Disturb corpus luteal function.

**A word of caution to all of you out there:** Be careful in reading the question - whether question is on Low dose progestins (Traditional pills) or on newer progestins containing desogestrel.

44. Ans. is a, i.e. Irregular vaginal bleeding may be a side effect Ref. Leon Speroff 7<sup>th</sup>/ed p 922

I have already discussed minipil/progesterone only pill/lactation pill/Estrogen free pill in detail earlier and hence you know minipill can be used during lactation (i.e. *option “c”* is correct).

It is not used in combination with other pills therefore *option “b”* is incorrect.

#### Minipill

*“Ectopic pregnancy is not prevented as effectively as intrauterine pregnancy. Although the overall incidence of ectopic pregnancy is not increased, When pregnancy occurs (with minipill use) the clinician must suspect that it is more likely to be ectopic. A previous ectopic pregnancy should not be regarded as a contraindication to the minipill.”*  
– Leon Speroff 7<sup>th</sup>/ed p 922

So *option “d”* is incorrect

**Main side effect of Minipill/progesterone only pill:** Irregular bleeding and amenorrhea (i.e. *option “a”* is correct).

Pearl index-3%

45. Ans. is a, b, c and e, i.e. Failure @ 0.3/100 WY; 150 mg/3 monthly delivered; Weight gain; and Anemia improves
46. Ans. is b, i.e. Does not have protective effect on Ca endometrium
47. Ans. is d, i.e. Hepatitis
48. Ans. is b, i.e 3 monthly

*Ref. Jeffcoate 7<sup>th</sup>/ed p 812; Dutta Obs 6<sup>th</sup>/ed p 548; Park 20<sup>th</sup>/ed pp 433-434; Leon Speroff 7<sup>th</sup>/ed pp 962-963*

*DMPA i.e. depot medroxyprogesterone acetate (depot provera) and Net en are progesterone only injectable contraceptives*  
DMPA is discussed in detail in preceding text:

**49. Ans. is a, i.e. Irregular bleeding**

*Ref. Dutta Obs 6<sup>th</sup>/ed p 548*

Norethisterone acetate is commonly used as an injectable steroid - 'NET-EN'

It is a progesterone based contraceptive like DMPA and its side effect are similar to those of DMPA.

The most frequent side effect is irregular bleeding.

NET-EN is given in doses of 200 mg at 2 monthly interval.

**Extra Edge: Combined injectable contraceptive.**

	Composition	Features
<ul style="list-style-type: none"> <li>Lunelle/cyclofem</li> <li>Mesigyna</li> </ul>	25 mg DMPA + 5 mg estradiol cypionate 50 mg NET-EN + 5 mg estradiol valerate	Monthly injection Monthly injection

**50. Ans. is b, i.e. Metrorrhagia**

*Ref. Novak 14<sup>th</sup>/ed p 283*

In progesterone only contraceptives whether injections/IUCDs/implants, the most common problem is-irregular vaginal bleeding i.e metrorrhagia

**Subdermal progesterone implants include:**

Norplant I	Norplant II/Jadelle	Implanon
<ul style="list-style-type: none"> <li>It has 6 rods containing <b>36 mg</b> of Levonorgestrel each</li> <li>Replaced after 5 years</li> </ul>	<ul style="list-style-type: none"> <li>It has 2 rods each containing 75 mg of LNG and releases the drug at the same dose as norplant 1</li> </ul>	<ul style="list-style-type: none"> <li>It has a single rod containing 68 mg of 3 keto-desogestrel (etonorgestrel)</li> <li>Most popular implant these days.<sup>o</sup></li> <li>Replaced after 3 years.<sup>o</sup></li> </ul>

**51. Ans. is c, i.e. Progesterone IUCD**

**52. Ans. is c, i.e. Premenstrual symptoms**

**53. Ans. is a, b, c, d and e, i.e. Endometriosis, Fibroid uterus, PID, Contraception, and Extrauterine endometriosis**

**54. Ans. is a and d, i.e. Progesterone containing IUCDs and Decreases menstrual blood.**

*Ref. Shaw 15<sup>th</sup>/ed p 228*

Mirena is a progesterone IUCD. It contains 52 mg levonorgestrel, eluting 20 µg daily.

**Life span-** 5 years

**Failure rate** = 0.2%

The biggest contraceptive advantage of progesterone IUCD's is-It can be given to nursing mothers.

For details see the text.

**55. Ans. is a, i.e. There is increased incidence of menorrhagia**

*Ref. Dutta Obs. 6<sup>th</sup>/ed p 537; Clinical Gynaecologic Endocrinology and Infertility by Leon Speroff 7<sup>th</sup>/ed p 979*

I have already discussed levonorgestrel releasing IUCD in detail in the preceding text.

LNG containing IUCDs do not cause menorrhagia, rather are used for management of menorrhagia as they decrease blood loss.

As far as **option 'd'** (i.e. irregular uterine bleeding it can be a problem initially) is concerned - since levonorgestrel is progesterone so it shares its property of causing irregular uterine bleeding.

*The other 2 options i.e. it can be used as hormone replacement therapy and is useful for the treatment of endometrial hyperplasia are correct as discussed earlier.*

**56. Ans. is b, i.e. Decreased ovulation**

*Ref. The Contraception Report' March 02, Vol. 13 No. 1*

Several mechanisms account for a potential reduced risk of upper-genital-tract infection in users of progestin releasing IUDs.

- First, the local effect of progestin on cervical mucus make it thick and relatively impenetrable to bacteria.
- Since uterine bleeding is eventually greatly decreased in users of the LNG-IUD (progestin releasing IUD), any retrograde menstruation (which might seed the fallopian tubes with bacteria) should be reduced as well.
- In addition, decidual changes in the endometrium may make it less susceptible to infection.

In other words, progestin-releasing IUDs may mimic the protective effect of combined oral contraceptives and depot medroxyprogesterone acetate against upper-genital-tract infection.

**Also know:**

- PID is common in non hormonal IUCD.
- IUCD related bacterial infections are due to contamination of endometrial cavity at the time of insertion.
- Actinomycosis infection is related to IUCD use.
- Most common side effect of IUCD's is increased vaginal bleeding.
- **Contraception of choice** in patients with current recent or recurrent PID is hormonal or barrier method:

57. **Ans. is a, i.e. 0.5**Ref. Leon Speroff 7<sup>th</sup>/ed p 981

LNG - IUD has a pregnancy rate of 0.2 100 women years (HWY) (here nearest is 0.5 so that is the answer).

**IUCDs**58. **Ans. is c, i.e. Has history of ectopic pregnancy**Ref. Parks 20<sup>th</sup>/ed p 427

The planned parenthood federation of America (PPFA) has described Ideal IUCD candidate as a woman.

- Who has no history of pelvic disease.
- **Who has born at least one child**
- **Has normal menstrual periods**
- **Is willing to check IUCD tail**
- Has access to follow up and treatment of potential problems
- Is in a monogamous relationship.

**Extra Edge:****Some important points from 'Leon Speroff' on patient selection for IUD.**

- Age and parity are not critical factors in selection, **the risk factors for STI's (sexually transmitted infection) are the most important considerations**
- Patients with heavy menstrual periods should be cautioned regarding the increase in menstrual bleeding associated with copper IUD. Women who are anticoagulated or have bleeding disorder are obviously not good candidates for copper IUCD, but might benefit from progestin IUCD.
  - Women who have abnormalities of uterus like bicornuate uterus are not good candidates for IUD insertion.<sup>Q</sup>
  - Patients with Wilson's disease are not recommended, copper containing IUCD as contraceptive
  - Immunosuppressed individuals should not use IUCD.
- Patients at risk for endocarditis should be treated with prophylactic antibiotics at the insertion and removal of IUCD.
- According to Speroff: cervical dysplasias are not contraindication for use of IUCD's<sup>Q</sup> but in patients with cervical stenosis it may be difficult to insert IUCD.
- No increase in adverse events has been observed with copper containing IUCD in women with either insulin dependent or non-insulin dependent diabetes. **Infact Cu containing IUCD's can be the ideal choice for a woman with diabetes especially if vascular disease is present.**

59. **Ans. is d, i.e. Inhibition of ovulation**Ref. Shaw 15<sup>th</sup>/ed p 229; Leon Speroff 7<sup>th</sup>/ed p 980**Mechanism of Action Of IUCD:**

Non medicated IUCD	Cu containing IUCD	Progestin releasing IUCD
<ul style="list-style-type: none"> <li>• Act as a foreign body in uterus and produce, a sterile inflammatory response and tissue injury of minor degree sufficient enough to be spermicidal. They prevent sperms from reaching the ova and therefore prevent both intrauterine and ectopic pregnancy</li> <li>• It provokes <b>uterine contractility and increases tubal peristalsis.</b></li> </ul>	<ul style="list-style-type: none"> <li>• Elute copper which bring about enzymatic and metabolic changes in the endometrial tissue &amp; also produce changes in cervical mucus and endometrial secretions.</li> </ul>	<ul style="list-style-type: none"> <li>• They cause decidualization <b>with atrophy of endometrial glands, therefore inhibit implantation</b></li> <li>• Alter cervical mucus causing inhibition of sperm penetration and capacitation.</li> <li>• In 40% cases, ovulation is also inhibited.</li> </ul>

*"The contraceptive action of all IUCD's is mainly in the uterine cavity. Ovulation is not affected and the IUCD is not an abortifacient. It is currently believed that the mechanism of action for IUCD's is the production of an intrauterine environment that is spermicidal."*

- Leon Speroff 7<sup>th</sup>/ed p 980

So, inhibition of ovulation is not the mechanism of action of IUCD's. (Except for progesterone containing IUCDs which inhibit ovulation, that too in only 40% cases)



60. Ans. is d, i.e. Progestasert

Ref. Shaw 15<sup>th</sup>/ed p 227

61. Ans. is a, i.e. CuT380A

Ref. Shaw 15<sup>th</sup>/ed p 227; Novak 14<sup>th</sup>/ed p 263

Most of the IUCDs have an average life span of 3 years.

Exceptions are:

- |  |  |
|--|--|
| • Nova T/ Multiload 375/Levonova                           | – 5 years  |
| • CuT 380 A (also known as Paragard)                       | – 10 years – Distributed free of cost                            |
| • Progestasert   | – 1 years  |
| • CuT200 B   | – 4 years, in US and 3 years in India and in European countries. |
| • Levonorgestrel containing IUCD can be used for: (Mirona) | – 7–10 years, but is approved for 5 years                        |

62. Ans. is a, i.e. Copper and silver

Ref. Shaw 15<sup>th</sup>/ed p 227

Nova-T is nothing but Cu-T, where silver is added to the copper wire thereby increasing lifespan of Cu-T from 3 years to 5 years in Nova-T.

63. Ans. is b, i.e. Remove the IUCD

64. Ans. is c, i.e. Remove the IUD to decrease the risk of infection

Ref. Dutta Obs 6<sup>th</sup>/ed p 540; Novak 14<sup>th</sup>/ed p 263; Pretest Obs and Gynae Q. No. 426, SK Chaudhary 7<sup>th</sup>/ed pp 110-111

A woman with an IUCD in place, with amenorrhea should have a pregnancy test and pelvic examination.

An intrauterine pregnancy can occur and continue successfully to term with an IUCD in place.

**A. If an intrauterine pregnancy is diagnosed and IUCD strings are visible:**

IUCD should be removed as soon as possible in order to prevent septic abortion, premature rupture of membranes, and premature birth. Also do an USG to know whether it is intrauterine or ectopic pregnancy

**B. If an intrauterine pregnancy is diagnosed and IUCD strings are not visible:**

- An ultrasound examination should be performed to localize the IUCD and determine whether expulsion has occurred.
- If the IUCD is present there are 3 options for management.
  - i. Therapeutic abortion
  - ii. If IUCD is not fundal in location: ultrasound guided intrauterine removal of IUCD.
  - iii. If IUCD is present in fundus of uterus: it should be left in place and pregnancy continued with the device left in place.
- If pregnancy continues with the device in place, the patient should be warned of the symptoms of intrauterine infection like fever or flue like symptoms, abdominal cramping or bleeding.
- At the earliest sign of infection, high dose intravenous antibiotic therapy should be given and the pregnancy evacuated promptly.

**Note:** Fetal malformations have not been reported to be increased with a device in place. – William Gynae 1<sup>st</sup>/ed p 120

Ref. SK Chaudhary 7<sup>th</sup>/ed p 114

65. Ans. is d, i.e. Laparoscopy

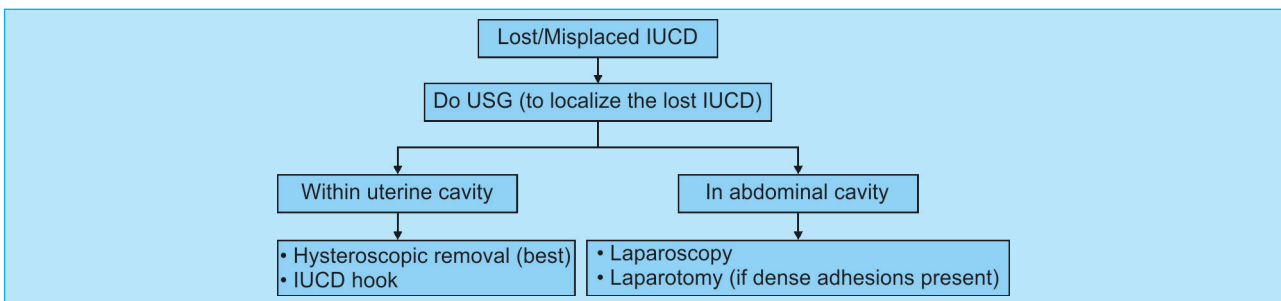
Copper can cause inflammatory reaction and can cause intestinal obstruction. Therefore, never wait and watch.

When Cu T is embedded within uterine cavity, hysteroscopic removal is the method of choice. It is preferred over IUCD hook. Hysteroscopy cannot visualize the Cu T that is in the abdominal cavity.

So when IUCD enters the abdominal cavity (partly or completely), laparoscopy is the preferred modality for retrieval.

Sometimes due to dense adhesions around the Cu T, a laparotomy may be required to remove it.

**Remember**



66. Ans. is c, i.e. Congenital malformation of uterus

Ref. Shaw 15<sup>th</sup>/ed p 228

67. Ans. is d, i.e. Pelvic tuberculosis

Ref. Shaw 15<sup>th</sup>/ed p 228

68. **Ans. is a and b, i.e. Undiagnosed vaginal bleeding and PID** Ref. Park 20<sup>th</sup>/ed p 427; Shaw 15<sup>th</sup>/ed p 228; Novak 15<sup>th</sup>/ed p 224

**Absolute contraindications of IUCD/WHO Category 4**

Please	Puerperal sepsis/Pregnancy
Don't	DUB
Try to	Gestation of trophoblastic disease
Put	<b>current</b> PID/STD or within the past 3 months puerperal sepsis
Condom	Cancer cervix Cancer endometrium

(Novak 15<sup>th</sup>/ed p 224)

**Mnemonic:** Please Don't Try to Put Condom

**Relative contraindications of IUCD**

– Park 20<sup>th</sup>/ed p 427; Jeffcoate 7<sup>th</sup>/ed pp 798-799; Shaw 14<sup>th</sup>/ed p 205

- Distortions of uterine cavity due to congenital malformations, fibroid<sup>Q</sup>
- Wilson disease
- Scarred uterus (Jeffcoate/Shaw)

According to WHO, IUCD can be used in valvular heart disease but antibiotics should be given before insertion.

69. **Ans. is b, c and e, i.e. PID; Uterine malformation; and Previous cesarean section**

70. **Ans. is b, c and e, i.e. PID; Uterine malformation; and Previous ectopic pregnancy**

Ref. Park 18<sup>th</sup>/ed p 364; Shaw 15<sup>th</sup>/ed p 228; Jeffcoate 7<sup>th</sup>/ed pp 798-799

In both the above question, I do not need to tell again that PID, uterine malformation and previous ectopic/previous cesarean section pregnancy are contraindications for IUCD use. Here I want to discuss about the use of IUCD in diabetics and HIV positive patients.

Some books mention diabetes as a contraindication for IUCD but according to Leon Speroff Cu containing IUCDs can be the ideal choice for women with diabetes especially if there is associated vascular disease.

*"No increase in adverse events has been observed with copper IUD use in women with either insulin dependant or non insulin dependant diabetes. Indeed, the IUCD can be an ideal choice for a woman with diabetes, especially if vascular disease is present."*

– Leon Speroff 7<sup>th</sup>/ed p 988

*"IUCDs-They are the contraceptive method of choice in woman with either type I or type II diabetes."*

– Current Concept in Contraception and Women Health, p 95

Earlier it was believed IUCD's are contraindicated in patients of HIV but now it is not so – rather IUCD's are the method of choice in HIV infected women.

HIV and AIDS – *"IUD's are the method of choice in these women owing to their high efficacy, minimal maintenance and no drug interaction."*

– Current Concept in Contraception and Women Health, p 97

Leon Speroff 7<sup>th</sup>/ed p 985 also supports the use of IUCD's in HIV infected females.

71. **Ans. is b, i.e. Bleeding**

Ref. Park 20<sup>th</sup>/ed p 428

**Complication of IUCD**

- M/C complication–Bleeding
- II<sup>nd</sup> M/C complication–Pain
- Infection–Doxycycline 200 mg/azithromycin 500 mg should be given 1 hour before insertion to reduce infection.
- Most typical infection associated with Cu T use is actinomyces.
- Ectopic pregnancy–It is seen that ectopic pregnancy is 50% less likely in women using IUCD than in women using no contraception.

## Emergency Contraception

72. **Ans. is d, i.e. Interrupting an early pregnancy**

Ref. Leon Speroff 7<sup>th</sup>/ed pp 925-926

Emergency Contraceptives are also called as **INTERCEPTIVES**.

It refers to a type of contraception that is used as an emergency to prevent pregnancy after an unprotected intercourse.

**Mechanism of action**

The mechanism of action is not known with certainty, but it is believed with justification that this treatment combines delay of ovulation (*Option 'a'*) with a local effect on endometrium (*Option 'c'*) and prevention of fertilization (*Option 'b'*). As far as *option 'd'* is concerned

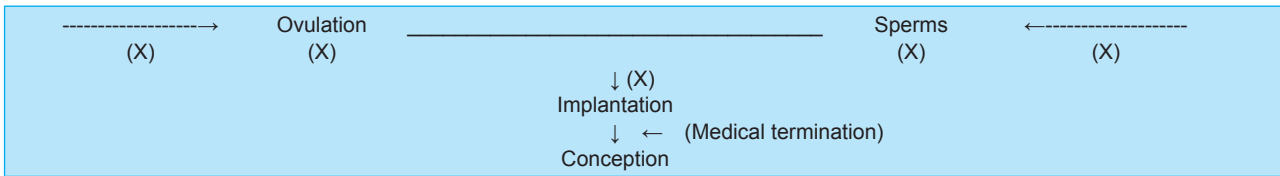
*"How much a post fertilization effect (option d) contributes to efficacy is not known, but it is not believed to be the primary mechanism."*

– Leon Speroff 7<sup>th</sup>/ed pp 925-926

*"Contrary to popular belief, it is not an abortifacient i.e. will not act after implantation has occurred."*

– Current Concepts in Contraception and Womens Health, p 108

**Mechanism of action of emergency contraception versus medical method of MTP.**



(X) steps inhibited by emergency contraception.

73. **Ans. is c and d, i.e. Contraception failure; and Unprotected sex** Ref. Dutta Obs. 6<sup>th</sup>/ed p 549; Leon Speroff 7<sup>th</sup>/ed p 925  
Sorry, friends I am not able to get you the exact answer. According to me both are correct.

**Indications for emergency contraception**

- Unprotected intercourse
- Condom rupture (Contraception failure)
- Missed pill (Contraception failure)
- Sexual assault/teenage assault
- Rape

– Dutta Obs. 6<sup>th</sup>/ed p 549

– Leon Speroff 7<sup>th</sup>/ed p 925

**Emergency contraception**

*“It is an important option for patients and should be considered when condom break, sexual assault occurs, if diaphragms or cervical caps dislodge or with the lapsed use of any method.”*

74. **Ans. is c and e, i.e. Danazol and misoprostol.**
75. **Ans. is c and e, i.e. Desogestrol and medroxyprogesterone acetate.**
76. **Ans. is c, i.e. Levonorgestrel.** Ref. Leon Speroff 7<sup>th</sup>/ed p 927; Novak 14<sup>th</sup>/ed pp 283-285

**Drugs used for Emergency contraception**

Drug	Dosage
1. <b>OCP's (Morning after pill)</b>	<b>Yuzpee's method</b> 2 tablets of ovral (EE=50 mg and Levonorgestrel .25 mg) followed by 2 tablets 12 hours later. <i>Remember</i> a total of 200 µg EE and 1 mg of Levonorgestrel is required as Emergency contraception. They should be started within 72 hours and for best results within 12 hours of exposure. High dose estrogen has replaced this method.
2. <b>Levonorgestrel alone- Most appropriate drug/progestrone for Emergency contraception – (3rd most effective)</b>	New and better alternative 0.75 mg is taken initially within 72 hours followed by another 0.75 mg 12 hours later. Available by name <i>E pill</i> under the National Family Welfare Programme. Other brands available are: I pill/ Ecee2/unwanted 72 It is the drug of choice for emergency contraception.
3. <b>Copper Intrauterine device, (2nd most effective)</b>	Insertion of an IUCD within maximum period of 5–7 days after accidental unprotected exposure. It prevents implantation but is not suitable for women with multiple sex partners and for rape victims.
4. <b>Mifepristone/RU-486</b>	A single dose of 10 mg given as soon as possible is effective in preventing in pregnancy in 95% cases. It is an anti-implantation agent. Mifepristone is also highly effective in inducing menstruation when taken on day 27 of the menstrual cycle (well beyond 72–120 hours window which is usually considered for postcoital contraception).
5. <b>Centchroman</b>	2 tablets (60 mg) to be taken twice at an interval of 12 hours within 24 hours of intercourse.
6. <b>Ulipristal—(most effective)</b>	It is a synthetic progesterone receptor modulator. Delays ovulation. Dose = 30 mg stat. It is as effective as levonorgestrel if taken within 72 hours and more effective than levonorgestrel between 72 and 120 hours.

**Note:** LNG-IUCD cannot be used for emergency contraception

As far as Danazol is concerned, it was earlier used as an emergency contraceptive but not nowadays.

*“The use of danazol for emergency contraception is not effective”.*

– Leon Speroff 7<sup>th</sup>/ed p 927

**Also Know:**

- Emergency contraception should be initiated as soon as possible **after exposure** and the standard recommendation is that it should not be initiated later than 72 hours.
- Greatest protection occurs, if it is started within 12 hours of exposure.
- Emergency contraception will be ineffective in the presence of an established pregnancy.

## 77. Ans. is d, i.e. 120 hours

Ref. Shaw 15<sup>th</sup>/ed p 237; Current Concepts in Contraception and Women Health, p 105, Leon Speroff 8<sup>th</sup>/ed p 1042

The standard recommendation is to start emergency contraceptive not later than 72 hours. The greatest protection is offered, if it is taken within 12 hours, as postponing the dose by 12 hours raises the chances of pregnancy by almost 50%. For this reason, the treatment should be initiated as soon as possible after sexual exposure.

**Note:** But here the question says - till how long are ECs effective or till how long can they be administered.

Shaw 14<sup>th</sup>/ed p 213 says

"The tables can be offered upto 120 hours, but its efficacy decreases with the longer coital - drug interval."

"Treatment should be initiated as soon after exposure as possible, and the standard recommendation is that it be no later than 120 h."

- Leon Speroff 8<sup>th</sup>/ed p 1042

According to current concepts in contraceptions and women health also -

**Emergency contraception can be given upto 5 days.**

This is because

"Emergency contraception is not an abortifacient i.e. it will not act after implantation has occurred. This is also the basis for the window period of 5 days for use effectiveness of EC, as the whole process from deposition of sperms to implantation takes about 5 days."

- Current Concepts in Contraception and Women Health p 108

## Permanent Method

## 78. Ans. is e, i.e. Medroxyprogesterone

Ref. Dutta Obs 6<sup>th</sup>/ed p 532

Methods of contraception (can be classified as)	
<p><b>Temporary methods</b> (used to postpone or space births)</p> <ul style="list-style-type: none"> <li>• <b>Barrier method<sup>a</sup></b></li> <li>• <b>Natural contraception<sup>a</sup></b></li> <li>• Oral contraceptive pills</li> <li>• Injectables</li> <li>• Implants</li> <li>• Intrauterine devices like Copper T, Levonorgestrel IUCD's</li> </ul>	<p><b>Permanent methods</b> (Surgical methods aim to purposefully and permanently destroy the Reproductive capacity of an individual)</p> <div style="text-align: center;"> <pre> graph TD     A[Permanent methods] --&gt; B[Female]     A --&gt; C[Male]     B --&gt; D[Tubectomy]     C --&gt; E[Vasectomy]           </pre> </div>

Electrocoagulation is using cauterization for the purpose of tubal ligation and clipping is done during laparoscopic tubal ligation, i.e. they are permanent methods.

Friends, here do not get confused by lines of *Shaws* which says some of these methods are reversible, it does not mean they are not permanent methods.

## 79. Ans. c, i.e. Essure

Ref. Williams 23/e p698-701

Essure is a permanent intratubal implant inserted transcervically using hysteroscope, not an abdominal technique for tubal ligation.

## 80. Ans. is d, i.e. Hysteroscopic tubal occlusion

Ref. Shaw 15<sup>th</sup>/ed p 241

Hysteroscopic tubal occlusion is done by 2 methods and both these methods have high failure rates.

Hysteroscopic tubal occlusion	
<p><b>Cauterization</b> (Failure rate 30%)</p> <ul style="list-style-type: none"> <li>• Due to high failure rate these methods are obsolete now</li> </ul>	<p><b>Sclerosants</b> (Failure rate 15%)</p>

## 81. Ans. is d, i.e. Laparoscopic tubal ligation with clips

Ref. Leon speroff 8<sup>th</sup>/ed pp 935, 929

### Reversal of tubal ligation

Sterilization procedure	Term pregnancy (range %)	Ectopic pregnancy (range %)
Spring-loaded clip	88 (75–100)	2 (0.4)
Ring occlusion (silastic bands)	75 (44–95)	2 (0–4)
Pomeroy ligation	59 (45–70)	2 (0–3)
Electrocoagulation	43 (26–58)	5 (0–9)

**Note:** Most suitable for reversal is clips followed by ring, BUT most commonly used for laparoscopic tubal ligation is silastic ring followed by clips

Least suitable for reversal is monopolar cautery followed by bipolar cautery technique.

82. **Ans. is c, i.e. Isthmoampullary**

83. **Ans. is c, i.e. Isthmus**

Ref. Dutta Obs 6<sup>th</sup>/ed p 553

I have given these 2 questions simultaneously so that you understand how the answer changes as the options of the question change. Sterilization is done at the junction of proximal and middle third – the loop formed consists mainly of isthmus and part of the ampullary region of the tube.

- Therefore, if in options isthmoampullary is given, it is the best choice but if isthmoampullary is not given Isthmus is the next best choice.

84. **Ans. is a, i.e. Isthmo-isthmic type**

85. **Ans. is a, i.e. Isthmo-isthmic anastomosis**

Ref. Jeffcoate 7<sup>th</sup>/ed p 825; Novak 14<sup>th</sup>/ed p 294

**Read the following lines**

*"It is important to select the site of tubal ligation carefully which should ideally be done at the tubal isthmus. This is because in the event of the patient desiring a tubal recanalization procedure, the isthmo-isthmic anastomosis carries the best chances of success".*

– Jeffcoate 7<sup>th</sup>/ed p 825

Ref. Dutta obs 7<sup>th</sup>/ed p 557

86. **Ans. is d, i.e. Dyspareunia**

**Post ligation syndrome-**

Some patients after tubal ligation can experience post-ligation syndrome characterized by menstrual irregularities like menorrhagia, or irregular periods along with pelvic pain or congestive dysmenorrhea and cystic ovaries.

**It is vascular in origin and its incidence can be reduced if the blood vessels adjacent to the mesosalpax are not unduly disturbed.**

87. **Ans. is b, i.e. 0.1%**

Ref. JB Sharma Obs 1/e p 672

*Read the text for explanation*

88. **Ans. is b, i.e. No sperms in ejaculate**

Ref. Textbook of Gynae Sheila Balakrishnan 1<sup>st</sup>/ed p 373, Dutta obs 7<sup>th</sup>/ed p 553

Sterility does not occur immediately after vasectomy.

Sperms remain in the semen for 15–20 ejaculations, requiring continued contraception for about 3 months. So the couple is advised to use some form of contraception for the next 3 months or 15–20 ejaculates, but this can vary from person to person. So the best thing to do is to repeat the semen analysis and confirm that the male partner has become azoospermic. This is the reason why after vasectomy, 2 separate semen analysis should be done to confirm the absence of sperms in the ejaculate and then additional contraception discontinued.

## Contraceptive of Choice

89. **Ans. is c, i.e. Diaphragm**

Ref. Shaw 15<sup>th</sup>/ed p 244

90. **Ans. is d, i.e. Condom**

Ref. Shaw 15<sup>th</sup>/ed p 244; Park 20<sup>th</sup>/ed p 425; Dutta Obs. 6<sup>th</sup>/ed p 280;

Current concepts in contraception and women health, p 96

Barrier contraceptives (diaphragm/condom) are the ideal contraceptives for patients with medical complications such as heart disease.

*"The primary advantage of the diaphragm is the almost total absence of risks and medical contraindications."* – Park 20<sup>th</sup>/ed p 425

- **Combined oral contraceptive pills are contraindicated in a woman with cardiac disease.** – Shaw 14<sup>th</sup>/ed p 219

- **IUCD is carefully considered in a cardiac and diabetic woman because of the possibility of pelvic infection.**

– Shaw 14<sup>th</sup>/ed p 219

- Depoprovera (DMPA) a progesterone only injectable contraceptive also is not a preferred agent for patients with cardiac disease although it is not contraindicated.

- Sterilization should be considered with completion of family at the end of first week<sup>Q</sup> in the puerperium under local anesthesia<sup>Q</sup> through abdominal route by minilap technique<sup>Q</sup>

- If the heart is not well compensated, the husband is advised for vasectomy.

91. **Ans. is b, i.e. Condom**

Ref. Shaw 15<sup>th</sup>/ed p 231

Barrier methods (especially condom) and OCP's both protect against PID, but the protection offered by OCP's is less than that by Barrier method.

*"The incidence of pelvic inflammatory disease (PID) is reduced, though it does not reach the same low level as seen with the barrier methods."*

– Shaw 14<sup>th</sup>/ed p 208

As far as diaphragm is concerned, it does not protect against HIV, whereas condom do. So I have chosen condoms as the answer.

92. **Ans. is b, i.e. Combined OCP**

93. **Ans. is a, i.e. Barrier method**

94. **Ans. is d, i.e. Progesterone only pill**

Ref. Read below

**For newly married couples** oral contraceptive pill is the method of choice provided there are no contraindications.

It has many noncontraceptive benefits along with effective contraception.

Barrier and Natural methods have high failure rate.

IUCD are not prescribed in nulliparous females due to increase risk of PID and infertility

**In a couple who are living separately** in two cities and meet only, occasionally contraception of choice is barrier method.

*"Condom are suitable for use in old age for couple who have infrequent coitus, during lactation, during holidays, subject who can not tolerate OCP, IUCD".*

*Ref. Practice of fertility control S.K. Chaudhuri 7<sup>th</sup>/ed p 71*

### **In Breastfeeding Females**

For lactating mothers, contraceptive should be chosen in such a way that in addition to providing effective contraception, they do not adversely affect the success of lactation or the health of the infant. Barriers have a high failure rate of 4-14% and not reliable for long-term control.

As estrogens decrease the quality and quantity of milk, COC pills are absolutely contraindicated in lactating mothers.

### **Lactation Amenorrhea Method (LAM)**

- Excessive secretion of prolactin, which controls lactation, inhibits the pituitary. Prolactin inhibits luteinizing hormone (LH) but has no effect on follicle-stimulating hormone (FSH). However, it partially inhibits ovarian response to both of these gonadotropins. As a result, while the prolactin level remains high, the ovary produces little estrogen and no progesterone. Hence, ovulation and menstruation are affected.
- LAM is effective only till 6 months postpartum. Beyond this, it is not a reliable method.
- Even for the 6 months, it is effective only if there is exclusive breastfeeding.
- **It any time in the first 6 months the menses starts, then it cannot be used as birth control.**
- POPs are safe with breastfeeding and very effective. They were mainly designed especially for lactating mothers.

### **95. Ans. is c, i.e. Vasectomy**

*Ref. Shaw 15<sup>th</sup>/ed p 238*

*Vasectomy consists of dividing the vas deferens and disrupting the passage of sperms. It is done through a small incision in the scrotum under local anesthesia (LA). There is no need to open the peritoneum.*

### **96. Ans. is a, i.e. OCPs**

*Ref: Leon speroff 8<sup>th</sup>/ed p 1026; text book of gynecology, sheila bala krishnan 1<sup>st</sup>/ed p 344, 345*

#### **In Epilepsy**

**"Consideration should be given to methods that neither affect antiepileptic drug metabolism nor the methods affected by drugs. These include intrauterine contraception with copper IUD, or levonorgestrel releasing IUD, long acting progestine only methods, barrier methods and sterilization."**

*Leon speroff 8<sup>th</sup>/ed p 1026*

Epilepsy/seizure disorder is a relative contraindication for the use of OCP's as antiepileptic drugs like phenytoin, carbamazepine and phenobarbitone induce the synthesis of liver enzyme thereby reducing the plasma levels of ethinyl estradiol in women on combined pills, thereby increasing the chances of contraceptive failure.

So in epilepsy OCPs should be avoided.

### **97. Ans. is a, i.e. Leads to immediate sterility**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 494-5*

- Vasectomy consists of dividing and excising a part of vas deferens (with spermatic cord).
- It leads to permanently ending fertility for men.
- Failure rate 0.15%.
- The sterility does not occur immediately after vasectomy. Sperms remain in semen for 15-20 ejaculations which is approximately 3-4 months, during which time an additional contraceptive method (condom by male or DMPA by wife should be used).

### **98. Ans. is b, i.e. Patients over 30 years of age.**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 248*

Tubal reconstruction surgery can be done for a number of reasons including for reversal of sterilisation procedure. The most favourable outcome is seen when it is done for reversal of sterilisation procedures.

#### **Factors for Poor Outcome Following Tuboplasty**

- Dense pelvic adhesions.
- Loss of fimbriae.
- Bilateral hydrosalpinx > 3 cm.
- Length of the reconstructed tube < 4 cm.
- Reversal done after 5 years of sterilization operation.
- Presence of other factors for infertility.

### **99. Ans. is b, i.e. 10-15 mm of Hg**

*Ref. SK Chaudhary 7<sup>th</sup>/ed p 209-211*

During laparoscopy, pneumoperitoneum is created with CO<sub>2</sub> or nitrous oxide. CO<sub>2</sub> is preferred because N<sub>2</sub>O can cause explosion in presence of volatile anesthetic drugs. About 2 litres of gas is introduced at 10 mmHg. The intraabdominal pressure during any laparoscopic surgery should be 10-15 mmHg. This eliminates the risk of hypercarbia or decreased venous return to heart.

### **100. Ans. is c, i.e. Vaginal diaphragm**

*Ref. SK Chaudhary 7<sup>th</sup>/ed p 103*

Since the patient wants contraception only for 6 months we could advise her some method of temporary contraception.

Complicated migraine is an (absolute contraindication for OC pills

As the patient has multiple fibroids and dysmenorrhea, Cu T should be avoided.

Hence, contraception of choice for her is vaginal diaphragm. It is a barrier method of contraception, which is to be used along with spermicidal agent.

**101. Ans. is d, i.e. Laparoscopy**

*Ref. SK Chaudhary 7<sup>th</sup>/ed p 114*

**In case or misplaced Cu T with Cu T seen inside abdominal cavity**

- Copper can cause inflammatory reaction and can cause intestinal obstruction.
- Therefore we should never wait and watch.
- When Cu T is embedded within uterine cavity, hysteroscopic removal is the method of choice. It is preferred over IUCD book. Hysteroscopy cannot be used in removal of Cu T that is in the abdominal cavity.
- When Cu t is seen in abdominal cavity it is removed by laparoscopy.

**102. Ans. is d, i.e. Mesigyna**

*Ref: Textbook of Gynae sheilabalakrishnan 1<sup>st</sup>/ed pp 350-351*

**Non oral hormonal contraceptives are:**

1. Hormone releasing IUCDs
2. Injectable contraceptive -
  - a. Progesterone only - DMPA  
- NET EN
  - b. Combined - cyclofem  
- mesigyna
  - c. Injectable vaccine - Antihcg injection.
3. Contraceptive implants:
  - Norplant I
  - Norplant II or Jadelle
  - Implanon
4. Vaginal ring

**103. Ans. is c, i.e. Unipolar cauterisation**

*Ref. Leon Speroff 7<sup>th</sup>/ed p 842; 8<sup>th</sup>/ed p 926*

**Female tubal sterilization methods-10 year cumulative failure rates:**

Unipolar cauterisation	- 0.75%
Postpartum tubal excision	- 0.75%
Silastic ring/fallope ring	- 1.77
Interval tubal exclusion	- 2.01
Bipolar coagulation	- 2.48
Hulka - clemens clips	- 3.65

**Note:** Although unipolar cauterization has least failure rates, but is not preferred method for female sterilization as it leads to serious gastrointestinal burns.

**104. Ans. is c, i.e. POPs**

**LARC method of contraception are Long acting Reversible contraceptive methods:**

LARC methods include:

- i. LARC Infection: DMPA/NET-en
- ii. Implants-Implanon, Norplant
- iii. IUCD's: CuT, LNG IUCD.
- iv. Transdermal patches
- v. Vaginal ring

**105. Ans. is c, i.e. OCP**

In a female with family history of ovarian cancer, best contraceptive is OCP.



Leiomyomata/Fibroids:  
Benign smooth muscle  
tumor of the uterus



Fibroid is an estrogen-  
dependent tumor

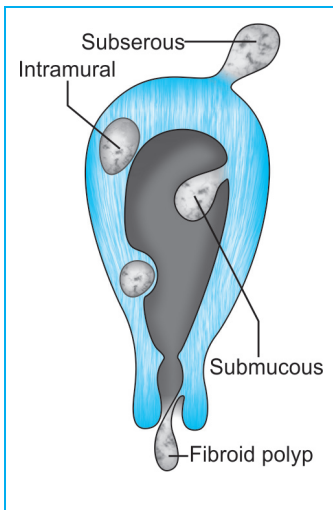


Fig. 11.1: Locations of fibroid



Diseases commonly  
associated with  
leiomyomas—

- Follicular cysts of ovary
- Endometrial hyperplasia
- Endometrial cancer
- Endometriosis

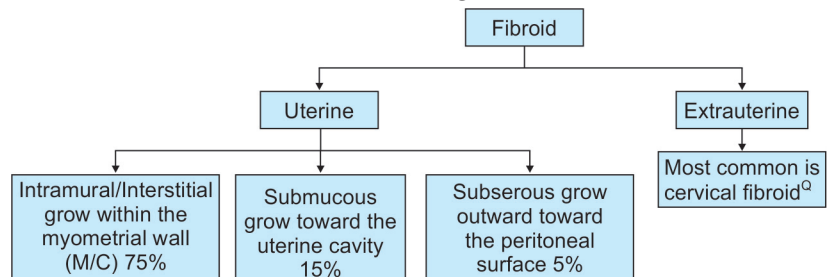


Fibroids are more common  
in—

- Nulliparous females
- Infertile females
- Black women

## FIBROIDS

- Fibroids are the most common benign solid tumors in females.<sup>Q</sup>
- It is the most common pelvic tumor.<sup>Q</sup>
- Most common age group affected is 35–45 years<sup>Q</sup>
- Fibroids are most commonly seen in nulliparous female.<sup>Q</sup>
- Locations of fibroid is described as follows (Fig. 11.1):



## Etiology/Pathogenesis of Fibroids

- Fibroid is monoclonal in origin.
- Multiple chromosomal abnormalities are detected in 50% of all fibroids—most common being translocation between the long arms of chromosomes 12 and 14 followed by deletion of long arm of chromosome Y.
- Fibroids are related to both estrogen and progesterone.
- Risk of fibroid increases as obesity increases
- Smoking is protective for fibroids
- Increasing parity decreases its incidence

## Most Common in Fibroid

- Most common (M/c) variety of fibroid
  - Intramural/interstitial (75%) followed by submucous (15%) and subserous (10%)
- Fibroid with maximal symptoms
- To start with, all fibroids are
- M/c fibroid to undergo malignant change
- M/c fibroid to cause retention of urine
- Torsion is most common in
- Fibroid causing pseudo Meigs syndrome
- M/c menstrual symptom of fibroid
- Inversion is seen in
- M/c symptom of fundal fibroid
- Fibroid which leads to maximum abortion
- Wandering or parasitic fibroid
- Lantern on dome of St Paul
- Pseudocervical fibroid
- M/c fibroid to undergo calcareous degeneration
  - Cervical fibroid
  - Fibroid polyp
  - Subserous fibroid



## Structure of Fibroids

- Fibroid is a well circumscribed tumor with a pseudocapsule which is formed by compressed adjacent myometrium
- The blood vessels supplying the fibroid lie in the capsule and run radially so that the center is the least vascular and periphery is the most vascular part of the fibroid
- Thus, calcifications begin from the periphery of fibroid and degenerations begin from the center.<sup>Q</sup>
- Most fibroids are slow growing

## Degenerations/Secondary Changes in a Fibroid

**MC**

<b>Avoid</b>	= Atrophy
<b>Red</b>	= Red degeneration
<b>Hot</b>	= Hyaline degeneration (MC)
<b>Fatty</b>	= Fatty degeneration or calcification
<b>Meat</b>	= Myxomatous degeneration
<b>of Chicken</b>	= Cystic degeneration
<b>(Mnemonic:</b>	<i>Avoid red hot fatty meat of chicken</i> )

### Red Degeneration of Fibroid (also called as Carneous Degeneration)

- It is seen mostly during pregnancy, especially mid pregnancy-2nd trimester<sup>Q</sup> (But can occur at other times as well and in nonpregnant females also).<sup>Q</sup>
- It is an aseptic condition.<sup>Q</sup>
- The myoma suddenly becomes acutely painful,<sup>Q</sup> enlarged<sup>Q</sup> and tender.<sup>Q</sup>
- **Patient presents with:**
  - Acute abdominal pain<sup>Q</sup>
  - Vomiting<sup>Q</sup>
  - Malaise<sup>Q</sup>
  - Slight fever<sup>Q</sup>
- Lab investigations:**
  - Moderate leukocytosis<sup>Q</sup>
  - Raised esr<sup>Q</sup>

### Pathological changes in the tumor

- Fibroid becomes soft, necrotic or homogenous especially in its center.
- It is stained Salmon pink<sup>Q</sup>, or red (due to diffusion of blood pigments from the thrombosed vessels).
- It has a fishy odor<sup>Q</sup> (due to secondary infection with coliform organisms)
- **Histologically:** There is evidence of thrombosis in some vessels.<sup>Q</sup>
- **Pathogenesis:** There is subacute necrosis of the myoma caused by an interference in blood supply (aseptic infarction).<sup>Q</sup>

### Management

- Conservative management<sup>Q</sup>
- Patient is advised rest<sup>Q</sup>
- Analgesics are given to relieve the pain.<sup>Q</sup>
- The acute symptoms subside in 3–10 days<sup>Q</sup> and pregnancy proceeds uneventfully.
- Diagnosis is by ultrasound.

### Differential Diagnosis

- Appendicitis,<sup>Q</sup> twisted ovarian cyst,<sup>Q</sup> pyelitis<sup>Q</sup> and accidental hemorrhage.<sup>Q</sup>



Smoking (both active and passive) is protective against fibroids as it leads to hyperestrogenism



Broad ligament of fibroids are of 2 types—

- Those which arise from the uterus and grow toward the broad ligament and displace the ureter laterally – they are known as false broad ligament fibroids
- Those which arise *de novo* from broad ligament and ureter is medial to this type of fibroid (i.e. ureter is between uterus and fibroid)



Calcifications begin from the periphery of fibroid and degenerations begin from the center.



- M/c degeneration – Hyaline degeneration
- Cystic degeneration is M/c in postmenopausal females and M/c in interstitial fibroid
- Calcareous degeneration is M/c in subserous fibroids

### Sarcomatous Change

- When a fibroid undergoes malignancy, the most common malignancy which is seen is leiomyosarcoma.
- Sarcomatous change is seen in only 0.2–0.5% of cases.<sup>Q</sup>
- The malignant process begins from the center.<sup>Q</sup>
- M/c in submucous followed by Intramural fibroid.<sup>Q</sup>
- Diagnosis is made by histological examination of the removed myoma.<sup>Q</sup>
- **Changes seen in myoma are:**
  - Sarcomatous Myoma is *yellowish gray in color* (normally pinkish white), with soft and friable consistency (instead of firm consistency).
  - *Non encapsulation of the tumor.* (Normally fibroid is surrounded by a pseudo capsule)
- Sarcomas with malignant behavior have *10 or more mitosis per ten high power field.*
- Development of sarcoma can be suspected clinically, when a leiomyoma (usually in a post-menopausal woman) becomes painful, tender, grows rapidly, and produces systematic upset and pyrexia.
- Overall 5 years survival rate in such patients = **20–30%**.



Least common change in fibroid

- Malignant change % = 0.2–0.5%
- M/c fibroid to become malignant – Submucous fibroid
- M/c malignancy – Leiomyosarcoma
- Endometrial cancer is associated with fibroids in 3% cases

### Symptoms of Fibroid

- Mostly fibroids are asymptomatic<sup>Q</sup> (M/C presentation)
- Most common symptom – Menstrual disturbances<sup>Q</sup>
- **Most common menstrual disturbance: Progressive menorrhagia<sup>Q</sup>** (seen in 30% cases).

#### Other Menstrual Symptoms:

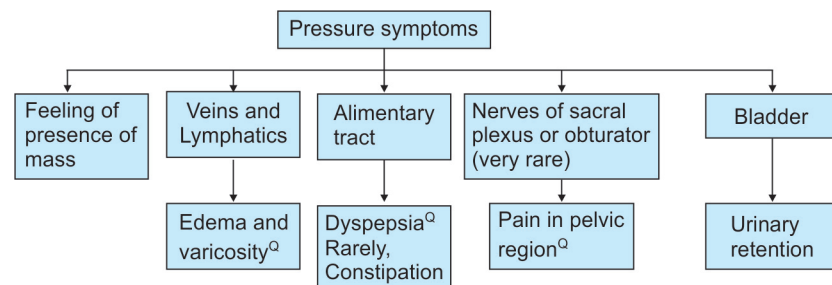
Metrorrhagia<sup>Q</sup> – (Continuous and irregular bleeding)<sup>Q</sup>

#### Causes:

- Ulceration of submucous fibroid or polyp.<sup>Q</sup>
- Sarcomatous change in leiomyoma.<sup>Q</sup>

**Dysmenorrhea** – congestive<sup>Q</sup> as well as spasmodic<sup>Q</sup> type seen.

- **Pressure symptoms**



M/c fibroid to cause infertility and abortions is submucous fibroid



- M/c fibroid to cause urinary retention – posterior cervical fibroid
- M/C fibroid to cause urinary frequency – Anterior cervical fibroid

- **Infertility:** As a sole cause, fibroid is responsible for < 3% cases of infertility.

#### Causes:

- Fibroid hinders with the ascent of the sperm.<sup>Q</sup>
- Interferes with implantation of fertilized ovum.<sup>Q</sup>
- Can cause associated disturbance in ovulation<sup>Q</sup>

**Note:** Presence of submucous fibroids decrease fertility rates and removing them increases fertility rates.

Subserous fibroids do not affect fertility rates but removing them increases fertility. Intramural fibroid slightly decreases fertility but removal does not increase fertility.

➤ **Pain:** A fibroid usually does not cause pain.

**Causes:**

- Malignancy<sup>Q</sup>
- It is being extruded from body as a polyp<sup>Q</sup>
- Associated endometriosis<sup>Q</sup>
- Torsion of a pedunculated fibroma<sup>Q</sup>
- Degeneration<sup>Q</sup>



**Mnemonic:** My PET Dog.

➤ Other rare features of fibroid:

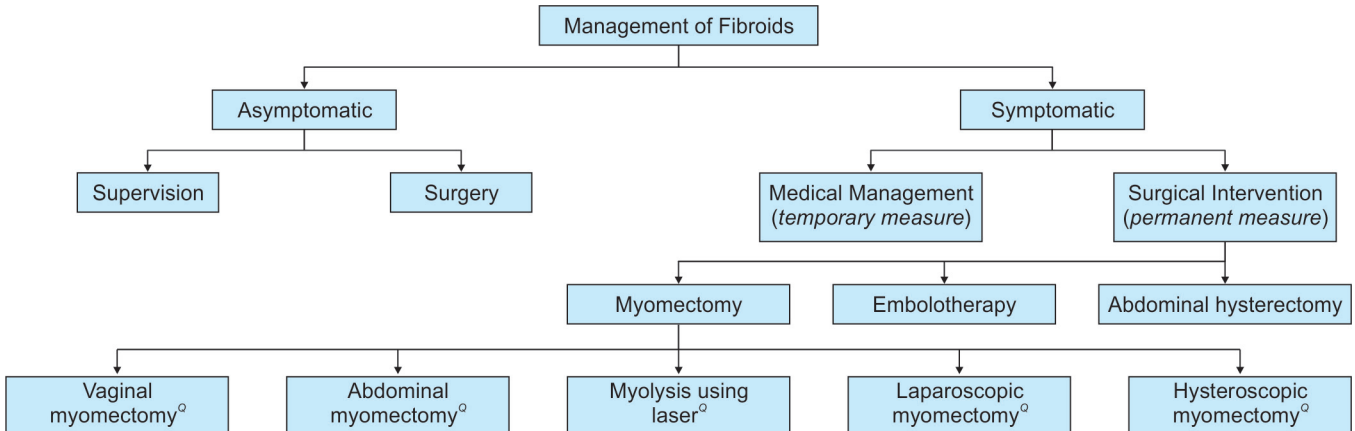
- **Polycythemia:** (Interesting as fibroids generally cause anemia due to blood loss. Polycythemia is seen in broad ligament fibroids).<sup>Q</sup>
- **Hypoglycemia and hypokalemia.**

**Investigations**

- M/c investigation done in fibroids or IOC is USG. (It is most readily available, least cost-effective but not as accurate as MRI at determining the precise location or size of fibroids especially in larger uteri or those with multiple fibroids)
- Best investigation to detect a small submucous fibroid – hysteroscopy.

**Differential diagnosis** adenomyosis

Fibroid	Adenomyosis
Presenting symptom	Menorrhagia and dysmenorrhoea
Irregular growth of uterus	Symmetrical growth of uterus
Non tender uterus	Tender to touch
Uterine size = 20 weeks pregnancy uterus	10–20 weeks pregnancy size uterus
IOC = USG	MRI Gold standard–HPE



**Management of Fibroids**

**Indications for Operating an Asymptomatic Fibroid<sup>Q</sup>:** —Jeffcoate 7<sup>th</sup>/ed, p 496

- Fibroids larger than 12–14 weeks pregnancy.<sup>Q</sup>
- Rapidly growing fibroids.<sup>Q</sup>
- Subserous and pedunculated fibroid prone to torsion.<sup>Q</sup>
- If it is likely to complicate a future pregnancy<sup>Q</sup>
- If there is doubt about its nature<sup>Q</sup>
- Unexplained infertility and unexplained recurrent abortion.<sup>Q</sup>

– Dutta Gynae 4<sup>th</sup>/ed p 264

➤ Uncertain diagnosis:<sup>Q</sup>If patient is symptomatic decide whether you give medical treatment or surgical treatment.



**Note**

According to the latest concept - Asymptomatic fibroids of any size can be managed expectantly.

**Indications of Medical Management<sup>Q</sup>**

- To treat anemia and recover hemoglobin levels before surgery.<sup>Q</sup>
- To reduce the size of large fibroid and facilitate surgery.<sup>Q</sup>

- Treatment of women approaching menopause to avoid surgery.<sup>Q</sup>
- In women with medical contraindication to surgery or those who are postponing surgery.<sup>Q</sup>
- For preservation of fertility in women with large myomas before conservative surgery like myomectomy.<sup>Q</sup>

### Indications of Surgical Management<sup>Q</sup>

Fibroids causing any symptoms like

- Menorrhagia<sup>Q</sup> or pressure symptoms<sup>Q</sup> like urinary retention (by a cervical or broad ligament fibroid) or chronic pelvic pain with<sup>Q</sup> severe dysmenorrhea, acute pelvic pain as in torsion of a pedunculated fibroid, or prolapsing submucosal fibroid
- Unexplained infertility
- Recurrent abortions due to submucous fibroid
- Rapidly growing fibroid.



Definitive management of symptomatic fibroids is surgery.

### Medical Management of Fibroid Aims at

- Decreasing the blood loss due to fibroid (as menorrhagia is the most common symptom of fibroid).
- Decreasing the size of fibroid.

But the main problem is that tumor may grow on cessation of treatment. Hence, main role of medical management is preoperative and in women nearing menopausal age to avoid surgery.

### A. Drugs to decrease size of fibroid

Mnemonic: U Are Gynae MD

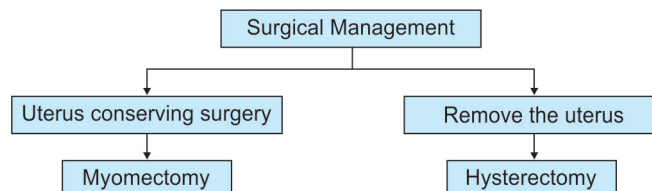
**MC**

**U:** Ullipristone  
**Are:** Aromatase 1 inhibitor–Letrozole  
**Gynae** GnRH agonist  
 GnRH antagonist  
**M** Mifepristone  
**D** Danazol/Gestrinone

### B. Drugs to decrease blood loss/menorrhagia in case of fibroids:

- All the drugs used to decrease size of fibroid can be used along with
- Progesterone releasing intrauterine devices–LNG IUCD
- OCP's (Low dose pills)
- Tranexamic acid–non-hormonal drug

### Surgical management



**Some Specific Indications for Hysterectomy**

- In patients > 40 years of age.<sup>Q</sup>
- Multiparous women.<sup>Q</sup>
- If fibroid is associated with malignancy.<sup>Q</sup>
- During myomectomy, if there is uncontrolled hemorrhage or other surgical difficulty.<sup>Q</sup>



Hysterectomy for fibroids can be done by

- Abdominal route
- Vaginal route—done, if size of uterus is < 12 weeks in size

**Myomectomy**

- Myomectomy is specifically indicated in an infertile woman or woman desirous of bearing child and wishing to retain the uterus.<sup>Q</sup>
- **Prerequisites:** Anemia should be corrected.<sup>Q</sup>
  - All other causes of infertility should be excluded.<sup>Q</sup>
  - Male factor infertility should be ruled out.<sup>Q</sup> (husband semen analysis should be normal)
  - Diagnostic D and C or hysteroscopy should be performed in case of irregular cycles, to detect any polyp and to rule out endometrial cancer<sup>Q</sup>
  - Hysteroscopy or hysterosalpinography (HSG) should be done to detect a fibroid encroaching the uterine cavity or a polyp or tubal block.<sup>Q</sup>



**Myomectomy**  
Myomectomy is the enucleation of myomata from the uterus leaving behind a potentially functioning organ capable of future reproduction<sup>Q</sup>

**Time of Myomectomy**

- It should be performed in immediate postmenstrual phase to reduce blood loss during surgery<sup>Q</sup>
- It should not be performed during pregnancy and at the time of cesarean section.<sup>Q</sup>
- Route of myomectomy
  - Laparoscopic
  - Abdominal
  - Hysteroscopic



Instrument used to decrease blood loss during myomectomy: Bonney's myomectomy clamp.<sup>Q</sup>  
**Note:** If Bonney's clamp or tourniquets are being used, they must be released after every 20 minutes during surgery as there can be accumulation of histamine like substances, which if suddenly released into circulation can cause shock.

- Myomectomy operation should always be followed by shortening of round ligament to prevent retroversion.<sup>Q</sup>
- Bonney's hood technique: is done in interstitial fibroid on the fundal posterior wall.<sup>Q</sup>

**Laparoscopic myomectomy:**

- Preferred as less operative time
- Less blood loss
- Less post-operative stay
- Early ambulation
- It is done in subserosal/intramural/type 2 submucosal (see next page FIGO classification of fibroid)
- Disadvantage—higher recurrence rate

**Hysteroscopic myomectomy:**

- Done for type 0 and type 1 submucosal fibroids.
- Associated with more blood loss
- Due to saline distension media—it can lead to electrolyte imbalance
- Perforation uterus can occur
- Risk of infection present

**Contraindications of Myomectomy**

- Big broad ligament fibroid (as many large vessels are present which can cause uncontrollable bleeding and thus the need to abandon myomectomy and do hysterectomy<sup>Q</sup>)
- Multiple tiny fibroids scattered through the uterine wall.<sup>Q</sup>
- Infected fibroid
- Pelvic or endometrial TB
- During pregnancy on following section



Contraindications for laparoscopic myomectomy:

- Medical conditions likely to be worsened with abdominal distension and Trendelenburg position for a long period
- Diffuse leiomyomas
- More than three myomas equal to or more than 5 cm
- Uterine size more than 16 weeks of gestation
- Myoma more than 15 cm in diameter
- Incision totaling to more than 15 cm.

### Results (Important)

- Pregnancy rate following myomectomy: 40–60%
- Recurrence rate: 30–50%
- Persisting menorrhagia: 1–5%<sup>Q</sup>
- 20–25% women subjected to myomectomy ultimately come for hysterectomy.
- Rupture of myomectomy scar during pregnancy is rare.
- Low-grade postoperative pyrexia is a rule and should not be treated by antibiotics (pyrexia is due to slight extravasation of blood in uterine wall or peritoneal cavity and settles spontaneously in 7–14 days).

### Measures to Control Blood Loss during Myomectomy ...Dutta Gynae 6<sup>th</sup>/ed p 604

- **Timing the surgery** in immediate postmenstrual phase.
- **Preoperative treatment with GnRH analogue** reduces the vascularity of the tumour and thereby reduces operative blood loss
- Injection of vasoconstrictive agents (commonly used is **vasopressin**) into the serosa overlying myoma.
- **Use of tourniquets:** To occlude the uterine vessels and also the ovarian vessels at the infundibulopelvic ligament.
- **Use of Victor Bonney's specially** designed clamp to reduce uterine artery blood flow. This clamp is placed around the uterine vessels and the round ligament.
- **Controlled hypotensive anaesthesia** (using sodium nitroprusside) to reduce venous tone and moderate degree of Trendelenburg position (enhance venous drainage) reduce operative blood loss.

### Embolotherapy

- *Uterine artery embolization* is done using **polyvinyl<sup>Q</sup> alcohol or gel foam<sup>Q</sup>**. It is performed by an *interventional radiologists* and involves catheterization of *the femoral artery to gain access to the hypogastric arteries*. Under fluoroscopic guidance the uterine arteries are occluded using gel foam, polyvinyl alcohol, in patients not suited for or not desirous of surgical therapy.
- In this manner, uterine blood flow is obstructed producing ischemia and necrosis.
- It shrinks the fibroid by 40–50% in selective young women<sup>Q</sup> and menorrhagia resolves by 90%. If patient is still symptomatic after year then surgery should be considered
- It can be used preoperatively before surgery to decrease blood cans during surgery on can be used aline for therapeutic purpose.

### Results

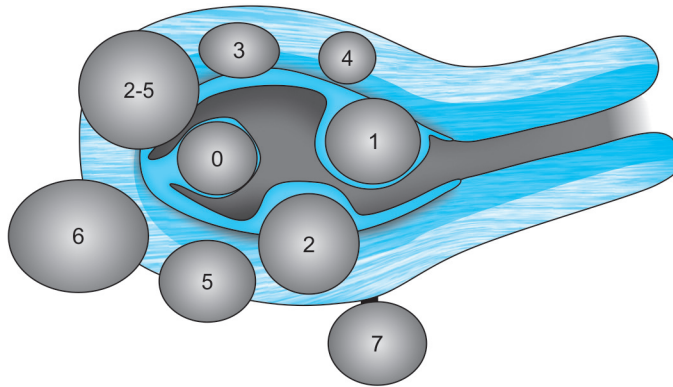
These patients experience:

- Lowered fertility rate<sup>Q</sup>
- Risk of placental insufficiency<sup>Q</sup>
- Uterine rupture in subsequent pregnancy<sup>Q</sup> because of interference with the blood supply and embolotherapy induced necrosis of the leiomyoma.
- Early ovarian failure, thus uterine artery embolization should not be done in females who desire future childbearing.
- Rate of reoperation is as high as 30% and reoperation rate is age-dependant, with higher likelihood in women over 40 years of age.
- **MRg HIFU**

**Magnetic resonance imaging-guided focused ultrasound surgery (MRgFUS)** is used in managing fibroid. In MRgFUS, fibroid tissue is heated and destroyed using targeted ultrasonic energy passing through the anterior abdominal wall.

- Normal uterine muscle cells, at a temperature  $\geq 57^{\circ}\text{C}$  remain intact following the procedure.
- The fibroid does not disappear; however, it shrinks in size leading to a reduction in symptoms.
- It is not appropriate for pedunculated myomas or those adjacent to bowel or bladder.
- Potential side effects include skin or nerve burns.
- It is not done in fibroids more than 5 in number degenerated fibroids, pedunculated fibroids  $2 > 12\text{ cm}$  from semi surface

**Extra edge**



**Fig. 11.2:** FIGO Classification of fibroids

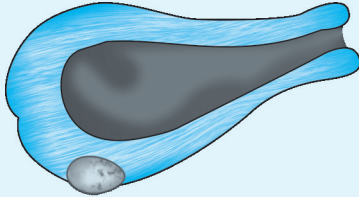
**FIGO Fibroid Classification**

FIGO Leiomyoma Classification System		
SM-Submucosal	0	Pedunculated intracavitary
	1	< 50% intramural
O-Other	2	$\geq 50\%$ intramural
	3	Contacts endometrium; 100% intramural
	4	Intramural
	5	Subserosal $\geq 50\%$ intramural
	6	Subserosal <50% intramural
	7	Subserosal pedunculated
Hybrid leiomyomas (impact both endometrium and serosa)	8	Other (specify e.g. cervical, parasitic)
	2-5	Two numbers are listed separated by a hyphen. By convention, the first refers to the relationship with the endometrium while the second refers to the relationship to the serosa. One example is below
	2-5	Submucosal and subserosal, each with less than half the diameter in the endometrial and peritoneal cavities, respectively.

## FIGURE BASED QUESTIONS

**F1.** Identify the fibroid based on FIGO classification:

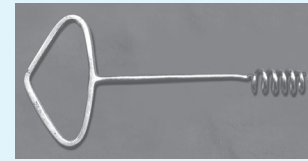
- a. Type 3
- b. Type 4
- c. Type 5
- d. Type 7



**Fig. F1**

**F2.** Identify the instrument:

- a. Myoma clamp
- b. Myoma screw
- c. Uterine manipulator
- d. IUCD removing hook



**Fig. F2**

**F3.** Identify the instrument shown in Figure F3

- a. Bonneys myoma screw
- b. Bonneys myoma clamp
- c. Cervical occlusion clamp
- d. Uterus holding forcep



**Fig. F3**

## QUESTIONS

1. All changes occur in fibroid uterus except: (AIIMS June 97)
  - a. Atrophy
  - b. Squamous metaplasia
  - c. Hyaline degeneration
  - d. Calcification
2. A pregnant woman with fibroid uterus develops acute pain in abdomen with low-grade fever and mild leukocytosis at 28 week. The most likely diagnosis is: (AIIMS Nov 03)
  - a. Preterm labor
  - b. Torsion of fibroid
  - c. Red degeneration of fibroid
  - d. Infection in fibroid
3. Not true about red degeneration of myomas is: (AIIMS May 02)
  - a. It occurs commonly during pregnancy
  - b. Immediate surgical intervention is needed
  - c. Due to interference with blood supply
  - d. Treated with analgesics
4. Red degeneration in uterine fibroid is most common in: (AI 99; AIIMS June 97)
  - a. Second trimester
  - b. Third trimester
  - c. Puerperium
  - d. First trimester
5. All are methods of managing fibroid uterus except: (AIIMS Nov 99)
  - a. Myomectomy
  - b. Radiofrequency ablation
  - c. Embolization of uterine artery
  - d. Laser myomectomy
6. Sucheta, a 29-year-old nulliparous women complains of severe menorrhagia and lower abdominal pain since 3 months. On examination there was a 14 weeks size uterus with fundal fibroid. The treatment of choice is: (AIIMS May 01)
  - a. Myomectomy
  - b. GnRH analogs
  - c. Hysterectomy
  - d. Wait and watch
7. To start with all fibroids are: (PGI Dec 98)
  - a. Interstitial
  - b. Submucous
  - c. Subserous
  - d. Ovarian
8. Calcareous degeneration occurs most commonly in which type of fibroids: (PGI 97)
  - a. Submucous
  - b. Subserous
  - c. Interstitial
  - d. Cervical
9. Uterine fibromyoma is associated with: (PGI June 02)
  - a. Endometriosis
  - b. Pelvic inflammatory disease
  - c. Ovarian Ca
  - d. Amenorrhoea
  - e. Tamoxifen
10. Treatment of red degeneration of fibroid during pregnancy: (PGI Dec 03)
  - a. Analgesics
  - b. Laparotomy
  - c. Termination of pregnancy
  - d. Removal at cesarean section
11. Submucosal fibroid is detected by: (PGI Dec 05, 02)
  - a. Hysteroscopy
  - b. Hysterosalpingography
  - c. USG (Transabdominal)
  - d. Laparoscopy
12. The drug which reduces the size of myoma includes: (PGI Dec 05)
  - a. GnRH agonist
  - b. Danazol
  - c. Progesterone
  - d. Mifepristone
  - e. Estrogen



13. Drugs that reduce the size of fibroid are: (PGI June 03)  
 a. Danazol                      b. GnRH analog  
 c. RU-486                      d. Estrogen  
 e. Progesterone
14. Decreased vascularity of fibroid is seen with:  
 a. GnRH agonist (PGI Dec 06)  
 b. Danazol  
 c. Mifepristone  
 d. Clomiphene citrate
15. Management options in a 26-year-old women with 7 × 8 cm size fibroid: (PGI June 09)  
 a. Follow-up                      b. OCP  
 c. Myomectomy                      d. Hysterectomy  
 e. Danazol
16. True regarding fibroid uteri: (PGI June 02)  
 a. Estrogen dependant tumor  
 b. Capsulated  
 c. Can lead to red degeneration in pregnancy for which urgent surgery is required  
 d. Danazol used in treatment
17. Malignant prevalence in fibroid is: (UP 99)  
 a. 0.5%                      b. 1%  
 c. 5%                      d. 10%
18. Least common complication of fibroid is: (AI 98)  
 a. Menstrual disorder                      b. Malignancy  
 c. Urinary retention                      d. Degeneration
19. In fibroid which is not seen: (AI 07)  
 a. Amenorrhea                      b. Pelvic mass  
 c. Infertility                      d. Menstrual irregularity
20. What is the earliest most common presenting feature of anterior cervical fibroid?  
 a. Frequency of urine                      b. Bleeding  
 c. Acute abdomen                      d. Constipation
22. All are prerequisites for myomectomy except:  
 a. Husbands semen analysis  
 b. D and C report  
 c. Hysterectomy consent  
 d. None of the above
23. All are complications of fibroid in pregnancy except:  
 a. Red degeneration  
 b. Obstructed labor  
 c. PPH  
 d. Placenta previa
24. Most common type of uterine polyp is:  
 a. Mucous polyp                      b. Fibroid  
 c. Placental polyp                      d. None
25. All of the following measures reduce bleeding during myomectomy except: (DNB 08)  
 a. Preoperative correction of anemia  
 b. Preop oc pills  
 c. Ligation of pedicle  
 d. GNRH analogues  
 e. Local injection of vasoconstrictive agents
26. Regarding imaging of uterine fibroids all are correct except:  
 a. Ultrasound is ideal to confirm the diagnosis  
 b. Saline Infusion Sonography (SIS) is more sensitive to detect any submucous fibroid  
 c. MRI is superior to USG to identify the exact location of myoma  
 d. CT scanning is an alternative to MRI
27. Concerning fibroids:  
 a. Use of GnRH analogues cause permanent reduction in size  
 b. Pregnancy following myomectomy is about 80%  
 c. Recurrence rate following myomectomy is about 30%  
 d. Growth factors (IGF-1, EGF) stimulates myoma to grow
28. The surgical treatment of uterine polyp includes:  
 a. Removal by twisting  
 b. Removal by morcellment  
 c. Hysteroscopy  
 d. All of the above

### NEW PATTERN QUESTIONS

21. All of the following are the indications for myomectomy in a case of fibroid uterus except:  
 a. Associated infertility  
 b. Recurrent pregnancy loss  
 c. Pressure symptoms  
 d. Red degeneration

## ANSWERS TO FIGURE BASED QUESTIONS

**F1. Ans. is c i.e. Type 5**

*Ref. Novaks Gynaec 15/e p445)*

The fibroid shown in the figure is subserosal with 50% intramural component. Hence it is type 5.

**F2. Ans. is b i.e. Myoma screw**

*Ref. Dutta Gyane 6/e p635*

**It is a myoma screw:**

**Uses:** To fix the myoma after the capsule is cut open to give traction while the myoma is enucleated of its bed (myomectomy)

To give traction in a big uterus (multiple fibroids are requiring hysterectomy while the clamps are placed.)

**F3. Ans. is d i.e. Bonneys myoma clamp**

*Ref. Dutta Gyane 6/e p635*

The clamp is used in myomectomy operation. It curtails the blood supply to the uterus temporarily, thereby minimizing the blood loss during operation. Simultaneous, bilateral clamping of the infundibulopelvic ligaments by rubber guarded sponge holding forceps may be employed.

The instrument is placed at the level of internal os with the concavity fitting with the convexity of the symphysis pubis. The round ligaments of both sides are included inside the clamp to prevent slipping of the instrument and preventing the uterus from falling back. The clamp is removed after suturing the myoma bed but before closing the peritoneal layers.

It is seldom used nowadays. Alternative methods are: Preoperative use of GnRH analogue, and/or intraoperative use of tourniquets, vasoconstrictive agents (vasopressin) and others.

## ANSWERS

**1. Ans. is b, i.e. Squamous metaplasia**

Fibromyoma can have following complications and degenerative changes:

Complications	Changes/Degenerations	
<ul style="list-style-type: none"> <li>Torsion<sup>Q</sup></li> <li>Hemorrhage<sup>Q</sup></li> <li>Infection<sup>Q</sup></li> <li>Ascites; pseudo-Meig's syndrome<sup>Q</sup> (Produced by pedunculated<sup>Q</sup> subserous fibroid)<sup>Q</sup></li> <li>Malignant change<sup>Q</sup> (rarest)</li> </ul>	<ul style="list-style-type: none"> <li>– Avoid</li> <li>– Red</li> <li>– Hot</li> <li>– Fatty</li> <li>– Meat</li> <li>– Of chicken</li> </ul>	<ul style="list-style-type: none"> <li>= Atrophy</li> <li>= Red degeneration</li> <li>= Hyaline degeneration (MC)</li> <li>= Fatty degeneration or calcification</li> <li>= Myxomatous degeneration</li> <li>= Cystic degeneration</li> </ul>
<i>(Mnemonic: Avoid Red hot fatty meat of chicken)</i>		

**Also know:**

- Most common degeneration: Hyaline degeneration.<sup>Q</sup>
- Degeneration starts from the central part, as fibroid is lined by a pseudocapsule. The blood vessels supplying the fibroid lie in the pseudocapsule.<sup>Q</sup> So the most vascular part of the fibroid is the peripheral part and least vascular is the central part.
- Calcification starts from the periphery (Womb stone) of fibroid.<sup>Q</sup>
- Most uncommon (rarest) change in fibroid is malignant change/sarcomatous change.<sup>Q</sup> It occurs in 0.5%<sup>Q</sup> cases of fibroid.

**2. Ans. is c, i.e. Red degeneration of fibroid**     *Ref. Shaw 15<sup>th</sup>/ed p 355; Dutta Obs 6<sup>th</sup>/ed p 314; High Risk Pregnancy 2<sup>nd</sup>/ed p 77*

Friends, the answer is quite obvious but let's see how other options can be ruled out.

**Option "a"** Preterm labor

Points in favor	Points against
<ul style="list-style-type: none"> <li>Patient is pregnant</li> <li>Pain in abdomen at 28 weeks (preterm labor is where labor starts before the 37<sup>th</sup> completed weeks. The lower limit is 28 weeks in developing countries and 20 weeks in developed countries)</li> </ul>	<ul style="list-style-type: none"> <li>• Preterm labor is diagnosed</li> <li>– When there are regular uterine contractions. (Not acute pain) With or without pain at least in every 10 minutes.</li> <li>– Dilatation of cervix is &gt; 2 cm</li> <li>– Effacement of cervix = 80%</li> <li>– Length of cervix as measured by TVS &lt; 2.5 cm and funneling of the internal OS.</li> <li>– Pelvic pressure backache, vaginal discharge, or bleeding. None of the above criteria are being fulfilled</li> </ul>

*Contd....*

Contd....

- Presence of leukocytosis and fever can also go against it as even if there is intra-amniotic infection causing preterm labor features like—fever, leukocytosis, uterine tenderness, and fetal tachycardia are absent. Rather, if these features are present it means a final stage of uterine infection has reached. And here our patient is having fever, leukocytosis without regular uterine contractions (off and on pair) but with acute pain in abdomen, so it can be ruled out

**Option “b”** Torsion of fibroid

Points in favor	Points against
<ul style="list-style-type: none"> <li>• Patient has fibroid (Though no mention has been made whether it is pedunculated or not, Remember torsion is seen in subserous pedunculated myomas)<sup>o</sup></li> <li>• Patient is complaining of acute pain in abdomen</li> </ul>	<ul style="list-style-type: none"> <li>• Torsion is not associated with fever and leukocytosis</li> </ul>

**Option “d”** Infection of fibroid

Points in favor	Points against
<ul style="list-style-type: none"> <li>• Presence of fibroid (Remember: Infection is common in submucous fibroids)<sup>o</sup></li> <li>• Fever</li> <li>• Leukocytosis</li> </ul>	<ul style="list-style-type: none"> <li>• Acute pain in abdomen (Infection of fibroid will not cause acute pain in abdomen).</li> <li>• Infection of fibroid occurs following abortion or labor (Here patient is pregnant but there is no history of abortion or labor)</li> <li>• Infection causes blood stained discharge (Not seen in this patient)</li> </ul>

So, from above discussion infection can be kept in +/- status. If we have no better option, we can think about it.

**Option “c”** i.e. Red degeneration of fibroid is the diagnosis—let’s have a look.

**Red degeneration of fibroid**

- It is seen mostly during pregnancy and mid pregnancy<sup>o</sup>
- The myoma suddenly becomes acutely painful<sup>o</sup>, enlarged,<sup>o</sup> and tender.<sup>o</sup>
- **Patient presents with:**
  - Acute abdominal pain<sup>o</sup>
  - Vomiting<sup>o</sup>
  - Malaise<sup>o</sup>
  - Slight fever<sup>o</sup>

**Lab investigations:** Show moderate leukocytosis<sup>o</sup> and raised ESR<sup>o</sup>

Thus, all the features given in the question favor the diagnosis of red degeneration.

**3. Ans. is b, i.e. Immediate surgical intervention is required**

Ref. Shaw 15<sup>th</sup>/ed p 355; Jeffcoate 7<sup>th</sup>/ed p 502

Let us see each option one by one.

*Red degeneration of fibroid commonly occurs during pregnancy. (Option “a” is thus correct)*

- The pathogenesis of fibroid is obscure but the initial change appears to be one of subacute necrosis which is presumably due to an interference with its blood supply. Some say that arterial or venous thrombosis is the basis of this and the lesion is the result of infarction. (Option “c” is thus correct). Ref. Jeffcoate 7<sup>th</sup>/ed p 502
- Red degeneration should be **managed conservatively with bed rest and analgesics** to relieve the pain. (**option “d”** is thus correct)
- There is no need for surgical intervention.

*For more details on Red Degeneration, refer to the preceding text*

**4. Ans. is a i.e. Second trimester**

Ref. Jeffcoate 7<sup>th</sup>/ed p 502

Friends, answer to this question was quite obvious as each one of us have mugged it up; but finding an appropriate reference was a difficult task.

Read for yourself what Dutta Obs. 6<sup>th</sup>/ed p 309 has to say—

*“Red degeneration; It predominantly occurs in a large fibroid during the second half of pregnancy or puerperium.”*

From the above statement answer could be second trimester, third trimester or puerperium.

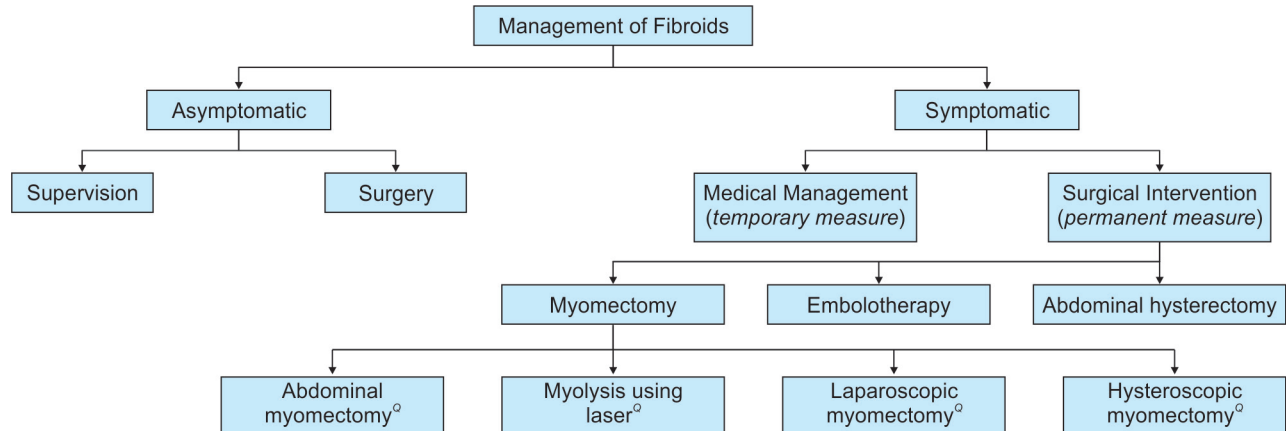
*“Red degeneration; manifests typically about midpregnancy when the leiomyoma suddenly become acutely painful, enlarged and tender.”* Ref. Jeffcoate 7<sup>th</sup>/ed p 502

This clears the doubts and confirms our answer, i.e. red degeneration is most common during second trimester (mid pregnancy).

Friends you should also keep in mind the following important points regarding **Fibroids and pregnancy**.

- Most fibroids do not increase in size during pregnancy.
- Only 5% females with fibroid have degeneration during pregnancy.

5. **Ans. is b, i.e. Radiofrequency ablation** Ref. Shaw 15<sup>th</sup>/ed pp 360-2; Jeffcoate 7<sup>th</sup>/ed pp 497-9; Dutta Gynae 5<sup>th</sup>/ed pp 269-73



6. **Ans. is a, i.e. Myomectomy**

Ref. Shaw 15<sup>th</sup>/ed p 360; Jeffcoate 7<sup>th</sup>/ed p 496-8

First, let us see whether we would like to go for medical management or surgical intervention.

The patient is presenting with:

- Severe menorrhagia<sup>o</sup>
- Chronic lower abdomen pain<sup>o</sup>

These indications are strong enough for surgical intervention. Earlier size of fibroid >12 weeks was also an indication for surgery but nowadays it is not.

Now comes the question – whether myomectomy or hysterectomy should be done.

**Indication of Myomectomy:** Myomectomy is specifically indicated in an infertile woman or woman desirous of bearing child and wishing to retain her uterus.

Since, our patient, Sucheta is just 29 years and nulliparous – Myomectomy should be done.

7. **Ans. is a, i.e. Interstitial**

Ref. Shaw 15<sup>th</sup>/ed p 352

- Most common variety of fibroid is intramural/interstitial (75%) followed by submucous (15%) and subserous (10%).
- To start with all fibroids are intramural/interstitial.<sup>o</sup>

8. **Ans. is b, i.e. Subserous**

Ref. Dutta Gynae 6<sup>th</sup>/ed p 265

*“Calcareous degeneration usually involves the subserous fibroids with small peduncle or myomas of postmenopausal women. It is usually preceded by fatty degeneration. There is precipitation of calcium carbonate or calcium phosphate within the tumor, when whole of the tumor is converted into a calcified mass it is termed as ‘womb stone’ ”*

Ref. Dutta Gynae 5<sup>th</sup>/ed p 265

9. **Ans. is a, i.e. Endometriosis**

Ref. Jeffcoate 7<sup>th</sup>/ed p 490

Diseases commonly associated with leiomyomas are:

- Follicular cysts of ovary<sup>o</sup>
- Endometrial hyperplasia<sup>o</sup>
- Endometrial cancer<sup>o</sup>
- Endometriosis<sup>o</sup>

- It is sometimes said salpingitis (i.e. pelvic inflammatory disease) is a common finding in patients of fibroid, but it is not true, the only possible link between the two is infertility (so **option “b”** is ruled out)
- Leiomyomas are associated with follicular cysts of ovaries (Not ovarian cancer-ruling out **option “c”**).
- Most common symptom of fibroid is menorrhagia and not amenorrhoea (so obviously amenorrhoea is not correct).

Now coming to the last option – Tamoxifen.

Tamoxifen causes Endometrial hyperplasia<sup>o</sup> and Endometrial cancer, not Fibromyoma.

10. **Ans. is a, i.e. Analgesics**

Ref. Shaw 15<sup>th</sup>/ed p 364; Dutta Obs 6<sup>th</sup>/ed p 309; Jeffcoate 7<sup>th</sup>/ed p 502

Management of red degeneration of fibroid.

- Patient is managed conservatively.<sup>o</sup>

- Patient is put to bedrest and given analgesics<sup>Q</sup> (to relieve the pain), sedatives<sup>Q</sup>, and if required, antibiotics.<sup>Q</sup>
- If because of mistaken diagnosis laparotomy is done, abdomen is closed without doing anything.
- Myomectomy should never be contemplated during cesarean section as vascularity of fibroid is increased during pregnancy (due to increased estrogen) leading to increased blood loss during cesarean section.<sup>Q</sup>

For more information about Red degeneration, refer to the preceding text.

11. Ans. is a, b and c, i.e. **Hysteroscopy; Hysterosalpingography; and USG (Transabdominal)**

Ref. John Hopkin's Manual of Obs and Gynae 4<sup>th</sup>/ed p 449; William's Gynae 1<sup>st</sup>/ed p 203; Dutta Gynae 6<sup>th</sup>/ed p 278-9

**USG: Ultrasound is the most readily available, least costly imaging technique to diagnose fibroid.**<sup>Q</sup> It checks the number<sup>Q</sup>, location<sup>Q</sup>, and size<sup>Q</sup> of fibroids and helps to reduce overlooking small fibroids during surgery (which might lead to persistence or recurrence of symptoms).

**Sonohysterography** - is instillation of saline into endometrial cavity during TVS

**Hysteroscopy or hysterosalpingography:** These methods are useful to detect **submucous fibroid** in unexplained infertility and repeated pregnancy wastage. The presence and site of submucous fibroid can be diagnosed by direct visualization during hysteroscopy or indirectly as a filling defect on HSG. Hysteroscopy also allows its excision under direct vision.

**Uterine Curettage:** It can also help in diagnosis of submucous fibroid by feeling of a bump during curettage.<sup>Q</sup>

**Laparoscopy:** is helpful if uterine size is less than 12 weeks, for detection of subserous fibroid and not submucous. It can also differentiate a pedunculated fibroid from an ovarian tumor not revealed by clinical examination and ultrasound.

12. Ans. is a, b and d, i.e. **GnRH against; Danazol; and Mifepristone**

13. Ans. is a, b and c, i.e. **Danazol; GnRH analogs and RU-486**

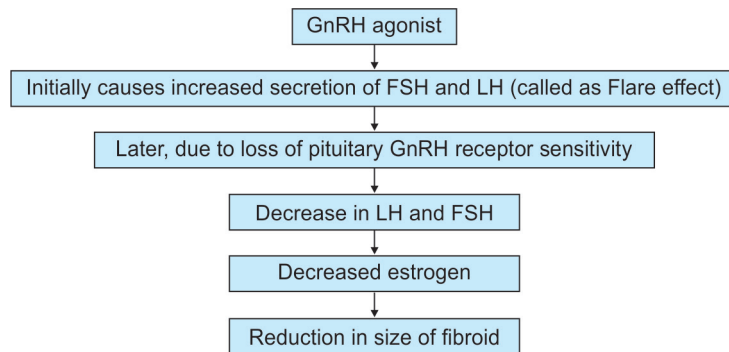
14. Ans. is a, b and c, i.e. **GnRH agonist, Danazol and Mifepristone**

Ref. Shaw's 14<sup>th</sup>/ed p 323; Dutta Gynae 4<sup>th</sup>/ed pp 261-2; William's Gynae 1<sup>st</sup>/ed pp 204-5

**M**

<b>U:</b>	Ulliprestone
<b>Are</b>	Aromatase 1 inhibitor-Letrozole
<b>Gynae</b>	GnRH agonist GnRH antagonist
<b>M</b>	Mifepristone
<b>D</b>	Danazol/Gestrinone

**Mechanism of action:**



GnRH analogs cause reduction in size (50%) when used for a period of 6 months. But size comes back to previous state after the drug is withdrawn and the hypoestrogenic state induced by GnRH-agonists causes significant loss after 6 months of therapy.

*"Because of these limitations of GnRH agonist therapy, The American College of Obstetricians and Gynaecologists currently recommends it only as a temporizing agent in women nearing menopause or as surgical pretreatment in selected women."*

Ref. William's Gynae 1<sup>st</sup>/ed p 205

**GnRH analogs are used preoperatively:**

- To decrease the vascularity and blood loss during surgery
- To induce amenorrhea - to build up hemoglobin in cases of anemia
- May facilitate laparoscopic or hysteroscopic surgery.

**GnRH antagonist:** They don't cause initial stimulatory effect and cause immediate suppression of pituitary and thus, decrease the size of fibroid.

**15. Ans. is a and c, i.e. Follow-up and Myomectomy**Ref. Williams Gynae 1<sup>st</sup>/ed p 205

The question here does not specify whether the fibroid is asymptomatic or symptomatic.

In case of asymptomatic fibroid-

*"Regardless of their size, asymptomatic leiomyomas usually can be managed expectantly by annual pelvic examination (ACOG 2001). If the assessment of the adnexa is hindered by uterine size or contour, some may choose to add annual sonographic surveillance."*

Ref. Williams Gynae 1<sup>st</sup>/ed p 203

So management of an asymptomatic fibroid is—simply follow-up

**In case of symptomatic fibroid -**

Medical management is a temporary measure and should be undertaken with the sole purpose of decreasing the size of fibroid or building hemoglobin levels, in females awaiting surgery. Now as far as - OCPs and Danazol is concerned,

**OCPs** - *"Because of the unpredictable effects of progestins on leiomyoma growth with the potential to worsen symptoms, the American Society for Reproductive Medicine (2004a) does not recommend either progestins or combination COCs for leiomyoma related symptoms."*

Ref. William's Gynae 1<sup>st</sup>/ed p 204

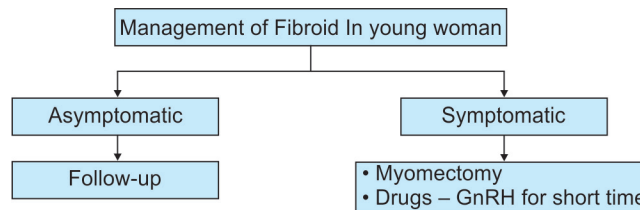
**Danazol** - *"Both danazol and gestrinone have found to shrink leiomyoma volume and improve bleeding symptoms. Unfortunately, their prominent side effects, which include acne and hirsutism, preclude their use as first-line agents."* Ref. William's Gynae 1<sup>st</sup>/ed p 204

Thus, option "b" i.e. OCP and option "e" i.e. danazol are ruled out.

**Surgical management:**

Between myomectomy and hysterectomy-

Myomectomy is preferred here because patient is too young (only 26 years) and may desire future pregnancy.

**16. Ans. is a and d, i.e. Estrogen dependant tumor; and Danazol is used in treatment**Ref. Shaw 15<sup>th</sup>/ed pp 352, 355, 359

As discussed earlier, fibroids are estrogen dependant tumors<sup>Q</sup> and don't have a true capsule but a pseudo capsule<sup>Q</sup>.

- Red degeneration occurs in pregnancy but does not require surgical management, rather it is managed conservatively.
- Danazol is used in medical management of fibroid to both decrease its vascularity as well as its size.

(Although it is not the first-line drug).

**17. Ans. is a, i.e. 0.5%****18. Ans. is b, i.e. Malignancy**Ref. Shaw 15<sup>th</sup>/ed pp 353-5; Jeffcoate 7<sup>th</sup>/ed pp 500-2

- Sarcomatous change is seen in 0.2-0.5% of fibroids. It is the least common complication of fibroid.
- Sarcomas with malignant behavior have  $\geq 10$  mitoses/high power field.
- M/c fibroid to undergo malignancy is Submucous followed by Intramural.

Ref. Textbook of Gynae Sheila Balakrishnan 1<sup>st</sup>/ed p163**19. Ans. is a, i.e. Amenorrhoea**Ref. Shaw 15<sup>th</sup>/ed pp 356-7; Jeffcoate 7<sup>th</sup>/ed pp 492-3

Fibroids do not lead to amenorrhoea, they lead to menorrhagia/metrorrhagia

**20. Answer is a, i.e. Frequency of urine**Ref. Dutta Gynae 6<sup>th</sup>/ed p 284

Symptoms of cervical fibroid are predominantly due to pressure effect on surrounding structures.

Anterior cervical fibroid irritates the trigone of bladder causing frequency of micturition or even retention due to pressure effects.

In lateral cervical fibroid, vascular obstruction may lead to hemorrhoids and rarely, edema of legs. The ureter is pushed laterally and below the tumor.

Posterior cervical fibroid predominantly presents with retention of urine and constipation.

**21. Ans. is d, i.e. Red degeneration**Ref. Shaw 15<sup>th</sup>/ed pp 360-2; Jeffcoat's 7<sup>th</sup>/ed p 502

From the given options the answer is quite obvious as red degeneration of fibroid is managed conservatively not by any surgery. But let us rule out other options also.

**Indication of myomectomy:** Myomectomy is specifically indicated in an infertile woman, in recurrent abortions and patients with symptomatic fibroid but desirous of bearing child and wishing to retain the uterus.

Thus, option a and b are ruled out. As far as pressure symptoms are concerned, it means fibroid is symptomatic and all symptomatic fibroids need surgical management which could either be myomectomy or hysterectomy.

**22. Ans. is d, i.e. None of the above**

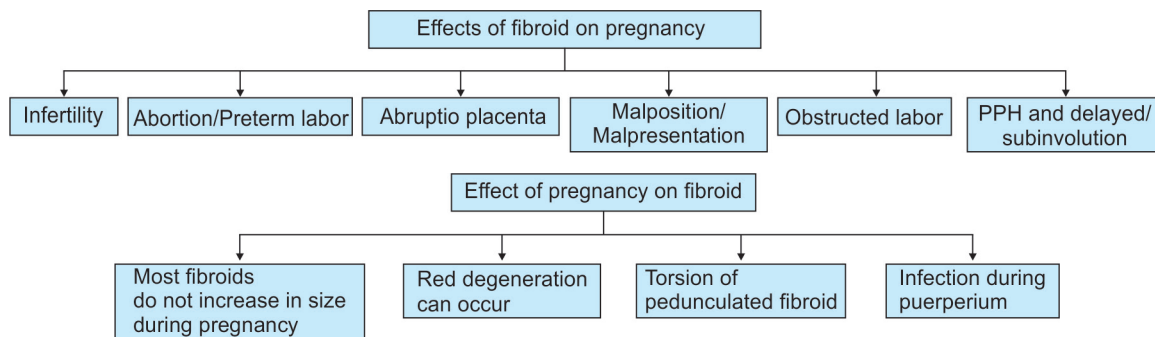
*Ref. Dutta Gynae 6<sup>th</sup>/ed p 269*

**Prerequisites for myomectomy:** Anemia should be corrected.<sup>Q</sup>

- All other causes of infertility should be excluded.<sup>Q</sup>
- Male factor infertility should be ruled out.<sup>Q</sup> (husband semen analysis should be normal).
- Diagnostic D and Cor endometrial biopsy should be performed in case of irregular cycles, to detect any polyp and to rule out endometrial cancer.<sup>Q</sup>
- Hysteroscopy or HSG: To detect a fibroid encroaching the uterine cavity or a polyp or tubal block.<sup>Q</sup>

**23. Ans. is d, i.e. Placenta previa**

*Ref. Jeffcoate 7<sup>th</sup>/ed pp 493-4*



Thus, placenta previa is not a complication of fibroid → Abruptio placenta is a complication.

**24. Ans. is a, i.e. Mucous polyp**

*Ref. Jeffcoate 7<sup>th</sup>/ed p 488*

- **M/C uterine polyp is mucous (endometrial/adenoma) polyp.**
- Polyps are mostly symptomless, if they become ulcerated, then features of menorrhagia/metrorrhagia are seen.
- M/C in postmenopausal females
- Predisposing factors: HRT, tamoxifen therapy and Increased patient age
- IOC = Hysteroscopy
- Management: Hysteroscopy-guided polypectomy.
- Rarely, polyps undergo malignant change (0.5%):
  - Endometrial polyp develops into adenocarcinoma
  - Fibroid polyp into sarcoma
  - Placental polyp into choriocarcinoma.

**25. Ans. is b, i.e. Preoperative OC pills**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 604*

**Measures to control blood loss during myomectomy**

- Preoperative GnRH analogs
- Moderate degree of edelenberg position to enhance venous return
- Timing the surgery in immediate postmenstrual phase.
- Hypotensive anaesthesia (using sodium nitro prudeside)
- Use of vasoconstrictive agents mainly vasopressin intraoperatively
- Use of victor Bonney's myomectomy clamp around blood vessels and round ligament
- Use of tourniquets around blood vessels
- Uterine artery embolisation (UAE)

**26. Ans. is d, i.e. CT scanning is an alternative to MRI**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 278-279*

The M/C investigation done to diagnose/detect fibroids is USG "USG is an useful diagnostic tool to confirm its diagnosis".

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 278*

Three dimensional ultrasonography can locate fibroids accurately.

Although MRI are better (more accurate) than USG but is not routinely used as it is expensive and not widely available.

CT scan has got limited contrast resolution than MRI.

For submucous fibroid hysteroscopy on saline infusion semiography can be done.

27. **Ans. is d, i.e. Growth factors (IGF-1 and EGF) stimulate myoma to grow**

Ref. Dutta Gynae 6th/ed p 272

**Option a:** Incorrect as regrowth of myoma occurs after 3 months of GnRH therapy

**Option b:** Is also incorrect as pregnancy rate following myomectomy is 50–60% and not 30%.

**Option c:** Recurrence rate is 1%, 10% and not 30% hence it is also incorrect.

**Option d:** “Epidermal growth factor (EGF), insulin like growth factor (IGF 1), transforming growth factor (TGF), stimulate the growth of the leiomyoma either directly or via estrogen” Dutta Gynae 6<sup>th</sup>/ed p 272. Hence option d is correct.

28. **Ans. is d, i.e. All of the above**

Ref. Dutta Gynae 6<sup>th</sup>/ed p 287, 288

Polyp	Management
Endometrial polyp	<b>Hysteroscopy and resection (best)</b> Removal by ovum forcep Incase of recurrence and, if family completed— uterine curettge hysterectomy
Cervical polyp	Twisting of the pedicle
Big fibroid in vagina	<ul style="list-style-type: none"> <li>• Removal of polyp by morcellation</li> <li>• If associated with inversion enucleate</li> </ul>



# CHAPTER

# 12

## Endometriosis and Dysmenorrhea

### Endometriosis

#### Etiology

- Not fully understood
- Many theories have been proposed to explain endometriosis.

Theory	Proposed by	Mechanism
Sampson's implantation theory	Sampson	Endometriosis occurs as a result of reflux of menstrual endometrium through the fallopian tubes and its subsequent implantation and growth on pelvic peritoneum and surrounding structures
Coelomic metaplasia	Meyer and Ivanoff	Endometriosis arises as a result of metaplastic changes in embryonic cell rests of embryonic mesothelium, which are capable of responding to hormone stimulation
Metastatic theory	Halban	Explains occurrence of endometriosis at less accessible sites like umbilicus, pelvic nodes, ureter, etc. The theory suggests embolization of menstrual fragments occurs through vascular or lymphatic channels. This leads to launching of endometriosis at distant sites
Histogenesis by induction		The theory proposes that an endogenous (undefined) biochemical factor can induce undifferentiated peritoneal cells to develop into endometrial tissue

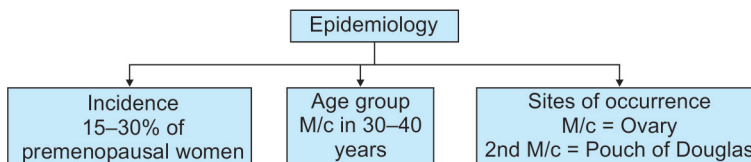


#### Endometriosis

The presence of endometrial tissue (glands and stroma) outside of the uterine cavity



Endometriosis can occur anywhere in body including abdominal wall, lung, pleura, brain, and arm



Risk Factors	Protective Factors
<ul style="list-style-type: none"> <li>• Family history (7–10 fold increased risk if affected 1<sup>st</sup> degree relative)</li> <li>• Obstructive anomalies of genital tract (earlier onset)</li> <li>• Nulliparity</li> <li>• High socioeconomic status due to late marriage and late childbirth</li> <li>• <i>In utero</i> exposure to DES</li> <li>• Hormone – estrogen dependant condition</li> </ul>	<ul style="list-style-type: none"> <li>• Regular exercise</li> <li>• Smoking</li> <li>• Pregnancy</li> </ul>



Endometriosis of ovary is called as endometrioma

### Scar Endometriosis is seen in

- Hysterotomy scar
- Classical cesarean section scar
- Myomectomy scar
- Ventrofixation scar
- Scar involving section of fallopian tube operation.



Endometriosis is classified according to a scoring system standardized by the American Society for Reproductive Medicine

### Pathology

#### Pathology

##### Peritoneum

- Earliest lesion is red petechial lesion later becoming cystic, dark brown or blue black in appearance called as **powder-burn appearance/ gunshot appearance**
- Presence of defects in peritoneum (usually scarring overlying implants) is called as **Allen-Masters syndrome**

##### Peritoneal cavity

- Contains yellowish brown fluid which has prostaglandin responsible for pain of endometriosis

##### Ovary

- Characteristic chocolate cyst (True cyst with columnar **lining epithelium**).
- Beneath the epithelium are pseudo-xanthoma cells which are brown colored due to ingested hemosiderin pigment



There is little correlation, between the extent of disease & symptomatology; pain coincides with the depth of the lesion



Classic triad of endometriosis

- Dysmenorrhea
- Infertility
- Dyspareunia

#### Extra Edge:

#### Classification of endometriosis:

**Minimal:** Isolated superficial disease on peritoneal surface.

**Mild:** Superficial multiple implants < 5 cms with no significant adhesions.

**Moderate:** Multifocal disease, both superficial and invasive and associated with adhesions in tube and/or ovaries.

**Severe:** Multifocal disease like in moderate cases along with large ovarian endometriomas and adhesions in tube, ovaries, and cul de sac



A sharp firm and exquisitely tender 'barb' on the uterosacral ligament = sine qua non of endometriosis

### Clinical Features

- May be asymptomatic
- M/c symptom is secondary dysmenorrhea commencing after 30 years and gradually increasing
- Dyspareunia occurs when pouch of douglas and rectovaginal septum are involved
- Deep-seated pelvic pain
- Premenstrual and postmenstrual spotting
- Infertility: 30-40% of patients with endometriosis will be infertile
- 15-30% of those who are infertile will have endometriosis.



Investigation of choice in endometriosis—Laparoscopy

### Examination Findings

- Fixed retroversion of uterus
- Firm fixed adnexal mass (endometrioma)
- Tender nodularity of uterine ligaments and cul-de-sac felt on rectovaginal examination

### Investigations

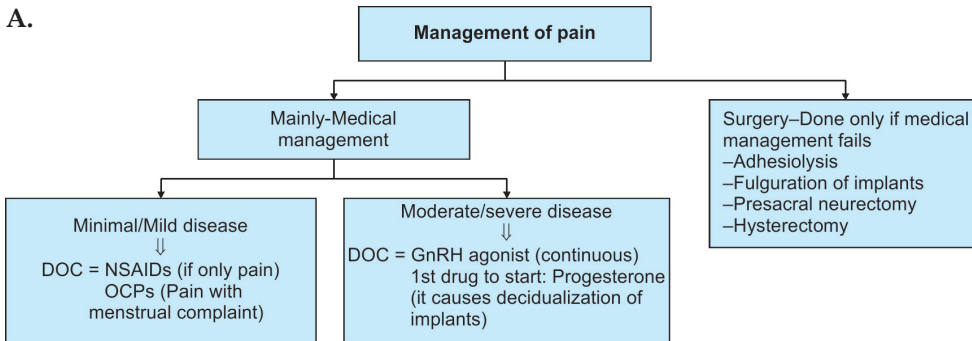
- **IOC = laparoscopy.** Gold standard: Histo pathological examination
- Others = **CA-125**-CA-125 levels are raised in endometriosis.
- Monocyte chemotactic protein (MCP-1) levels are raised in peritoneal fluid of women with endometriosis

**Treatment**

Treatment is justified in all patients regardless of clinical profile as endometriosis progresses in 30–60% patient’s within an year of diagnosis.

Management of Endometriosis: consists of

- A. Managing pain
- B. Managing infertility



**M**  
**Drugs which can be used: In pain management**  
 Proctor–Progesterone (Oral/ Mirera/DMPA injection)  
 And  
 Gamble–GnRH agonist  
 Always–Aromatase inhibitor– Letrozole  
 Offer–OCP  
 Good–Gestrinone  
 Deals–Danazol (Androgenic side effects)

**M**  
 Pain is proportional to depth of invasion

**B. Management of Infertility**

> In minimal/mild endometriosis the cause of infertility is ovarian, either oogenesis is defective or ovum pickup is defective. Hence, management is superovulation with clomiphene followed by intrauterine insemination.

This should be tried for 3 cycles and if patient does not conceive in 3 cycles, do IVF.

> In moderate/severe endometriosis, causes of infertility are both:

Ovarian (as discussed above) and tubal – there is distorted tubal anatomy and formation of dense adhesions in the tubes.

Management = IVF

Results of infertility management are better with advanced endometriosis as IVF is the management

**W**  
 Drugs used in endometriosis can either function as pseudo–pregnancy drugs which bring about decidualization eg. cyclic OCP progesterone or Pseudomenopause (use for short term <6 months due to osteoporotic potential) eg. danazol, GnRH agonists

**Management of Endometrioma**

Laparoscopic management of the endometrioma is the preferred management

**Recent Advances**

—Novak 15<sup>th</sup>/ed p 527

- Latest edition of Novaks 15th/ed, p 506 and John Hopkins Manual of obs and gynae 4th/ed, p 459—mention increased risk of ovarian cancer (Endometrioid and clear cell variety ) in women with endometriosis.
- Definitive surgery to remove all visible evidence of endometriosis is not recommended as a prophylactic measure to reduce the risk of development of ovarian cancer.
- However, long term use of OCPs is the preferred method.
- Evidence for an association with melanoma and non hodgkins-lymphoma is increasing but needs to be verified.
- Endometriosis is also associated with hyperprolactinemia and galactorrhea.

**W**  
 Recurrence rate: Medical therapy = 30–50% conservative surgery = 14–14%

**?**  
 Best time to become pregnant in a Patient of endometriosis is immediately after surgery

**Adenomyosis**

Adenomyosis is a condition where there is ingrowth of endometrium (both gland + stroma) directly into the myometrium.<sup>Q</sup> Earlier it was called endometriosis interna.

**?**  
 Endometriosis of ovary, i.e. endometrioma, bladder and bowel cannot be managed medically & should be managed surgically

- Age group** : Elderly patients > 40 years<sup>Q</sup>  
**Parity** : Multiparous<sup>Q</sup>  
**Symptoms** : Most common symptom: *Menorrhagia*<sup>Q</sup>  
 2nd most common symptom: *Dysmenorrhea*<sup>Q</sup>  
 Presenting feature: Menorrhagia and citalies Dysmenorrhea

**On per vaginal examination:** Symmetrical enlargement of uterus<sup>Q</sup> (not more than 12–14 weeks of pregnancy)<sup>Q</sup>, mobility not restricted, no associated adnexal pathology.

**Halban's sign – tender, softened uterus** on premenstrual bimanual examination.

### Diagnosis

- It is mainly clinical.
- MRI (Junctional zone thickness >12 mm) is IOC
- Gold standard–histopathological examination

### Management

- TOC–Surgery (total hysterectomy)<sup>Q</sup> in most of the patient, as most of the patients are elderly.
- In younger women–localized excision can be tried or Levonorgestrel containing IUCDs can also be tried.

## Menstruation and Pain

### Dysmenorrhea

Dysmenorrhea means painful menstruation of sufficient magnitude so as to incapacitate day to day activities.

Primary/Spasmodic	Secondary/Congestive
<ul style="list-style-type: none"> <li>• No pelvic pathology is responsible for the pain</li> <li>• Mostly seen in adolescents</li> <li>• M/C in affluent society</li> <li>• Almost always confined to ovulatory cycle, hence pain appears within 6 months–1 year after onset of menarche (when cycles become ovulatory)</li> <li>• Pain appears within 2 years of menarche</li> <li>• Pain appears on 1<sup>st</sup> day of menstrual period and usually lasts for 12 hours.</li> <li>• Pain never persists beyond 48 hours</li> <li>• Pain is spasmodic and confined to lower abdomen. May radiate to back and medial aspect of thigh</li> <li>• Systemic discomfort present</li> <li>• Pain is usually cured after 24 years of age and following pregnancy and delivery.</li> </ul>	<ul style="list-style-type: none"> <li>• Pain is due to presence of pelvic pathology.</li> <li>• Pain seen years after menarche (mostly in parous females)</li> <li>• Can be seen in anovulatory cycles also</li> <li>• Patients mainly complain of deep seated pelvic pain. Pain is dull, situated in back and front without any radiation</li> <li>• No systemic discomfort seen</li> <li>• Pain appears 3–5 days prior to the period and is relieved with the start of the period.</li> </ul>

Contd...

Contd...

Primary/Spasmodic	Secondary/Congestive
<p>Treatment of spasmodic dysmenorrhea-</p> <ol style="list-style-type: none"> <li>1. Prostaglandin synthetase inhibitor- M/C used drug.</li> <li>2. OCP's × 3 – 6 cycles- if pain is not relieved by analgesics and antispasmodics Principle- makes the cycles anovulatory and hence pain is relieved.</li> <li>3. Surgery – rarely required e.g. <ul style="list-style-type: none"> <li>○ Dilatation of cervical canal</li> <li>○ Paracervical block.</li> <li>○ Presacral neurectomy (LPSN) and uterosacral nerve ablation (LUNA)</li> </ul> </li> </ol>	<p>Important causes are</p> <ul style="list-style-type: none"> <li>• PID</li> <li>• Endometriosis</li> <li>• Adenomyosis</li> <li>• IUCD in utero</li> <li>• Uterine fibroid</li> <li>• Polyps</li> <li>• Cervical stenosis</li> <li>• Congenital malformation of uterus like bicornuate uterus</li> </ul> <p><b>Management:</b> Treatment of the underlying cause.</p>

**Also Know**

The phenomenon of ovulation bleeding or mucus tinged with blood at the time of ovulation is called as mittlebutt.<sup>Q</sup> This may be associated with ovulation pain, although each may occur independently.

**Mittelschmerz/Ovular Pain**

- A female giving history of sharp pain in lower abdomen, every month, 2 weeks before menstruation suggests mittelschmerz as the diagnosis.
- Mittelschmerz is synonymous to painful ovulation. Pain is associated with rupture of ovarian follicle at the time of ovulation

**Characteristics**

- It appears in the mid-menstrual period.<sup>Q</sup>
- Pain is usually situated in the hypogastrium or to one iliac fossa.<sup>Q</sup>
- Pain is usually located on one side and does not change side according to which ovary is ovulating.<sup>Q</sup>
- Nausea and vomiting is conspicuously absent.<sup>Q</sup>
- It rarely lasts for more than 12 hours.<sup>Q</sup>
- It may be associated with slight vaginal bleeding or mucoid discharge.<sup>Q</sup>
- The probable factors are:
  - Increased tension of graffian follicle just prior to rupture.<sup>Q</sup>
  - Peritoneal irritation by follicular fluid following ovulation.<sup>Q</sup>
  - Contraction of tubes and uterus.<sup>Q</sup>

**Management**

- Assurance and analgesics
- In refractory cases, cycles are made anovular by giving OCPs.

**Premenstrual Disorders**

- Frequently women of reproductive age experience symptoms during the late luteal phase of their menstrual cycle, and collectively these complaints are termed **premenstrual syndrome (PMS) or premenstrual dysphoric disorder (PMDD)**
- It is mostly seen in women aged to 30–45 years

**Symptoms**

The patients must have at least **five** of the following symptoms for most of the time during the premenstrual week, with symptoms remitting completely in the postmenstrual week (in order to make the diagnosis, the symptoms must be characteristic of PMS/PMDD, limited to luteal phase and not attributable to a general medical condition):

**Right ovarian vein**

**syndrome:** Right ovarian vein crosses the ureter at right angle. During premenstrual period, due to pelvic congestion or increased blood flow, there may be marked engorgement in the vein → pressure on ureter → stasis → infection → pyelonephritis → pain.



A young female giving history of pain in lower abdomen, every month- two weeks before menstruation suggests Mittelschmerz as the diagnosis.

- Depressed mood, hopelessness, self-depreciation
- Anxiety tension
- Affective lability
- Anger, irritability, and interpersonal conflict
- Decreased interest in usual activities
- Difficulty in concentrating
- Decreased energy
- Appetite changes or cravings
- Changes in sleep
- Feeling overwhelmed or out of control
- Physical symptoms such as breast tenderness, headache, bloating

The symptoms markedly interfere with work, family, or academic responsibilities; are not only exacerbations of another existing disorder and are corroborated by at least 2 months of prospective daily ratings.

### Pathophysiology of Premenstrual Syndromes (PMS)

The exact causes of premenstrual disorders are unknown, although several different biologic factors have been suggested. Of these, estrogen and progesterone, as well as the neurotransmitters,  $\gamma$ -amino butyric acid (GABA), and serotonin have been implicated.

### Treatment of PMS

Conservative Measures	Inhibition of Ovulation	Medications directed at symptoms
<ul style="list-style-type: none"> <li>• Elimination of caffeine from diet</li> <li>• Smoking cessation</li> <li>• Counselling, emotional support</li> <li>• Low-fat, high-fiber diet, and essential fatty acids in diet.</li> <li>• Regular exercise</li> <li>• Adequate sleep</li> <li>• Stress reduction</li> </ul>	<ul style="list-style-type: none"> <li>• Oral contraceptives (especially drospirenone containing)</li> <li>• GnRH agonist</li> </ul>	<ul style="list-style-type: none"> <li>• For fluid retention: diuretics</li> <li>• For pain: prostaglandin synthetase</li> <li>• For mastalgia: evening primrose oil and pyridoxine</li> <li>• For anxiety/depression: SSRI like fluoxetine and preferred Tricyclic antidepressants can also be used.</li> </ul>

## QUESTIONS

1. All are true regarding endometriosis, except:  
(AIIMS Dec 94)
  - a. Hormone dependent condition
  - b. Can involve lung, pleura
  - c. Contains clear fluid
  - d. Ovary is the most common site
2. True about endometriosis is/are: (PGI June 06)
  - a. MC in 3<sup>rd</sup> or 4<sup>th</sup> decade
  - b. Premenstrual spotting
  - c. Endometrial sarcoma is most common malignancy associated with it
  - d. True cyst
  - e. 1<sup>st</sup> degree relative seen
3. Endometriosis is commonly associated with:  
(PGI Dec 02)
  - a. B/L chocolate cyst of ovary
  - b. Adenomyosis
  - c. Fibroid
  - d. Luteal cyst
  - e. Endometritis
4. Pain in endometriosis correlates with: (PGI June 00)
  - a. Depth of invasion
  - b. Multiple sites
  - c. CA 125
  - d. Stage of disease
5. A 35-year-old woman presents with infertility and palpable pelvic mass. Her CA-125 level is 90 mIU/mL diagnosis is: (AIIMS May 2010)
  - a. Ovarian Ca
  - b. Endometrioma
  - c. Tuberculosis
  - d. Borderline ovarian tumor
6. All are used in treatment of endometriosis except:
  - a. Medroxyprogesterone acetate (AIIMS Dec 97)
  - b. Tibolone
  - c. OCP
  - d. Danazol
7. Treatment of endometriosis include: (PGI Dec 02)
  - a. Estrogen
  - b. Progesterone
  - c. OCP
  - d. Danazol
  - e. GnRH
8. Drugs used in endometriosis are: (PGI Dec 01)
  - a. Testosterone
  - b. Danazol
  - c. GnRH
  - d. Progesterone
  - e. Estrogen
9. Cause of secondary dysmenorrhea in a young female:  
(PGI June 05)
  - a. Tuberculosis
  - b. Adenomyosis
  - c. CIN
  - d. Endometriosis
  - e. Subserous fibroid

## NEW PATTERN QUESTIONS

10. Scar endometriosis can occur following:
  - a. Classical Cesarean Section
  - b. Hysterotomy
  - c. Episiotomy
  - d. All of the above
11. Endometriosis is explained by:
  - a. Sampson's Implantation theory
  - b. Metastatic epithelium
  - c. Histogenesis by induction
  - d. Coelomic metaplasia theory
  - e. All of the above
12. Best investigation to establish the diagnosis of endometriosis is:
  - a. Laparoscopy
  - b. USG
  - c. X-ray pelvis
  - d. CT Scan
13. A 40-year-old primiparous woman suspected to be suffering from endometriosis is subjected to diagnostic laparoscopy. Findings indicate - uterus normal, both the ovaries show presence of chocolate cysts; endometriotic deposits are seen on the round ligament right side, both the fallopian tubes and the pouch of Douglas; moderately dense adhesions are present between the fallopian tubes and the pouch of Douglas. The treatment of choice in this case is:
  - a. Total hysterectomy with bilateral salpingo-oophorectomy
  - b. Danazol therapy
  - c. Progesterone therapy
  - d. Fulguration of endometriotic deposits
14. True regarding adenomyosis is:
  - a. Most common in nullipara
  - b. Progestin are agents of choice for medical management
  - c. Presents with menorrhagia, dysmenorrhea, and an enlarged uterus
  - d. More common in young women
15. False statement regarding spasmodic dysmenorrhea is:
  - a. Often cured by delivery of a child
  - b. Pain usually appears on the first day of menstruation
  - c. Pain persists for 2-3 days
  - d. Rare above age of 35 years

16. All are used in treating spasmodic dysmenorrhea except: (DNB 02)
- Bromocriptine
  - Ibuprofen
  - Mefenamic acid
  - Norethisterone and ethinyl estradiol
17. A 20-year-old woman gives a history of sharp pain in the lower abdomen for 2-3 days every month approximately 2 weeks before the menses. The most probable etiology for her pain is: (AI 03)
- Endometriosis
  - Dysmenorrhea
  - Pelvic tuberculosis
  - Mittelschmerz
18. Which of the following is NOT to be given in cyclic mastalgia is: (UP 01)
- Evening primrose oil
  - Danazol
  - Tamoxifen
  - Estrogen
19. Which of the following modalities have shown best result for pre menstrual syndrome? (AIIMS Nov 02)
- SSRI
  - Progesterone
  - Oestrogen
  - Anxiolytics



## ANSWERS

## 1. Ans. is c, i.e. Contains clear fluid

Ref. Shaw 15<sup>th</sup>/ed p 466 for option a, 466-7 for option c; Jeffcoate 7<sup>th</sup>/ed p 370 for option 'd'; p 372 for option 'b'

Endometriosis is occurrence of functioning endometrial tissue (glands + stroma) outside the uterine cavity.

*Whatever the initial genesis of endometriosis its further development depends mainly on estrogen (Option "a").*

- It can occur anywhere in body, Most common site being ovary<sup>Q</sup> (Option "d"). – Shaw 14<sup>th</sup>/ed p 420
- Can also involve lungs and pleura<sup>Q</sup> (Option "b"). – Jeffcoate 7<sup>th</sup>/ed p 370
- In endometriosis ovary contains tarry dark brown fluid (due to presence of blood pigments like hemosiderin) and cul de sac has yellow brown fluid. – Jeffcoate 7<sup>th</sup>/ed p 372

Clear fluid is not seen anywhere, So, Option "c" is incorrect.

2. Ans. is a, b, d and e, i.e. Most common in 3<sup>rd</sup> or 4<sup>th</sup> decade; premenstrual spotting; and true cyst; and 1<sup>st</sup> degree relative seen

Ref. Shaw 15<sup>th</sup>/ed p 466-9; Jeffcoate 7<sup>th</sup>/ed p 368-70; CGDT 10<sup>th</sup>/ed p 715

As discussed in the preceding text-

- i. Endometriosis occurs most commonly in 3<sup>rd</sup> or 4<sup>th</sup> decade i.e "option a" is correct.
- ii. If first degree relative is affected, there are 7-10 fold increased chances of a female having endometriosis i.e option e is correct.
- iii. Endometrioma/chocolate cyst is a true cyst—"option d" is correct.
- iv. Premenstrual spotting is seen in endometriosis— thus proving "option b" is correct.
- iv. Endometriosis is associated with granulosa cell tumors of ovary but not with endometrial sarcomas.

## 3. Ans. is a, i.e. B/L chocolate cyst of ovary

Ref. Shaw 15<sup>th</sup>/ed p 466; Jeffcoate 7<sup>th</sup>/ed p 370; Novak 14<sup>th</sup>/ed p 1145, 15<sup>th</sup>/ed p 517

*"The ovary is the most common site and involved in 30–40% of cases. The lesion is nearly always bilateral. It sometimes appears as multiple burnt match head spots on the surface of the ovary and sometimes as the typical tarry cysts in a disorganised organ surrounded by dense adhesions."*

– Jeffcoate 7<sup>th</sup>/ed p 370

**Chocolate cysts of ovary:**

- They are true cysts<sup>Q</sup>
- The cysts enlarge with cyclic bleeding. The serum gets absorbed in between periods and the content inside becomes chocolate, tarry brown in color.<sup>Q</sup>
- Histology
  - Lining epithelium is columnar epithelium<sup>Q</sup>.
  - Beneath the epithelium are large macrophages called as *pseudoxanthoma cells* which have brown cytoplasm due to ingested blood pigments like hemosiderin.
- Treatment of chocolate cyst/endometrioma.

Laparoscopic management is the preferred management

...Novak 15<sup>th</sup>/ed p 527

**Before concluding lets rule out other options.**

- *Adenomyosis* is associated with endometriosis but vice versa is not true; similarly *fibroid uterus* is associated with endometriosis but vice versa is not true (Ruling out options "b" and "c").
- Multiple luteal cysts in the ovary are seen in case of
  - Pregnancy
  - Multiple pregnancy<sup>Q</sup>
  - HCG therapy<sup>Q</sup>
  - Hydatidiform Mole<sup>Q</sup>
  - Choriocarcinoma<sup>Q</sup>

Thus option "d" is incorrect.

There is no association between endometritis and endometriosis i.e. option "e" is incorrect.

## 4. Ans. is a, i.e. Depth of invasion

Ref. Gynecology for Post Graduates and Practitioners by Bijoy Sree  
Sen Gupta 2<sup>nd</sup>/ed p 133; William's Gynae 1<sup>st</sup>/ed p 230; Novak 14<sup>th</sup>/ed p 1144, 15<sup>th</sup>/ed p 512

*"Deep penetrating endometriosis is a form of the disease which was described by Koninck's group. These lesion can extend 10 mm or more down from the peritoneal surface and the deeper lesions appear to have a closer associations with pain than infertility, whereas less deep lesions have a closer association with infertility than pain."*

– Bijoy Sree Sen Gupta 2<sup>nd</sup>/ed p 133

**Dysmenorrhea:**

– Williams Gynae 1<sup>st</sup>/ed p 230

*"Cyclical pain with menstruation is noted commonly in women with endometriosis. Typically, endometriosis associated dysmenorrhea precedes menses by 24–48 hours and is less responsive to NSAIDs and combination oral contraceptives. This pain is thought to be more severe in comparison with primary dysmenorrhea and Crammer and associates demonstrated a positive correlation between the severity of dysmenorrhea and the risk of endometriosis. Furthermore, deeply infiltrating endometriosis, that is disease that extends > 5 mm under the peritoneal surface, also appears to have positive correlation to the severity of dysmenorrhea."*

From above lines it is clear that pain in endometriosis coincides with the depth of lesion.

As far as other options are concerned –

*"The levels of CA-125 correlate with severity of the disease, but since there is a wide variety of conditions in which the levels are elevated its greatest use may be in monitoring a patient serially for recurrence."* (ruling out **"option c"**) – Jeffcoate 7<sup>th</sup>/ed p 375

*"Most studies have failed to detect a correlation between the degree of pelvic pain and severity of endometriosis. Some women with extensive disease have no pain, whereas others with only minimal disease may experience severe pelvic pain and dyspareunia may be associated with infiltrating subperitoneal endometriosis."* (ruling out **"option d"**). – Novak 14<sup>th</sup>/ed p 1144, 15<sup>th</sup>/ed p 512

**5. Ans. is b, i.e. Endometrioma**

Ref. Novak Gynecology 14<sup>th</sup>/ed pp 1466, 1146, 1147; William's Gynae 1<sup>st</sup>/ed pp 232, 210  
Textbook of Gynae, Sheila Balakrishnan p 185

In this question we have insufficient information to make any definite diagnosis. At the best we can try to make the most probable diagnosis.

**CA-125**

- This is a non-specific tumor marker
- CA-125 is a glycoprotein which is normally not produced by ovarian epithelium but may be produced by both malignant and benign epithelial ovarian tumors.
- Cut off level of CA-125 is < 35 U/mL.
- Levels of CA 125 can be raised in

↑ CA-125	
Neoplastic conditions	Non-neoplastic/Benign conditions
<b>Gynecological</b> <ul style="list-style-type: none"> <li>• Ovarian cancer (nonmucinous)</li> <li>• Endometrial cancer</li> <li>• Tubal cancer</li> </ul> <b>Non-gynecological</b> <ul style="list-style-type: none"> <li>• Lung cancer</li> <li>• Breast cancer</li> <li>• Ca Pancreas</li> <li>• Colon cancer</li> </ul>	<ul style="list-style-type: none"> <li>• Endometriosis</li> <li>• Peritoneal inflammation, including PID</li> <li>• Tuberculosis</li> <li>• Hemorrhagic ovarian cysts</li> <li>• Liver disease</li> <li>• Leiomyoma</li> <li>• Pregnancy</li> <li>• Menstruation</li> </ul>

- Thus, Ca-125 levels, can be raised in all the four options, given in the question
- Palpable mass may also be present in all the four conditions.
- Infertility is a feature of endometriosis and tuberculosis. But for ovarian cancers, infertility (due to use of ovulation inducing drugs) is a risk factor, not a feature or presenting symptom.
- Coming to Age: Patient is 35 years old.
- Age of 35 years favors endometrioma (endometriosis) the most.
- Peak incidence of invasive epithelial ovarian cancer (most common ovarian cancer) is at 56–60 years of age and for border line tumor average age is 46 years approximately (Novak 14<sup>th</sup>/ed p 1466)
- Patient with tuberculosis are in their twenties commonly, the maximum age incidence at diagnosis being 28 years.
- Also in tuberculosis, CA 125 has least significance as it is neither used for diagnosis nor for follow up
- Thus, based on age and infertility → the most probable diagnosis is endometrioma/endometriosis.
- Our answer is further supported by following lines from – Textbook of gynae, Sheila Balakrishnan 1<sup>st</sup>/ed p 185  
Serum ca 125 *"This is useful in post menopausal women when a high level may indicate malignancy. In the reproductive age group, the predictive value is not good as the marker may be raised in endometriosis"*.  
In young females if the value of Ca-125 is >200 IU/mL, it is considered to indicate malignancy.

**6. Ans. is b, i.e. Tibolone**

Ref. Shaw 15<sup>th</sup>/ed pp 472-3; Novak 14<sup>th</sup>/ed p 1164-9

**7. Ans. is b, c, d and e, i.e. Progesterone, OCP, Danazol and GnRH**

**8. Ans. is b, c and d, i.e. Danazol, GnRH, and Progesterone**

Ref. Shaw 15<sup>th</sup>/ed pp 472-3; Novak 14<sup>th</sup>/ed pp 1164-9

Drugs used in the management of endometriosis

**Hormone Therapy**

**Proctor**–Progesterone-First line management –  
**and**

**Gamble**–GnRH analogue

**Always**–Antiprogesterone-mifepristone

**Offer**–OCP

**Good**–Gestrinone

**Deals**–Danazol

**Empirical Therapy**

- Oral progestins- continuous administration NSAIDs
- Injectable progestin-DMPA
- LNG-IUS

**Mnemonic – Proctor and Gamble Always Offer Good Deals****Note:**

Superficial peritoneal and ovarian implants may respond well to medical management but large endometriomas and extra pelvic endometriosis are unlikely to respond and will ultimately require surgical excision.

**9. Ans. is a, d and e, i.e. Tuberculosis, endometriosis and subserous fibroid**

Ref. Dutta Gynae 5<sup>th</sup>/ed p 174-5; Jeffcoate 7<sup>th</sup>/ed p 622-3; Textbook of Gynae Sheila Balakrishnan 1<sup>st</sup>/ed p 203

**Causes of secondary dysmenorrhea:**

- PID
- Endometriosis
- Adenomyosis
- IUCD
- Uterine fibroid
- Polyps
- Cervical stenosis
- Congenital malformation of uterus like bicornuate uterus

**Management :** Treatment of the underlying cause.

**10. Ans. is d, i.e. All of the above**

Ref. Jeffcoate 7<sup>th</sup>/ed p 371

Endometriosis sometimes occurs in abdominal wall scars following operations on uterus or tubes and is known as *scar endometriosis*.

Operations most likely to be followed by scar endometriosis:

- Hysterotomy<sup>Q</sup>
- Classical cesarean section<sup>Q</sup>
- Myomectomy<sup>Q</sup>
- Ventrofixation<sup>Q</sup>
- Following operations for section of fallopian tube<sup>Q</sup>
- Following operations for removal of pelvic endometriosis<sup>Q</sup>
- Episiotomy<sup>Q</sup>

**11. Ans. is e, i.e. All of the above**

Ref. Shaw 15<sup>th</sup>/ed pp 465, 466

Endometriosis is the occurrence of ectopic endometrial tissue (both glands and stroma) outside the cavity of uterus.

**Several theories have been propounded to explain endometriosis.**

Theory	Proposed by	Mechanism
Sampson's implantation theory	Sampson	Endometriosis occurs as a result of reflux of menstrual endometrium through the fallopian tubes and its subsequent implantation
Coelomic metaplasia	Meyer and Ivanoff	Endometriosis arises as a result of metaplastic changes in embryonic cell rests of embryonic mesothelium, which are capable of responding to hormone stimulation.
Metastatic theory	Halban	Explains occurrence of endometriosis at less accessible sites like umbilicus, pelvic nodes, ureter, etc. The theory suggests embolization of menstrual fragments occurs through vascular or lymphatic channels. This leads to launching of endometriosis at distant sites.
Histogenesis by induction		Proposes that an endogenous (undefined) biochemical factor can induce undifferentiated peritoneal cells to develop into endometrial tissue.

**12. Ans. is a, i.e. Laparoscopy**

Ref. Shaw 15<sup>th</sup>/ed p 470; Novak 14<sup>th</sup>/ed pp 1145-46, 15<sup>th</sup>/ed p 516

Diagnostic laparoscopy is the gold standard for diagnosing endometriosis.

**Typical lesion:** Powder burn/Gun shot lesions (*black, dark brown, or bluish cysts with old hemorrhage surrounded by variable degree of fibrosis*)

**Other non-typical findings could be:**

- Red implants<sup>Q</sup>
- Serous or clear vesicles
- White plaques/scarring
- Yellowish brown discoloration of peritoneum<sup>Q</sup>
- Sub ovarian adhesions<sup>Q</sup>
- Presence of defects in the peritoneum (usually scarring overlying implants) is called as **Allen masters syndrome**.
- Histological confirmation of laparoscopic impression is essential for diagnosis of endometriosis.

**13. Ans. is d, i.e. Fulguration of endometriotic deposits**

Ref. William's Gynae 1<sup>st</sup>/ed p 235; Bijoy Sree Sen Gupta 2<sup>nd</sup>/ed p 138

In the question it is given, dense adhesions and chocolate cyst are present which cannot be fully treated by medical therapy and so, some form of surgery is required.

Main question is whether we would like to go for conservative surgery or radical surgery (i.e. TAH with BSO)

**Remember:** mostly in endometriosis conservative surgery is done.

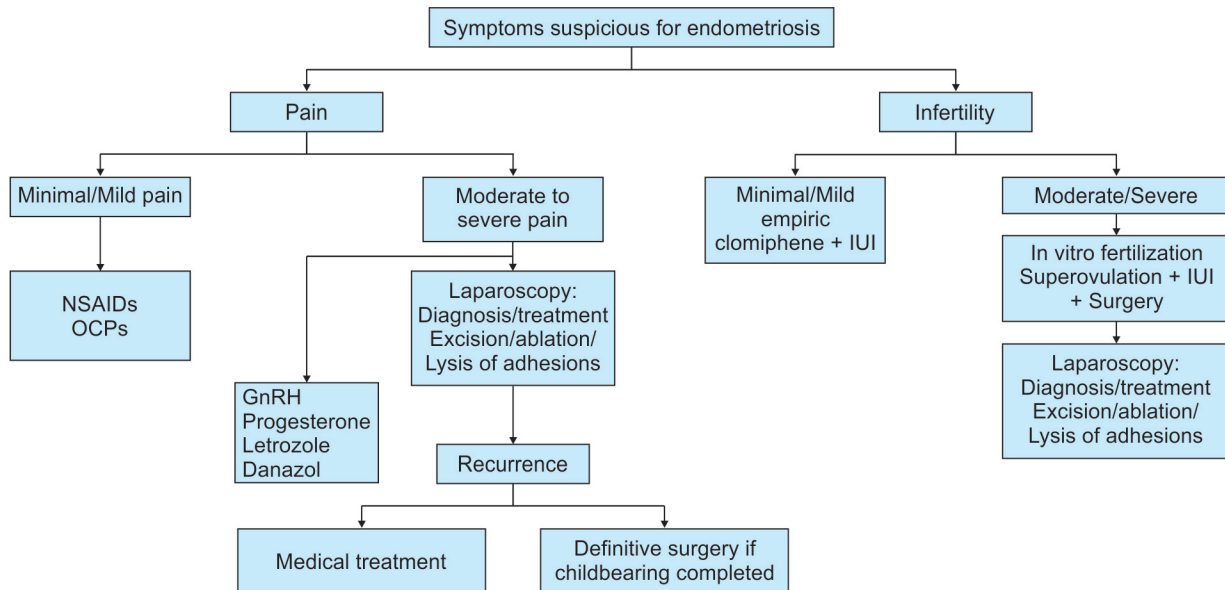
**Conservative surgery:** The clinical situations involving conservative surgery include ovarian endometrioma, pelvic adhesions, peritoneal implants and deep infiltrative rectovaginal septum disease. In addition, laser laparoscopy can be used in order to perform uterine nerve ablation.

– Bijoy Sree Sen Gupta 2<sup>nd</sup>/ed p 138

According to *William's Gynae 1<sup>st</sup>/ed p 239* –

*"Hysterectomy with bilateral oophorectomy should be reserved for women who have completed childbearing and recognise the risk of premature hypoestrogenism including possible osteoporosis and decrease libido."*

#### Diagnostic and treatment algorithm for women with presumptive or proven endometriosis.



#### 14. Ans. is c, i.e. Presents with menorrhagia, dysmenorrhea and an enlarged uterus

Ref. Shaw 15<sup>th</sup>/ed pp 474-5; Novak 15<sup>th</sup>/ed pp 484-5

As discussed in text-*adenomyosis is a condition where there is ingrowth of endometrium (both gland + stroma) directly into the myometrium.*<sup>Q</sup> Earlier it was called as *Endometriosis interna*

*It is more common in Multiparous<sup>Q</sup> females (i.e. option a is correct).*

*It is more common in elderly patients (>40 years, i.e. option d is incorrect).*

*Mainly manifests as menorrhagia, dysmenorrhea and enlarged uterus (i.e. option c is correct.)*

#### 15. Ans. is c, i.e. Pain persists for 2-3 days.

#### 16. Ans. is a, i.e. Bromocriptine

Ref. Dutta Gynae 5<sup>th</sup>/ed pp 174-5, 6<sup>th</sup>/ed p 179-181; Jeffcoate 7<sup>th</sup>/ed pp 622-3; textbook of Gynae Sheila Balakrishnan 1<sup>st</sup>/ed p 203

Spasmodic dysmenorrhoea is another name for primary dysmenorrhoea. (i.e. no pelvic pathology is responsible for pain)

#### Characteristics of spasmodic dysmenorrhoea

- Seen in adolescent girls
- Pain appears within 2 years of menarche
- Family history may be present
- Pain is spasmodic nature. It is located in lower abdomen and may radiate to back and medial aspect of thigh.
- Associated systemic discomfort seen
- Pain begins few hours before a rest of menstruation and lasts for 12-24 hours, but never 48 hours more than
- Pain is often cured after child birth
- Management: NSAID's or OCP's

#### 17. Ans. is d, i.e. Mittelschmerz

Ref. Dutta Gynae 4<sup>th</sup>/ed p 172, 5<sup>th</sup>/ed p 178

- A female giving history of sharp pain in lower abdomen, every month, 2 weeks before the menstruation suggests mittelschmerz as the diagnosis.
- Mittelschmerz is synonymous to painful ovulation. Pain is associated with rupture of ovarian follicle at the time of ovulation

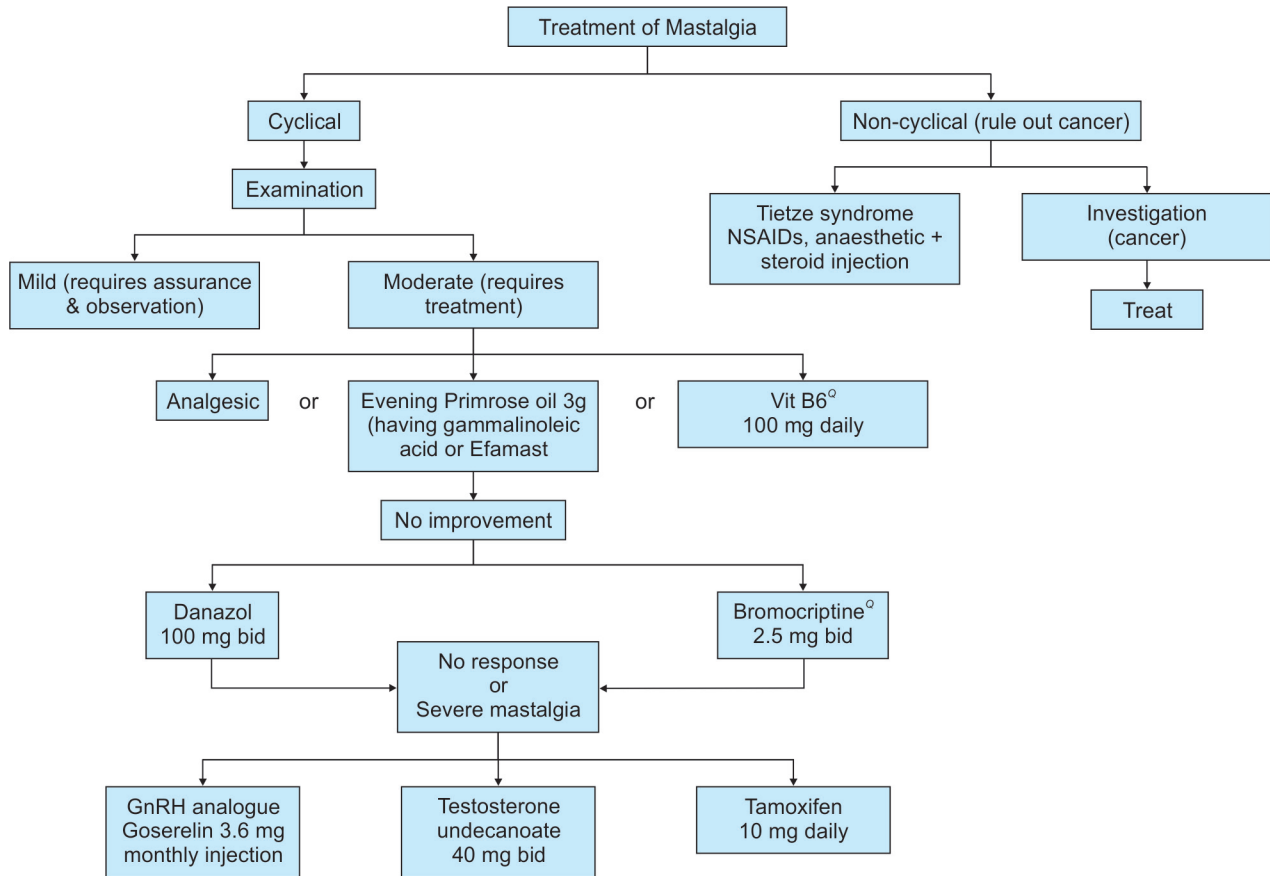
**For more details refer to the preceding text.**

18. Ans. is d, i.e. Estrogen

Mastalgia is painful breast:  
It can be:

Ref. Shaw 15<sup>th</sup>/ed pp 477, 478

Cyclical	Non-cyclical
<ul style="list-style-type: none"> <li>• Mostly seen in young women</li> <li>• It occurs for a few days before menstruation</li> <li>• It is usually bilateral diffuse and most severe during luteal phase of menstrual</li> </ul>	<ul style="list-style-type: none"> <li>• Mostly seen in older women</li> <li>• May be a symptom of breast carcinoma, cyst Tietze syndrome (Chest wall pain)</li> <li>• It has no relation to menstrual cycle</li> <li>• It is often focal.</li> </ul>



19. Ans. is a, i.e. SSRI

Ref. William's Gynae 1<sup>st</sup>/ed p 300; Jeffcoate 7<sup>th</sup>/ed p 629; Novaks 15<sup>th</sup>/ed pp 311, 312; Leon speroff 8<sup>th</sup>/ed p 578; John hopkins manual of obs and gynae 4<sup>th</sup>/ed p 462

Premenstrual disorders:

- Frequently women of reproductive age experience symptoms during the late luteal phase of their menstrual cycle, and collectively these complaints are termed **premenstrual syndrome (PMS)** or **premenstrual dysphoric disorder (PMDD)**
- It is mostly seen in women aged to 30–45 years

Treatment of PMS:

Conservative measures	Inhibition of ovulation	Medications directed at symptoms
<ul style="list-style-type: none"> <li>• Elimination of caffeine from diet</li> <li>• Smoking cessation</li> <li>• Counselling, emotional support</li> <li>• Low-fat, high-fiber diet and essential fatty acids in diet.</li> <li>• Regular exercise</li> <li>• Adequate sleep</li> <li>• Stress reduction</li> </ul>	<ul style="list-style-type: none"> <li>• Oral contraceptives (especially drospirenone containing)</li> <li>• GnRH agonist</li> </ul>	<ul style="list-style-type: none"> <li>• For fluid retention: diuretics</li> <li>• For pain: Prostaglandin synthetase</li> <li>• For mastalgia: evening primrose oil and pyridoxine</li> <li>• For anxiety/depression: SSRI like fluoxetine preferred</li> <li>• Tricyclic antidepressants can also be used</li> </ul>

**Choice of treatment in PMS**

Amongst all the drugs used-SSRI's have shown the best results

*"For premenstrual dysphoric disorder, selective serotonin re uptake inhibitor (SSRI'S) proved effective in clinical trials".*

– Novak 15<sup>th</sup>/ed p 312

*"Women who meet strict criteria for diagnosis of PMS or PMDD, including socioeconomic dysfunction, are candidates for treatment with an SSRI (fluoxetine, sertraline, paroxetine, venlaflexine), administered daily or only during the luteal phase"*

– Leon speroff 8<sup>th</sup>/ed p 578

*"SSRIs are the most effective pharmacologic treatment for moderate to severe PMS and PMDD"*

– John hopkins manual of obs and gynae 4<sup>th</sup>/ed p 462

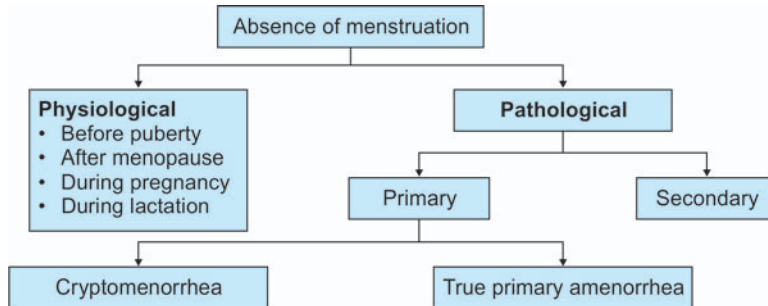
**Remember:** The most significant side effect of SSRI is sexual dysfunction including decreased libido and anorgasmia.

# CHAPTER

# 13

## Disorders of Menstruation

### Amenorrhea



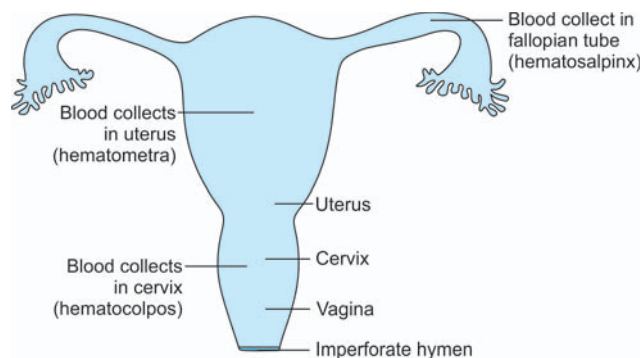
### Cryptomenorrhea

**Definition:** Occurrence of menstrual symptoms without external bleeding. Menstrual blood fails to come out from genital tract due to obstruction in the outflow passage.

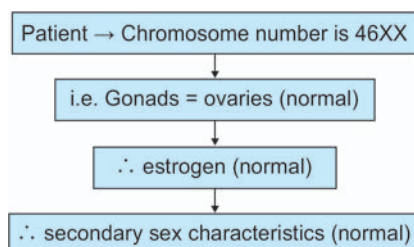
#### Causes

Congenital	Acquired
<ul style="list-style-type: none"> <li>• Imperforate hymen (M/c cause)</li> <li>• Transverse vaginal septum</li> </ul>	Cervical stenosis following: <ul style="list-style-type: none"> <li>• Amputation</li> <li>• Cauterization</li> <li>• Conization</li> </ul>

### Pathology



### Symptoms



**1° Amenorrhea**—Condition where a female has not attained menarche by the **age of 14 years in the absence of development of secondary sexual characteristics** or no menarche by the age of **16 years regardless of the presence of normal growth and development** of secondary sexual characteristics.

**2° Amenorrhea**—Absence of menstruation for 3 normal cycles or for 6 months or more in a previously normally menstruating female



#### In Females

For normal development of Gonads (ovaries). Absence of Y chromosome & presence of XX (2X) chromosomes is required.

- Ovary
  - ↓ secretes
  - Estrogen
  - (Required for normal development of secondary sexual characteristic in females)
- Absence of Y chromosome
  - ↓
  - Absent testis
  - ↓
  - Mullerian inhibiting factor is absent
  - ↓
  - i.e. Mullerian duct grows normally and forms fallopian tubes, uterus, cervix, upper part of vagina.

In a normal looking female, with normal secondary sexual characteristic always rule out cryptomenorrhea.

Never do P/V examination in a virgin females. To know whether uterus is present/absent & to assess the size of the uterus – do a **Per Rectal examination**, never Per vaginal examination.

In imperforate hymen after doing local examination and before proceeding to management, Per Rectal examination is a must to confirm the presence of uterus.

### In Cryptomenorrhea

- A female with normal secondary sexual characteristics complains of primary amenorrhea
- H/o cyclical abdominal pain is present
- Patient may complain of urinary symptoms as hematocolpos can cause pressure symptoms.

**O/E** – A tumor, dull on percussion is found in lower abdomen (partly due to distended vagina & partly due to overfill bladder).

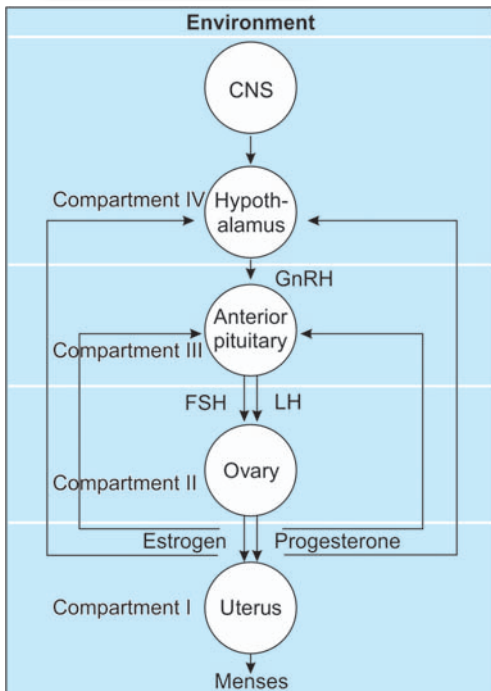
### Local Examination

On separating labia, bluish bulging hymen is seen. Per Rectal examination shows uterus is present.

### Management

Urgent surgical management by giving a cruciate incision on the hymen (the collected blood automatically drains out).

## Primary Amenorrhea



Before going into the details of primary amenorrhea lets first understand the basic requirement for a female to menstruate normally.

- An intact outflow tract which connects the uterine cavity with outside and a normally developed uterus with its endometrium lining.
- Proper quantity and sequence of steroid hormones i.e. estrogen and progesterone which inturn originate from ovary.
- The maturation of follicular apparatus is guided by gonadotropins- FSH and LH (released by pituitary).
- The secretion of these hormones is inturn dependant on gonadotropin releasing hormone (re-leased by hypothalamus).

So, broadly we can classify the causes of amenorrhea into the following compartments.

- Compartment I** Disorders of the out flow tract or uterine target organs.
- Compartment II** Disorders of the Ovary
- Compartment III** Disorders of the Pituitary
- Compartment IV** Disorders of the CNS (hypothalamic) factors.

### Major Causes of Primary Amenorrhea (Compartment Wise)

Normally the endogenous GnRH released in a pulsatile manner which releases LH & FSH. This in turn leads to release of estrogen. When GnRH is given continuously from outside, it binds to GnRH receptors and inhibits endogenous GnRH & thus decreases LH, FSH & estrogen.

<b>Compartment I (Disorders of outflow tract/uterus)</b>	Mullerian Anomalies <sup>o</sup> (2 <sup>nd</sup> M/C cause of primary amenorrhea) Androgen insensitivity syndrome (Testicular feminization syndrome) <sup>o</sup>
<b>Compartment II (Disorders of Ovary)</b>	Gonadal dysgenesis (M/C cause of Primary Amenorrhea) <sup>o</sup> Turners syndrome: 45XO <sup>o</sup> Pure gonadal dysgenesis: 46 XX <sup>o</sup> Swyers syndrome: 46 XY <sup>o</sup> Savage syndrome: Resistant ovary syndrome



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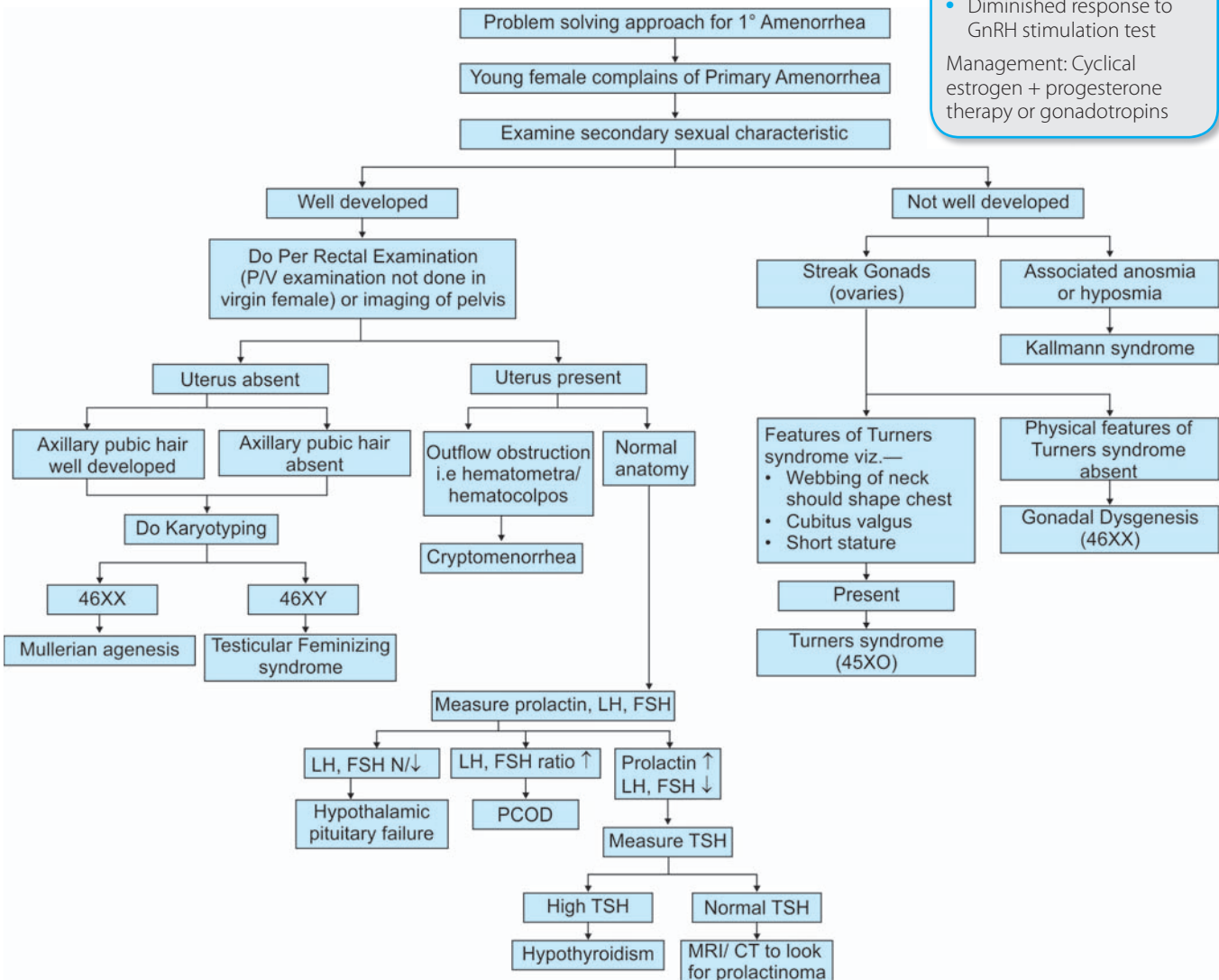
Compartment III (Disorders of Anterior Pituitary)	Neoplasia Prolactinomas <sup>o</sup> /Craniopharyngiomas <sup>o</sup> Hypopituitary states – Simmond's disease <sup>o</sup> / Chiari Frommel syndrome <sup>o</sup> Forbes Albright syndrome (Not very important)
Compartment IV (Disorders of CNS)	Kallmann syndrome <sup>o</sup> (Amenorrhea + Anosmia) Adrenal hypoplasia

M/c cause of Primary Amenorrhea – Turner syndrome  
2nd M/c cause – MRKH syndrome  
3rd M/c cause – Testicular feminizing syndrome/Androgen insensitivity syndrome

The details of Mullerian agenesis (MRKH syndrome), testicular feminizing syndrome, and Turners syndrome have been dealt in previous chapters.

### Secondary Amenorrhea

**Kallmann syndrome**  
Genetic condition characterised by hypogonadotropic hypogonadism (hypothalamic failure) and anosmia  
• ↓GnRH levels – absent Secondary sexual characteristics, anovulation, infertility, anosmia  
• Diminished response to GnRH stimulation test  
Management: Cyclical estrogen + progesterone therapy or gonadotropins





Pregnancy is a cause of secondary amenorrhea as well as physiological amenorrhea.

- Causes of physiological amenorrhea-
  - Before puberty.
  - After menopause
  - During pregnancy
  - During lactation.
- Lactation leads to amenorrhea as hypothalamic GnRH secretion is suppressed by negative feedback of excess prolactin, thereby lowering FSH and LH levels.



**Premature ovarian failure/premature menopause** is amenorrhea associated with depletion of oocytes before the age of 40 years.



#### Levels of Prolactin and associated Menstrual disorders

Increased levels of prolactin adversely affect GnRH secretion which leads to amenorrhea. This is the reason for amenorrhea in prolactinomas and during lactational period.

#### Also Know

##### Ashermann's syndrome

is amenorrhea due to intrauterine synechiae formation. M/C cause of Ashermann's syndrome is vigorous uterine curettage in postpartum period but the syndrome can also occur after myomectomy, cesarean section, and tuberculosis endometritis. IOC = Hysteroscopy  
Other Ix = HSG which shows honeycomb appearance.

##### Management

Hysteroscopic adhesiolysis followed by insertion of CuT to prevent reformation of synechiae and cyclical estrogen and progesterone.

Secondary amenorrhea is defined as absence of menstruation for 3 normal cycles or for 6 months or more in a woman with previous normal menstrual pattern in absence of pregnancy...  
– Williams gynae p365

#### Important causes of Secondary Amenorrhea (Compartment wise)

<b>Compartment I</b> (Disorders of outflow tract/uterus)	<ul style="list-style-type: none"> <li>• Acquired obstruction (gynatresia) of cervical canal causing severe stenosis or atresia following electrocauterization, chemical burns, cervical amputation in Fothergill's repair, conization, CIN, or genital tuberculosis.</li> <li>• Asherman's syndrome<sup>o</sup> Following excessive curettage or endometrial tuberculosis</li> <li>• V V F (cause unknown)</li> </ul>
<b>Compartment II</b> (Disorders of Ovary)	<ul style="list-style-type: none"> <li>• Ovary Tumor – Masculinizing tumors/PCOD<sup>o</sup></li> <li>• Trauma – Surgical extirpation/Radiotherapy</li> <li>• Infections – Mumps, Tuberculosis rarely pyogenic infections</li> <li>• Premature ovarian failure</li> </ul>
<b>Compartment III</b> (Pituitary)	<ul style="list-style-type: none"> <li>• Hyperprolactinemia/prolactin tumor/prolactinoma</li> <li>• Insufficiency as in Simmond's disease, Sheehan's syndrome</li> <li>• Empty sella syndrome</li> <li>• Infiltrative disease</li> </ul>
<b>Compartment IV</b> (Hypothalamus)	<ul style="list-style-type: none"> <li>• GnRH deficiency</li> <li>• Vigorous exercise/excessive stress</li> <li>• Weight loss</li> <li>• Eating disorders – anorexia and Bulimia</li> <li>• Tumor (including craniopharyngioma, germinoma, endodermal sinus tumor, eosinophilic granuloma, and glioma)</li> <li>• Radiation</li> <li>• Pseudocyesis</li> <li>• Infection (TB)</li> <li>• Infiltrative disease (sarcoidosis)</li> </ul>

Besides these some other causes of secondary amenorrhea are

- Pregnancy-M/C cause of secondary amenorrhea
- Hypothyroidism<sup>o</sup> (V. Imp. cause, should be ruled out in every case)
- Hyperprolactinemia
- Diabetes
- Tuberculosis
- Renal disease/liver disease
- Addison disease/Cushing's syndrome/acromegaly
- Drugs (phenothiazines, reserpine, antidepressants, OCPs).
- Malabsorption syndrome
- AIDS

#### Sheehan's Syndrome

- It is the syndrome which results from ischaemic necrosis of most of the anterior pituitary<sup>o</sup> due to spasm in its arterioles occurring at the time of severe hemorrhage or shock complicating childbirth.
- Only the anterior pituitary is affected because in parturient woman, blood supply to the pituitary gland is modified to the advantage of the posterior lobe and disadvantage of the anterior lobe so, when spasm occurs, posterior lobe is protected.
- When 75% of anterior pituitary is destroyed, manifestations of Sheehan's syndrome appear and when 95% is destroyed – fully developed Simmond's syndrome is seen.

- Hormones of anterior pituitary are affected in order of frequency = GH, FSH, and LH, TSH and ACTH.

**Clinical Features**

**Symptoms<sup>Q</sup>**

- Failure of lactation after delivery<sup>Q</sup> (due to ↓ Prolactin)
- Secondary amenorrhoea<sup>Q</sup> (↓ LH/↓ FSH)
- Loss of libido<sup>Q</sup>
- Increased sensitivity to cold (hypothyroidism)<sup>Q</sup> (↓ TSH)

**Signs**

- Absence of axillary sweating<sup>Q</sup>
- Loss of axillary and pubic hair<sup>Q</sup> (Signs of adrenal cortical failure)
- Decrease in skin pigmentation<sup>Q</sup>
- Anemia due to lack of pituitary erythropoietic factor
- Weakness, lethargy<sup>Q</sup>
- Hypothyroidism<sup>Q</sup> and hypothermia<sup>Q</sup>
- Hypoglycemia<sup>Q</sup> (due to decreased insulin tolerance)<sup>Q</sup>
- All genital organs show atrophy, uterus is smaller than in postmenopausal women<sup>Q</sup> as there is decrease in FSH, LH and estrogen although dormant ovaries retain their ova till menopause<sup>Q</sup>

**Lab Investigation**

Most common is prolactin deficiency along with decreased levels of FSH<sup>Q</sup>, LH<sup>Q</sup>, TSH<sup>Q</sup>, ACTH<sup>Q</sup>, oestrogens<sup>Q</sup>, and urinary 17-keto steroids<sup>Q</sup>

**Management**

The treatment of Sheehan’s syndrome includes: *Life-long hormone substitute of estrogen, progesterone, thyroid, and adrenal hormone.*

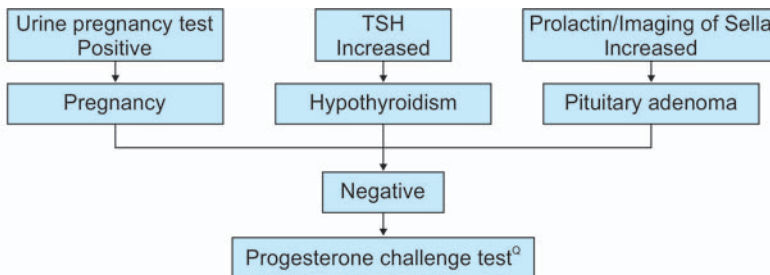
**Stein Leventhal Syndrome**

Another name for PCOS (dealt in detail earlier).

**Premature Menopause**

Is defined as secondary amenorrhoea before 40 years of age, due to ovarian failure. It is clinically defined as secondary amenorrhea for atleast 3 months with raised FSH, raised FSH/LH ratio and low E<sub>2</sub> levels in a women under 40 years of age.

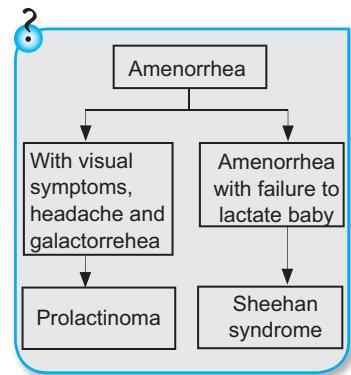
**Work up for a case of Secondary Amenorrhea**

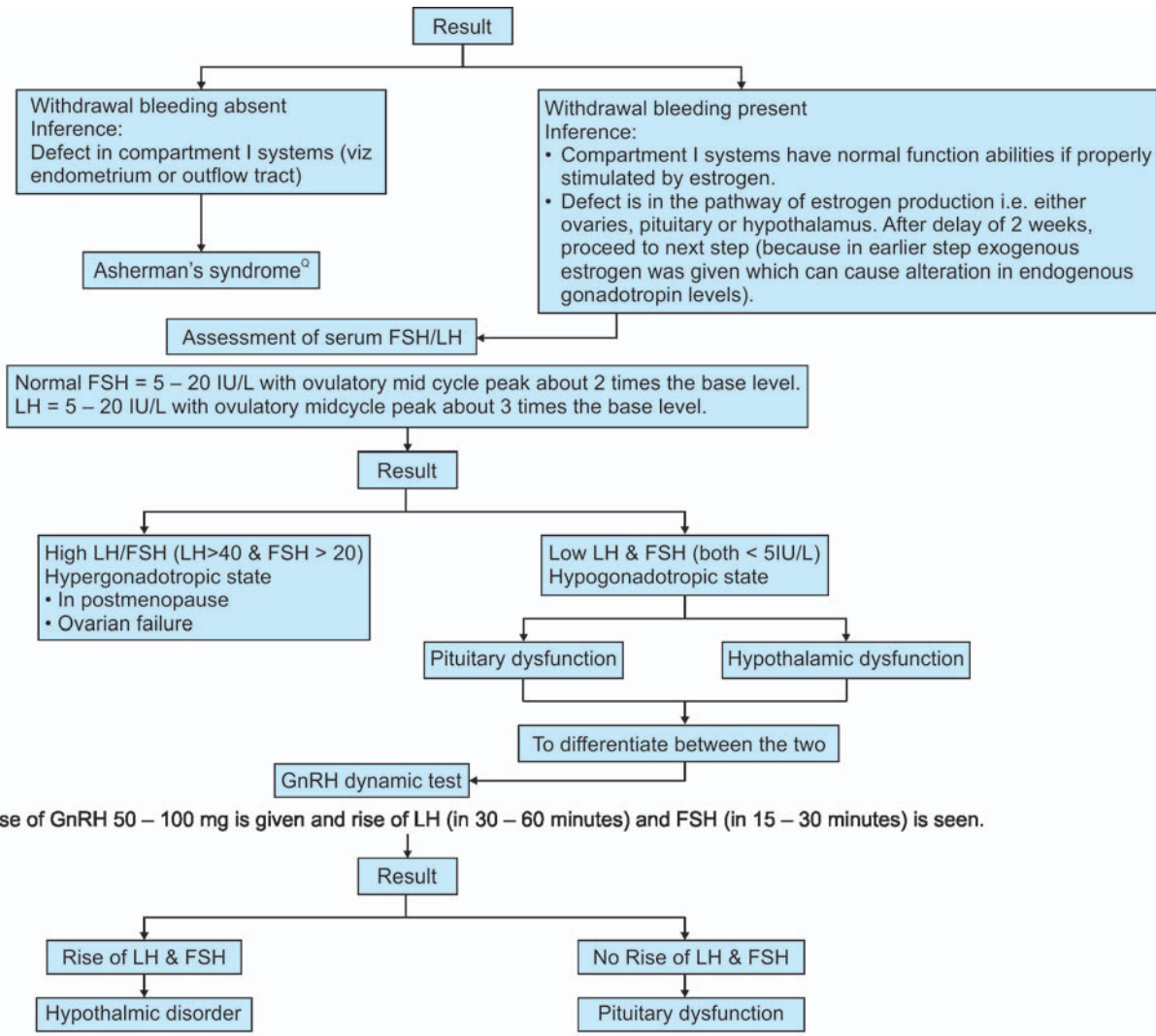
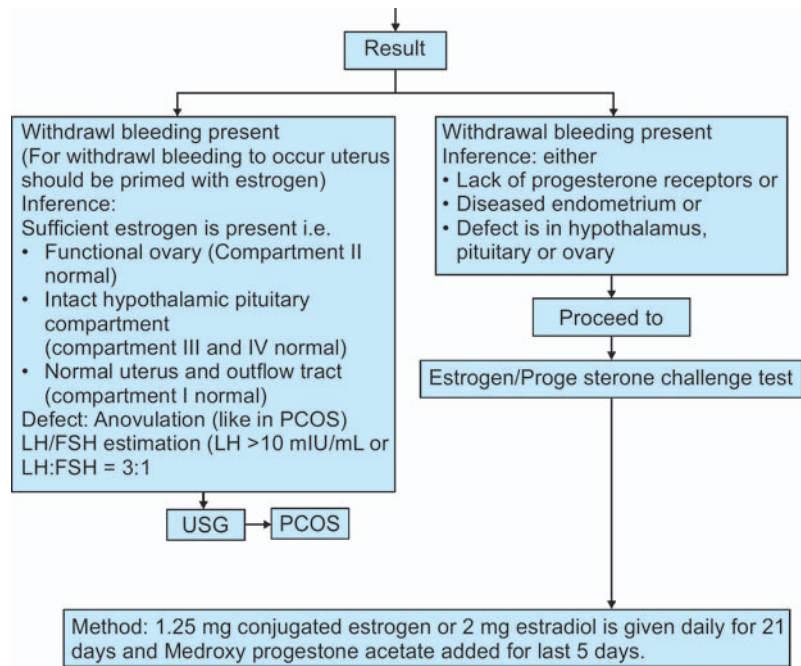


Purpose: To assess the level of endogenous estrogen and competence of outflow tract.  
 Method: Progesterone totally devoid of estrogenic activity (like MDPA, micronized progesterone) is given for 5 days and then withdrawn.

**Prolactinoma–**

- M/c pituitary adenomas
- Types:
  - Microadenoma (<1 cm)
  - Macroadenoma (>1 cm)
- Patients have increased prolactin which decreases GnRH, leading to 2° amenorrhea
- Galactorrhea
- Due to mass effects of the tumor–(as the tumor lies near optic chiasma)–visual disturbances & headache are complained of.



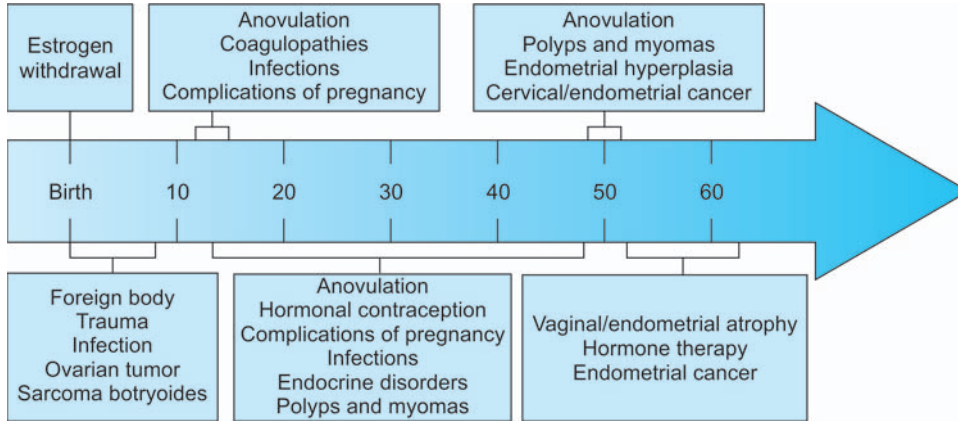


I.V. dose of GnRH 50 – 100 mg is given and rise of LH (in 30 – 60 minutes) and FSH (in 15 – 30 minutes) is seen.

Note: Friends it is quite difficult to understand the above chart in one go, you will have to go through it 3 – 4 times to understand it well.

## DUB – Dysfunctional Uterine Bleeding

### Causes of DUB

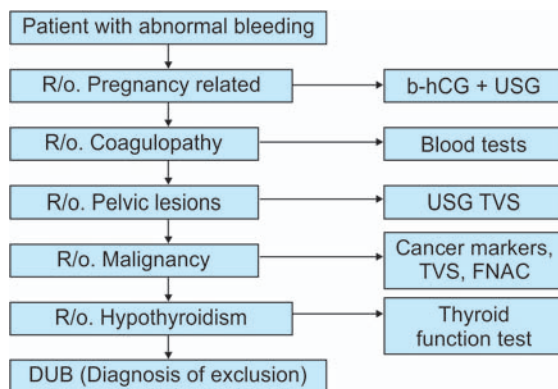


DUB is defined as a state of abnormal uterine bleeding without any clinically detectable organic pelvic pathology.

### Type of DUB

- DUB is of two types :
1. Anovulatory (80%)
  2. Ovulatory (20%)
- Anovulatory (80%) :
- Threshold bleeding of puberty menorrhagia
  - Metropathia hemorrhagica<sup>Q</sup>/cystic glandular hyperplasia<sup>Q</sup>
  - Premenopausal DUB (Atrophy of endometrium).
- Ovulatory (20%) :
- Irregular ripening<sup>Q</sup> of corpus luteum
  - Irregular shedding<sup>Q</sup> of corpus luteum/Halban’s disease
  - IUCD insertion
  - Following sterilization operation.

### Algorithm of Diagnostic Rules in DUB

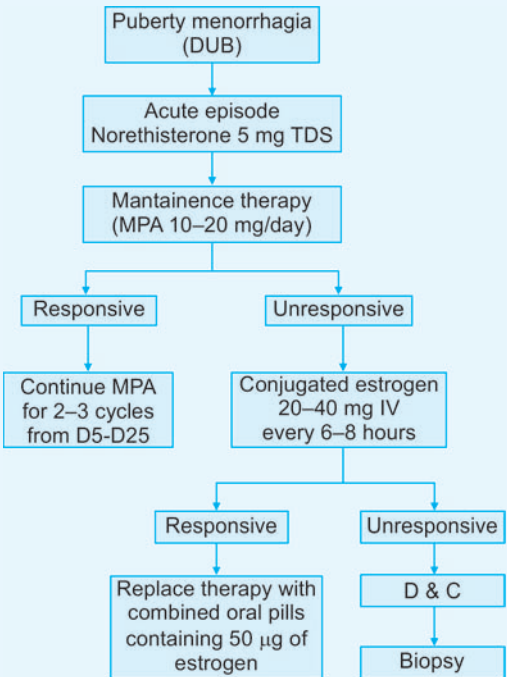


### Management options in different age groups

Age group	Investigations	Treatment
I <b>Puberty menorrhagia</b> Since in this age group bleeding is usually anovulatory DOC=cyclical	<ul style="list-style-type: none"> <li>• Rule out bleeding disorders by coagulation studies, CBC, platelet count</li> <li>• TSH levels</li> <li>• USG</li> </ul>	<ul style="list-style-type: none"> <li>• Reassurance</li> <li>• Psychological support</li> <li>• Correction of anemia</li> </ul> Non hormonal T/t: <ul style="list-style-type: none"> <li>– NSAID’s - mefenamic acid</li> <li>– Antifibrinolytics - Tranexamic acid</li> </ul>

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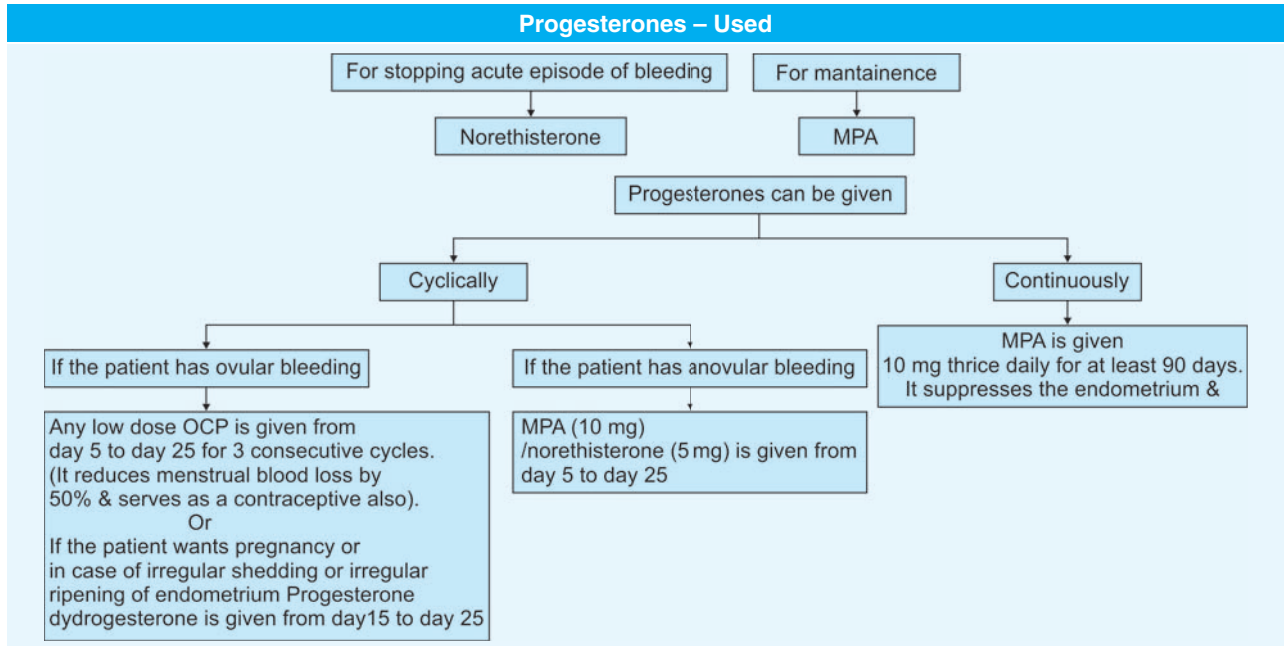
Age group	Investigations	Treatment
<p>progestin therapy (Leon speroff 8/e, 607)</p>	<p>Note These 2 investigations USG &amp; TSH should be done in all groups</p> <ul style="list-style-type: none"> <li>• If female has been sexually active               <ul style="list-style-type: none"> <li>○ During pregnancy test</li> <li>○ Cultures for gonorrhoea, Trichomonas, and Chlamydia testing</li> </ul> </li> <li><b>Investigation never done in this age group</b> <ul style="list-style-type: none"> <li>○ P/V examination</li> <li>○ Dilatation and curettage</li> </ul> </li> </ul>	<div style="text-align: center;">  <pre> graph TD     A[Puberty menorrhagia (DUB)] --&gt; B[Acute episode Norethisterone 5 mg TDS]     B --&gt; C[Maintenance therapy (MPA 10-20 mg/day)]     C --&gt; D[Responsive]     C --&gt; E[Unresponsive]     D --&gt; F[Continue MPA for 2-3 cycles from D5-D25]     E --&gt; G[Conjugated estrogen 20-40 mg IV every 6-8 hours]     G --&gt; H[Responsive]     G --&gt; I[Unresponsive]     H --&gt; J[Replace therapy with combined oral pills containing 50 µg of estrogen]     I --&gt; K[D &amp; C]     K --&gt; L[Biopsy]           </pre> </div> <ul style="list-style-type: none"> <li>• In patients with von Willebrand's disease, Desmopressin is the DOC</li> <li>• In young sexually-active females, Levonorgestrel IUCD-Mirena can also be used.</li> </ul>
<p>II <b>Reproductive age</b> – (In this age group, it is necessary to rule out pregnancy complications, fibroids, polyps and premalignant conditions like endometrial hyperplasia and CIN)</p>	<ul style="list-style-type: none"> <li>• TSH</li> <li>• USG</li> <li>• UPT</li> <li>• Endometrial sampling (by dilatation and curettage/hysteroscopy and biopsy)</li> <li>• Papsmear</li> <li>• Colposcopy</li> </ul>	<p>Mgt</p> <ol style="list-style-type: none"> <li>1. Antifibrinolytic drugs like tranexamic acid</li> <li>2. Prostaglandin synthetase inhibitor—mefenamic acid</li> <li>3. <b>To stop bleeding:</b> Norethisterone preparations (5 mg TDS × 5 or 7 days). Then regulate cycle by using either OCPs (in case of ovular bleeding) or medroxyprogesterone acetate (In anovular bleeding from D5–D25)</li> <li>4. <b>Cyclic Therapy</b> <ol style="list-style-type: none"> <li>a. <b>In ovular bleeding where patient doesnot want pregnancy:</b> Any <b>low dose combined oral pills</b> are effective when given from 5th to 25th day of cycle for 3 consecutive cycles. It causes endometrial atrophy. It is more effective as compared to progesterone therapy as it suppress the hypothalamopituitary axis more effectively and has contraceptive benefits also. <i>“Treatment with an estrogen progestin contraceptive is the better choice for those who likely still ovulate or want to avoid pregnancy.”</i> —Leon speroff 8<sup>th</sup>/ed p 607</li> <li>b. <b>In ovular bleeding, where the patient wants pregnancy or in cases of irregular shedding or irregular ripening of the endometrium:</b> Dydrogesterone 1 tab (10 mg) daily or twice a day from 15th to 25th day may cure the state.</li> <li>c. <b>In anovulatory bleeding:</b> Cyclic progestogen preparation of <b>medroxyprogesterone acetate (MPA)</b> 10 mg or norethisterone 5 mg is used from 5th to 25th day of cycle for 3 cycles.</li> </ol> </li> </ol>

Contd...

Contd...

	Age group	Investigations	Treatment
			<p><b>Continuous progestins Therapy</b>            Continuous progestins: Progestins also inhibit pituitary gonadotropin secretion and ovarian hormone production. Continuous therapy can be in the form of oral therapy or Mirena</p> <ol style="list-style-type: none"> <li>Medroxyprogesterone acetate 10 mg thrice daily is given and treatment is usually continued for at least 90 days.</li> <li>Levonorgestrel IUD – Mirena LNG IUS.                LNG-IUS is recommended as a first line therapy for a woman with heavy menstrual bleeding in the absence of any structural or histological abnormality. <i>“Can be used in all women as a first line of treatment of menorrhagia in place of oral medications. It is particularly useful for reproductive age women who also desire contraception” —William Gynae 1st/ed, p 188</i></li> </ol> <ol style="list-style-type: none"> <li><b>GnRH agonist</b> The subtherapeutic doses reduce the blood loss whereas in therapeutic doses produce amenorrhea. It is valuable as short-term use in severe DUB, particularly if the woman is infertile and wants pregnancy. The drugs are used subcutaneously or intranasally. It improves anemia, and is helpful when used before endometrial ablation. A varying degree of hypoestrogenic features may appear.</li> <li><b>Danazol:</b> Danazol is suitable in cases with recurrent symptoms and in patients waiting for hysterectomy. The dose varies from 200–400 mg daily in 4 divided doses continuously for 3 months. A smaller dose tends to minimize the blood loss and a higher dose produces amenorrhea. It reduces blood loss by 60 percent.</li> <li><b>Mifepristone (RU 486):</b> It is an anti-progesterone (19 nor-steroid). It inhibits ovulation and induces amenorrhea and reduces myoma size</li> </ol> <p><b>Surgical methods</b></p> <ol style="list-style-type: none"> <li><b>Dilatation and Curettage</b> can be used to control an acute episode of bleeding and is used for diagnostic purpose and not for therapeutic purpose as its effects are temporary. Ideally hysteroscopy and directed biopsy should be considered both for the purpose of diagnosis and therapy. Presently, dilatation and curettage should be used neither as a diagnostic tool nor for the purpose of therapy.</li> <li>Endometrial ablation                It is an alternative to hysterectomy in those reproductive age females who do not desire future pregnancy</li> <li>Hysterectomy is generally not required in this age group but in older age group.</li> </ol>
III	<p><b>Perimenopausal/post menopausal age</b>            Always rule out cancers first in Perimenopausal age-M/C cause after ruling out cancers is anovulatory</p>	<ul style="list-style-type: none"> <li>Never wait and watch Histopathological diagnosis should be made</li> <li>Do hysteroscopy and biopsy along with papsmear and colposcopy.</li> <li>Fractional curettage is preferred to blind D and C.</li> </ul>	<p><b>In perimenopausal age-</b> treatment is</p> <ul style="list-style-type: none"> <li>Progesterone – DMPA – Mirena</li> <li>Endometrial ablation</li> <li>Hysterectomy</li> </ul> <p><b>In postmenopausal age-</b>            Their is no role of hormonal therapy, do-</p> <ul style="list-style-type: none"> <li>Endometrial ablation</li> <li>Hysterectomy</li> </ul>

## Uses of Progesterone in DUB



### Uterus Conserving Surgeries for DUB -Endometrial Ablation/Resection

The various surgeries included in Endometrial Ablation are :

- Transcervical resection of endometrium (TCRE)
- Roller ball endometrial ablation
- Laser (Nd YAG) endometrial ablation
- MEA (microwave of 9.2 GHz is used for endometrial ablation)
- Uterine thermal balloon.

#### Indications

- Failed medical treatment
- Women who do not wish to preserve menstrual or reproductive function
- Uterus – normal size or not bigger than 10 weeks pregnancy size
- Small uterine fibroids (< 3 cm)
- Women who want to avoid longer surgery
- Woman who prefers to preserve her uterus.

#### Prerequisites

- Patient's family should be complete
- There should be no evidence of malignancy

#### Technique

**Laser ablation** of the endometrium using the Nd:YAG laser through hysteroscope is an alternative to hysterectomy. It is employed as an elective alternative to hysterectomy or when hysterectomy has been medically contraindicated. Tissue destruction to a depth of 4-5 mm produces a therapeutic Ashermann's syndrome and amenorrhea.

In **Uterine thermal balloon**: Endometrium is destroyed using a thermal balloon with hot normal saline (87°C) for 8-10 minutes. No dilatation of the cervical canal is needed. This procedure is suitable for women who are not suitable for general

In endometrial ablation surgeries, whole of endometrium is destroyed, thus, it should not be done in females who desire future pregnancy.

#### Contraindications of endometrial ablation

- Pregnancy
- Acute pelvic infection
- Endometrial hyperplasia
- Genital cancer
- Women wishing to preserve fertility
- Expectation of amenorrhea
- IUCD in place



anesthetic or long duration surgery. The success rate is similar to TCRE. No pretreatment endometrial thinning is required. **This is considered as a first line therapy and is done as a day care basis.**

**Microwave endometrial ablation:** Endometrial tissue upto a depth of 6 mm is ablated. Temperature in the region is 75–80°C.

**Novasure:** Endometrial ablation is done using a bipolar radio frequency mounted on an expandable frame.

Radio frequency energy vaporizes or coagulates the endometrium up to the myometrium. The procedure is quick, simple, and safe. Women with uterine cavity < 4 cm, PID, cesarean delivery are contraindicated.

**Transcervical resection of the endometrium (TCRE)** through continuous flow resectoscope is quicker and less costlier than laser ablation. It can be carried out even under paracervical block. Resectoscope loop must remove the basal layer of endometrium along with superficial layer of myometrium, otherwise regeneration of endometrium causes failure of operation.

**Result:** Ablation of endometrium upto a depth of 4–5 mm using laser, roller ball, thermal balloon, microwave, is an effective method. Resection of endometrium upto the basal layer is also a quicker and less costlier method. Overall, amenorrhea occurs in 30–40 percent of women, about 50 percent have decreased bleeding and 10 percent may need repeat procedure or hysterectomy.

**Complication:** most important is uterine perforation and fluid absorption leading to fluid overload.

**Hysterectomy** is not recommended as a first line therapy for heavy menstrual bleeding (HMB) or DUB. However, hysterectomy is justified when the conservative treatment fails or contraindicated and the blood loss impairs the health and quality of life. Presence of endometrial hyperplasia and atypia on endometrial histology is an indication for hysterectomy.

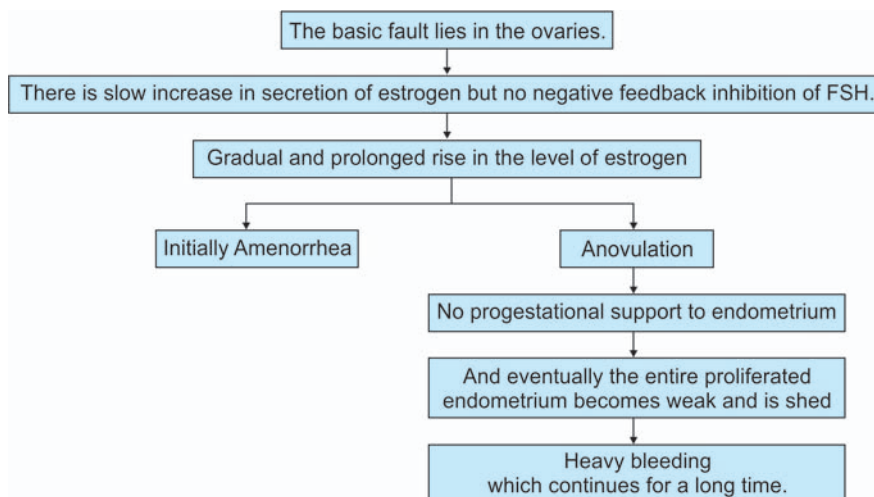
### Metropathia Hemorrhagica

*It is a specialized form of DUB.*

Mostly seen in premenopausal women.

**Maximum age incidence:** Between ages 40–45 years.

### Pathology



**Changes in the Uterus:** Symmetrical enlargement of the uterus to a size of 8 – 10 weeks due to hypertrophy of muscles.

**Microscopic appearance:**

- Hyperplasia of all endometrial components.
- Intense cystic glandular hypertrophy.<sup>Q</sup>
- Some glands are small and some large giving appearance of “swiss cheese”.<sup>Q</sup>
- Glands are empty and lined by columnar epithelium.
- Secretory changes are absent.<sup>Q</sup> (no cork screw glands seen)
- Follicular cysts containing estrogen present on ovaries.

**Signs and Symptom:** Patient complains of prolonged amenorrhea (of 6–8 weeks) followed by excessive painless bleeding (anovulatory bleeding).

**HOT TOPICS****Abnormal Uterine Bleeding (AUB) (FIGO, ACOG-2011)**

Any uterine bleeding outside the normal volume, duration, regularity or frequency is considered abnormal uterine bleeding (AUB).

Normal Menstruation	
Cycle interval	28 days (21–35 days)
Menstrual flow	4–5 days
Menstrual blood loss	35 mL (20–80 mL)

In order to create an universally accepted nomenclature to describe abnormal uterine bleeding, International Federation of Gynecology and Obstetrics (FIGO) and American College of Obstetricians and Gynecologists (ACOG) introduced newer system of terminology to describe AUB.

The newer classification system is known by the acronym **PALM-COEIN (FIGO-2011)**. It is used to classify the abnormal uterine bleeding on the basis of etiology. **Polyp, adenomyosis, leiomyoma, malignancy and coagulopathy, hyperplasia, ovulatory dysfunction, endometrial, iatrogenic, and not yet classified** are the different etiological factors expressed by one (or more) letters.

**Etiopathology of AUB**

Classification of AUB (FIGO-2011)			
Structural causes (PALM)		Nonstructural systemic causes (COEIN)	
• Polyp	AUB-P	Coagulopathy	AUB - C
• Adenomyosis	AUB-A	Ovulatory dysfunction	AUB - O
• Leiomyoma	AUB-L	Endometrial	AUB - E
– Submucosal myoma	AUB-L SM	Iatrogenic	AUB - I
– Other myoma	AUB-LO		
• Malignancy and hyperplasia	AUB-M	Not yet identified	AUB - N

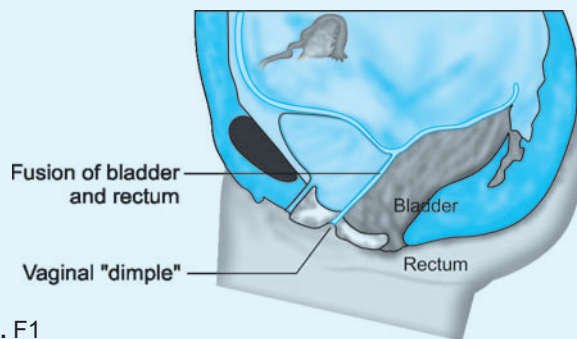
**Management Options for a Case with AUB**

- Women with AUB with age ≥ 45 years should have endometrial biopsy (D/C or hysteroscopy directed biopsy) as an initial step of management.
- Adolescent girls with AUB or heavy menstrual bleeding need exclusion of bleeding disorders besides other investigations. Complete hemogram, platelet count, prothrombin time, and partial thromboplastin time need to be done.

## FIGURE BASED QUESTION

**F1.** A 16-year-old girl was brought to gynae OPD by her parents with C/O primary amenorrhea. The findings discovered by the gynecologist are represented in the Fig. F1. The patient was diagnosed as having complete vaginal agenesis. Congenital vaginal agenesis is associated with all except:

- Non-functioning uterus
- Non-functioning ovaries
- Normal female karyotype
- Normal secondary sexual characteristics



**Fig. F1**

## QUESTIONS

- A 13-year-old young girl presents in the casualty with acute pain in the lower abdomen. She has history of cyclical pain for last 6 months and she has not attained her menarche yet. On local genital examination, a tense bulge in the region of hymen was seen. The most probable diagnosis is: (AIIMS May 06)
  - Mayer Rokitansky Kuster Hauser syndrome
  - Testicular feminization syndrome
  - Imperforate hymen
  - Asherman's syndrome
- The commonest cause of primary amenorrhoea is: (AIIMS Nov. 03)
  - Genital tuberculosis
  - Ovarian dysgenesis
  - Mullerian duct anomalies
  - Hypothyroidism
- Which is not primary amenorrhea? (AI 09/AI 2011/AIIMS May 2010)
  - Sheehan's syndrome
  - Kallmann's syndrome
  - Mayer Rokitansky Koster Hauser syndrome
  - Turner syndrome
- A woman has 2 kids. She presents with galactorrhea and amenorrhea for 1 year. The most probable diagnosis is: (AIIMS May 02)
  - Pregnancy
  - Pituitary tumor
  - Sheehan's syndrome
  - Metastasis to pituitary from other carcinoma
- Mrs. Sinha having her youngest child of 6 years age presents to her family physician with complaints of pruritis vulvae and amenorrhoea. On examination she is found to have loss of pubic and axillary hairs, patch of vitiligo and hypotension. She is lethargic and has cold intolerance. She has got multiple skin infections and anemia. All of the following should be used to treat her, except: (AIIMS Nov. 01)
  - Cortisol
  - Insulin
  - Ethinyl estradiol
  - Thyroid extract
- Hypothalamic amenorrhoea is seen in: (AIIMS Nov. 01)
  - Asherman syndrome
  - Stein-leventhal syndrome
  - Kallmann syndrome
  - Sheehan's syndrome
- Primary amenorrhoea with anosmia is seen in: (AIIMS June 00)
  - Kallmann syndrome
  - Laurence Moon Biedl syndrome
  - Foster - Kennedy syndrome
  - Sheehan's syndrome
- A 19-year-old patient complains of primary amenorrhoea. She had well developed breast and pubic hair but on examination there was absence of uterus and vagina. Likely diagnosis is: (AIIMS Nov 2010)
  - XXY
  - Mullerian agenesis
  - Gonadal dysgenesis
  - Klinefelter syndrome
- A 35-year-old lady is not having her menses for last 4 months. She has high serum FSH and LH level with low estradiol. The likely cause is: (AIIMS Nov. 99)
  - Panhypopituitarism
  - Polycystic ovarian disease
  - Exogenous estrogen administration
  - Premature menopause
- A 30-year-old woman para 2+0, hypertension have menorrhagia. Which is best treatment for her? (AIIMS May 2011)
  - Combined pills
  - Mirena
  - Hysterectomy
  - Transcervical resection of endometrium

11. A 45 years old lady presented with dysfunctional uterine bleeding. On transvaginal USG thickness of endometrium was found to be 8 mm. What should be the next step in the management of this patient? (AIIMS Nov 08/AIIMS Nov 2011)
- Histopathology
  - Hysterectomy
  - Progesterone
  - OCP
12. Raja Devi 45 years old women present with history of poly-menorrhoea for last six months. The first line of management is: (AI 02)
- Hysterectomy
  - Progesterone for 3 cycles
  - Dilatation and curettage
  - Oral contraceptive for 3 cycles
13. In a 45 years old lady with DUB for 6 months duration best line of management is: (AIIMS June 00)
- Progesterone for 6 months
  - OCP for 6 months
  - Dilation and curettage
  - Hysterectomy
14. Commonest cause of post menopausal bleeding in India is: (AI 07; AIIMS May 07)
- Ca endometrium
  - Ca cervix
  - Ca vulva
  - Ovarian tumour
15. A teenage girl presented in OPD with moderate acne and history of irregular menses. What treatment will you give? (AIIMS Nov 2010)
- Oral isotretinoin
  - Oral acitretin
  - Oral minocycline
  - Cyproterone acetate
16. Primary Amenorrhoea: (PGI Dec 08)
- Absence of Menarche by 14 years without secondary sexual characters
  - Absence of Menarche by 16 years with secondary sexual characters
  - Absence of secondary sexual characters by years
17. Causes of secondary amenorrhoea are: (PGI June 01)
- Turner's syndrome
  - Endometriosis
  - Asherman's syndrome
  - Thyroiditis
  - PCOD
18. Lady recovered from severe PPH, complains of failure of lactation and menstruation, which of the following can be seen: (PGI Dec 08)
- Increased Excretion of Na<sup>+</sup>
  - Retention of Water
  - Increased Prolactin
  - Increased GnRH
  - Increased TSH
19. A patient with amenorrhoea had bleeding after giving a trial of progesterone. This implies: (PGI Dec. 01)
- Sufficient estrogen
  - Sufficient progesterone
  - Normal ovarian function
  - Intact endometrium
  - Intact pituitary axis
20. Positive progesterone challenge test in a patient of secondary amenorrhoea, seen in: (PGI June 04)
- Asherman Syndrome
  - Endometrial TB
  - Hypopituitarism
  - Premature ovarian failure
  - PCOD
21. Withdrawal bleeding with progesterone seen in otherwise amenorrhoeic woman due to: (PGI Dec. 97)
- Hypogonadotrophic hypogonadism
  - Anovulation
  - Ovarian failure
  - TB endometritis
22. In a case of secondary amenorrhoea who fails to get withdrawal bleeding after taking E and P, the fault lies at the level of: (PGI June 05)
- Pituitary
  - Hypothalamus
  - Ovary
  - Endometrium
23. Child with primary amenorrhoea with negative progesterone challenge test but positive combined progesterone and estrogen test. Diagnosis may be: (PGI June 07)
- Mullerian agenesis
  - PCOD
  - Asherman syndrome
  - Prolactinoma
24. Average blood loss in normal menstruation:
- 50 mL
  - 80 mL
  - 100 mL
  - 120 mL
  - 10 mL
25. Menorrhagia is defined as blood loss per vagina more than: (AIIMS Nov. 99)
- 80 mL
  - 110 mL
  - 150 mL
  - 50 mL
26. Polymenorrhoea Means: (PGI Dec 08)
- Menses < 21 days
  - Menses >35 days
  - Painful menses
  - DUB
27. Initial evaluation in adolescent with abnormal uterine bleeding: (PGI June 05)
- Haemogram
  - Platelet count
  - USG
  - D & C
  - Examination under anesthesia

28. Most common cause of puberty menorrhagia:  
(PGI June 07)
- Anovulation
  - Malignancy
  - Endometriosis
  - Bleeding disorder
29. Puberty menorrhagia is treated by: (PGI June 02)
- Progesterone
  - Progesterone and estrogen
  - GnRH analogues
  - Danazol
  - Surgery
30. Causes of dysfunctional uterine bleeding can be:  
(PGI Dec. 01)
- Uterine polyp
  - Fibroid
  - Granulosa cell tumour
  - Irregular ripening of endometrium
  - Irregular shedding of endometrium
31. The most common histological finding of endometrium in DUB is:  
(PGI June 99)
- Hypertrophic
  - Hyperplastic
  - Cystic glandular hyperplasia
  - Dysplastic
32. Treatment of DUB in young female is: (PGI 95)
- Hormones
  - Radiotherapy
  - D & C
  - Hysterectomy
33. Treatment for 32 years old multipara with dysfunctional uterine bleeding (DUB) is:  
(PGI Dec 00)
- Progesterone
  - Danazol
  - Prostaglandins
  - Endometrial ablation
  - Hysterectomy
34. A 45-year-old female presenting with dysmenorrhoea and menorrhagia most probably has:  
(PGI Dec 97)
- DUB
  - Endometriosis
  - Fibroid
  - Endometrial Ca
35. All are causes of postmenopausal bleeding except:  
(PGI Dec 00)
- Carcinoma in situ of cervix
  - Ca. endometrium
  - Ca. ovary
  - Ca. fallopian tube
36. Post-menopausal bleeding is associated with all except:  
(PGI Dec 04)
- Ca cervix
  - CIN
  - Ca ovary
  - Endometrial Ca
  - Ca fallopian tube
37. A woman of 50 years who attained menopause, coming with one episode of bleeding P/V. Which of the following to be done:  
(PGI June 09)
- Assess for H/o HRT
  - Hysterectomy
  - PAPs smear
  - Endometrial biopsy
  - DUB
38. Evaluation of a patient with post menopausal bleeding is done by:  
(PGI June 05)
- Pap smear
  - USG
  - Endometrial biopsy
  - Dilatation & curettage
39. Cryptomenorrhoea occurs due to: (AI 95)
- Imperforate hymen
  - Asherman's syndrome
  - Mullerian agenesis
  - All
40. A 35-year-old mother of two children is suffering from amenorrhoea from last 12 month. She has a history of failure of lactation following second delivery but remained asymptomatic thereafter. Skull X-ray shows empty sella diagnosis is:  
(AI 02)
- Menopause
  - Pituitary tumor
  - Sheehan's syndrome
  - Intraductal papilloma of breast
41. A 35-year-old female patient Radha having children aged 5 and 6 years has history of amenorrhoea and galactorrhea. Blood examination reveals increased prolactin. CT of head is likely to reveal: (AI 02)
- Pituitary adenoma
  - Craniopharyngioma
  - Sheehan's syndrome
  - Pinealoma
42. In a woman presenting with amenorrhoea headache, blurred vision and galactorrhea appropriate investigation:  
(AI 97)
- Prolactin levels
  - LH
  - FSH
  - HCG
43. A middle aged female presents with increasing visual loss, breast enlargement and irregular menses. Investigation of choice would be: (AI 97)
- S. calcitonin
  - S. prolactin
  - S. hemoglobin concentration
  - S. calcium
44. Primary amenorrhoea with absent uterus, normal breasts and scanty pubic hair is seen in: (AI 2010)
- Mayer Rokitansky Kuster hauser Syndrome
  - Turner Syndrome
  - Noonan Syndrome
  - Testicular feminizing syndrome
45. A patient had a spontaneous abortion, then she came with amenorrhoea and FSH 6 pm IU/mL. What the most probably diagnosis?  
(AI 10)
- Ovarian failure
  - Uterine Synechia
  - Pregnancy
  - Pituitary failure
46. Lactational amenorrhoea is due to:
- Prolactin induced inhibition of GnRH
  - Prolactin induced inhibition of FSH
  - Oxytocin induced inhibition of GnRH

47. All of the following conditions are associated with primary amenorrhoea except: (AI 97)
- Testicular feminization syndrome
  - Stein-Leventhal syndrome
  - Turner's syndrome
  - Mayer Rockitansky Kuster Hauser Syndrome
48. The most common cause of secondary amenorrhoea in India is: (AI 05)
- Endometrial tuberculosis
  - Premature ovarian failure
  - Polycystic ovarian syndrome
  - Sheehan's syndrome
49. Evidence based treatment for menorrhagia is all except: (AI 09/AIIMS May 2010)
- OCPs
  - Progesterone for three months cyclically
  - Tranexamic acid
  - Ethamsylate
50. Which of the following is not indicated in menorrhagia: (AI 02)
- |                   |                    |
|-------------------|--------------------|
| a. NSAID's        | b. Clomiphene      |
| c. Norethisterone | d. Tranexamic acid |

### NEW PATTERN QUESTIONS

51. Abnormal uterine bleeding is/are: (PGI May 2013)
- Blood loss of more than 80 ml
  - Cycle duration is more than 35 days or less than 21 days
  - Bleeding period lasting 7 days or more
  - Irregular bleeding during a regular cycle
52. Metrorrhagia is produced by the following except:
- |                  |                       |
|------------------|-----------------------|
| a. Fibroid polyp | b. CA endometrium     |
| c. IUD           | d. Intramural fibroid |
53. In DUB, there is:
- Increased estrogen
  - Decreased receptors of progesterone
  - Decreased receptors of estrogen
  - Pituitary imbalance of hormones
54. Halban's disease is due to:
- Persistent corpus luteum
  - Deficient corpus luteum
  - Persistent trophoblast
  - Deficient trophoblast
55. Metropathica hemorrhagica is best treated by:
- |                        |                |
|------------------------|----------------|
| a. Curettage of uterus | b. Progestogen |
| c. Estrogen            | d. Clomiphene  |
56. The most common source of vicarious menstruation is:
- |          |           |
|----------|-----------|
| a. Heart | b. Lungs  |
| c. Nose  | d. Kidney |
57. Most common endometrial pattern in dysfunctional uterine bleeding:
- Normal
  - Hyperplastic with Swiss-Cheese pattern
  - Nonsecretory
  - Atrophic
58. Most common cause of menorrhagia in childbearing period:
- Fibroid
  - Dysfunctional uterine bleeding
  - Pelvic endometriosis
  - Adenomyosis
59. Primary amenorrhoea is most commonly associated with:
- Developmental defect of the genital tract
  - Tuberculosis
  - Endocrine disorders
  - Chromosomal abnormality
60. Dysfunctional uterine bleeding is commonly met in all except:
- Adolescence
  - Following childbirth
  - Premenopausal period
  - Postmenopausal period
61. Withdrawal bleeding following administration of progestogen in a case of secondary amenorrhoea indicates all except:
- Absence of pregnancy
  - Production of endogenous estrogen
  - Endometrium is responsive to estrogen
  - Defect in pituitary gonadal axis
62. The following are the features of anovular menstruation except:
- The only symptom may be failure of conception
  - It is usually associated with painless periods
  - May be associated with premenstrual syndrome
  - May be associated with DUB
63. Anita 15-year-old, complains of heavy periods since 2 montsh. O/E: wt 40 kg and BP 120/80 mmHg. All of the following investigations are indicated, except:
- S. TSH
  - Platelet count
  - Bleeding and clotting time
  - Estradiol levels
64. Period of amenorrhoea followed by massive bleeding is seen in premenopausal women with:
- Irregular ripening
  - Irregular shedding
  - Metropathia hemorrhagica
  - All of the above
65. The investigation of choice in a 55-year-old postmenopausal women who has presented with postmenopausal bleeding is:
- Pap smear
  - Fractional curettage
  - Transvaginal ultrasound
  - CA-125

## ANSWER TO FIGURE BASED QUESTIONS

## F1. Ans. is b, i.e. Non-functioning ovaries

Complete vaginal agenesis is seen in mullerian duct agenesis. Ovaries are functioning in this case.  
The rest all options have been discussed in detail earlier

## ANSWERS

## 1. Ans. is c, i.e. Imperforate hymen

Ref. Shaw 15<sup>th</sup>/ed pp 96-97

A young girl who has not attained menarche but has history of cyclical pain for last 6 months, presenting to casualty with acute abdomen and on examination a tense bulge in the region of hymen – clearly point towards “Imperforate hymen” as the diagnosis.  
For details see the preceding text.

## 2. Ans. is b, i.e. Ovarian dysgenesis

Ref. Leon Speroff 7<sup>th</sup>/ed p 420; Shaw 15<sup>th</sup>/ed p 284

- Most common cause of Primary Amenorrhea = Gonadal dysgenesis<sup>o</sup>/ovarian dysgenesis
- 2<sup>nd</sup> most common cause of Primary Amenorrhea = Mullerian agenesis (Mayer Rokitansky Kuster Hauser Syndrome).<sup>o</sup>  
“Mullerian agenesis is a relatively common cause of primary amenorrhea, more frequent than congenital androgen insensitivity and second only to gonadal dysgenesis.”  
– Leon Speroff 7<sup>th</sup>/ed p 420
- 3<sup>rd</sup> most common cause is testicular feminizing syndrome.

## 3. Ans. is a, i.e. Sheehan’s syndrome

Ref. Shaw 14<sup>th</sup>/ed p 256-257

- Kallmann’s syndrome is due to hypothalamic dysfunction characterized by a deficiency of gonadotropin releasing hormone (GnRH) causing a hypogonadotropic hypogonadism. This is associated with anosmia. It can occasionally be associated with optic problems, such as color blindness or optic atrophy, nerve deafness, cleft palate, cryptorchidism, renal agenesis, and mirror movement disorder.
- MRKH syndrome, also known as Mullerian agenesis is due to anatomical absence of uterus. This is the second most common cause of primary amenorrhea.
- Turner’s syndrome is a type of gonadal dysgenesis and is overall the most common cause of primary amenorrhea
- Sheehan’s syndrome is postpartum pituitary necrosis. It leads to secondary amenorrhea and not primary amenorrhea.

## 4. Ans. is b, i.e. Pituitary tumor

Ref. Novak 14<sup>th</sup>/ed pp 1104, 1109; Harrison 17<sup>th</sup>/ed pp 2205-2206; Williams Gynae 1<sup>st</sup>/ed p 338 onwards

The female in the question is presenting with galactorrhea and amenorrhea for 1 year which raises the suspicion for pituitary tumor i.e. prolactinoma/pituitary adenoma.

**Pituitary Adenomas:**

- Most common Pituitary adenoma is Prolactinomas.

Microadenomas	Macroadenomas
< 1 cm in diameter <sup>o</sup>	> 1 cm in diameter <sup>o</sup>
Female–male ratio = 20:1 <sup>o</sup>	Female–male ratio = 1:1 <sup>o</sup>
5% of microadenomas progress to macroadenomas.	Prolactin levels > 100 µg/L
30% resolve spontaneously	

**Presentation:**

- |                     |  |
|---------------------|--|
| Women present with: | <ul style="list-style-type: none"> <li>• Galactorrhea<sup>o</sup></li> <li>• Features of hypogonadism:<br/>(as prolactin inhibits GnRH) <ul style="list-style-type: none"> <li>– Amenorrhea<sup>o</sup> / Oligomenorrhea</li> <li>– Delayed puberty, Anovulation</li> <li>– Infertility<sup>o</sup></li> </ul> </li> </ul> |
| Men present with:   | <ul style="list-style-type: none"> <li>• Impotence</li> <li>• Loss of libido</li> <li>• Infertility.</li> </ul>  |

**In both sexes, they can cause symptoms due to mass effects of the tumor:**

- Cavernous sinus syndrome consisting of:
    - Headaches
    - Visual defects (Most common Bitemporal hemianopsia)
    - Cranial nerve palsies especially III, IV, and VI
  - Raised serum prolactin levels
  - X-Ray sella shows space occupying lesion.
- Investigations: In all cases of hyperprolactinemia:
- MRI should be performed
  - TSH levels should be measured.

**Management:****Microadenoma with no desire of fertility:**

- Asymptomatic patients with microadenomas rarely progress to macroadenomas and are managed conservatively.
- If patient has osteopenia, (due to hypoeestrogenemia caused by ↑ Prolactin levels) = estrogen replacement or OCP's.
- Monitor patients with regular serial prolactin levels and MRI (every 12 months).

**For symptomatic microadenomas:**

- Medical management by dopamine agonist viz bromocriptine and cabergoline (which increase dopamine levels, thus decreasing prolactin levels) are the mainstay of therapy.
- Other dopamine agents like pergolide, lisuride (both ergot derivatives) and quinagolide (non ergot derivative) can also be used.

**Macroadenomas:** Long-term Bromocriptine therapy with periodic serum prolactin measurements (6 monthly) and MRI (6 monthly).

**Surgery indications:**

- Tumors unresponsive to Bromocriptine
- Tumors causing persistent visual field loss.

**5. Ans. is b, i.e. Insulin**Ref. Jeffcoate 7<sup>th</sup>/ed pp 582-583

Well friends let's first diagnose the disorder with which Mrs. Sinha is suffering, then only we can debate about its management.

- The anterior pituitary hormones are affected in order = GH, FSH and LH, TSH, and ACTH
- In the question: **Mrs. Sinha has:**
  - Amenorrhea: due to ↓ FSH/LH
  - Cold intolerance due to ↓ TSH
  - Hypotension
  - Loss of axillary hair
  - Loss of pubic hair due to ↓ ACTH (Adrenal cortical failure)
  - Decreased skin pigmentation (vitiligo)

**All these can be explained by:** Sheehan's syndrome (and the question also says her youngest son is 6 years old which should hint at something: **Remember** - in **AIIMS** they have a meaning for each and every word).

Sheehan's syndrome is characteristically caused by ischemic necrosis of most of the anterior pituitary which results from spasm in its arterioles occurring at the time of severe haemorrhage or shock (usually postpartum) complicating child birth.

*"The syndrome may develop slowly over 8-10 years time."*

- Dutta Gynae 6<sup>th</sup>/ed p 465

The treatment of Sheehan's syndrome includes: Lifelong hormone substitute including estrogen, progesterone, thyroid, and adrenal hormone.

- Internet link [www.nlm.nih.gov/medlineplus/ency/article/001175.htm](http://www.nlm.nih.gov/medlineplus/ency/article/001175.htm).

Replacement therapy with appropriate hormones including corticosteroid and thyroid are needed

Dutta Gynae 6<sup>th</sup>/ed p 465**6. Ans. is a, i.e. Kallmann Syndrome**Ref. Shaw 15<sup>th</sup>/ed p 284; Harrison 17<sup>th</sup>/ed p 2198**Lets see all options one by one.**

Asherman's syndrome	Is caused by endometrial synechiae most common after an overzealous curettage. The defect lies in the endometrium (Compartment I)
Stein Leventhal syndrome	The PCOS involves the ovaries (Compartment II)
Sheehan's syndrome	This syndrome results from ischemic necrosis of the anterior pituitary (Compartment III)

**Lets see all options one by one.**

Kallmann syndrome	This syndrome results from defective hypothalamic GnRH synthesis and is associated with anosmia or hyposmia due to olfactory bulb agenesis or hypoplasia. (i.e. Kallman syndrome involves hypothalamus or Compartment IV).
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**Also know:**

**Kallmann syndrome may be associated with:**

- Optic atrophy<sup>Q</sup>
- Color blindness<sup>Q</sup>
- Nerve deafness
- Cleft palate
- Renal anomalies
- Cryptorchidism<sup>Q</sup>
- Neurologic abnormalities



**Males with Kallmann syndrome present with:**

- Delayed puberty
- Micropenis
- Anosmia

Due to low LH, FSH, and testosterone levels

**Females present with:**

- Primary amenorrhea<sup>Q</sup>
- Failure of secondary sexual development<sup>Q</sup>
- Anosmia.

**Management:** Cyclical estrogen/progestin therapy or gonadotropins.

**Extra Edge:**

**Other congenital hypothalamic syndromes leading to Amenorrhea are:**

- Prader willi syndrome<sup>Q</sup>
- Laurence Moon Biedl syndrome<sup>Q</sup>
- Septo-optic dysplasia<sup>Q</sup>
- Frohlich's syndrome.<sup>Q</sup>

**7. Ans. is a, i.e. Kallmann Syndrome**

Ref. Shaw 15<sup>th</sup>/ed p 70; Harrison 17<sup>th</sup>/ed p 2198

Friends, you know the answer to this question quite well. Here I would like to point out that in solving PGME Questions of previous years, it is not only important to know the correct answer with its details, it is equally important to know the details of incorrect options (as Questions might be asked on these incorrect options in future).

So, let's know:

**Laurence Moon Biedl Syndrome**

It is an autosomal recessive disorder characterized by GnRH deficiency (hypogonadism) (FSH < 40 mIU/ml) and associated with:

- Obesity
- Mental retardation
- Polydactyly
- Retinitis Pigmentosa

**Sheehan's syndrome:** described in detail earlier

**Foster Kennedy Syndrome: Do not get confused with this option:** It is the same Foster Kennedy Syndrome as you have read in Ophthalmology, characterized by papilloedema in one eye and optic atrophy in the other. It results from raised intracranial pressure and simultaneous optic nerve compression secondary to tumor - classically, a meningioma of the olfactory groove, or more commonly, due to meningioma of the sphenoid wing.

**8. Ans. is b, i.e. Mullerian agenesis**

Ref Jeffcoates 7<sup>th</sup>/ed pp 197-198; Leon Speroff 7<sup>th</sup>/ed pp 455-457,460-461,1261-1262

In the question a 19 year old girl is presenting with primary amenorrhea, she has well developed breast and pubic hair but on examination uterus and vagina are absent. Since her breast and pubic hair both are well developed- this means her secondary sexual characteristics are well developed.

This means in this female amount of estrogen is adequate, which means she has normally functioning ovaries.

Thus, options **XXX** (presence of Y Chromosome means- gonads are testis), **Klinefelter's syndrome** (genotype = 47XXY- again since Y chromosome is present, gonads are testes i.e. they are males) are ruled out and in gonadal dysgenesis- gonads are incompletely formed and are streak gonads, M/c example is Turner's syndrome - genotype 45XO. Since gonads are streak, therefore estrogen is insufficient so secondary sexual characteristics are not well developed. In Turners thus by exclusion, our answer is **option b-** i.e. **Mayer Rokitansky kuster hauser syndrome.**

*"Patients with mullerian agenesis, typically present in late adolescence or as young adults, well after menarche was expected, with primary amenorrhea as their only complaint. They exhibit normal, symmetrical breast and pubic hair development, no usable vagina and have no symptoms or signs of cryptomenorrhea because the rudimentary uteri contain no functional endometrium."*

- Leon speroff 8<sup>th</sup>/ed p 455

**9. Ans. is d, i.e. Premature menopause**

Ref. Shaw 14<sup>th</sup>/ed p 60

- Premature menopause is defined as secondary amenorrhea before 40 years of age, due to ovarian failure. It is clinically defined as secondary amenorrhea for atleast 3 months with raised FSH, raised FSH/LH ratio and low estrogen levels in a women under 40 years of age.
- In case of PCOD or Stein-Leventhal syndrome, estrogen level is normal, LH is raised, LH/FSH ratio is raised.
- Panhypopituitarism leads to decreased LH and FSH levels which in turn leads to decreased estrogen.
- Exogenous oestrogen reduces FSH and LH by its feedback mechanism.

Conditions	Gonadotropins (LH, FSH)	Estrogen
Premature menopause	Both increased	Decreased
Pan hypopituitarism	Both decreased	Decreased
Exogenous estrogen	Both decreased	Increased
PCOD	LH increased, FSH normal	Increased

**Also know:** Categories of Amenorrhea based on Gonadotropin and Estrogen and Levels

Type of Hypogonadism	LH/FSH	Estrogen	Primary Defect
Hypergonadotropic	High	Low	Ovary
Hypogonadotropic	Low	High	Hypothalamus / pituitary
Eugonadotropic	Normal	Normal	Varied

**Remember:** For diagnosis of premature ovarian failure serum FSH levels should be  $> 40$  mIU/ml on 2 occasions, atleast 1 month apart.

**10. Ans. is b, i.e. Mirena**

*Ref. Novak 15<sup>th</sup>/ed p 788; Williams Gynae 1<sup>st</sup>/ed pp 187-188*

We have discussed in the preceding text, management options for females of reproductive age group -

In this particular question, female is 30 years old i.e. very young so we should not choose hysterectomy or endometrial ablation as the management of choice because in future she might desire pregnancy.

Patient is hypertensive, hence OCPs are contraindicated, so our answer by exclusion is Mirena which is logically also correct, as this patient has 2 children so she may not desire pregnancy presently.

Thus, Mirena serves 2 purposes in this female-

- I. Controls bleeding
- II. Contraceptive benefit.

In future, if she desires pregnancy, she may get mirena removed.

Our answer is further supported by the following lines -

*"The LNG IUS can be used in all women as a first line of treatment of menorrhagia in place of oral medications. It is particularly useful in reproductive aged women who desire contraception."*

*– Williams Gynae 1<sup>st</sup>/ed p188*

*"Heavy menstrual bleeding that doesnot respond to oral medication may be managed by endometrial ablation using coagulation, resection or vaporisation provided that patient is willing to forgo future fertility. Alternatively if future fertility is desired, a levonorgestrel releasing intrauterine device can provide virtually equal clinical outcome."*

*– Novak 15<sup>th</sup>/ed p788*

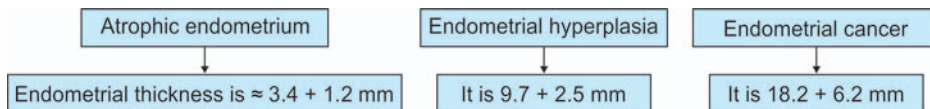
**11. Ans. is a, i.e. Histopathology**

*Ref. Williams Gynae 1<sup>st</sup>/ed p 180*

A 45 years old lady is presented with DUB -

- Chances of endometrial hyperplasia/neoplasia are high.
- TVS findings show thickness of endometrium as 8 mm. First, lets understand what does this signify -  
Endometrial thickness has been correlated with endometrial cancer risk in peri-and postmenopausal women.

**In postmenopausal females with:**



Sensitivities of 95 - 97% have been reported using a measurement of  $\leq 4$  mm for exclusion of endometrial cancer.

*Women with endometrial thickness  $> 5$  mm warrant additional evaluation with saline infusion sonography (SIS), or hysteroscopy or endometrial biopsy.*

**• Summary of diagnostic procedures in case of DUB, if endometrial neoplasia is suspected:**

- There is no clear sequence to the use of endometrial biopsy, TVS, saline infusion sonography (SIS), and hysteroscopy when evaluating abnormal uterine bleeding.
- TVS - as it is well tolerated, cost effective, and requires minimal technical skill is the first logical step. In addition, TVS can determine whether a lesion is diffuse or focal
- If endometrial hyperplasia/neoplasia is suspected on TVS: then endometrial biopsy is done.
- If there is a focal lesion - either hysteroscopy or saline infusion sonography (SIS) is done.

**Extra Edge:**

- Clear cut endometrial thickness guidelines have not been established for premenopausal females.
- It is generally seen that normal endometrial thickness in premenopausal women does not exceed 4 mm on day 4 of menstrual cycle and 8 mm by day 8.
- A persistent finding of endometrial thickness  $\geq 12$  mm independent of cycle day should prompt further evaluation in these women, especially in those with risk factors for endometrial carcinoma.

**12. Ans. is c, i.e. Dilatation and curettage**Ref. CGDT 9<sup>th</sup>/ed p 629; Jeffcoate 7<sup>th</sup>/ed p 610**13. Ans. is b, i.e. OCP for 6 months**

Friends, I have given these questions (12 and 13) together, so that you understand the difference between the two.

**Question 12 asks:** Polymenorrhea in a 45 years old woman for 6 months – first line of management.

**Whereas question 13 asks -DUB** in a 45 years old woman for 6 months – best line of management.

As far as first line of management is concerned if such a patient comes to me, definitely I would investigate the patient to rule out endometrial cancer. In this process I would perform hysteroscopy and biopsy but since they are not given in options so I would go for a diagnostic D and C.

*“In the later reproductive years, even more care must be given to exclude pathological cause because of the possibility of endometrial cancer. Aspiration, curettage, or both should clearly establish anovulatory or dyssynchronous cycles as the cause before hormone therapy is started.”*

– Jeffcoate 7<sup>th</sup>/ed p 609

*“Above 40, anovulatory DUB is again the commonest cause, but endometrial malignancy must be excluded and so endometrial sampling is performed as a first line investigation.”*

Ref. Text book of gynae Shiela Balakrishnan 1<sup>st</sup>/ed p58

As far as the therapy is concerned, in perimenopausal age group–

*“In this age group, anovulatory DUB is definitely more common, but endometrial pathology, especially endometrial malignancy must be ruled out”*

Ref. Text book of gynae Sheila Balakrishnan 1<sup>st</sup>/ed p56

And as we know in anovulatory DUB – medical therapy of choice is - Progesterone

As far as D & C is concerned: dilatation and curettage is basically for diagnostic purpose, its therapeutic benefit is very short lived

*“Therapeutic curettage is of no value in the treatment of polymenorrhea.”*

– Jeffcoate 7<sup>th</sup>/ed p 610

For hysterectomy-

*The place of surgery in the treatment of excessive bleeding without an organic basis varies with the age of the patient; it should be a last resort in young girls but may be considered earlier in women above the age of 40 years. Nevertheless, in the latter group it is good practice to exclude organic disease by ultrasound and endometrial aspiration, to try medical therapy, and proceed to hysterectomy if the response is inadequate or not sustained.*

– Jeffcoate 6<sup>th</sup>/ed p 575

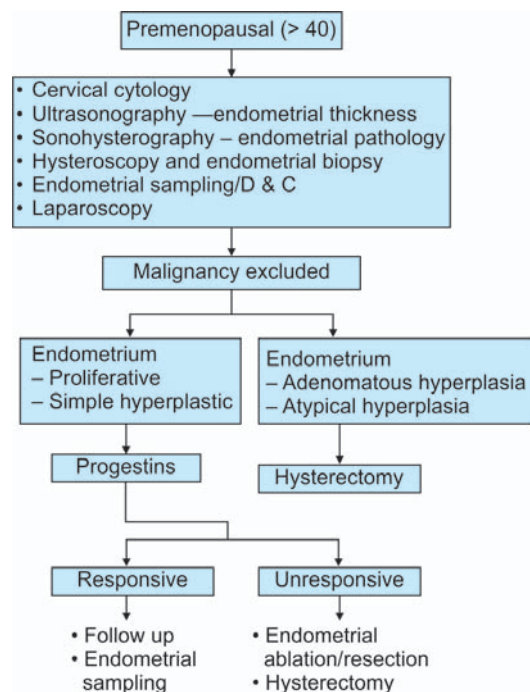
*When the patient is above 40 years of age, and when the hemorrhage fails to respond to simpler measure, hysterectomy is indicated. It is the treatment of choice in all cases of persistent or recurrent postmenopausal bleeding for which there is no obvious cause.*

– Jeffcoate 7<sup>th</sup>/ed p 611

From above lines it is clear that hysterectomy is the last resort, first medical management is tried in perimenopausal females.

**Hysterectomy** personally I feel is not the best treatment as it is a major surgery, has its own complications and high rate of morbidity. I will not advise hysterectomy to all patients who come to me with the complain of DUB I will advise medical therapy and then proceed to hysterectomy if it fails. This is what we do in general practice.

Management protocol of DUB in perimenopause females

**14. Ans. is b, i.e. Ca cervix** Ref. Gynae. for PG's by Bijoy Sree Sen Gupta 2<sup>nd</sup>/ed p 156-157; Shaw 15<sup>th</sup>/ed p 392; Jeffcoate 7<sup>th</sup>/ed p 471

Friends, all the options given in the question can cause postmenopausal bleeding. The main question is most common cause in India –

*“In the developed world Post Menopausal Bleeding (PMB) is a frequent presentation of endometrial carcinoma. The scenario is different in the developing world where carcinoma cervix is still the leading malignancy of the genital tract and the leading cause of PMB.”*

– Bijoy Sree 2<sup>nd</sup>/ed p 156

- Remember-**
- M/C cancer causing postmenopausal bleeding in India-Ca Cervix
  - M/C cancer causing postmenopausal bleeding world wide-Ca endometrium
  - M/C cause of postmenopausal bleeding in india-Ca cervix
  - M/C cause of postmenopausal bleeding worldwide-Endometrial atrophy

*Causes of Post Menopausal Uterine Bleeding with their frequency of occurrence.*

– Novak 15<sup>th</sup>/ed pp 1256, 427

In 15/e two different tables are given on two different pages. I am giving both of them here.

Table 35.3, p 1256	Cause	Percentage	Table 14.16, p 427	Cause	Percentage
	Endometrial atrophy (MC)	60 – 80%		Exogenous estrogens	30
	Estrogen Replacement therapy	15 – 25%		Atrophic endometritis/vaginitis	30
	Endometrial Polyps	2 – 12%		Endometrial cancer	15
	Endometrial hyperplasia	5 – 10%		Endometrial or cervical polyps	10
	Endometrial cancer	60 – 80% 10%		Endometrial hyperplasia	5

**15. Ans. is d, i.e. Cyproterone acetate**

Ref - Read Below

A teenage Girl is presenting with H/O irregular menses and acne both of which could mean excessive androgen production in females

Excessive androgen production in females leads to:

- |                     |                      |
|---------------------|----------------------|
| i. Hirsutism        | ii. Irregular Menses |
| iii. Acne           | iv. Seborrhea        |
| v. Temporal Balding | vi. Clitoromegaly    |

*“The physical manifestations of androgen excess generally reflect the extent to which androgen levels are elevated. Hirsutism is the most common complaint associated with androgen excess and essentially all women with hirsutism have an increased production rate of testosterone and androstenedione.”*

– Leon Speroff 8<sup>th</sup>/ed p 542

The management of excessive androgen production is -

- i. Oral contraceptive pills-

**Principle for using OCP's**

**Estrogen component of OCP's-**

Increases sex hormone binding globulin (SHBG) resulting in decreased free testosterone.

**Progesterone** suppresses LH resulting in decreased ovarian androgens.

The best oral contraceptives should be those which utilize a progestin with minimal androgenicity i.e. pills containing desogestrel, gestodene e.g. femilon and novelon.

OCP's are effective in 60 – 100% patients with hirsutism, acne and seborrhea.

**Remember:** Hormone therapy must be continued for 6 months before judging its effectiveness.

**Anti-androgens Cyproterone acetate:** It is an antiandrogen which inhibits gonadotropin secretion and interferes with androgen action on the target organs by competing for the androgen receptors.

It should be administered along with ethinyl-estradiol to prevent menstrual irregularities and ovulation. It is available as combined estrogen – progestin oral contraceptive (2 mg cyproterone acetate and 35 µg ethinyl estradiol as (Ginette or Diane 35)

**“A combined pill containing 35 mcg ethinyl estradiol and 2 mg of an anti-androgen cyproterone acetate (Diane 35 or Ginette) is the drug of choice in teenagers with irregular period and hirsutism. The effect on acne and seborrhea is evident shortly after starting treatment but 6-12 cycles are needed for a demonstrable effect on hirsutism.**

**16. Ans. is a and b, i.e. Absence of Menarche by 14 years without secondary sexual characters; and Absence of Menarche by 16 years with secondary sexual characters**

Ref. Shaw 15<sup>th</sup>/ed p 284

Primary amenorrhea is a condition when a female has not attained menarche by the age of 14 years in the absence of growth or development of secondary sexual characteristics.

OR

No menarche by the age of 16 years<sup>Q</sup> regardless of the presence of normal growth and development of secondary sexual characteristics.

**17. Ans. is c, d and e, i.e. Asherman's syndrome; Thyroiditis; and PCOD**

Ref. Shaw 14<sup>th</sup>/ed pp 259-260

*Secondary amenorrhea is defined as absence of menstruation for 3 normal cycles or for 6 months or more in a woman with previous normal menstrual pattern in absence of pregnancy*

– Williams Gynae p 365

Important causes of Secondary Amenorrhea (Compartment wise)	
Compartment I (Disorders of outflow tract/uterus)	<ul style="list-style-type: none"> <li>Acquired obstruction (gynatresia) of cervical canal causing severe stenosis or atresia following electro-cauterization, chemical burns, cervical amputation in fothergill's repair, conization, CIN or genital tuberculosis.</li> <li>Asherman's syndrome<sup>o</sup> Following excessive curettage or endometrial tuberculosis</li> <li>V V F (cause unknown)</li> </ul>
Compartment II (Disorders of Ovary)	<ul style="list-style-type: none"> <li>Ovary Tumor – masculinizing tumors/PCOD<sup>o</sup></li> <li>Trauma – surgical expiration/radiotherapy</li> <li>Infections – mumps, tuberculosis rarely pyogenic infections</li> <li>Premature ovarian failure</li> </ul>
Compartment III (Pituitary)	<ul style="list-style-type: none"> <li>Hyperprolactinemia</li> <li>Insufficiency as in Simmond's disease, Sheehan's syndrome</li> <li>Empty sella syndrome</li> <li>Infiltrative disease</li> </ul>
Compartment IV (Hypothalamus)	<ul style="list-style-type: none"> <li>GnRH deficiency</li> <li>Vigorous exercise/Excessive stress</li> <li>Weight loss</li> <li>Eating disorders – anorexia and Bulimia</li> <li>Tumor (including craniopharyngioma, germinoma, endodermal sinus tumor, eosinophilic granuloma, and glioma)</li> <li>Radiation</li> <li>Pseudocystitis</li> <li>Infection (TB)</li> <li>Infiltrative disease (sarcoidosis)</li> </ul>

Besides these some other causes of secondary amenorrhea are:

- Pregnancy-M/C cause of secondary amenorrhea
- Hypothyroidism<sup>o</sup> (V.Imp. cause, should be ruled out in every case).
- Hyperprolactinemia
- Diabetes
- Tuberculosis
- Renal disease/Liver disease
- Addison's disease/Cushing's syndrome/Acromegaly
- Drugs (phenothiazines, reserpine, antidepressants, OCPs).
- Malabsorption syndrome
- AIDS

Among the options given: asherman's syndrome, PCOD, and thyroiditis (as it leads to hypothyroidism) are the causes of secondary amenorrhea.

18. Ans. is a, i.e. Increased excretion of Na<sup>+</sup>

Ref. Read below

Now, friends this is a tricky question. As far as diagnosis of this female is concerned there is no doubt that she is having Sheehan's syndrome.

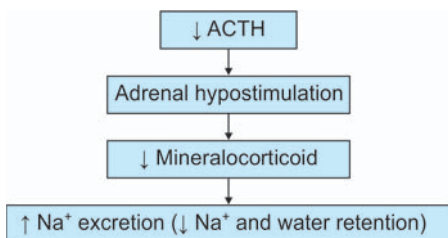
As discussed earlier in next-

Levels of prolactin

Levels of GnRH are all decreased in Sheehan syndrome

Levels of TSH

Along with this, level of ACTH is also decreased.



19. Ans. is a, d and e, i.e. Sufficient estrogen; Intact endometrium; and Intact pituitary axis

Ref. Dutta Gynae 5<sup>th</sup>/ed p 447, 6<sup>th</sup>/ed p 469; Leon Speroff 7<sup>th</sup>/ed pp 404-409

20. Ans. is e, i.e. PCOD

21. Ans. is b, i.e. Anovulation

Ref. Dutta Gynae. 5<sup>th</sup>/ed p 447; Williams Gynae 1<sup>st</sup>/ed p 377

**If a patient is having positive progesterone challenge i.e. bleeding occurs after giving progesterone it means:**

If withdrawal bleeding occurs, it proves— (i) The intact hypothalamopituitary ovarian axis and (ii) There is adequate endogenous estrogens (serum E2 level more than 40 pg/ml) to promote progesterone receptors in the endometrium, (iii) Anatomically patent outflow tract and (iv) Endometrium is responsive.

The defect lies in production of progesterone (as when progesterone is supplemented from outside, it results in withdrawal bleeding) and since progesterone is produced mainly by corpus luteum, so, the defect is anovulation.

The main cause of Anovulation in a case of 2<sup>o</sup> amenorrhea is polycystic ovarian disease.

22. Ans. is d, i.e. Endometrium

Ref. Dutta Gynae 5<sup>th</sup>/ed p 447

Read the question carefully, it says absence of withdrawal bleeding after estrogen-progesterone challenge test.

**Estrogen-progesterone challenge test**

**Procedure:** Ethinyl estradiol (.02 mg) or conjugated equine estrogen (1.25 mg) is given daily for 25 days. MDPA 10 mg daily is added from day 15 to 25 (Alternatively estrogen is given for 21 days and progesterone is added in last 5 days).

↓ The test creates a condition similar to normal menstrual cycle

Withdrawl bleeding occurs	No withdrawl bleeding
Means endometrium and outflow tract are normal and if provided by normal hormonal levels, results in menstruation. Defect lies in production of estrogen i.e. either in ovary <sup>o</sup> / Pituitary <sup>o</sup> /Hypothalamus	<b>Means their is a defect in endometrium<sup>o</sup></b> or outflow tract <sup>o</sup> (As despite normal hormonal sequence no bleeding occurs).

23. Ans. is d, i.e. Prolactinoma

Ref. Dutta Gynae 6<sup>th</sup>/ed p 467

**This child is presenting with primary amenorrhea with:**

- Negative progesterone challenge test - which rules out PCOD (which may sometimes manifest as primary amenorrhea)
- When next step was done i.e., estrogen, progesterone combined test – It comes out to be positive i.e., compartment I system (uterus, endometrium and outflow tract) is normal if properly stimulated by estrogen which rules out mullerian agenesis and Ashermann's syndrome.
- Positive estrogen progesterone combined test means the defect is in the production of estrogen i.e., either ovaries, pituitary, or hypothalamus.

So from the given options we have to look for a cause which involves either of the above sites, which in this case is prolactinoma.

24. Ans. is a, i.e. 50 mL

Ref. Novak 14<sup>th</sup>/ed p 461; Shaw 15<sup>th</sup>/ed p 283

25. Ans. is a, i.e. 80 mL

Ref. Shaw 15<sup>th</sup>/ed p 283

26. Ans. is a and d, i.e. Menses <21 days; and DUB

Shaw 15<sup>th</sup>/ed p 283

- A normal menstrual cycle lasts from **21 – 35 days<sup>o</sup>**, with 2 – 6 days<sup>o</sup> of flow and an **average blood loss of 20 to 60 ml<sup>o</sup>**.
- Mean blood loss per cycle is 35 mL (since 35 mL is not given in option, so 50 mL is being taken as the correct answer).
- Mean duration of menses is 4.7 days.<sup>o</sup>

**Irregularities in Normal Menstrual Cycle:**

Definitions of Menstrual cycle irregularities	
<i>Oligomenorrhea</i>	Infrequent, irregularly timed episodes of bleeding occurring at intervals of more than 35 days
<i>Polymenorrhea</i>	Frequent but regularly timed episodes of bleeding occurring at intervals at intervals of 21 days or less
<i>Menorrhagia</i>	Regularly timed episodes of bleeding that are excessive in amount (>80 mL) and/or duration of flow (>5 days)
<i>Metrorrhagia</i>	Irregularly-timed bleeding
<i>Menometrorrhagia</i>	Excessive prolonged bleeding that occurs at irregularly timed, frequent intervals
<i>Hypomenorrhea</i>	Regularly timed bleeding that is decreased in amount
<i>Intermenstrual bleeding</i>	Bleeding (usually not of excessive amount) that occurs in between menstrual cycle otherwise, normal menstrual cycle.

**Note:** *Polymenorrhea, irregular ripening and irregular shedding of endometrium are forms of ovulatory DUB.*

– Dutta Gynae 6<sup>th</sup>/ed p 187

27. Ans. is a, b and c, i.e. Haemogram; Platelet count; and USG

Ref. Novak 14<sup>th</sup>/ed pp 450-454, 15<sup>th</sup>/ed pp 390-397; Dutta Gynae 6<sup>th</sup>/ed p 55

28. Ans. is a, i.e. Anovulation

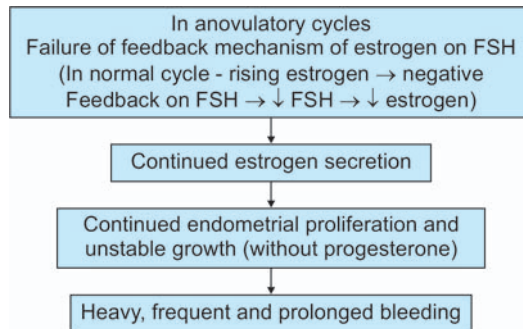
29. Ans. is a, b and c, i.e. Progesterone; Progesterone and estrogen; and GnRH analogues

Ref. Shaw 15<sup>th</sup>/ed p 302; Novak 15<sup>th</sup>/ed pp 394-397; Dutta Gynae 6<sup>th</sup>/ed p

Puberty menorrhagia is excessive cyclical regular bleeding occurring in adolescents.

Most of the adolescent females have irregular periods for a variable period following menarche due to anovulatory cycles. Anovulatory bleeding can be too frequent, prolonged or heavy particularly after a long interval of amenorrhea.

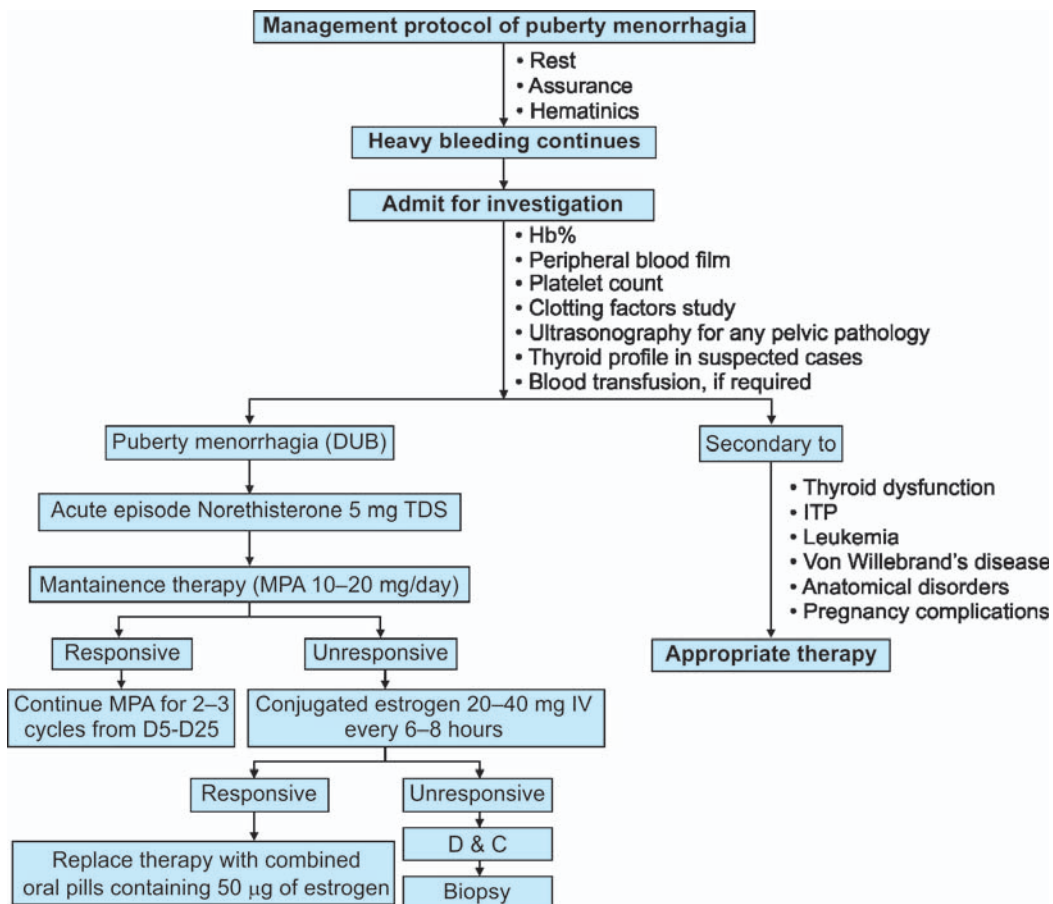
**Physiology:**



#### Causes of puberty menorrhagia-

Most common cause - anovulation

2nd most common cause is - Bleeding disorders - blood dyscrasias and coagulation disorders.



**Remember**

- In DUB- Progesterone of choice:
  - (i) For acute bleeding–Norethisterone
  - (ii) For maintenance purpose–DMPA
- In patients with von Willebrands disease - Desmopressin is the DOC
- In young sexually active females. Levonorgestrel IUCD- Mirena can also be used.

**Role of dilatation and curettage in puberty menorrhagia:** *“D & C is done only in rare cases of puberty menorrhagia - when intrauterine clots are seen on USG (as the cause of bleeding) to rule out endometrial tuberculosis.”* – Novak 15<sup>th</sup>/ed p 396

*“If a girl fails to respond to hormonal therapy curettage of endometrium is necessary to rule out genital tuberculosis which is seen in 4% of these young girls.”* – Shaw 14<sup>th</sup>/ed p 271

D & C is not a part of initial evaluation in adolescents (so, option “d” ruled out).

**Use of GnRH analogues:**

*“For adolescent patients with coagulopathies or malignancy requiring chemotherapy, long term therapeutic amenorrhea with menstrual suppression using GnRH analogues can be achieved.”* – Novak 14<sup>th</sup>/ed p 454, 15<sup>th</sup>/ed p 397

**30. Ans. is d and e, i.e. Irregular ripening of endometrium; and Irregular shedding of endometrium**

*Ref. Shaw 15<sup>th</sup>/ed pp 301-302 Table 22.2*

DUB is defined as a state of abnormal uterine bleeding without any clinically detectable organic pelvic pathology.

**DUB is of 2 types:** 1. Anovulatory (80%)  
2. Ovulatory (20%)

- Anovulatory (80%):
- Threshold bleeding of puberty menorrhagia
  - Metropathia hemorrhagica<sup>Q</sup>/cystic glandular hyperplasia<sup>Q</sup>
  - Premenopausal DUB (Atrophy of endometrium).
- Ovulatory (20%):
- Irregular ripening<sup>Q</sup> of corpus luteum
  - Irregular shedding<sup>Q</sup> of corpus luteum
  - IUCD insertion
  - Following sterilization operation.

**31. Ans. is b, i.e. Hyperplastic**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 189*

**Endometrial pattern in DUB**

- Normal secretory endometrium = 60%
- Hyperplastic endometrium = 30%
- Irregular shedding
- Irregular ripening = 10%
- Atrophic pattern

Since normal secretory endometrium is not given in options so, we will see 2<sup>nd</sup> most common which is hyperplastic endometrium.

**32. Ans. is a, i.e. Hormones**

*Ref. Dutta Gynae 5<sup>th</sup>/ed p 187; Novak 14<sup>th</sup>/ed p 465*

**In reproductive age group:** In most cases abnormal bleeding can be managed effectively by medical therapy.

- **Medical Therapy.**

**(A) Hormones**

- Norethisterone acetate
- Medroxyprogesterone acetate
- Dydrogesterone
- Equine conjugated estrogen
- Combined estrogens and progestogens (contraceptive pills)
- 19 Norsteroid derivative (Gestrinone)
- Danazol (17  $\alpha$ -ethinyl testosterone)
- Progestin releasing IUCD LNG – IUS
- Mifepristone (RU 486)
- GnRH analogues
- Desmopressin

**(B) Prostaglandin synthetase inhibitors (PSI)**

- Fenamates (Mefenamic acid)

**(C) Antifibrinolytic agents**

- Tranexamic acid (TA)

- **Surgical therapy:**

- It is reserved for situations in which medical therapy has been unsuccessful or is contraindicated.
- Surgical treatment depends on the cause of bleeding.



**33. Ans. is a and d, i.e. Progesterones; and Endometrial ablation**Ref. Novak 15<sup>th</sup>/ed p788; Williams Gynae 1<sup>st</sup>/ed p187

Now in this question, patient is 32 years old and is multiparous- so LNG- IUCD will be best option for her i.e option a-progesterones is correct.

Since, it is a multiple choice question so here we can also mark endometrial ablation as correct option, because she is multiparous and if she doesnot require future pregnancy -we can do endometrial ablation.

*"Heavy menstrual bleeding that doesnot respond to oral medication may be managed by endometrial ablation using coagulation, resection or vaporization provided that patient is willing to forgo future fertility. Alternatively, if future fertility is desired, a levonorgestrel releasing intrauterine device can provide virtually equal clinical outcome."*  
– Novak 15<sup>th</sup>/ed p788

**As far as other options are concerned-**

Danazol-it should not be used in young females, as it leads to androgenic side effects

Hysterectomy-it should not be done at 32 years unless and until absolutely indicated.

Prostaglandins-are not used for managing DUB, rather prostaglandin synthetase inhibitors are used.

**34. Ans. is b and c, i.e. Endometriosis; and Fibroid**Ref. Read Below, Shaw 15<sup>th</sup>/ed pp 302-303

Well friends, here we will have to weigh each option one by one.

**Option "a": DUB**– Shaw 14<sup>th</sup>/ed pp 271-272

- Metropathia hemorrhagica is seen in age group of 40 – 45 years which coincides with the age of the patient given in the question.
- But in DUB (as 80% cases are due to anovulatory bleeding) pain is characteristically absent. Bleeding is always painless and acyclical and continues for 2 – 8 days. In about half the cases, it is preceded by a short period of amenorrhea (metropathia hemorrhagica).

So, option "a" is ruled out.

**Option "b": Endometriosis**

- Dysmenorrhea (secondary and progressive in nature) and menstrual irregularities including menorrhagia are specifically seen in endometriosis.
- As far as age is concerned.

– Shaw 15<sup>th</sup>/ed pp 468-469

*"Active endometriosis is seen most commonly between the ages of 30 and 40 years. It can however occur at any time between the menarche and the menopause, even before the age of 20 years."*

– Jeffcoate 7<sup>th</sup>/ed p 368

So, endometriosis is one of the possible differential diagnosis.

**Option "c": Fibroid**

- Age group: Seen in women of child bearing age group. Seen in 40% of women above the age of 40 years.
- Fibroids most commonly cause symptoms between the ages of 35 and 45 years. (So age is consistent with the patients age).
- Fibroid uterus causes menorrhagia and dysmenorrhea. So, the possibility of fibroid is high.

– Shaw 15<sup>th</sup>/ed p 357**Option "d": Endometrial carcinoma**

- It is not a case of endometrial Ca because, endometrial Ca is common in 55 – 60 years.
- Patient presents with irregular and heavy cycles.
- The lower abdominal pain in advanced stage is due to parametrial involvement. (Not dysmenorrhea)

– Shaw 15<sup>th</sup>/ed p 416– Shaw 15<sup>th</sup>/ed p 418; Jeffcoate 7<sup>th</sup>/ed p 508**35. Ans. is a, i.e. Carcinoma in situ of cervix****36. Ans. is b, i.e. CIN**Ref. Novak 14<sup>th</sup>/ed p 490; CGDT 10<sup>th</sup>/ed pp 577-578; Jeffcoate 7<sup>th</sup>/ed p 614

Postmenopausal bleeding is defined as bleeding which occurs after 12 months amenorrhea in a middle aged women.

**Causes of Post Menopausal Bleeding:**

<ul style="list-style-type: none"> <li>• Exogenous estrogen (HRT)</li> <li>• Vaginitis - tubercular, candida, chlamydia, senile</li> <li>• Endometrial hyperplasia</li> <li>• Cervical cancer</li> <li>• Uterine sarcoma</li> <li>• DUB - ovulatory/anovulatory ulcer/Foreign body</li> <li>• Bleeding from urethra, bladder, rectum which is mistaken for vaginal bleeding.</li> </ul>	<ul style="list-style-type: none"> <li>• Endometritis - tubercular, senile pyometra &amp; hematometra</li> <li>• Endometrial/cervical polyp</li> <li>• Endometrial cancer (correct option)</li> <li>• Ovarian cancer (correct option)</li> <li>• Fallopian tube carcinoma</li> <li>• Injuries - direct trauma / Decubitus</li> </ul>
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As far as Fallopian tube carcinoma is concerned. Most common age group = 50 – 60 years.

**Most common symptom:** Watery discharge which tracks from the tube through the uterus and vagina (hydrops tubal profluens).It is typically colourless, profuse in amount and escapes continuously or in gushes. The discharge ultimately becomes blood stained from ulceration of growth and female presents as *post menopausal bleeding*. (correct option).

Cervical cancer is a cause of postmenopausal bleeding, but cervical carcinoma in situ which is seen at 25 – 35 years of age and CIN which is seen in women in their 20's is not a cause of post menopausal bleeding.

**Remember:**

"CIN is most commonly detected in women in their 20's, peak incidence of carcinoma in situ is in women aged 25 – 35, while incidence of cervical cancer rises after the age of 40."

– CGDT 10<sup>th</sup>/ed p 833

37. Ans. is a, c and d, i.e. Assess for H/o HRT; PAP smear; and Endometrial biopsy

38. Ans. is a, b, c and d, i.e. Pap smear; USG; Endometrial biopsy; and Dilatation & curettage

Ref. CGDT 10<sup>th</sup>/ed pp 577-578; Novak 15<sup>th</sup>/ed p 427, 1256

- Postmenopausal bleeding is more likely to be caused by pathological disease than is bleeding in younger women and must always be investigated.
  - i. Most common cause of postmenopausal bleeding is – **Endometrial and vaginal atrophy**  
They can be diagnosed by clinical examination.  
*In vaginal atrophy* – examination reveals thin tissue with echymosis.  
*In vulvar dystrophy* – white area and cracking of skin of vulva may be present  
*Investigation to be done in these cases is* – cytological study of material obtained from the cervix and vagina, which reveal immature epithelial cells with or without inflammation (i.e. Pap smear is correct option).
  - ii. Another cause of postmenopausal bleeding is – **the use of exogenous hormones** i.e. HRT (hormone replacement therapy) – so careful history about the use HRT becomes vital (i.e. option a is correct).
  - iii. Third important cause is **tumors of the reproductive tract**.

**Tumors of the reproductive tract causing postmenopausal bleeding:**

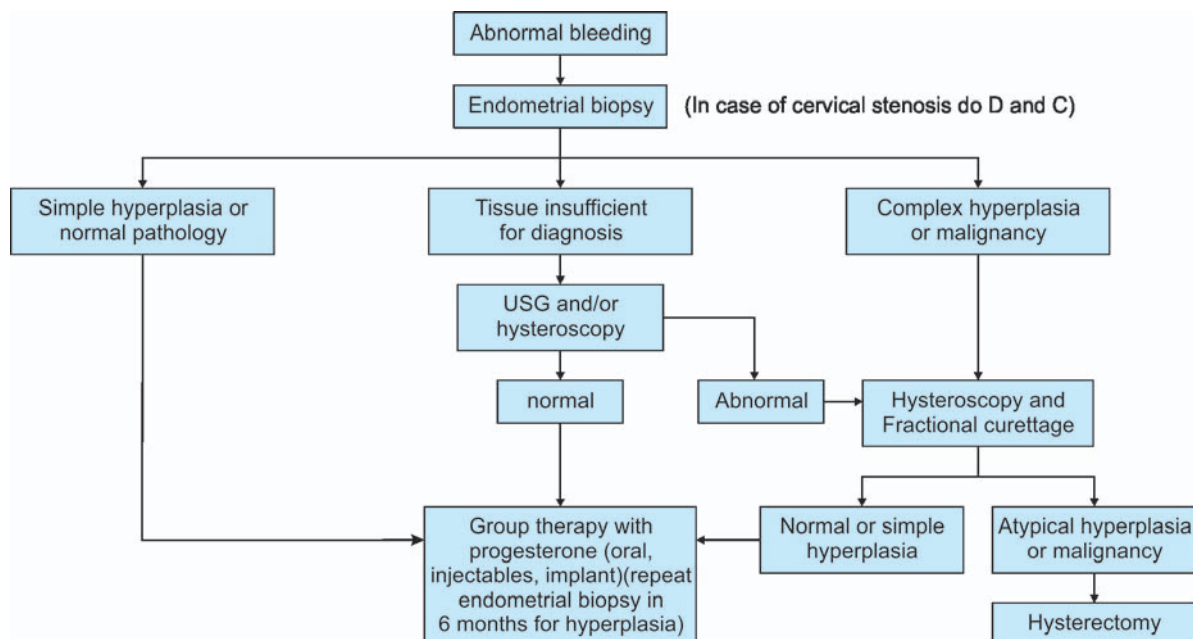
- Endometrial hyperplasia
- Endometrial polyps
- Endometrial cancer (M/C cancer causing postmenopausal bleeding world wide)
- Cervical cancer (M/C cancer causing postmenopausal bleeding in India)
- Uterine sarcoma
- Fallopian tube carcinoma
- Ovarian CA – especially estrogen secreting tumor

The investigations done to rule them out are:

- Pap smear
- Transvaginal sonography
- **Hysteroscopy** and biopsy
- Endometrial aspiration/biopsy
- Dilatation and curettage

**As far as hysterectomy is concerned:**

The patient is presenting with a single episode of bleeding which does not warrant hysterectomy. A diagnosis should be established before going for hysterectomy.

**Extra Edge: Management of Postmenopausal abnormal bleeding:**

## 39. Ans. is a, i.e. Imperforate hymen

Ref. Dutta Gynae 6<sup>th</sup>/ed p 450; Shaw 15<sup>th</sup>/ed pp 96-97

- Cryptomenorrhea is defined as occurrence of menstrual symptoms without external bleeding. Menstrual blood fails to come out from genital tract due to obstruction in the outflow passage.
- Causes:

Congenital	Acquired
Imperforate hymen (commonest) Transverse vaginal septum Atresia of upper third vagina & cervix	Cervical stenosis following: <ul style="list-style-type: none"> <li>• Amputation</li> <li>• Cauterization</li> <li>• Conization</li> <li>• 'Radium' treatment for malignant conditions</li> </ul>

## 40. Ans. is c, i.e. Sheehan's syndrome

Ref. Williams Gynae 1<sup>st</sup>/ed p 374; Leon Speroff 7<sup>th</sup>/ed p 438; Jeffcoate 7<sup>th</sup>/ed pp 582-583

Friends, here before arriving to any diagnosis lets first see the causes of:

**Empty Sella:**

- Congenital incompleteness of the sellar diaphragm.
- Secondary to surgery/radiotherapy or infarction of pituitary tumor.
- Secondary to infarction and necrosis of pituitary gland.

Now from the given causes: either pituitary tumor or Sheehan's syndrome can cause an empty sella on X-ray.

Pituitary tumours (micro/macroadenoma) are prolactin secreting tumors and hence, cause galactorrhea (not lactational failure) with amenorrhea and are so, ruled out.

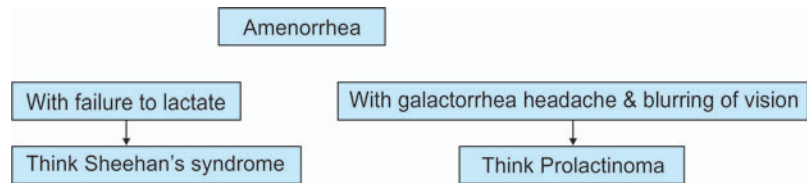
So, the obvious answer by exclusion is Sheehan's Syndrome.

**Sheehan's syndrome:**

- It is the syndrome which results from ischemic necrosis of most of the anterior pituitary<sup>Q</sup> due to spasm in its arterioles occurring at the time of severe hemorrhage or shock, complicating childbirth.

**Clinical Features: Symptoms<sup>Q</sup>**

- Failure of lactation after delivery<sup>Q</sup>
- Secondary amenorrhea<sup>Q</sup>
- Loss of libido<sup>Q</sup>
- Increased sensitivity to cold (hypothyroidism)<sup>Q</sup>

**Always Remember:**

## 41. Ans. is a, i.e. Pituitary adenoma

Ref. Novak 14<sup>th</sup>/ed pp 1104,1109; Harrison 17<sup>th</sup>/ed pp 2205-2206; Williams Gynae 1<sup>st</sup>/ed p 338 onwards

Patient is presenting with amenorrhea; galactorrhea with raised prolactin levels. So lets rule out some of the options:

**Sheehan's Syndrome**

- In Sheehan's syndrome there is failure of lactation (due to ischemic necrosis of anterior pituitary) and not galactorrhea (so, option "c" ruled out).

**Pinealoma:**

- If you go through the list of causes of hyperprolactinemia given in Harrison 17<sup>th</sup>/ed p 2205; Table 333-8 - Pinealoma is not one of the causes. (as there is no reason for a pineal gland tumor to raise prolactin levels), ruling out option "d".

**That leaves us with 2 options:**

**Pituitary adenoma and craniopharyngioma:** Both are pituitary tumors which can present with amenorrhea galactorrhea, and raised prolactin levels.

Now comes the age factor - Craniopharyngiomas present usually before 20 years (Harrison 17<sup>th</sup>/ed p 2201) of age and so by exclusion: **Option "a"** i.e. Pituitary adenoma seems more likely as the cause.

*"In patients with both galactorrhea and amenorrhea approximately two-thirds will have hyperprolactinemia, in that group approximately one third will have a pituitary adenoma."*

— Novak 14<sup>th</sup>/ed p 1104

So, pituitary adenoma is more common than craniopharyngioma and this confirms our answer.

## 42. Ans. is a, i.e. Prolactin levels

Ref. Harrison 17<sup>th</sup>/ed p 2205; Williams Gynae 1<sup>st</sup>/ed pp 338-340

A woman presenting with headache, blurred vision and galactorrhea, raises the suspicion of a pituitary prolactinoma and so, appropriate investigations would be:

- S. prolactin (most important)<sup>Q</sup>
- TSH (as patients with hypothyroidism have elevated TRH which acts to stimulate the release of prolactin)
- X Ray skull<sup>Q</sup> (shows space occupying lesion)
- MRI<sup>Q</sup>
- Contrast enhanced CT.<sup>Q</sup>

43. **Ans. is b, i.e. S. prolactin**

A middle aged female is presenting with:

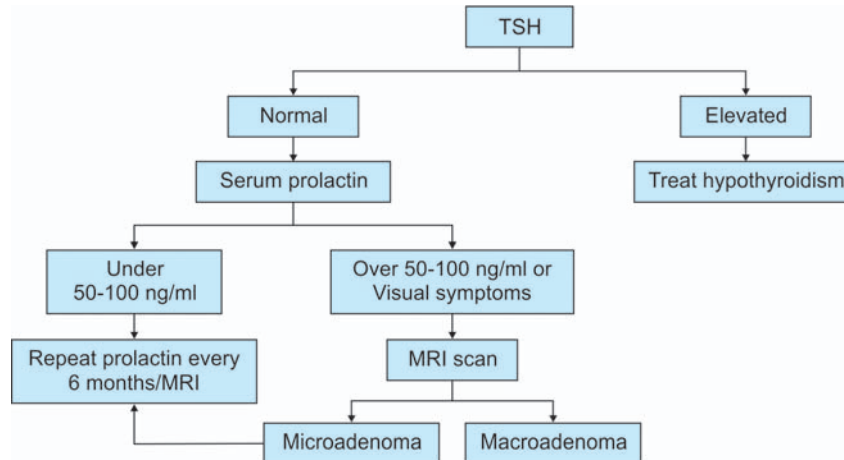
- Increasing visual loss<sup>Q</sup>
- Breast enlargement<sup>Q</sup>
- Irregular menses<sup>Q</sup>

All these features can be explained by pituitary adenoma.

- Most common type of pituitary adenomas are prolactinomas.
- Prolactinoma can be diagnosed by raised serum prolactin levels so, the investigation of choice here is serum prolactin level.

**Also know:** Work up of patient with ammenorrhea, galactorrhea, and hyperprolactinemia

Ref. Harrison 16<sup>th</sup>/ed p 2086

44. **Ans. is d, i.e. Testicular feminizing syndrome**

The patient is presenting with primary amenorrhea along with well developed breast and scanty pubic hair and axillary hair -leave no doubt regarding Testicular feminizing syndrome as the diagnosis. For details see chapter-sexuality and intersexuality of the guide.

Ref. Novak 14<sup>th</sup>/ed pp 1037-1038

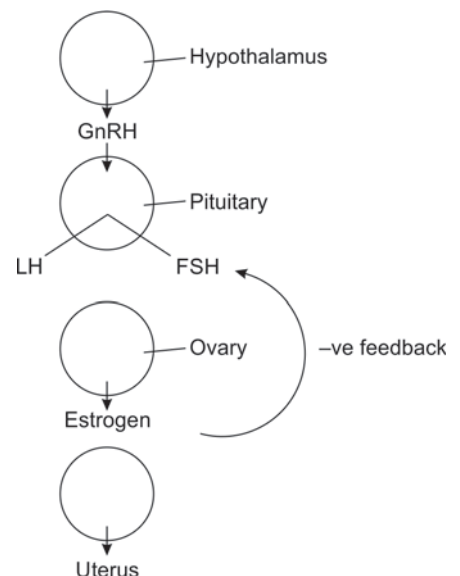
45. **Ans. is b, i.e. Uterine Synechia**

Ref. Leon speroff 7<sup>th</sup>/ed pp 415-425, 8<sup>th</sup>/ed p 443 for FSH significance and 459 for asherman syndrome

**Explanation:**

Normal FSH values range from 5 to 20 mIU/mL. In the question, FSH levels are 6 mIU/mL, that means this is a case of secondary amenorrhea with normal FSH values.

- In case of pituitary failure – as is evident from the flow diagram → values of FSH should be lower than the normal values. So **Option 'd'** is ruled out
- In case of ovarian failure → estrogen is deficient so negative feedback on FSH will be absent, thus values of FSH will be more than normal. In case of ovarian failure/menopause, FSH is above 40 m IU/mL so **option a** is also ruled out.
- Normal FSH and amenorrhea point towards uterine pathology. The patient had a spontaneous abortion following which a curettage is generally required which would be responsible for intrauterine synechia (Asherman's Syndrome). Thus, the most probable diagnosis is uterine synechia.

**Remember**

Hyperprolactinemia leads to decreased levels of FSH.

46. **Ans. is a, i.e. Prolactin induced inhibition of GnRH**

Ref. Leon Speroff 7<sup>th</sup>/ed p 582; John hopkins manual of obs and gynae 4<sup>th</sup>/ed p 472

- In breastfeeding females, prolactin levels are increased in response to suckling stimulus of breast feeding.
- Besides Prolactin, FSH concentrations are normal and LH concentrations are low.

- Despite the presence of gonadotropin the ovary during lactational hyperprolactinemia does not display follicular development and does not secrete estrogen.
- These observations suggest that high concentrations of prolactin can work at both central level (by inhibiting pulsatile secretion of GnRH) and peripheral level i.e. ovarian sites (by inhibiting synthesis of progesterone and by changing testosterone/dihydrotestosterone ratio i.e. increasing local antiestrogen concentrations) to produce lactational amenorrhoea and anovulation.
- The principle of GnRH suppression by prolactin is reinforced by the demonstration that, treatment of amenorrhoeic, lactating women with pulsatile GnRH, fully restores pituitary secretion and normal ovarian cyclic activity.

47. **Ans. is b, i.e. Stein-Leventhal syndrome**

Ref. Shaw 15<sup>th</sup>/ed pp 284-285

The **Stein-Leventhal Syndrome** also known as **Polycystic Ovarian Disease (PCOD)** is an important cause of Secondary Amenorrhoea in young women.

Testicular Feminizing syndrome, Turners syndrome and Mayer Rokitansky Kuster Hauser syndrome are causes of Primary amenorrhoea.

48. **Ans. is a, i.e. Endometrial tuberculosis**

Ref. Read below

In a country like India where most of the population belongs to middle, lower middle, and lower class: Endometrial tuberculosis seems to be the most common cause of secondary amenorrhoea.

49. **Ans. is d, i.e. Ethamsylate**

Ref. Williams Gynae 1<sup>st</sup>/ed p 187

50. **Ans. is b, i.e. Clomiphene**

Ref. Dewhurst's textbook of Obs. & Gynae. 7<sup>th</sup>/ed p 401; Gyanaecology by Soutter – Stanton 2<sup>nd</sup>/ed p 435; Shaw 12<sup>th</sup>/ed p 242

**Medical Management of Menorrhagia:**

A. Prostaglandin synthetase inhibitor	B. Antifibrinolytic	C. Hormones
<ul style="list-style-type: none"> <li>• Mefenamic Acid</li> </ul>	<ul style="list-style-type: none"> <li>• Tranexamic acid</li> </ul>	<ul style="list-style-type: none"> <li>• Progesterones</li> <li>• Estrogen</li> <li>• OCP's</li> <li>• Danazol/Gestrinone (androgen)</li> <li>• GNRH analogues</li> </ul>

**NSAID's**

- **Rationale:** Its use stems from the suspected role of prostaglandins in the pathogenesis of DUB.
- **Advantages:**
  - It is required only during menstruation
  - It provides relief from dysmenorrhoea
- **Tranexamic acid:** It is an antifibrinolytic drug which exerts its effects by reversibly blocking lysine binding sites on plasminogen. The resulting decreased plasmin levels diminish fibrinolytic activity within endometrial vessels to prevent bleeding.

*"Clinically, the drug has been shown effective to reduce bleeding in upto half of the women with DUB related to menorrhagia."*

– Williams Gynae 1<sup>st</sup>/ed p 187

According to latest RCOG guidelines tranexamic acid is the first line DOC for menorrhagia

**Progesterone's**

*"With the introduction of potent orally active progestins, they have become the mainstay in the management of DUB in all age groups and practically replaced the isolated use of oestrogens and androgens."*

– Dutta Gynae 5<sup>th</sup>/ed p 187

**Estrogen:** High dose estrogen therapy may be useful in controlling acute bleeding episodes because it promotes rapid endometrial growth to cover denuded surface. Conjugated equine estrogens are administered orally at dosages up to 10mg daily given in four divided doses. Similarly the drug can be given intravenously in 25 mg doses every 4 hours for up to 3 doses. Once bleeding has slowed, patients can be transitioned to an oral taper using COCs.

**Androgens – Danazol** – It is suitable for recurrent symptoms and in patients waiting for hysterectomy. A smaller dose tends to minimize the blood loss and higher dose produces amenorrhoea.

**Gestrinone** – can also be used like Danazol.

**Mifepristone** – It is an antiprogestone. It inhibits ovulation and induces amenorrhoea but is not commonly used for DUB (this drug is not mentioned in Williams Gynae for management of DUB)

**Gonadotropin Releasing hormone agonists (GnRH agonist)** – Its subtherapeutic doses decrease the blood loss whereas therapeutic doses produce amenorrhoea.

It is valuable for short term use in severe DUB, particularly if the woman is infertile and wants pregnancy.

- As far as ethamsylate is concerned:
  - It is a hemostatic agent but its action and efficacy is inconsistent.
  - Though in some books it is given ethamsylate may be used but Williams Gynae. specifically says:
 

*"Because of its inconsistent efficacy, in United States ethamsylate does not have a clinical role in the treatment of menorrhagia."*

– Williams Gynae 1<sup>st</sup>/ed p 187

## 51. Ans. is all.

Any uterine bleeding outside the normal volume, duration, regularity or frequency is considered **abnormal uterine bleeding (AUB)**. Nearly 30% of all gynecological outpatient attendants are for AUB.

Normal Menstruation	
Cycle interval	28 days (21–35 days)
Menstrual flow	4–5 days
Menstrual blood loss	35 mL (20–80 mL)

Abnormal menstrual bleeding pattern have been traditionally expressed by terms like menorrhagia, metrorrhagia, polymenorrhea, and oligomenorrhea. In order to create an universally accepted nomenclature to describe abnormal uterine bleeding, International Federation of Gynecology and Obstetrics (FIGO) and American College of Obstetricians and Gynaecologists (ACOG) introduced newer system of terminology to describe AUB. The newer classification system is known by the acronym PALM-COEIN (FIGO-2011). It is used to classify the abnormal uterine bleeding on the basis of etiology. Polyp, adenomyosis, leiomyoma, malignancy and coagulopathy, hyperplasia, ovulatory dysfunction, endometrial, iatrogenic, and not yet classified are the different etiological factors expressed by one (or more) letters.

The term dysfunctional uterine bleeding (DUB), discussed above is a type of AUB, whereas no systemic or locally identifiable structural cause is found.

Etiopathology of AUB

The common causes of abnormal uterine bleeding with the PALM-COEIN classification are shown below. The letter within the parenthesis indicate the pathology.

Classification of AUB (FIGO-2011)			
Structural causes (PALM)		Nonstructural systemic causes (COEIN)	
• Polyp	AUB-P	Coagulopathy	AUB - C
• Adenomyosis	AUB-A	Ovulatory dysfunction	AUB - O
• Leiomyoma	AUB-L	Endometrial	AUB - E
– Submucosal myoma	AUB-L SM	Iatrogenic	AUB - I
– Other myoma	AUB-LO		
• Malignancy and hyperplasia	AUB-M	Not yet identified	AUB - N

## 52. Ans. is d, i.e. Intramural fibroid

Ref. Dutta Gynae 6<sup>th</sup>/ed p 186

**Metrorrhagia:** It is defined as irregular, acyclical bleeding from uterus, amount of bleeding is variable. Metrorrhagia also includes irregular bleeding in the form of contact bleeding or intermenstrual bleeding.

**Menometrorrhagia:** When the bleeding is so irregular and excessive that the menstruation cannot be identified.

<b>Causes of Acyclical bleeding</b>	<ul style="list-style-type: none"> <li>• DUB - usually during adolescence, following childbirth and abortion and preceding menopause<sup>o</sup></li> <li>• <b>Submucous fibroid</b><sup>o</sup></li> <li>• <b>Uterine polyp</b><sup>o</sup></li> <li>• Carcinoma cervix and <b>endometrial carcinoma</b>.<sup>o</sup></li> </ul>
<b>Causes of Contact bleeding</b>	<ul style="list-style-type: none"> <li>• Carcinoma cervix<sup>o</sup></li> <li>• Mucous polyp of cervix<sup>o</sup></li> <li>• Vascular ectopy of cervix specially during pregnancy, pill use<sup>o</sup></li> <li>• Infection: chlamydial, tubercular<sup>o</sup></li> <li>• Cervical endometriosis<sup>o</sup></li> </ul>
<b>Causes of Intermenstrual bleeding</b>	<ul style="list-style-type: none"> <li>• Urethral caruncle<sup>o</sup></li> <li>• Ovular bleeding<sup>o</sup></li> <li>• Breakthrough bleeding in pill users<sup>o</sup></li> <li>• <b>IUCD in utero</b><sup>o</sup></li> <li>• Decubitus ulcer<sup>o</sup></li> </ul>

**Remember:** Metrorrhagia is seen in submucous myomas when they become polypoidal and ulcerated, otherwise all fibroids cause menorrhagia.

## 53. Ans. is a, i.e. Increased estrogen

Ref. Shaw 15<sup>th</sup>/ed p 301

DUB is mainly anovulatory-

Bleeding occurs due to the hypertrophy and hyperplasia of the endometrium induced by a high titer of estrogen in the circulating blood.

This is the reason why initially due to lack of progesterone patients complain of amenorrhea and later on, due to excessive estrogen they complain of excessive bleeding.

54. **Ans. is a, i.e. Persistent corpus luteum** Ref. Shaw 15<sup>th</sup>/ed p 307; Jeffcoate 7<sup>th</sup>/ed p 604; Dutta Gynae 6<sup>th</sup>/ed p 178, 5<sup>th</sup>/ed p 184  
**Halban's disease:**

- Rare, self-limiting process.
- Also called irregular shedding.
- It is due to persistent corpus luteum<sup>o</sup> due to incomplete withdrawal of LH even on 26 in day of cycle. The CL continues to secrete progesterone
- Menstruation comes on time, is prolonged but not heavy. Slight bleeding continues intermittently for several days after proper flow.
- **On D & C done on 5-6th of cycle** – endometrial tissue shows presence of progestational changes (proliferative endometrium) along with secretory endometrium. Pregnandiol is found in urine during menstruation.
- **Treatment** – spontaneous cure or NSAIDs for 6 months.

Also know-Irregular ripening of corpus luteum-

- It is due to poor formation and function of corpus luteum.<sup>o</sup>
- The endometrium is without adequate hormonal support, so slight losses or spotting occur for many days before the proper flow starts.

**Diagnosis:**

- Serum progesterone <5 ng/mL (or urinary pregnandiol <3 mg) in luteal phase.
- Endometrial study prior to or soon after spotting reveals patchy areas of secretory changes amidst proliferative endometrium.

**Management:** Administration of progestogens in premenstrual phase.

55. **Ans. is b, i.e. Progesterone** Ref. Dutta Gynae 5<sup>th</sup>/ed pp 184,187, 6<sup>th</sup>/ed p  
As discussed in the preceding text **metropathica hemorrhagica** is a type of anovulatory DUB, hence logically speaking it should be best treated by progesterone therapy.

It is mostly seen in premenopausal women.

Patients complain of a variable period of amenorrhea followed by excessive painless bleeding.

On HPE-cystic glandular hyperplasia, Swiss cheese pattern is seen, and secretory changes are absent

**Treatment:**

- In DUB due to anovular causes: Progesterones are the mainstay of therapy.
- They diminish the effects of estrogen on target cells by inhibiting oestrogen receptors.

56. **Ans. is c, i.e. Nose** Ref. Jeffcoate 7<sup>th</sup>/ed p 634  
Vicarious menstruation is a rare condition in which extragenital bleeding occurs at regular intervals corresponding to menstrual period. The commonest form of vicarious bleeding is epistaxis and this is a feature in 30% cases. Other sites affected are alimentary tract, lungs, breast, gums, lips, kidney, rectum, retina and conjunctiva.

It occurs most often at the extremes of menstrual life and in individuals with nervous and vascular instability. It ceases with menopause.

The epithelium over the inferior turbinate bones is already influenced by estrogen and so epistaxis is most common form of vicarious menstruation.

57. **Ans. is a, i.e. Normal** Ref: Dutta Gynae 6<sup>th</sup>/ed p 189  
Already explained, see Ans 31 for explanation

58. **Ans. is b, i.e. Dysfunctional uterine bleeding** Ref. Dutta Gynae 6<sup>th</sup>/ed p 185



**Common causes of menorrhagia:**

- Dysfunctional uterine bleeding
- Fibroid uterus
- Adenomyosis
- Chronic tubo-ovarian mass

59. **Ans. is d, i.e. Chromosomal abnormality** Ref. Leon Speroff 7<sup>th</sup>/ed p 420; Shaw 15<sup>th</sup>/ed p 284  
As discussed earlier:  
M/C cause of primary amenorrhea is Turners syndrome (ovarian dysgenesis)

60. **Ans. is d, i.e. Postmenopausal period (read below)**

Now this one needs only common sense to answer.

Bleeding which occurs in a postmenopausal woman is called as postmenopausal bleeding and not DUB.

61. **Ans. is d, i.e. Defect in pituitary gonadal axis** Ref. Dutta Gynae 6<sup>th</sup>/ed p 467; Leon Speroff 7<sup>th</sup>/ed p 404-409  
As discussed earlier withdrawal bleeding following administration of progesterone suggests:

- The uterus is sufficiently primed with estrogen, i.e. production of endogenous estrogen is normal which means. Ovaries and hypothalamic pituitary axis are functioning normally.
- The outflow tract (uterus) is normal and endometrium is responsive to estrogen.
- There is a defect in production of progesterone (so pregnancy ruled out).

**62. Ans. is c, i.e. May be associated with premenstrual syndrome**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 182*

PMS is associated with ovulatory menstrual cycle. Rest all features are of anovulatory cycle.

**63. Ans. is d, i.e. Estradiol levels**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 55*

**Explanation**

Important causes of puberty menorrhagia are:

- HPO axis immaturity (anovulation)
- Bleeding disorders
- Endocrinological causes

Hence TSH, platelet count and BT/CT are done. Estradiol levels are of no utility in the workup of this patient.

*Note:* Always rule out bleeding disorder in patients of puberty menorrhagia.

**64. Ans. is c, i.e. Metropathia hemorrhagica**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 188-189*

Discussed in detail in preceding text

**65. Ans. is b, i.e. Fractional curettage**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 560*

**Explanation:**

Postmenopausal bleeding most commonly occurs due to atrophic changes but can also occur due to Ca endometrium or Ca cervix.

Hence, in case of postmenopausal bleeding, ruling out both endometrial and cervical cancer is always a priority.

Hence, fractional curettage is the right answer. TVS can detect uterine pathology, but histopathological diagnosis is a must in such cases. Pap is positive only in 30-50% of Ca endometrium and so not useful. TVS and CA-125 are screening methods for ovarian CA and hence not applicable here.



# CHAPTER

# 14A

## Gynecological Oncology: Uterine Cancer

### Endometrial Hyperplasia

It represents a spectrum of morphological and biological alteration of endometrium (both in glands<sup>o</sup> and stroma<sup>o</sup>), ranging from an exaggerated physiological state to carcinoma in situ.

They are clinically important because:

- They cause abnormal bleeding.<sup>o</sup>
- Either precede or occur simultaneously with endometrial carcinoma.

### Types of Endometrial Hyperplasia

Simple	Complex
<ul style="list-style-type: none"> <li>• It results from circumstance in which there is prolonged, increased oestrogen production:                             <ol style="list-style-type: none"> <li>i. Follicular cysts of ovary<sup>o</sup></li> <li>ii. PCOD<sup>o</sup></li> <li>iii. Granulosa and Theca cell tumours of ovary<sup>o</sup></li> <li>iv. HRT<sup>o</sup></li> </ol>                             In perimenopausal age they are associated with glucose intolerance.<sup>o</sup> </li> </ul> <p><b>Pathology</b></p> <ul style="list-style-type: none"> <li>• Glands are large, cystic with increased glands/stromal ratio<sup>o</sup></li> <li>• Scanty mitosis<sup>o</sup></li> <li>• Glands lined by columnar<sup>o</sup> epithelium</li> <li>• Stroma is sparsely cellular</li> </ul>	<ul style="list-style-type: none"> <li>• Less obviously connected with increased estrogen</li> <li>• Mostly, cause is unknown</li> <li>• Can be associated with:                             <ul style="list-style-type: none"> <li>– PCOD<sup>o</sup></li> <li>– Glucose Intolerance<sup>o</sup></li> </ul> </li> </ul> <p><b>Pathology</b></p> <ul style="list-style-type: none"> <li>• Glands number is increased, size is increased and Glands are thrown into folds (over crowding of glands)</li> <li>• Numerous mitosis<sup>o</sup></li> <li>• Glands are lined by stratified squamous epithelium<sup>o</sup></li> <li>• Stroma is densely cellular<sup>o</sup></li> </ul>

### Chances of Progression to Carcinoma

Type of hyperplasia	Progression to cancer
• Simple without atypia	1% <sup>o</sup>
• Complex without atypia	3% <sup>o</sup>
• Simple with atypia	8% <sup>o</sup>
• Complex with atypia	29–30% <sup>o</sup>

### Management of Endometrial Hyperplasia

Depends on the patient's age and the presence or absence of cytological atypia.

### Non Atypical Hyperplasia

Since the chances of malignancy in this category are less (1% for simple hyperplasia and 3% for complex), hence they are managed medically:



The four main types of endometrial hyperplasia are:

1. Simple hyperplasia without atypical cells.
2. Complex hyperplasia without atypical cells
3. Simple hyperplasia with atypical cells
4. Complex hyperplasia with atypical cells



Characteristics of Atypical cells

- Large in size<sup>o</sup>
- Loss of polarity<sup>o</sup>
- Irregular shape<sup>o</sup>
- Hyperchromatic nucleus<sup>o</sup> and prominent nucleoli<sup>o</sup>
- Altered nucleus cytoplasmic ratio.<sup>o</sup>



Minimum chances of progression to carcinoma are with simple hyperplasia without atypia (also called as cystic glandular hyperplasia) and maximum chances of carcinoma are with complex hyperplasia with atypia.<sup>9</sup>

- **Premenopausal women:** Progesterone therapy-  
Options:
  - Medroxyprogesterone acetate for 21 days a month daily for 3 months.
  - Progesterone containing IUCD.
- **Post menopausal women:**  
Simple hyperplasia without atypia—generally followed without therapy.  
Complex hyperplasia without atypia—cyclical/continuous progesterone therapy.  
These patients should be followed annually by endometrial biopsy.

### Atypical Hyperplasia

In this category chances of malignancy are high (simple-8%, complex-30%, hence they are managed surgically).

- **Ideal treatment is—Hysterectomy**
- **Premenopausal women willing to preserve fertility:** High dose progesterone therapy after full information of risk of a undiagnosed cancer or progression to cancer. In these cases periodic TVS and endometrial biopsy is necessary.

## Endometrial Carcinoma

### Epidemiology

- Most common gynecological malignancy in developed countries and the 4th most common cancer in women
- 20% of women develop endometrial carcinoma in lifetime
- Mean age of presentation is 60 years: peak incidence occurs from 55 to 70 years
- Majority are diagnosed early
- 5 year survival for stage I disease is more than 90%
- Overall 5 year survival for all stages is 60-70%

### Risk Factor

Endometrial cancer occurs as a result of unopposed estrogen exposure in body.

#### Mnemonic-Family Has OLD AUNTIS

<b>F</b>	Family history
<b>H</b>	Hypertension
<b>O</b>	Obesity
<b>L</b>	Late menopause/Early menarche
<b>D</b>	Diabetes
<b>A</b>	Atypical endometrial hyperplasia
<b>U</b>	Unopposed estrogen or increased estrogen in body as in : HRT, Fibroid, PCOD and Feminizing ovarian tumours
<b>N</b>	Nulliparity
<b>T</b>	Therapy: Tamoxifen Therapy and Radiation Therapy
<b>I</b>	H/O infertility/menstrual irregularity
<b>S</b>	Senile endometritis/Pyometra

Approximately 5% of endometrial cancer is hereditary, with majority of these presenting as a part of the **Lynch II or Hereditary Non Polyposis Colorectal Cancer (HNPCC) syndrome**. Besides endometrial cancer, individuals in this family are at increased risk of colorectal cancer, ovarian, urinary, biliary, gastric and small intestinal cancer. Abnormal bleeding at any age should be evaluated by tissue



Remember: Most common gynaecological cancer in developed countries is endometrial cancer.

- Most common gynaecological cancer in developing countries like India is cervical cancer.
- M/C Female genital tract worldwide—Ca cervix



- Estrogen replacement without concomitant progesterone carries a relative risk of 4.5 to 8 & persists for 10 years after treatment is stopped.
- BMI > 30 kg/m<sup>2</sup> will triple the risk of endometrial cancer
- A woman taking Tamoxifen has an annual risk of 2 in 1000 of developing endometrial cancer and 40% of women will develop cancer more than 12 months after stopping therapy
- Women with HNPCC syndrome have 39% risk of developing endometrial cancer by the age of 70 years.
- OCP's decrease endometrial cancer risk by 40%, even upto 15 years after discontinuation and the protection increases with the length of use.

biopsy in women of HNPCC families. Routine surveillance may consist of yearly USG and endometrial biopsy commencing at the age of 30–35.

### Protective Factors

- Oral contraceptive pills (combined pills with addition of progesterone to HRT).
- Smoking (as it decreases levels of estrogen, decreases weight and is associated with earlier age of menopause).
- Multiparity
- Phytoestrogens
- Green tea
- Coffee
- Physical exercise

### Classification

- Adenocarcinoma/endometrioid (most common 80%). **Note:** Uterus is lined by columnar epithelium hence logically speaking also, the most common to occur in uterus is adenocarcinoma.
- Adenosquamous carcinoma (15%) or adenocarcinoma with squamous differentiation.
- Papillary serous adenocarcinoma
- Mucinous adenocarcinoma
- Clear cell carcinoma

### Histological Differences in Endometrial Cancer

On the basis of histology endometrial cancer can be classified into two main types:

Features	Type I (Endometrioid) (80%)	Type II (Nonendometrioid) (20%)
Unopposed estrogen	Present	Absent
Menopausal status	Pre-and perimenopausal	Postmenopausal
Hyperplasia	Present	Absent
Race	White	Black
Grade	Low	High
Myometrial invasion	Minimal	Deep
Specific subtypes	Endometrioid, Adeno CA grade 1,2	Serous, clear cell, Adeno CA-grade 3
Behavior	Stable	Aggressive
Associated gene	pTEN/Kras	p53

Papillary serous cancer:

- Seen in 5-10% of endometrial cancers.
- Associated with BRCA 1 & BRCA 2 gene.
- It metastasizes early by spreading through peritoneum therefore in its staging omentectomy and peritoneal biopsy should be done.

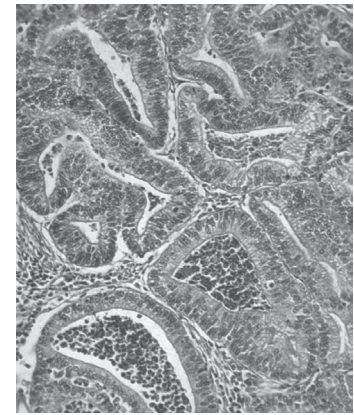
### Clear Cell Carcinoma

- It accounts for < 5% of all endometrial carcinomas.
- Most characteristic histological finding is presence of “hobnail cells”.
- It characteristically occurs in older women and is very aggressive type of endometrial cancer.



#### Histological criteria for diagnosis of endometrial Ca:

- Back to back arrangement of glands
- Desmoplastic stroma
- Excessive papillary pattern
- Squamous cell differentiation



**Fig. 14A.1:** Histology of uterine cancer



- M/C variety of endometrial cancer is adenocarcinoma
- Most malignant variety is clear cell carcinoma and papillary serous tumor.



- Mucinous variety of endometrial CA needs to be differentiated from Adeno CA of endocervix. It is done by using vimentin stain.



- % of patients of post menopausal bleeding with endometrial CA-10%.



- M/C cause of postmenopausal bleeding—senile endometritis.
- M/C cancer causing of PMB—In India—Ca cervix



When hysteroscopy is performed to detect endometrial cancer distension media should be CO<sub>2</sub> and not saline so as to minimize the risk of teratogenicity by introducing malignant cells into peritoneal cavity via transtubal migration.



#### Remember:

- **For postmenopausal bleeding:** 1st investigation is TVS in endometrial cancer - IOC is Endometrial Aspiration Biopsy.
- **Gold standard** for diagnosing endometrial cancer - Fractional curettage.

- Prognosis is similar to or worse than papillary serous carcinoma.
- In staging: Omentectomy and peritoneal biopsy done

### Clinical Features

- **Age group:** Peak incidence of endometrial cancer is seen at 60 years but in 25% cases it can occur before menopause or in young females.
- **A nulliparous postmenopausal female in the sixth or seventh decade presents with:**
- Irregular vaginal bleeding:- M/C complaint
- Postmenopausal bleeding :- Most specific complaint
- Discharge per vagina (1%):
  - Brown, watery offensive discharge
  - Watery discharge free from blood (hydrorrhoea<sup>®</sup>).
- Pelvic pressure/discomfort.
- Referred pain in hypogastrium or both iliac fossae (Simpson's pain).
- Pain is not severe and tends to occur at the same time each day, lasting only 1-2 hrs.
- In some older patients, bleeding may not occur due to cervical stenosis, causing hematometra/pyometra.

### Investigations

- **Screening:** Routine screening for Ca endometrium is not done, as Pap smear is positive only in 50% of patients of Ca endometrium.
- In patients of HNPCC—changes of malignancy are high: hence screening required. **Screening method**
  - Pelvic examination, endometrial sampling and TVS done every 6 or 12 monthly.
  - Screening begins at age of 35 years.
  - Best method to prevent Ca in these patient is—prophylactic hysterectomy with bilateral salpingo oophorectomy after completing childbirth.

### TVS

It is the **1st step taken in women** who present with post menopausal bleeding to decide whether endometrial sampling is needed or not. If endometrial thickness is less than 4 mm, further testing may be deferred. But if there is recurrence of bleeding, a tissue diagnosis is essential. Other factors to be assessed are the presence of a polypoidal endometrial mass or fluid collection as the latter may indicate pyometra.

### Endometrial Sampling

This could be done by any of the following methods-

- Office endometrial aspiration biopsy
- Traditional fractional curettage
- Hysteroscopy and directed biopsy.

### Endometrial Aspiration Biopsy

It is the **IOC for endometrial cancer**. Diagnostic accuracy: 92–98%

Endometrial aspiration biopsy can be performed in outpatient setting as it does not require any anesthesia and has the advantage of being simple, quick, safe, inexpensive, convenient. It is combined with endocervical curettage to rule out cancer cervix. It is done using a vibra aspirator, Sharman curette, or Pipelle endometrial sampler (Fig. 14A.2).

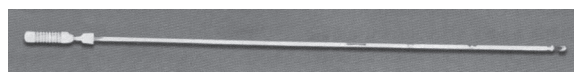


Fig. 14A.2: Pipelle endometrial sampler

## Fractional Curettage

Fractional curettage is the **Gold standard investigation** used for ruling out endometrial cancer. Here the endocervical canal is curetted first followed by dilation and endometrial curettage.

### ➤ Indications:

- Cervical stenosis;
- If clinical suspicion of malignancy is high;
- If bleeding recurs after a negative report on endometrial aspiration.

## Hysteroscopy and Biopsy

It is not recommended routinely for endometrial cancer as most of the cancers are detected easily by endometrial aspiration biopsy and hysteroscopy is good for focal lesions.

## Pap Smear

It is not a reliable test for diagnosis of Endometrial carcinoma. Only 30–50% patients with endometrial carcinoma have positive pap test and they are women with advanced disease.

## Staging

- **Staging for endometrial cancer is done surgically**, and because many patients have early-stage diseases at the time of diagnosis, this is often the only intervention necessary. Surgical staging includes hysterectomy (TAH) and bilateral salpingo-oophorectomy (BSO), cytoreduction of all visible disease, and pelvic and paraortic lymph node sampling.
- With the above procedures; Omentectomy and peritoneal biopsy is done in case of papillary serous and clear cell CA.
- Lymphadenectomy is also done in serous clear cell CA and in tumors where >50% myometrium is involved.

### FIGO Staging of Endometrial Cancer

Stage I	- Tumor confined to uterus
	A = only endometrium involved
	B = < 50% of myometrium involved
	C = ≥ 50% of myometrium involved
Stage II	- Tumor involves cervix
	A = Glands involved.
	B = Stroma Involved.
Stage III	- Local spread.
	A = Serosa/adenexa/positive peritoneal cytology
	B = Vaginal metastasis
	C = Pelvic & para aortic lymph nodes involved
Stage IV	- Metastases
	A = Regional metastasis (Bladder/Bowel, involved)
	B = Distant metastasis including abdominal metastasis and inguinal lymphnode metastasis
Each stage has 3 grades	G1 – Well differentiated tumor
	G2 – Moderately differentiated tumor
	G3 – Poorly differentiated tumor

## Revised Staging of Ca Endometrium (2009)

In 2009 FIGO revised the staging for cancer endometrium. In this new staging system, positive cytology no longer changes the stage, but is still reported.



**Staging for endometrial cancer is surgical i.e. total hysterectomy with bilateral salping ophorectomy** with pelvic and paraaortic lymphnode sampling being performed at the time of staging only.

- Papillary serous variety and clear cell CA- Omentectomy and peritoneal biopsy is also done.



### Prognostic factors in endometrial cancer

- **Most important prognostic factor is lymph node metastasis.**<sup>Q</sup>
- **Age** at diagnosis (older the patient poorer the prognosis).
- **Stage of the disease.**<sup>Q</sup>
- **Histologic type** (endometrioid adenocarcinoma have good prognosis, clear cell carcinoma have poor prognosis).<sup>Q</sup>
- **Histologic grade.**<sup>Q</sup>
- **Myometrial penetration** (Increasing depth of invasion is associated with increasing likelihood of extrauterine spread and recurrence).
- **Extension to cervix**– Involvement of cervix, isthmus or both is associated with increased risk of extrauterine disease and lymph node metastasis.
- **Role of peritoneal cytology is controversial.**
- **Tumor size** (≥ 2 cm– means more lymph node metastasis).
- **Hormone receptor status** (receptor positive–better prognosis).
- **Ploidy status:** Aneuploid have got better prognosis compared to diploid tumors.
- **Oncogene expression:** HER: 2/neu, k-ras poor prognosis.

Stage IA	= Cancer confined to uterus and anything < 50% of myometrium .
Stage IB	= Cancer confined to uterus but 50% or more of myometrium involved.
Stage II	= Endocervical stroma involved. Note endocervical glandular involvement is non-considered stage I.
Stage IIIA	= Tumor invades serosa or adnexa. Positive cytology has to be reported separately without changing the stage.
Stage IIIB	= Vaginal and/or parametrial involvement
Stage IIIC1	= Metastasis to pelvic lymph node
Stage IIIC2	= Metastasis to Para-aortic lymph node.
Stage IV	= No change



In all gynaecological cancers FIGO staging system is being followed except in cancer vulva where both FIGO and TNM staging can be done.

### Spread

- Most common mode of spread is direct extension.<sup>Q</sup>
- Lymphatic spread occurs to pelvic and para-aortic nodes
- Hematogenous spread (usually to lungs) is rare.

### Management

#### Principle of Management

- Remember–In cancer endometrium, staging is surgical, i.e. already we have performed TAH+BSO + dissected any enlarged lymph node (LN) or performed selective pelvic and paraaortic lymphadenectomy.
- Thus treatment is mainly postoperative management
- **Postoperative management of choice in patients with endometrial cancer is always radiotherapy.** In stage III and IV:- Chemotherapy is given along with Radiotherapy.
- **Only Patients with stage IA grade 1 and 2 donot require postoperative radiotherapy.**



At the time of surgical staging of endometrial cancer TAH and BSO are done but if cervical involvement is known preoperatively, i.e. in case of stage II disease-radical/Wertheims hysterectomy is preferred.



#### Indications for pelvic and paraaortic lymph node dissection in Endometrial cancer.

- i. Tumor histology-
  - Clear cell carcinoma
  - Papillary serous carcinoma
  - Squamous carcinoma.
- ii. Adenocarcinoma grade III
- iii. More than half of the myometrium involved.
- iv. Tumour extends to isthmus-cervix
- v. Extrauterine disease.
- vi. Tumor size > 2 cms

Stagewise	Management
Stage I A grade 1 and 2	Surgery –(TAH) + (BSO) + LN dissection-(pelvic lymphadenectomy) if Tm size is > 2 cms. (No other postoperative therapy required).
Stage IA grade III and IB (all grades)	Surgery –TAH + BSO+Pelvic and paraaortic lymphadenectomy followed by radiotherapy (after 4-6 weeks)
Stage II	Modified radical hysterectomy with LN dissection (pelvic and paraaortic) followed by radiotherapy
Stage III and stage IV	Debulking surgery followed by chemotherapy and radiotherapy

### Choice of Radiotherapy

Radiation Type	Used in
Vaginal Vault Radiation	Grade 3 tumor and Lymph vascular space invasion
Whole Pelvis External Beam Radiation (Radiation field encloses upper half of vagina inferiorly, Lower border of L4 vertebral body superiorly and 1 cm lateral to margins of bony pelvis)	Extrauterine pelvic disease including adnexal spread, parametrial involvement and pelvic lymph node metastases, in absence of extrapelvic disease
Extended field radiation including entire pelvis, common iliac lymph nodes and para aortic lymph nodes	Endometrial cancer with positive para aortic lymph nodes

Contd...

Contd...

Radiation Type	Used in
Whole abdomen radiation therapy	Done in stage III /IV Serous or carcinosarcoma Note-After the publication of GOG122, demonstrating the superiority of chemotherapy over whole abdominal radiotherapy in advanced endometrial cancer, the utilization of whole abdomen RT is not common...Novak 15 <sup>th</sup> /ed p 1278



**Indications for adjuvant Radiotherapy in Cancer endometrium**

- i. Grade III tumor (poor histology differentiation)
- ii. Papillary serous/clear cell histology
- iii. Lower uterus/cervical involvement
- iv. Myometrial involvement  $\geq$  than 50%
- v. Pelvic lymph node involved
- vi. Extrauterine involvement

**Hot Topic**

**Recurrent Endometrial Cancer**

M/C time of recurrence is within first two years  
 M/C symptom of local recurrence vaginal bleeding  
 M/C symptom of pelvic recurrence – pelvic pain  
 M/C site of recurrence – Vagina and pelvis  
 M/C site of extrapelvic recurrence – Lung, lymph node (aortic), Liver, brain and bones

**Management**

- > For patients with recurrent endometrial tumors with hormone receptors positive, **initial treatment is progestin.**
- > If patient has contraindication to progesterone then Tamoxifen can be used.
- > In Recurrent Cancers: which are hormone negative initial management is local management
- > If patient is operable-surgery is done
- > If patient is inoperable-RT is given
- > If local T/t cannot be given-Palliative chemotherapy is given.

**Uterine Sarcoma**

- > It is a rare uterine tumor accounting for 2-6% of all uterine malignancies
- > Arises from stromal components (endometrial stroma, mesenchymal or myometrial tissues)
- > Mostly seen in post menopausal age group
- > Vaginal bleeding is most common presenting symptom
- > Behaves more aggressively and is associated with poorer prognosis
- > 5-year survival rate – 35%

**M/C Varieties of Uterine Sarcoma are**

Endometrial Stromal Sarcoma (ESS)	Leiomyosarcoma	Carcinosarcoma (Mixed Mullerian Tumor)
<ul style="list-style-type: none"> <li>• Arises from stromal cells</li> <li>• Least aggressive of the sarcomas</li> <li>• M/c age = Perimenopausal and postmenopausal females</li> </ul>	<ul style="list-style-type: none"> <li>• Occurs when fibroid becomes malignant</li> <li>• (0.1 – 0.5%) fibroids undergo malignancy</li> <li>• M/c age = 43–53 years</li> <li>• Differentiating feature of leiomyosarcomas is <math>&gt;</math> 10 mitosis 10 high power field.</li> </ul>	<ul style="list-style-type: none"> <li>• M/c variety</li> <li>• M/c age = 62 years</li> <li>• M/c - post menopausal bleeding</li> <li>• M/c mode of spread - Blood borne</li> <li>• Most aggressive sarcomas</li> </ul>
	<ul style="list-style-type: none"> <li>• No whorled appearance and no capsule</li> </ul>	<ul style="list-style-type: none"> <li>• M/c type of cells seen MMT are spindle cells.</li> </ul>



**Mixed mullerian tumors** are diagnosed on the basis of **ten or more mitotic figures per ten high power fields (HPFs)**. Those tumors with 5 to 10 mitotic figures per 10 HPFs are referred to as smooth muscle tumors of uncertain malignant potential. Tumors with  $<$  5 mitotic figures per 10 HPFs and little cytological atypia are classified as cellular leiomyosarcomas.

**Treatment**

First step is always exploration. TAH + BSO (done in all patients except premenopausal females with leiomyosarcoma where we donot do bilateral



Uterine sarcomas may be pure (single cell type) or mixed (more than one cell type). The tumor is termed homologous when the tissue elements are native (e.g. smooth muscle or heterologous when tissue elements are not native (cartilage, striated muscle, bone). This is due to totipotent nature of endometrial stromal cells.

salpingoophorectomy) followed by chemotherapy. (Doxorubicin, Ifosfamide, Paclitaxel, carboplatin). Novak 15/e, p 1292.

### **Staging of Sarcoma**

Uterine sarcomas were staged previously as endometrial cancers, which did not reflect their clinical behavior. Now they are staged as follows:

Stage IA	= Tumor limited to uterus < 5 cm
Stage IB	= Tumor limited to uterus > 5 cm
Stage IIA	= Adnexal involvement
Stage IIB	= Tumor extends to extrauterine pelvic tissue
Stage IIIA	= Tumor invades one site of abdominal tissue
Stage IIIB	= Tumor invades more than one site of abdominal tissues
Stage IIIC	= Metastasis to pelvic and/or para-aortic lymph nodes
Stage IVA	= Tumor invades bladder and/or rectum
Stage IVB	= Distant metastasis.

### **Embryonal Rhabdomyosarcoma**

- > Most common malignant tumor of the genital tract in girls.
- > Mostly arises from the submucosa of cervix or vagina.
- > **Age**-90% cases occur before the age of 5, peak incidence at 2 years of age.
- > **Hallmark**-pinkish, grape like polypoidal soft growth arising from the cervix.
- > **Clinical features**-Blood stained watery vaginal discharge is the main symptom.
- > **Treatment**-Initial staging with Chest X-ray and CT Scan.
- > **Later**-Chemotherapy (VAC-Vincristine, Actinomycin D and Cyclophosphamide) followed by surgery is the treatment of choice.
- > **Prognosis**-poor.
- > **Recurrence**-common.



## QUESTIONS

1. The risk of endometrial cancer is highest with the following histological pattern of endometrial hyperplasia: *(AIMS May 06)*
  - a. Simple hyperplasia without atypia
  - b. Simple hyperplasia with atypia
  - c. Complex hyperplasia without atypia
  - d. Complex hyperplasia with atypia
2. The risk of complex hyperplasia of endometrium with atypia progressing to malignancy in a postmenopausal woman is: *(AIIMS 04, 05)*
  - a. 3%
  - b. 8%
  - c. 15%
  - d. 28%
3. Percentage change of cystic glandular hyperplasia turning to malignancy: *(PGI June 05)*
  - a. 0.1%
  - b. 2%
  - c. 1%
  - d. 10%
  - e. 15%
4. Endometrial hyperplasia is seen in: *(AI 04)*
  - a. Endodermal sinus tumor
  - b. Dysgerminoma
  - c. PCOD
  - d. Ca cervix
5. What is the ideal treatment for a 55-years-female with Simple hyperplasia of endometrium with Atypia? *(AI 08)*
  - a. Simple hysterectomy
  - b. Medroxy progesterone acetate (MPA)
  - c. Levonorgesterol (LNG)
  - d. IUCD
6. All of the following are known risk factors for development of endometrial carcinoma except:
  - a. Obesity *(AI 03, 02)*
  - b. Family history
  - c. Use of hormone replacement therapy
  - d. Early menopause
7. Risk for endometrial cancer is: *(PGI 04, 00)*
  - a. Obesity
  - b. Pregnancy before 20 years age
  - c. PCOD
  - d. Combined OC pills
  - e. Artificial menopause
8. All are the risk factors for endometrial carcinoma except: *(PGI June 09)*
  - a. Multiparity
  - b. Obesity
  - c. Early menopause
  - d. Unopposed estrogen therapy
  - e. Hypertension
9. Long-term tamoxifen therapy may cause: *(AI 99, 98; PGI 99)*
  - a. Endometrium Ca
  - b. Ovary Ca
  - c. Cervix Ca
  - d. Vagina Ca
10. Which of the following is not seen with corpus cancer syndrome in cancer endometrium? *(AIIMS Nov 2010)*
  - a. Multiparity
  - b. Diabetes mellitus
  - c. Hypertension
  - d. Obesity
11. A 50-year-old woman, nulliparous, diabetic and obese presenting with post-menopausal bleeding likely diagnosis is: *(PGI 99)*
  - a. Carcinoma in situ of cervix
  - b. Carcinoma endometrium
  - c. DUB
  - d. None of the above
12. True about endometrial carcinoma: *(PGI 01)*
  - a. Predisposed by diabetes mellitus, hypertension and obesity
  - b. Adenosquamous type is most common
  - c. Commonly associated with Ca cervix
  - d. Common age group affected is between 20 and 40 years
13. The most malignant endometrial carcinoma is:
  - a. Adenocarcinoma *(JIPMER 03)*
  - b. Adenoacanthoma
  - c. Mixed adenosquamous carcinoma
  - d. Clear cell carcinoma
14. Investigation of choice in a 55-year-old post menopausal woman who has presented with postmenopausal bleeding: *(AI 06, 98)*
  - a. Pap smear
  - b. Fractional curettage
  - c. Transvaginal ultrasound
  - d. CA - 125 estimation
15. The stage of cancer endometrium with invasion of 10 mm of myometrium is: *(AI 00)*
  - a. Ia
  - b. Ib
  - c. IIb
  - d. IIa
16. Carcinoma endometrium with positive superficial inguinal lymph node status is classified as stage: *(AI 99)*
  - a. I
  - b. II
  - c. III
  - d. IV
17. True about endometrial carcinoma in clinical stage III: *(PGI June 09)*
  - a. Vaginal metastasis
  - b. Para aortic lymph node involvement
  - c. Pelvic lymph node involvement
  - d. Peritoneal involvement
  - e. Inguinal lymph node involvement

18. Lymph nodes not involved in Ca endometrium is:  
(AIIMS 97)
- Para-aortic
  - Presaral
  - Inferior mesenteric
  - Inguinal
19. A perimenopausal lady with well differentiated adenocarcinoma of uterus has more than half myometrial invasion, vaginal metastasis and inguinal lymph node metastasis. She is staged as:  
(AIIMS 96, 03)
- Stage IIIB
  - Stage IIIC
  - Stage IVA
  - Stage IVB
20. A lady presented with carcinoma endometrium involving >50% of myometrium extending to vagina and positive peritoneal cytology but no involvements of para aortic and pre aortic nodes. What is the stage of disease? (AIIMS Nov 2010)
- III A
  - III B
  - III C1
  - III C2
21. Stage III B endometrial Ca-true is:  
(PGI June 08, Dec. 06)
- Vaginal metastasis
  - Lymph node metastasis
  - Bowel involvement
  - Lung metastasis
  - Serosa involved
22. Stage-IIIB endometrial carcinoma true is/are:  
(PGI June 09)
- Vaginal metastasis
  - Lymph node metastasis (paraaortic)
  - Pelvic lymph node involvement
  - Positive peritoneal cytology
  - Rectal invasion
23. Choice of adjuvant treatment for endometrial carcinoma stage I A grade I is:  
(AI 04)
- Radiotherapy
  - Chemotherapy
  - Chemotherapy + Radiotherapy
  - No treatment
24. The following are indications for postoperative radiotherapy in a case of carcinoma endometrium except:  
(AIIMS 04, 05)
- Myometrial invasion of more than half thickness
  - Positive lymph nodes
  - Endocervical involvement
  - Tumor positive for estrogen receptors
25. Indication for radioterhapy in carcinoma endometrium include all except: (AIIMS Nov. 07)
- Pelvic node involvement
  - Deep myometrial involvement
  - Enlarged uterine cavity
  - Poor differentiation
26. Indication of adjuvant radiotherapy in Ca endometrium is/are:  
(PGI 05)
- Cervical involvement
  - Lymph node involvement
  - Carcinoma in situ
  - Papillary serous tumor
  - Estrogen receptor positive
27. Which of the following direct lymph node dissections in endometrial carcinoma?
- Penetration into half of myometrium
  - Clear cell carcinoma
  - Fundal involvement
  - Peritoneal metastasis
  - Papillary serous carcinoma
28. An 80-year-old female who has never taken estrogen, develops pink vaginal discharge. An endometrial biopsy shows an adenocarcinoma of the endometrium. Papanicolaou smear is negative. Of the following what is the most important indicator of prognosis?  
(AI 04)
- Body habitus
  - Level of CA-125
  - Nutritional status
  - Histologic type of tumor
29. Following can cause endometrial cancer:(AP 2008)
- Metropathia hemorrhagica
  - Gynandroblastoma
  - Dysgerminoma
  - All of the above
30. A female patient has adenocarcinoma uterus along with sarcoma of uterus. It is known as:  
(AIIMS June 00)
- Homologous sarcoma
  - Sarcoma uterus
  - Mixed Mullerian carcinogenesis
  - Heterologous sarcoma
31. All are true regarding sarcoma botryoides except:  
(PGI 01)
- Seen in vagina
  - Grape like clusters are seen
  - Seen in elderly women
  - It is an adenocarcinoma
  - Familial incidence is common
32. True statement regarding sarcoma botryoides:  
(PGI May 2010)
- Involvement of vagina
  - Grape like growth seen
  - Common in old age
  - Malignant

### NEW PATTERN QUESTIONS

33. Primary carcinoma body of the uterus may be of following types except:
- Adenocarcinoma
  - Adenosquamous carcinoma
  - Clear cell type
  - Large cell keratinising type
34. The following are precursors of endometrial carcinoma except:
- Atypical adenomatous hyperplasia
  - Atrophic endometrium
  - Adenocarcinoma in situ
  - Cystic hyperplasia

## ANSWERS

1. **Ans. is d, i.e. Complex hyperplasia with atypia**

2. **Ans. is d, i.e. 28%**

3. **Ans. is c, i.e. 1%** *Ref. Jeffcoate 7<sup>th</sup>/ed p 422-3; Novak 14<sup>th</sup>/ed p 1346; 15<sup>th</sup>/ed p 1252-3; Williams Gynae 1<sup>th</sup>/ed p 689*  
 Friends, let's first try to figure out this question on the basis of our basic knowledge of neoplasia. We all have read time and again that in 'Neoplasia' atypical cells are present, therefore obviously out of the given options, either option "b" or "d" is correct and since neoplasia is most likely to occur in complex situations therefore out of the given options even if I don't know anything about endometrial hyperplasia I would have gone for option "d".

**As discussed in the preceding text:**

Endometrial hyperplasia is of following four varieties:

1. Simple hyperplasia without atypical cells
2. Complex hyperplasia without atypical cells
3. Simple hyperplasia with atypical cells
4. Complex hyperplasia with atypical cells.

Logically speaking least chances of malignant transformation are with simple hyperplasia without atypia and maximum chances are with complex hyperplasia with atypia.

**Chances of Progression to Carcinoma:**

Type of hyperplasia	
• Simple without atypia	1% <sup>o</sup>
• Complex without atypia	3% <sup>o</sup>
• Simple with atypia	8% <sup>o</sup>
• Complex with atypia	29–30% <sup>o</sup>

Thus, from the table it is reaffirmed that minimum chances of progression to carcinoma are with simple hyperplasia without atypia (also called as cystic glandular hyperplasia) and maximum chances of carcinoma are with complex hyperplasia with atypia.<sup>o</sup>

4. **Ans. is c, i.e. PCOD**

*Ref. Jeffcoate 7<sup>th</sup>/ed p 422-3*

Endometrial hyperplasia specially simple hyperplasia results from circumstances in which there is prolonged, increased oestrogen production example:

- Follicular cysts of ovary
- PCOD
- Granulosa and theca cells
- HRT.

5. **Ans. is a, i.e. Simple hysterectomy**

*Ref. Jeffcoate 7<sup>th</sup>/ed p 425; Williams Gynae. 1<sup>st</sup>/ed p 691*

**Management of Atypical Endometrial Hyperplasia:**

*"Hysterectomy is the best treatment for women at any age with atypical endometrial hyperplasia because the risk of concurrent subclinical invasive disease is high."* ... Williams Gynae 1<sup>st</sup>/ed p 691

*"In presence of atypia, response to progesterone therapy is poor and relapse rate is high. Nearly one-third of them will progress to cancer and one-fourth may already have associated undiagnosed cancer. In women approaching or past menopause, hysterectomy is a safer choice in those with complex or atypical hyperplasia."* ... Jeffcoate 7<sup>th</sup>/ed p 425

**So Remember: Best management of atypical hyperplasia is hysterectomy.**

**Also Know: Management of Endometrial Hyperplasia:**

Management depends on the patient's age and the presence or absence of cytological atypia.

**Non atypical hyperplasia:**

- **Premenopausal women:** Progesterone therapy-  
**Options:** – Medroxyprogesterone acetate for 21 days a month daily for 3 months.  
 – Progesterone containing IUCD.
- **Postmenopausal women**  
 Simple hyperplasia without atypia – Generally followed without therapy.

Complex hyperplasia without atypia – Cyclical/continuous progesterone therapy.  
These patients should be followed annually by endometrial biopsy.

#### Atypical hyperplasia:

- Ideal treatment is hysterectomy
- Premenopausal women willing to preserve fertility – High dose progesterone therapy after full information of risk of a undiagnosed cancer or progression to cancer. In these cases periodic TVS and endometrial biopsy is necessary.

6. Ans. is d, i.e. Early menopause

7. Ans. is a and c, i.e. Obesity; and PCOD

8. Ans. is a and c, i.e. Multiparity; and Early menopause

*Ref. Shaw 15<sup>th</sup>/ed pg 416-7; Williams Gynae 1<sup>st</sup>/ed p 688; Novak 14<sup>th</sup>/ed p 1345, 15<sup>th</sup>/ed pp 1251-2*

Friends, this is the most frequently asked question on endometrial cancer. Mug up predisposing factors by heart.

**Endometrial carcinoma occurs as a result of unopposed estrogen exposure in body.**

Predisposing factors are:

<b>F</b>	Family history
<b>H</b>	Hypertension
<b>O</b>	Obesity
<b>L</b>	Late menopause/early menarche
<b>D</b>	Diabetes
<b>A</b>	Atypical endometrial hyperplasia
<b>U</b>	Unopposed estrogen or increased estrogen in body as in: HRT, Fibroid, PCOD and Feminizing ovarian tumour
<b>N</b>	Nulliparity
<b>T</b>	Therapy: tamoxifen therapy and radiation therapy
<b>I</b>	H/o infertility/menstrual irregularity

**Mnemonic:** Family has OLD AUNTI

#### Hereditary:

Approximately 5% of endometrial cancer is hereditary, with majority of these presenting as a part of the Lynch 11 or hereditary non polyposis colorectal cancer (HNPCC) syndrome. Aside from endometrial cancer, individuals in this family are at increased risk of colorectal cancer, ovarian, urinary, biliary, gastric and small intestinal cancer. Abnormal bleeding at any age should be evaluated by tissue biopsy in women of HNPCC families. routine surveillance may consist of yearly USG and endometrial biopsy commencing at the age of 30–35.

#### Protective factors:

- Oral contraceptive pills (combined addition of Progesterone to HRT).
- Smoking (as it decreases levels of estrogen, decreases weight and is associated with earlier age of menopause).

9. Ans. is a, i.e. Endometrium Ca

*Ref. Shaw 15<sup>th</sup>/ed pg 417, Novak 14<sup>th</sup>/ed p 1345, 15<sup>th</sup>/ed p1251-2*

**Long-term tamoxifen therapy is a predisposing factor for endometrial hyperplasia and cancers.**

#### Malignancies caused by long-term tamoxifen therapy:

- Carcinoma endometrium-it is the most common carcinoma associated with it.
- Uterine sarcoma.
- Rarely liver cancer with long-term high dose.

#### Non malignant effects of tamoxifen on uterus:

- Endometrial hyperplasia
- Endometriosis
- Fibroid uterus
- Ovarian cysts
- Menstrual irregularities or amenorrhea.

10. Ans. is a, i.e. Multiparity

*Ref. Jeffcoates 7<sup>th</sup>/ed p 504, Dutta Gynae 5<sup>th</sup>/ed p 351*

Combination of diabetes, obesity and hypertension in association with endometrial carcinoma is called as the Corpus Cancer Syndrome.

**11. Ans. is b, i.e. Carcinoma endometrium**Ref. Jeffcoate 7<sup>th</sup>/ed p 503; Novak 14<sup>th</sup>/ed p 1349

A 50-year-old woman nulliparous, diabetic and obese (all predisposing factors for carcinoma endometrium) female is presenting with postmenopausal bleeding (most common complaint in Ca endometrium). The most likely diagnosis is carcinoma endometrium.

**12. Ans. is a, i.e. Predisposed by diabetes mellitus, hypertension and obesity** Ref. Jeffcoate 7<sup>th</sup>/ed p 503-5; Shaw 15<sup>th</sup>/ed pp 417 for option a, 418 for option b, 416 for option c & option d; Novak 14<sup>th</sup>/ed p 1345, 15<sup>th</sup>/ed p 1256-7**Endometrial cancer:**

- Lets see each option regarding endometrial cancer one by one:
  - Predisposed by diabetes mellitus, hypertension and obesity correct
  - Adenosquamous type is most common—incorrect as the most common variant is adenocarcinoma
  - Commonly associated with cancer cervix incorrect as cancer cervix and endometrial cancer are not related to each other.
  - Common age group affected is between 20 and 40 years incorrect as endometrial cancer occurs in postmenopausal females (6th–7th decade).

**13. Ans. is d, i.e. Clear cell carcinoma**Ref. Devita cancers 8<sup>th</sup>/ed p 1545, Table 42.3.2; Dutta Gynae 4<sup>th</sup>/ed p 334; Novak 14<sup>th</sup>/ed p 1354; Williams Gynae 1<sup>th</sup>/ed p 9691**Endometrial cancers can be histologically classified as:**

Features	Type I (Endometrioid)	Type II (Nonendometrioid)
Unopposed estrogen	Present	Absent
Menopausal status	Pre-and perimenopausal	Postmenopausal
Hyperplasia	Present	Absent
Race	White	Black
Grade	Low	High
Myometrial invasion	Minimal	Deep
Specific subtypes	Endometrioid	Serous and clear cell
Behavior	Stable	Aggressive

Thus it is clear non endometrioid/type II endometrial cancer (clear cell carcinoma) have poor prognosis.

**Also know:**

Clear cell carcinoma:

- It accounts for < 5% of all endometrial carcinoma.
- Most characteristic histological finding is presence of “hobnail cells”.
- It characteristically occurs in older women and is very aggressive type of endometrial cancer.
- Prognosis is similar to or worse than papillary serous carcinoma.



Thus remember M/C variety of endometrial cancer = Adenocarcinoma  
Most malignant is Clear cell Carcinoma / Papillary Serous variety.

**14. Ans. is b, i.e. Fractional curettage** Ref. Devita cancers-8<sup>th</sup>/ed p 1546, p 344; Jeffcoate 7<sup>th</sup>/ed p 509; Novak 14<sup>th</sup>/ed p 1350; 15<sup>th</sup>/ed p 1257-8; Bijoy Sree Sen Gupta 2<sup>th</sup>/ed p 616-7; Dutta Gynae 5<sup>th</sup>/ed p 344

In a woman with postmenopausal bleeding chances of endometrial carcinoma are very high. Therefore such a patient should be evaluated so as to rule out endometrial carcinoma. Hence fractional curettage should be done.

Investigations for endometrial carcinoma

... Novak 15<sup>th</sup>/ed p 1257

- i. **Endometrial Aspiration Biopsy:** “It is the accepted first step in evaluating a patient with abnormal uterine bleeding or suspected pathology. The diagnostic accuracy of an office based endometrial biopsy is 90-98% when compared with subsequent findings at dilatation and curettage (D and C)”.

... Novak 15<sup>th</sup>/ed p 1257

“Endometrial sampling should be performed in any woman with irregular or heavy bleeding older than age 35. Although a formal dilatation and curettage has been the standard technique for diagnosis, outpatient endometrial biopsy has replaced it in most situations”

....Devita 8<sup>th</sup>/ed p 1546

Endometrial biopsy can be performed in outpatient setting and has the advantage of being simple, quick, safe, inexpensive, convenient and avoiding the need of anaesthesia.

- ii. **Dilatation and Fractional Curettage:** *"Fractional curettage is not only the definite method of diagnosis but can detect the extent of growth."* ... Dutta Gynae 5<sup>th</sup>/ed p 344
- iii. **Hysteroscopy and biopsy:** It is nowadays the investigation of choice for endometrial cancer but most of the cancers are detected easily by endometrial aspiration biopsy and it is reserved for those cases where there is cervical stenosis or patient cannot tolerate endometrial aspiration, bleeding recurs after a negative endometrial biopsy or specimen is inadequate.
- iv. **Transvaginal ultrasound:** May be useful adjunct to endometrial biopsy for evaluating abnormal uterine bleeding and selecting patients for additional testings.  
If endometrial thickness is > 4 mm, a polypoidal endometrial mass is present or a collection of fluid is present within the uterus, in postmenopausal females always follow up with histopathological diagnosis.
- v. **Pap smear:** It is not a reliable test for diagnosis of endometrial carcinoma. Only 30–50% patients with endometrial carcinoma have positive pap test and they are women with advanced disease.

**Remember:**

- First investigations in case of endometrial cancer – Endometrial aspiration biopsy.
- Best investigation for diagnosing endometrial cancer – Hysteroscopy and biopsy.

**15. Ans. is b, i.e. Ib**

*Ref. Novak 15<sup>th</sup>/ed p 1265; Shaw 15<sup>th</sup>/ed p 420*

FIGO staging and revised FIGO staging has been given in the preceding text.

**According to older staging**

- If tumor involves myometrium, it belongs to either stage Ib or Ic. Normal thickness of myometrium is 10–20 mm, therefore, if 10 mm of myometrium is involved. It should ideally be included in stage Ic but since Ic is not given in options, IInd best option is Ib.

Now if we think from newer revised staging it says

In stage IA–Tumor is confined to uterus and either it is limited to endometrium or less than half of myometrium is involved.

Stage IB–Tumor confined to uterus with more than or equal to half of myometrial invasion

Thickness of 10 mm means more than half of myometrium, i.e. stage Ib.

**16. Ans. is d, i.e. Stage IV**

*Ref. Novak 15<sup>th</sup>/ed p 1265; Shaw 15<sup>th</sup>/ed p 420*

In general inguinal lymph node metastasis are very frequently asked in exams–

**Remember:**

- In ca endometrium–Inguinal LN are involved in stage IV B
- In ca ovary–Inguinal LN are involved in stage III C
- In ca cervix–Lymph nodes rarely involved–Inguinal LN
- In vulva cancer–Sentinel lymph nodes, i.e., first lymph nodes involved are–inguinal lymph node.

**17. Ans. is a, b, c and d, i.e. Vaginal metastasis; Para aortic lymph node involvement; Pelvic lymph node involvement; and Peritoneal involvement**

*Ref. Novak 15<sup>th</sup>/ed p 1265; Shaw 15<sup>th</sup>/ed p 420*

Kindly see FIGO staging given in preceding text.

**18. Ans. is c, i.e. Inferior mesenteric**

*Ref. AJCC Cancer Staging Manual 6<sup>th</sup>/ed p 267*

Lymphatic drainage of uterus: ∴ Lymph nodes involved in ca endometrium. ... BDC Vol II, 3<sup>rd</sup>/ed p 319

- |                                  |  |
|----------------------------------|--|
| • Upper lymphatics (from fundus) | – Para aortic                                |
| • From cornua                    | – Superficial Inguinal nodes.                |
| • Middle lymphatics (from body)  | – External iliac nodes.                      |
| • Lower lymphatics (from cervix) | – External iliac node, Internal iliac nodes. |

**Besides these other regional lymph node involved in CA endometrium are:**

- Parametrial LN
- Presacral LN
- Pelvic LN
- Obturator.

19. **Ans. is d, i.e. Stage IVB** *Ref. Novak 15<sup>th</sup>/ed p1265; Shaw 15<sup>th</sup>/ed p 420*  
The lady in above question has cancer spread to inguinal lymph nodes i.e. stage IVB.

20. **Ans. is b, i.e. III B** *Ref. Williams gynae 2/e, p 830; shaw 15<sup>th</sup>/ed p 420; Novak 15<sup>th</sup>/ed p 1265*

**Explanation:**

As discussed earlier, 50% myometrial invasion means stage IC, positive peritoneal cytology puts it in stage III A  
Vaginal metastasis means stage III B cancer and since this is the highest stage.  
Therefore, this patient has endometrial cancer belonging to stage III B.

21. **Ans. is a and e, i.e. Vaginal metastasis; and Serosa involved**

22. **Ans. is a and d, i.e. Vaginal metastasis; and Positive peritoneal cytology** *Ref. Novak 15<sup>th</sup>/ed p 1265; Shaw 15<sup>th</sup>/ed p 420*

**Before answering these questions I want all of you to quickly revise staging of Ca Endometrium.**

- Vaginal metastasis means stage IIIB<sup>Q</sup>
- Lymph node involvement is seen from stage IIIC onwards.
- Bowel involvement /rectal involvement means stage IVA.
- Lung metastasis means stage IVB.
- Serosa involvement/positive peritoneal cytology means stage IIIA. The question is about stage IIIB, so everything involved before it is also included.

23. **Ans. is d, i.e. No treatment** *Ref. Shaw 15<sup>th</sup>/ed p 420; Novak 15<sup>th</sup>/ed p 1275*  
As discussed in preceding text – Stage Ia grade 1 and grade II require no post operative treatment.  
Rest for all stages–post operative management is radiotherapy in endometrial cancer.

24. **Ans. is d, i.e. Tumour positive for estrogen receptors**

25. **Ans. is c, i.e. Enlarged uterine cavity**

26. **Ans. is a, b and d, i.e. Cervical involvement; Lymph node involvement; and Papillary serous tumor**

*Ref. COGDT 9<sup>th</sup>/ed p 924; Shaw 15<sup>th</sup>/ed p 420; Novak 15<sup>th</sup>/ed p 1275; Onwards*

**Indications of adjuvant radiotherapy:**

- Extrauterine extension.
- Lower uterine or cervical involvement.
- Papillary serous or clear cell histology.
- Poor histologic differentiation (Grade III).
- Myometrial penetration greater than 1/2 of thickening.
- Pelvic node involvement.

Tumor positive for estrogen receptors suggest well differentiated disease, So no adjuvant radiotherapy is recommended.

27. **Ans. is a, b and e, i.e. Penetration into half of myometrium; Clear cell carcinoma; and Papillary serous carcinoma**

*Ref. Novak 15<sup>th</sup>/ed p 1271*

**Indications for lymph node (pelvic and Para-aortic) dissection in endometrial cancer**

1. Tumour histology:
  - Clear cell carcinoma
  - Papillary serous carcinoma
  - Squamous carcinoma
2. Adenocarcinoma (endometrioid) III.
3. More than half of myometrial invasion
4. Isthmus- cervix extension
5. Extrauterine disease.
6. Tumor size > 2 cm

**Note:** In absence of these factor only bilateral pelvic lymphadenectomy is performed if the tumor size is greater than 2 cm. Para aortic lymphadenectomy would be performed if pelvic lymph nodes are positive.  
Lymphadenectomy is altogether omitted for patient with above risk factors absent, absence of cervical involvement and tumor size less than 2 cm.

**As far as Peritoneal metastasis is concerned:**

“Positive peritoneal cytology in itself is not a marker of poor prognosis, i.e. is not an indication for lymph node dissection unless and until associated with other poor prognostic markers as above.” *... Novak 14<sup>th</sup>/ed p 1358*

28. **Ans. is d, i.e. Histologic type of tumor** *Ref. John Hopkins Manual of Obs & Gynae 4<sup>th</sup>/ed p 564; Novak 15<sup>th</sup>/ed p 1266–8*  
 “The most significant prognostic factors for recurrence and survival are stage, grade and depth of myometrial invasion. Age, histologic type, LVSI and progesterone receptor activity also have prognostic significance.”  
*.. John Hopkins Manual of Obs & Gynae 4<sup>th</sup>/ed p 564*

#### Prognostic factors in endometrial adenocarcinoma

- Most important prognostic factor is lymph node metastasis<sup>Q</sup>
- Age at diagnosis (older the patient poorer the prognosis).
- Stage of the disease.<sup>Q</sup>
- Histologic type (endometrioid adenocarcinoma have good prognosis, clear cell carcinoma have poor prognosis).<sup>Q</sup>
- Histologic grade.<sup>Q</sup>
- Myometrial penetration (Increasing depth of invasion is associated with increasing likelihood of extrauterine spread and recurrence).
- Extension to cervix Involvement of cervix, isthmus or both is associated with increased risk of extrauterine disease and LN metastasis.
- Tumor size (> 2 cm—more lymph node metastasis).
- Hormone receptor status (receptor positive—better prognosis).
- Ploidy status: Aneuploid have got better prognosis compared to diploid tumors.
- Oncogene expression: HER: 2/neu, k-ras poor prognosis.  
 Role of Peritoneal cytology on prognosis is controversial.

29. **Ans. is a, i.e. Metropathia hemorrhagica** *Ref. Shaw 14<sup>th</sup>/ed p 340, 341, 338; Dutta Gynae 5<sup>th</sup>/ed p 184 for option a*

#### Endometrial cancer is mainly caused by excessive estrogen

- Metropathia hemorrhagica is the same as cystic glandular hyperplasia and is a causative factor for endometrial cancer. *Ref. Dutta Gynae 5<sup>th</sup>/ed p 184*
- Gynandroblastoma is a virilising tumor which secretes androgens (not estrogens) and so doesnot lead to endometrial cancer *Ref. Shaw 14<sup>th</sup>/ed p 34*
- Dysgerminoma is a neutral tumor which doesnot secrete either male or female sex hormones but secretes placental alkaline phosphatase, LDH and BHCG and therefore doesnot lead to endometrial cancer. *Ref. Shaw 14<sup>th</sup>/ed 3386*

30. **Ans. is c, i.e. Mixed Mullerian carcinogenesis** *Ref. COGDT 10<sup>th</sup>/ed p 866*

#### Mixed mullerian carcinoma is a mixture of both carcinomatous and sarcomatous element.

- Represent 50% of all uterine sarcoma.
- Most common combination is of serous carcinoma with endometrial sarcoma.
- Most commonly occur in postmenopausal women.

#### Remember:

- *Most common histologic type* of uterine sarcoma is carcinosarcoma.<sup>Q</sup>
- *Most common symptom* of uterine sarcoma is bleeding.
- Surgery is main stay of treatment followed by chemotherapy.

#### Also know:

**Heterologous tumors:** If sarcoma component of mixed mullerian tumors mimic extra uterine tissue (viz – striated muscle cell, cartilage, adipose tissue and bone) it is known as *Heterologous tumor*.

**Homologous tumor:** If mesenchymal/sarcomatous component of mixed mullerian tumor consists of malignant endometrial or smooth muscle differentiation, the term homologous is used.

31. **Ans. is c, d and e, i.e. Seen in elderly women; It is an adenocarcinoma; and Familial incidence is common**

*Ref. Robbin's Pathology 7<sup>th</sup>/ed p 1071–2*

32. **Ans. is a, b, and d, i.e. Involvement of vagina; Grape like growth seen; and Malignant**

*Ref. William Gynae 1<sup>st</sup>/ed p 683*

Embryonal Rhabdomyosarcoma is the most common malignancy of the vagina in infants and children.

Most common subtype of embryonal rhabdomyosarcoma is sarcoma botryoides

- *Seen in infants and children less than 5 years of age.*

*“This rare tumor develops almost exclusively in girls younger than 5 years, although vaginal and cervical sarcoma botryoides have been reported in females aged 15 to 20 years.”*

*William Gynae 1<sup>st</sup>/ed p 683*

*“Sarcoma botryoides are usually seen in patients who are younger than 5 years of age.”*

*COGDT 10<sup>th</sup>/ed p 831*

In infants and children, sarcoma botryoides is usually found in vagina, in reproductive age females rhabdomyosarcoma is seen within the cervix and after menopause within the uterus.



The gross appearance of the tumor resembles pinkish bunch of grapes—it can be in the form of multiple polyp like structures or can be a solitary growth with pedunculated appearance.

Histologically—its characteristic finding is “rhabdomyoblast.”

**Clinical features**

The presenting features are:

- Blood stained vaginal discharge
- Anaemia and cachexia

**Management**

Chemotherapy—vincristine actinomycin D and cyclophosphamide followed by conservative surgery to excise residual tumor is the treatment of choice. Newer studies have revealed that primary chemotherapy without surgery is adequate for most patients.

**33. Ans. is d, i.e. Large cell keratinsing type**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 355*

Microscopically, endometrial carcinoma may be of following varieties:

- Adenocarcinoma (endometrioid 80%).
- Adenocarcinoma with squamous elements.
- Papillary serous carcinoma (5–10%) (virulent).
- Mucinous adenocarcinoma (5%).
- Clear cell adenocarcinoma (5%).
- Secretory carcinoma (1%).
- Squamous cell carcinoma.
- Mixed carcinoma.

**34. Ans. is b, i.e. Atrophic endometrium**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 330*

**Premalignant Lesions of Endometrium are:**

**Simple hyperplasia:** Endometrium is thick. The glands are dilated and have outpouching and invaginations. They are crowded and have irregular outlines. The stroma is more dense and cellular.

**Complex hyperplasia:** Endometrium is thicker. The gland are crowded and arranged back to back with reduced stroma. Most glands have irregular outlines. There are papillary processes and intraluminal bridges within the glands. Epithelial pseudostratification is present.

**Atypical hyperplasia:** The endometrial glands have cytologic atypia. The gland outlines are of complex hyperplasia in type. The nuclei of the glands show enlargement, irregular size and shape, hyperchromasia and coarse chromatin.

**Carcinoma-in-situ:** Commonly describes a lesion with severe cytologic as well as architectural abnormalities of the glands.

# CHAPTER

# 14B

## Gynecological Oncology: CIN Cancer Cervix



### Benign lesions of cervix

Nabothian cyst/inclusion cyst.

- Retention cysts of the cervical glands
- Seen on the external os.
- No treatment required. If at all they become large, treatment is ablation
- Endocervical polyps, treatment is polypectomy.

### Dysplasia

Represents a change in which there is *alteration in cell morphology and disorderly arrangement of the cells of the stratified squamous epithelium*. It is a premalignant lesion.

#### Characteristics of Dysplastic Cell

- Vary in size<sup>o</sup>, shape<sup>o</sup> and polarity<sup>o</sup>.
- Have altered nucleo-cytoplasmic ratio (N/C ratio is increased).<sup>o</sup>
- Have large, irregular **hyperchromatic nuclei** with marginal condensation of chromatin material.<sup>o</sup>
- Have several mitotic figures.
- The basement membrane, however, is intact and there is no stromal infiltration.

### CIN

Term **CIN (Cervical Intraepithelial Neoplasia)** has almost universally replaced WHO classification of dysplasia. It is a term used to describe the condition of cervix when a part or the full thickness of stratified squamous epithelial cells is replaced by dysplastic cells

WHO	CIN	Description	Bethesda classification
Mild dysplasia	CIN I	Dysplastic cells seen in lower 1/3 of epithelial lining of cervix	LSIL <sup>o</sup>
Moderate dysplasia	CIN II	Dysplastic cells seen in 2/3 of epithelial lining of cervix	HSIL <sup>o</sup>
Severe dysplasia	CIN III	Dysplastic cells seen in more than 2/3 of epithelial lining of cervix	HSIL <sup>o</sup>
	Carcinoma in situ	Dysplastic cells seen full thickness but basement membrane is intact	HSIL <sup>o</sup>

**In Invasive carcinoma:** Breach of basement membrane seen.

**Note :** LSIL = Low squamous intraepithelial lesion.

HSIL = High squamous intraepithelial lesion.

### Cervical Metaplasia

#### ALSO KNOW

- The cervix is composed of columnar epithelium which lines the endocervix and squamous epithelium which covers the ectocervix. The point at which they meet is known as **squamocolumnar junction** (Transformation zone).



CIN occurs at squamocolumnar junction/Transformation zone.<sup>o</sup>



Squamous metaplasia is a normal process and occurs in all young females.

- Under the influence of hormones the subcolumnar cells transform into squamous cells. This changing of one type of epithelium into the other is called as **metaplasia**.

#### Metaplastic cells are:

- Normal cells.<sup>Q</sup>
- No Nuclear atypia.<sup>Q</sup>
- Do not transform into malignant cells.<sup>Q</sup>
- Squamous metaplasia is a normal process and occurs in all young females.

#### The Transformation zone/Squamous Columnar Junction

- It lies originally at the level of external os but rarely remains restricted to the external os.
- It is a dynamic point that changes in response to puberty, pregnancy, menopause and hormone stimulation.



- With advancing age, it recedes inside the endocervix.
- It moves out during pregnancy, puberty and in females taking OCPs.

- The only way to know where original SCJ was located in a female is to look for nabothian cyst or cervical cleft opening which indicate presence of columnar epithelium.

#### Factors Predisposing to CIN/Ca Cervix

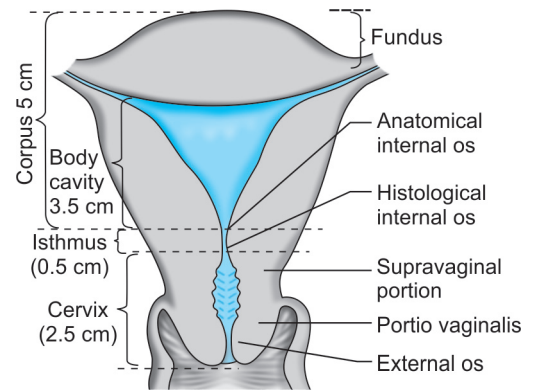
- **Human Pappiloma virus infection** (*most important*)
- **Factors increasing the risk of sexually transmitted infections-**
  - Coitus before 18 years of age<sup>Q</sup>
  - Multiple sex partners<sup>Q</sup>
  - Multiparity<sup>Q</sup>
  - Poor personal hygiene<sup>Q</sup>
  - Poor socioeconomic status<sup>Q</sup>
- Smoking<sup>Q</sup> (predisposes to squamous cell CA).
- Immunosuppressed individuals<sup>Q</sup>
- Women on OCP<sup>Q</sup> or progesterone therapy for long time, are predisposed to *adenocarcinoma* of endocervix
- In utero exposure to diethylstilbestrol (DES).

#### Human Papilloma Virus: DNA Virus

- The M/C etiological factor associated with cancer cervix is **Human Papilloma Virus (HPV)**.
- **High risk HPV** include 16, 18, 31, 33, 35, 39, 45, 52, 56, 58, 59, 68.
- **Low risk HPV** associated with genital warts are **subtypes 6 and 11**.
- Almost 80% women are infected by HPV at some point in their lives.
- HPV is epitheliotropic. It infects basal epithelial cells. The cytological changes were first recognised by **Koss and Durfee in 1956** and called as **koilocytosis**.
- Viral proteins required for malignant transformation are **E6 and E7 oncoproteins**.
- Viral proteins required for replication are **E1 and E2**.
- **HPV DNA detection is used along with pap smear as a screening procedure** in females more than 30 years of age.



- M/C HPV subtype a/w Ca cervix is HPV-16.
- HPV subtype most specific for Ca cervix is HPV-18.
- M/C HPV subtype a/w squamous cell carcinoma is HPV-16.
- M/C HPV subtype a/w adenocarcinoma is HPV-18.



**Fig. 14B.1:** Coronal section showing different parts of uterus

- **Polymerase chain reaction (PCR) or southern blot or hybrid capture technique** is used for HPV DNA detection.

### Rate of Progression of CIN

	CIN I	CIN II	CIN III
Regression to normal	60%	40%	30%
Persistence	30%	35%	50%
Progression to CIN III	10%	20%	—
Progression to cancer	< 1%	5%	20%



#### Cancers caused by HPV

##### Females

Ca cervix  
Ca vagina  
Ca vulva  
Oral Ca

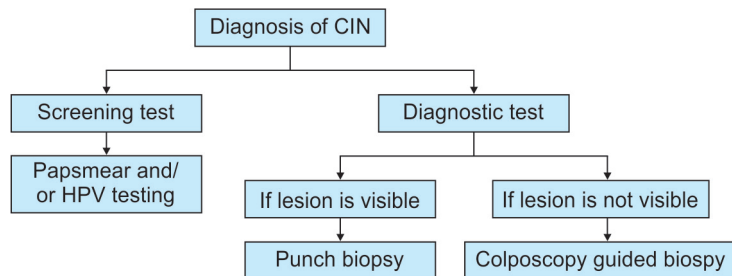
##### Males

Penile Ca  
Anal Ca  
Oral Ca

### Epidemiology of CIN

#### Age

CIN	M/c in 20–30 years
Ca in situ	30–35 years.
Ca cervix	Bimodal peak
	1st peak seen at 35–39 years.
	2nd peak seen at 55–60 years.



- For hormonal study, sample is taken from the lateral wall of vagina
- For cytological study, (Pap smear) sample is taken from the posterior wall of vagina.

### Diagnosis

#### Pap Smear (Exfoliative Cytology)

- **Time for initiating pap smear:** 21 years of age regardless of the age of first sexual intercourse.
  - **Instrument used:** Ayres spatula and endocervical brush
  - **Method:** Ayres spatula is rotated through 360° over portio vaginalis of cervix and 1st slide is prepared
- With cytobrush, 2nd slide is prepared from endocervix
- Control slide prepared from posterior wall/posterior fornix of vagina
  - **Fixative used :** 95% ethyl alcohol and ether.

**Note:** Liquid base cytology is being used now a days.

Preservative used in liquid based cytology is Methanol.

If liquid based cytology is being done it should be repeated every 2 years till female is 30 years of age then 3 yearly.



- Yearly screening can reduce the risk of cancer cervix by 91%.
- A single pap smear performed during lifetime reduces the risk of cervical cancer by 50%.

- Screening guidelines for cancer cervix are formulated by American Society for Colposcopy and Cervical Pathology (ASCCP) and have been revised by the American College of Obs and Gynae in 2013.

### Revised Guideline for Pap Smear: Cervical Cancer Screening

- Age to begin pap smear = 21 years
- Women aged 21-29 years should have a pap test every 3 years (earlier it was done annually)
- Women aged 30-65 years should have a pap test and HPV testing every 5 years. It is acceptable to have a pap test alone every 3 years.
- Women should stop having cervical cancer screening after the age of 65 years if they do not have a H/O moderate or severe dysplasia or cancer and they have had either three negative pap test results in a row or two negative co-test results in a row within 10 years, with the most recent test performed within the past 5 years.
- Women, who have a history of cervical cancer, are infected with HIV or have been exposed to DES should have annual screening done. In HIV positive females, if three consecutive tests are normal, they can have testing once in every 3 years instead of annual.

### Pap Smear Results

The pap smear report can have the following terminologies as per the Bethesda system:

- Within normal limits
- Infection (organism should be specified)
- Reactive and Reparative changes
- Atypical squamous cells of undetermined significance (ASC-US)
- Low grade squamous intraepithelial lesion (LSIL)
- High grade squamous intraepithelial lesion (HSIL)
- Squamous cell carcinoma



**In Bethesda system:** The most common cytological abnormality encountered is atypical squamous cells (ASC). The category ASC is further divided into ASCUS (atypical squamous cells of unknown significance), and ASC-H (atypical squamous cells where HSIL cannot be ruled out) which indicates cells that are suggestive of, but do not fulfill the criteria for squamous intraepithelial lesion.



The Bethesda Classification System is based on cytological results of a pap test that permits the examination of cells but not tissue structure. The diagnosis of cervical intraepithelial neoplasia (CIN) or cervical carcinoma requires a tissue sample, obtained by biopsy of suspicious lesions (done during colposcopy), to make a histologic diagnosis. That is why pap smear should always be followed by colposcopy or punch biopsy to confirm the diagnosis.

### Management Strategies of Various Cytological Abnormalities

Depending on the Report of pap smear, which is a cytological report, further investigations are done:

Pap smear report	Next step
Normal/reactive/infective	Resume pap smear as per ACOG guidelines
ASCUS	Options are: <ul style="list-style-type: none"> <li>• Repeat pap smear after 6 months</li> <li>• If female is <math>\geq 30</math> years, do HPV-DNA testing</li> <li>• If pap smear report this time is <math>\geq</math>ASCUS or if HPV-DNA testing is positive—colposcopy is done</li> <li>• Best method of following ASCUS is immediate colposcopy (biopsy)</li> </ul>
LSIL	<ul style="list-style-type: none"> <li>• Colposcopy (Gold standard) <math>\pm</math> endocervical curettage</li> <li>• If lesion is visible—punch biopsy</li> </ul>

Contd...



**Limitation of colposcopy**  
Upper 2/3rd of endocervix is not visualized by colposcopy.

Contd...

Pap smear report	Next step
HSIL	<ul style="list-style-type: none"> <li>Colposcopy (Gold standard) ± endocervical curettage</li> <li>If lesion is visible—punch biopsy</li> </ul>

**Definitive Diagnostic Procedures for CIN**

Colposcopy	Cone biopsy	Punch biopsy
Done to confirm findings of abnormal pap smear when lesion is not visible.	Done to confirm findings of colposcopy if there is a discrepancy in pap smear result and colposcopy.	Done to confirm findings of abnormal pap's when lesion is visible.

**Colposcopic Directed Biopsy**

**Colposcopy is the Gold standard technique for evaluation of an abnormal cervical cytology smear/pap smear.**

- It is an outpatient procedure that is simple, quick and well tolerated.
- It allows examination of the lower genital tract and anus with a microscope (magnification = 30 times).

**Method**

- The first step to visualize cervix under magnification.
- **Leukoplakia** must be looked for before applying acetic and otherwise it gets confused with acetowhite areas. Biopsy sample should be taken.
- Biopsy sample should also be taken from any rough area or raised area of cervix.
- Any abnormal blood vessel pattern viz reticular blood vessels, comma-shaped blood vessels or punctate blood vessels should be biopsied.
- Then 3-5% acetic acid should be applied on cervix gently but liberally.

**Principle**

- *Application of acetic acid to normal epithelium:* Glycogen producing epithelium of cervix does not produce any effect and it appears pink during colposcopy.
- *Application of acetic acid to dysplastic epithelium:* When acetic acid is applied to dysplastic epithelium which have large nuclei with abnormally large amounts of chromatin (i.e. protein), acetic acid coagulates the proteins of the nucleus and cytoplasm, making the proteins opaque and white, therefore, dysplastic cells and cancerous cells appear white (known as Aceto white areas).
- *Application of acetic acid to metaplastic epithelium:* The immature metaplastic cells have large nuclei and also show some effects of the acetic acid. Since metaplastic epithelium is very thin, it does not appear white but instead appear grey and filmy.

**Indications of Colposcopy**

- Abnormal pap smear cytology
- To locate abnormal areas<sup>Q</sup>
- To obtain directed biopsies<sup>Q</sup>
- Conservative therapy under colposcopy guidance<sup>Q</sup>
- For follow up of cases treated conservatively<sup>Q</sup>

... Shaw 14<sup>th</sup>/ed p 362



**Cervicography** refers to photographs taken from cervix

- Iodine used in schillers = 0.3%
- Iodine used in lugols = 5%
- Down staging of cancer cervix is done by simple speculum examination.



**Adenocarcinoma of cervix**  
It does not have any specific colposcopic appearance, all the abnormal blood vessels can be seen in adenocarcinoma. Since adenocarcinoma tend to develop within the endocervix, endocervical curettage is required as a part of colposcopic examination. They are best diagnosed by conization.



HPV Triage strategy for screening includes:

1. Liquid based thin layer cytology (pap smear)
2. HPV DNA testing using hybrid capture technique. If papsmear shows atypical cells and HPV DNA is positive then go to third step.
3. Colposcopy.

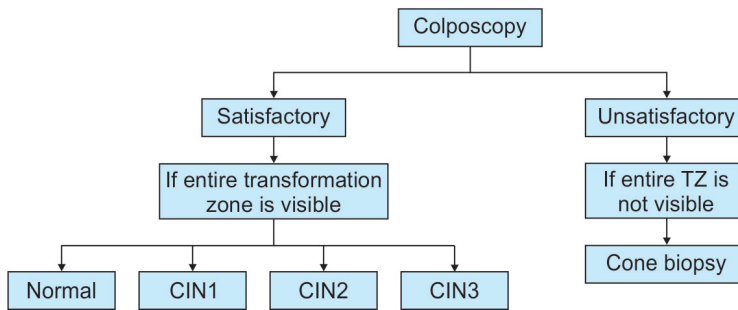
**Note:** Colposcopy, i.e. simply visualizing the cervix after application of acetic acid is used in triage screening whereas colposcopic directed biopsy is a definitive diagnostic procedure.

Absolute Contraindications	Relative contraindications
None	Anticoagulant therapy if patient requires biopsy
	Upper or lower reproductive tract infection
	Uncontrolled severe hypertension
	Uncooperative or overly anxious patient

**Abnormal findings on colposcopy indicative of dysplasia are:**

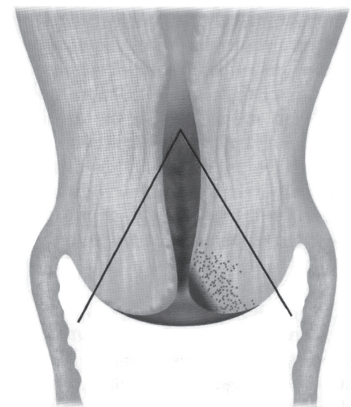
- Aceto white epithelium: Dysplastic epithelium turns white after application of acetic acid and is called as aceto white epithelium.
- Leukoplakia or hyperkeratosis: It is an area of white, thick epithelium which is appreciated prior to application of acetic acid and may indicate HPV infection/ Keratinizing CIN, Keratinizing carcinoma, Chronic trauma from diaphragm, pessary and radiotherapy.
- Mosaicism or punctuation: Reflecting abnormal vascular pattern of surface capillaries.
- Atypical vessels: With bizarre capillaries in corkscrew, comma shape or spaghettini like configuration. (They suggest early stromal invasion).

**Result-Colposcopy report is a histopathology report**



**Cone Biopsy/Conization**

- It involves removal of a cone of the cervix which includes entire squamocolumnar junction, stroma with glands and considerable part of endocervix.
- The tissue so obtained is divided into 12 to 16 segments and each one blocked and sectioned separately.
- Procedure is done under general anaesthesia.
- **Cone biopsy or conization is both diagnostic as well as therapeutic procedure.**



**Fig. 14B.2:** Cone biopsy

Indications of Cone biopsy	
Diagnostic	Therapeutic
Limits of the lesion can not be visualised with colposcopy. <sup>o</sup>	Cancer in situ in young females
The squamocolumnar junction is not seen at colposcopy. <sup>o</sup>	Cancer cervix Stage 1A1 in young females
Endocervical curettage is positive in HSIL	
Microinvasive carcinoma or adenocarcinoma in situ is suspected based on biopsy, colposcopy or cytology results	
Lack of correlation between cytology, biopsy and colposcopy results.	

**?** Cone biopsy can lead to incompetent os and subsequent recurrent second trimester abortions.

### Complications of Cone Biopsy

- Bleeding<sup>Q</sup> (M/C complication)
- Infection<sup>Q</sup>
- Cervical stenosis<sup>Q</sup>
- Incompetent os<sup>Q</sup>

### Management of CIN

#### Preventive Measures

#### HPV vaccines

- HPV vaccines have been developed from the inactivated capsid coat of the virus.
- **HPV vaccines were earlier of two types. During its Feb 2015, meeting Advisory Committee on Immunization Practises (ACIP) recommended 9-valent HPV vaccine (9V HVP) as one of the three vaccines for preventive HPV.**

Characteristic	Bivalent (2V HPV)	Quadrivalent (4V HPV)	9 Valent (9V HPV)
Brand name	Cervarix	Gardasil	Gardasil-9
HPV subtypes	16, 18	6, 11, 16, 18	6, 11, 16, 18, 31, 33, 45, 52, 58
Protects against	CIN, Ca cervix	Anogenital warts, CIN, Ca cervix	Anogenital warts CIN, Ca cervix, vulva intraepithelial neoplasia, vaginal intraepithelial neoplasia
Manufacturer	GlaxoSmithKline	Merck & Co	Merck & Co
Manufacturing	Trichoplusia insect line infected with L1 encoding baculovirus	Saccharomyces cerevisiae expressing L1	Saccharomyces cerevisiae expressing L1
Adjuvant	500 mcg aluminium hydroxide with monophosphoryl	225 mcg Al(OH) PO <sub>4</sub> SO <sub>4</sub>	500 mcg Al(OH) PO <sub>4</sub> SO <sub>4</sub>
Dose	0.5 ml	0.5 ml	0.5 ml
Administration	1/m	1/m	1/m
Administered to males or females	Only females	Both males and females	Both males and females
Age in females Ideal age range	11-12 years 9-26 years	11-12 years 9-26 years	11-12 years 9-26 years
Age in males Ideal age range	×	11-12 years 9-26 years	11-12 years 9-15 years—FDA approved 9-26 years—ACIP recommendation



#### Age group for HPV vaccine

Ideal = 11 to 12 years  
Can be given from 9 to 26 years.

#### Contraindications

- Pregnancy
- Hypersensitivity

#### Important points:

- For population who are seronegative and HPV-DNA negative for HPV 16 and HPV 18 at vaccination and have received all three dosages of vaccine. The efficacy is 100%.



- This protection is documented to last for 6.4 years to 7.5 years after vaccination
- To increase the period of efficacy they are combined with an adjuvant.
  - Adjuvant in quadrivalent vaccine and 9 valent vaccine: Aluminium hydroxyphosphate sulfate.
  - In bivalent vaccine: Aluminium hydroxide combined with monophosphoryl lipid A.
  - These adjuvants are theorized to function as a link between HPV and activation of innate immune system.

**?** Screening practises should remain same in both vaccinated and unvaccinated persons.

**Definitive Treatment**

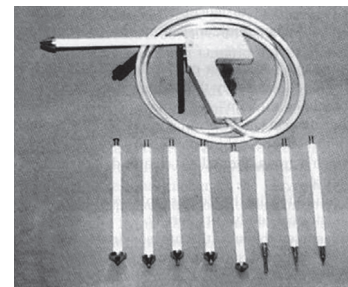
**Options**

Ablative methods	Surgical Excisional methods
<ul style="list-style-type: none"> <li>• Cryosurgery</li> <li>• Laser ablation or vaporization</li> </ul>	<ul style="list-style-type: none"> <li>• Large loop excision of transformation zone (LLETZ) or loop electroexcisional procedure.(LEEP)</li> <li>• Conization</li> <li>• Hysterectomy</li> </ul>
<p><b>Aim:</b> To destroy the entire transformation zone of the cervix (upto to a depth of 6–8 mm from the surface).</p>	
<p>Major disadvantage is follow up with histopathological examination, is not possible after the procedure as SCJ recedes into the endocervix.</p>	

**Comparison of Ablative Techniques for Managing CIN**

**Ablative techniques for CIN management**

Cryotherapy	CO <sub>2</sub> Laser
<ul style="list-style-type: none"> <li>• Destroys the surface epithelium of cervix by crystallising intracellular water.</li> <li>• Aim should be to produce an ice ball that extends 5-10 mm beyond the margin of lesion.</li> </ul>	<ul style="list-style-type: none"> <li>• Best method to treat CIN I/II if it extends to vaginal fornices.</li> </ul>
<ul style="list-style-type: none"> <li>• Temp = -22°C Agent used = N<sub>2</sub>O or CO<sub>2</sub></li> </ul>	
<ul style="list-style-type: none"> <li>• Depth of destruction = 5 mm. (Method = freeze – thaw – freeze = 3 min- 5 min- 3 min).</li> <li>• Aim should be produced.</li> </ul>	<ul style="list-style-type: none"> <li>• Depth of destruction = 7 mm.</li> </ul>
<ul style="list-style-type: none"> <li>• Can be used only if, lesion is on ectocervix. (Not on endocervix.)</li> </ul>	<ul style="list-style-type: none"> <li>• Major advantage: It can be used if vaginal extension of CIN is present.</li> </ul>
<ul style="list-style-type: none"> <li>• No evidence of microinvasive/invasive cancer.</li> <li>• Vagina is not involved.</li> </ul>	<ul style="list-style-type: none"> <li>• No evidence of microinvasive invasive cancer.</li> </ul>
<ul style="list-style-type: none"> <li>• Postoperative complication M/C vaginal discharge cervical stenosis or cervical dystocia (uncommon)</li> </ul>	<ul style="list-style-type: none"> <li>• No vaginal discharge</li> </ul>



**Fig. 14B.3:** Cryosurgery probe

**Criteria for employing ablative methods for treating CIN:**

- Entire lesion should be visualised within the transformation zone (TZ)
- Noevidence of microinvasion or macroinvasion.
- No endocervical glandular involvement
- No discrepancy in cytology, colposcopy and biopsy report.

### LEEP (Loop electro excisional procedure)/LLETZ (Large loop excision of transformation zone)

- A loop of very thin stainless steel wire is used for excision of the transformation zone. The tissue effect of electricity depends on size of loop and wattage. If a low power or large diameter wire is used, effect is electrocautery and tissue damage is more. If high watt (35-55 w) & small loop (0.5 mm) is used effect is electrosurgical.
- Done under local anaesthesia
- Tissue upto a depth of 10 mm or more can be removed and sent for histopathological examination.
- Complications are minimal.
- **Currently, it is the method of choice for treating CIN II and CIN III at any age.**

LEEP/LLETZ is the best management of CIN III in all age groups .  
Earlier in females < 40 yrs: LEEP was the procedure of choice and in females > 40 yrs hysterectomy was the choice but now for all age groups TOC is LEEP/LLETZ.

### Hysterectomy indications: Earlier, it was TOC for treating CIN in females > 40, but now it is done only if –

- Other associated gynecological problems (fibroid, prolapse) which need hysterectomy
- Adenocarcinoma in situ in females
- Recurrent/repetitive CIN 2/3 despite less invasive treatment in females who have completed their family.
- Patients not willing for follow-up.

#### Stagewise Management of CIN:

- CIN I – observation. Do yearly HPV - DNA testing or Papsmear every 6–12 months. If HPV DNA testing is negative or 2 consecutive papsmear are negative then return to routine screening.

If HPV DNA is positive or Pap smear show lesions as ASC – US (atypical squamous cells of unknown significance) ,ASC-H (Atypical squamous cells – HSIL cannot be ruled out) or higher lesions like CIN, 2 then do colposcopy.

**Note:** If CIN I occurs in adolescent age group - follow up with annual cytology. In these patients follow up with HPV – DNA is not useful.

- CIN I persists for 2 years – Cryotherapy/LEEP.
- CIN II – LEEP or cryotherapy
- CIN III – LEEP (any age group)
- Recurrent CIN III – Hysterectomy
- CIN extending to vaginal fornices – Laser ablation/Hysterectomy.

### Cervical Glandular Intraepithelial Neoplasia (CGIN)

- It is a rare premalignant condition often diagnosed on a cervical cone removed for CIN.
- IOC: Cone Biopsy. Screening with cytology and colposcopy not effective
- TOC: Hysterectomy if family is completed
- Diagnostic excisional procedure can be considered for women who want to maintain fertility. An endocervical curettage needs to be performed at the time of the resection.

### Cancer Cervix

#### Epidemiology

- Cervical cancer is overall the most common gynaecological malignancy in the world, and the second most frequently diagnosed cancer in women worldwide after breast cancer (*John Hopkins Manual of Obs and Gynae. p 541*)

Incidence of major genital malignancies per 100,000 women

	Developed countries	Developing countries
Ca cervix	4-15	30-40
Ca body uterus	10-20	5
Ca ovary	12-15	4-6

- M/C age group-Bimodal peak = 1st peak seen at 35–39 years
- 2nd peak seen at 60 to 65 years.
- Mean age for cervical cancer = 52.2 years.
- M/C in low socioeconomic status.

### Risk Factors

Same as CIN

### Screening

- i. By paps test (as discussed)
- ii. **Downstaging for cervical cancer** is defined as “the detection of the disease at an earlier stage when it is still curable. Detection is done by nurses and other paramedical health workers using a simple speculum for visual inspection of the cervix”. Compared to cytological screening it is suboptimal. But in places where prevalence of cancer is high and cytological screening is not available, “downstaging screening” is useful. **The strategy is, however, not expected to lower the incidence of cancer cervix, but it can certainly minimize the cancer death through early detection.**

### Downstaging Procedure

A female primary health care worker is trained for 2–3 weeks to perform speculum examination. They are trained to distinguish a normal cervix from an abnormal one.

### Characters of a normal cervix

Pink in color, round in shape, smooth surface and does not bleed on touch. Whereas an abnormal cervix has the following characters—reddish, red or white area of patch, growth or ulcer on the surface and bleeds on touch.

Once the abnormality is suspected, the case is referred to a center where diagnosis and treatment of premalignant and malignant lesions are done.

### Pathogenesis

Endocervix is lined by columnar epithelium and ectocervix is lined by squamous epithelium. Thus in all females in the cervix columnar epithelium changes to squamous epithelium, i.e. metaplasia occurs normally in the cervix and is physiological (not premalignant). The site at which this change occurs is called the transformation zone.

The metaplastic cells, when they get disorganised under the influence of some carcinogenic factor like HPV, it results in dysplasia. Dysplasia is not physiological and is premalignant.

- Thus M/C site for cancer cervix will be where cells are changing from one type to other, i.e. transformation zone.
- M/C histological variety of cancer cervix is squamous cell carcinoma.
- Since endocervix is lined by columnar epithelium, hence adenocarcinoma can also be seen.
- M/C site for adenocarcinoma will be endocervix.



M/C gynaecological cancer in developed countries– Endometrial cancer  
M/C gynaecological cancer in developing countries- Cancer cervix  
Overall M/C gynaecological cancer worldwide -Cancer cervix due to increase in incidence of the cancer.



Down staging of cancer cervix is done by per speculum examinations

## Histology

Squamous cell carcinoma (Epidermoid carcinoma)	Adenocarcinoma
<ul style="list-style-type: none"> <li>Accounts for 80% of carcinoma cervix<sup>o</sup></li> <li>Arises from squamocolumnar junction<sup>o</sup></li> <li>Squamous cell carcinoma can be further classified as:               <div style="text-align: center;"> <pre> graph TD           A[Squamous cell carcinoma] --&gt; B[Large cell Keratinizing type (M/C)]           A --&gt; C[Large cell non Keratinizing type]           A --&gt; D[Small cell Worst prognosis]           A --&gt; E[Ca Verrucous Ca associated with HPV-6]           E --- F["Slow growing, locally invasive neoplasm. Radical resection is the mainstay of therapy. It resembles condyloma accuminata."]               </pre> </div> </li> </ul>	<ul style="list-style-type: none"> <li>Accounts for 20% of carcinoma cervix<sup>o</sup></li> <li>Arises from endocervix<sup>o</sup></li> <li>M/C in young females</li> <li>Recently increased in incidence because of use of OCP, Progesterone pills for long time.</li> <li>M/C subtype of adenocarcinoma is mucinous endocervical adenocarcinoma. associated with HPV 18. Adenoma malignum is an extremely well differentiated adeno CA with favourable diagnosis</li> </ul>



- M/C cause of death in patients of Ca cervix is renal failure.
- lInd M/C common cause of death is haemorrhage.

## Clinical Features

### Symptoms

- **Bleeding per vagina:** Most common symptom is irregular vaginal bleeding. Most specific symptom-postcoital bleeding.
- **Discharge:** It is at first creamy and later becomes dirty brown in colour and is very offensive<sup>o</sup>. The odour is caused by infection of necrotic tissue with saprophytes.

### Symptoms of Advanced Stage

- Deep pelvic pain<sup>o</sup> often unilateral and radiating to hip or thigh.
- Urinary incontinence, dysuria, increased urinary frequency, ureteric colic.
- Rectal pain
- Low backache/Flank pain due to hydronephrosis.
- Triad of sciatic pain, leg edema and hydronephrosis is associated with extensive pelvic involvement by tumor.
- Weight loss, anorexia, malaise, etc.

### Signs

- Four cardinal signs:
  - Hardness<sup>o</sup>
  - Friability<sup>o</sup>
  - Fixation<sup>o</sup>
  - Bleeds on touch<sup>o</sup>

## Complications

**Mnemonic:** Private FUND

... Jeffcoates 7<sup>th</sup>/ed p 472

<b>Private</b>	<b>Pyometra</b>
<b>F</b>	<b>Fistula:</b> <ul style="list-style-type: none"> <li>- Vesico vaginal</li> <li>- Vesico cervical</li> <li>- Recto vaginal</li> </ul>
<b>U</b>	<b>Uraemia</b>
<b>N</b>	<b>Nephrosis:</b> <ul style="list-style-type: none"> <li>- Hydronephrosis</li> <li>- Pyonephrosis</li> </ul>
<b>D</b>	<b>Death (most common cause of death is uraemia).</b>

**Mode of Spread**

- **Direct extension:** The tumor spreads directly to adjacent organs viz uterus, vagina.  
**Note:** In staging of cervical cancer, extension of tumor to the uterus is disregarded i.e. it doesnot change the stage of cancer.
- **Lymphatic spread:** The lymphnodes involved in cancer cervix are:

Primary group	Secondary group
<b>H</b> = Hypogastric	Common iliac
<b>O</b> = Obturator	Para aortic
<b>P</b> = Presacral and parametrial	Inguinal
<b>E</b> = External iliac	

➤ **Hematogenous spread**

- M/C route of spread – Lymphatic
- M/C site involved after hematogenous spread – lungs
- M/C site involved is: Lymphnodes.

**Staging**

Staging for cancer cervix is clinical and requires a set of investigations -as recommended by FIGO.

Physical examination	Radiological studies	Procedure
<ul style="list-style-type: none"> <li>• Palpate lymph node</li> <li>• Examine vagina</li> </ul>	<ul style="list-style-type: none"> <li>• Chest X-ray</li> <li>• Skeletal X Ray</li> </ul>	<ul style="list-style-type: none"> <li>• Biopsy</li> <li>• Conisation</li> </ul>
<ul style="list-style-type: none"> <li>• Bimanual rectovaginal examination</li> </ul>	<ul style="list-style-type: none"> <li>• IVP</li> </ul>	<ul style="list-style-type: none"> <li>• Endocervical Curettage</li> </ul>
	<ul style="list-style-type: none"> <li>• Barium enema</li> </ul>	<ul style="list-style-type: none"> <li>• Colposcopy</li> </ul>
		<ul style="list-style-type: none"> <li>• Hysteroscopy</li> </ul>
		<ul style="list-style-type: none"> <li>• Cystoscopy</li> </ul>
		<ul style="list-style-type: none"> <li>• Proctoscopy</li> </ul>

**FIGO Staging of Cancer Cervix**

**Stage I:** Carcinoma confined to cervix (extension to corpus is disregarded)

- A = Microscopic cancer (<5 mm depth and <7 mm wide)
- A1 = < 3 mm deep.
- A2 = 3-5 mm deep.
- B = Clinically visible lesion
- B1 = < 4 cms in size
- B2 = ≥ 4 cms in size



- M/C lymph node involved in Ca cervix is obturator LN
- Sentinel lymph node is-Para cervical or ureteric LN



Sentinel lymph node biopsy is most useful in which gynaecological cancer - Vulval cancer > cervical cancer.



**Remember**

USG/CT scan /MRI/PET Laparoscopy/Laparotomy and lymphangiography are not included in the investigations approved by FIGO.



Mnemonic for the various procedures advised by FIGO: BS4C Exam  
**B** = **B**iopsy  
 S<sub>4</sub>-4 types of scopy's i.e hysteroscopy/colposcopy/cystoscopy/proctoscopy  
**C** = **C**onization  
**Exam** = **E**ndocervical curettage



The most important prognostic factor for cancer cervix is clinical stage

- LN status > Depth of invasion

**Stage II:** Carcinoma involves upper 2/3rd of Vagina

A = Parametrium not involved

B = Parametrium involved

**Stage III:** Carcinoma involves lower 1/3rd of Vagina

A = Pelvic side wall not involved

B = Pelvic sidewall involved/non functioning kidney, hydronephrosis, hydroureter

**Stage IV:** Metastasis of the carcinoma

A = Regional Metastasis (bladder and/or rectum involved)

B = Distant metastasis

#### Revised Staging for Ca Cervix

Stage I = No change

Stage IIA = Without parametrial involvement is further divided into-

A1 Tumor size < 4 cms size

A2 Tumor size  $\geq$  4 cms size

Stage IIB = No change

Stage III/ IV = No Change.

#### Note:

- In staging, ureter is involved in stage 3B. Bladder is involved in stage 4A.
- Ovaries are not involved by cancer cervix
- Superficial inguinal lymphnodes are not involved by Ca cervix.

## Management of Cancer Cervix

### Principle

- All stages of cancer cervix (I-IV) are radiosensitive
- Stages of Ca cervix that are operable (Radical/Wertheim's hysterectomy) are IA1, IA2, IB, and IIA
- Stages IIB-IV are not operable and have to be treated with radiotherapy only
- In squamous cell cancers, before giving radiotherapy, a chemotherapeutic agent is given to increase the sensitivity of the cells to radiation called as radiosensitiser.
- In cancer cervix cisplatin is used as a radiosensitiser, so from stages IIB to IVA-management of choice is chemoradiation.
- Use of cisplatin has resulted in reduction in local recurrence and distant metastasis.
- Stages IA1, IA2, IB1 are radiosensitive and surgically operable, but surgery is preferred over radiotherapy for these stages because of the following reasons:
  - Preservation of ovarian function
  - Preservation of vagina for coital function
  - Psychological benefit to the patient
- Other indications for the selection of radical surgery over radiation-
  - Concomitant inflammatory bowel disease.
  - Previous radiation for any other disease
  - Presence of simultaneous adenexal neoplasm.
- In stages IB2, IIA1, IIA2 - Recent studies have shown better results with chemoradiation than surgery.

### Surgery in Cancer Cervix

#### Hysterectomy depends on stage:

- In stage IA1 - simple hysterectomy (Type I)

- > In stage IA2 - Wertheim's hysterectomy (Type II)
- > In stage IB1 - Radical hysterectomy (Type III)
- > Ca cervix almost never spreads to ovary so when radical hysterectomy is done, oophorectomy is not required in young females

- > Radical trachelectomy-involves **removal of 80% cervix, parametria (Mackenrodt's ligaments) and vaginal cuff along with pelvic lymphadenectomy**
- > Radical trachelectomy is an option for women with stage IA2 and IB1 disease who desire uterine preservation and fertility.
- > **Indication** of doing trachelectomy-Low risk disease
  - Negative nodes
  - Size of tumor <2 cms
- > A cerclage is done between uterus and vagina after the procedure
- > If patient conceives after trachelectomy-do cesarean section.

### Radiation in Cancer Cervix

Radiation treatment plan in cancer cervix consists of a combination of:

#### i. External beam radiotherapy (EBRT)

- Isotope used Cesium
- EBRT is done to treat the regional lymphnodes and to decrease the tumour volume.

#### ii. Brachytherapy:

- > EBRT is followed by brachytherapy delivered by intracavitary application to provide a treatment boost to the central tumour.
  - Intracavitary therapy alone may be used in patients with early disease with negligible incidence of lymph node metastasis
  - Isotopes used:
    - » Low-dose rate technique Cs-137
    - » High-dose rate techniques Ir-192.
  - Intensity modulated radiation therapy (IMRT) computer-generated algorithms that accurately distinguish between target treatment volumes and normal tissue.
  - Two important reference points in the brachytherapy of cancer cervix are:

	Point A	Point B
Location	2 cm above and 2 cm lateral to external os	2 cm above and 5 cm lateral to external os
Structure present	Paracervical/parametrial lymph node	Obturator lymph node
dose of radiation	8000 cGy or 80 Gy	6000 cGy or 60 Gy

- > ABS criteria (American Brachytherapy Society):
  - Point A: Early stage - Dose 80-85 Gy  
Locally advanced - stage ( $\geq$  IB2) = 85-90 Gy
  - Point B: Early stage - 50-55 Gy  
Late stage - 55-60 Gy

**Note:** In routine pelvic radiation - inguinal lymphnodes are not included.



Management of cancer cervix Stage III B is chemoradiation if it is not given in the options go for radiotherapy alone and not chemotherapy.



Cancer cervix does not involve:

- Ovaries
- Inguinal lymphnodes



In young females with cancer cervix while performing radical hysterectomy/ Wertheim's hysterectomy structure which should not be removed is ovaries.



Radiation therapy should not be used in patients with diverticulosis, pelvic or tubo ovarian abscess.

### Stagewise Management of Ca Cervix

Stage	Management	Comment
Stage IA1	<b>No lymphovascular space invasion</b> <b>Young female</b> - conization <b>Older female</b> - simple hysterectomy with bilateral salpingo-oophorectomy <b>In case of LVSI</b> <b>Young females</b> - Radical Trachelectomy and pelvic lymphadenectomy <b>Older females</b> - Simple or Wertheim's hysterectomy with pelvic lymphadenectomy	Pelvic lymphadenectomy is not needed as <1% chances of pelvic node metastasis No postoperative management
Stage IA2	<b>Family not complete</b> Radical trachelectomy and pelvic lymphadenectomy <b>Family complete</b> Wertheim's hysterectomy (Type II) with pelvic lymphadenectomy	Incidence of nodal metastasis—3 to 8% Postoperative management given if intermediate or high-risk factors present
Stage IB1	<b>Family not complete</b> If size of tumor < 2 cms, radical trachelectomy, pelvic lymphadenectomy and para aortic LN sampling <b>Family complete</b> Wertheim's hysterectomy (Type II) with pelvic and para aortic lymphadenectomy	Postoperative management given if intermediate or high-risk factors present
Stage IB2 and IIA	<b>Both options</b> • Primary chemoradiation (better) • Surgery: Type III radical hysterectomy, pelvic lymphadenectomy and para aortic lymphadenectomy	Postoperative management given
Stage IIB-IIIB	Chemoradiation	Cisplatin used as radiosensitizer
Stage IV	CT and palliative pelvic radiation therapy	



#### Intermediate risk factors:

##### 3S

Size-large

Stromal invasion > 1 cms deep

Lymph vascular Space invasion present.

#### High risk factors include:

##### 3Ps

Positive margins

Positive lymphnodes

Parametrial involvement.

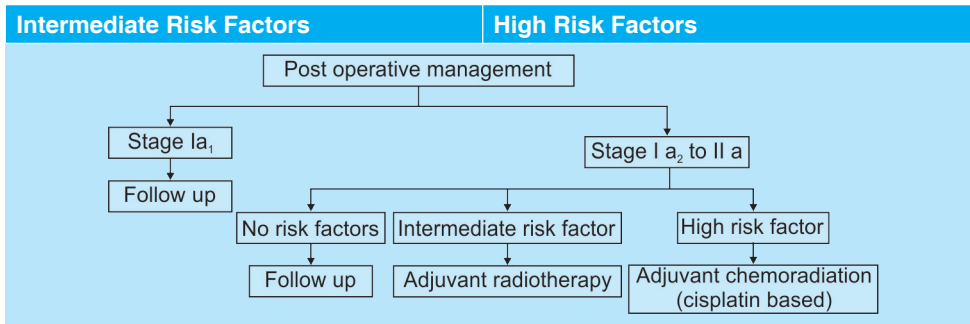
### Post Operative Management of Cancer Cervix

Once surgery is performed in cancer cervix, patient is reassessed for the presence or absence of risk factors:

Intermediate Risk factors	High Risk Factors
• Large tumor size	• Positive or close margins
• Cervical stromal invasion to middle or deep one third (> 1 cms)	• Positive lymphnodes
• Lymph vascular space invasion	• Microscopic parametrial involvement

Contd...





### Comparison Between Surgery and Radiotherapy for Management of Cancer Cervix

	Surgery	Radiation
Survival	85%	85%
Serious complications	Urological fistulas 1-2%	Interstinal and urinary strictures and fistulas 1.4–5.3%
Vagina	Initially shortened but may lengthen with regular intercourse	Fibrosis and possible stenosis, particularly in postmenopausal patients
Ovaries	Can be conserved	Destroyed
Chronic effects	Bladder atony in 3%	Radiation fibrosis of bowel and bladder in 6–8%
Surgical mortality	1%	1% (from pulmonary embolism during intracavitary therapy)



- Cervical cancer is the M/C malignancy in pregnancy.
- Symptoms of cervical cancer in pregnant and non pregnant women remain same

### Carcinoma Cervix in Pregnancy

Cancer cervix is the most common malignancy in pregnancy.

- PAP smear should be performed ideally on all pregnant women at the first antenatal visit and if required colposcopy and biopsy should be done. Punch biopsy can also be performed any time during pregnancy
- If there is a need to perform a diagnostic cone biopsy, it should be done in second trimester – (12-20 weeks)
- **CIN 1, 2 & 3** can be managed after pregnancy, vaginal delivery is possible
- Treatment modalities for Ca cervix are same as in nonpregnant women
- Cervical stage is the most important prognostic factor for cervical cancer during pregnancy
- **Stage 1A1:** vaginal delivery and then simple extrafascial hysterectomy or therapeutic conization after 6 weeks postpartum. If cesarean is being done it can be followed by hysterectomy directly.
- **Stage 1A2:** vaginal delivery and then Wertheim's hysterectomy and pelvic lymph node dissection after 6 weeks or immediately after cesarean section.
- **Stage, 1B, IIA:** If detected in first trimester = immediate Wertheim's hysterectomy on pregnant uterus.
- If detected in late second or third trimester: wait (treatment can be delayed up to 4-6 weeks) for fetal lung maturity and then classical caesarean section followed immediately by Wertheim's hysterectomy
- **Stage IIB-IV :** If detected in first trimester: Immediate radiotherapy (patient will spontaneously abort before 4000 cGY are delivered. If detected in late second or third trimester wait for fetal maturity, classical caesarean section and then radiotherapy begun postoperatively.

### Recurrent Cervical Cancer

- Cervical cancer detected within **first 6 months** of treatment is termed as **persistent** cancer. Disease diagnosed **≥6 months later** is **recurrent cancer**.
- Treatment of recurrent cervical cancer depends on the mode of primary therapy and the site of recurrence.
- Patients who were treated initially with surgery should be considered for radiation therapy and those who had radiation therapy should be considered for surgical treatment. (Pelvic exenteration surgery).
- Chemotherapy is palliative only and is reserved for patients who are not considered curable by either surgery or radiation therapy.



Cervical cancer detected within first 6 months of treatment is termed as persistent cancer. Disease diagnosed after 6 months is recurrent cancer

#### Stump Carcinoma

- Rare these days
- Earlier it was common when subtotal hysterectomy was done.
- It developed 2 years after hysterectomy.
- Incidence = 1%.

#### Treatment

- Early stages – surgery – Radical parametrectomy with upper vaginectomy and pelvic lymphadenectomy, i.e. cervix + upper vagina + parametrium + LN removed.
- Advanced stages – Radiotherapy.

## QUESTIONS

### CIN

1. True about CIN: (PGI Dec 04)
  - a. Premalignant lesion
  - b. HPV predisposes
  - c. Pap smear can detect it
  - d. Chlamydia infection can predispose
  - e. Occurs at squamocolumnar junction
2. A patient is diagnosed to have CIN II. She approaches you for advice. You can definitely tell her the risk of malignancy as: (AI 98; AIIMS 01)
  - a. 15%
  - b. 60%
  - c. 30%
  - d. 5%
3. All of the following changes are seen in dysplasia of squamocolumnar junction, except: (AIIMS 97)
  - a. Breaking of basement membrane
  - b. Change of epithelium
  - c. Hyperchromatic nuclei
  - d. Increased mitotic figure
4. In a cervix low grade squamous intraepithelial lesion (LSIL) in Bethesda system includes: (PGI May 2010)
  - a. CIN 1
  - b. CIN 2
  - c. CIN 3
  - d. Squamous metaplasia
5. Pap smear is useful in the diagnosis of all EXCEPT: (AIIMS May 02)
  - a. Gonorrhoea
  - b. Trichomonas vaginalis
  - c. Human papilloma virus
  - d. Inflammatory changes
- 6A. Acetic acid staining of cervix shows following except: (AIIMS May 02)
  - a. Squamous dysplasia
  - b. Cervical carcinoma in situ
  - c. Cervical polyp
  - d. Cervical dysplasia
- 6B. Colposcopic features suggestive of malignancy are all except: (PGI 99)
  - a. Condyloma
  - b. Vascular atypia
  - c. Punctuation
  - d. White epithelium
- 6C. In colposcopy following are visualised except:
  - a. Upper 2/3rd endocervix
  - b. Cervical carcinoma in situ
  - c. Cervical polyp
  - d. Cervical dysplasia
- 6D. All of the following are indications of colposcopy: (PGI Dec 05)
  - a. Suspicious pap smear
  - b. Obvious mass seen
  - c. Suspected invasive carcinoma
  - d. Patient who refuse biopsy
7. Rekha a 45-year-old woman has negative pap smear with +ve endocervical curettage. Next step in management will be: (AI 01)
  - a. Colposcopy
  - b. Vaginal hysterectomy
  - c. Conization
  - d. Wertheim's hysterectomy
8. Pap smear of Lelawati 45 years female shows CIN grade III. Which of the following is the next step in management: (AIIMS 00)
  - a. Punch biopsy
  - b. Large loop excision
  - c. Colposcopy directed biopsy
  - d. Cone biopsy
9. Cone biopsy is indicated in all the following conditions except: (AIIMS 00)
  - a. Indefinite diagnosis on colposcopy
  - b. CIN-III
  - c. Cervical metaplasia
  - d. Microinvasive carcinoma
10. Cone biopsy of cervix is indicated in all cases showing: (PGI 04)
  - a. Parametrial invasion
  - b. Abnormal pap smear
  - c. Endometrial Ca
  - d. Endocervical curettage positive
  - e. Clear cell Ca
11. Therapeutic conisation is indicated in: (AIIMS 00)
  - a. Microinvasive carcinoma
  - b. CIN (III)
  - c. Unsatisfactory colposcopy with cervical dysplasia
  - d. Cervical metaplasia
12. Young lady comes with mild erosion of cervix and pap smear shows dysplasia, next step is: (PGI Dec 98)
  - a. Antibiotics
  - b. Colposcopy
  - c. Cryosurgery
  - d. Conization
13. A 45 years old lady complains of contact bleeding. She has positive pap smear. The next line of management is: (AIIMS 99)
  - a. Colposcopy directed biopsy
  - b. Cone biopsy
  - c. Repeat pap smear
  - d. Hysterectomy
14. A 35-year-old lady with post coital bleeding management is: (AIIMS Nov 09; May 08)
  - a. Clinical examination and pap smear
  - b. Visual examination with lugol iodine
  - c. Visual examination with acetic acid
  - d. Colposcopy
15. Treatment of choice of stage III CIN in 40-year-old female is: (AIIMS 97; PGI 96)
  - a. Hysterectomy
  - b. Laser coagulation
  - c. Cryocoagulation
  - d. Cone excision
16. A 40-year-old woman presents with abnormal cervical cytology on PAP smear suggestive of CIN (III). The next best step in management is: (AI 2010)
  - a. Hysterectomy
  - b. Colposcopy and LEEP
  - c. Colposcopy and cryotherapy
  - d. Conization

17. A female 35 years P3 L3 with CIN III on colposcopic biopsy what would you do? (AI 09)  
 a. LEEP                                      b. Conization  
 c. Hysterectomy                          d. Cryotherapy
18. A 55-year-old lady presenting to out patient department (OPD) with postcoital bleeding for 3 months has a 1 × 1 cm nodule on the anterior lip of cervix. The most appropriate investigation to be done subsequently is: (AI 03)  
 a. Pap smear                                  b. Punch biopsy  
 c. Endocervical curettage                  d. Colposcopy
19. A 50-year-old women present's with post coital bleeding. A visible growth on cervix is detected on per speculum examination. Next investigation is: (AI 01)  
 a. Punch biopsy                              b. Colposcopic biopsy  
 c. Pap smear                                  d. Cone Biopsy
20. Meena 45-years-old female presents with post coital bleeding. On per speculum examination a friable mass is found in cervix. Next step in management is: (AIIMS Nov 00)  
 a. Colposcopy directed biopsy  
 b. 6 monthly pap smear  
 c. Only observation  
 d. Punch biopsy
21. A patient complaints of post coital bleed; no growth is seen, on per speculum examination; next step should be: (AI 01)  
 a. Colposcopy biopsy                      b. Conisation  
 c. Repeat pap smear                        d. Culdoscopy
22. Investigation of choice in postcoital bleeding in a 60-year-old lady is: (AIIMS 96, 97; AI 96)  
 a. Pap smear                                  b. Colposcopy and biopsy  
 c. Pelvic ultrasound                        d. Cone excision of cervix

## CARCINOMA CERVIX

23. True about Ca cervix: (PGI Dec 06)  
 a. 90% associated with HPV  
 b. Nulliparity  
 c. OCP  
 d. Immunocompromised patients
24. Predisposing factors for Ca cervix: (PGI Dec 08)  
 a. Multiple sex partners                  b. Genital warts  
 c. HPV 16, 18                                d. Virginity  
 e. Late menarche
25. Risk factor for Ca Cervix: (PGI Dec 04)  
 a. HPV    b. Smoking  
 c. Late Menarche                          d. Nulliparity  
 e. Early sexual intercourse
26. Carcinoma cervix is more common in: (PGI 01)  
 a. HIV patient                                b. Multiparity  
 c. Smoking                                    d. Nulliparity  
 e. Family history
27. Which of the following is not a risk factor for CA cervix? (AIIMS Nov 2013)  
 a. Low parity  
 b. Multiple sexual partner  
 c. Early sexual intercourse (< 16 years)  
 d. Smoking
28. M/C agent responsible for Ca cervix is: (AI 07)  
 a. HPV 16                                      b. HPV 18  
 c. HPV 31                                      d. HPV 36
29. HPV associated with adenocarcinoma of cervix: (PGI 05)  
 a. Type 6                                      b. Type 18  
 c. Type 11                                     d. Type 42
30. Most common type of human papilloma virus causing Ca cervix are: (PGI 03)  
 a. 16 and 18                                  b. 1 and 33  
 c. 6 and 11                                    d. 2 and 14  
 e. 2 and 5
31. High risk HPV includes: (PGI 02)  
 a. Type 16                                      b. Type 18  
 c. Type 11                                      d. Type 12
32. HPV type teast commonly associated with carcinoma cervix: (PGI Nov 2012)  
 a. 6    b. 11  
 c. 16    d. 18  
 e. 33
33. Cervix carcinoma arises from: (PGI Dec 08)  
 a. Squamocolumnar junction  
 b. Isthmus  
 c. Cervical lip  
 d. Internal os
34. Earliest symptom of carcinoma cervix is: (PGI 99)  
 a. Irregular vaginal bleeding  
 b. Post coital bleed  
 c. Foul smelling discharge  
 d. Pain
35. A case of carcinoma cervix is found in altered sensorium and is having hiccups. Likely cause is: (AI 01)  
 a. Septicemia                                b. Uremia  
 c. Raised ICT                                 d. None of the above
36. Which investigation is not done in FIGO staging of CA cervix: (AIIMS 96)  
 a. Cystoscopy                                b. Chest X-ray  
 c. Pelvic ultrasound                        d. IVP
37. All of the following investigations are used in FIGO staging of carcinoma cervix except: (AIIMS Nov 08)  
 a. CECT                                        b. Intravenous pyelography  
 c. Cystoscopy                                d. Proctoscopy
38. Carcinoma cervix extends upto lateral pelvic wall. The stage would be: (AI 97)  
 a. Stage I                                      b. Stage II  
 c. Stage III                                    d. Stage IV
39. Which is/are feature(s) of stage Ib2 cancer cervix: (PGI Nov 12)  
 a. Microinvasive carcinoma with stromal invasion <3 mm  
 b. Microinvasie carcinoma with stromal invasion <5 mm  
 c. Microinvasive carcinoma with 6mm carcinoma with stromal invasion >5 mm  
 d. Size of lesion ≤ 4 cm  
 e. Size of lesion > 4 cm

40. Which of the following statements about squamous cell carcinoma of cervix is false: (AI 08)
- Common at squamocolumnar junction
  - CT scan is mandatory for staging
  - Post coital bleeding is a common symptom
  - HPV 16 and 18 are associated with high risk of carcinogenesis
41. In Ca cervix lymphatic spread involve which of the following lymph node/nodes: (PGI 02)
- Obturator LN
  - External iliac LN
  - Inguinal LN
  - Femoral LN
  - Hypogastric LN
42. LN involved in cervical cancer: (PGI Dec. 05)
- Inguinal LN
  - Obturator LN
  - Hypogastric LN
  - External Iliac LN
  - Femoral LN
43. Best treatment of carcinoma in situ of cervix: (PGI 98)
- Simple hysterectomy
  - Conization
  - Laser
  - Cryosurgery
  - All
44. A 42-year-old female P3 + 0 + 0 + 3 is found to have carcinoma in situ. Best treatment would be: (AI 97)
- Hysterectomy
  - Wertheim's hysterectomy
  - Conisation
  - Wait and watch
45. In microinvasive cervical cancer, most common treatment is: (PGI 97)
- Conization
  - Laser
  - Simple hysterectomy
  - Radical hysterectomy
46. False statement about treatment of Ca cervix: (PGI June 05)
- Radiotherapy is helpful in all stages
  - Prognosis of surgery good if done in early stages
  - When radiotherapy is given, para-aortic LNs should be included
  - Chemotherapy is reserved for late stages
  - From stage Ib onwards same prognosis with surgery and RT
47. A lady undergoes radical hysterectomy for stage Ib ca cervix. It was found that cancer extends to lower part of body of uterus and upper part of cervix next step of management will be: (AIIMS May 2010)
- Chemotherapy
  - Radiotherapy
  - Chemoradiation
  - Follow-up
48. Treatment of Ca cervix stage IB includes: (PGI Nov 10)
- Surgery
  - Chemotherapy
  - Radiotherapy
  - Cryotherapy
  - Leep
49. Treatment of stage IIa cervical cancer includes: (PGI Nov 12)
- Radical hysterectomy
  - Radical hysterectomy with pelvic lymph node dissection
  - Total abdominal hysterectomy with B/L salpingo oophorectomy
  - Chemoradiation
50. Treatment of stage III B carcinoma cervix is: (AIIMS Nov 2010/AIIMS May 2012 Nov 2012)
- Wertheim procedure
  - Schauta's procedure
  - Chemotherapy
  - Intracavitary brachytherapy followed by external beam RT
51. True statement regarding Ca cervix involving parametrium but not pelvic involvement: (PGI May 2010)
- Stage II A
  - Stage II B
  - Radiotherapy should be given
  - Hysterectomy can be useful
  - Staging should be done after cystoscopy
52. Cervical cone biopsy in a case of carcinoma cervix causes all, except: (AIIMS May 94)
- Bleeding
  - Cervical stenosis
  - Infection
  - Spread of malignancy
53. A 55-year-old woman was found to have Ca cervix, FIGO stage 2-3, locally advanced. What would be the management?: (AIIMS May 2012)
- Surgery plus chemotherapy
  - Radiotherapy plus chemotherapy
  - Chemotherapy
  - Radiotherapy plus HPV vaccine

### NEW PATTERN QUESTIONS

54. All are signs of inoperability of carcinoma of cervix except
- Cervix of cervix and parametrium to lateral pelvic wall
  - Presence of extrapelvic metastasis
  - Involvement of bladder
  - Extensive infiltration of vagina
55. If stage Ib cervical cancer is diagnosed in a young woman, while performing radical hysterectomy which structure would you not remove:
- Uteroseval and uterovesical ligament
  - Pelvic LN
  - Both ovaries
  - Upper third of vagina
56. Point B in the treatment of carcinoma cervix receives the dose of:
- 7000 cGy
  - 6000 cGy
  - 5000 cGy
  - 10,000 cGy
57. HPV triage strategy includes all except:
- Conventional pap smear
  - Liquid based cytology
  - Hybrid capture 2 for HPV DNA
  - Colposcopy
58. M/C site of metastasis of Ca cervix is
- Lymph node
  - Lungs
  - Bone
  - Abdominal cavity

59. A 55-year-old woman is diagnosed with invasive cervical carcinoma by cone biopsy. Pelvic examination and rectal examination reveal the parametrium is free of disease but upper part of vagina is involved with tumor. IVP and sigmoidoscopy are negative but CT scan of abdomen and pelvis shows grossly enlarged pelvic and para aortic nodes. Thus patient is classified as stage:
- a. IIa
  - b. IIb
  - c. IIIa
  - d. IIIb
  - e. IV
60. An intravenous pyelogram (IVP) showing hydronephrosis in the work up of a patient with cervical cancer otherwise confined to a cervix of normal size would indicate stage:
- a. I
  - b. II
  - c. III
  - d. IV
61. Concerning invasive cervical carcinoma all are correct except:
- a. Radical hysterectomy is not indicated for stage Ia disease, if the excision margins are free of the disease
  - b. MRI imaging is safe for staging even during pregnancy
  - c. Radical trachelectomy and pelvic lymphadenectomy can be done for stage IIa disease
  - d. Pregnancy rate is about 35% within 1 year following radical trachelectomy
62. The following statements are related to the treatment of carcinoma cervix stage 1B except:
- a. Surgery and radiotherapy have got almost equal 5-year-survival rate
  - b. Surgery has got higher morbidity than radiotherapy
  - c. Radiotherapy has got few limitations
  - d. In younger age group, radiotherapy is preferred

## ANSWERS

1. **Ans. is a, b, c, d and e, i.e. Premalignant lesion; HPV predisposes; Pap smear can detect it; Chlamydia infection can predispose; and Occurs at squamocolumnar junction**

Ref. Shaw 15<sup>th</sup>/ed p 400; Novak 14<sup>th</sup>/ed p 1404

As discussed in the preceding text, all the options are correct. I am not repeating explanation for all the options but just for option d, i.e. Chlamydia infection predisposes to CIN. STD's predispose to CIN and Chlamydia is an STD.

*"Infection with the herpes virus was previously thought to be the initiating event in cervical cancer; however, infection with human papilloma virus (HPV) has now been determined to be the causal agent in the development of cervical cancer, with herpes virus and Chlamydia trachomatis likely acting as cofactors."*

... Novak 14<sup>th</sup>/ed p 1404

2. **Ans. is d, i.e. 5%**

Ref. CGDT 10<sup>th</sup>/ed p 840, Table 50.2

**Rate of progression of CIN**

	CIN I	CIN II	CIN III
Regression to Normal	60%	40%	30%
Persistence	30%	35%	50%
Progression to CIN III	10%	20%	
Progression to cancer	< 1%	5%	20%

3. **Ans. is a, i.e. Breaking of basement membrane**

Ref. Robbin's 7<sup>th</sup>/ed p 1076, Shaw 15<sup>th</sup>/ed p 400

**Dysplasia:** Represents a change in which there is alteration in cell morphology and disorderly arrangement of the cells of the stratified squamous epithelium. It is a premalignant lesion.

**Characteristics of Dysplastic cell:**

- Vary in size<sup>o</sup>, shape<sup>o</sup> and polarity<sup>o</sup>.
- Have altered nucleo-cytoplasmic ratio (N/C ratio is increased).<sup>o</sup>
- Have large, irregular **hyperchromatic nuclei** with marginal condensation of chromatin material.<sup>o</sup>
- **Have several mitotic figures.**
- **The basement membrane, however, is intact and there is no stromal infiltration.**

**CIN: Term CIN (Cervical Intraepithelial Neoplasia):** has almost universally replaced WHO classification of dysplasia.

Classification system		
WHO	CIN	Description
Mild dysplasia	CIN I	Dysplastic cells seen in lower 1/3 <sup>rd</sup> of epithelial lining
Moderate dysplasia	CIN II	Dysplastic cells seen in 2/3 of epithelial lining
Severe dysplasia	CIN III	Dysplastic cells seen in more than 2/3 of epithelial lining

**Carcinoma in situ (CIS):** It represents full thickness dysmaturity but basement membrane is intact.

**Invasive carcinoma:** Breach of basement membrane seen.

4. **Ans. is a, i.e. CIN 1**

Ref. Shaw 15<sup>th</sup>/ed p 400

In Bethesda system:

LSIL = CIN 1

HSIL = CIN 2, CIN 3/Ca in situ

5. **Ans. is a, i.e. gonorrhea**

Ref. Novak 15<sup>th</sup>/ed p = ?

The Papanicolaou test (also called Pap smear, Pap test, cervical smear, or smear test) is a screening test to detect premalignant and malignant processes in the transformation zone.

Abnormal results are reported according to the Bethesda System. They include:

- **Squamous cell abnormalities (SIL)**
  - A typical squamous cells of undetermined significance (ASC-US)
  - Low grade squamous intraepithelial lesion (LGSIL or LSIL)
  - A typical squamous cells cannot exclude HSIL (ASC-H)
  - High-grade squamous intraepithelial lesion (HGSIL or HSIL)
  - Squamous cell carcinoma
- **Glandular epithelial cell abnormalities**
  - Endocervical and endometrial abnormalities can also be detected by pap smear
  - **A number of infectious processes, including yeast, candidiasis, herpes simplex virus, and trichomoniasis** can also be detected however, it is not very sensitive at detecting these infections, so absence of detection on a Pap does not mean absence of the infection.

- 6A. Ans. is c, i.e. Cervical polyp Ref. Novak 14<sup>th</sup>/ed p 576  
 6B. Ans. is a, i.e. Condyloma Ref. Novak 14<sup>th</sup>/ed p 576  
 6C. Ans. is a, i.e. Upper 2/3rd endocervix Ref. Novak 14<sup>th</sup>/ed p 576  
 6D. Ans. is a and c, i.e. Suspicious pap smear; and Suspected invasive carcinoma

Ref. Shaw 15<sup>th</sup>/ed p 403; CGDT 10<sup>th</sup>/ed p 837; Williams Gynae 1<sup>st</sup>/ed p 630

See the preceding text for explanation.

7. Ans. is c, i.e. conization Ref. Novak 15<sup>th</sup>/ed p , Textbook of Gynaccology Sheila Balakrishnan 1<sup>st</sup>/ed p 255  
 In the question, Rekha has negative pap smear along with positive endocervical curettage – it could mean endometrial cancer which has extended to cervix or adeno carcinoma of endocervix. To distinguish between the two – conization should be done. Colposcopy is of no use as it cannot usualize upper part of endocervix.
8. Ans. is c, i.e. Colposcopy directed biopsy Ref. CGDT10<sup>th</sup>/ed p 837, 841; Harrison 17<sup>th</sup>/ed p 608; Williams Gynecology 1<sup>st</sup>/ed p 628, Table 29-6
- Pap smear is only a screening test. To confirm we need to do a biopsy.
  - In all visible lesions punch biopsy should be done
  - In case of invisible lesion colposcopic directed biopsy is the gold standard. Thus in this case since it is not mentioned growth is visible so we do colposcopy guided biopsy.
9. Ans. is c, i.e. Cervical metaplasia
10. Ans. is b, and d, i.e. Abnormal pap smear; Endocervical curettage positive
11. Ans. is a, i.e. Microinvasive carcinoma Ref. Shaw 15<sup>th</sup>/ed p 405; Novak 14<sup>th</sup>/ed p 584-5, 15/ed p 604

**Cone biopsy or conization is both diagnostic as well as therapeutic procedure**

Indications of Cone biopsy	
Diagnostic	Therapeutic
<ul style="list-style-type: none"> <li>• Limits of the lesion cannot be visualised with colposcopy.<sup>o</sup></li> <li>• The squamocolumnar junction is not seen at colposcopy<sup>o</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Ca in situ in young females</li> <li>• Cancer cervix stage 1A1 in young females (microinvasive cancer)</li> </ul>
<ul style="list-style-type: none"> <li>• In endocervical curettage histological findings are positive for CIN - II or CIN - III<sup>o</sup>, CA in situ</li> </ul>	
<ul style="list-style-type: none"> <li>• Micro Invasive carcinoma or adenocarcinoma in situ is suspected based on biopsy, colposcopy or cytology results</li> </ul>	
<ul style="list-style-type: none"> <li>• Lack of correlation between cytology, biopsy &amp; colposcopy results.</li> </ul>	

**Complications of cone biopsy**

- Bleeding<sup>o</sup> (M/C complication)
  - Infection<sup>o</sup>
  - Cervical stenosis<sup>o</sup>
  - Incompetent os<sup>o</sup>
12. Ans. is b, i.e. Colposcopy Ref. Jeffcoate 7<sup>th</sup>/ed p 410-1; Dutta Gynae. 4<sup>th</sup>/ed p 250  
 A young lady is presenting with erosion which on cytology shows dysplasia. Now what will be the next step:  
 Friends, here first of all it is important to know that erosion (ectopy): *is a condition in which the squamous covering of the vaginal aspect of the cervix is replaced by columnar epithelium lining the endocervix.*  
 It appears as a bright red area continuous with the endocervix and with a clearly defined outer edge.  
 It often bleeds on touch and has to distinguished from carcinoma, tuberculosis, syphilitic and other ulcers of the cervix.  
*"Although a cervical smear may be helpful, the distinction may not be possible except by colposcopy or biopsy".*  
... Jeffcoate 7<sup>th</sup>/ed p 411

Here in the question: Pap smear has already been done and it shows dysplasia which should be confirmed by colposcopy.

**Extra Edge:**

**Management of cervical erosion:**

- If it is detected during pregnancy treatment should be deferred for atleast 12 weeks postpartum.
- Management:
  - Thermal cauterization<sup>o</sup>
  - Cryosurgery<sup>o</sup>
  - Laser vaporisation<sup>o</sup>

**Aim:** To destroy columnar epithelium so that on healing it is replaced by squamous epithelium.



13. **Ans. is a, i.e. Colposcopy directed biopsy** *Ref. CGDT 10<sup>th</sup>/ed p 837, 841 fig. 50-6; Williams Gynae 1<sup>st</sup>/ed p 628 Table 29.6*  
45 years old patient presenting with post coital bleeding and positive pap smear raises suspicion of carcinoma cervix / CIN which needs to be confirmed (as pap smear is only a screening procedure).

In the question it is not mentioned whether lesion is visible nor the size of lesion is given so we take it to be invisible. As already discussed for invisible lesion, colposcopy should be done to confirm the diagnosis.

14. **Ans. is d, i.e. Colposcopy**

*Ref. Novak 15/e p 1305*

VIA - Visual inspection with acetic acid  
VIL - Visual inspection with Lugoli's iodine  
Normal areas appear brown  
Abnormal areas appear white

In asymptomatic women, cervical cancer is mostly identified through evaluation of abnormal cytological screening tests. The false negative rate for pap tests in presence of invasive cancer is upto 50%, so a negative pap test should never be relied on in a symptomatic patient. *Novak 14/e p 1305*

In our question patient is symptomatic, so pap test is not reliable.

In symptomatic patient or any patient suspected to have cancer cervix – steps done:

1. General physical examination (including examination of supraclavicular, axillary and inguinofemoral nodes).
2. Pelvic examination, speculum examination of cervix to detect any suspicious area.
3. When obvious tumor growth is present cervical biopsy is sufficient for diagnosis.
4. If gross disease is not present, a colposcopic examination with cervical biopsies and endocervical curettage is done.
5. If diagnosis cannot be established by colposcopy and directed biopsies, which may be the case with adenocarcinoma, – cervical conisation may be necessary.

15. **Ans. is a, i.e. Hysterectomy**

*Ref. Shaw 15<sup>th</sup>/ed p 405; Jeffcoate 7<sup>th</sup>/ed p 421; Novak 14<sup>th</sup>/ed p 586*

The best method for treating CIN III these days is LLETZ /LEEP whether the patient is young or old.

Since in the question LEEP/LLETZ is not given – we will go for hysterectomy.

16. **Ans. is b i.e. Colposcopy and LEEP**

*Ref. William 1<sup>st</sup>/ed p 635; Novak 14<sup>th</sup>/ed p 582, 583; Devita 8<sup>th</sup>/ed p 1506.*

The patient in the question has CIN (III) on pap smear. PAP smear is only a screening procedure and is not diagnostic, hence for confirming the diagnosis, we will have to do colposcopy

**“Colposcopy is the primary technique for evaluation of an abnormal cervical cytology smear”** *COGDT 10<sup>th</sup>/ed p 837*

**Option ‘d’** conization should be done only if.

- There is a discrepancy between the result of colposcopy and PAP smear.
- It entire TZ is not visualized on colposcopy (unsatisfactory colposcopy).

Thus **option ‘d’** is ruled out.

In the previous question we have discussed that the procedure of choice for treating CIN III these days is ‘LEEP i.e. Loop Electro surgical excision procedure’

**“Leep is the procedure of choice for treating CIN II and CIN III because of its ease of use, low cost and proven of tissue for histological evaluation”**

*Ref. COGDT 10<sup>th</sup>/ed p 840*

**“Although CIN can be treated with a variety of techniques the preferred treatment for CIN II and CIN III has become LEEP”**

*Ref. Novak 14<sup>th</sup>/ed p 582.*

**“LEEP is now considered the preferred treatment for noninvasive squamous lesions”**

*Devita 8<sup>th</sup>/ed p 1506.1*

So our answer is Colposcopy and LEEP.

Now when we are doing the procedure, we can either perform it in 2 steps, i.e.

**1st Step:** Diagnostic Colposcopy

↓

Confirm CIN III

**2nd Step: Therapeutic colposcopy with LEEP. This approach should be adopted in young females. In older females we can perform the procedure in single step, i.e. with out confirming CIN histologically, directly perform LEEP while doing colposcopy. This is called as “See and treat LEEP”**

See and treat LEEP refers to the practice of diagnosing and treating on a single visit and has been prepared for patients with evidence of high grade dysplasia (CIN III > CIN II) on PAP smear on adequate colposcopic examination. The main problem with this approach is that an excision procedure may be performed unnecessarily and hence it should not be performed in young women. Older women who have completed their families and have evidence of high grade dysplasia can be adequately managed by the “see and treat LEEP approach.

Now let's rule out other options:

**Option ‘c’** Colposcopy and Cryosurgery

**“Cryosurgery is generally not favored for the treatment of CIN 3 due to higher rates of disease persistence following treatment and lack of histologic specimen to exclude occult invasive cancer”**

*William gyane 1<sup>st</sup>/ed p 634*

*"Patients with HSILs are usually treated with a LEEP if there is no suspicion of occult invasion on cytologic or colposcopic examination. If patients do not meet these criteria, a conization should be performed. The use of ablative therapy with cryotherapy or CO<sub>2</sub> laser ablation has declined in recent years because low grade dysplasia are often followed without treatment and high grade lesions are usually treated with excision (LEEP) to permit histological examination."* Devita 8<sup>th</sup>/ed p 1506.

So **Option 'b'** is ruled out

As far as hysterectomy (**option 'a'**) is concerned – Earlier it was said- hysterectomy is the TOC in CIN III if female is above 40 years and has completed her child bearing.

The current recommendations are:

LEEP is the procedure of choice for managing CIN II/ CIN III in all age groups.

**17. Ans. is a, i.e. LEEP**

Ref. CGDT 10<sup>th</sup>/ed p 840; Jeffocate 7<sup>th</sup>/ed p 421

As discussed in the previous question – Loop Electrosurgical Excision Procedure (LEEP) has now become the procedure of choice for treating CIN II and CIN III in all age groups. Therefore in this patient we will go for LEEP.

**18. Ans. is b, i.e. Punch biopsy**

**19. Ans. is a, i.e. Punch biopsy**

**20. Ans. is d, i.e. Punch biopsy**

Ref. Novak 15<sup>th</sup>/ed p 1306

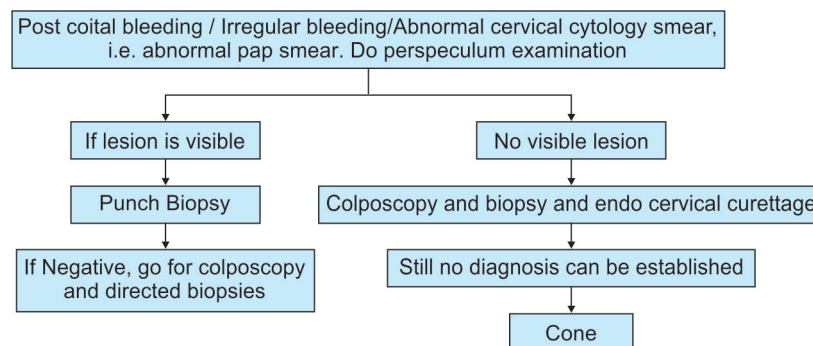
**21. Ans. is a, i.e. Colposcopy biopsy**

Ref. Novak 15<sup>th</sup>/ed p 1306

**22. Ans. is b, i.e. Colposcopy and biopsy**

An old lady presenting to OPD with post coital bleeding with a lesion visible on cervix- raises the suspicion carcinoma cervix in this case because CIN is asymptomatic as discussed in Q14. In such cases pap smear is of no use and directly biopsy should be done. Since lesion is visible we will go for punch biopsy.

**Investigation Protocol for Diagnosis of Carcinoma Cervix:**



**23. Ans. is a, c and d, i.e. 90% associated with HPV; OCP; and Immunocompromised patients**

**24. Ans. is a, b and c, i.e. Multiple sex partners; Genital warts and HPV 16, 18**

**25. Ans. is a, b and e, i.e. HPV; Smoking; and Early sexual intercourse**

**26. Ans. is a, b and c, i.e. HIV patient, multiparity and smoking.**

Ref. CGDT 10<sup>th</sup>/ed p 834, Shaw 14<sup>th</sup>/ed p 359

**27. Ans. is a i.e. Low parity**

**Factors Predisposing to CIN/Ca cervix:**

- Human Papilloma virus infection
- Sexually transmitted infections:
  - Coitus before 18 years of age<sup>Q</sup>
  - Multiple sex partners<sup>Q</sup>
  - Multiparity<sup>Q</sup>
  - Poor personal hygiene<sup>Q</sup>
  - Poor socioeconomic status<sup>Q</sup>
- Smoking<sup>Q</sup>,
- Immunosuppressed individuals<sup>Q</sup>
- Women on OCP<sup>Q</sup>, Progesterone therapy for long time are predisposed to **adenocarcinoma** of endocervix.
- In utero exposure to DES

*"HPV is central to the development of cervical neoplasia. HPV - DNA is found in 95% of all squamous cell carcinoma & 90% of all adenocarcinomas."*

28. Ans. is a, i.e. HPV 16

29. Ans. is b, i.e. Type 18

30. Ans. is a, i.e. 16 and 18

Ref. Novak 14<sup>th</sup>/ed p 568; 15<sup>th</sup>/ed p 581; COGDT 10<sup>th</sup>/ed p 843

31. Ans. is a, and b, i.e. Type 16; and Type 18

Ref. Williams Gynae 1<sup>st</sup>/ed p 619; Dutta Gynae 6<sup>th</sup>/ed p 323

32. Ans. is a and b i.e. 6 and 11.

Read the text for explanation.

33. Ans. is a, i.e. Squamocolumnar junction

Ref. Shaw 15<sup>th</sup>/ed p 400; Novak 14<sup>th</sup>/ed p 564; Williams Gynae 1<sup>st</sup>/ed p 619

**Note:**

- M/C site for carcinoma cervix = Squamo columnar junction
- M/C site for adenocarcinoma of cervix = Endocervix.

34. Ans. is a, i.e. Irregular vaginal bleeding

Ref. Jeffcoate 7<sup>th</sup>/ed p 471; Williams Gynae. 1<sup>st</sup>/ed p 652

*"In its very early stage, invasive carcinoma of cervix causes no symptoms and is discovered accidentally or as a result of routine search. Symptoms come with surface ulceration and consist only of irregular uterine bleeding or discharge or both. These being peri- or postmenopausal in half the cases. The first episode of bleeding commonly follows coitus, straining at stool or trauma."*

... Jeffcoates 7<sup>th</sup>/ed p 471

*"For those with symptoms, however, early stage cervical cancer may create a watery, blod tinged vaginal discharge. Intermittent vaginal bleeding that follows coitus or douching may also be noted."*

... Williams Gynae. 1<sup>st</sup>/ed p 652

*The earliest symptom of invasive cervical cancer is usually abnormal vaginal bleeding, often following coitus or vaginal douching. This may be associated with clear or foul smelling vaginal discharge.*

"Devita 8<sup>th</sup>/ed p 1502

Thus earliest symptom is irregular vaginal bleeding which usually follows coitus. So I am taking option 'a', i.e. irregular vaginal bleeding as the correct answer.

- Also Know:**
- CIN is most commonly detected in women in their 20's.
  - Peak incidence of carcinoma in situ: 25 - 35 years<sup>Q</sup>
  - Ca cervix has bimodal peak - first at 35-39 years<sup>Q</sup> and second at 60-64 years<sup>Q</sup>.

35. Ans. is b, i.e. Uremia

Ref. Jeffcoate 7<sup>th</sup>/ed p 472

*"The ultimate cause of death in their order of frequency and importance - uraemia cachexia associated with recurrent haemorrhage, infection and interference with nutrition, complication of treatment and remote metastasis to vital organs (rare)."*

Hiccups and altered sensorium are nonspecific signs of uraemia and so the likely cause in this case is uraemia.

**Also know:**

Uraemia in carcinoma cervix occurs when tumor involves ureter and results in blockage.

M/C cause of death in cancer cervix =Renal failure/uremia

Second M/C cause of death in cancer cervix=Hemorrhage.

36. Ans. is c, i.e. Pelvic ultrasound

37. Ans. is a, i.e. CECT

Ref. Dutta Gynae. 5<sup>th</sup>/ed p 328, 6<sup>th</sup>/ed p 341; Novak 14<sup>th</sup>/ed p 1410

**Staging Procedures in Ca cervix (As recommended by FIGO).**

Physical examination	Radiological studies	Procedure
• Palpate lymph node	• Chest X-ray	• Biopsy
• Examine vagina	• Skeletal X Ray	• Conisation
• Bimanual recto vaginal examination	• IVP	• Endocervical Curettage
	• Barium enema	• Colposcopy
		• Hysteroscopy
		• Cystoscopy
		• Proctoscopy
		Mnemonic: <b>BS<sub>4</sub>C Exam</b>
		<b>B</b> = Biopsy
		<b>C</b> = Conization
		<b>S<sub>4</sub></b> = 4 types of scopy's
		<b>Exam</b> = Endocervical curettage

**Note:** USG, CECT, MRI, PET, Laproscopy, Laparotomy and Lymphangiography are optional and not to be included in FIGO staging so for staging results of USG,CECT and MRI are not taken into consideration.

## 38. Ans. is c, i.e. Stage III

Ref. Novak 15<sup>th</sup>/ed p 1317, Devita 8<sup>th</sup>/ed p 1501 table 42-2-2 and p 1503

As discussed in the staging given in preceding text carcinoma extending to pelvic wall means stage III.

## 39. Ans. is c and e, i.e. microinvasive carcinoma with 6 mm carcinoma with stromal invasion &gt; 5mm and size of lesions 4 cms.

Read the text for explanation.

## 40. Ans. is b, i.e. CT scan is mandatory for staging

Ref. Jeffcoates 7<sup>th</sup>/ed p 470-72; COGDT 10<sup>th</sup>/ed p 834-5, 843

Let's see each option separately –

**Option 'a'** is Squamous cell carcinoma is common at squamous columnar junction.**Histologically Ca cervix is of 2 types.**... Jeffcoates 7<sup>th</sup>/ed p 470

Squamous cell carcinoma (Epidermoid carcinoma)	Adenocarcinoma
Accounts for 80% of carcinoma cervix <sup>o</sup>	Accounts for 20% of carcinoma cervix <sup>o</sup>
Arises from squamocolumnar junction <sup>o</sup>	Arises from Endocervix <sup>o</sup>

So, **Option 'a'** is correct.**Option 'b'**: CT scan is mandatory for staging – As discussed in previous question CT scan is not included in FIGO staging. So option b is incorrect.**Option 'c'**: Post coital bleeding is a common symptom. This is quite true and we have dealt with it earlier.**Option 'd'**: HPV 16 and HPV18 is associated with high risk of carcinogenesis.... COGDT 10<sup>th</sup>/ed p 834-5, 843As we have discussed earlier HPV 16 & 18 is categorised as High Risk HPV. Therefore, **option 'd'** is correct.

So, I am left with option 'b' as the option of choice.

## 41. Ans. is a, b and e, i.e. Obturator LN; External iliac LN; and Hypogastric LN

## 42. Ans. is b, c and d, i.e. Obturator LN; Hypogastric LN; and External iliac LN

Ref. Williams Gynae 1<sup>st</sup>/ed p 649; Devita 7<sup>th</sup>/ed 1297

Primary group	Secondary group
H = Hypogastric	Common iliac
O = Obturator	Para aortic
P = Presacral and parametrial	Inguinal
E = External iliac	

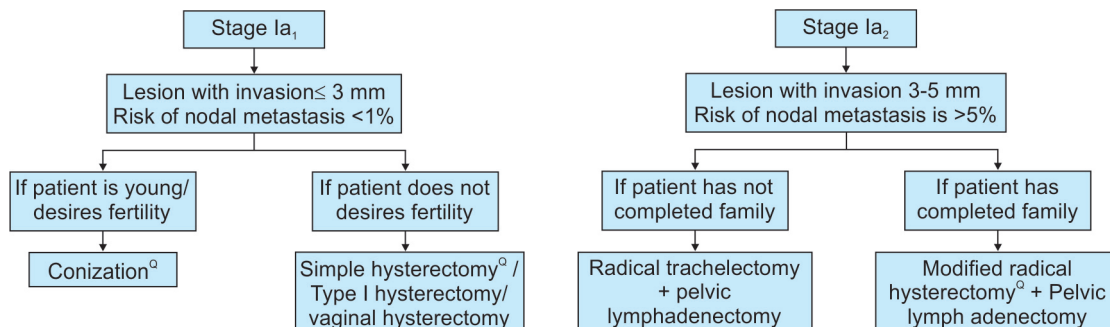
## 43. Ans. is a and b, i.e. Simple hysterectomy; and Conization

## 44. Ans. is a, i.e. Hysterectomy

Ref. Harrison 17<sup>th</sup>/ed p 608; Novak 14<sup>th</sup>/ed p 581; Jeffcoate 6<sup>th</sup>/ed p 398**"Carcinoma in situ (stage 0) can be managed successfully by cone biopsy or by abdominal hysterectomy."**... Harrison 17<sup>th</sup>/ed p 608

Friends, carcinoma in situ is managed in young women with cone biopsy, whereas in older women or females who had completed their families (&gt; 40 years), simple hysterectomy is the TOC.

## 45. Ans. is c, i.e. Simple hysterectomy

Ref. Shaw 15<sup>th</sup>/ed p 413; Novak 14<sup>th</sup>/ed p 1417-8; Williams Gynae. 1<sup>st</sup>/ed p 657A micro invasive carcinoma is one in which stromal invasion is < 5 mm from the base<sup>o</sup> and lateral spread < 7mm with no vascular or lymphatic involvement (Stage Ia of Ca cervix)<sup>o</sup>.**Microinvasive Ca can be further subdivided as:**

46. **Ans. is c and e, i.e. When radiotherapy is given paraaortic LN should be included and from stage Ib onwards same prognosis with Surgery and Radiotherapy**

*Ref. Novak 14<sup>th</sup>/ed p 1417-8, 1436; 15<sup>th</sup>/ed p 1326, 1333, William Gynae 1<sup>st</sup>/ed p 658-9*

I have discussed management of cancer cervix in detail in preceding text.

**Option "a":** Radiotherapy is helpful in all stages. ... *Correct*

**Option "b":** Prognosis of surgery is good if done in early stages. ... *Correct*

**Option "c":** When radiotherapy is given para aortic LN should be included. It is incorrect as routine radiotherapy for cancer cervix does not include para aortic lymph nodes. If para aortic lymph nodes are involved then only extended field radiotherapy should be given.

*"The routine use of extended field radiation for prophylactic para aortic radiation without documentation of distant metastasis to para aortic nodes was evaluated and is not practiced because of increased enteric morbidity associated with this treatment modality."* ... *Novaks 15<sup>th</sup>/ed p 1326*

**Note:**

- IOC to know whether para-aortic lymph nodes are involved is PET/CT imaging studies.
- Radiotherapy for para aortic lymph nodes leads to bowel complications and to avoid these complications, extra peritoneal dissection of para aortic nodes is recommended and the dose of radiation should be reduced to 5000 cGy or less. When this approach is used, post radiotherapy bowel complications occur in < 5% patients and 5 year survival rate is 15–26% in patients with positive para aortic nodes.

**Option "d":** Chemotherapy is reserved for last stages. ... *Correct*

**Option "e":** From stage 1B onwards same prognosis with surgery and RT.

The only data which I could get on this is –

*"Stages 1B1, 1B2 and 2A (size of lesion <4 cms)-these patients can be managed by surgery or primary chemoradiation. Several studies showed similar survival rates and outcomes. In bulky stages 1B2 and 2A2 -chemoradiation should be preferred but if patient wishes to conserve ovary then surgery should be done but it has increased morbidity because most of these patients have intermediate or high risk factors present for which post operative radiotherapy or chemoradiation has to be given."* *Ref. Novak Gynae 15<sup>th</sup>/ed p 1333*

47. **Ans. is d, i.e. Follow-up** *Ref. Novak Gynae 14<sup>th</sup>/ed p 1436, 1426, 1418-1, 1408*

Postoperatively it was found that carcinoma extends to the lower part of uterus. Now this is a trap because uterine extension has no significance in cancer cervix and does not change the staging.

48. **Ans. is a, b and c, i.e. surgery, chemotherapy and radiotherapy** *Ref. Novak Gynae 15<sup>th</sup>/ed p 1332; Devita 8<sup>th</sup>/ed p 1508-9*

In the question—since no risk factor has been mentioned assuming that none are present, we would simply think to follow-up the patient.

49. **Ans. is b and d, i.e. Radical hysterectomy with pelvic lymph node dissection and chemoradiation.**

Read the text for explanation.

50. **Ans. is d, i.e. Intracavitary brachytherapy followed by external beam RT.**

*Ref. Novak 14<sup>th</sup>/ed p 1436, 1427; Shaw 15<sup>th</sup>/ed p 414*

As discussed in the preceding text, best treatment for stage III B of invasive cancer is chemoradiation. Since this option is not given – we will go for next best option, i.e. Radiotherapy

Generally from stage II B-IV A when radiotherapy is given - external beam pelvic radiation precedes brachytherapy. But again since we don't have this option, we are going for vice versa (which is not incorrect).

51. **Ans. is b, c, and e, i.e. Stage IIB:Radiotherapy should be given; Staging should be done after cystoscopy.**

*Ref. COGDT 10<sup>th</sup>/ed p 848-9; Novak 14<sup>th</sup>/ed p 1407-9; Shaw 15<sup>th</sup>/ed p 412-5*

**Cancer cervix involving the parametrium but not the pelvis refers to stage IIB** (i.e. **option 'a'** is incorrect and **option 'b'** is correct).

Management of choice for stage II b is – chemoradiation (i.e. 5 days Radiotherapy along with cisplatin added on any one day). i.e. **option 'c'** is correct.

Surgery–(Radical/wertheims hysterectomy) is not done for stage IIB. (i.e. **option 'd'** is incorrect).

Procedures done for Surgical staging of Ca cervix as advised by FIGO includes cystoscopy and thus cystoscopy should be done before staging (i.e. **option 'e'** is correct).

52. **Ans. is d, i.e. Spread of malignancy**

*Ref. Shaw 15<sup>th</sup>/ed pg 406; Jeffcoate 7<sup>th</sup>/ed p 421; Williams Gynae 1<sup>st</sup>/ed p 635*

**Complications of Cone biopsy are:**

- Hemorrhage<sup>a</sup>
- Sepsis (infection)<sup>a</sup>
- Cervical stenosis<sup>a</sup>
- Pregnancy complications which include:
  - Mid trimester abortions<sup>a</sup>
  - Preterm labour<sup>a</sup>
  - Cervical dystocia<sup>a</sup>

**Also Know:**

- Cone biopsy should be done under general anaesthesia.
- The cone should include the entire outer margin and the endocervical lining but internal OS is spared.
- A small cone is preferred in younger women to avoid pregnancy complications.

**53. Ans is b, i.e. Radiotherapy plus chemotherapy**

*Ref. Williams Gynae 2<sup>nd</sup>/ed p 787; Novak 14<sup>th</sup>/ed p 1436*

As discussed in detail in preceding text best for cervical cancer of (stages II B to IV A) is chemoradiation (i.e. chemotherapy and radiotherapy), where by cisplatin is used as a radiosensitiser to increase the sensitivity of the cells to radiotherapy before giving radiotherapy.

Since in this question -chemotherapy + radiotherapy is given as one of the options, hence, we will mark it as the correct option.

**54. Ans. is none**

*Ref. (Read below)*

**Signs of inoperability of cancer cervix are:**

- a. Complete fixity of cervix and parametrium to lateral pelvic wall
- b. Extensive infiltration of vagina
- c. Presence of extrapelvic metastasis
- d. Extensive infiltration of bladder
- e. Presence of VVF.

**55. Ans. is c, i.e. Both ovaries**

*Ref. Textbook of Gynaeceology sheila Balakrishnan 1<sup>st</sup>/ed p 255*

Cancer cervix rarely involves the ovaries.

∴ When radical/modified radical hysterectomy are being performed in young females, ovaries should not be removed.

**56. Ans. is b, i.e. 6000 cGy**

*Ref. Novak, 14<sup>th</sup>/ed p 1428; John Hopkins manual of obs and gynae 4<sup>th</sup>/ed p 554*

Two important points in the radiotherapy of cancer cervix are

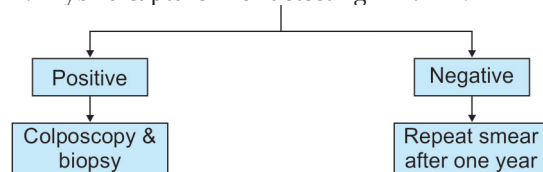
	Point A	Point B
Location	2 cm above and 2 cm lateral to external os	2 cm above and 5 cm lateral to external os
Structure present	<b>Paracervical/parametrial lymph node</b>	Obturator lymph node
Dose of radiation	7000 – 8000 cGy	4000-6000 cGy

**57. Ans. is a, i.e. Conventional pap smear**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 323-4*

HPV triage strategy includes:

- i. Pap smear test-**by liquid based thin layer cytology**
- ii. Hybrid capture 2 for detecting HPV DNA



This triage strategy can detect CIN II and III lesions effectively and reduces the load of colposcopy clinic.

**58. Ans. is b, i.e. Lungs**

*Ref. Dutta Gyane 6<sup>th</sup>/ed p 346*

Metastasis to distant organs in case of cancer cervix is seen in lungs (36%) > lymph node (30%) > bone (16%) and abdominal cavity (7%)

**59. Ans. is a, i.e. Stage II a**

Now here – in this patient

On examination – Parametrium is not involved and upper part of vagina is involved so stage will be IIa – clinically. Remember cervical cancer is still staged clinically by using investigations recommended by FIGO.

CT scan results, while clinically useful are not useful to stage the disease.

No matter whatever finding are reported on CT scan it does not affect the staging so Answer remains is Stage 11a.

**60. Ans. is c, i.e. Stage III**

**Now here** - the investigation done is IVP which is one of the recommended investigations by FIGO therefore results of IVP are important for staging. By definition, a positive IVP would mean ureter is involved i.e. extension to pelvic side wall and i.e. Stage 111 b.

Such staging applies even if there is no palpable tumor beyond the cervix.

**Remember-** FIGO stage is based on careful clinical examination and the results of specific radiological studies and procedures. These should be performed and stage should be assigned before any definitive therapy is administered. The clinical stage should never be changed on the basis of subsequent findings.

**61. Ans. is c, i.e. Radical trachelectomy and pelvic lymph adenectomy can be done for stage IIA disease**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 352*

For stage I a, surgery of choice is conization in young females and simple hysterectomy in older females.

Radical hysterectomy is not done in stage I a (i.e. option a is correct).

MRI is a safe investigation during pregnancy, hence in cancer cervix occurring during pregnancy, it can be done (i.e. option b is correct)

Laparoscopic assisted vaginal radical trachelectomy with pelvic and aortic lymphadenectomy (LAVRT) was designed (Daniel Dargent 1987) to treat early invasive cervical cancer. This is done in a young woman where childbearing function is to be preserved. Initially, pelvic and aortic lymph node dissection is done. Vaginal radical trachelectomy is done only when these nodes are negative. Vaginal part includes resection of cervical, vaginal, paracervical and paravaginal tissues. Vaginal cuff is resected circumferentially about 2 cm below the cervicovaginal junction. Ideally, the resected cervical tissue margins should be free of disease as evaluated by frozen section.

**Indications of trachelectomy are:** (i) preservation of fertility, (ii) early stage disease (stage IA1, A2, IBI), (iii) small tumor volume (< 2 cm), (iv) no pelvic node metastasis, (v) cancer margin is at 1 cm below the internal os on MRI.

This trachelectomy is not done in stage IIA disease

**62. Ans. is d, i.e. In younger age group, radiotherapy is preferred**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 195*

As explained in the text, in younger age group we prefer surgery with preservation of ovaries and not radiotherapy

# CHAPTER

# 14C

## Gynecological Oncology: Ovarian Tumors



### Risk of malignancy index (RMI)

$RMI = U \times M \times \text{value of CA125}$   
 U = Ultrasound score  
 M = Menopausal score

### ULTRASOUND FINDINGS

(1 point for each)

- Multilocular cyst
- Evidence of solid areas
- Evidence of metastases
- Presence of ascites
- Bilateral lesions

U = 1 (for ultrasound scores of 0 or 1)

U = 3 (for ultrasound scores of 2-5)

### MENOPAUSAL STATUS

- Postmenopausal: M = 3
- Premenopausal: M = 1

If **RMI > 200**: Gynecologic Oncology referral is recommended

### Ultrasound Characteristics of Benign vs Malignant Ovarian Tumors

Physical examination	Benign tumor	Malignant tumor
Mobility	Mobile	Fixed, large and multiloculated
Consistency	Cystic	Solid or firm
Laterality	Unilateral	Bilateral
Cul-de-sac	Smooth on P/V examination	Nodular on P/V examination
Radiography		
Size	Usually < 10 cm size	Any size
Septations	< 2 mm thickness	Multiple septations > 3 mm in size
Calcification	Seen in teratoma	Usually absent
Omental caking	Absent	Seen
Ascites	Absent	Present
Intraoperative	Unilateral cyst with no adhesion Capsule intact	Solid areas with adhesion, rupture may occur. Capsule is breached

### Physiological/Functional Cysts

Type	Description	Presentation	Ultrasound/Cytology	Treatment
<b>Functional Tumors (all benign)</b>				
Follicular cyst	<ul style="list-style-type: none"> <li>• Follicle fails to rupture during ovulation</li> </ul>	<ul style="list-style-type: none"> <li>• Usually asymptomatic</li> <li>• May rupture, bleed, tort, infarct causing pain ± signs of peritoneal irritation</li> </ul>	<ul style="list-style-type: none"> <li>• 4–8 cm mass, unilocular, lined with granulosa cells</li> </ul>	<ul style="list-style-type: none"> <li>• If &lt;6 cm, wait 6 weeks then re-examine as cyst usually regresses with next cycle</li> <li>• OCP (ovarian suppression) – will prevent development of new cysts</li> <li>• Treatment usually laparoscopic</li> <li>• Painful, multiloculated, or partially solid masses warrant surgical exploration</li> </ul>
Lutein cyst	<ul style="list-style-type: none"> <li>• Corpus luteum fails to regress after 14 days, becoming cystic or hemorrhagic</li> </ul>	<ul style="list-style-type: none"> <li>• More likely to cause pain than follicular cyst</li> <li>• May delay onset of next period</li> </ul>	<ul style="list-style-type: none"> <li>• Larger and firmer than follicular cysts</li> <li>• Show a cob web like appearance</li> </ul>	<ul style="list-style-type: none"> <li>• Same as for follicular cysts</li> </ul>
Theca-lutein cyst	<ul style="list-style-type: none"> <li>• Due to atretic follicles stimulated by abnormal β-hCG levels</li> </ul>	<ul style="list-style-type: none"> <li>• Associated with molar pregnancy, ovulation induction with clomiphene pregnancy</li> </ul>		<ul style="list-style-type: none"> <li>• Conservative</li> <li>• Cyst will regress as β-hCG levels fall</li> </ul>

Contd...



Contd...

Type	Description	Presentation	Ultrasound/Cytology	Treatment
Luteoma of pregnancy	<ul style="list-style-type: none"> <li>Usually bilateral</li> <li>Due to prolonged elevation of <math>\beta</math>-hCG</li> </ul>	<ul style="list-style-type: none"> <li>Associated with multiple pregnancy</li> </ul>		<ul style="list-style-type: none"> <li>Same as for theca-lutein</li> <li>Regresses postpartum</li> </ul>

## Benign Ovarian Tumors

- Benign epithelial tumors = M/C = 80%
  - Serous cystadenoma = M/C but overall, M/C benign tumor is dermoid cyst.
  - Mucinous cystadenoma
  - Endometrioid cystadenoma
  - Brenner Tumor
- Benign sex cord tumors
  - Theca cell tumor
  - Fibroma
- Benign germ cell tumors
  - Mature cystic teratoma (dermoid cyst)
  - Mature solid teratoma
- Gonadoblastoma

## Benign Epithelial Tumors

Serous cystadenoma	Mucinous cystadenoma	Brenner Tm/transitional tumor
<ul style="list-style-type: none"> <li>M/c benign epithelial tumor of ovary</li> <li>Thin walled, unilocular cyst filled with serous fluid and lined by cells similar to those lining the fallopian tube</li> <li>B/L in 20% cases</li> <li>Chances of malignancy = 40%</li> <li>Psammoma bodies seen</li> </ul>	<ul style="list-style-type: none"> <li>2nd M/c benign epithelial tumor of ovary</li> <li>Thick walled, mucoid material containing tumor which may be unilocular or multilocular (M/c), lined by single columnar epithelium</li> <li>Chances of malignancy = 10%</li> <li>Pseudomyxoma peritoneii is a rare complication</li> </ul>	<ul style="list-style-type: none"> <li>Rare solid tumor resembling fibroma of ovary</li> <li>Mostly benign</li> <li>M/c age – Peri and postmenopausal females</li> <li>Walthard cell nests are seen and cells have coffee bean nuclei</li> </ul>

## Benign Sex Cord Tumors

### Theca Cell Tumor

- Almost always benign
- Presents after menopause
- Unilateral
- Tumor secretes estrogen which can lead to postmenopausal bleeding, endometrial hyperplasia and endometrial cancer.

### Fibroma

- Arises from stromal cells
- Hard in consistency
- Microscopy shows spindle shaped cells
- When fibroma is accompanied with ascites and hydrothorax (usually right side) it is called as Meigs syndrome.



90% of all ovarian tumors in the reproductive age group are Benign. Physiological cysts are very common in this age group and must be considered as a possibility.



For detailed classification of ovarian tumors – see section malignant ovarian tumor/ovarian cancer.



Brenner tumor – histologically shows Walthard cell rests of transitional cells with coffee bean nuclei, and its cut section is gritty.



- M/C ovarian tumor over all epithelial tumors (80%)
- 80% of epithelial tumors are benign
- M/C benign epithelial tumor of ovary is serous cystadenoma
- M/C benign tumor of ovary is Dermoid cyst (Williams gynae 1/e p 214; 2/e p 267)



**Meigs syndrome** Combination of fibroma with ascites and hydrothorax, usually right sided is called as Meigs syndrome. Seen in 1-5% patients.

**Criteria for diagnosis of Meig's syndrome**

- Tumor must be ovarian, solid and benign.
- Both hydrothorax and ascites must be present.
- Removal of the tumor must result in their spontaneous and permanent cure.

Pseudomeigs syndrome – When ascites and hydrothorax occur with Brenner, Thecoma and granulosa cell tumor it is called as Pseudomeigs syndrome.



**Dermoid cyst:**

- Most common benign tumor of ovary in reproductive age group.<sup>Q</sup>
- Most common benign neoplasm diagnosed during pregnancy.<sup>Q</sup>
- Most common Germ cell tumor (overall).<sup>Q</sup>
- It is the commonest tumor to undergo torsion.



If teeth or bone are seen in X-ray in adnexal mass, it is pathognomic for teratoma.

## Benign Germ Cell Tumor

### Dermoid Cyst (Mature cystic teratoma)

#### KNOW IN-DEPTH

➤ **Dermoid cyst is a benign teratoma.**

➤ Teratomas are the most common germ cell neoplasm.

**On the basis of maturity teratoma can be divided into:**

**a. Mature (Benign) teratoma = dermoid cyst**

- Most common *benign tumor of ovary* in reproductive age group.<sup>Q</sup>
- Most common benign neoplasm diagnosed during pregnancy.<sup>Q</sup>
- Most common Germ cell tumor.<sup>Q</sup>
- It is the commonest tumor to undergo torsion.
- It frequently arise in association with mucinous cystadenoma:
- Age for combined tumor is 20–30 years.
- Age for simple dermoid cyst is 40–50 years.
- *Bilateral* in 10% to 15% of cases.
- Lining epithelium is stratified squamous epithelium (if dermoid cyst undergoes malignant change - Squamous cell Ca is seen).
- *Dermoid cyst usually contain derivatives of ectoderm, endoderm and mesoderm. Most common tissue element in dermoid cyst is ectodermal.*<sup>Q</sup>
- It may attain a size of 20 cms (generally 15 cms).
- **Characteristically they are unilocular cyst containing hair and cheesy sebaceous material, teeth, bones, thyroid tissue and cartilage.**
- On cross section – they typically show an area of localized growth from which hair projects, teeth and bone are seen. It is called as Rokitansky protuberance or dermoid process.
- *Malignant change in a dermoid cyst occurs in 0.5–2% cases in patients more than 40 years. Most common malignancy which develops is, squamous cell carcinoma.*

**b. Immature (Malignant) teratoma**

- Rare, mostly solid, differ from benign teratomas in the component tissue which resembles that observed in the fetus or embryo rather than mature adult tissue.
- Tumor occur *chiefly in prepubertal adolescents and young women.*
- Tumor grade is correlated with prognosis and extra-ovarian spread.
- c. Monodermal or specialized teratomas = (Struma ovarii and carcinoid)**
- Rare group of tumor, struma ovarii composed entirely of mature thyroid tissue which is hyperfunctional.
- Patients usually present with hyperthyroidism.
- Most of the tumors are innocent, but malignant thyroid tumor have been recorded.

## Gonadoblastoma

This is a benign neoplasm which can arise in dysgenetic gonads in the presence of Y chromosome like in Androgen Insensitivity Syndrome and Swyer's syndrome.

Although these tumors are essentially benign, 50% of them are accompanied by malignant germ cell tumor – dysgerminoma.

## Pseudomyxoma Peritonei

#### Also Know

**Pseudomyxoma peritonei** is a condition in which the neoplastic epithelium secretes large amounts of gelatinous mucinous material. So the peritoneal cavity is filled with mucinous material. It is most commonly seen secondary to:

- Appendicular carcinoma (*well differentiate carcinoma*).
- Ovarian mucinous carcinoma; mucinous cystadenoma.
- Mucocoele of appendix (less commonly seen).

Even after removal of the ovarian tumors, these cells continue to secrete mucin.

Tendency of *recurrence* is present.

**Prognosis** is Poor.

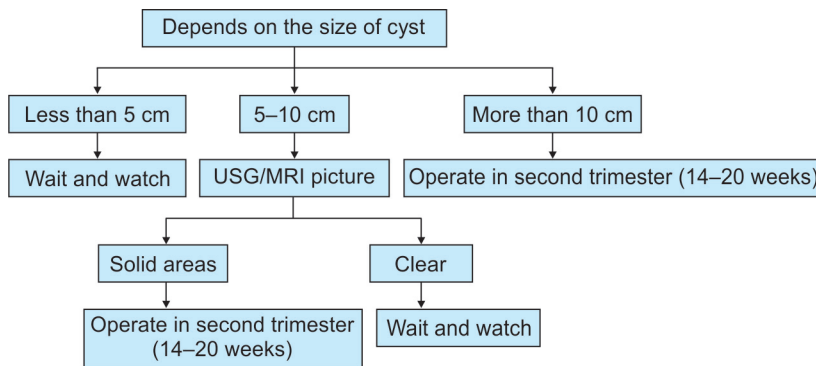
**Management:** Hysterectomy with BSO with removal of mucin peritoneal implants along with appendix.

### Ovarian Cysts in Pregnancy

#### HOT TOPIC

- M/C ovarian cyst diagnosed in pregnancy- Dermoid cyst
- M/C ovarian tumor to undergo torsion in pregnancy- Dermoid cyst
- M/C time for ovarian cyst to undergo torsion in pregnancy- end of first trimester and /or puerperium

### Management of Ovarian Cyst in Pregnancy



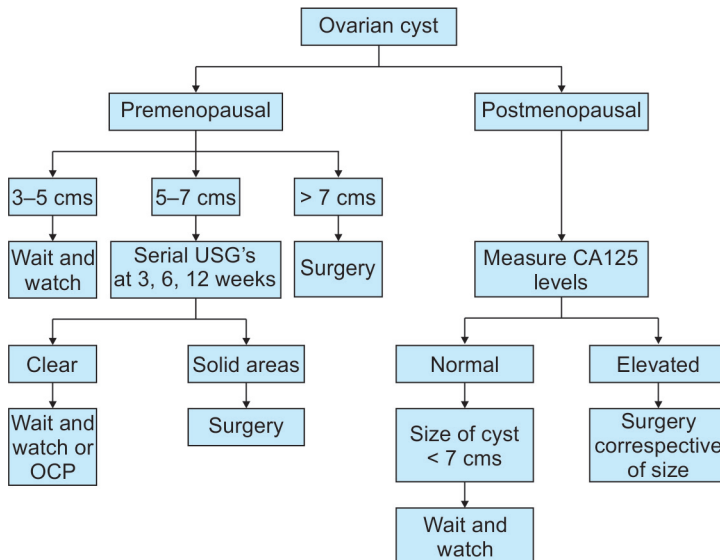
In cases of emergency (e.g., torsion, rupture) do surgery, irrespective of size and weeks of gestation.

### Management of Ovarian Cyst

General principles:- **Surgery for ovarian mass.**

#### Indications

1. Any ovarian mass which shows high risk features on USG.
2. Any ovarian mass >7 cm & adnexal mass > 10 cm irrespective of age.
3. Raised CA125 levels in postmenopausal femels (>65 IU/mL)
4. Acute complication of ovarian cyst.
5. For diagnostic purpose.



#### Complications of Ovarian Cyst

- Torsion (M/c tumor to undergo torsion – Dermoid cyst Management = immediate surgery → Detorsion and cystectomy, preserving the ovary)
- Rupture of cyst (M/c with corpus luteum cyst)
- Haemorrhage in cyst (M/c with serous cystadenoma)
- Infection pseudomyxoma peritonei (M/c in mucinous cystadenoma)
- Malignancy (risk of malignancy is maximum in – Serous cystadenoma (40%) Least (1–2%) in Dermoid cyst)



#### Risk Factors for developing Ovarian Cancer

- N = Nulliparity
- O = Ovulation induction by Clomiphene/ Gonadotropins
- C = Cackasian
- H = Family history
- I = Increased age (> 60)
- L = Late menopause, early menarche
- D = Delayed child bearing

## Malignant Ovarian Tumor/Ovarian Cancer

### Etiology

The theory which explains the etiology of ovarian cancer is 'Theory of incessant ovulation' which means as frequency of ovulation increases, risk of ovarian cancer increases.

- Risk factors:
  - Advancing age (average age 60 years)
  - Early menarche and late menopause
  - Family history of ovarian cancer, breast, endometrial and colorectal cancer
  - Personal/family history of breast CA
  - Multiple cycles of gonadotropins/clomiphene citrate for ovulation induction
  - Low parity/infertility
  - Women workers in asbestos industry
  - Caicasons
  - Dysgenetic gonad
  - Post-menopausal palpable ovary (volume > 8 cm<sup>3</sup>)
- **Factors reducing the risk of ovarian cancer** (all those conditions which decrease frequency of ovulation)
  - Use of OC pills/DMPA (since they cause anovulation)
  - Multiparity
  - Breast feeding
  - Pregnancy
  - Anovulation
  - Tubal ligation
  - Hysterectomy
- Hereditary Breast Ovarian Cancer
  - Most hereditary ovarian cancers are associated with mutations in **BRCA 1** located on chromosome 17. Small proportions have mutations in BRCA 2 gene located on chromosome 13.
  - The mutations are inherited in an autosomal dominant patterns.
  - Hereditary ovarian cancers occur in women approximately 10 years younger than those with nonhereditary tumors.
  - **Lynch II Syndrome/HNPCC - hereditary non polyposis colorectal cancer**  
It includes multiple adenocarcinomas and involves a combination of familial colon cancer (Lynch I); a high-rate of ovarian, endometrial, breast cancers; genitourinary cancer and hereditary nonpolyposis coli.



Women with first degree relative with ovarian cancer have a 5% lifetime risk of developing the disease and those with two first degree relatives with ovarian cancer have a 7% risk.



Women with HNPCC have a 40% to 60% lifetime risk for ovarian cancer. Mutations in three DNA mismatch repair genes, MLH1, MSH-2 AND MSH6 account for over 95% of mutations found in Lynch syndrome.



Women with BRCA gene mutations have a life time risk of breast cancer of 82%,  
 BRCA1 → Ovarian cancer 45%  
 BRCA2 → Ovarian cancer 25%  
 HNPCC → Ovarian cancer 15%



In women with BRCA1 and BRCA2 mutations, chances of ovarian cancer can be reduced by prophylactic bilateral Salpingo oophorectomy on completion of childbearing or 35 years of age.

### Epidemiology

- Life time risk of developing ovarian cancer is 1 in 70 (1.4%)
- Fifth leading cause of cancer related death worldwide in females, after - lung > breast > colorectal > pancreatic > ovarian cancer
- 65% of ovarian cancers are epithelial
- 35% of ovarian cancers are nonepithelial
- 5-10% of epithelial ovarian cancers have hereditary predisposition.

## Classification

Ovarian Cancer	Arises from	Types	Age Group
Epithelial	Coelomic epithelium	Serous, Mucinous Endometrioid Clear cell, Brenner Undifferentiated	Peri/ postmenopausal (45 + years)
Sex cord stromal	Gonadal stromal	Granulosa cell tumor, Sertoli-Leydig tumor	Reproductive (20 – 40 years)
Germ cell tumors	Primitive germ cells	Dysgerminoma, Endodermal sinus tumor, Embryonal, Teratoma, Chorio carcinoma	Prepubertal-pubertal (15–20 years)
Others	Metastatic	Krukenberg	

## Low Malignant Potential Tumors/Borderline Tumors

- Approximately 10% of all epithelial tumors are borderline of which 30 % are of mucinous variety
- Tumor cells display malignant characteristic histologically but no invasion is identified.
- They remain confined to a single ovary for a very long time are slow growing and have a good prognosis (5 year survival >99%).
- Common in age group-30-50 years unlike there malignant counterparts which are seen in age >50 years.

### The criteria for the diagnosis of borderline tumors

- Epithelial hyperplasia in the form of pseudostratification, tufting, cribriform, and micropapillary architecture
- Nuclear atypia and increased mitotic activity
- Detached cell clusters
- Absence of destructive stromal invasion (i.e., without tissue destruction)

- Metastasis is uncommon and occurs rarely
- Treated with surgery, no proven benefit of chemotherapy.

## Neoplastic Ovarian Tumors

### Epithelial Tumors

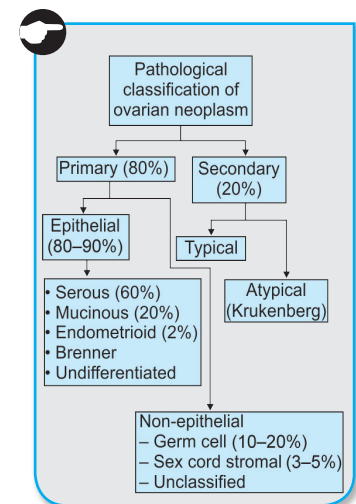
Derived from the ovarian surface epithelium. Epithelial tumors comprise 50-60% of all ovarian tumors but malignant epithelial tumors comprise 90% of all ovarian cancers.

### Varieties of epithelial cell tumors

Serous (histology resembles the lining of fallopian tubes)  
Mucinous (histology resembles endocervical epithelium)  
Endometrioid (histology resembles endometrial lining)  
Clear cell (histology resembles vaginal mucosa)  
Transitional cell (Brenners' – histology resemble bladder)

### Important Points to Remember: In Epithelial Tumors

- Malignant epithelial tumours include both cystic and solid types



Pseudomyxoma peritonei is a condition associated with mucinous neoplasms, usually of gastrointestinal origin, and is characterized by gelatinous mucus or ascites in the abdomen.

**?**  
Hobnail cells are characteristic of clear cell carcinoma.

- Only 19% of ovarian cancers (epithelial cancers) are recognized while disease is in localized stage. Approx 70% are diagnosed in stage III.
- Symptoms – Nonspecific like bloating, early satiety, weight loss, constipation, anorexia.
- Physical examination – Most important sign is presence of a pelvic mass.

**Remember**  
Two tests in post menopausal females tests for ovarian cancer are measurement of CA - 125 levels and transvaginal USG. In premenopausal females Ca125 levels are not measured.

- These are bilateral in 50 percent cases
- Cystic type is more common than the solid
- These may arise *de novo* as malignant or more commonly, they result from malignant changes of benign cystic tumors.
- Serous.** The serous histologic subtype resembles cells of the fallopian tube and is the most common, accounting for over 50% of all malignant ovarian tumors. Approximately one third are malignant, one sixth are LMP, and half are benign.
- The mean age of patients at diagnosis is 57 years.
- Psammoma bodies are present in 25%.
- Mucinous tumors** – lined by cells that resemble the cells of the endocervical glands.
- Primary ovarian mucinous tumors account for 3% to 4% of epithelial tumors.
- Sixty percent of mucinous tumors are stage I, and most are unilateral.
- They are large, cystic, and multiloculated.
- CA-125 levels may not be markedly elevated.
- Poor prognosis than serous variety.
- Endometrioid tumors** resemble the histology of the endometrium.
- Most of them are malignant; 20% may be LMP.
- Associated with endometrial cancer, and endometriosis.
- Endometrioid tumors have a better prognosis because of their early stage at diagnosis.
- Clear cell.** The most chemoresistant type of ovarian cancer are most commonly associated with paraneoplastic syndromes.
- Histologically Hobnail-shaped cells are characteristic of the clear cell carcinoma.
- **Brenner tumor** – Mostly benign, very rarely malignant.

**Diagnosis of Epithelial Ovarian Tumors**

**Assessment of levels of CA125**

- CA - 125 is a glycoprotein secreted by *malignant epithelial tumors* of ovary.
- Levels of Ca 125 correlate with *volume of tumour* and is elevated in 50% of Stage I tumour and 90% of tumours with Stage II or higher.
- CA - 125 level is also useful for *follow up* after treatment. Level > 35 units/ml suggests residual tumour.
- **CA - 125 is raised in :** ... Harrison 16<sup>th</sup>/ed p 554

Benign gynaecological condition	Malignant condition
• Pregnancy	Endogenous – Endometrial Ca
• PID	Pneumocystis – Pancreas Ca
• Endometriosis	Carinii – Colon Ca
• Uterine fibroid	Causes – Cervix Ca
• About 1% of normal females	T – Fallopian tubes Ca
<b>Mnemonic:</b> CA - 125 is raised in pregnant patient with endometrial fibroid B and PID	B – Breast Ca
	Of – Ovarian epithelial Ca (MC cause)
	Lung – Lung Ca
	<b>Mnemonic:</b> Endogenous Pneumocystis Carinii Causes TB Of Lungs

- Normal levels > 35 IU/mL
- In a postmenopausal women with an asymptomatic pelvic mass and CA - 125 ≥ 65 U/ml is very sensitive for diagnosis of ovarian epithelial tumour.
- In menopausal females - levels > 200 IU/mL are diagnostic.
- Although CA 125 is raised in many cancers it is specific for epithelial ovarian cancer.

**Ultrasound:** Ultrasound is an invaluable investigation in presence of pelvic mass.

USG features suggestive of Malignancy

- Solid or echogenic area
- Multilocularity
- Thick and fronded septation
- Bilaterality
- Papillary projection
- Ascites
- Increases vascularity on Doppler

Staging of ovarian cancer is surgical i.e. staging is done following laparotomy where TAH + BSO + Infracolic omentectomy and sampling of pelvic and para-aortic lymph nodes is performed first for staging purpose.

**FIGO Staging for Ovarian Cancer (Surgical)**

STAGE I: Tumor confined to ovaries			
OLD		NEW (2014)	
IA	Tumor limited to 1 ovary, capsule intact, no tumor on surface, negative washings/ascites.	IA	Tumor limited to 1 ovary, capsule intact, no tumor on surface, negative washings.
IB	Tumor involves both ovaries otherwise like IA	IB	Tumor involves both ovaries otherwise like IA.
IC	Tumor involves 1 or both ovaries with any of the following: capsule rupture, tumor on surface, positive washings/ascites.	<i>IC Tumor limited to 1 or both ovaries</i>	
		IC1	Surgical spill (Intra operative capsule rupture)
		IC2	Capsule rupture before surgery or tumor on ovarian surface.
		IC3	Malignant ascites or peritoneal washings.

Stage II: Tumor involves 1 or both ovaries with pelvic extension (below the pelvic brim) or primary peritoneal cancer			
OLD		NEW	
IIA	Extension and/or implant on uterus and/or Fallopian tubes	IIA	Extension and/or implant on uterus and/or Fallopian tubes
IIB	Extension to other pelvic intraperitoneal tissues	IIB	Extension to other pelvic intraperitoneal tissues and pelvic nodes.
IIC	IIA or IIB with positive washings as cites		



Tumor markers in ovarian cancers

Ovarian Tumor	Tumor Marker
Epithelial ovarian tumors	
Serous variety	CA 125
Mucinous variety	Ca 19 – 9, CEA
Serous and mucinous	OCCA, OCA
Endodermal sinus/Yolk sac tumor	AFP
Choriocarcinoma	HCG
Dysgerminoma	LDH, Alkaline phosphatase
Granulosa cell tumor	Inhibin



Inguinal lymph nodes are involved in—  
 Ca ovary – stage IV B  
 Ca Endometrium – stage IVB  
 Ca Cervix – not involved.



**Surgical Staging Procedures for Ovarian Cancer**

- Midline vertical incision
- Obtain ascites for cytologic evaluation or Washings from the pelvis, gutters, and diaphragm
- Inspection and palpation of all organs and surfaces
- Hysterectomy + Bilateral salpingo-oophorectomy
- Infracolic omentectomy
- Sampling pelvic and para-aortic lymph nodes
- Random multiple biopsy specimens from peritoneal sites, Pelvic side walls, surfaces of the rectum and bladder, Cul-de-sac, Lateral abdominal gutters, diaphragm

**Note:** In mucinous tumor one additional step appendicectomy done.

STAGE III: Tumor involves 1 or both ovaries with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to the retroperitoneal lymph nodes			
OLD		NEW	
IIIA	Microscopic metastasis beyond the pelvis.	<i>IIIA (Positive retroperitoneal lymph nodes and/or microscopic metastasis beyond the pelvis.</i>	
		IIIA1	Positive retroperitoneal lymph nodes only
		IIIA 1(i)	Metastasis ≤ 10 mm
		IIIA 1(ii)	Metastasis > 10 mm
		IIIA2	Microscopic extrapelvic (above the brim) peritoneal involvement ± positive retroperitoneal lymph nodes
IIIB	Macroscopic, extrapelvic, peritoneal metastasis ≤ 2 cm in greatest dimension.	IIIB	Microscopic extrapelvic ≤ 2 cm ± positive retroperitoneal lymph nodes. Includes extension to capsule of liver/spleen.
IIIC	Macroscopic, extrapelvic, peritoneal metastasis > 2 cm in greatest dimension and/or regional lymph node metastasis.	IIIC	Microscopic extrapelvic, peritoneal metastasis > 2 cm ± positive retroperitoneal lymph nodes. Includes extension to capsule of liver/spleen.

Stage IV: Tumor involves 1 or both ovaries with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to the retroperitoneal lymph nodes			
OLD		NEW	
IV	Distant metastasis excluding peritoneal metastasis. Includes hepatic parenchymal metastasis.	IV A	Pleural effusion with positive cytology
		IVB	Hepatic and/or splenic parenchymal metastasis, metastasis to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside of the abdominal cavity)

**Other major recommendations are as follows:**

- Histologic type including grading should be designated at staging
- Primary site (ovary, fallopian tube or peritoneum) should be designated where possible
- Tumors that may otherwise qualify for stage I but involved with dense adhesions justify upgrading to stage II if tumor cells are histologically proven to be present in the adhesions.

**Spread**

Modes of spread of ovarian cancer are –

- Transcoelomic (Tumor exfoliation)
- Lymphatic (pelvic + para-aortic LN)



- Direct
- Hematogenous

## Management of Epithelial Ovarian Tumors

In ovarian cancers similar to endometrial cancer – staging is surgical i.e. hysterectomy with bilateral salpingo Ophorectomy has already been performed. Therefore treatment basically consists of postoperative management. The preferred post operative treatment in ovarian tumors is chemotherapy. 6 cycles of carboplatin and paclitaxel and in advanced cases cisplatin and paclitaxel.

### Stagewise Management of Ovarian Tumors

Stage	Management
Low malignant potential tumors	Surgical staging. No postoperative treatment required
Stage I (A or B) Grade I and II	Surgical staging. No postoperative treatment required <b>Note:</b> In a young woman who wish to preserve fertility if intraoperative findings are consistent with stage I , unilateral salpingo oophorectomy may be performed. The uterus and the contralateral ovary can be removed later when the patient has completed child bearing.
Stage I (A or B) Grade III and all grades of Stages IC and II	Surgical staging followed by three to six cycles of chemotherapy postoperatively.
Advanced ovarian cancer – Stage III/IV	Cytoreduction or debulking surgery followed by six cycle of platinum based chemotherapy (carboplatin + paclitaxel preferred) each cycle given after 3 weeks.

**Neoadjuvant therapy** i.e. initial treatment with chemotherapy followed by interval debulking surgery.

### Indications

- Patients with medical conditions which prohibit initial surgery.
- In patients in whom suboptimal debulking is likely.

**Posttreatment Surveillance** plan consists of physical examination with rectovaginal examination, CA-125 testing, and CT scan every 3 months for the first 2 years.

### Prognosis

Depends on

- i. Stage
- ii. Histology of tumor
- iii. **Grade**  
Grade 1 – well differentiated  
Grade 2 – Moderately differentiated  
Grade 3 – Poorly differentiated
- iv. Amount of residual tumor left after debulking
- v. Age of the patient (younger patients have better prognosis)
- vi. Tumor ploidy – Diploid tumors having better prognosis than aneuploid
- vii. Absence of ascites.



**Debulking**, also called **cytoreduction**, is defined as removal of as much tumor as possible during surgical exploration. Optimal cytoreduction implies that tumor nodules no larger than 1 cm in diameter are left behind and survival improves as the amount of residual diseases decreases.



Primary cytoreductive surgery, or debulking is central in the treatment of advanced disease because maximal cytoreduction is one of the most powerful predictor of survival in patients with advanced cancer. The determination of residual disease does not include the total volume of tumor cells left behind but rather the diameter of the largest single residual nodule.



In stage III tumors – Chemotherapy can also be given intraperitoneally.

#### Advantage

- Better compliance
- Better results in overall survival

#### Disadvantage

- Increase in toxic events
- Catheter related complications



The 'gold standard' for identifying residual disease is second look laparotomy.



- Most common germ cell Tumor – Mature teratoma or Dermoid cyst<sup>o</sup> (Benign in nature).
- Most common malignant GCT – Dysgerminoma.<sup>o</sup>
- Second most common malignant GCT – Endodermal sinus Tumor. (Yolk Sac tumor)
- Most common benign Tumor of ovary – Dermoid cyst<sup>o</sup>



#### Dysgerminoma

- M/c malignant GCT
- Most radiosensitive
- Best prognosis amongst all germ cell tumors
- Worst prognosis in germ cell tumors is with endodermal sinus tumor.

## Germ Cell Tumors of Ovary

- They are unilateral tumors
- Account for 5% of all ovarian tumors
- M/C age group = 10–20 years
- In this age group 70% tumors are Germ cell tumors.
- Rare after 30 years.
- Metastasis is late feature.

### Germ Cell Tumors of Ovary

#### Mnemonic : YES PCT

**Y** - Yolk sac Tumor (Endodermal sinus Tm)

**E** - Embryonal carcinoma

**S** - Seminoma ≈ Dysgerminoma

**P** - Polyembryoma

**C** - Choriocarcinoma

**T** - Teratoma ≈ Dermoid

In contrast to slow growing epithelial ovarian tumors, germ cell malignancies grow rapidly and are characterised by subacute pelvic pain.

## Endodermal Sinus Tumor/Yolk Sac Tumor

### Endodermal sinus tumour / Yolk sac tumor:

- Endodermal sinus (yolk sac) tumour is third most common malignant germ cell tumour of ovary affecting mostly children or young women. (Age group 14–20 years).
- Tumour is *highly malignant* and is *most rapidly growing tumour of whole body*.
- **It is the most deadly malignant ovarian germ cell tumor.**
- Histologically the pathognomonic finding is *Schiller - Duval bodies*<sup>o</sup> which is a single papilla lined by tumour cells with a central blood vessel.
- Due to high rate of growth, tumour usually presents with acute abdomen.
- **Unilateral in 100% cases therefore biopsy of opposite ovary is contraindicated.**
- Almost all cases are associated with raised AFP and Alpha 1 antitrypsin.
- *Treatment:* Chemotherapy.
- It has a high propensity for rapid growth, peritoneal spread and distant hematogenous dissemination to the lungs.

## Dysgerminoma

- Commonest *malignant germ cell tumour*<sup>o</sup> of ovary.
- They are the most common ovarian malignancy detected during pregnancy.
- Primarily affect *young women* (average age of incidence is 20 years<sup>o</sup>).
- Usually *unilateral*<sup>o</sup> but they are the only germ cell malignancy with a significant rate of bilateral ovarian involvement – 15 to 20%.
- Can be found at gonadal as well as extra gonadal sites.<sup>o</sup>
- Pathologically it is a solid neoplasm with *areas of softening*<sup>o</sup> due to degeneration. "*Consistency is fleshy*"
- **Histologically** as in seminoma, it *mimics the pattern of primitive gonad, lymphocytic infiltration* may be seen (good prognostic sign).<sup>o</sup>
- Clinically as with all germ cell tumours most dysgerminoma are diagnosed at an early stage.
- Unlike other germ cell tumours it *does not secrete AFP* and HCG is only rarely secreted, however it *secretes LDH and placental alkaline phosphatase*, which are used as tumour marker of dysgerminoma.

- M/C, route of spread is via lymphatics but hematogenous and direct spread are also seen.
- It can metastasise to opposite ovary and an uncommon site of metastasis seen is lower vertebra.

### Management of Dysgerminoma

- The treatment of *early dysgerminoma* i.e. Stage IA  
*Surgical* – including resection of the primary lesion (unilateral salpingo-oophorectomy) and proper surgical dissection, without postoperative chemotherapy.
- Rest all cases – surgery (fertility sparing i.e. removing only the affected ovary or debulking surgery) followed by chemotherapy.

### Chemotherapy :

- The most frequently used chemotherapy regimens for germ cell tumors are :
  - **BEP** – Bleomycin, Etoposide, Cisplatin (best regime)
  - **VBP** – Vinblastin, Bleomycin, Cisplatin
  - **VAC** – Vincristine, Actinomycin, Cyclophosphamide

### In case of Recurrent Disease :

If **primary treatment was surgery** – chemotherapy can be given (BEP regime).

If **primary treatment was chemotherapy** –

- Radiation therapy can be given (Major disadvantages - loss of fertility if pelvic and abdominal irradiation is required).

OR

- Chemotherapy in the form of POMB - ACE (i.e. Vincristine, bleomycin, cisplatin, etoposide, actinomycin D, methotrexate and cyclophosphamide) is given.

### Sex Cord Stromal Tumors (SCST)

- Least common (3%) of ovarian tumors
- Unilateral
- Remain confined to ovary for a long time
- LN metastasis is a feature rare
- M/C age-perimenopausal females but can occur at any age.
- Diagnosed at early stage.
- Best prognosis

### Classification

Granulosa stromal cell tumour	Androblastoma	Gynandroblastoma
<ul style="list-style-type: none"> <li>• Granulosa cell tumour</li> <li>• Tumours in thecoma fibroma group               <ul style="list-style-type: none"> <li>– Thecoma</li> <li>– Fibroma</li> <li>– Unclassified</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Sertoli cell tumour</li> <li>• Sertoli leydig cell tumour</li> <li>• Leydig cell tumour</li> </ul>	

### Granulosa Cell Tumor

- **Age** : It can be seen at any age. Most common before puberty and *after 40 years*. (Maximum incidence at 52 years).
- Tumour secretes estrogen which is responsible for its clinical features.



Dysgerminomas are also seen in phenotypic females with abnormal gonads like:

- Pure gonadal dysgenesis (46XY with bilateral streak gonads, swyer syndrome)
- Mixed gonadal dysgenesis
- Testicular feminization syndrome (46XY)
- Klinefelter syndrome
- For patients in whom karyotype reveals Y chromosome, both ovaries should be removed although uterus may be left in situ for possible future embryo transfer.



Dysgerminoma in pregnancy—

- M/c ovarian tumor detected during pregnancy – Dermoid
- M/c malignant tumor detected in pregnancy – Dysgerminoma.

### Early stage dysgerminoma (Stage Ia)

- Tumor can be removed intact and pregnancy continued.

### Advanced disease

- Continuation of pregnancy depends on the gestational age of fetus.
- Chemotherapy can be given in the second and third trimester in the same dosages as given for the nonpregnant patient without apparent detriment to the fetus.

If it occurs		
Before puberty	Reproductive age	Postmenopausal
Precocious puberty	Initially it leads to amenorrhoea (Due to suprathreshold level of estrogen) f/b prolonged bleeding (similar to metropathia hemorrhagica).	

➤ Most common symptoms are : Menometrorrhagia and post menopausal bleeding.

#### Pathology

- They are low grade malignancies.
- Almost always unilateral<sup>Q</sup> (B/L in < 2%)
- Encapsulated tumours and have smooth surface.

**On microscopy:** Granulosa cells exhibit coffee bean nucleus and call exner bodies.<sup>Q</sup>

**Metastasis:** It is peculiar in case of granulosa cell tumour, it first involves opposite ovary followed by metastasis in lumbar region.

Secondary deposits are also seen in mesentery, liver and mediastinum.

#### Malignant transformation

- Since they secrete estrogen, 25–50% are associated with *Endometrial hyperplasia*.
- 5 per cent of tumours are associated with endometrial cancer.

**Recurrence:** is common but manifests late.

**Marker:** Granulosa cell tumour secrete inhibin which is a useful marker for it. **Management:** Surgery is the TOC. Type of surgery depends on age of occurrence.

Women of reproductive age stage IA ↓ Unilateral salpingo-oophorectomy	Postmenopausal ↓ TAH + BSO.
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**Prognosis** – good.

**Note:** For premenopausal females in whom uterus is left intact in granulosa cell Tumor -an endometrial biopsy should be done because of possibility of coexisting adenocarcinoma endometrium.

### Masculinising Tumors

Arrhenoblastoma/ Androblastoma Hilus cell Tm	Adrenal cortical Tm/ Lipoid cell Tm of ovary	Gynandroblastoma
<ul style="list-style-type: none"> <li>• Affect child bearing age group (10–35 years)</li> </ul> <b>It includes :</b> <ul style="list-style-type: none"> <li>• Sertoli Cell Tumor (SCT)</li> <li>• Leydig cell Tumor</li> <li>• Sertoli – Leydig cell Tumor</li> </ul>	<ul style="list-style-type: none"> <li>• Seen in postmenopausal females</li> <li>• Characterised by presence of Reinke's crystals</li> </ul>	<ul style="list-style-type: none"> <li>• Combination of granulosa cell tumour &amp; arrheno blastoma</li> </ul>

**Presentation :** They are low grade malignancies

All masculinizing tumors cause defeminization, followed by masculinization.

**Patient complain of:** • altered body contour

- scanty and irregular menstruation followed by amenorrhoea
- flattening of breast
- increased hair growth – hirsutism



- Granulosa cell tumor is associated with endometrial cancer
- GCT are relatively insensitive to adjuvant chemotherapy and radiotherapy.
- Levels of Inhibin B correlate with the risk of recurrence of granulosa cell tumor.

- clitoromegaly
- receding hair line
- hoarseness of voice

**Diagnosis:** Serum Testosterone levels raised >200 ng/dl and increased androstenedione. (DHEAS may be normal which helps to differentiate it from a masculinizing adrenal tumor)

### Metastatic Ovarian Carcinoma

First Type	Second Type ( <i>Krukenberg Tumour</i> )
<ul style="list-style-type: none"> <li>• They are metastatic tumors from Intestine, Gall bladder, pancreas, corpus, and cervix</li> <li>• They are most commonly bilateral</li> <li>• They have irregular surface</li> <li>• The method of ovarian infiltration is by surface implantation or retrograde implantation</li> </ul>	<ul style="list-style-type: none"> <li>• They are metastatic tumors from stomach (70%), large bowel (15%) and breast (6%)</li> <li>• They are always bilateral.<sup>Q</sup></li> <li>• They have a smooth surface which may be slightly bossed.</li> <li>• Always arise by retrograde lymphatic spread.</li> </ul>



M/c tumor to metastasize to ovary – GIT tumor  
Second M/c – Breast tumor

### Krukenberg Tumor

- Krukenberg tumor by definition *represent carcinoma of stomach metastasised to ovary*. But the eponym is commonly used to denote any gastric cancer metastatic to ovary
- Tumor arise by *retrograde lymphatic spread*<sup>Q</sup> i.e. carcinoma cells pass from the stomach to the superior gastric lymphnode which also receive lymphatics from ovary.

### Characteristics of Krukenberg Tumor

- Always bilateral<sup>Q</sup>
- Have smooth surface<sup>Q</sup>
- No tendency to form adhesions
- Freely mobile
- No infiltration through the capsule.
- Histologically tumour has signet ring cells in the background of myxomatous stroma.
- They retain the shape of normal ovary.<sup>Q</sup>
- Have waxy consistency.<sup>Q</sup>

### Histological Characteristics of Ovarian Tumors

Feature	Associated tumour
Call exner bodies & coffee bean nuclei	Granulosa cell tumour
Schiller duval bodies	Endodermal sinus tumor
Reinke's crystal	Hilus cell tumour
Psammoma bodies	Serous epithelial tumours
Walthard cell nest	Brenner tumour
Signet ring cell	Krukenberg tumour
Hobnail cell	Clear cell tumour
Large polygonal cell with lymphocytic infiltration and fibrous septa	Dysgerminoma
Skin, teeth, cartilage	Teratoma

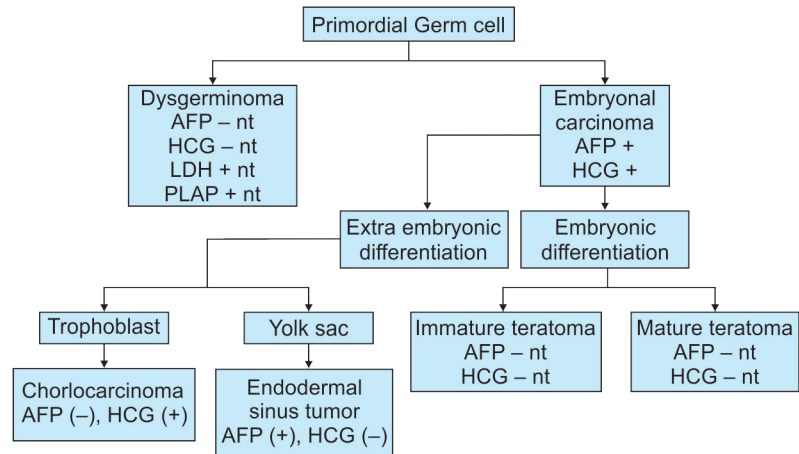
## Tumor Markers of Ovarian Neoplasm



### Remember

- Fertility sparing surgery in ovarian cancers is U/L salpingo-oophorectomy: Aspiration and cystectomy are never done.
- Indications of U/L BSO in ovarian cancers
- Epithelial ovarian Tms- Stage 1 in young females
- Germ cell Tumors
- Granulosa cell Tumor- stage 1A in young female
- Borderline Tumors

Epithelial cell Tumor-Serous variety	<ul style="list-style-type: none"> <li>• CA 125</li> <li>• Mucinous variety-Ca 19-9,CEA</li> <li>• Both serous and mucinous variety- OCCA, OCA</li> </ul>
Germ cell Tumors (In individual tumors see flow chart given below)	<ul style="list-style-type: none"> <li>• Alpha fetoprotein</li> <li>• Lactic dehydrogenase</li> <li>• Human chorionic gonadotropin</li> <li>• Placental alkaline phosphatase</li> </ul>
Granulosa cell tumor	Inhibin



## FIGURE BASED QUESTION

- F1. Figure 1 shows specimen of 'Para ovarian cyst'. All of the following are true in relation to para ovarian cyst except:
- It is a true broad ligament cyst
  - It usually arises from epoophoron
  - Malignant transformation is frequent
  - More chances of ureteric injury during surgical removal

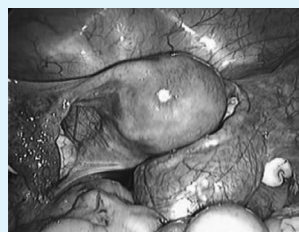


Fig. F1

## QUESTIONS

## General

- All of the following are known risk factors for the development of ovarian carcinoma except: (AIIMS 03)
  - Family history of ovarian carcinoma
  - Use of oral pills
  - Use of Clomiphene
  - BRCA - 1 positive individual
- Which of the following strategy has been recommended to reduce the heredity risk for ovarian cancer in women with BRCA - 1 and BRCA - 2 mutations? (AIIMS 05)
  - Use of oral contraceptive pills
  - Screening with transvaginal ultrasound
  - Screening with CA - 125
  - Prophylactic oophorectomy
- Most common ovarian tumor in less than 20 years is: (AIIMS 97)
  - Epithelial tumour
  - Germ cell tumour
  - Metastatic tumour
  - Sexcord stromal tumour
- Which of the following is the most radiosensitive ovarian tumors? (AIIMS 97)
  - Dysgerminoma
  - Dermoid cyst
  - Serous cystadenoma
  - Endodermal sinus tumour
- MC ovarian tumour in younger age group or M/C malignant Tm in young age group: (PGI June 05/04)
  - Dysgerminoma
  - Dermoid
  - Mucinous cystadenoma
  - Fibroma
  - Granulosa cell tumour
- All of the following are true about Borderline tumors except:
  - 10% of all epithelial tumours are borderline.
  - they have a good prognosis.
  - Metastases are common
  - Absence of stromal invasion
- According to WHO classification of ovarian tumours, Brenner tumor of ovary belongs to:
  - Epithelial tumours
  - Sex cord stromal tumours
  - Germ cell tumours
  - Metastatic tumours

## Epithelial Cell Tumors

- Ovarian tumours are commonly arise from: (UP 05)
  - Stroma
  - Surface epithelium
  - Germinal epithelium
  - Endoderm
- True about Brenner tumor: (PGI 03)
  - Usually bilateral
  - Resembles fibroma
  - Accounts for 20% of all ovarian tumors
  - Common in postmenopausal age group
- A 25-year-old married nullipara undergoes laparoscopic cystectomy for ovarian cyst which on histopath reveals ovarian serous cisadenocarcinoma. What should be the next management? (AIIMS Nov 08)
  - Serial Ca-125 measurement and follow-up
  - Hysterectomy and bilateral pingo oophorectomy
  - Hysterectomy + Radiotherapy
  - Radiotherapy
- Chemotherapeutic drug effective in the treatment of epithelial ovarian cancer is: (Karn 02)
  - Carboplatin
  - Paclitaxel
  - Cyclophosphamide
  - Methotrexate karnataka

## Sex Cord Tumors

- Which of the following are masculinizing tumors of the ovary? (AI 97)
  - Granulosa cell tumor
  - Dysgerminoma
  - Dermoid Cyst
  - Arrhenoblastoma
- Which of the following is correct regarding granulosa cell tumour of ovary? (AIIMS 96)
  - Common in puberty
  - Associated with Ca endometrium
  - Malignant change occur rarely
  - It is bilateral
- True about granulosa cell tumours: (PGI Dec 05)
  - MC malignant tumour of ovary
  - It secretes hormones
  - Associated with endometrial hyperplasia
  - Chemotherapy sensitive

## Germ Cell Tumor

15. The most common pure germ cell tumour of the ovary:
  - a. Choriocarcinoma
  - b. Dysgerminoma (AI 05)
  - c. Embryonal cell tumor
  - d. Malignant Teratoma
16. Which of the following is the most common pure malignant germ cell tumor of the ovary? (AIIMS 04, 05)
  - a. Choriocarcinoma
  - b. Gonadoblastoma
  - c. Dysgerminoma
  - d. Malignant teratoma
17. Malignant germ cell tumours of ovary includes all of the following except: (PGI 04)
  - a. Choriocarcinoma
  - b. Arrhenoblastoma
  - c. Brenner's tumor
  - d. Serous cystadenoma
  - e. Teratoma
18. Features of dysgerminoma are: (PGI June 06)
  - a. Unilateral
  - b. Post-menopausal
  - c. Virilising
  - d. Cut section gritty
  - e. ↑ AFP
19. True about dysgerminoma: (PGI June 09)
  - a. Radiosensitive
  - b. Most common malignant germ cell tumor
  - c. Bilateral
  - d. ↑ AFP
  - e. Common in postmenopause
20. True about dysgerminoma of ovary: (PGI Dec. 04)
  - a. Blood spread seen
  - b. Schiller-Duval bodies seen
  - c. Increase alfa fetoprotein
  - d. Bleomycin, etoposide and cisplatin given
  - e. Radiosensitive
21. Chemotherapy for dysgerminoma is: (AP 05)
  - a. Cisplatin, etoposide, bleomycin
  - b. Cyclophosphamide, vincristine, prednisolone
  - c. Adriamycin, cyclophosphamide, cisplatin
  - d. Methotrexate, oncovin, cyclophosphamide
22. A 12 years old female is admitted as a patient of dysgerminoma of right ovary 4 x 5 cm in size with intact capsule. Best treatment will be: (AIIMS 01)
  - a. Ovarian cystectomy
  - b. Oophorectomy on the involved side
  - c. Bilateral oophorectomy
  - d. Hysterectomy with bilateral salpingo oophorectomy
23. True about dermoid cyst of ovary: (PGI 03)
  - a. It is teratoma
  - b. Frequently undergo torsion
  - c. X-ray is diagnostic
  - d. Invariably turns to malignancy
  - e. Contains sebaceous material and hairs
24. True about Yolk sac tumor: (PGI 02)
  - a. Also called endodermal sinus tumour
  - b. Always have elevated AFP level
  - c. Schiller Duval bodies seen
  - d. Highly malignant
  - e. Arise from epithelial cells of ovary

25. True about endodermal sinus tumors: (PGI Dec 05)
  - a. Schiller duval bodies seen
  - b. It is a benign tumour
  - c. ↑ HCG
  - d. It is seen in young individuals
  - e. It is a malignant tumour

## Krukenberg Tumor

26. All of the following are true about Krukenberg's tumor except: (AI 96)
  - a. Has a rough surface
  - b. Shape of ovary is maintained
  - c. Usually bilateral
  - d. Arises usually from stomach carcinoma
27. Smt. Pushpa is a suspected case of ovarian tumors. On laparotomy bilaterally enlarged ovaries with smooth surface was seen: (AIIMS 00)
  - a. Granulosa cell tumor
  - b. Krukenberg tumor
  - c. Dysgerminoma
  - d. Primary adenocarcinoma
28. The following tumours commonly metastasise to the ovary, except: (J & K 05)
  - a. Malignant melanoma
  - b. Stomach
  - c. Oesophagus
  - d. Lymphoma

## Presentation/Complication

29. A 55-year-old female presents with abdominal pain, distension, ascites and dyspnea. Her CA 125 levels are elevated. The most likely diagnosis is: (AI 2012)
  - a. Ca ovary
  - b. Ca cervix
  - c. Ca lung
  - d. Symphoma
30. Pain of ovarian carcinoma is referred to: (AIIMS May 2010)
  - a. Back of thigh
  - b. Cervical region
  - c. Anterior surface of thigh
  - d. Medial surface of thigh
31. True about Meig's syndrome: (PGI Dec 06)
  - a. Lymphatic dysplasia
  - b. 2-30 years age
  - c. Associated with ascites and pleural effusion
  - d. No treatment required
32. All are components of Meig's syndrome, except: (AIIMS 97; AI 95)
  - a. Pleural effusion
  - b. Ovarian tumour
  - c. Ascites
  - d. Pericardial effusion
33. Meig's syndrome is associated with: (PGI 95, 99)
  - a. Teratoma
  - b. Brenner tumour
  - c. Theca cell tumour
  - d. Fibroma
34. The most common complication of an ovarian tumor is: (AI 95)
  - a. Torsion
  - b. Hemorrhage
  - c. Infection
  - d. Hyaline change



35. Most common ovarian cyst to undergo torsion: (AI 07)  
 a. Benign cystic teratoma b. Dysgerminoma  
 c. Ovarian fibroma d. Brenner's tumour
36. Pseudomyxoma peritonei is seen in: (PGI 98)  
 a. Serous cystadenoma  
 b. Pseudomucinous cyst  
 c. Mucinous cystadenoma  
 d. Teratoma
37. The pseudomyxoma peritonei occurs as a complication of the following ovarian tumours: (AIIMS May 06)  
 a. Serous cystadenoma b. Mucinous cystadenoma  
 c. Dysgerminoma d. Gonadoblastoma
38. Attacks of flushing and cyanosis occur in which type of ovarian tumors: (AIIMS 79; AMU 82)  
 a. Struma ovarii  
 b. Krukenberg's tumor  
 c. Arrhenoblastoma  
 d. Carcinoid tumors of ovary  
 e. Granulosa cell tumor  
 (Ref. Shaw 15<sup>th</sup>/ed p 378)
44. A lady has ovarian mass, X-ray pelvis shows a radio-opaque shadow. The probable diagnosis is: (AIIMS 98)  
 a. Mucinous cyst adenoma  
 b. Serous cyst adenoma  
 c. Dysgerminoma  
 d. Dermoid cyst
45. A 20-year female presents with a ovarian mass 6 × 6 × 6 cm in size. Ultrasonography reveals solid structures in the mass. Her serum biomarkers such as AFP, fÖ-hCG and CA 125 are normal, however, her serum alkaline phosphatase was found to be elevated. The most likely diagnosis is: (AIIMS Nov 2011)  
 a. Dysgerminoma  
 b. Endodermal sinus tumor  
 c. Malignant teratoma  
 d. Mucinous cystadenocarcinoma
46. Smt. Pushpa is a suspected case of ovarian tumors. On laparotomy bilaterally enlarged ovaries with smooth surface was seen: (AIIMS 00)  
 a. Granulosa cell tumor b. Krukenberg tumor  
 c. Dysgerminoma d. Primary adenocarcinoma
47. Reinke's crystals are found in: (AIIMS 95)  
 a. Arrhenoblastoma b. Granulosa cell tumor  
 c. Dysgerminoma d. Hilus cell tumor
48. Which are seen in endodermal sinus tumor?  
 a. Schiller-duval bodies b. Reed-Sternberg cells  
 c. Reinke's crystals d. Russell bodies

## Diagnosis

39. In a suspected case of ovarian cancer, imaging work up is required for all of the following except: (AI 06)  
 a. Detection of adnexal lesion  
 b. Characterization of lesion  
 c. Staging  
 d. Asses resectability
40. A 45-year-old female is having bilateral ovarian mass, ascites and omental caking on CT scan. There is high possibility that patient is having: (AI 03)  
 a. Benign ovarian tumor  
 b. Malignant epithelial ovarian tumor  
 c. Dysgerminoma of ovary  
 d. Lymphoma of ovary
41. Feature in USG suggestive of ovarian malignancy is: (PGI 99)  
 a. Papillary pattern b. Septations  
 c. Bilaterality d. Clear fluid
42. A 24-year-old woman presents with new onset right lower quadrant pain, and you palpate an enlarged, tender right adnexa. Which of the following sonographic characteristics of the cyst in this patient suggests the need for surgical exploration now instead to observation for one menstrual cycle?  
 a. Lack of ascites b. Unilocularity  
 c. Papillary vegetation d. Diameter of 3 cm
43. A 20-year-old young girl, presents with history of rapidly developing hirsutism and amenorrhea with change in voice. To establish a diagnosis you would like to proceed with which of the following tests in blood? (AI 02)  
 a. 17 OH progesterone b. DHEA  
 c. Testosterone d. LH + FSH estimation

## Tumor Markers

49. In a case of Dysgerminoma of ovary one of the following tumor markers is likely to be raised: (AI 05)  
 a. Serum HCG  
 b. Serum alpha fetoprotein  
 c. Serum lactic dehydrogenase  
 d. Serum inhibin
50. Which is raised in dysgerminoma? (AI 09)  
 a. AFP b. LDH  
 c. HCG d. CA-A 19-9
51. All of the following are the markers for malignant germ cell tumors of ovary except: (AIIMS 05)  
 a. CA - 125 b. Alpha fetoprotein  
 c. β HCG d. LDH
52. CA - 125 is a tumor marker for: (AIIMS 97, 98)  
 a. Carcinoma ovary b. Carcinoma endometrium  
 c. Carcinoma vagina d. Carcinoma cervix
53. CA - 125 is specifically associated with: (PGI 02)  
 a. Colon Ca b. Breast Ca  
 c. Ovarian Ca d. Bronchogenic Ca  
 e. Pancreatic Ca
54. CA - 125 is specific marker of: (PGI 99)  
 a. Choriocarcinoma  
 b. Teratoma  
 c. Epithelial cell carcinoma of ovary  
 d. Seminoma

55. A lady with CA ovary in follow-up with raised CA 125 level, next step: (AIIMS May 08)
- CT
  - PET
  - MRI
  - Clinical exam and serial follow up of CA 125
56. Placental alkaline phosphatase is marker of: (PGI 96)
- Theca cell tumor
  - Teratoma
  - Choriocarcinoma
  - Dysgerminoma
57. Marker for granulosa cell tumor: (AIIMS May 08)
- CA 19-9
  - Ca 50
  - Inhibin
  - Teratoma

### Unilateral/Bilateral

58. All of the following ovarian tumours usually occur bilaterally, except: (AIIMS 95)
- Metastatic mass
  - Dysgerminoma
  - Cyst adenoma of ovary
  - Dermoid cyst
59. Bilateral germ cell tumour is: (AIIMS May 07)
- Dysgerminoma
  - Immature teratoma
  - Embryonal cell carcinoma
  - Endodermal sinus tumour
60. Which ovarian tumor is likely to involve the opposite ovary by metastasis? (AI 96)
- Granulosa cell tumor
  - Dysgerminoma
  - Gynandroblastoma
  - Endodermal sinus tumor

### Staging

61. Surgical staging of ovarian Ca all done except: (AI 09)
- Peritoneal washing
  - Peritoneal biopsy
  - Omental biopsy
  - Palpation of organs
62. Laparotomy performed in a case of ovarian tumor revealed unilateral ovarian tumor with ascites positive for malignant cells and positive pelvic lymph nodes. All other structures were free of disease. What is stage of the disease? (AI 03)
- Stage II b
  - Stage III a
  - Stage III b
  - Stage III c
63. Bilateral ovarian cancer with; capsule breached; ascites positive for malignant cells. Stage is: (AI 01; AIIMS 07)
- I
  - II
  - III
  - IV
64. A 55-year-old female patient has carcinoma ovary with bilateral involvement with ascitic fluid in the abdomen. The stage is: (AIIMS 99)
- II
  - III
  - IV
  - IC
  - Dysgerminoma

65. What is the stage of ovarian Ca with superficial liver metastasis with B/L ovarian mass? (PGI Dec 06)
- Stage I
  - Stage II
  - Stage III
  - Stage IV
  - Ca in situ

### Ovarian Cysts and Their Management

66. Which ovarian cyst does not undergo malignancy: (AIIMS 92)
- Mucinous
  - Papillary
  - Dermoid
  - Granulosa Theca
- (Ref. Shaw 15<sup>th</sup>/ed pg -377 for option c, 379 for option d, 375 for option a, 374 for option b)
67. All are true about serous cystadenoma of the ovary except: (UP 04)
- Bilateral
  - Unilateral
  - Concentric calcification
  - Multiloculated, sticky, gelatinous fluid
- (Ref. Shaw 15<sup>th</sup>/ed pg -374; Dutta Gynae 5<sup>th</sup>/ed p 282)
68. A 35-year-old patient on USG shows 3 × 4 cm clear ovarian cyst on right side. Next line of management is: (PGI Dec 08)
- Laparoscopy
  - OC pills
  - Wait and watch
  - Ca-125 estimation
69. Kruti, 56 years old, complained of pain in abdomen, with USG showing 4 cm bilateral ovarian mass with increased vascularity. Next line of managements: (AI 2007)
- USG guided ovarian tapping
  - Wait and watch
  - Surgery
  - OC pills x three cycles.

### Pregnancy and Cysts

70. Most common ovarian tumour in pregnancy is: (AIIMS 96)
- Mucinous cyst adenoma
  - Dermoid cyst
  - Metastasis
  - Dysgerminoma
71. Which of the following ovarian tumor is most prone to undergo torsion during pregnancy? (AI 06)
- Serous cystadenoma
  - Mucinous cystadenoma
  - Dermoid cyst
  - Theca lutein cyst
72. A 15 cms X 15 cms ovarian cyst has been diagnosed in an 8 weeks pregnant lady. Further Management includes: (PGI Nov 10)
- Only follow up without surgical intervention
  - Laparotomy at 14-16 weeks
  - Cesarean delivery and ovariectomy at term
  - Surgery after delivery
  - Immediate operation

73. Which is/are used in management of stage III ovarian cancer:
- Debulking
  - Mantle field irradiation
  - Abdomino-pelvic radiotherapy is very effective
  - Chemotherapy
  - Cytoreduction

### NEW PATTERN QUESTIONS

74. Lutein cysts are associated with all except:
- Gestational trophoblastic tumours
  - Clomiphene administration
  - Bilaterality
  - Use of OCP's
75. The following statements are related to Krukenberg tumour except:
- It is always secondary
  - The most common primary site is pylorus of the stomach
  - The tumour is bilateral
  - 'Signet ring' looking cells are characteristic
76. Sex cord stromal tumours of the ovary include all except:
- Luteomas
  - Gynandroblastomas
  - Sertoli-Leydig cell tumours of the ovary
  - Theca-fibroma
77. True regarding neoplasms of the ovary are:
- Stromal invasion is commonly present in ovarian tumours of borderline malignancy
  - Lymphocytic infiltration is characteristic to dysgerminoma
  - Presence of ascites and pleural effusion in Brenner tumour indicates poor prognosis
  - Endometrioid carcinoma of the ovary may coexist with endometrial adenocarcinoma
78. A 52 years postmenopausal female presents unilocular with a ovarian cyst of 6 cms with normal Ca125 levels management is:
- USG guided ovarian tapping
  - Wait and watch
  - Surgery
  - OCP

## ANSWER TO FIGURE BASED QUESTION

- F1. Ans. is c, i.e. Malignant transformation is frequent**  
In para ovarian cysts-malignant transformation is rare.

## ANSWERS

## 1. Ans. is b, i.e. Use of oral pills

Ref. CGDT 10<sup>th</sup>/ed p 871 - 872

See the text for explanation.

## 2. Ans. is d, i.e. Prophylactic oophorectomy

Ref. Novak 14<sup>th</sup>/ed p 1471; Devita 7<sup>th</sup>/ed p 1369; Wililams Gynae 1<sup>st</sup>/ed p 718-719; Recent Advances in Gynae - Studs

## As discussed in previous question:

- BRCA-1 and BRCA-2 are tumour suppressor genes.
- Individuals who inherit mutations of BRCA-1 and BRCA-2 are highly susceptible for the development of hereditary breast or ovarian cancer. The mutations are inherited as autosomal dominant.

## Strategies for prevention of hereditary ovarian cancer

- Genetic testing for susceptibility to ovarian cancer is rapidly becoming integrated into the clinical practice of oncology. Strategies have been adopted to reduce the incidence of ovarian cancer in patient with BRCA-1 and BRCA-2 mutations.

## a. Prophylactic oophorectomy:

*"The only proven way to prevent ovarian cancer is surgical oophorectomy. As another possible site of disease among these high risk patients is fallopian tube therefore should be removed. IN BRCA 1 or BRCA-2 mutation carriers, prophylactic bilateral salpingo-oophorectomy (BSO) may be performed on either completion of childbearing or at age 35. In these patients, the procedure is approximately 90% effective in preventing epithelial ovarian cancer. In women with HNPCC, the risk reduction approaches 100%."*  
... William Gynae 1<sup>st</sup>/ed p 719

- Additional benefit of prophylactic oophorectomy is that the risk of breast cancer is reduced by 50-80%.

## b. Oral contraceptive pills:

- Data received from a multicenter control of genetic screening centers indicates that the use of oral contraceptive pill is associated with 50% decreased risk for developing ovarian cancer in women who have mutation in either in BRCA - 1 or BRCA - 2. However there is short term increased risk of developing breast cancer.

## c. Role of screening with CA 125 and transvaginal ultrasound:

*"In BRCA1- BRCA2 mutation carriers who donot wish to undergo prophylactic surgery a combination of through pelvic examination, transvaginal sonographic examination and CA125 blood testing should be done".*

... Williams Gynae 1<sup>th</sup>/ed p 719

- Best method of prevention: Prophylactic hysterectomy and BSO at 35 years or as soon as family is complete.
- 2nd line: OCP's + screening
- Screening: TVS + Ca 125 started at 35 years and done every 6 or 12 months, breast screening by MRI and mamography at 30 years done annually.

## 3. Ans. is b, i.e. Germ cell tumour

Ref. Shaw 15<sup>th</sup>/ed pg -376

## 4. Ans. is a, i.e. Dysgerminoma

Ref. Bailey & Love 24<sup>th</sup>/ed p 221

*"Below the age of 20 years 60% of the tumours are of germ cell origin and in girls under the age of 10 years almost 85% are of germ cell origin and are invariably malignant."*

*"Dysgerminoma is the most common malignant germ cell tumour accounting for about 40% of all ovarian cancers of germ cell origin."*

... Novak 14<sup>th</sup>/ed p 1506

*"Dysgerminomas are the most common malignant germ cell tumours of the ovary and have been considered the female - equivalent of seminoma."*

... Devita 7<sup>th</sup>/ed p 1391

Most common germ cell tumour of ovary is dermoid cyst (mature teratoma). It is benign in nature.

## Remember:

- Most common ovarian tumour (overall) – Epithelial cell tumour.
- Most common tumour in young woman is – Germ cell tumour. ... Shaw 14<sup>th</sup>/ed p 555
- Most common malignant tumour of ovary – Serous cystadenocarcinoma.
- Most common benign tumour of ovary (overall) – Dermoid cyst. ... Williams Gynae 1<sup>st</sup>/ed p 214
- Most common benign epithelial tumor of ovary – Serous cystadenoma. Jeffcoate 7<sup>th</sup>/ed p 531
- Most common germ cell tumour – Mature teratoma (Dermoid cyst).
- Most common malignant GCT – Dysgerminoma.

- Most common ovarian tumour in pregnancy (but in remains undiagnosed) – Serous cystadenoma.
- Most Common benign tumour diagnosed in pregnancy – Dermoid cyst.
- Overall most common ovarian tumour diagnosed in pregnancy – Dermoid cyst.
- Most common malignant ovarian tumor detected during pregnancy – Dysgerminoma.
- Germ cell Tumor with best prognosis Dysgerminoma
- Germ cell tumor with worst prognosis- endodermal sinus tumor
- Germ cell tumor which has maximum bilaterality- Dysgerminoma
- Germ cell tumor which presents as acute abdomen- Endodermal Sinus Tumor
- Most common ovarian tumour to undergo torsion during pregnancy – Dermoid cyst.
- Most common ovarian tumour to involve opposite ovary by metastasis – Granulosa cell tumour.
- Most radiosensitive ovarian tumour – Dysgerminoma.. *Ref. Bailey & Love 24<sup>th</sup>/ed p 221*
- Most rapidly growing ovarian tumour – Yolk sac Tm- (Endodermal Sinus Tumor)
- Most connective tissue tumour – Fibroma.

#### Ovarian Tumour: Causing:

- *Pseudomyxoma peritonei* – Mucinous cystadenoma.
- *Meig's syndrome* – Ovarian fibroma
- *Pseudomeig's syndrome:*
  - Brenner's tumour
  - Granulosa cell tumour
  - Thecoma
- Ovarian tumour associated with hyperpyrexia and hypercalcemia – Mesonephroid tumour.
- Ovarian tumour arising from epithelium of urinary tract – Brenner Tm
- Feminizing tumours:
  - Granulosa cell tumour
  - Theca cell tumour
  - Fibromas
- Virilising tumour:
  - Androblastoma
  - Hilus cell Tm
  - Gynadroblastoma
  - Adrenal cortical tumour
- Largest benign ovarian Tm – Mucinous cyst adenoma
- Mucinous tumours are associated with:
  - Dermoid cyst (MBD)
  - Brenner's tumour
  - Dysgerminoma.
- Tumour with lymphocytic infiltration:

#### 5. Ans. is a, i.e. Dysgerminoma

*Ref. Shaw 15<sup>th</sup>/ed p 378, 377, 375, 379, 381*

Most common tumor at young age is Germ cell tumor. Amongst the options given, malignant germ cell tumor is Dysgerminoma so it will be our answer of choice.

#### The age incidence of tumours given in the options:

- Dysgerminoma* – 10–20 years
- Dermoid cysts* – Can occur at any age. Maximum age incidence in between 40–50 years.
- Mucinus cystadenoma* – Between 30–60 years.
- Granulosa cell tumour* – Mostly in postmenopausal or > 40 years.
- Ovarian fibroma* – No particular age incidence.

#### 6. Ans. is c, i.e. Metastases are common

*Ref. Textbook of Gynacecology sheila Balakrishnan 1<sup>st</sup>/ed p 255*

See the text for exploration.

#### 7. Ans. is a, i.e. Epithelial tumours

*Ref. Textbook of Gynacecology sheila Balakrishnan 1<sup>st</sup>/ed p 252*

#### Cancer of Ovary

Ovarian Cancer	Arises from	Types	Age Group
Epithelial	Coelomic epithelium	Serous, mucinous endometrioid clear cell, Brenner undifferentiated	Peri/postmenopausal (45 + years)
Sex cord stromal	Gonadal stromal	Granulosa cell tumor, Sertoli-Leyding tumor	Reproductive (20 – 40 years)
Germ cell tumors	Primitive germ cells	Dysgerminoma, endodermal sinus tumor, embryonal, teratoma, choriocarcinoma	Prepubertal-pubertal (15–20 years)
Others	Metastatic	Krukenberg	

8. **Ans. is b, i.e. Surface epithelium**

Ref. Shaw 14<sup>th</sup>/ed p 334

Epithelial tumors are derived from the ovarian surface epithelium. In general, epithelial tumors comprise 50-60% of all ovarian tumors but malignant epithelial tumors comprise 90% of all ovarian cancers.

9. **Ans. is b, and d, i.e. Resembles fibroma; and Common in postmenopausal age group**

Ref. Shaw 15<sup>th</sup>/ed p 376

**Brenner tumour is also called as Transitional cell tumour:**

- It is a rare epithelial neoplasm of ovary resembling fibroma.<sup>Q</sup>
- It is an essentially benign tumour.<sup>Q</sup>
- Tumour is generally seen in women around menopause and is generally unilateral.<sup>Q</sup>
- Cause menopausal bleeding and Pseudomeig syndrome (ascites and hydrothorax).<sup>Q</sup>
- Malignant change is very rare.
- Histologically it shows walthard cell rests of transitional cells<sup>Q</sup>, cells have coffee bean nuclei, cut section is gritty.

10. **Ans. is a, i.e. Serial Ca-125 measurement and follow-up**

Ref. Novak 14<sup>th</sup>/ed p 1479-1480; 15<sup>th</sup>/ed p 1371

Here the patient is 25 years old nullipara and cystectomy sample shows serous cysadenocarcinoma - Probably the disease is limited to the ovary removed, hence to be called stage Ia.

Doing an oophorectomy here will suffice as the patient is young and nullipara. Next step is to follow the patient with regular CA 125 estimations. Though the levels of CA 125 are not specific but in this condition where the follow up is after a known cause there is ample sensitivity.

*"Fertility preservation in early stage ovarian cancer - The uterus and the contralateral ovary can be preserved in women with stage Ia, grade 1 to 2 disease who desire to preserve fertility. The conditions of the women should be monitored carefully with routine periodic pelvic examination and determinations of serum CA 125 levels. Generally, the other ovary and the uterus are removed at the completion of childbearing."*

Novak 14<sup>th</sup>/ed p 1479-1480; 15<sup>th</sup>/ed p 1371

11. **Ans. is a and b, i.e. Carboplatin; and Paclitaxel**

Ref. Novak 14<sup>th</sup>/ed p 1493

**Role of Chemotherapy in Epithelial ovarian tumors**

In early stage (Stage I)	In advanced stages
Low risk patients No adjuvant therapy required.	Combination chemotherapy: intraperitoneal cisplatin and paclitaxel or I.V. carboplatin & paclitaxel are the treatments of choice for patients with advanced disease.
High risk patients like stage IA or IB grade III, (i.e. poorly differentiated or in whom there are malignant cells in ascitic fluid or in peritoneal washings) and stage IC any grade cancer require adjuvant chemotherapy	In patients who cannot tolerate combination chemotherapy, single agent, I.V. administered carboplatin can be given.
<i>Recommendations for therapy</i> – treatment with CARBOPLATIN & PACLITAXEL chemotherapy for three to six cycles seems to be desirable in younger patients whereas a short course of a single agent, either carboplatin or paclitaxel may be preferable to older women.	In patients who have hypersensitivity to paclitaxel or carboplatin alternative drugs used are: – Docetaxel – Liposomal doxorubicin – Topotecan – Etoposide

12. **Ans. is d, i.e. Arrhenoblastoma**

Ref. Shaw 15<sup>th</sup>/ed p 380-381

**Masculinizing Tumors develop from Sex cord of Embryonic gonad and include**

- Arrhenoblastoma/ Androblastoma Hilus cell Tm
- Adrenal cortical Tm/Lipoid cell Tm of ovary
- Gynandroblastoma

13. **Ans. is b, i.e. Associated with Ca endometrium**

Ref. Shaw 15<sup>th</sup>/ed p 379; Novak 14<sup>th</sup>/ed p 1520-1521

**Granulosa cell tumour is a sex cord tumour.**

- **Age:** It can be seen at any age. Most common before puberty and *after 40 years*. (Maximum incidence at 52 years). Hence option a i.e. it is common is puberty is incorrect  
... Williams Gynae 1<sup>st</sup>/ed p 747
- Tumour secretes estrogen which is responsible for clinical features like precocious puberty, menometrorrhagia and post menopausal bleeding.
- They are low grade malignancies.
- Almost always unilateral<sup>Q</sup> (B/L in < 2%) i.e. option d incorrect

**Malignant transformation:**

- Since they secrete estrogen, 25-50% are associated with *Endometrial hyperplasia*.
- 5 per cent of tumours are associated with endometrial cancer.

*"There is a strong evidence that carcinoma of the endometrium may be associated with feminizing tumors of the ovary in postmenopausal women."*

... Shaw 15<sup>th</sup>/ed p 380

**Marker:** Granulosa cell tumour secrete inhibin which is a useful marker for it.

**Prognosis:** Is good with 5 year survival rate being 90%.

**Metastasis:** It is peculiar in case of granulosa cell tumour, it first involves opposite ovary followed by metastasis in lumbar region.

**14. Ans. is b and c, i.e. It secretes hormones; and Associated with endometrial hyperplasia**

Ref. Novak 14<sup>th</sup>/ed p 1520 - 1521, 15<sup>th</sup>/ed p 1408

- Most common malignant tumour of ovary is *Serous cystadenocarcinoma* (**Option "a"** is incorrect).
- Granulosa cell tumor secretes estrogen and so, in 25 - 50% cases is associated with endometrial hyperplasia. (**Option "b"** and **"c"** are correct).
- Surgery is the TOC.

**Management:** Surgery is the TOC. Type of surgery depends on age of occurrence.

Children and women of reproductive age

Postmenopausal



Unilateral salpingo-oophorectomy



TAH + BSO.

*"There is no evidence that adjuvant chemotherapy will prevent recurrence of disease."*

...Novak 14<sup>th</sup>/ed p 1523, 15<sup>th</sup>/ed p 1408

*"The mainstay of treatment for patients with an ovarian SCST (Sex Cord Stromal Tumors) is complete surgical resection due to their relative insensitivity to adjuvant chemotherapy or radiation."*

... Williams Gynae 2<sup>nd</sup>/ed p 892

(So, **Option "d"** is incorrect)

**15. Ans. is b, i.e. Dysgerminoma**

**16. Ans. is c, i.e. Dysgerminoma**

**17. Ans. is b, c and d, i.e. Arrhenoblastoma; Brenner's tumor; and Serous cystadenoma**

Ref. CGDT 10<sup>th</sup>/ed p 875; Devita 7<sup>th</sup>/ed p 1391; Novak 14<sup>th</sup>/ed p 1506; 15<sup>th</sup>/ed p 1394; Williams Gynae 1<sup>st</sup>/ed p 741

**Germ cell Tumors of ovary:**

**Mnemonic: YES PCT**

- Y - Yolk sac Tumor (Endodermal sinus Tm)
- E - Embryonal carcinoma
- S - Seminoma ≈ Dysgerminoma
- P - Polyembryoma
- C - Choriocarcinoma
- T - Teratoma ≈ Dermoid

In contrast to slow growing epithelial ovarian tumors, germ cell malignancies grow rapidly and are characterised by subacute pelvic pain.

- *Most common germ cell Tumor - Mature teratoma or Dermoid cyst*<sup>Q</sup> (Benign in nature).
- *Most common malignant GCT - Dysgerminoma.*<sup>Q</sup>
- *Second most common malignant GCT - Endodermal sinus Tumor. (Yolk Sac tumor)*
- *Most common benign Tumor of ovary - Dermoid cyst*<sup>Q</sup>

... Williams Gynae 1<sup>st</sup>/ed p 214; Merck manual online medical library on Internet; Jeffcoate 7<sup>th</sup>/ed p 531

**18. Ans. is a, i.e. Unilateral**

Ref. Shaw 15<sup>th</sup>/ed p 378; CGDT 9<sup>th</sup>/ed p 937

**19. Ans. is a and b, i.e. Radiosensitive; and Most common malignant germ cell tumor**

Ref. Shaw 15<sup>th</sup>/ed p 378

**20. Ans. is a, d and e, i.e. Blood spread seen; Bleomycin, etoposide and cisplatin given; and Radiosensitive**

Ref. Novak 14<sup>th</sup>/ed p 1508-9, 1511, 15<sup>th</sup>/ed p 1395-1397

**Dysgerminoma:**

- Commonest *malignant germ cell tumour*<sup>Q</sup> of ovary.
- They are the most common ovarian malignancy detected during pregnancy.
- Primarily affect *young women* (average age of incidence is 20 years<sup>Q</sup>) and not postmenopausal females.
- Usually *unilateral*<sup>Q</sup> but they are the only germ cell malignancy with a significant rate of bilateral ovarian involvement - 15 to 20%.
- Pathologically it is a solid neoplasm with *areas of softening*<sup>Q</sup> due to degeneration. ... CGDT 10<sup>th</sup>/ed p 875
- *"Consistency is fleshy"* Ref. Novak 15<sup>th</sup>/ed 1395
- Unlike other germ cell tumours it *does not secrete AFP* and HCG is only rarely secreted, however it *secretes LDH and placental alkaline phosphate*, which are used as tumour marker of dysgerminoma.

M/C, route of spread is via lymphatics (Novaks 15/e, p1396) but hematogenous and direct spread are also seen.

- Dysgerminoma is the *most radio sensitive tumour.*<sup>Q</sup> But treatment of choice is *surgery* (unilateral salpingo oophorectomy) *along with proper surgical staging followed by Bleomycin, Etoposide and Cisplatin (BEP) based chemotherapy* as fertility can be preserved.

Chemotherapy is helpful in metastatic spread

- They have the best prognosis of all malignant ovarian germ cell variants.
- Recurrence rate is high.

21. Ans. is a, i.e. Cisplatin, etoposide, bleomycin

Ref. Novak 14<sup>th</sup>/ed p 1511

**Management of Dysgerminoma:**

- The treatment of *early dysgerminoma*.  
Surgical – including resection of the primary lesion (unilateral oophorectomy) and proper surgical dissection.
- *Metastatic Disease* – Chemotherapy or Radiation therapy.

**Chemotherapy:**

The most frequently used chemotherapy regimens for germ cell tumors are:

- **BEP** – Bleomycin, Etoposide, Cisplatin
- **VBP** – Vinblastin, Bleomycin, Cisplatin
- **VAC** – Vincristine, Actinomycin, Cyclophosphamide

Results suggest that patients with advanced stage, incompletely resected dysgerminoma have an excellent prognosis when treated with cisplatin based combination chemotherapy. **The best regimen is 4 cycles of BEP.**

22. Ans. is b, i.e. Oophorectomy of the involved side

Ref. Devita 7<sup>th</sup>/ed p 1391; Williams Gynae 1<sup>st</sup>/ed p 741

**Though Dysgerminoma is most radiosensitive tumour known**, treatment of choice is oophorectomy of involved side followed by cisplatin based chemotherapy to preserve fertility, as dysgerminoma is seen in young women with average age incidence being 20 years.

**BEP:** Bleomycin, Etoposide, Cisplatin

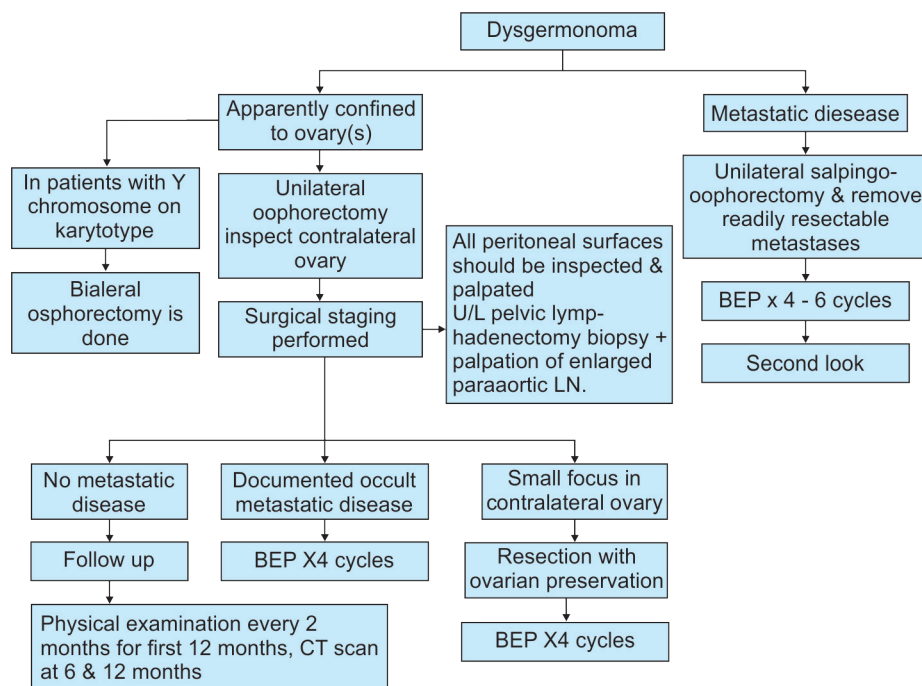
23. Ans. is a, b, c and e, i.e. It is teratoma; Frequently undergo torsion; X-ray is diagnostic; and Contains sebaceous material and hairs

Ref. Shaw 15<sup>th</sup>/ed p 376-7; Williams Gynae 1<sup>st</sup>/ed p 214-5

**Dermoid cyst: Dermoid cyst is a benign teratoma.**

- It is most common *benign tumour of ovary* in reproductive age group.<sup>Q</sup>
- Most common benign neoplasm diagnosed during pregnancy.<sup>Q</sup>
- Most common Germ cell tumor.<sup>Q</sup>
- It is the commonest tumor to undergo torsion.
- **Characteristically they are unilocular cyst containing hair and cheesy sebaceous material, teeth, bones, thyroid tissue and cartilage.**
- **If teeth or bone are seen in X-ray in adnexal mass, this finding is pathognomic for teratoma and thus X-ray is diagnostic.**
- *Malignant change in a dermoid cyst occurs in 0.5 – 2% cases in patients > 40 years. Most common malignancy which develops is, squamous cell carcinoma.*

Ref. Textbook of Gynaecology Sheila Balakrishnan 1<sup>st</sup>/ed p 183





24. Ans. is a, b, c and d, i.e. Also called endodermal sinus tumour; Always have elevated AFP level; Schiller Duval bodies seen; and Highly malignant

25. Ans. is a, d and e, i.e. Schiller duval bodies seen; It is seen in young individuals; and It is a malignant tumour

Ref. Williams Gynaecology 1<sup>st</sup>/ed p 742; Jeffcoates 7<sup>th</sup>/ed p 541; Novak 15<sup>th</sup>/ed p 1403

#### Endodermal sinus tumor/Yolk sac tumor:

- Endodermal sinus (yolk sac) tumour is third most common malignant germ cell tumour of ovary affecting mostly children or young women. (Age group 14–20 years. ... Novak 15<sup>th</sup>/ed p 1403)  
(M/C, being Dysgerminoma, 2<sup>nd</sup> M/C Immature teratoma)
- Tumour is *highly malignant* and is *most rapidly growing tumour of whole body*.
- Histologically the pathognomonic finding is *Schiller - Duval bodies*<sup>Q</sup> which is a single papilla lined by tumour cells with a central blood vessel.
- Due to high rate of growth, tumour usually presents with acute abdomen.
- **Unilateral in 100% cases therefore biopsy of opposite ovary is contraindicated.**
- Almost all cases are associated with raised AFP and Alpha 1 antitrypsin.
- **It is the most deadly malignant ovarian germ cell tumor.**
- *Treatment:* Chemotherapy.
- It has a high propensity for rapid growth, peritoneal spread and distant hematogenous dissemination to the lungs.

26. Ans. is a, i.e. Has a rough surface

Ref. Shaw 15<sup>th</sup>/ed p 425-6

27. Ans. is b, i.e. Krukenberg tumor

Ref. Shaw 15<sup>th</sup>/ed p 425-6; CGDT 10<sup>th</sup>/ed p 877

#### Krukenberg tumor:

- Krukenberg tumor by definition *represent carcinoma of stomach metastasised to ovary*. But the eponym is commonly used to denote any gastric cancer metastatic to ovary
- Tumour arise by *retrograde lymphatic spread*<sup>Q</sup> i.e. carcinoma cells pass from the stomach to the superior gastric lymphnode which also receive lymphatics from ovary.

#### Characteristics of Krukenberg Tumour:

- Always bilateral<sup>Q</sup>
- Have smooth surface<sup>Q</sup>
- No tendency to form adhesions
- Freely mobile
- No infiltration through the capsule.
- Histologically tumour has signet ring cells in the background of myxomatous stroma.
- They retain the shape of normal ovary.<sup>Q</sup>
- Have waxy consistency.<sup>Q</sup>

28. Ans. is c, i.e. Oesophagus

Ref. Novak 14<sup>th</sup>/ed p 1525-7

*About 5 - 6% of Ovarian tumors are metastatic from other organs. The metastatic tumors can arise from metastasis from the following sites.*

Gynaecologic	Gastrointestinal tract	Breast	Lymphoma and Leukemia	Melanoma	Carcinoid Tm
• Tubes (13%)	• Stomach		(Most common		
• Endometrium	(Characteristic Krukenberg tumour)		Burkitt's lymphoma)		
• Cervix (Rare < 1%)					
• Colon					
• Small intestine					
• Appendix					

*Note:* M/C tumor to metastasize to ovary-GIT tumor

Second M/C site is Breast tumor.

29. Ans. is a, i.e. Ca ovary

Ref. Jeffcoates 7<sup>th</sup>/ed p 543; Novaks 15<sup>th</sup>/ed p1366

- M/c age incidence for primary ovarian neoplasms is 40-60 years, peak age incidence being 55–60 years. Ovarian malignancies generally present with vague symptoms like abdominal pain, dyspepsia, and patient may also experience irregular menses and if pelvic mass compresses the bladder or rectum she may have urinary frequency or constipation. In advanced stages patients have symptoms related to presence of ascites, omental metastasis or bowel metastasis like abdominal distension, dyspnea, bloating, nausea, anorexia or early satiety. In the patient given in the question all these symptoms are present (which could be seen in other cancers as well) plus her Ca 125 levels are raised, which favors the diagnosis of ovarian cancer in her.

**Remember**

The most important sign of epithelial ovarian cancer is the presence of a pelvic mass on physical examination. For postmenopausal patients with an adnexal mass and a very high serum CA125 level (>200U/ml), there is 96% positive predictive value for ovarian malignancy.

30. **Ans. is d, i.e. Medial surface of thigh**

*Ref. Lasts Anatomy 10th/ed p 302*

**Ovarian pain is referred along the medial side of thigh**

The obturator nerve during its course, when runs in front of the internal iliac vessels is separated from the normally situated ovary by only the parietal peritoneum lining the pelvic wall, thus pain from the ovary may be referred along the nerve to the skin on the medial side of thigh.

**Also know**

**Simpson Pain-** colicky pain in patients of Ca Endometrium. It is referred to the hypogastrium or to both iliac fossas. It is not severe and tends to appear at the same time each day lasting only 1–2 hours.

31. **Ans. is c and d, i.e. Associated with ascites and pleural effusion; and No treatment required**

32. **Ans. is d, i.e. Pericardial effusion**

33. **Ans. is d, i.e. Fibroma**

*Ref. Comprehensive Gynaecology by Arthus L Herbst 2<sup>nd</sup>/ed p 533; Jeffcoate 7<sup>th</sup>/ed p 543*

**Meig's syndrome:**

- **Ascites and right sided hydrothorax** in association with **fibroma** of ovary is called as *Meig's syndrome*.
- It can also be seen in Brenner's tumour and Granulosa cell tumour where it is called as *Pseudomeig's syndrome*.
- True meig's syndrome is rare, occurring in **< 5 per cent** of fibromas.
- Hydrothorax can be bilateral also.
- Ascites is caused by transudation of fluid from the ovarian fibroma. Hydrothorax develops secondary to flow of ascitic fluid into the pleural space via lymphatics of the diaphragm.
- Ascites occurs (*in 50% cases*) when tumour size is **> 6 cms**.
- Tumours producing Meig's syndrome manifest in *the late childbearing period* i.e., 30–40 years.
- Both ascites and hydrothorax resolve spontaneously after removal of the tumour.

**Criteria for diagnosis of Meig's syndrome:**

- Tumour must be ovarian, solid and benign.
- Both hydrothorax and ascites must be present.
- Removal of the tumour must result in their spontaneous and permanent cure.

**Pseudomeig syndrome:**

- Can be seen in association with either benign or malignant tumour.
- Hydrothorax could be a manifestation of pulmonary metastasis.
- Syndrome can result from overstimulation of the ovaries with gonadotropins but, in such cases, the peritoneal exudate is more likely to be caused by an electrolyte imbalance rather than by ovarian tumour.

34. **Ans. is a, i.e. Torsion**

*Ref. Shaw 15<sup>th</sup>/ed p 382*

**Complications of Ovarian tumour (TRIP):****T Torsion**

- Most common complication
- Seen in 12% cases
- Most common in benign tumours
- Most common tumour to undergo torsion is dermoid cyst.

*.... Jeffcoate 7<sup>th</sup>/ed p 548*

**R Rupture**

- Which can be traumatic or spontaneous.

**I Infection**

- Rare complication
- Seen following acute salpingitis or during puerperium as a part of an ascending genital tract infection.

**P Pseudomyxoma peritonei**

- Peritoneal cavity is filled with coagulated mucinous material.

**In ovarian Tumors**

- Most common in mucinous cystadenoma and mucinous carcinoma.

**Also seen in:** – Mucocoele of appendix.

– Carcinoma of large intestine.

– Appendix cancer overall is the M/C cause of pseudomyxoma peritonei.

## 35. Ans. is a, i.e. Benign cystic teratoma

Ref. Novak 14<sup>th</sup>/ed p 510

*"A benign cystic teratoma is the most common neoplasm to undergo torsion, and it to the M/C benign tumor diagnosed during pregnancy."*

... Novak 14<sup>th</sup>/ed p 510

A benign cystic teratoma is synonymous to dermoid cyst.

## 36. Ans. is c, i.e. Mucinous cystadenoma

## 37. Ans. is b, i.e. Mucinous cystadenoma

Ref. Novak 14<sup>th</sup>/ed p 1462-3

**Pseudomyxoma peritonei** is a condition in which the neoplastic epithelium secretes large amounts of gelatinous mucinous material. It is most commonly seen secondary to:

- Appendicular carcinoma (*well differentiate carcinoma*).
- Ovarian mucinous carcinoma; mucinous cystadenoma.
- Mucocoele of appendix (*less commonly seen*).

Even after removal of the ovarian tumours, these cells continue to secrete mucin.

Tendency of *recurrence* is present.

**Prognosis** is Poor.

**Management:** Hysterectomy with BSO with removal of mucin peritoneal implants along with appendix.

## 38. Ans. is d, i.e. Carcinoid Tumors of ovary

Ref. Shaw 15<sup>th</sup>/ed p 378**Carcinoid tumour of Ovary:**

- It is sometimes primary and sometimes metastatic.
- Also called *Argentaffinoma*.
- Occurs as a malignant change in benign dermoid cyst.
- Presence of solid yellow tumour with histological property of reducing silver salts derived from specialized Kulchitsky cells of intestine.
- *It produced 5 - HT which causes attacks of flushing and cyanosis.*<sup>Q</sup>

## 39. Ans. is c, i.e. Staging

Ref. Novak 14<sup>th</sup>/ed p 1477; Jeffcoate 7<sup>th</sup>/ed p 550

*"FIGO staging is based on finding at surgical exploration."*

... Novak 14<sup>th</sup>/ed p 1477

*"Whenever malignancy is suspected, a staging laparotomy should be carried out."*

... Jeffcoates 7<sup>th</sup>/ed p 550**Role of Imaging in Ovarian tumour:**

- **Used for** - delineating the site and size of lesion.
- **Characterization of lesion** into benign or malignant.  
Detects early metastasis.
- To **asses resectability**.
- To **exclude** extraperitoneal metastasis( *like liver parenchyma, enlarged pelvic and paraaortic nodes, hydroureter and hydronephrosis*)

**Imaging Modality of Choice is USG:** for delineating the site and size of lesion, to devise scoring systems for differentiating benign from malignant tumours and for screening.

**Other modalities:** Regarding imaging used for ovarian Ca.

- **Direct radiological examination of abdomen:** for evidence of fetal skeleton, calcification of leiomyoma or teeth in a dermoid cyst.
- **Colour flow imaging:** to increase the specificity of diagnosis of malignant tumours.
- **CT and MRI:** used to evaluate the tumour and the extent of spread but are more useful in monitoring the progress of the disease.

**Extra edge:**

**The risk of Malignancy Index (RMI) Scoring System**

Feature	RMI 1 Score	RMI 2 Score
Ultrasound features:	0 = None	0 = None
• Multilocular cyst	1 = One abnormality	1 = One abnormality
• Solid areas	3 = Two or more abnormalities	4 = Two or more abnormalities
• Bilateral lesions		
• Ascites		
• Intra-abdominal metastases		
Premenopausal	1	1
Postmenopausal	3	4
Ca 125 U/ml		

RMI score = Ultrasound score x Menopausal score x Ca 125 level in U/mL

### The Risk of Malignancy Scoring System

There are 2 scoring systems, RMI 1 and RMI 2, each of which calculates scores by using ultrasound features, menopausal status, and pre-operative CA 125 level according to the equation:

RMI score = Ultrasound score x Menopausal score x Ca 125 level in U/mL

- The RMI scoring system is the method of choice for predicting whether or not an ovarian mass is likely to be malignant.
- Women with an RMI score > 200 have a high risk of ovarian cancer.

#### 40. Ans. is b, i.e. Malignant epithelial ovarian tumor

Ref. COGDT 10<sup>th</sup>/ed p 879

*"Malignant ovarian tumour are often bilateral solid and present with ascites."*

Omental caking on CT is also a sign of malignancy.

Physical examination	Benign tumour	Malignant tumour
Mobility	Mobile	Fixed, large and multiloculated
Consistency	Cystic	Solid or firm
Laterality	Unilateral	Bilateral
Cul-de-sac	Smooth on P/V examination	Nodular on P/V examination
<b>Radiography</b>		
Size	Usually < 10 cm size	Any size
Septations	< 2 mm thickness	Multiple septations > 3 mm in size
Calcification	Seen in teratoma	Usually absent
Omental caking	Absent	Seen
Ascites	Absent	Present
Intra operative	Unilateral cyst with no adhesion	Solid areas with adhesion, rupture
	Capsule intact	may occur.
		Capsule is breached

#### Note-USG characteristics of dermoid cyst

- USG shows a cyst with internal echoes due to hair and sebum present in the cyst.
- Rokitansky protuberance appears like a hyperechoic area along cyst wall
- Posterior acoustic shadow due to hair.

**Other options :** Dysgerminoma of ovary is seen in 1st or 2nd decade with mean age of 20 years; therefore is unlikely in women of 45 years. But it can present with ascites and secondaries in omentum.

#### Remember

Benign tumours of ovary causing ascites are:

- Ovarian fibroma (*Meig's syndrome*).
- Theca cell tumour
- Brenner's tumour (*Pseudomeig syndrome*)
- Granulosa cell tumour (*Rarely*).

... Shaw 13<sup>th</sup>/ed p 403

#### Also know:

#### Pelvic Mass Evaluation: Criteria for Gynecologic Oncology Referral

Premenopausal women	Postmenopausal Women
Very elevated CA-125 (>200 U/mL)	Elevated CA-125
Ascites	Ascites
Evidence of abdominal or distant metastasis	Evidence of abdominal or distant metastasis
Family history of one or more first degree relatives with ovarian or breast cancer	Family history of one or more first degree relatives with ovarian or breast cancer
	Nodular or fixed pelvic mass

#### 41. Ans. is b and c, i.e. Septations; and Bilaterality

#### 42. Ans. is c, i.e. Papillary vegetation

Ref. Sutton 2<sup>nd</sup>/ed p 1083

#### USG features of malignant ovarian tumour:

- *Hypoechoic solid area* within the mass (*highly echogenic solid areas due to fat or calcification are typical of dermoids*).
- Thick (more than 3 mm) *nodular septations* / papillary vegetations
- Size of *mass greater than 7 cm*, although very large but simple cysts are usually benign cystadenomas.
- *Central* rather than peripheral *vascularity*.
- RI less than 0.6. *RI greater than 0.8 is suggestive of benign disease* but there is an indeterminate range of 0.6 – 0.8.

*In Q 42-Presence of papillary vegetation is suggestive of malignancy and hence is an indication for laparotomy.*

## 43. Ans. is c, i.e. Testosterone

Ref. Shaw 15<sup>th</sup>/ed p 380; Williams Gynae 1<sup>st</sup>/ed p 391

*"Specifically women with an abrupt onset, typically within several months or sudden worsening of virilising signs should prompt concern for a hormone producing ovarian or adrenal tumor. Serum testosterone levels may be used to exclude these tumours."*

... Williams Gynae 1<sup>st</sup>/ed p 391

**Rapidly developing hirsutism with amenorrhoea and change in voice is suggestive of masculinizing tumour like Arrhenoblastoma or androblastoma which are invariably associated with raised testosterone (T > 200 ng/dl).**

All **masculinizing tumour** have similar presentation *characterized by defeminization such as breast atrophy and amenorrhoea, hirsutism, a hoarseness of voice, muscular development, clitoromegaly and receding hair line.*

**Removal of tumour** restores the secondary sexual character but **hoarseness** of voice is permanent.

**Note:**

- Most common cause of hirsutism in young girls - PCOD (80% cases).
- PCOD is not associated with hoarseness and hirsutism is not rapidly developing.
- In PCOD - testosterone levels though raised are less than 200 ng/dl.

Friends here it is important to know that we are measuring the levels of testosterone and not DHEA because main source of DHEA is adrenal gland and not ovary.

## 44. Ans. is d, i.e. Dermoid cyst

Ref. Sutton 2<sup>nd</sup>/ed p 1085

*An ovarian mass with radio opaque shadow on X-ray points towards dermoid cyst as the diagnosis.*

**Causes of Pelvic Calcification are:**

- Fibroids:* popcorn type
- Dermoid cyst:* it is the commonest ovarian mass to calcify
- Other ovarian masses:* cystadenoma / carcinoma, fibromas
- Pseudomyxoma peritonei
- Fallopian tube calcification (rare):* suggest TB
- Uterine* i.e. endometrial calcification from chronic endometritis.

## 45. Ans. is a, i.e. Dysgerminoma

Ref. Novak 15<sup>th</sup>/ed p 1394, 14<sup>th</sup>/ed p 1505; Shaw 14<sup>th</sup>/ed p 338**M/C tumor in young females is- Germ cell tumor**Ref. Shaw 14<sup>th</sup>/ed p 555

*Hence in this female it could either be a dysgerminoma, endodermal sinus tumor or malignant teratoma, all of which are germ cell tumors (mucinous cystadenocarcinoma is ruled out)*

The mass in this female has solid component as revealed on USG so it is most probably malignant

M/C malignant GCT is dysgerminoma, furthermore in the patient- levels of

CA 125 are normal i.e. mucinous cyst adenocarcinoma again ruled out

Alpha-fetoprotein is normal, hence endodermal sinus tumor ruled out

Alkaline phosphatase is elevated hence diagnosis of dysgerminoma is confirmed

*"Unlike other germ cell tumors dysgerminoma is not associated with raised AFP and rarely increases HCG, however placental alkaline phosphatase and lactate dehydrogenases are commonly produced by dysgerminoma and may be useful in monitoring the disease."*

Ref. Novak 14<sup>th</sup>/ed p 1505

## 46. Ans. is b, i.e. Krukenberg tumor

Ref. Shaw 15<sup>th</sup>/ed p 379

Already explained.

## 47. Ans. is d, i.e. Hilus cell tumor

Ref. Shaw 15<sup>th</sup>/ed p 381

## 48. Ans. is a, i.e. Schiller-duval bodies

Ref. CGDT 9<sup>th</sup>/ed p 938; Shaw 13<sup>th</sup>/ed p 362

**Call exner bodies are small cyst like spaces found in cases of granulosa cell tumour.**

Feature	Associated tumour
Call exner bodies & coffee bean nuclei	Granulosa cell tumour
Schiller duval bodies	Endodermal sinus tumor
Reinke's crystal	Hilus cell tumour
Psammoma bodies	Serous epithelial tumours
Walthard cell nest	Brenner tumour
Signet ring cell	Krukenberg tumour
Hobnail cell	Clear cell tumor
Large polygonal cell with lymphocytic infiltration and fibrous septa	Dysgerminoma
Skin, teeth, cartilage	Teratoma

49. Ans. is c, i.e. Serum lactic dehydrogenase

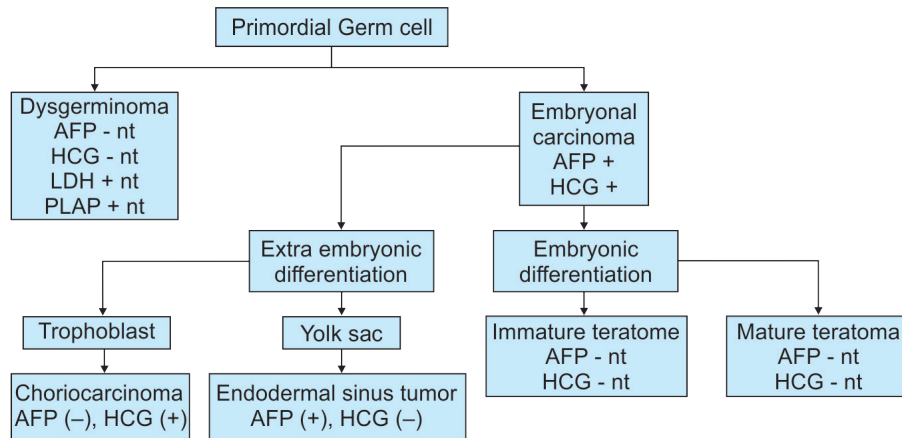
Ref. Novak 14<sup>th</sup>/ed p 1505; Shaw 15<sup>th</sup>/ed p 378

50. Ans. is b, i.e. LDH

Ref. Shaw 15<sup>th</sup>/ed p 378

*"Unlike other germ cell tumour dysgerminoma is not associated with raised AFP and rarely increase HCG; however placental alkaline phosphatase and lactate dehydrogenase are commonly produced by dysgerminomas and may be useful in monitoring the disease."*

... Novak 14<sup>th</sup>/ed p 1505



**AFP** - Alpha Feto Protein

**LDH** - Lactic Dehydrogenase

**HCG** - Human Chorionic Gonadotropin

**PLAP** - Placental Alkaline Phosphatase

51. Ans. is a, i.e. CA - 125

Ref. Novak 14<sup>th</sup>/ed p 1505; Shaw 15<sup>th</sup>/ed p 378, 387

*CA 125 is tumour marker of epithelial cell neoplasm (not for germ cell tumour).*

52. Ans. is a, i.e. Carcinoma ovary

Ref. Shaw 15<sup>th</sup>/ed p 387

53. Ans. is c, i.e. Ovarian Ca

Ref. Shaw 15<sup>th</sup>/ed p 387

54. Ans. is c, i.e. Epithelial cell carcinoma of ovary

Ref. Shaw 15<sup>th</sup>/ed p 387; Williams Gynae 1<sup>st</sup>/ed p 722

- CA - 125 is a glycoprotein secreted by *malignant epithelial tumours* of ovary. Therefore it is a marker of epithelial cell carcinoma of ovary.
- CA - 125 level correlates with *volume of tumour* and is elevated in 50% of Stage I tumour and 90% of tumours with Stage II or higher.
- CA - 125 level is also useful for *follow up* after treatment. Level > 35 units/ml suggests residual tumour.

**Remember:**

- Two best screening test for ovarian ca are measurement of CA - 125 levels and transvaginal USG.

- **CA - 125 is raised in:**

... Harrison 16<sup>th</sup>/ed p 554

Benign condition	Malignant condition	
• Pregnancy	Endogenous	- Endometrial Ca
• PID	Pneumocystis	- Pancreas Ca
• Endometriosis	Carinii	- Colon Ca
• Uterine fibroid	Causes	- Cervix Ca
• About 1% of normal females	T	- Fallopian tubes Ca
<b>Mnemonic:</b> CA - 125 is raised in pregnant patient with endometrial fibroid and PID	<b>B</b> <b>O</b> <b>Lung</b>	- Breast Ca - Ovarian epithelial Ca (MC cause) - Lung Ca
<b>Mnemonic:</b>	Endogenous Pneumocystis Carinii Causes TB Of Lungs	

- In a postmenopausal women with an asymptomatic pelvic mass and CA - 125  $\geq 65$  U/ml is very sensitive for diagnosis of ovarian epithelial tumour.
- Although CA 125 is raised in many cancers it is specific for epithelial ovarian cancer.

## 55. Ans. is b, i.e. PET

Ref. Novaks Gynae 14<sup>th</sup>/ed p 1496

In a case of treated ovarian cancer - Treatment assessment is done by:

- **Tumor marker CA 125** - It is a reliable indicator of disease response or progression.
  - If CA 125 levels decreases after treatment - It indicates response to treatment.
  - If CA 125 levels increase after treatment - It indicates relapse after treatment.
  - A review of the literature suggests that an elevated Ca 125 level predicts persistent disease at second look surgery in 97% of the cases but CA 125 is not sensitive enough to exclude subclinical disease in many patients.
  - Follow up in a patients of ovarian cancer is done by physical and pelvic examination along with estimation of CA 125 levels. Patient is advised to visit every 3–4 months for the first 2 years and then 6 monthly for 5 years.
- Clinical examination and CA 125 together can detect 90% of recurrences. Radiological procedures are not required in all cases.
- But since here CA 125 is elevated and we have to choose one option - the best is **PET** as:
  - CT scan cannot distinguish between a relapsed tumour and fibrosis whereas PET scan will exactly demonstrate whether it is a relapsed tumour or a fibrosis. (In a patient treated with chemotherapy or radiotherapy fibrosis is common. It can present as a mass so it is essential to differentiate between relapsed tumour and fibrosis.)

## 56. Ans. is d, i.e. Dysgerminoma

Ref. Novak 14<sup>th</sup>/ed p 1505

Placental alkaline phosphatase and LDH are tumour markers of dysgerminoma.

## 57. Ans. is c, i.e. Inhibin

Ref. William Gynae 1<sup>st</sup>/ed p 747

Ovarian Tumor	Tumor Marker
– Epithelial ovarian tumors Serous variety Mucinous variety Serous and mucinous	CA 125 Ca 19 – 9, CEA OCCA, OCA
– Endodermal sinus/Yolk sac tumor	AFP
– Chorio carcinoma	HCG
– Dysgerminoma	LDH, Alkaline phosphatase
– Granulosa cell tumor	Inhibin

## 58. Ans. is d, i.e. Dermoid cyst

Ref. Williams Gynae 1<sup>st</sup>/ed p 741

## 59. Ans. is a, i.e. Dysgerminoma

Ref. Jeffcoate 6<sup>th</sup>/ed p 522; Novak 14<sup>th</sup>/ed p 1519, 1517, 1514

*“Dysgerminomas are the only germ cell malignancy with a significant rate of bilateral involvement 15 to 20%.”*

**Remember**

A *“Fundu”* – Germ cell tumours are unilateral and maximum bilaterality is seen in dysgerminoma amongst germ cell tumour and that too only in 15 - 20% cases.

So, the other germ cell tumor will obviously be less bilateral therefore our answer to [Question 58](#) is *dermoid cyst*.

**Other important fundas-**

- Endodermal sinus tumors are unilateral in 100% cases.
- Granulosa cell tumors are U/L in 98% of cases and bilateral in only 2% of cases

**In Q 59-**

Endodermal sinus tumor as I have said is U/L in 100% cases so it is ruled out, Dysgerminoma is bilateral in 15–20% cases.

Lets have a look at embryonal cell carcinoma-

**Embryonal cell carcinoma**

- *The primary lesions tend to be large, and about two thirds are confined to one ovary at the time of diagnosis.*

... Novak 14<sup>th</sup>/ed p 1519

## 60. Ans. is a, i.e. Granulosa cell tumor

Ref. Shaw 15<sup>th</sup>/ed p 379-80

*“The metastasis of granulosa cell tumour is interesting because the opposite ovary first become involved, then metastasis develop in the lumber region, secondary deposits become scattered in the mesentery, the liver and mediastinum.”*

*Granulosa cell tumour and theca cell tumour are feminizing tumours that originate from sex cord stroma.*

**Feminizing Tumors of Ovary:**

	Granulosa cell tumour	Theca cell tumour
<b>Incidence</b>	Common	Rare
<b>Age</b>	Occurs at any age but most common after 40 years.	Occur after menopause
<b>Presentation</b>	In prepubertal girls it leads to precocious puberty, hypertrophy <sup>o</sup> of breast. In adults – leads to amenorrhoea followed by prolonged bleeding (metropathia hemorrhagica) <sup>o</sup> In postmenopausal women – Causes Postmenopausal bleeding <sup>o</sup> <i>Metastases to opposite ovary first is characteristic feature.<sup>o</sup></i>	Usually presents as postmenopausal bleeding. <sup>o</sup>
<b>Microscopy</b>	<b>Exhibits:</b> Coffee bean nuclei. Call exner bodies.	It has spindle shaped cells together with fat laden cells.

**Remember:**

- Both these tumors cause endometrial hyperplasia and so, risk of carcinoma endometrium is increased.<sup>o</sup>
- Both these tumors can become luteinized to form a luteoma, they may then produce progesterone as well as oestrogen and convert the endometrium to a secretory one.  
Besides granulosa tumor complain other tumor which can show metastasis to opposite ovary is dysgerminoma but it is not very significant. ... *Novak 13<sup>th</sup>/ed p 1286; 14<sup>th</sup>/ed p 1509*
- Both these tumors can cause pseudomeig syndrome. ... *Dutta Gynae 4<sup>th</sup>/ed p 277*

**61. Ans. is c, i.e. Omental biopsy***Ref. Williams Gynae 1<sup>st</sup>/ed p 729; Novak 14<sup>th</sup>/ed p 1478***Surgical staging is done in all cases of ovarian cancer.**

- Typically, the abdominal incision must be adequate to identify and resect any disease that may have been missed on physical examination or imaging tests.
- The operation begin by aspirating free ascitic fluid or collecting peritoneal washing followed by visualization and palpation of all peritoneal surfaces and viscera proceeding in a clockwise manner from cecum.
- Next an extrafascial (simple) hysterectomy and BSO are performed and infracolic omentectomy done.
- In the absence of gross extraovarian disease, peritoneal biopsies are obtained, along with a biopsy or scraping of the right diaphragm.
- Finally, a pelvic and infrarenal para-aortic lymphadenectomy is complete.

Note: Infracolic omentectomy is done: Not omental biopsy

**62. Ans. is d, i.e. Stage II b***Ref. Novak Internet-FGO site p 427*

From the new staging, given in preceding text it is seen that if there is retroperitoneal or inguinal lymphnode involved, it is in stage IV B, and, pelvic lymphnode involvement is included in stage IIB.

For this – refer to *AJCC Cancer Staging Manual 6<sup>th</sup>/ed p 276* which says.**63. Ans. is a, i.e. Stage I***Ref. Novak 14<sup>th</sup>/ed p 1477; Shaw 15<sup>th</sup>/ed p 427***64. Ans. is d, i.e. Stage Ic***Ref. Novak 14<sup>th</sup>/ed p 1477; Shaw 15<sup>th</sup>/ed p 427***Bilateral involvement and malignant ascites is seen in category IC.**

- In IC also- according to new classification it is IC 3.

**65. Ans. is c, i.e. Stage III***Ref. Shaw 15<sup>th</sup>/ed p 427*

- Superficial liver metastasis is included in Stage III.
- Metastasis to liver parenchyma is included in Stage IV.

**66. Ans. is None***Ref. Shaw 15<sup>th</sup>/ed p 377 for option c, 379 for option d, 375 for option a, 374 for option b***Rate of malignant transformation of different tumors:**

Serous cystadenoma	– 25%-40%	.... <i>Ref. Textbook of Gynaecology sheila Balakrishnan 1<sup>st</sup>/ed p 180</i>
Granulosa cell tumor	– 50%	
Mucinous cystadenoma	– 5% -10%	.... <i>Ref. Textbook of Gynaecology sheila Balakrishnan 1<sup>st</sup>/ed p 181</i>
Dermoid	– 1.7%-2%	.... <i>Ref. Textbook of Gynaecology sheila Balakrishnan 1<sup>st</sup>/ed p 183</i>

*In ovarian cysts- "The risk of malignancy is maximum with serous cystadenoma (40%) and least with dermoid cyst (1-2%)."**Ref. Textbook of Gynaecology Sheila Balakrishnan 1<sup>st</sup>/ed p 187***Note:** M.C malignancy seen with dermoid cyst is squamous carcinoma.**67. Ans. is d, i.e. Multiloculated, sticky, gelatinous fluid***Ref. Shaw 15<sup>th</sup>/ed p 374; Dutta Gynae 5<sup>th</sup>/ed p 282***Serous cystadenoma:**



- Most common of cystic neoplasms.
- It accounts for 50% of all ovarian tumors, of these 60% are benign, 15% are borderline, 25% of malignant.
- Occur in 3<sup>rd</sup>, 4<sup>th</sup> and 5<sup>th</sup> decade of life.
- Half cases are bilateral (*option "a" and "b" are true*).

*It is a unilocular cyst.*

- Delicate papillary excrescences may be seen on the surface and within the loculi of a benign cyst.
- Histologically – the benign variety shows cystic spaces and the lining of the tumor consists of tall columnar ciliated epithelium resembling the endosalpinx.
- **The loculi contain a thin serous straw coloured fluid**, which may be blood stained when malignant transformation occurs.

Rate of malignant transformation-40%

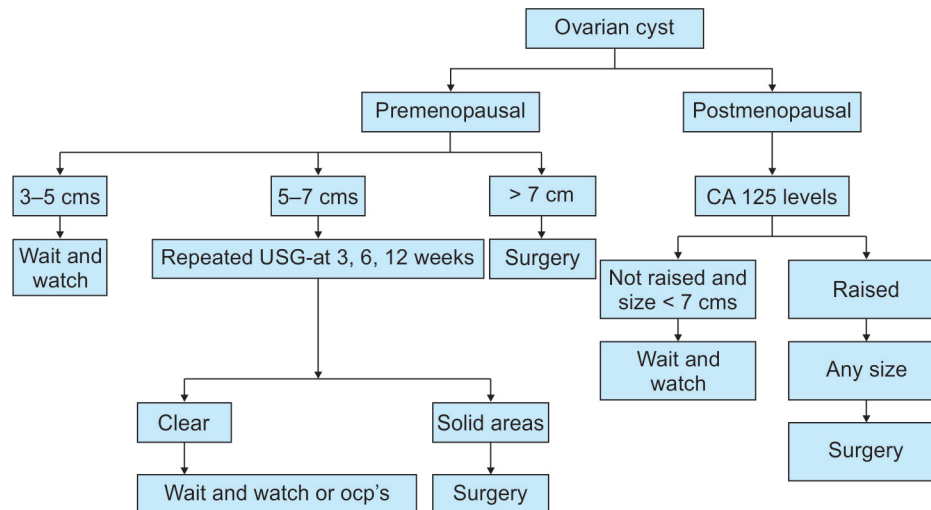
- *Option "d" (Dutta Gynae, 5/e, p 282):* Mucinous cystadenoma have glistening surface and cut surface shows loculi filled with mucinous material. The content is thick, viscid, and mucin. The cyst is frequently multiloculated.

68. Ans. is c, i.e. Wait and watch

Ref. Novak 14<sup>th</sup>/ed p 472

**Explanation:**

The patient is premenopausal and has a 3 x 4 cm clear ovarian cyst, so she is best managed by giving OC pills for 1-2 cycles and then repeating the USG.



**Note:** OCP's are not given routinely for ovarian masses as they decrease the risk of developing new cysts but do not hasten the resolution of existing cyst

69. Ans. is c, i.e. Surgery

Ref. Novak 14<sup>th</sup>/ed p 472

As explained in text.

Any ovarian mass with signs of malignancy (B/L ↑ vascularity) require surgery irrespective of the size.

The exact nature and extent of surgery is only decided intraoperatively, depending upon the frozen section (pathology) report.

70. Ans. is b, i.e. Dermoid cyst

71. Ans. is c, i.e. Dermoid cyst

Ref. Dutta Obs. 6<sup>th</sup>/ed p 310; Williams Gynae 1<sup>st</sup>/ed p 214

72. Ans. is b, i.e. Laparotomy at 14-16 weeks

Ref. Williams obs 23<sup>th</sup>/ed p 905-6

*"Dysgerminomas are the most common malignant tumor diagnosed during pregnancy but overall most common is dermoid cyst."*

... Williams Gynae 1<sup>st</sup>/ed p 214

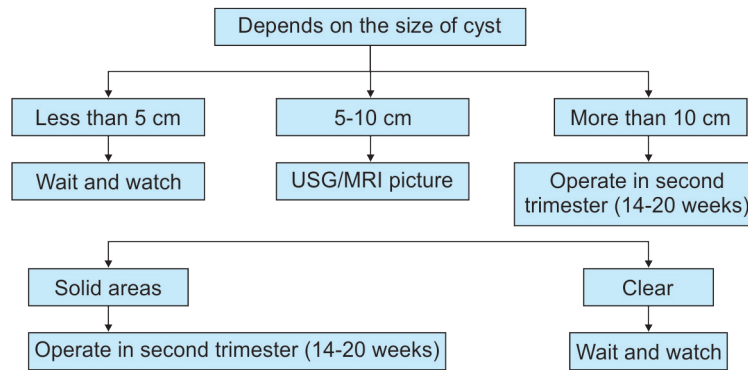
**Ovarian cysts in pregnancy**

M/C ovarian cyst diagnosed in pregnancy- Dermoid cyst

M/C ovarian tumor to undergo torsion in pregnancy- Dermoid cyst

M/C time for ovarian cyst to undergo torsion in pregnancy- end of first trimester and/or puerperium.

**Management:**



In cases of emergency (e.g., torsion, rupture) do Surgery, irrespective of size and weeks of gestation.

73. **Ans. is a, d and e, i.e. debulking; Chemotherapy; and Cytoreduction.**

*Ref. Shaw 15<sup>th</sup>/ed p 428; Dutta Gynae 6<sup>th</sup>/ed p 378-9*

Management of Advanced stage disease (stages III and IV) in ovarian cancer:

- **Advanced stage disease:** Exploratory Laparotomy → Cytoreductive or debulking surgery. This includes: Total abdominal hysterectomy bilateral salpingo-oophorectomy, complete omentectomy, retroperitoneal lymph node sampling and resection of any metastatic tumor. Optimum cytoreductive surgery is aimed to reduce the residual tumor load < 1-2 cm in diameter. Lesser the residual tumor volume (< 1 cm), better is the survival.
- **Chemotherapy:** Chemotherapy is used widely following surgery to improve the result in terms of survival. Drugs are given for five or six cycles at 3-4 weekly interval.
- **Combination chemotherapy:** Paclitaxel (175 mg/m<sup>2</sup>) and carboplatin (400 mg/m<sup>2</sup>) are commonly used.
- **Neoadjuvant chemotherapy and interval cytoreductive surgery:** Few cycles of chemotherapy followed by interval primary cytoreductive surgery may be done. Indications are: (i) Advanced epithelial ovarian cancer, (ii) High risk for surgery, (iii) Associated comorbid conditions (pleural effusion), (iv) Predicted to be suboptimally resected. Patient should have histological diagnosis of the tumor (biopsy). Benefits of neoadjuvant chemotherapy are: (i) Rapid clinical improvement. (ii) Subsequent surgery is easier and morbidity is reduced, (iii) Optimum cytoreduction with minimal residual disease may be possible.
- **Radiotherapy:** There is very little scope of radiotherapy as an adjunct to surgery because of the advent of chemotherapy.

74. **Ans. is d, i.e. Use of OCP's**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 290*

Lutein cysts are usually bilateral and caused by excessive chorionic gonadotropin secreted in cases of gestational trophoblastic tumors. These may also be formed with administration of gonadotropins or even clomiphene to induce ovulation. These are usually lined either by theca lutein cells called theca lutein cyst or by granulosa lutein cells, called granulosa lutein cyst.

Spontaneous regression is expected within few weeks following effective therapy of the tumors with the gonadotropin level returning back to normal.

75. **Ans. is a, i.e. It is always secondary**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 387*

- Krukenberg tumor is generally a metastatic tumor to the ovary. But "krukenberg tumor may be a primary tumor"
- Dutta Gynae 6<sup>th</sup>/ed p 387*
- The most common primary sites from where metastases to the ovaries occur are gastrointestinal tract (pylorus, colon and rarely small intestine), gallbladder, pancreas, breast and endometrial carcinoma.
- These are usually bilateral tumors which maintain shape of the ovary. Histologically 'signet ring' looking cells are characteristic of krukenberg tumor.
- In most patients with Krukenberg's tumors, the prognosis is poor. Median survival being less than a year. Rarely, no primary site can be identified and the Krukenberg's tumor may be a primary tumor.

**Also know:** Metastatic tumors from the GI tract can be associated with sex hormone (estrogen and androgen) production. Patient may present with postmenopausal bleeding.

76. **Ans. is a, i.e. Luteoma**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 384*

**SEX CORD Stromal Tumors**

- Granulosa cell tumors
- Thecomas, fibromas
- Sertoli-Leydig cell tumors (androblastoma)

- Gynandroblastoma (mixed)

Sex cord stromal tumors constitute 6–10 percent of all ovarian neoplasms. Peak incidence is over the age of 50. As 15–30 percent of these tumors produce hormones, they are also known as '*functioning tumors*'.

77. **Ans. is b and d, i.e. Lymphocytic infiltration is characteristics to dysgerminoma; and Endometrioid carcinoma of the ovary may coexist with endometrial adenocarcinoma**

Stromal invasion is absent. The epithelium shows multilayering, cellular atypia, pleomorphism and mitotic activity. Brenner tumour may present with the features of Meigs' syndrome and treatment prognosis is satisfactory. 20% of ovarian endometrioid carcinoma is associated with endometrial carcinoma.

78. **Ans. is b, i.e. Wait and watch**

*Novaus 141e, p 1366*

In postmenopausal women with unilocular cyst measuring 8–7 or less with normal several CA125 levels, expectant management is acceptable.



Any suspicious lesion of the vulva should be biopsied.

**Vulva**

**Premalignant Lesions of Vulva**

<ul style="list-style-type: none"> <li>• VIN</li> <li>• Lichen sclerosis</li> </ul>	<ul style="list-style-type: none"> <li>• Paget's disease</li> <li>• Squamous hyperplasia/hyperplastic dystrophy</li> </ul>	<ul style="list-style-type: none"> <li>• Bowen disease erythroplasia of queyrat</li> </ul>
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**Classification of Epithelial Vulvar Diseases**

Non-neoplastic epithelial disorders of skin and mucosa	
<ul style="list-style-type: none"> <li>• Lichen sclerosis</li> <li>• Squamous hyperplasia (earlier called as hyperplastic dystrophy)</li> </ul>	
Mixed neoplastic and non-neoplastic epithelial disorders	
Intraepithelial neoplasia	
Squamous intraepithelial neoplasia	Nonsquamous intraepithelial neoplasia
<ul style="list-style-type: none"> <li>• VIN 1</li> <li>• VIN 2</li> <li>• VIN 3</li> <li>• VIN 1</li> </ul>	<ul style="list-style-type: none"> <li>• Paget's disease</li> <li>• Tumor of melanocyte and Noninvasive</li> </ul>
Invasive tumors	



**Non-neoplastic disorders of vulvar epithelium**  
**Hyperplastic dystrophy (squamous cell hyperplasia)**

- Surface thickened and hyperkeratotic
- Most common symptom pruritis seen in post menopausal females
- Treatment-1% fluorinated corticosteroid ointment bid for 6 weeks

**Lichen sclerosis**

- Subepithelial fat becomes diminished, labia becomes thin and atrophic, labial fusion .
- Symptoms- pruritis, dyspareunia, burning
- Most common in postmenopausal women
- Treatment-ultrapotent topical steroid .05%, clobetasol x 2-4 weeks then taper down.

**Treatment of Vulval Intraepithelial Neoplasia**

- Treatment of choice - Surgery
  - Wide local excision done in young patient with localized lesion
  - Skinning vulvectomy - (Remove epidermis, not the underlying fibro fatty tissue) done in -Young patient with multicentric lesion
  - Simple vulvectomy done in elderly patient with extensive lesion
- CO<sub>2</sub> laser can be used in multicentric lesions
- Topical 5 Fluorouracil

**Paget's Disease of Vulva**

Mostly confined to epithelium. It occurs in two forms Intraepithelial Paget's disease and invasive Paget's disease

- M/C in postmenopausal women
- Patients complain of itching, irritation and bleeding
- The lesion has slightly raised margins, it is erythematous, with islands of white epithelium.
- **Histologically, it is characterized by Paget cells, Velvety red lesion**
- 10-15% patients with vulvar Paget's disease have an underlying adenocarcinoma of sweat glands.

- 10% patients of vulvar Paget's disease also have associated breast, colon or genitourinary cancer.
- So workup of Paget's disease should include colonoscopy, cystoscopy, mammography and colposcopy.

### Treatment

- Intraepithelial paget – Wide local excision
- Invasive paget – Radical vulvectomy with lymph node dissection
- Recurrence rate is very high.
- Management of recurrence - laser ablation

### Vulval Cancer

- M/C variety- Squamous cell carcinoma
- Most common symptom of vulval cancer - pruritis
- Most common site: Labia majora and minora
- Most common type of spread: Lymphatics (First lymphnode involved-Superficial Inguinal lymphnode, and then Deep inguinal LN and femoral group of lymphnodes).
- For lateral tumors only ipsilateral lymphnodes involved whereas for midline lesions, B/L lymphnodes are involved
- Sentinel lymphnode biopsy is helpful in vulval cancer
- Most important prognostic factor- Lymph node status.

### FIGO Staging of Vulval Cancer

- Stage I -** Tumor confined to vulva or perineum (No nodes)  
 IA – Size  $\leq$  to 2 cms stromal invasion  $<$  1 mm  
 IB – Size  $>$  2 cms stromal invasion  $>$  1 mm
- Stage II -** Tumor of any size with spreads to lower urethra, lower vagina or anus, with negative nodes.
- Stage III -** Tumor of any size spread to lower urethra, lower vagina or anus and regional lymphnode metastasis (i.e. inguinal, femoral lymphnodes involved)
- Stage IVA -** Tumor invades upper urethra, upper vagina, bladder mucosa, rectal mucosa or fixed or ulcerated inguinofemoral nodes
- Stage IVB -** Any distant metastasis including pelvic LN.

### Treatment of Vulval Cancer

Microinvasive cancer, i.e. Stage IA or invasion  $<$ 1 mm Wide local excision/ simple partial vulvectomy, no need for lymphadenectomy.  
 Stage IB and II and some III- Radical vulvectomy/Modified radical vulvectomy with thorough inguinofemoral lymphadenectomy.  
 If lesion is central do B/L lymphnode dissection otherwise if it is  $>$ 2 cms from midline do ipsilateral inguinofemoral lymphadenectomy.

Postoperative radiotherapy to be given if 2 or more groin nodes involved or disease free margin is  $<$ 8 cms

**Note :** In simple partial vulvectomy dissection is carried upto the superficial layer of urogenital fascia.  
 In modified radical/radical vulvectomy - dissection done upto the deep fascia of urogenital diaphragm, i.e. the perineal membrane.



HPV 16 and 18 are the most common risk factors for developing vulvar carcinoma:

- Sentinel lymphnode for vulvar carcinoma is superficial inguinal lymph node
- Sentinel lymph node biopsy is useful for knowing the spread of vulvar carcinoma
- In vulvar carcinoma both TNM and FIGO staging can be done



### Investigations Done in Vulvar Carcinoma

- Physical examination
- Always biopsy
- +/-Colposcopy

### Prognosis of Vulvar Carcinoma

- Depends on nodal involvement (single most important predictor followed by tumor size)
- Lesion > 3 cm are associated with poor prognosis
- Overall 5-year survival rate =79%

### Vaginal Carcinoma

- Primary cancer of vagina are very rare.
- Most common age group is elderly females > 70 years.
- Most common histologic type is squamous cell carcinoma.
- Most common site is upper third of posterior wall of vagina.

### Symptoms

- Mostly asymptomatic
- Patient may present with painless abnormal vaginal bleeding (including post coital bleeding).
- Foul smelling discharge per vaginum.

### Signs

- On per speculum examination-ulcerative/exophytic growth on vagina.
- Cervix appears normal.

### Lymphatic Drainage

- Tumor arising in upper vagina: drains to pelvic lymph node.
- Tumor arising in lower part: drains to inguinal lymph node.

### VAIN-Vaginal Intraepithelial Neoplasia

#### TREATMENT

- VAIN 1-No treatment
- VAIN 2-Laser
- VAIN 3-Surgical excision.

### Vaginal cancer staging

Stage 0	Vaginal intraepithelial neoplasia (VAIN)
Stage I	Carcinoma limited to the vaginal wall.
Stage II	Carcinoma extending beyond the vagina, but not extending to the pelvic side walls.
Stage III	Carcinoma extends upto the pelvic walls.
Stage III	Carcinoma extending beyond the true pelvis/or involving the bladder and/or rectum, or evidence of distal metastasis.

Clear cell adenocarcinoma occurs due to DES exposure to mother in first trimester. Most common lesion due to DES exposure is vaginal adenosis (benign lesion).

### Management

- Stage I – Tumor involving upper 1/3<sup>rd</sup> vagina – Radical hysterectomy + Radical vaginectomy + bilateral pelvic lymphadenectomy
- Tumor involving lower 1/3<sup>rd</sup> vagina – Radical vulvectomy + Bilateral inguino femoral lymphadenectomy + Radical vaginectomy.
- (*Note:* Carcinoma involving the distal third of the vagina necessitates dissection of groin nodes.)
- Tumor involving middle 1/3<sup>rd</sup> of vagina – External Radiotherapy + Brachytherapy
- Stages II and III – Radiotherapy
- Stage IV – Pelvic exenteration + Radiotherapy

## QUESTIONS

1. Most common vaginal carcinoma is: (PGI 99)
  - a. Squamous cell carcinoma
  - b. Adenocarcinoma
  - c. Botryoid's tumor
  - d. Columnar hyperplasia
2. Involvement of pelvis in a case of vaginal carcinoma of stage: (AI 97)
  - a. I
  - b. II
  - c. III
  - d. IV
3. Common differential diagnosis of verrucous carcinoma is: (AIIMS 96)
  - a. Condylomata lata
  - b. Condylomata acuminata
  - c. Adenocarcinoma
  - d. Tuberculosis
4. Which is most commonly implicated in genital (vulval) warts? (AIIMS May 08)
  - a. HPV 16
  - b. HPV 18
  - c. HPV 31
  - d. HPV 6
5. True about Ca vulva associated/predisposed by: (PGI 02)
  - a. Paget's disease
  - b. Vulval intraepithelial neoplasia
  - c. Bowen's disease
6. Vulval Ca, True statements: (PGI Dec 09)
  - a. Squamous hyperplasia predisposes
  - b. Paget's disease of vulva predisposes
  - c. Lichen sclerosis
  - d. Condylomata acuminata
  - e. Dystrophy
7. True about carcinoma vulva: (PGI 04)
  - a. Spreads to superficial inguinal nodes
  - b. Spreads to iliac nodes
  - c. Seen after menopause
  - d. Viral predisposition
  - e. Radiotherapy given
8. Brachytherapy is used in: (PGI 00)
  - a. Stage Ib Ca cervix
  - b. Ovarian Ca
  - c. Stage IV Ca vagina
  - d. Stage II fallopian tube Ca
9. All of these secrete hormone, except: (AIIMS May 93)
  - a. Granulosa cell tumor
  - b. Dysgerminoma
  - c. Hilus cell tumor
  - d. Theca cell tumor
10. Pyometra commonly occurs following: (AIIMS Dec 94)
  - a. Carcinoma endometrium
  - b. Carcinoma cervix
  - c. Carcinoma urethra
  - d. Senile endometritis
11. Pyometra is a complication associated with all of the following conditions except: (AI 03)
  - a. Carcinoma vulva
  - b. Carcinoma cervix
  - c. Carcinoma endometrium
  - d. Pelvic radiotherapy
12. Characteristic feature of carcinoma fallopian tube: (MAHE 01)
  - a. Watery discharge P/V
  - b. Hemorrhage
  - c. Pain
  - d. Sepsis
13. Patient diagnosed as squamous cell intraepithelial lesion which of the following has the highest risk for progression to carcinoma: (AIIMS Nov 07)
  - a. Low grade squamous intraepithelial neoplasia
  - b. High grade squamous intraepithelial neoplasia
  - c. Squamous intraepithelial associated with HPV 16
  - d. Squamous intraepithelial neoplasia associated with HIV
14. Sentinel biopsy most effective in: (AI 2010)
  - a. Cervix cancer
  - b. Endometrium ca
  - c. Vulval ca
  - e. Vaginal ca
15. The treatment of leukoplakia of vulva is: (UPSC 85; PGI 86)
  - a. Irradiation
  - b. Simple vulvectomy
  - c. Radical vulvectomy
  - d. Estrogen cream
16. All of the following are used for screening cancers in females except: (AIIMS Nov 2014)
  - a. CA-125: Ovarian cancer
  - b. Office endometrial aspirate: Endometrial carcinoma
  - c. Pap smear: Cervical cancer
  - d. Mammography: Breast cancer
17. Which of the following most commonly causes intraorbital metastasis in female? (AIIMS Nov 13)
  - a. Breast cancer
  - b. Cervical cancer
  - c. Ovarian cancer
  - d. Endometrial cancer

## NEW PATTERN QUESTIONS

18. Most common recurrence sites or metastatic sites of malignancy following pelvic surgery are all except:
  - a. Carcinoma cervix – Lateral pelvic wall and central pelvis
  - b. Carcinoma ovary – Lung
  - c. Chorionepithelioma – Suburethral region in anterior vaginal wall
  - d. Carcinoma body – Vault of vagina
19. The most common site of vulval cancer:
  - a. Labia majora
  - b. Labia minora
  - c. Prepuce of the clitoris
  - d. Bartholin's gland

20. The following statements are related to clear cell carcinoma of the vagina except:
- Common to those whose mothers were given diethylstilbestrol during early pregnancy
  - Vaginal adenosis may progress to this conditions
  - The middle one-third is the commonest site
  - May be multicentric and may involve even the cervix as well
21. The following primary tumours are common in the vulva except:
- Adenocarcinoma
  - Basal cell carcinoma
  - Choriocarcinoma
  - Squamous cell carcinoma
22. All of the following statements hold true for melanoma of vulva *except*:
- It is the 2nd M/C vulval cancer
  - M/C site is labia majora
  - May arise from junctional nevus
  - Has a poor prognosis



## ANSWERS

1. **Ans. is a, i.e. Squamous cell carcinoma**

*Ref. Dutta Gynae. 4<sup>th</sup>/ed p 314; Shaw 15<sup>th</sup>/ed p 398*

2. **Ans. is c, i.e. III**

*Ref. Shaw 15<sup>th</sup>/ed p 399; Table 29.5*

**Vaginal carcinoma:**

Most common histologic type is squamous cell carcinoma.

Most common site is upper third of posterior wall of vagina.

**Lymphatic Drainage:**

- Tumor arising in upper vagina: drain to pelvic lymph node.
- Tumor arising in lower part: drain to inguinal lymph node.

**Vaginal cancer staging**

Stage 0	Vaginal intraepithelial neoplasia (VAIN)
Stage I	Carcinoma limited to the vaginal wall.
Stage II	Carcinoma extending beyond the vagina, but not extending to the pelvic side walls.
Stage III	Carcinoma extends upto the pelvic walls.
Stage IV	Carcinoma extending beyond the true pelvis/or involving the bladder and/or rectum, or evidence of distal metastasis.

3. **Ans. is b, i.e. Condylomata acuminata**

*Ref. Novak 14<sup>th</sup>/ed p 1412*

Verrucous carcinoma is variant of squamous cell carcinoma of cervix.

*"Verrucous carcinomas may resemble giant condyloma accuminatum, are locally invasive and rarely metastasise."*

*... Novak 14<sup>th</sup>/ed p 1412*

Condylomata accuminata is an STD (due to HPV 6 and HPV 11 infection) and has a verrucous appearance.

4. **Ans. is d, i.e. HPV 6**

*Ref. Williams Gynae 1<sup>st</sup>/ed p 619*

*"Low Risk HPV types 6 and 11 cause nearly all genital warts."*

*... Williams Gynae 1<sup>st</sup>/ed p 67*

**Genital Warts:**

- Genital warts are lesions created from productive infection with HPV (most common type 6 and 11).
- They display various morphologies and appearances ranging from flat papules to the classic verrucous, polyphytic lesions, termed "*condyloma acuminata*".
- **Sites:** External genital warts may develop at sites in the lower reproductive tract, urethra, anus, or mouth.
- **Diagnosis :** They are typically diagnosed by clinical infection, and biopsy is not required unless co-existing neoplasia is suspected. HPV serotyping is not required for routine diagnosis.

**Treatment:**

- Condyloma acuminata may remain unchanged or resolve spontaneously.
- Effect of treatment on future viral transmission is unclear. However, many women prefer removal, and lesions can be destroyed with sharp or electrosurgical excision, cryotherapy, or laser ablation. In addition, very large, bulky lesions may be managed with cavitation ultrasonic surgical aspiration.

**Medical Management of Genital Warts:**

- Topical 5-percent imiquimod cream (immunomodulator)
- Podophyllin (antimitotic agent)
- Trichloroacetic acid (proteolytic agent)
- Bichloroacetic acid (proteolytic agent)
- Intralesion injection of interferon

**Note:** Intralesion injection of interferon has high cost, is painful and is inconvenient to administer, So this therapy is not recommended as a primary modality and is best reserved for recalcitrant cases.

**Therapy of choice:** No data suggest the superiority of one treatment. Thus in general treatment should be selected based on clinical circumstances and patient and provider preferences.

5. **Ans. is a, b and c, i.e. Paget's disease; Vulvar intraepithelial neoplasia; and Bowen's disease**

*Ref. Dutta Gynae. 5<sup>th</sup>/ed p 307*

**Premalignant lesion of vulva:**

- Vulvar intraepithelial neoplasia VIN (most common)
- Chronic vulvar dystrophies
- Lichen sclerosis
- Erythroplasia of Queyrat
- Paget's disease
- Condyloma accuminata
- Squamous cell hyperplasia

Bowen's disease is a type of VIN where among the ordinary atypical cells, large bloated cells called Bowen cells are also present.

6. **Ans. is a, b, c, d and e, i.e. All are correct**

*Ref. Novak 14<sup>th</sup>/ed p 591-5; Dutta Gynae 5<sup>th</sup>/ed p 321-5*

In the past the term "*Chronic vulvar dystrophy*" used to denote disorders of epithelial growth and differentiation which predisposed to vulval cancer.

But the International Society for Study of Vulvar Diseases (ISSVD) recommended that the old dystrophy terminology be replaced by newer classification.

**Classification of Epithelial Vulvar Diseases:**

Non-neoplastic epithelial disorders of skin and mucosa	
<ul style="list-style-type: none"> <li>Lichen sclerosis</li> <li>Squamous hyperplasia (earlier called as hyperplastic dystrophy)</li> </ul>	
Mixed neoplastic and non-neoplastic epithelial disorders	
Intraepithelial neoplasia	
Squamous intraepithelial neoplasia	Non-squamous intraepithelial neoplasia
<ul style="list-style-type: none"> <li>VIN 1</li> <li>VIN 2</li> <li>VIN 3</li> <li>VIN 1</li> </ul>	<ul style="list-style-type: none"> <li>Paget's disease</li> <li>Tumor of melanocyte, Noninvasive</li> </ul>
Invasive Tumors	

*"The malignant potential of the non-neoplastic epithelial disorders is low but patients with lichen sclerosis and concomitant hyperplasia may be at high risk."*

*... Novak 14<sup>th</sup>/ed p 591*

So I am taking option "a" and "c" as correct.

**Condyloma accuminata** (vulvar warts) are caused by HPV type 6 and 11.

Most common site posterior fourchette and lateral areas.

The virus can be transmitted to this site from other parts of body or can be transmitted sexually.

Long standing condyloma can undergo malignant change.

*"Malignant change is also associated with chronic inflammatory diseases such as the venereal granulomas and vulvar warts with 20-30 years standing."*

*... Jeffcoates 7<sup>th</sup>/ed p 446*

**Paget's disease:**

- Most cases of vulvar Paget's disease are nonsquamous intraepithelial neoplasia associated with proliferation of atypical glandular cells of the apocrine type.
- "Some patients with vulvar paget's disease have an underlying adenocarcinoma, although the precise frequency is difficult to ascertain."*
- The characteristic histological feature is the presence of "Paget cell" in the epidermis - The cells are large round - oval in shape, with abundant pale cytoplasm. Mucopolysaccharide may be present in its cytoplasm.
- It predominantly affects postmenopausal white women and presenting symptom is usually pruritis and vulvar sclerosis. The lesion has an eczematoid appearance and usually begins on hair bearing portions of vulva.
- A second synchronous or metachronous primary neoplasm is associated with Paget's disease in 4% cases. Associated carcinomas have been reported in the apocrine sweat gland, bartholin gland, cervix, colon, bladder, gallbladder and breast.

*... Novak Gynae 14<sup>th</sup>/ed p 593*

7. **Ans. is a, b, c, d and e, i.e. Spreads to superficial inguinal nodes; Spreads to iliac nodes; Seen after menopause; Viral predisposition; and Radiotherapy given**

*Ref. Shaw 15<sup>th</sup>/ed p 395; Dutta Gynae. 5<sup>th</sup>/ed p 321-2; Williams Gynae. 1<sup>st</sup>/ed p 668-72*

**Vulval cancer:**

- 2-4% of all malignancies of female genital tract.
- Age:** occurs in 6th or 7th decade.
- Most common histologic type is epidermoid cancer (squamous cell CA) seen in 90% cases.**
- Nulliparous**, women of **low parity** are predisposed to vulval CA.
- The etiology is same as of carcinoma in situ cervix (that is viral predisposition by viruses - HIV, HPV, HSV-II).
- Most common site - Labia majora (Anterior 2/3rd) followed by clitoris and labia minora.
- Associated with cervical cancer in 20% cases.
- Presents with pruritis and visible lesion. All though pain, bleeding and ulceration also may be the initial complains.
- Spread of tumor - mainly by direct spread and lymphatics.
- First superficial inguinal nodes are involved and then it spreads to deep nodes and via glands of Cloquet to external iliac nodes, obturator and common iliac nodes in late stages.

**Staging :** Mainly clinical:

- Both FIGO staging and TNM staging are done in case of vulval cancer.
- Recommended is FIGO staging

**Note:** Vulval cancer is the only genital malignancy which can be staged using TNM staging.<sup>Q</sup>

**Treatment:**

- Early stages : Radical/Partial Vulvectomy with inguinal nodes dissection.
- Late stages : chemotherapy and radiotherapy.

**Prognosis:**

- Overall survival rates of women with vulval cancer are excellent.
- Lymphnode involvement is the single most important prognostic factor.
- Presence of inguinal lymphnode metastasis reduces the overall survival rate by 50%.

**Note:**

- "*Skinning vulvectomy*" refers to removal of only the skin and superficial subcutaneous tissue. This surgery plays no role in the treatment of invasive vulvar cancer but may be used in noninvasive disease such as cases with widespread multifocal VIN 3.
- Sentinel node biopsy - At present, the Gynecologic Oncology Group (GOG) is conducting a multicenter trial to evaluate the benefit of sentinel node biopsy for vulvar cancer.

**8. Ans. is a, i.e. Stage Ib Ca cervix**

Ref. Dutta Gynae. 4<sup>th</sup>/ed p 352-3, 342; Shaw 15<sup>th</sup>/ed p 414

- Radiotherapy is recommended in advanced stages of Ca cervix i.e. stage IIB onwards.<sup>Q</sup>
- Brachytherapy is commonly used.
- For larger tumors initially external radiation then brachytherapy is given.
- In small tumors brachytherapy is given first followed by external radiation.
- For **stage IB and IIA** - both surgery and radiotherapy yield similar results.
- There is very little scope of radiotherapy in ovary tumors. Only Granulosa cell tumor and dysgerminoma are radiosensitive and in them also external radiotherapy is instituted for elderly woman. ... Dutta 5<sup>th</sup>/ed p 365-8
- Vaginal squamous cell Ca is only moderately sensitive to irradiation.
- In all advanced cases exenteration operation is done. ... Shaw 14<sup>th</sup>/ed p 358
- **Fallopian tube carcinoma** - Total hysterectomy with Bilateral Salpingo-oophorectomy along with omentectomy followed by external pelvic radiation is the Treatment of Choice in cancer of Fallopian Tube.

... Dutta Gynae 5<sup>th</sup>/ed p 356

Ref. Shaw 15<sup>th</sup>/ed p 378

**9. Ans. is b, i.e. Dysgerminoma**

Dysgerminoma:

*"The tumor is neutral and does not secrete either male or female sex hormones but secretes placental alkaline phosphatase, lactate dehydrogenase and beta hCG.*

Granulosa cell tumor	:	Secretes estrogen
Theca cell tumor	:	Secretes estrogen
Hilus cell tumor	:	Secretes androgens

**10. Ans. is a, i.e. Carcinoma endometrium**

**11. Ans. is a, i.e. Carcinoma vulva**

Ref. Jeffcoate 7<sup>th</sup>/ed p 350

Pyometra is collection of pus or mixture of pus and blood within the uterus.

**Causes:**

- Most common cause : *carcinoma endometrium*.<sup>Q</sup>
- 2nd most common cause : *senile endometritis*.<sup>Q</sup>

**Other causes:**

- Congenital atresia of the vagina/cervix.
- Stenosis of cervix/vagina following :
  - Operations
  - Burns
  - Radiotherapy
  - Senile
  - Tuberculous
  - Puerperal
- Endometritis:
  - *Ca endometrium (most common)*<sup>Q</sup>
  - Ca cervix
  - Ca corporis
- Carcinoma:
  - *Ca endometrium (most common)*<sup>Q</sup>
  - Ca cervix
  - Ca corporis

**12. Ans. is a, i.e. Watery discharge P/V**Ref. Shaw 15<sup>th</sup>/ed p 421

- *Fallopian Tube Carcinoma accounts for 0.3% of all cancers of female genital tract.*
- *Most common site* is the ampulla of the tube.
- *Most common type* is adenocarcinoma.
- The fallopian tube is frequently involved in secondary to carcinoma of ovary, endometrium, gastrointestinal tract, breast and peritoneum.
- Women with mutation in **BRCA I** and **BRCA II** have higher risk of developing fallopian tube carcinoma (therefore, a prophylactic surgery in these women should include a complete removal of both tubes along with the ovaries).
- Most common symptom is Vaginal discharge (**prominent watery vaginal discharge** called as *Hydrops tubal profluens*). Later due to ulceration – watery discharge becomes blood stained and may take the form of perimenopausal/postmenopausal bleeding.

**Always remember:**

- In perimenopausal and postmenopausal women with unusual, unexplained or persistent vaginal discharge, even in absence of bleeding, the clinician should always keep the possibility of occult tubal cancer in mind.
- **Triad of :**
  - Vaginal discharge
  - Pelvic pain
  - Pelvic mass

} is seen in 15% of patients

**On examination :** Pelvic mass may be felt.**Spread :** Since the fallopian tube is richly supplied by lymphatics, spread to the pelvic and para-aortic nodes occurs early.**Treatment :** *Surgery + chemotherapy + radiotherapy.***13. Ans. is b, i.e. High grade squamous intraepithelial neoplasia**Ref. Shaw 15<sup>th</sup>/ed p 402; Williams Gynae 1<sup>st</sup>/ed p 629

There are various nomenclatures/classification systems for reporting of Pap smear.

The one which is classically used is by WHO, which uses the terms CIN-I, CIN-II and CIN-III (as discussed in chapter on CIN). Another system as discussed earlier is **Bethesda** which classified the disease as **LSIL=low grade squamous intraepithelial lesion** and **HSIL high grade squamous intraepithelial lesion** and as discussed in chapter on cancer cervix chances of progressing to cancer are maximum with HSIL which includes CIN1, CIN11 and ca in situ.

**14. Ans. is c, i.e. Vulval ca**Ref: Novak 14<sup>th</sup>/ed p 1425-6, 1562-3

- The sentinel node is a specific lymph node (or nodes) that is the first to receive drainage from a malignancy and is the primary site of nodal metastasis.
- In theory, the presence or absence of metastatic disease in the sentinel node should reflect the status of the nodal basin as a whole. Thus a negative sentinel lymph node would allow omission of lymphadenectomy of the whole nodal basin.
- It is detected through perilesional injection of radiolabelled technetium-99 or blue dye followed by intraoperative identification of the sentinel lymph nodes.
- *Sentinel lymph node detection has become an integral part of the management strategy for breast cancer and melanoma.*

**Amongst Gynaecological Cancers:**

Preliminary studies suggest that a sentinel node can be identified in most patients of vulval cancer.

... Novak 14<sup>th</sup>/ed p 1562

Investigation are being carried out to detect sentinel node in cervical cancer. But at this time – the role of sentinel node detection is purely investigational and complete lymphadenopathy when indicated, remains the standard of care.

... Novak 14<sup>th</sup>/ed p 1426

Although in both Ca cervix and Ca vulva, role of sentinel lymph node biopsy is not yet confirmed but vulval cancer is a better bet.

**15. Ans. is b and d, i.e. Simple vulvectomy; and Estrogen cream**Ref. Jeffcoate 7<sup>th</sup>/ed p 403-5**Treatment of leukoplakia :**

Treatment of the cause	General treatment	Empirical measures (when cause can not be treated)
<ul style="list-style-type: none"> <li>• Anemia correction</li> <li>• Folic acid and vit B12 (given in case of deficiency)</li> <li>• Treatment of candidiasis</li> </ul>	<ul style="list-style-type: none"> <li>• Sedatives - to prevent scratching and to ensure sleep</li> <li>• Cold cream application</li> <li>• Washing with 1% sodium bicarbonate</li> <li>• Use of loose and light cotton underclothing</li> </ul>	<ul style="list-style-type: none"> <li>• Corticosteroids (mainstay of therapy)<sup>o</sup></li> <li>• Estrogens and testosterone<sup>o</sup></li> <li>• Local analgesia</li> <li>• Division of cutaneous nerves; nerve block</li> <li>• Cod liver oil or cream of zinc oxide &amp; olive oil</li> <li>• Local applications</li> <li>• For refractory lesion intralesional injection of triamcinolone acetonide may be tried.</li> </ul>

### Role of Vulvectomy

- When a non-neoplastic epithelial disorder is localized, local excision or partial vulvectomy may be the best method of biopsy. Otherwise vulvectomy should be reserved for those cases in which atypical epithelial activity is found histologically. In these cases, it need not be accompanied by lymphadenectomy.
- If there is no threat of cancer, empirical vulvectomy should be avoided. It is mutilating and gives poor results. The disorder sooner or later recurs in 50% cases treated by vulvectomy. There is no role of vulvectomy in children and lichen sclerosis.

16. **Ans. b. Office endometrial aspirate: Endometrial carcinoma** *Ref. Novak's 14/e p1348 Harrison 18/e p661-662; Park 21st/129*  
Office endometrial aspirate is not used for screening of Endometrial carcinoma.

Transvaginal ultrasound and endometrial sampling have been advocated as screening tests for endometrial cancer but benefit from routine screening has not been shown.

*"Screening for endometrial cancer should currently not be undertaken because of lack of an appropriate, cost-effective and acceptable test that reduces mortality. Routine PAP testing is inadequate test that reduces mortality. Routine PAP testing is inadequate and endometrial cytology assessment is too insensitive and non-specific to be useful in screening for endometrial cancer even in high-risk population."* Novak's 14/e p1348

Screening test	Disease screened
Papanicolaou (Pap's) smear	Cervical cancer
Mammography	Breast cancer
CA-125	Ovarian cancer

### Screening test

**Screening test** is used to search for an **unrecognized disease or defect**, in apparently healthy individuals, by means of **rapidly applied tests, examination or other procedures**.

Screening test	Disease screened
Papanicolaou (Pap's) smear	Cervical cancer <sup>Q</sup>
Mammography	Breast cancer <sup>Q</sup>
Bimanual oral examination	Oral cancer <sup>Q</sup>
ELISA	HIV <sup>Q</sup>
Urine for sugar, Random blood sugar	Diabetes mellitus <sup>Q</sup>
AFP	Developmental anomalies in fetus <sup>Q</sup>
DRE + PSA	Prostate cancer <sup>Q</sup>
Fecal occult blood test	Colorectal cancer <sup>Q</sup>
CA-125	Ovarian cancer <sup>Q</sup>

17. **Ans. is a, i.e. Breast cancer**

*Ref. Journal of head and neck oncology 2011*

Orbital metastasis occurs in 2 to 3% of cancers. Metastasis of breast cancer accounts for majority of ocular and orbital metastasis.

18. **Ans. is b, i.e. Carcinoma ovary - Lung**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 360, 354,376*

**Endometrial cancer/cancer body uterus** *-Dutta gynae 6<sup>th</sup>/ed p 360*

**Recurrent disease:** Common sites for recurrence are the vagina and the pelvis. The extrapelvic metastases are seen in the lung, lymph nodes (aortic), liver, brain and bones. Majority (60%) of recurrences are seen within 2 years of initial therapy.

- Radiation therapy is the choice for isolated recurrence following surgical treatment:
- Exenterative surgery for recurrent endometrial cancer is of limited value.
- Hormonal therapy and chemotherapy have been used depending on the individual case.

**Cancer cervix: Recurrent disease**

*-Dutta gynae 6<sup>th</sup>/ed p 354*

Risk factors for recurrent disease are: Large tumor size, lymphovascular space invasion, positive lymph nodes, advanced stage disease.

**Most common site** of recurrence is pelvic side wall. Features of disease recurrence are: Pain in the pelvis, back, unilateral leg edema, ureteral obstruction, vaginal bleeding, palpable tumor in the pelvis and lymphadenopathy. Single agent or multiagent chemotherapy with cisplatin, paclitaxel or ifosfamide is used. Palliative radiation therapy may be used to those who have been treated initially with surgery.

**Follow-up:** The majority of the recurrences occur in the first 2 years. As such, the follow-up protocols should be at 3–4 months interval for the first 2 years then at 6 months interval for next 2 years and thereafter annually. Thorough physical examination is done including examination of supraclavicular and inguinal lymph nodes. Cervical or vaginal cytology is performed. Chest X-ray is done annually.

**Cancer Ovary** –Dutta gynae 6<sup>th</sup>/ed p 376

**Metastasis**

The most common sites of metastases are—peritoneum (85%), omentum (70%), contralateral ovary (70%), liver (35%), lung (25%) and uterus (20%). Thus option b is incorrect.

**19. Ans. is a, i.e. Labia majora**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 334*

**Sites for vulval cancer**

The commonest site is labium majus followed by clitoris and labium minus.

**20. Ans. is c, i.e. The middle one-third is the commonest site**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 339*

**Clear cell adenocarcinoma of vagina–**

Primary vaginal adenocarcinoma is rare. This is found in adolescent girls who have had history of intrauterine exposure to diethylstilbestrol in the first trimester of pregnancy.

The approximate risk of an offspring to develop the clear cell adenocarcinoma of the vagina following DES exposure is 1 in 1000 or less. These patients are more likely to develop vaginal adenosis but, rarely clear cell adenocarcinoma.

**The lesion usually involves the upper-third of the anterior vaginal wall.** The cervix may also be involved.

**Treatment:** Radical hysterectomy, vaginectomy with pelvic lymphadenectomy is the treatment of choice.

Radiotherapy is reserved for advanced cases.

**21. Ans. is c, i.e. Choriocarcinoma**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 334*

**Histological types of vulval cancers**

- Squamous cell carcinoma–90%
- Melanoma 5%
- Adenocarcinoma (Bartholin's gland)
- Basal cell carcinoma
- Sarcoma

**22. Ans. is b, i.e. M/C site is labia majora**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 337*

**Melanoma** is the second most common vulval cancer. **The common sites are the clitoris and labia minora.** It may arise from a junctional nevus. Radical vulvectomy and bilateral regional lymphadenectomy (en-block) is the preferred treatment. Pelvic lymphadenectomy does not alter the prognosis. Radiation therapy, adjuvant chemotherapy, or immunotherapy are ineffective. Overall prognosis is poor.

# CHAPTER

# 15

# Gynecological Diagnosis and Operative Surgery

## QUESTIONS

- Hysteroscopy means visualization of: (PGI June 05)
  - Genital tract
  - Fallopian tube
  - Uterine cavity
  - Cervix
  - Abdominal cavity
- For hysteroscopy, following are/is used: (PGI Dec 08)
  - Distilled Water
  - Air
  - Glycine
  - CO<sub>2</sub>
- Hysteroscopy can diagnose all, except: (PGI June 98)
  - Asherman's syndrome
  - Septate uterus
  - Adenomyosis
  - TB endometritis
- Hysteroscopy is used in all EXCEPT: (AIIMS May 02)
  - Uterine synechia
  - Abnormal vaginal bleeding
  - Infertility
  - Recurrent still birth and abortions
- Asherman's syndrome can be diagnosed by all except: (AIIMS Nov 07)
  - Hysterosalpingography
  - Saline sonography
  - Endometrial culture
  - Hysteroscopy
- Best gas used for creating pneumoperitoneum at laparoscopy is: (AI 98)
  - N<sub>2</sub>
  - O<sub>2</sub>
  - CO<sub>2</sub>
  - N<sub>2</sub>O
- Laparoscopy is best avoided in patients with: (UPSC 97)
  - Hypertension
  - Diabetes
  - Obesity
  - COPD
- Laparoscopy is contraindicated in: (MCI March 11)
  - Ectopic pregnancy
  - PID
  - Endometriosis
  - Peritonitis
- A 26-year-old female with 3 living issues having cervical erosion which bleeds to touch, diagnosis can be done by: (PGI Dec 03)
  - Pap smear
  - Excision biopsy
  - Hysteroscopy
  - Colposcopy
- Occurrence of ovulation is indicated by: (PGI Dec 03)
  - LH
  - FSH
  - Estradiol
  - Progesterone
  - Cortisol
- Time of ovulation is detected by: (PGI June 03)
  - Urine LH
  - Urine FSH
  - Urine HCG
  - Serum Estradiol
  - BBT
- Which of the following methods for assessment of female infertility during a menstrual cycle can best predict timing of ovulation: (AI 2010)
  - BBT
  - Fern Test
  - Spin Barkeit Phenomenon
  - Hormonal Study
- Best indicator of ovarian reserve is: (AIIMS Nov 07)
  - FSH
  - Estradiol
  - LH
  - FSH/LH Ratio
- Goniometer is used for: (AIIMS Nov 07)
  - Amount of vaginal secretions
  - To measure width of genital hiatus
  - Gonococcal colony count
  - Urethrovesical angle
- Feature of post ovulatory endometrium on ultrasound is: (Delhi 03)
  - Single hyperechoic thin line
  - Three line sign
  - Prominent halo
  - Prominent posterior enhancement
- Luteal phase defect is best diagnosed by: (Delhi 97)
  - Serum progesterone levels
  - Endometrial biopsy
  - Basal body temperature
  - Ultrasonography
- Chassarmoir surgery is done in case of:
  - Uterine inversion
  - VVF repair
  - Ureterovesical fistula repair
  - Retroverted uterus
- All of the following are advantages of vaginal hysterectomy over abdominal hysterectomy except:
  - Better tolerated by elderly and obese patients
  - Lesser risk of postoperative thromboembolism
  - Other visceral structures can be easily visualized
  - Corrects prolapse of other organs

19. Maximum chances of ureteric injury are with: (AI 06)
- TAH
  - Wertheims hysterectomy
  - Anterior colporrhaphy
  - Vaginal hysterectomy
20. Transcervical endometrial resection (TCRE) is used in:
- Endometriosis (PGI June 99)
  - DUB
  - Carcinoma endometrium
  - Submucous fibroid

### NEW PATTERN QUESTIONS

21. Cryosurgery is effective in all except:
- Chronic cervicitis
  - Squamous intraepithelial lesion (SIL)
  - Condyloma accuminata
  - Cases with severe dysplasia or CIS lesion
22. Regarding outpatient hysteroscopy all are correct except:
- Abnormal uterine bleeding is an indication
  - Normal saline as distension medium can be used
  - It is less accurate than saline infusion sonography (SIS)
  - It is not reliable to exclude endometrial carcinoma
23. To minimize ureteric damage, the following preoperative and operative precautions may be taken except:
- Cystoscopy
  - Direct visualization during surgery
  - Ureter should not be dissected off the peritoneum for a long distance
  - Bladder should be pushed downwards and outwards while the clamps are placed near the angles of vagina
24. Indications of rectal examination in gynecology are all except:
- In cases with müllerian agenesis
  - In virgin females
  - To differentiate rectocele from enterocele
  - For staging of ovarian malignancy
25. The advantages of cryosurgery over electrocauterization are all except:
- Less discomfort to the patient
  - Postoperative bleeding is much less
  - Postoperative vaginal discharge is also much less
  - Cervical stenosis is extremely rare
26. Position of the patient should be as described except:
- Diagnostic laparoscopy – Trendelenburg with about 30° tilt
  - Colposcopy – Lithotomy
  - Transvaginal sonography in gynecology – Lithotomy with full bladder
  - Hysteroscopy – Lithotomy
27. Absolute contraindications of laparoscopy are:
- Diaphragmatic hernia
  - Generalized peritonitis
  - Patient on anticoagulant therapy
  - Previous incomplete laparoscopy
28. As regard the use of laser in gynecology, all are correct except:
- Management of CIN, VIN, VAIN
  - Laser laparoscopy for ectopic pregnancy
  - Laser hysteroscopy for presacral neurectomy
  - It acts by tissue cutting, vapourization or coagulation



## ANSWERS

1. Ans. is c, i.e. Uterine cavity
2. Ans. is c and d, i.e. Glycine and CO<sub>2</sub>
3. Ans. is c, i.e. Adenomyosis *Ref. Novak 14<sup>th</sup>/ed p 787, 15<sup>th</sup>/ed p 786-2, Shaw 15<sup>th</sup>/ed p 494; Williams Gynae 1<sup>st</sup>/ed p 950-1*
  - *Hysteroscopy is the endoscopic technique of visualizing the interior of uterus directly.*<sup>Q</sup>
  - It is both diagnostic and therapeutic.

**Patient Preparation:**

- In premenopausal women, hysteroscopy is ideally performed in the early proliferative phase of menstrual cycle, when endometrium is relatively thin. This allows small masses to be easily identified and removed.
- Alternatively agents like progestins, combined pills, Danazol and GnRH agonist can be administered prior to anticipated surgery.
- Hysteroscope consists of a rigid 4 mm diameter telescope so, cervix has to dilated to 4 mm<sup>Q</sup> for insertion of hysteroscope.

**Distension media:**

- Because the anterior and posterior uterine walls are in apposition, a distention medium is required to expand the endometrial cavity for viewing.
- Distension media includes CO<sub>2</sub> Saline and low viscous fluids such as sorbitol, mannitol and glycine solutions.
- To expand the cavity, intrauterine pressure of *these media must reach 45 to 80 mm of hg.* it should not exceed 100mg of Hg because high pressure can result in increased intravasation of medium into the patient's circulation and fluid volume overload.

Most common media used for diagnostic purpose – CO<sub>2</sub>  
 Most common media used for therapeutic purpose – Glycine

- Contraindication:**
- Infection (except in case of misplaced IUCD)
  - Pregnancy
  - Genital malignancy

**Diagnostic Indications of hysteroscopy:**

Friends, lets not mug up the diagnostic indications of hysteroscope by any mnemonic but lets understand them.

*A hysteroscope can visualize the interior of uterus so, it can diagnose*

- *Any congenital malformation of uterus and can also help in differentiating between a bicornuate uterus from a septate uterus.*<sup>Q</sup>
- *Any uterine synechiae (as in Ashermann syndrome).*<sup>Q</sup>
- Misplaced IUCD.<sup>Q</sup>
- Submucous fibroid<sup>Q</sup>

*A hysteroscope can visualize the cornua so, it can diagnose*

- Any cornual pathology

*Hysteroscope can directly visualize the endometrium so, it can diagnose*

- Endometrial lesions like - endometrial polyp, endometrial hyperplasia, endometrial cancer, endometrial T.B.<sup>Q</sup>
- Pregnancy related conditions like : Molar tissue or products of conception.<sup>Q</sup>

**Besides these hysteroscopy is also indicated in<sup>Q</sup>:**

- Unexplained abnormal uterine bleeding<sup>Q</sup>
  - Premenopausal<sup>Q</sup>
  - Postmenopausal<sup>Q</sup>
- Selected infertility cases: In case of
  - Abnormal HSG<sup>Q</sup>
  - Unexplained infertility<sup>Q</sup>
- Recurrent spontaneous abortion
  - The therapeutic indications of hysteroscope are (here also don't mug up, just try to understand them).<sup>Q</sup>
    - To excise uterine septum<sup>Q</sup>
    - To lyse adhesions in Ashermann's syndrome<sup>Q</sup>
    - To retrieve lost IUCD<sup>Q</sup>
    - Hysteroscopic myomectomy<sup>Q</sup>
    - Polypectomy<sup>Q</sup>
    - Endometrial ablation for menorrhagia<sup>Q</sup>
    - Tubal occlusion for control of fertility<sup>Q</sup>
    - Intratubal ballooning in tubal blockage<sup>Q</sup>

**As far as adenomyosis is concerned** – it can be suspected on hysteroscopy by appearance of diverticuli but definitive diagnosis requires transvaginal ultrasonography.

For management of adenomyosis hysterectomy is the definitive treatment

*“Endometrial ablation and resection using hysteroscopy has been used to successfully treat dysmenorrhea and menorrhagia caused by adenomyosis. However, complete eradication is problematic.”* ... Williams Gynae 1<sup>st</sup>/ed p 209

**Also know :**

Technique for visualization of	
Cervix	Colposcopy
Fallopian tube	
– To see its mucosa	Salpingoscopy
– To see its lumen	Falloscopy
Abdominal cavity	Laparoscopy

**4. Ans. is d, i.e. Recurrent still birth and abortions**

Ref. Novak 14<sup>th</sup>/ed p 787, 1302; Shaw 15<sup>th</sup>/ed p 494, 495

**Hysteroscopy is used undoubtedly in :**

- Uterine synechiae i.e. Asherman syndrome - Hysteroscopy is the gold standard technique for diagnosing uterine synechiae (Asherman syndrome) as well as managing it.
- Abnormal vaginal bleeding hysteroscopy has nearly replaced standard D and C for the management of abnormal uterine bleeding as it allows for the direct visualization of any uterine abnormality as well as simultaneously it can treat them.
- In case of Infertility - *“Endoscopic evaluation of the intrauterine cavity is the primary method for defining intrauterine abnormalities (leading to infertility)”*. ... Williams Gynae 1<sup>st</sup>/ed p 438
- In case of recurrent abortions also hysteroscopy is useful  
*“Hysteroscopy forms an integral part of the procedures done to evaluate the cause of recurrent pregnancy loss.”*  
... Novak's 14<sup>th</sup>/ed p 1302

But hysteroscopy is not useful in recurrent still births.

**5. Ans. is c, i.e. Endometrial culture**

Ref. Williams Gynae 1<sup>st</sup>/ed p 420; Leon Speroff 7<sup>th</sup>/ed p 419

**Asherman's syndrome:**

- It is an acquired uterine defect characterized by the presence of uterine synechiae and subsequent destruction of the lining endometrium.
- M/C cause for Asherman syndrome - Post partum curettage  
2nd M/C cause - curettage done for MTP  
Other causes - uterine surgery like cesarean section, myomectomy, Sheehan's syndrome  
Infectious causes - TB, Schistosomiasis
- Most characteristic symptom = Hypomenorrhea (scanty bleeding <20 ml or <2 days) or 2° amenorrhea  
Others - Infertility  
Abortion
- **Diagnosis:** ... William Gynae 1<sup>st</sup>/ed p 420-1
- When Asherman syndrome is *suspected, HSG is indicated. Intrauterine adhesions, characteristically appear as irregular, angulated filling defects* within the uterine cavity.
- At times, *uterine polyps, leiomyomas, air bubbles* and *blood clots* may masquerade as adhesions.  
Transvaginal USG or saline infusion sonography may help clarify these difficult cases.
- A definitive diagnosis requires hysteroscopy. (Investigation of choice)

**Treatment:**

- Adhesiolysis *via hysteroscopy*.
- Placement of an *intrauterine device* or Pediatric foley's catheter with the bulb filled with 3ml of fluid, to avoid contact between the ends of the adhesions.
- Treatment with *estrogen* to stimulate endometrial growth. (Since estrogen alone can lead to endometrial, cancer. Estrogen and progesterone should be given together).

**Prognosis:**

- Approximately 70-80% of patients with this condition have achieved successful pregnancy. But pregnancy can be complicated by premature labor, placenta accreta, placenta previa and/or PPH.
- Recurrence rate is high.

6. Ans. is c, i.e. CO<sub>2</sub>

7. Ans. is d, i.e. COPD

8. Ans. is d, i.e. Peritonitis

Ref. Williams Gynae 1<sup>st</sup>/ed p 932, COGDT 10<sup>th</sup>/ed p 801-2

#### Important points to remember on laparoscopy:

- CO<sub>2</sub> is currently the insufflation gas of choice for laparoscopy. It fulfills most of the requirements for an ideal insufflation gas, being colorless, noninflammable and rapidly excreted from the circulation.
  - Other alternative is N<sub>2</sub>O : But it is expensive, less soluble in blood and supports combustion.
  - Instrument used for creating pneumoperitoneum is vercess needle.
  - It should be inserted at an angle of 45 degrees to the spine.
  - Flow rate of CO<sub>2</sub> for creating pneumoperitoneum is 200 – 2000 ml/min & pressure between 10 – 15 mm of Hg. In many patients, this correlates with an infusion of 2.5 to 3 litres of gas
- .... Williams Gynae 1<sup>st</sup>/ed p 934

#### Contraindications of laparoscopy

Absolute	Relative
<ul style="list-style-type: none"> <li>• Intestinal obstruction<sup>Q</sup></li> <li>• Generalized peritonitis<sup>Q</sup></li> <li>• Massive hemorrhage<sup>Q</sup></li> <li>• Cancer involving anterior abdominal wall<sup>Q</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Previous periumbilical surgery<sup>Q</sup></li> <li>• Cardiac or pulmonary disease<sup>Q</sup></li> <li>• Shock<sup>Q</sup></li> </ul>

#### Additional factors weighing against performing laparoscopy surgery are :

- Extremes of weight.<sup>Q</sup>
- Intrauterine pregnancy after first or early 2nd trimester.<sup>Q</sup>
- Presence of large mass.<sup>Q</sup> i.e. abdominal tumor, large uterus
- IBD (inflammatory bowel disease)<sup>Q</sup>
- Known severe intraperitoneal adhesions.<sup>Q</sup>
- Umbilical hernia and diaphragmatic hernia.

9. Ans. is a, b and d, i.e. Pap smear; Excision biopsy; and Colposcopy Ref. Dutta Gynae. 5<sup>th</sup>/ed p 257-9; Jeffcoate 7<sup>th</sup>/ed p 410-2  
Cervical erosion (ectopy) is condition where the squamous epithelium of ectocervix is replaced by columnar epithelium of endocervix.

#### Etiology:

Congenital Hormonal	Acquired Infection
<ul style="list-style-type: none"> <li>• During pregnancy</li> <li>• In pill users</li> </ul>	<ul style="list-style-type: none"> <li>• Chronic cervicitis</li> </ul>

#### Symptoms :

- Mostly asymptomatic
- Patient may present with vaginal discharge - Excessive and mucoid in consistency. It may be mucopurulent, offensive and irritant in presence of infection or may be even blood stained due to premenstrual congestion.
- Contact bleeding specially during pregnancy and "pill use" either following coitus or defecation.
- Associated cervicitis may produce *backache, pelvic pain and infertility.*

#### Signs :

- On per speculum examination a bright red area is seen surrounding and extending beyond the external os in the ectocervix, **which is neither tender nor bleeds on touch.**

#### Differential diagnosis :

- Carcinoma cervix<sup>Q</sup>
- Ectropion<sup>Q</sup>
- Tuberculous ulcer<sup>Q</sup>
- Syphilitic and other ulcers of cervix.<sup>Q</sup>

#### Diagnosis:

"All cases should be subjected to cytological examination from the cervical smear to exclude dysplasia or malignancy. In doubtful cases, colposcopy and/or cervical biopsy should be done."  
.... Dutta Gynae 5<sup>th</sup>/ed p 259

"Although a cervical smear may be helpful, the diagnosis and distinction (between ectopy and its differential diagnosis) may not be possible except by colposcopy or biopsy."  
... Jeffcoate 7<sup>th</sup>/ed p 412

In the given question the female is multiparous and is having cervical erosion which bleeds on touch, which may signify early cervical cancer and therefore pap smear/colposcopy/cone biopsy all should be done.

10. Ans. is a, c and d, i.e. LH; Estradiol; and Progesterone

11. Ans. is a, d and e, i.e. Urine LH; Serum estradiol; and BBT

12. Ans. is d, i.e. Hormonal study

Ref. Leon Speroff 8<sup>th</sup>/ed p 1161-4; Dutta Gynae 5<sup>th</sup>/ed p 228

a. LH Surge

*"Evaluation of ovulation is an important part of any female fertility investigation. All of the different methods are useful and no one method is necessarily best. When circumstances require accurate prediction of ovulation as in couples having infrequent intercourse or those who require timely insemination, monitoring urinary LH excretion generally is the most cost-effective and appropriate choice".*

Leon speroff 7<sup>th</sup>/ed p 1036

*"Ovulation predictor kits (LH kits) are noninvasive and widely available, require relatively little time and effort. Their greatest advantage over other methods is the ability to accurately predict when ovulation will occur"*

*"LH ovulation predictor kits are probably the most convenient home monitoring methods of predicting ovulation"*

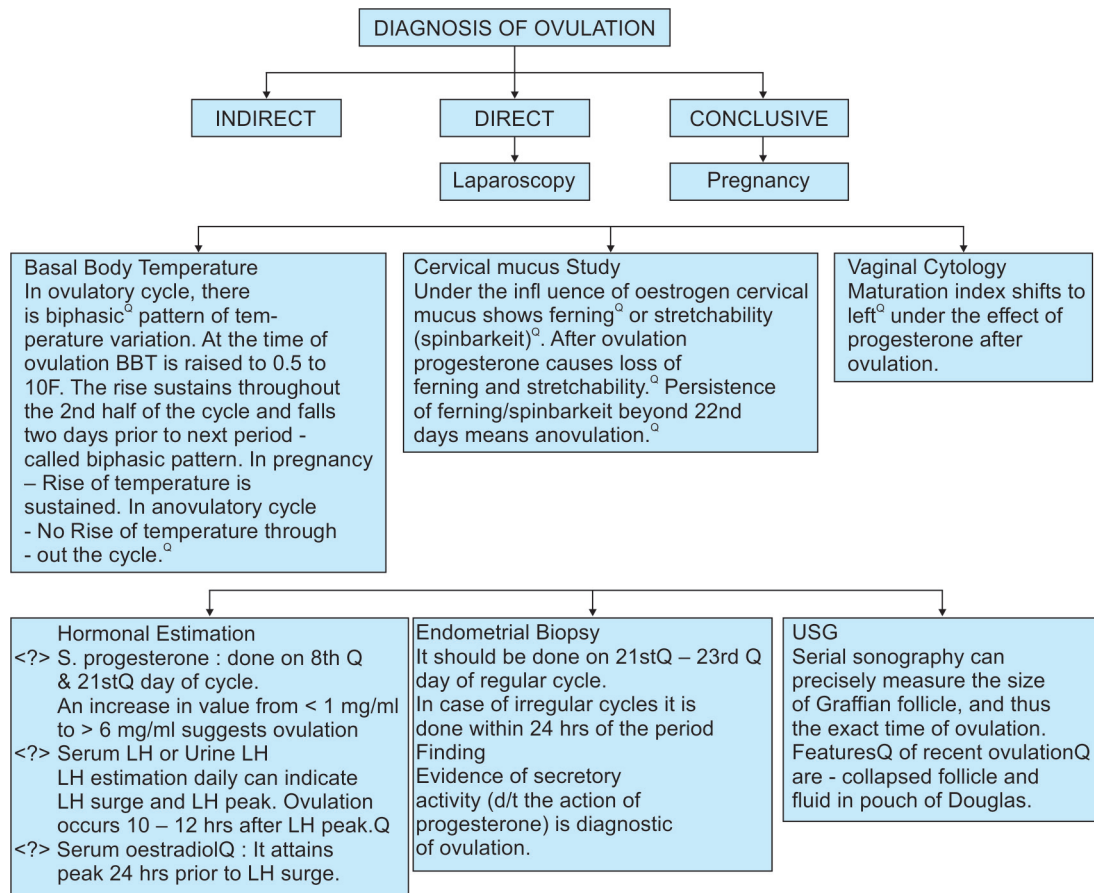
Ref. Cambridge Guide to Infertility management and Assisted reproduction/68

**Note: Ovulation occurs because of LH surge**

Onset of LH surge to ovulation = 36 hours

Onset of LH peak to ovulation = 12 hours

- Preovulatory estradiol levels should reach 200 pg/ml and maintained for 24-48 hrs, then only LH surge begins



b. Serum Progesterone levels

- It is the simplest method to assess ovulation in a female with regular menstruation

Test - Should be performed 1 week before the next menstruation (i.e on Day 21 if menstrual cycle is of 28 days).

If serum progesterone levels on day 21 are <5ng/ml it indicates luteal phase defect.

More than 8-15 ng/ml indicate ovulation

≥ 25 ng/ml indicate pregnancy

13. Ans. is a, i.e. FSH

Ref. Novak 14<sup>th</sup>/ed p 1203-5, Williams Gynae 1<sup>st</sup>/ed p 434; Harrison 17<sup>th</sup>/ed p 223

*"Ovarian reserve refers to the size of the nongrowing or resting, primordial follicle population which presumably determines the number of growing follicles and the quality or reproductive potential of their oocytes."*

... Novak 14<sup>th</sup>/ed p 1203

- Determination of the ovarian reserve is important in the treatment of infertility.
- The ovary is generally thought of as an egg bank from which the woman draws eggs during her reproductive life. While each month when one egg is released by ovulation about one thousand additional eggs are lost by atresia.
- Few if any oocytes are replenished during the reproductive years.
- Thus with advanced maternal age the number of eggs that can be successfully recruited for a possible pregnancy declines.

*In short Ovarian reserve tests evaluate quantity and quality of egg in an individual woman at a particular point of time. The tests for measuring ovarian reserve are :*

Serum day 3 FSH and estradiol levels	Clomiphene citrate challenge test	Serum Inhibin B	TVS
<ul style="list-style-type: none"> <li>• An elevated baseline FSH on day 3 indicates decreased ovarian reserve due to aging of ovaries</li> <li>• FSH &gt; 40 mIU and serum estradiol indicates absence of ovarian follicles.</li> <li>• Serum FSH is the best predictor of ovarian reserve</li> </ul>	<ul style="list-style-type: none"> <li>• This test helps to detect those cases of decreased ovarian reserve which show normal day 3 FSH.</li> <li>• It measures serum FSH &amp; estradiol on day 3 &amp; again on day 10 after administering clomiphene citrate (100 mg) from D5 to D9</li> </ul>	Is produced by ovarian granulosa cells predominantly during the follicular phase of menstrual cycle. In women with decreased ovarian reserve there is decreased Inhibin B.	Assesses atrial follicle number & ovarian size

**Note:** Ideally the levels of estrogen should be decreased in older women but paradoxically it is seen that values of estradiol are raised on day 3. Values of estrogen >80pg/ml are considered abnormal.

- Amongst all the test – **Screening is done by Serum Day 3 FSH.**

*“In general a simple day 3 - FSH measurement is probably adequate as an initial screen. However consideration should be given to performing a (CCT clomiphene citrate in challenge test) in any woman with a borderline FSH level or who is older than 40 Years.”*

... Williams Gynae 1<sup>st</sup>/ed p 434

#### Also know :

Ovarian reserve test should be performed in case of -

- Woman with a smoking history
- Poor response to gonadotropins
- Age > 35 years
- Family history of early menopause
- If there is history of ovarian surgery chemotherapy or irradiation.

#### Extra Edge :

**Recently Mullerian Inhibiting Substance - MIS (also known as Antimullerian Hormone - AMH)** has been investigated as a marker for ovarian reserve and for ovarian responsiveness to stimulation. It is produced by the Granulosa cells of preantral, and small antral follicles and inhibits the initiation of primordial follicle growth. The serum levels of MIS in women with normal cycles declines with age and becomes undetectable by the time of menopause. As the ovarian primordial follicle count decreases, the serum MIS concentration also decreases, making this hormone an ideal candidate for the early detection of ovarian reserve depletion.

AMH test can be done on any day of a woman's cycle unlike FSH level test, which has to be done on day 2 or 3 of the menstrual cycle.

Since AMH is produced only in small ovarian follicles, blood levels of this substance have been used to measure the size of the pool of growing follicles in women.

- Research shows that the size of the pool of growing follicles is heavily influenced by the size of the pool of remaining primordial follicles. Therefore, AMH blood levels are thought to reflect 'ovarian reserve'
- With increasing female age, the size of their pool of remaining microscopic follicles decreases. So does, their blood AMH levels.

AMH levels (ng/ml)	Interpretation
4.0–6.8	Optimal fertility
2.2–4.0	Satisfactory fertility
0.3–2.2	Low fertility
<0.3	Very low fertility
>6.8	High levels (PCOS and granulosa cell tumor)

14. **Ans. is d, i.e. Urethrovesical angle**

Goniometer is used to measure urethrovesical angle.

15. **Ans. is d, i.e. Prominent posterior enhancement**

Ref. *Transvaginal Ultrasound by Melvin G. Dodson 1<sup>st</sup>/ed p 86*

**Friends this is a very important Question**

**IMPORTANT :** I have summarized here the appearances of endometrium on transvaginal ultrasound during different stages of normal menstrual cycle.

**a. Early menses (days 1–4)**

Hypoechoic central echo with a thick hyperechoic endometrial echo and posterior enhancement similar to the luteal phase.

**b. Late menses (days 3–7)**

Single hyperechoic thin lines (central endometrial echo)  
Hypoechoic halo  
Hypoechoic central echo representing blood is gone  
Anterior posterior thickness of the entire endometrial echo complex is only 1 – 3 mm.

**c. Early follicular phase (days 5–9)**

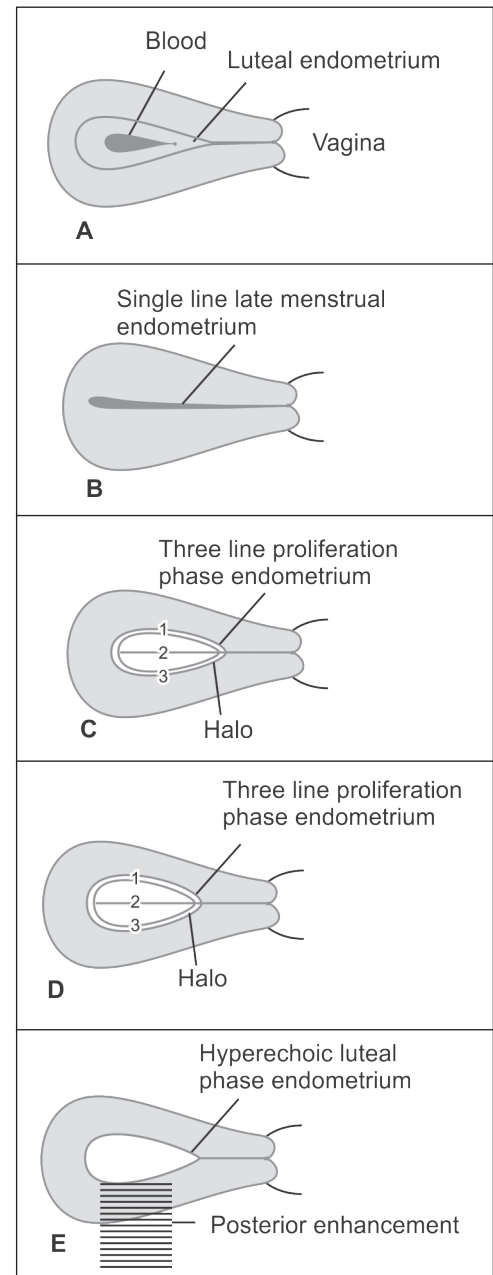
Halo present  
Relatively thin anterior posterior endometrial thickness (< 6 mm)  
No posterior enhancement<sup>o</sup>  
Three line sign.<sup>o</sup>

**d. Late follicular phase (days 10–14)**

As above with thicker endometrial echo complex (> 6 mm).

**e. Luteal phase**

Maximum endometrial thickness  
Hyperechoic endometrium  
Loss of halo<sup>o</sup>  
Loss of three line sign<sup>o</sup>  
Prominent posterior enhancement<sup>o</sup>



16. **Ans. is b, i.e. Endometrial biopsy**

Ref. *Shaw 14<sup>th</sup>/ed p 30-1; Dutta Gynae 5<sup>th</sup>/ed p 230; Novak 15<sup>th</sup>/ed p 1161*

In luteal phase defect (LPD) as the name suggests there is decreased progesterone secretion which leads to premenstrual spotting and recurrent 1st trimester abortions

Best method of diagnosing - LPD is endometrial biopsy done on day 21 day 23 of cycle (a lag of 48 hrs or more between the chronological dating and histological dating is diagnostic of LPD).

It can also be diagnosed by serum progesterone levels- If serum progesterone done on day 21 of the cycle is < 5ng/ml-it indicates LPD.

17. **Ans. is b, i.e. VVF repair**

Ref: Shaw 14<sup>th</sup>/ed p 168

Surgery	Done in
1. Kelly stitch/Boney's Test/ Marshall Marchetti Krantz Surgery	Stress Urinary Incontinence
2. Chassar Moir Technique/Latzko technique/layer technique	VVF Repair
3. Boari Flap Technique	Uretrovaginal Fistula repair
4. Purandare Sling/Fothergill's Repair/Manchester Repair/Ward Mayo Hysterectomy/ Lefort's Colpocleisis	Prolapse Uterus
5. Strassman Unification Surgery	Bicornuate/Didelphic uterus (Indication for operation , if bicornuate or didelphic uterus lead to >3 Abortion)
6. Hysteroscopic Septal Resection (M/c done), Jones/Thompkins/ Williams metroplasty	Septate Uterus
7. McIndoe Vaginoplasty	MRKH Syndrome/Vaginal agenesis (Best time to perform this surgery is just before/just after marriage)
8. Mc Donald/Shirodkar Cerclage	Incompetent Internal os
9. Baldy Webster operation, Modified Gilliams operation, Laparoscopic ventrosuspension	Retroversion of the uterus
10. Haultains Operation(via abdominal route), Spinellis operation (via vaginal route)	Inversion of uterus

18. **Ans. is c, i.e. other visceral structures can be easily visualized**

**Vaginal Hysterectomy**

Advantages	Disadvantages
<ul style="list-style-type: none"> <li>• Can be done in obese patients</li> <li>• Less postoperative complications</li> <li>• Less morbidity and mortality</li> <li>• Less postoperative pain</li> <li>• Less hospital stay</li> <li>• No abdominal scar</li> <li>• Early resumption of day to day activities</li> </ul>	<ul style="list-style-type: none"> <li>• Exploration of abdominal organs and pelvic organs cannot be done</li> <li>• Tubo-ovarian pathologies cannot be simultaneously dealt</li> <li>• Difficult to perform if uterus is &gt;12 weeks size and if pelvic adhesions are present</li> <li>• Concurrent surgical procedures cannot be done</li> </ul>

19. **Ans. is b, i.e. Wertheims hysterectomy**

Ref. COGDT 10<sup>th</sup>/ed p 779; Dutta Gynae 5<sup>th</sup>/ed p 408

Terminology	Structures Removed
• Total hysterectomy /Simple Hysterectomy	Whole uterus+ whole of cervix (TAH; Type I hysterectomy)
• Pan hysterectomy	
• Modified radical hysterectomy/Wertheim's hysterectomy (Type II hysterectomy)	TAH+BSO+ medial half of cardinal ligaments + medial half of uterosacral ligaments + only enlarged pelvic lymph nodes + uterine artery below the origin of uterine artery + 1 cm vagina
• Radical/Modified Wertheims hysterectomy	TAH+BSO+ whole of cardinal and uterosacral ligaments and +com (Type III) + Complete pelvic lymph node dissection +upper third of vagina + whole of uterine artery
• Extended Radical hysterectomy (Type IV)	Radical hysterectomy + 3/4th of vagina+ Periureteral tissue + Superior vesical artery.

- So now common sense tells us that, since in Wertheims hysterectomy, we are removing the medial half of cardinal ligament, there are maximum chances of injuring the ureter and furthermore wertheims hysterectomy is done in case of cancers and a lot of adhesions are present during surgery which increases the chances of ureteric injury
- Ureters are very prone to injury during cutting of medial half of cardinal ligaments. But I am sure you need references also

"About 75% of ureteral injuries result from Gynecological operations and 75% of them occur following abdominal Gynecological procedures" ....Dutta 5<sup>th</sup>/ed p 408

- From the above lines it is clear that, in abdominal operations, ureters are more prone to injury than in vaginal operations (ruling out Options "c" and "d")  
"The reported incidence of ureteral injury during Gynecologic procedures ranges from about 0.5% in simple hysterectomies for benign disease upto 1.6% for laparoscopic cases and to as high as 30% for some older series of Wertheim's Radical Hysterectomies."  
..... CGDT 10<sup>th</sup>/ed p 779

#### Also know

Piver Rutledge classification of types of hysterectomy

Type I	Total Abdominal Hysterectomy.
Type II	Wertheims hysterectomy
Type III	Radical hysterectomy/ Meigs hysterectomy
Type IV	Extended radical hysterectomy
Type V	Complete pelvic extenteration

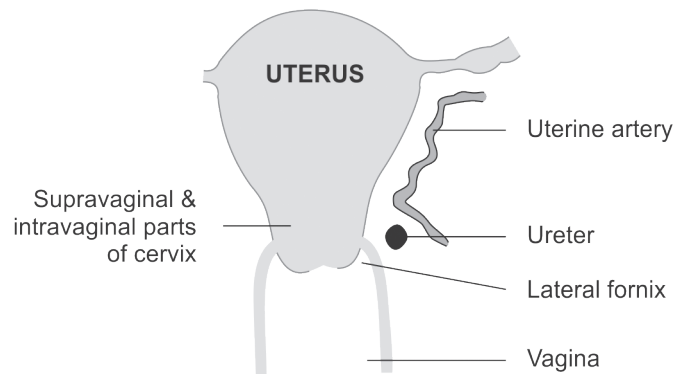


Figure showing the relative position of ureter in relation to uterus and uterine artery

#### 20. Ans. is b i.e. DUB

Ref. Shaw 15<sup>th</sup>/ed pg -305; Bijoy Sree Sen Gupta 2<sup>nd</sup>/ed p 151 - 152; Williams Gynae 1<sup>st</sup>/ed p 188

**Transcervical endometrial resection (Hysteroscopic endometrial ablation) is a technique for management of DUB.**

**Aim** of the procedure is to produce a therapeutic Asherman's syndrome and produce amenorrhea.

It destroys the endometrium → formation of synchea → Asherman syndrome → amenorrhea.

It is essential to destroy endometrial functionalis and basalis as well as 3mm of myometrial depth.

**Procedure :** After appropriate inspection of the landmarks and endometrial cavity, a wire loop electrode is used to resect several strips of endomyometrium, to a depth of 4mm. Resected tissue is used for pathologic examination and documentation of the absence of cellular atypia. After a few strips are resected initially from the posterior uterine wall, resection of almost all the remaining surface with loop electrode by vaporization is performed. The procedure should be performed soon after menstruation or the woman should be given progesterone, danazol or GnRH to suppress the endometrium.

**Result :** Short term and long term studies show amenorrhea rates of 20–50%, overall improved bleeding patterns (including amenorrhea) in 85–95%, with failure rates of 5–10% which requires additional surgery i.e. hysterectomy.

#### Extra Edge:

- A COG recommends endometrial sampling prior to ablation surgery. Women with endometrial hyperplasia or cancer should not undergo ablation.
- **Absolute contraindications for endometrial ablation :**
  - Genital tract malignancy
  - Women wishing to preserve their fertility
  - Pregnancy
  - Expectation of amenorrhea
  - Acute pelvic infection
  - Prior uterine surgery - Classical cesarean delivery, transmural myomectomy
  - Uterine size > 12wks

... Williamss Gynae 1<sup>st</sup>/ed p 188

#### 21. Ans. is d, i.e. Case with severe dysplasia or CIS lesion

Ref. Dutta Gynae 6<sup>th</sup>/ed p 591

#### Cryosurgery

This is a procedure whereby destruction of the tissue is effective by freezing.

#### Indications

- Cervical ectopy
- Benign cervical lesions— such as CIN (ideal for minor degree and localized CIN), condyloma acuminata, leukoplakia, etc.
- Condyloma acuminata of vulva and VIN diagnosed colposcopically and not more than 2 cm in size.
- VAIN, condyloma acuminata or vault granulation tissue following hysterectomy.
- As a palliative measure to arrest bleeding in carcinoma cervix or large fungating recurrent vulvar carcinoma.



**Principle:** It consists of a 'probe', the tip of which is cooled to a temperature below freezing point ( $-60^{\circ}\text{C}$ ). **Freezing produces cellular dehydration by crystallization of intracellular water and ultimately death of cells.** This is effective by rapid expansion of gas which is passed through it. Carbon dioxide is widely used while nitrous oxide and liquid nitrogen are also used.

The application to the cervix freezes the tissue to a depth of about 3 mm. Healing is complete in 6 to 10 weeks.

**22. Ans. is c, i.e. It is less accurate than saline infusion sonography (SIS)**

As discussed in Q.5 and 6, abnormal uterine bleeding is an indication for performing hysteroscopy and normal saline can be used as a distention media (i.e. both options a and b are correct).

As for as results of hysteroscopy are concerned, they are comparable with saline infusion sonography (SIS) (i.e. option c is in correct)

A positive hysteroscopy is more reliable and has moral significance than a negative one, hence option d is also correct.

**23. Ans. is a, i.e. Cystoscopy (Read below)**

New this question can be done with common sense as to minimize ureteric damage, all the options given in the questions hold good except cystoscopy. What is the role of visualizing bladder prevent ureteric surgery. Rather if it would have been IVP, then it would be correct.

**24. Ans. is d, i.e. for staging of ovarian malignancy**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 107*

**Indication of Rectal examination**

- Children or in adult virgins
- Painful vaginal examination
- Carcinoma cervix – to note the parametrial involvement (base of the broad ligament and the uterosacral ligament can only be felt rectally) or involvement of the rectum
- To corroborate the findings felt in the pouch of Douglas by bimanual vaginal examination
- Atresia (agenesis) of vagina
- Patients having rectal symptoms
- To diagnose rectocele and differentiate it from enterocele.

**25. Ans. is c, i.e. Postoperative vaginal discharge is also much less**

*Ref. read below*

After cryosurgery there will be profuse vaginal discharge for about 2–3 weeks

**26. Ans. is c, i.e. Transvaginal sonography (TVS) (in gynecology lithotomy with full bladder.**

As the position described in the question are correct with respect to the surgery except for TVS.

In TVS, the position is dorsal with legs drawn up and not lithotomy Full bladder may or may not be required.

**27. Ans. is d, i.e. previous incomplete laparoscopy**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 615*

**Contraindications of Laparoscopy**

- Severe cardiopulmonary disease
- Patient hemodynamically unstable
- Generalized peritonitis
- Significant hemoperitoneum
- Intestinal obstruction
- Extensive peritoneal adhesion
- Large pelvic tumor
- Pregnancy > 16 weeks
- Advanced malignancy
- Anticoagulation therapy.

*Note:* previous incomplete laparoscopy is an indication for performing a repeat laparoscopy and not a contraindication.

**28. Ans. is c, i.e. Laser hysteroscopy for presacral neurectomy**

Laser hysteroscopy is used for endometrial ablation and septum resection. Presacral neurectomy is done by loser laparoscopy.

# CHAPTER

# 16

## Miscellaneous Question Bank

### QUESTIONS

- CA 125 is elevated in all except : (AIIMS June 98)
  - Tuberculosis
  - Endometriosis
  - Ovarian tumor
  - Polycystic ovarian disease
- A 21-year-old unmarried woman has premenstrual fullness of breast and pain, the likely diagnosis is: (AIIMS June 98)
  - Galactocele
  - Fibroadenoma
  - Fibroadenosis
  - Mastitis
- Corpus luteum cyst occurs due to: (AIIMS Nov 99)
  - HCG
  - Estrogen
  - HPL
  - Progesterone
- In those mammals which are seasonal breeder, the females are receptive only once in a year ; the cycle is termed as: (AIIMS May 06)
  - Follicular
  - Menstrual
  - Estrous
  - Luteal
- Which of the following is true regarding precocious puberty? (AI 94)
  - Sexual maturity is attained early
  - Mental function is increased
  - No reproductive function
  - Body proportions are enlarged
- Menstruation is defined as precocious if it starts before the child reaches the age of: (AIIMS Nov 04)
  - 8 years
  - 14 years
  - 10 years
  - 20 years
- Primary peritonitis is more common in females because: (AI 01)
  - Ostia of fallopian tubes communicate with abdominal cavity
  - Peritoneum overlies the uterus
  - Rupture of functional ovarian cysts
  - None of the above
- Post menopausal estrogen production is due to :
  - Peripheral aromatization of androstenedione
  - Adrenal - direct production (PGI June 00)
  - Ovarian tumor
  - Ovary testosterone secretion
- 40 years female, mass in pelvis detected clinically, following investigations should be done except :
  - CT
  - Pap smear
  - Laparoscopy (PGI 00)
  - USG
- A female presents to gynecological OPD with complain of cyclical pain, dyspareunia and infertility. The best investigation to establish the diagnosis would be- (AIIMS Nov 2012)
  - TVS
  - Diagnostic laparoscopy
  - Hormonal study
  - Aspirate from the pouch of douglas

### NEW PATTERN QUESTIONS

- These are the names with associated conditions – match the following:
 

a. Henry Turner	1. Repair of bladder fistula
b. John Tanner	2. Primary amenorrhoea with delayed secondary sex characters
c. Marion Sims	3. Surgery for carcinoma cervix
d. Joe Meige	4. Staging of puberty changes
- Causes of vulval pain are due to all except:
  - Neuralgia of the genitofemoral nerve
  - Herpes
  - Vulval vestibulitis syndrome
  - Lichen sclerosus
- Match the names associated in the treatment of stress incontinence:
 

a. Osteitis pubis	1. Raj and Stamey
b. Rectus sheath	2. Marshall-Marchetti Krantz
c. Cystoscopy	3. Aldridge sling
d. Cystourethroplasty	4. Howard Kelly
- Match the following appropriately:
 

a. Asherman's syndrome	1. Chronic pelvic pain
b. Rokitansky-Küster-Hauser syndrome	2. Secondary amenorrhoea
c. Toxic shock syndrome	3. Primary amenorrhoea
d. Ovarian remnant syndrome	4. Menstruation and use of tampons

## ANSWERS

## 1. Ans. is d, i.e. Polycystic ovarian disease (PCOD)

Ref. Novak Gynecology 14<sup>th</sup>/ed pp 1466, 1146, 1147;  
William's Gynae 1<sup>st</sup>/ed pp 232, 210.  
Textbook of Gynae Sheila balakrishnan p 185

## CA-125

- This is a non-specific tumor marker
- CA-125 is a glycoprotein which is normally not produced by ovarian epithelium but may be produced by both malignant and benign epithelial ovarian tumors.
- Cut off level of CA-125 is < 35 U/mL.
- Levels of CA 125 can be raised in

↑ CA-125	
Neoplastic conditions	Non-neoplastic/Benign conditions
<b>Gynecological</b> <ul style="list-style-type: none"> <li>• Ovarian cancer (nonmucinous)</li> <li>• Endometrial cancer</li> <li>• Tubal cancer</li> </ul> <b>Non-gynecological</b> <ul style="list-style-type: none"> <li>• Lung cancer</li> <li>• Breast cancer</li> <li>• Ca Pancreas</li> <li>• Colon cancer</li> </ul>	<ul style="list-style-type: none"> <li>• Endometriosis</li> <li>• Peritoneal inflammation, including PID</li> <li>• Tuberculosis</li> <li>• Hemorrhagic ovarian cysts</li> <li>• Liver disease</li> <li>• Leiomyoma</li> <li>• Pregnancy</li> <li>• Menstruation</li> </ul> <p style="text-align: right;">physiological</p>

## 2. Ans. is b, i.e. Fibroadenosis

Ref. 7<sup>th</sup>/ed p 186-8

An unmarried 21 year old female is complaining of premenstrual fullness of breast and pain : lets rule out some options.

## Option "a" Galactocele

- Presents as a solitary sub areolar cyst and always dates from lactation. It contains milk.
- Since, our patient is unmarried, it is ruled out.

## Option "c" Fibroadenoma

- Presents as a freely mobile lump (breast mouse) without any pain. It occurs in 15–25 yrs. old female (age is consistent with patient) but then fibroadenoma does not cause pain.

## Option "d" Mastitis

- Occurs mainly in lactating female and pain is not premenstrual but constant in nature.

## Option "b" Fibroadenosis

- It is usually seen in women of 4th and 5th decade of life (also not rare in young females) with complain of an intermittent mammary discomfort or an area of lumpiness or nodularity in the breast.
- The changes are generally bilateral. Pain is cyclical with a premenstrual exacerbation.
- Most likely the girl in question is suffering from fibroadenosis though her age is not consistent with the fibroadenosis.

## 3. Ans. is a, i.e. HCG

Ref. Shaw 15<sup>th</sup>/ed p 369

## Lutein cysts of ovary

Granulosa lutein cyst	Theca lutein cyst
<ul style="list-style-type: none"> <li>• Functional, non neoplastic enlargement of the ovary.</li> <li>• Persistent corpus luteum cyst may cause local pain, tenderness or delayed menstruation</li> <li>• Cysts are often palpable clinically</li> <li>• Usually resolve spontaneously</li> </ul>	<ul style="list-style-type: none"> <li>• They are associated with trophoblastic disease<sup>o</sup>, chorionic gonadotrophin therapy (HCG)<sup>o</sup> &amp; clomiphene therapy<sup>o</sup></li> <li>• They are bilateral and filled with straw coloured fluid.</li> <li>• They resolve spontaneously after elimination of the H mole, therapeutic curettage, destruction of choriocarcinoma or discontinuation of gonadotropin therapy</li> </ul>

## Also know:

## Characteristic features of functional cysts of ovary :

- Size < 7cm
- Unilocular
- Filled with clear fluid
- Regress after some time

4. **Ans. is b, i.e. Estrous**

Ref. Taber's Dictionary 19<sup>th</sup>/ed p 714

**Estrous:** It is cyclical period of sexual activity in nonhuman female mammals, marked by congestion of and secretion by the uterine mucosa, proliferation of vaginal epithelium, swelling of the vulva, ovulation, and acceptance of the male by the female. During estrus, the animal is said to be "in heat".

**Also Know:**

**Estrus cycle** – The sequence from the beginning of one estrus period to the beginning of the next.

- It includes :
- Proestrus
  - Estrus
  - Metestrus followed by
  - Diestrus (period of quiescence).

5. **Ans. is a, i.e. Sexual maturity is attained early**

Ref. Shaw 15<sup>th</sup>/ed p 56

6. **Ans. is b, i.e. 10 years**

Ref. Shaw 15<sup>th</sup>/ed p 56

**Precocious puberty** is the appearance of appropriate secondary sexual characters before the age of 8 years and occurrence of menstruation before 10 years of chronological age.

**Also know :** *Delayed puberty* : is considered delayed when the secondary sexual characters do not appear by the age of 14, and menarche is not established by 16 years of age.

7. **Ans. is a, i.e. Ostia of fallopian tubes communicate with abdominal cavity**

Ref. Sabiston 16<sup>th</sup>/ed p 777

Primary peritonitis refers to inflammation of peritoneal cavity without a documented source of contamination.

*"It occurs more commonly in children than adults and in women than in men. The later distribution is explained by entry of organisms into the peritoneal cavity through the fallopian tubes."*

8. **Ans. is a, i.e. Peripheral aromatization of androstenedione**

Ref. Shaw 15<sup>th</sup>/ed p 62

- In menopause estrogen levels decrease by 66%.
- **Main source of estrogen production postmenopausally is by peripheral aromatization of androstenedione.**
- Main estrogen after menopause - oestrone.

Also know :

- *Main estrogen during reproductive year is oestradiol.<sup>o</sup>*
- *Main estrogen in pregnancy is oestriol.<sup>o</sup>*

9. **Ans. is b, i.e. Laparoscopy**

Ref. Novak 15<sup>th</sup>/ed p 410-8

*Friends, before knowing the investigations which should be done in a 40 year old female with pelvic mass detected clinically. It is important to know the D/D of pelvic mass in woman of reproductive age.*

**Conditions diagnosed as a pelvic mass in women of reproductive age :**

- |  |  |
|--|--|
| • Full urinary bladder                     | • Urachal cyst   |
| • Sharply anteflexed or retroflexed uterus | • Pregnancy (with or without concomitant leiomyomas) / ectopic pregnancy |
| • Ovarian or adnexal masses                | • Matted bowel loops & omentum   |
| • Functional cysts                         | • Peritoneal cyst  |
| • Inflammatory masses :                    | • Stool in sigmoid colon   |
| – Tubo-ovarian masses                      | • Neoplastic tumors :  |
| – Diverticular abscess                     | – Benign   |
| – Appendiceal abscess                      | – Malignancy   |
| • Paraovarian or paratubal cysts           |  |
| • Intraligamentous myomas                  |  |

**Less common conditions that must be excluded:**

- Pelvic kidney
- Carcinoma of the colon, rectum and appendix
- Carcinoma of the fallopian tube
- Retroperitoneal tumors (anterior sacral meningocele)
- Uterine sarcoma or other malignant tumors.

**Investigations to done :**

- Complete pelvic examination including rectovaginal examination
- Lab investigation - complete hemogram, ESR, test of stool or occult blood
- **Pap smear**
- Urine pregnancy test

- Endometrial sampling with endometrial biopsy or D and C
- If urinary symptoms are prominent : studies of urinary tract may be necessary
- **Pelvic ultrasonography**
- Hysteroscopy (for intrauterine pathology)
- HSG
- MRI (for uterine anomalies)
- **CT Scan.**

**10. Ans is b i.e. Diagnostic laparoscopy**

*Ref. Williams Gynae 2<sup>nd</sup>/ed p 286, 287, 290, 291*

Clinical features of infertility, dyspareunia, and cyclical pain (i.e. dysmenorrhea) are highly suggestive of endometriosis and the investigation of choice/gold standard investigation for the diagnosis of endometriosis is laparoscopy

Friends, if in the same scenario – next or first investigation was asked – Answer would have been TVS

TVS is the mainstay for evaluating symptoms associated with endometriosis. It is accurate in detecting endometriosis and aids exclusion of other causes of pain. (Endometriosis can be diagnosed by TVS with adequate sensitivity in most settings, if they are 20 mm in diameter or greater), Since TVS is non-invasive wherever a patient comes with such symptoms, it is the first investigation done; however, IOC is always laparoscopy however, imaging of superficial endometriosis or endometriotic adhesions is inadequate.

**11. Ans. is a = 2; b = 4; c = 1; d = 3**

**12. Ans. is d, i.e. Lichen sclerosis**

*Ref. Dutta Gynae 6<sup>th</sup>/ed p 264*

**Vulvar pain syndrome**

Vulvar pain sensation may be burning, stinging or irritation. It may be due to several reasons:

- Aphthous ulcer
- Vulval dermatoses
- Herpes genitalis
- Pudendal or genitofemoral nerve neuralgia
- Vulvodynia (burning vulva syndrome)
- Vulvar vestibulitis syndrome
- Referred pain from urethral or vagina
- Psychological.



**Vulvodynia** is a severely painful socially debilitating disease where infection, invasive disease or inflammation have been excluded. It is characterized by burning sensation over the vulva (burning vulva syndrome). It is often seen in perimenopausal or postmenopausal women. Exact etiology is not known. Clinical examination does not reveal any abnormality in many cases. Treatment is unsatisfactory. Tricyclic antidepressant (amitriptyline) is found helpful. A dose of 60 mg/day for 3–6 months is given. Gabapentin is also beneficial. Psychosexual counseling and behavior therapy are needed for some cases. Surgery is contraindicated.

**13. Ans. is a = 2; b = 3; c = 1; d = 4**

**14. Ans. is a = 2; b = 3; c = 4; d = 1**

# Latest Papers

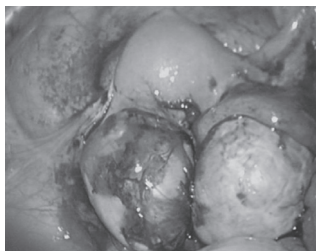
## AIIMS NOVEMBER 2015

1. Which of these is not a noncontraceptive use of levonorgestrel?

- a. Endometriosis
- b. PreMenstrual Tension
- c. Complex endometrial hyperplasia
- d. Emergency contraception

2. A 28-year-old female patient presented with lower abdominal pain along with dysmenorrhea. The following finding was seen on laparoscopic examination. What is the likely diagnosis? (Color Fig. 1)

- a. Krukenberg tumor
- b. Polycystic ovaries
- c. Endometriosis
- d. Cystadenoma of ovary



3. Which of the following statements is true about Swyer syndrome?

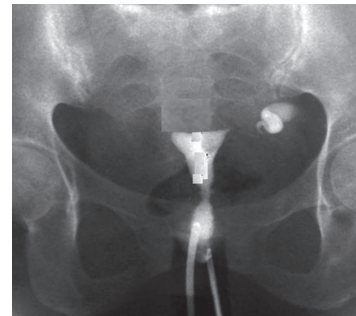
- a. Can be fertile with surrogacy
- b. Can be fertile with ovum donation
- c. Presents with primary fertility
- d. Gonadectomy is indicated for all patients

4. Which of these is seen in Asherman syndrome:

- a. Oligomenorrhea
- b. Hypomenorrhea
- c. Metromenorrhagia
- d. Polymenorrhea

5. HSG image below shows: (Color Fig. 37)

- a. Endometrial polyp
- b. Genital TB
- c. Fibroid uterus
- d. Asherman syndrome



6. What is the most likely cause for beaded appearance of fallopian tubes with clubbed ends of fimbriae on HSG?

- a. Genital Tuberculosis
- b. Chlamydia
- c. Nisseria Gonorrhoea
- d. Endometriosis

7. All of these can be used for postcoital contraception except:

- a. Desogestrol
- b. Copper-T
- c. Levonorgestrol
- d. OCP

8. Which of these is diagnostic of menopause?

- a. Serum FSH > 40
- b. Serum LH > 20
- c. Serum FSH < 40
- d. Serum estradiol < 30

9. What is the first sign of puberty in a girl?

- a. Thelarche
- b. Menarche
- c. Adrenarche
- d. Pubarche

10. Ulipristal acetate is a/an:

- a. GnRH agonist
- b. Androgen antagonist
- c. Selective estrogen receptor modulator
- d. Selective progesterone receptor modulator

## EXPLANATIONS

### 1. Ans. is b i.e. PreMenstrual Tension

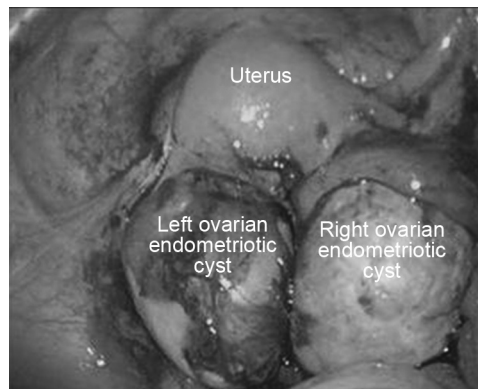
See Q. 52 of chapter 10 for Explanation

Ref. Williams Obstetrics 24/e p701

### 2. Ans. is c i.e. Endometriosis

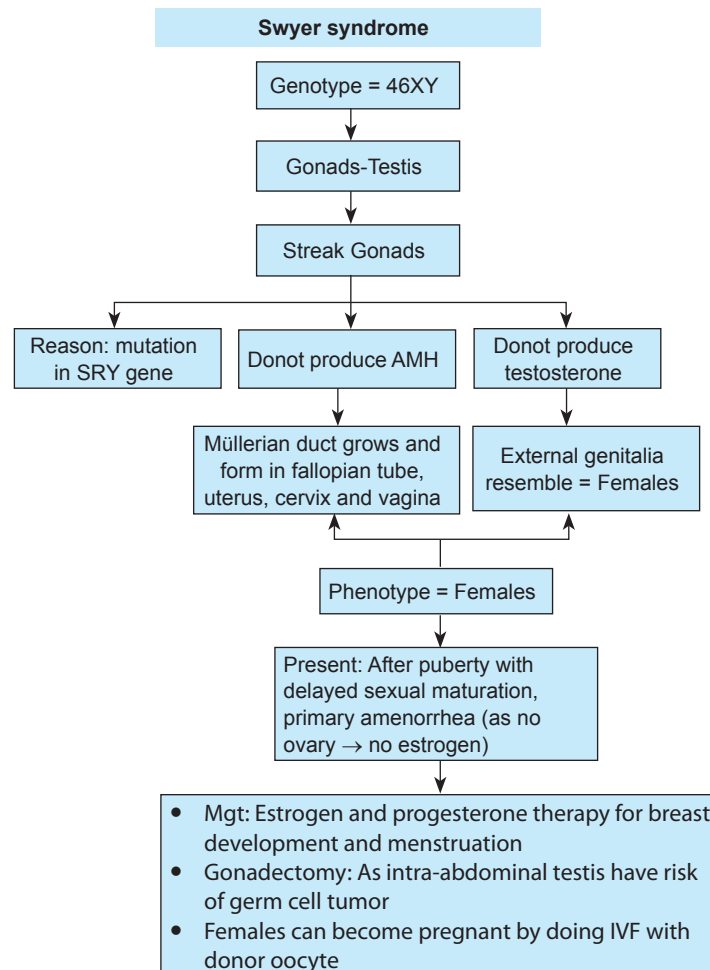
As seen in the figure, the cysts are showing blue gray color. It is chocolate cyst seen in endometriosis.

Ref. Shaw's Textbook of Gynecology 15/e p471



### 3. Ans. is b i.e. Can be fertile with ovum donation

Ref. Shaw's Textbook of Gynecology 15/e p145



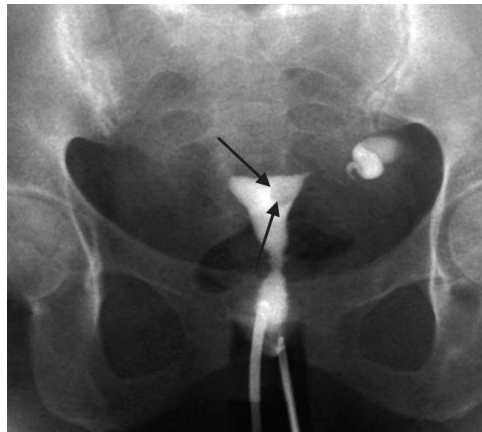
**4. Ans. is b i.e. Hypomenorrhea**

Repeat

*Ref. Shaw's Textbook of Gynecology 15/e p250***5. Ans. is a i.e. Endometrial polyp***Ref. Shaw's Textbook of Gynecology 15/e p103*

The HSG shows a filling defect, characteristically seen in Endometrial polyps. Polyps may be seen as pedunculated or sessile-filling defects within the uterine cavity. This is not a preferred method for evaluation compared with the other modalities.

Although not always necessary for a diagnosis, polyps are well characterized on sonohysterography and appear as echogenic, smooth, intracavitary masses outlined by the fluid. The typical appearance of an endometrial polyp at sonohysterography is as a well-defined, homogenous, polypoid lesion that is isoechoic to the endometrium with preservation of the endometrial-myometrial interface. There is usually a well-defined vascular pedicle within the stalk.

**6. Ans. is a i.e. Genital Tuberculosis***Ref. Shaw's Textbook of Gynaecology*

As discussed in chapter on PID of the book beaded appearance of the tube signifies TB of the genital tract.

**7. Ans. is a i.e. Desogestrol***Ref. Shaw's Textbook of Gynecology 15/e p471*

See chapter 10 for details

**8. Ans. is a i.e. Serum FSH > 40***Ref. Shaw's Textbook of Gynecology 15/e p62***Diagnostic Criteria for Menopause**

- Estrogen (E2) low at 10–20 pg/ml
- Estrone (E1) – 30–70 pg/ml
- E2/E1 < 1
- Urine FSH > 40 IU/L

**9. Ans. is a i.e. Thelarche***Ref. Ghai essential pediatrics 8/e p531-535*

The first sign of puberty in girls is Growth spurt. The first visible sign of puberty in girls is: Thelarche (appearance of breast budding)

**10. Ans. is d i.e. Selective progesterone receptor modulator***Ref. Harrison's Principles of Internal medicine 19/e p2391*

Ulipristal acetate (trade name EllaOne in the European Union, Ella in the US for contraception, and Esmya for uterine fibroid) is a selective progesterone receptor modulator (SPRM).

**1. Pharmacodynamics**

As an SPRM, ulipristal acetate has partial agonistic as well as antagonistic effects on the progesterone receptor. It also binds to the glucocorticoid receptor, but is only a weak antiglucocorticoid relative to mifepristone, and has no relevant affinity to the estrogen, androgen and mineralocorticoid receptors. Phase II clinical trials suggest that the mechanism might consist of blocking or delaying ovulation and of delaying the maturation of the endometrium.

**2. Medical Uses**

- Emergency contraception: For emergency contraception, a 30 mg tablet is used within 120 hours (5 days) after an unprotected intercourse or contraceptive failure. It has been shown to prevent about 60% of expected pregnancies, and prevents more pregnancies than emergency contraception with levonorgestrel.
- Treatment of uterine fibroids: Ulipristal acetate is used for preoperative treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age in a daily dose of a 5 mg tablet. Treatment of uterine fibroids with ulipristal acetate for 13 weeks effectively controlled excessive bleeding due to uterine fibroids and reduced the size of the fibroids.



**3. Interactions**

Ulipristal acetate is metabolized by CYP3A4 in vitro. Ulipristal acetate is likely to interact with substrates of CYP3A4, like rifampicin, phenytoin, St John's wort, carbamazepine or ritonavir. Therefore, concomitant use with these agents is not recommended. It might also interact with hormonal contraceptives and progestogens such as levonorgestrel and other substrates of the progesterone receptor, as well as with glucocorticoids.

**4. Adverse Effects**

Common side effects include abdominal pain and temporary menstrual irregularity or disruption. Headache and nausea were observed under long-term administration (12 weeks), but not after a single dose.

**5. Contraindications**

Ulipristal acetate should not be taken by women with severe liver diseases because of its CYP-mediated metabolism. It has not been studied in women under the age of 18.

Pregnancy: Unlike levonorgestrel, and like mifepristone, ulipristal acetate is embryotoxic in animal studies. Before taking the drug, a pregnancy must be excluded.

## AIIMS MAY 2015

1. **A 18-year-old girl presented to the gynecology OPD with amenorhea. On examination she was found to have Tanner's Stage V breasts and no pubic and axillary hairs. Ultrasound revealed absent uterus and nondeveloped gonads. What is the likely diagnosis?**
  - a. Androgen insensitivity Syndrome
  - b. Turner's syndrome
  - c. Cryptomenorrhea
  - d. Mayer Rokitansky kuster hauser syndrome
2. **A lady underwent vaginal hysterectomy for Carcinoma cervix. Following the surgery after her urethral catheter was removed, she complained of urinary incontinence. On examination she has normal voiding as well as continuous incontinence. Methylene blue dye was instilled in her bladder through her urethra and she was given oral Phenazopyridine dye. After some time her pads were checked and it showed yellow staining at the top most pad, while the middle or bottom pads were unstained. She is likely to have:**
  - a. Ureterovaginal fistula
  - b. Vesicovaginal fistula
  - c. Urethrovaginal fistula
  - d. Vesicouterine fistula
3. **Which of these is not a support of the uterus?**
  - a. Urogenital diaphragm
  - b. Pelvic diaphragm
  - c. Perineal body
  - d. Rectovaginal septum
4. **A 10-year-old girl presents with a mass in lower abdomen involving umbilical and the hypogastrium. On examination it is cystic and mobile and the examiner is unable to insinuate fingers between the mass and the pelvic bone. What is the likely diagnosis?**
  - a. Duplication of small intestine
  - b. Mesenteric cyst
  - c. Omental cyst
  - d. Ovarian cyst
5. **A lady with abdominal mass was investigated. On surgery, she was found to have bilateral ovarian masses with smooth surface. On microscopy they revealed mucin secreting cells with signet ring shapes. Diagnosis?**
  - a. Dysgerminoma
  - b. Krukenberg tumor
  - c. Mucinous adenocarcinoma of the ovaries
  - d. Dermoid cyst
6. **Drug not given in PCOD in a 30-year-old lady with infertility?**
  - a. Tamoxifen
  - b. Clomiphene
  - c. Oral contraceptive
  - d. Spironolactone
7. **A 32-year-old P2L2 lady comes five days after unprotected sexual intercourse. What will be your advice for contraception in this lady?**
  - a. Levonorgestrol 0.75 mg
  - b. Copper IUD
  - c. Two tablets of high dose OCP, repeated after 24 hours
  - d. Laparoscopic tubectomy
8. **According to the 2010 WHO criteria what are the characteristics of normal semen analysis.**
  - a. Volume 1.5 ml, count 15 million, morphology 4% progressive motility 32%
  - b. Volume 2.0 ml, count 20 million, morphology 4% progressive motility 32%
  - c. Volume 1.5 ml, count 20 million, morphology 4% progressive motility 32%
  - d. Volume 2.0 ml, count 15 million, morphology 40% progressive motility 32%

## EXPLANATIONS

1. **Ans. is a i.e. Androgen insensitivity syndrome**

*Ref. Williams Obstetrics 24/e p149*

See Ans. 22, Chapter 6 of the guide

2. **Ans. is a i.e. Ureterovaginal fistula**

*Ref. Shaw's Textbook of Gynecology 15/e, p186*

The site of the fistula can be determined by the complaint and also by Methylene Blue 3 Swab test.

Complaint	Urogenital fistula
• H/O normal voiding + Continuous dribbling of urine from vagina	Ureterovaginal fistula
• Continuous dribbling of urine from vagina but no normal voiding	Vesicovaginal fistula
• No continuous leakage but when patient urinates, urine comes out from urethra and vagina	Urethrovaginal fistula

For details of methylene blue 3 swab test-Refer chapter 8 of the guide.

Observation	Interpretation
Upper most swab soiled with urine (yellow) but not with dye. Remaining 2 swabs unstained	Ureterovaginal fistula
Upper and lower remain dry but middle swab soaked with dye. The upper two swabs remain dry but lower soiled with dye	Vesicovaginal fistula

In the question, the lady is having normal voiding as well as continuous in continence and on methylene blue 3 swab test, she has yellow staining on upper most pad while other two pads are unstained.

This means she is having ureterovaginal fistula.

**3. Ans. is d i.e. Rectovaginal septum**

*Ref. Shaw's Textbook of Gynecology 15/e p331*

For details see chapter 8 of the guide

**4. Ans. is d i.e. Ovarian cyst of pelvic swellings**

*Ref Shaw's Textbook of Gynecology 15/e p79, 385*

As described in the examination, the swelling is typically arising from the pelvis as the hand cannot be insinuated.

Only an ovarian cyst is a pelvis swelling among the given options.

Abdominal Palpation of pelvic swellings

The sensitive ulnar border of the left hand is used from above downwards to palpate swellings arising from the pelvis. The upper and lateral margins of such swellings can be felt but the lower border cannot be reached, i.e. the hand cannot be insinuated between the mass and the pelvis.

**5. Ans. is b i.e. Krukenberg tumor**

*Ref. Shaw's Textbook of Gynecology 15/e p425*

A Krukenberg tumor refers to a malignancy in the ovary that metastasized from a primary site, classically the gastrointestinal tract, although it can arise in other tissues such as the breast.

They are almost always bilateral (80%), consistent with its metastatic nature. They have smooth surfaces which maybe slightly bossed and they are freely movable in the pelvis. There is not tendency to form adhesions and there is no infiltration through the capsule. The tumor retains the shape of the normal ovary and has a peculiar solid waxy consistency. Microscopically, Krukenberg tumors are often characterized by cellular or myxomatous stroma with scattered mucin-secreting signet-ring cells in the tissue of. the ovary; when the primary tumor is discovered, the same signet ring cells are typically found.

**6. Ans. is d i.e. Spironolactone**

*Ref. Shaw's Textbook of Gynecology 15/e p371*

See Q. 24 of chapter 4 for explanation

**7. Ans. is b i.e. Copper IUD**

*Ref. Williams Obstetrics 24/e p714; JB Sharma Obs, p698*

Since the couple presented five days after unprotected sex and the family is complete, intrauterine devices are best for emergency contraception. Only copper containing IUD's can be used and not LNG-containing (like Mirena)

LNG tablet, can be given up till 120 hours. But its efficacy will be much less.

**8. Ans. is a i.e. Volume 1.5 ml, count 15 million morphology 4% progressive motility 32%**

Morphology 4% and progressive motility 32%

Semen characteristics	WHO 1999	WHO 2010
Volume (ml)	≥ 2	≥ 1.5
Sperm count (10 <sup>6</sup> /mL)	≥ 20	≥ 15
Total sperm count (10 <sup>6</sup> )	≥ 40	≥ 39
Total motility (%)	≥ 50	≥ 40
Progressive motility	≥ 25%	≥ 32%
Vitality (%)	≥ 75	≥ 58
Morphology (%)	14	≥ 4

## PGI MAY 2015

- 1. All are true about polycystic ovarian disease (PCOD) except:**
  - a. Testosterone > 2 ng/ml
  - b. Infertility
  - c. High FSH/LH ratio
  - d. ↑ Insulin level
  - e. ↑ E<sub>2</sub>/oestron (E<sub>1</sub>) ratio
- 2. Not true about Endometriosis:**
  - a. Sampson gave implantation theory
  - b. Cause infertility
  - c. Laparoscopy is gold standard for diagnosis
  - d. Common in low socio-economic group
- 3. A young lady can be counselled for sterilization operation in all except:**
  - a. A woman having no child may undergo sterilization
  - b. Women with HIV either taking or not ART can go for sterilization
  - c. Husband consent is present
  - d. Young lactating women more than 25 years can go for sterilization
  - e. If the couple has 3 or more living children, the lower limit of age of the husband or wife may be relaxed at the discretion of the operating surgeon
- 4. Nulliparous women have high risk of following cancer:**
  - a. Cervical cancer
  - b. Vaginal cancer
  - c. Breast cancer
  - d. Ovarian cancer
  - e. Endometrial Ca
- 5. True about testosterone in female:**
  - a. > 50% testosterone secreted from ovary
  - b. > 80% testosterone secreted from ovary
  - c. ~ .05% ng/ml is plasma concentration
  - d. Slight decrease in the secretion at time 0/5 ovulation
  - e. Daily production of testosterone is 0.2–0.3% mg
- 6. True about Nonoxynol-9:**
  - a. Decrease risk of HIV
  - b. Prevent STD infection
  - c. Remain effective for 1–2 hours after application
  - d. Spermicidal action
  - e. Causes itching of vagina in female and itching of penis in male
- 7. Appropriate time of IUCD insertion is/are:**
  - a. Immediately after delivery
  - b. 1 week after delivery
  - c. Post-puerperal period
  - d. Before menstruation
  - e. Any time during lactation period
- 8. True about combined oral contraceptive:**
  - a. Pelvic examination is mandatory before prescribing COC
  - b. Pregnancy resumes soon after discontinuation of pill
  - c. Protect from endometrial cancer, & ovarian cancer
  - d. HIV antiviral drugs reduce effectiveness of COC
  - e. Pregnancy rate equal to non-hormonal contraceptive after discontinuation
- 9. True about implanon:**
  - a. Releases > 76 µg/day of drug
  - b. Prevent STD
  - c. Life span is 3 years
  - d. Contains LNG
  - e. Has 6 implants
- 10. True about progestogen only pill:**
  - a. Weight gain occurs
  - b. Cause irregular bleeding
  - c. It can be given to lactating mother
  - d. Should not be given to women over 35 years
  - e. Protect from breast cancer
- 11. True about Dysgerminoma:**
  - a. Rare tumor in pregnancy
  - b. Always b/l
  - c. Total abdominal hysterectomy is usually done
  - d. Unilateral salpingo-oophorectomy is generally done
  - e. Constitute 30% of all malignant germ cell tumour
- 12. True about Klinefelter syndrome:**
  - a. Leg are more in length than trunk
  - b. Intrauterine fertilization can not be successful even with TESA & ICSI
  - c. Gynecomastia
  - d. FSH and luteinizing hormone (LH) are decreased
- 13. Diagnosis of Endometrial carcinoma can be made from:**
  - a. Papanicolaou smear
  - b. Fractional curettage
  - c. Aspiration cytology from uterine
  - d. Hysteroscopy & biopsy
  - e. Colposcopy

## EXPLANATIONS

### 1. Ans. is c and e i.e. High FSH/LH ratio and $\uparrow E_2$ /oestrone ( $E_1$ ) ratio

As discussed in the chapter of PCOD

In PCOS: LH is increased and FSH decreased

$\therefore$  FSH/LH ratio will be low (opposite will be true i.e. LH/FSH will be high)

Similarly in PCOD= levels of  $E_2$  are less but  $E_1$  which is mainly formed by conversion of testosterone to estrogen is high.

$\therefore E_2/E_1$  ratio will low

Rest all options are correct, and discussed in detail in chapter 4 of the guide

### 2. Ans. is d i.e. Common in low socio-economic group

As discussed in chapter on endometriosis–It is more common in high socio-economic status, not low.

Rest all options are correct and have been discussed in chapter.

### 3. Ans. is a i.e. A woman having no child/may undergo sterilization

*Ref. Shaws Gynecology 16/e p281-82*

#### Female sterilization

- Tubal ligation can be done at any convenient time to the patient. Postpartum ligation is done within the first week of delivery when the patient is already hospitalized. Interval sterilization is done when the woman is not pregnant or any time after 6 weeks of delivery. It can be combined with caesarean section
- Indications
  - Multiparity
  - Need of permanent method
  - Obstetrics- Three caesarean deliveries
  - Medical diseases at high risk of pregnancy
  - Psychiatric problems
  - Breast cancer
  - Eugenic conditions- repeat fetal malformations such as hemophilia, Rh incompatibility, Wilson's disease, Tay Sachs disease & Marfan syndrome
- Contraindication
  - Young women less than 25 years (as dictated by GOI)
  - Parity less than one child (as per the government rule)
  - Local infection
  - Prolapse- tubectomy can be done at the time of repair surgery

#### Government guidelines for sterilization *Park 23/e p508-09*

- The age of the husband should not ordinarily be less than 25 years nor should it be over 50 years
  - The age of the wife should not be less than 20 years or more than 45 years
  - The motivated couple must have 2 living children at the time of operation
  - If the couple has 2 or more living children, the lower limit of age of the husband or wife may be relaxed at the discretion of the operating surgeon
  - It is sufficient if the acceptor declares having obtained the consent of his/her spouse to undergo sterilization operation without outside pressure, inducement or coercion & he/she knows that for all practical purposes, the operation is irreversible, & also that the spouse has not been sterilized earlier
4. Ans. is c, d and e i.e. breast cancer, ovarian cancer and endometrial cancer.  
Remember: A simple funda- All hyperestrogenic conditions are M/C in nulliparous females.

#### Conditions M/C in Nulliparous Females

- PCOD
- Fibroid
- Endometriosis
- Endometrial hyperplasia
- Cancer endometrium
- Cancer ovary
- Cancer breast

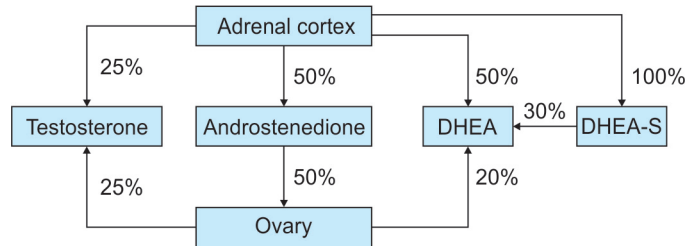
### 5. Ans. is a, and e i.e. > 50% Testosterone secreted from ovary, and daily production of testosterone is 0.2–0.3% mg

*Ref. Leon Speroff 8/e, page 537*

#### Testosterone in Females-

- Testosterone production occurs from adrenals (25%), ovaries (25%) and from peripheral conversion of androstenedione (50%)

- Production rate is between 0.1–0.4 mg/day
- Normal serum concentration is 20–80 mg/dl
- 80% of circulating testosterone is bound to sex hormone binding globulin, 19% to albumin, Thus only 1% is free.



**6. Ans. is c, d and e i.e. Remain effective for 1–2 hrs after application, spermicidal action and cause itching of vagina in female and itching of penis in male**

*Ref. Leon Speroff 8/e, p1129-1131*

- Nonoxynol-9 is spermicidal agent
- All spermicidal agents-have low efficacy with failure rate 20–25%
- Effectiveness lasts for 1–2 hrs only.
- They do not prevent HIV or STD infection(Rather HIV infection chances increases)
- Only side effects in minor allergy in the form of itching
- There is a possible association between spermicidal use and congenital abnormalities on spontaneous abortions, if pregnancy occurs.

**7. Ans. is a, b, c, d and e Immediately after delivery, 1 week after delivery, post peripheral period, (before menstruation and anytime during lactation period.**

*Ref. JB Sharma Obs- 680, Leon Speroff 8/e, p1113*

**Timing of insertion:**

1. Interval insertion- Insertion-6weeks after parturition or MTP or abortion
2. Insertion immediately after delivery or 1<sup>st</sup> trimester(Abortion, spontaneous or induced)
3. Insertion at the time of caesarean section
4. Insertion immediately after menstruation (as cervix is more open-although insertion can be done at anytime of menstrual cycle after being sure patient is not pregnant)
5. After 2<sup>nd</sup> trimester abortion-Insertion should be done after uterine involution
6. Post cortical insertion-As an emergency contraceptive

*Ref. JB Sharma, Obs, p680*

Insertion during lactation period- IUD can be safely inserted during lactational period after ruling our pregnancy, IUD does not affect lactation in any way. It is preferable to use smaller device during this period.

Immediate post partum insertion- IUD is inserted following delivery of the placenta both after normal delivery and caesarean section. Govt. of India is recommending it now. Large and long sponge holding forceps (Keely's forceps) have been devised to place the IUD near fundus. Expulsion rate is slightly high.

**8. Ans. is b,d and e, i.e. pregnancy resumes soon after discontinuation of pill, HIV antiviral drug reduce effectiveness of COC, pregnancy rate equal to non hormonal contraception after discontinuation.**

*Ref Leon Speroff, 8/e, page 996-100*

- Many women can be prescribed hormonal contraception without clinical breast and pelvic examination (Thus, option 'a' is incorrect)

Leon Speroff, 8/e, page 1015

Leon Speroff 8/e, page 1015 says—pelvic examination is not mandatory before prescribing CoCs in all women. Patients requiring further evaluation can be identified with careful medical history and measurement of BP. Subsequently, in view of the increased safety profile of low dose OCPs, for young healthy women with no risk factors, patients should be seen only after every 12 months for measurement of BP, urinalysis, breast examination, palpitation of liver and pelvic examination with pap smear.

Women with risk factors should be seen every 6 months by trained personnel. In females also, breast and pelvic examination is done yearly. Blood lipid profile and glucose levels should be checked only:

- i. Once in young women
- ii. Women > 35 years
- iii. Women with family H/O heart disease, diabetes, hypertension
- iv. Women with xanthesis
- v. Obese women
- vi. Diabetic women

- OCPs protect from endometrial and ovarian cancers but not cervical cancer (Therefore option 'c' is incorrect)
- HIV drugs reduce the effectiveness of OCPs i.e. option 'd' is incorrect.
- Reproduction after discontinuation of OCPs

#### According to Leon Speroff 8/e

It is unlikely that women discontinuing low-dose steroid contraception experience any significant delay in achieving pregnancy compared with the experience in general population.

This is in contrast to the earlier findings that ovulation returns 3 months after stopping OCPs and to the finding that OCP users took 24 months, IUC users 14 months and diaphragm users 10 months to become pregnant.

#### 9. Ans. is c i.e. 3 years

Ref. JB Sharma Obs, p696-697

- Implanon is a long-acting single rod subdermal implant
- Rod measures 4 cm in length
- It contains 68 mg of etonogestrel dispersed in ethylene risyle acetate polymer
- Initial release rate is 60–70 µg/day and declines to 25–30 mcg at the end of third year
- Recommended use 3 years
- In UK, nexplanon has now replaced implanon.

#### 10. Ans. is a, b and c i.e. weight gain occurs, causes irregular bleeding and it can be given to lactating mothers

Ref. JB Sharma Obs, p694-695

As discussed in the chapter on contraception, Minipills or progesterone only pills are most effective means of contraception in lactating females.

- They should be taken everyday at the same time (hence, they are not good for unorganised females)
- Ectopic pregnancy is not prevented as effectively as intrauterine pregnancy. Although overall incidence of ectopic pregnancy is not increased
- Main side effect—breakthrough bleeding
- Other minor side effects—weight gain, acne and formation of follicular cysts in ovary
- Immediate return to fertility in lactating women with recent gestational diabetes
- Good choice for females in whom estrogen is C/I like smokers more than 35 years of age
- Can be used in females with previous episodes of vascular thrombosis
- It protects from endometrial and ovarian cancer

#### 11. Ans. is d and e, i.e. unilateral salpingo-oophrectomy is generally done and constitutes 30% of all malignant germ cell tumors.

Ref. Dutta Gyne 5/e p367, Nov. Ans 14/e p1506-1508

For details of dysgerminoma- see chapter 14c of the guide

#### 12. Ans is a and c, i.e. Legs are more in length than tronk and gynaeromastia.

Ref. Leon Speroff 8/e p1261-1262

#### 13. Ans is b, c and d i.e. Fractional cumettage, aspiration cytology from uterus and hysteroscopy and biopsy.

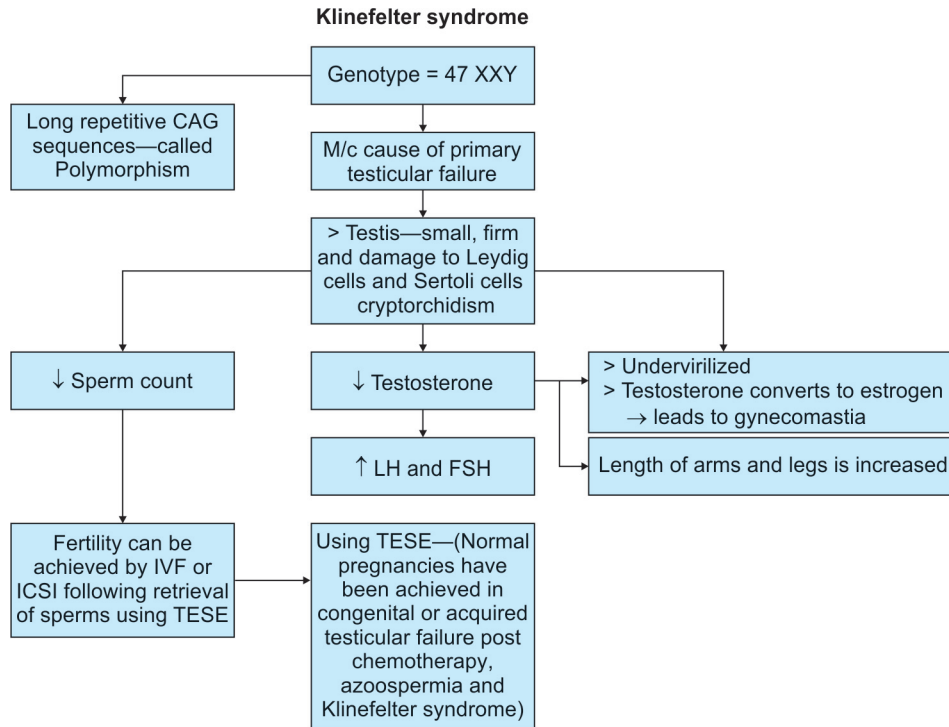
Ref. Dutta Gyne, 5/e p356-357

#### Diagnosis of Endometrial Carcinoma

- Papanicolaou smear is not a reliable diagnostic test for endometrial carcinoma (positive only in 30% cases)
- Endometrial biopsy: Using curette or cannula has been done with reliability (90%). Histology is the definitive diagnosis
- USG and color Doppler
- Hysteroscopy
- Fractional curettage: It is not only the definite method of diagnosis but can detect the extent of growth
- CT scan of pelvis and abdomen: To detect LN metastases
- MRI: Can detect myometrial invasion
- PET scan

"Endometrial carcinoma: Pap smear is only 50% sensitive and not reliable"- Shaw's Gynecology 16/e p510.

"Colposcopy is used for cervical cancer. Aim- to study cervix when pap smear detects abnormal cells, to locate abnormal areas & take a biopsy, to study the extent of abnormal lesions, conservative surgery under colposcopic guidance & followup of conservative therapy cases."- Shaw's Gynecology 16/e p490.





## PGI NOVEMBER 2014

1. **Which of the following is true about endometrial carcinoma:**
  - a. Less aggressive in post menopausal women
  - b. More common in diabetes
  - c. Common after 40 year of age
  - d. Associated with PCOD
  - e. Associated with hereditary nonpolyposis colorectal cancer syndrome (HNPCC)
2. **True about Trichomonas vaginitis:**
  - a. Important cause of recurrent abortion
  - b. T.vaginalis is a flagellated protozoa
  - c. Metronidazole is used for treatment
  - d. Strawberry cervix
  - e. Curdy discharge
3. **True about Mirena:**
  - a. Effective life is 2 year
  - b. LNG containing IUD
  - c. Cause endometrial hyperplasia
  - d. Suppression of endometrium
  - e. No significant effect on ovaries
4. **All are true about LNG except:**
  - a. Cause Endometrial suppression
  - b. Can be used in emergency contraception
  - c. Can not be given to lactating women
  - d. Devoid of estrogenic side-effects
5. **IUCD is absolutely contraindicated in:**
  - a. HIV positive women
  - b. Previous ectopic tubal pregnancy
  - c. Mild anaemia
  - d. Undiagnosed vaginal bleeding
6. **True about ovulation and menstruation:**
  - a. Temperature decrease at time of ovulation
  - b. Estrogen have a role in proliferative phase
  - c. LH surge occurs before ovulation
  - d. 80 ml blood loss is normal

## EXPLANATIONS

1. **Ans. is b, c, d and e i.e. More common in diabetes, common after 40 years of age, associated with PCOD and associated with hereditary nonpolyposis colorectal cancer syndrome (HNPCC)**  
*Ref. Novars Gyne 4/e p1251, 1256*  
 For details see chapter 14A of the guide
  2. **Ans. is b, c and d i.e T. Vaginalis is a flagellated protozoa, metronidazole is used for treatment, and strawberry cervix.**  
*Ref. Dutta obs 7/e p167*  
 Infection in genital tract may be responsible for sporadic abortion but its relation to recurrent abortion is inconclusive.  
 Rest all options- have been explained earlier in the book.
  3. **Ans. is b, d and e i.e. LNG containing IUD, suppression of endometrium and no significant effect on ovaries**  
*Ref. Leon Speroff 8/e p1102*  
 For all options see chapter 10 of guide
  4. **Ans. is c i.e. cannot be given to lactating women.**  
 For explanation see chapter 10 of guide
  5. **Ans. is d i.e. Undiagnosed vaginal bleeding**  
 Absolute-WHO-category 4 contraindications for IUCD
 

**M**

Please- Periperal Sepsis, pregnancy  
 Don't- DUB  
 Try to- Gestational Trophoplastic disease  
 Put- current PID/STD or within 3 months, known pelvic TB  
 Condom- Ca Cervix  
 Ca endometrium
- Relative C/I:-**  
 Wilson disease  
 Breast CA for miera  
 Distortions of uterine cavity due to congenital malformations or fibroid  
 Note: Ectopic pregnancy is not a C/I for use of IUCD  
 Undiagnosed vaginal bleeding is a C/I for IUCD  
*Ref. JB Sharma 1/e, page 682*
6. **Ans. is b, c, and d i.e Estrogen has a role in proliferative phase, LH surge occurs before ovulation and 80ml blood loss is normal**  
*Ref. Shaw 15/e p46,32*  
 All the options have been explained earlier in the guide

# Annexures

## Annexure 1

### Lining of Female Genital Tract

Organ/Structure	Epithelial lining
<ul style="list-style-type: none"> <li>Bartholin's gland</li> <li>Bartholin's duct (<i>Jeffcoate 7/e, p 24</i>)</li> <li>Adult vagina</li> <li>Newborn vagina</li> <li>Uterus</li> <li>Cervix (endocervix, cervical canal)</li> <li>Ectocervix</li> <li>Fallopian tube</li> </ul>	<ul style="list-style-type: none"> <li>Single layer of low columnar cell</li> <li>Multilayered columnar cells (Not transitional)</li> <li>Stratified squamous epithelium</li> <li>Transitional epithelium</li> <li>Columnar epithelium</li> <li>High columnar epithelium</li> <li>Squamous epithelium</li> <li>Ciliated columnar epithelium</li> </ul>

### Blood Supply of Genital Tract

Organ	Supplied By
Uterus	Uterine artery (branch of ant. div. of internal iliac artery) and ovarian artery.
Cervix	Descending cervical artery (branch of uterine artery).
Vagina	Vaginal artery (Separate branch of int. iliac artery or may come from uterine artery), branches of int. pudendal, middle and inferior rectal arteries.
Organ	Supplied By
Fallopian tube	Medial 2/3 <sup>rd</sup> – uterine artery, lateral 1/3 <sup>rd</sup> – ovarian artery.
Ovary	Ovarian artery (branch of aorta).
Vulva	Internal pudendal artery (terminal branch of int. iliac artery).

## Annexure 2

### Lymphatic Drainage of Female Genitalia

Organ	Lymphatic drainage
<b>Ovaries</b>	Para-aortic lymph node (lateral aortic nodes)
<b>Fallopian Tube</b>	<ul style="list-style-type: none"> <li>Along ovarian lymphatic</li> <li>Along cornua</li> <li>Lateral aortic lymph node</li> <li>Superficial inguinal lymph node</li> </ul>
<b>Uterus</b> <ul style="list-style-type: none"> <li>Fundus</li> <li>Body</li> <li>Cornus</li> </ul> <b>Cervix</b>	<ul style="list-style-type: none"> <li>Lateral aortic lymph node</li> <li>External iliac lymph node</li> <li>Superficial inguinal lymph node (along round ligament)</li> <li>H – Hypogastric lymph node/internal iliac</li> <li>O – Obturator lymph node</li> <li>P – Presacral lymph node and parametrial lymph node (sentinel lymph node)</li> <li>E – External iliac lymph node.</li> </ul>

(**Note:** Cervix does not drain into superficial inguinal lymph node So cancer cervix rarely involves inguinal lymph node).

M/c lymph node involved in cancer cervix–obturator lymph node.

1<sup>st</sup> lymph node involved in cancer cervix–parametrial lymph node or paracervical lymph node (also called as ureteric lymph node).

Contd...

Organ	Lymphatic drainage
<b>Vagina :</b> <ul style="list-style-type: none"> <li>• Upper part</li> <li>• Middle part</li> <li>• Lower</li> </ul>	<ul style="list-style-type: none"> <li>• Same like cervix.</li> <li>• Internal iliac lymph node.</li> <li>• Superficial inguinal lymph node.</li> </ul>
<b>Vulva</b>	<ul style="list-style-type: none"> <li>• Superficial inguinal lymph node (sentinel lymph node)</li> <li>• Deep inguinal lymph node</li> <li>• Internal iliac nodes</li> </ul>
<b>Clitoris</b>	<ul style="list-style-type: none"> <li>• Superficial + deep inguinal lymph node.</li> <li>• The anterior most lymph node of deep inguinal group is called as lymph node of cloquet/ Rosenmuller lymph node</li> </ul>

### Annexure 3

#### pH of vagina at different ages:

Age	Vaginal pH
Newborn infants	Between 4–5
6 weeks old child	6–8
Puberty	Charges from alkaline to acidic
Reproductive age group	4–5.5
Pregnancy	3.5–4.5
Menstruation	6–8
Menopause	6–8

### Annexure 4

#### Some Important Measurements

Structure	Measurement
<ul style="list-style-type: none"> <li>• Isthmus which forms lower uterine segment</li> <li>• Female urethra</li> <li>• Posterior vaginal wall</li> <li>• Anterior vaginal wall</li> <li>• Uterus (Nulliparous)</li> </ul>	5–6 mm <sup>Q</sup> 35–40 mm <sup>Q</sup> 11.5 cm 9 cm 8 cm × 6 cm × 4 cm
Structure	Measurement
<ul style="list-style-type: none"> <li>• Cervix</li> <li>• Ovary</li> <li>• Fallopian tube</li> <li>• Mature ovum</li> <li>• Mature/ripe graafian follicle</li> <li>Just before ovulation site of graafian follicle</li> </ul>	2.5–3.5 cm 3 × 2 × 1 cms 10–12 cm 120–140 microns 5–8 mm 16–24 mm (≈ 20 mm)
<b>Some important angles to remember:</b> <ul style="list-style-type: none"> <li>• Angle of anteflexion (angle between cervix and uterus)</li> <li>• Angle of anteversion (angle between cervix and vagina)</li> <li>• Urethrovesical angle</li> </ul>	120–130° 90° 100°

## Annexure 5

### Male and female derivatives of embryonic urogenital structures

Embryonic structures	Derivatives	
	Male	Females
Labioscrotal swelling	Scrotum <sup>o</sup>	Labia majora <sup>o</sup>
Genital folds	Ventral aspect of penis	Labia minora
Genital tubercle <sup>o</sup>	Penis <sup>o</sup>	Clitoris <sup>o</sup>
Urogenital sinus	Urinary bladder Urethra except navicular fossa Prostate gland Prostatic utricle Bulbourethral glands	Urinary bladder Urethral and paraurethral glands Lower part of Vagina Bartholin's glands
Paramesonephric duct/ Mullerian duct	Appendix of testes Prostatis utriculis	Hydatid of Morgagni, uterus, cervix, fallopian tubes, upper part of vagina
Mesonephric duct/Wolffian duct	Ductus epididymis Seminal vesicles	Duct of epoophoron Gartner's cyst
Mesonephric tubules	Ductus efferentes Paradidymis	Epoophoron (cranial end) Paroophoron (caudal end)
Genital ridge	Testis	Ovary

## Annexure 6

### Origin of female genital tract

Part of female genital system	Originates from
Ovary	Genital ridge
Fallopian tubes Uterus Cervix Upper part of vagina	Mullerian/paramesonephric duct
Lower part of vagina	Urogenital Sinus

## Annexure 7

### Culture Media and DOC of Various Organism

#### Culture Medium

Organism	Culture Medium
Trichomonas	Feinberg-Whittington media/Diamond media
Candida	Sabouraud's media
Chlamydia	McCoy cells/HeLa cells
TB	LJ media/Bactec

#### DOC

Condition	Drug of choice
Trichomonas vaginitis Nonpregnant Pregnant	Metronidazole (2 g single dose) Metronidazole in 2 <sup>nd</sup> & 3 <sup>rd</sup> trimester
Candidiasis	Antifungals
Bacterial vaginosis	
HSV	Acyclovir or Fancyclovir

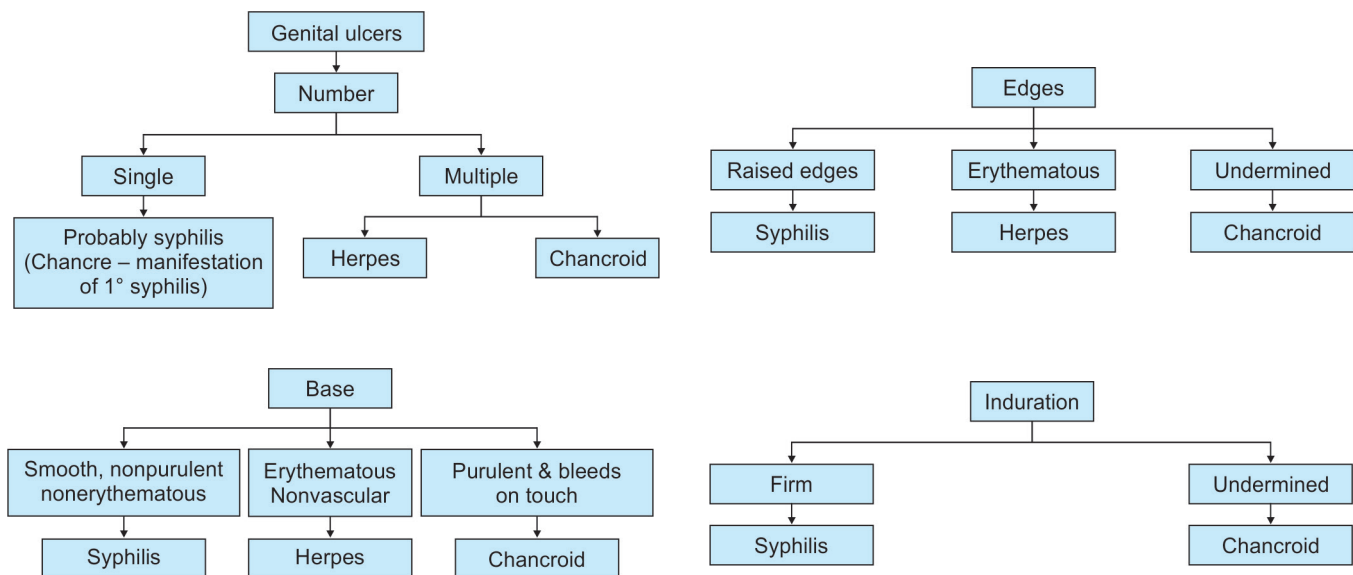
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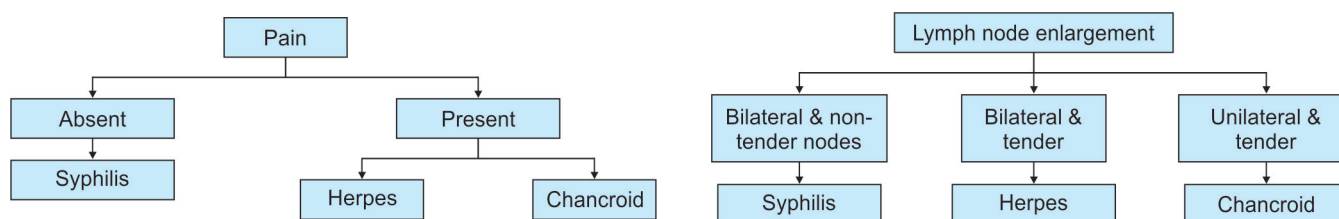
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Condition	Drug of choice
Syphilis	Benzathine penicillin
Chancroid	Azithromycin or Ceftriaxone or Erythromycin
Granuloma Inguinale/Donovanosis caused by <i>Calymmatobacterium (Klebsiella) granulomatis</i>	Doxycycline or Azithromycin Ciprofloxacin or Erythromycin
<b>Gonococcal infection:</b> <b>Uncomplicated:</b> Nonpregnant	Single dose = Ceftriaxone + Azithromycin or Doxycycline (100 mg B/D × 7 days) Ceftriaxone or Cefixime.
Pregnant	If patient is allergic to cephalosporin → Spectinomycin <b>Note:</b> for Gonococcal endocarditis antimicrobials should be continued for 4 weeks & for meningitis 10–14 days
Chlamydia Non pregnant	1 <sup>st</sup> Choice Single dose = Azithromycin + contact tracing 2nd choice = Doxycycline or Erythromycin
Pregnant	1 <sup>st</sup> Choice Azithromycin or Amoxicillin 2nd choice = Erythromycin
Genital warts/HPV Pregnancy	see the text Trichloroacetic acid (80–90% solution applied once a week) or cryotherapy or Laser ablation or surgery
Scabies Non pregnant Pregnant & young children	Lindane 10% Crothamine lotion cream or 5% Permethrin cream

## Annexure 8

### Clinical Features of Genital Ulcers





## Annexure 9

### Types of Hysterectomies and Structures Removed

Hysterectomy	Structure Removed
Simple Hysterectomy/Total abdominal hysterectomy/Extrafascial hysterectomy/Type I hysterectomy	Uterus + Cervix
Wertheim's hysterectomy/Modified Radical hysterectomy (Type II hysterectomy)	Uterus + cervix + 1 cm vagina + medial half of cardinal and uterosacral ligament + uterine artery after it has given branch to ureter + selective removal of enlarged lymph nodes
Radical hysterectomy/Type III hysterectomy/Meigs hysterectomy	Uterus + cervix + 2 cms of vagina (upper 1/3) + whole of cardinal and uterosacral ligament + whole of uterine artery + pelvic lymphadenectomy
Type IV hysterectomy	Same like Type III but upper 3/4 of vagina removed + periureteral tissues + superior vesical artery
Type V hysterectomy (Rarely done)	Same like Type IV + distal ureter and bladder also removed

## Annexure 10

### Pearl Index: WHO category 1 (user independent)

Contraception	Perfect use rate	Typical use
Implants	0.5%	.05%
Sterilization		
Male	0.1%	0.15%
Female	0.5%	0.5%
IUCD		
Mirena	0.2%	0.2%
CuT	0.6%	0.8%

### WHO category 2 (user dependent)

Contraception	Perfect use rate	Typical use
OCP's	0.3%	8.7%
Vaginal ring	0.3%	8%
Transdermal patch	0.3%	8%
DMPA	0.3%	3%
Diaphragm	20%	20%
<b>Sponge</b>		
Nulliparous	9	16
Parous	26	32
Condom		
Male	2	16
Female	5	21



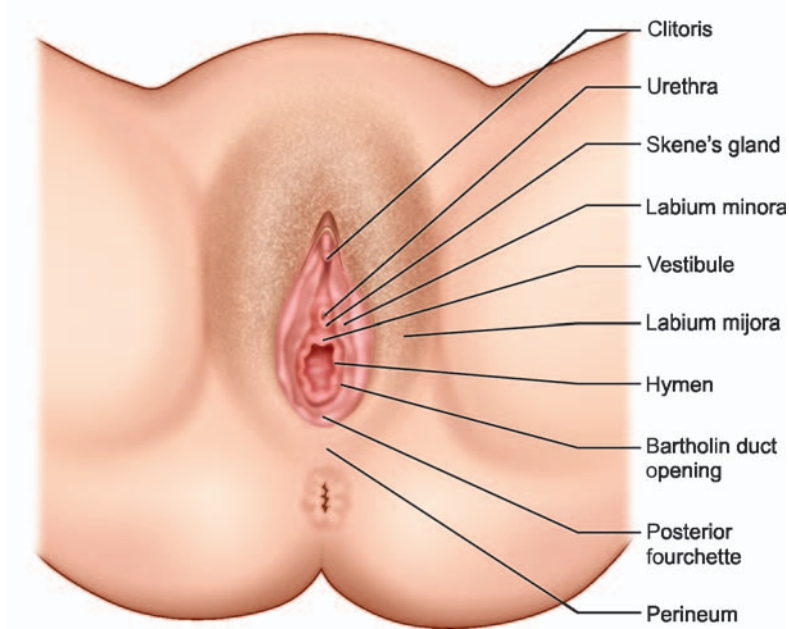


# COLOR PLATES

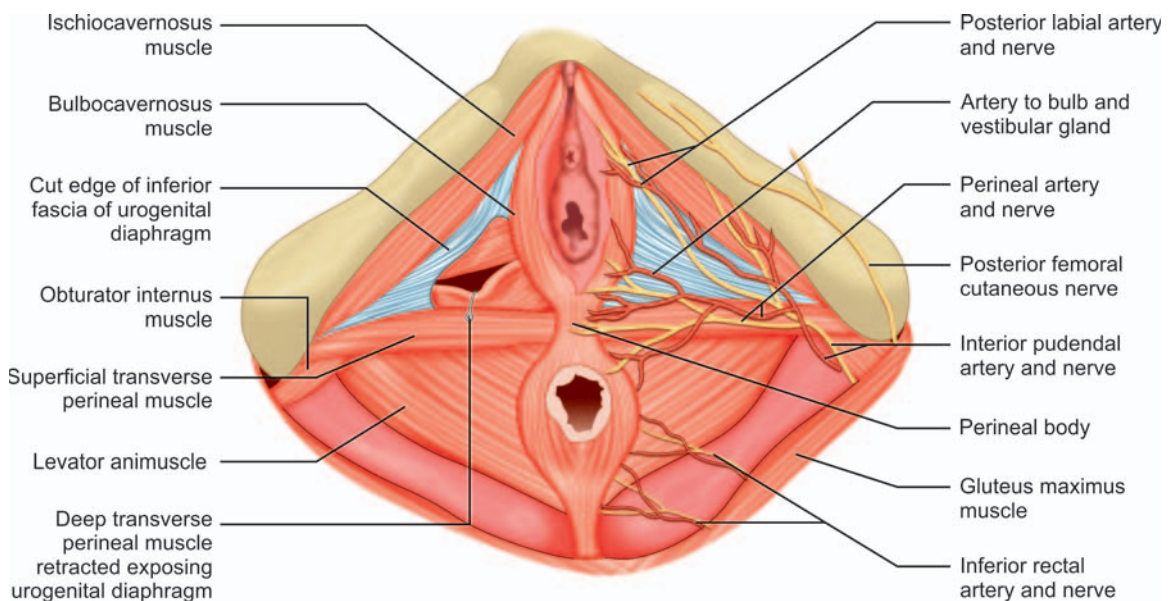




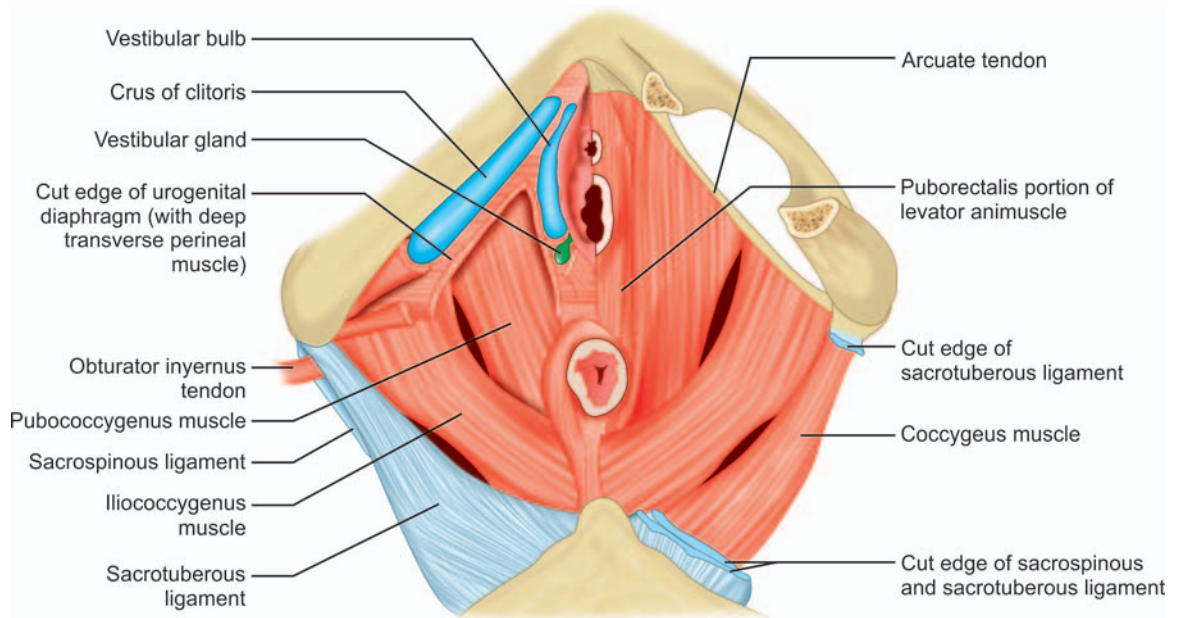
## COLOR PLATES



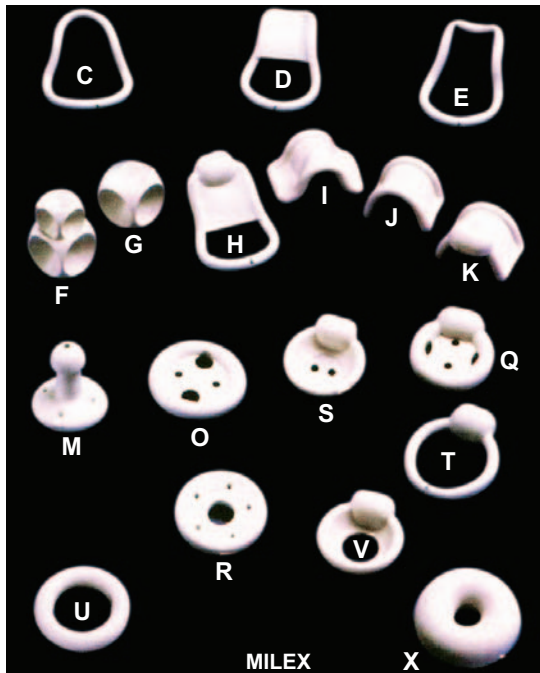
**Fig. 1:** Vulva and perineum



**Fig. 2:** Superficial perineal compartment

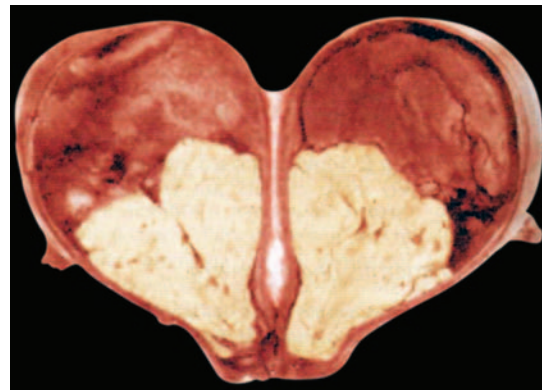


**Fig. 3:** Deep perineal compartment

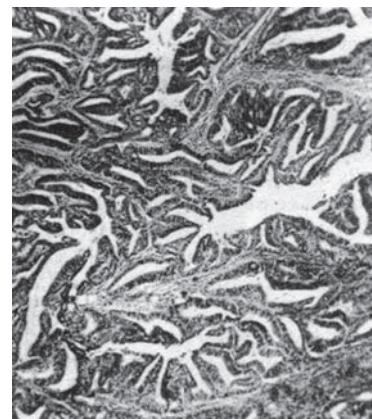


C: Smith (Silicone); D: Hodge with Support (Silicone); E: Hodge (Silicone); F: Tandem-Cube (Silicone); G: Cube (Silicone); H: Hodge with Support + Knob (Silicone); I: Regula (Silicone); J: Gehrung (Silicone); K: Gehrung with Knob (Silicone); L: Gellhorn Flexible (Silicone); M: Gellhorn Flexible (Silicone); N: Ring with Support (Silicone); O: Ring with Knob (Silicone); P: Ring with Support + Knob (Silicone); Q: Ring with Support + Knob (Silicone); R: Shaatz (Silicone); S: Incontinence Dish with Support (Silicone); T: Ring Incontinence (Silicone); U: Ring (Silicone); V: Incontinence Dish (Silicone); W: Ring (Silicone); X: Donut (Silicone)

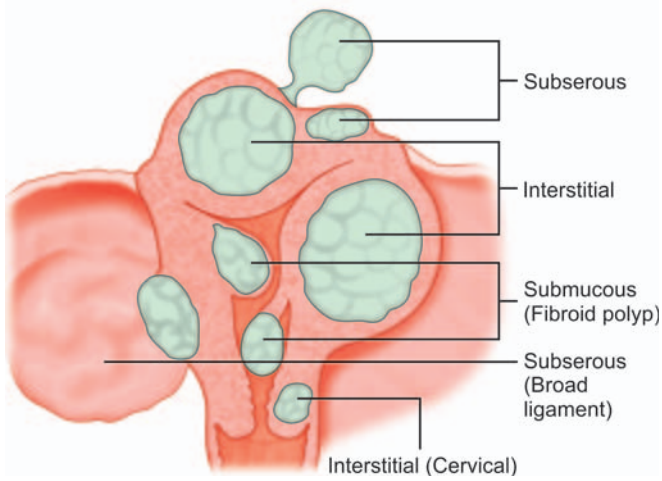
**Fig. 4:** Pessaries used to treat the various degrees of prolapse



**Fig. 5:** An adenocarcinoma arising in the region of the isthmus of the uterus and blocking the cervix to cause a haematometra above the growth



**Fig. 6:** A well-differentiated adenocarcinoma of the endometrium



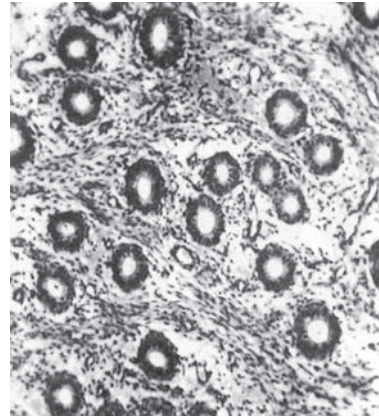
**Fig. 7:** The sites of uterine leiomyomas



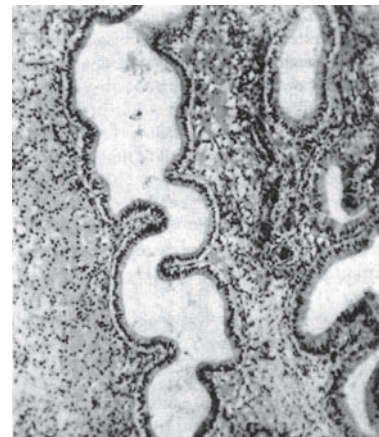
**Fig. 8:** An endometrial polyp



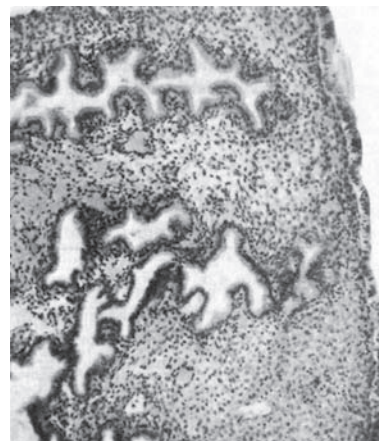
**Fig. 9:** Fibroids intracavitary



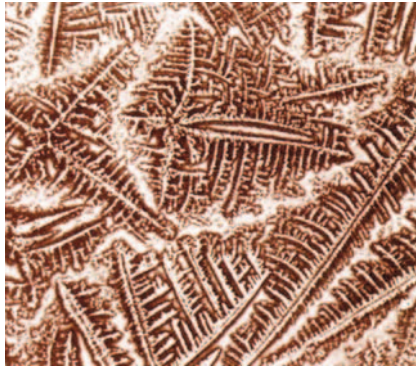
**Fig. 10:** The early proliferative phase with small regularly shaped nonsecretory glands. The glands generally appear in cross-section at this stage because they tend to lie parallel to the surface of the endometrium (Photomicrograph 85x)



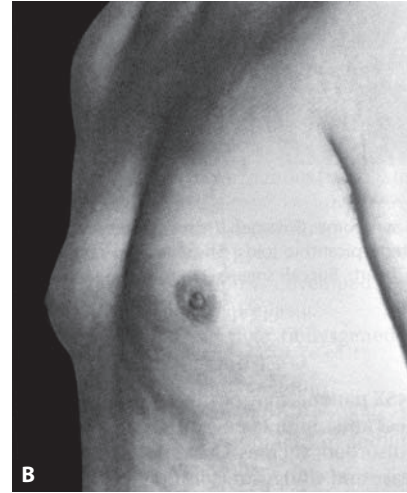
**Fig. 11:** The early secretory phase. The glands are larger and less regular in outline. The lining cells show globules of secretion lying basal to the nucleus, the so-called subnuclear vacuolation (Photomicrograph)



**Fig. 12:** The late secretory phase with 'sawtooth' glands in longitudinal section. The stroma near the endometrial surface shows the decidual reaction typical of the premenstrual phase (Photomicrograph 85x)



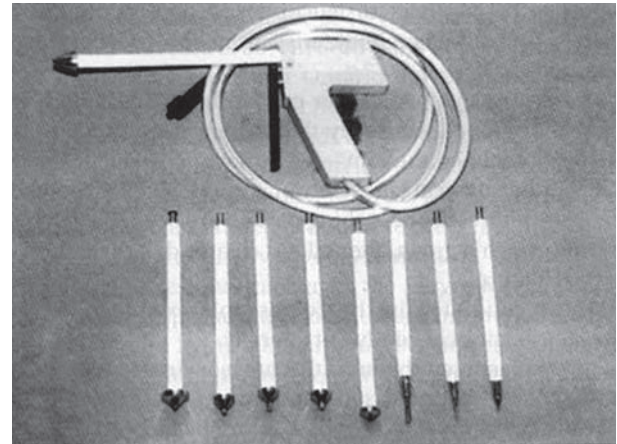
**Fig. 13:** The late secretory phase with 'sawtooth' glands in longitudinal section. The stroma near the endometrial surface shows the decidual reaction typical of the premenstrual phase (Photomicrograph 85x)



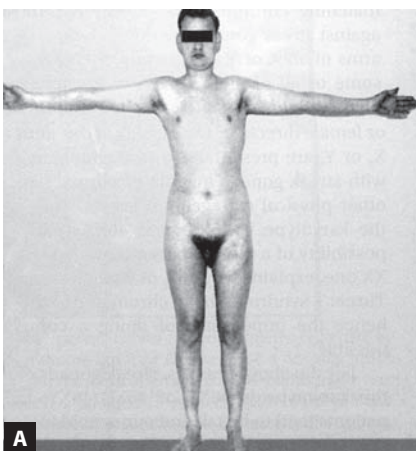
**Figs. 15A and B:** Klinefelter's syndrome. Man aged 28 years, married but infertile and complaining of gynecomastia. Chromosomes 47XXY (Professor Sir Cyril Clarke's case) (A) An apparently normal male but tall. The scrotum is small and contains very hypoplastic testes, (B) Slight



**Fig. 14:** Turner's syndrome with presumed streak gonads. The patient, aged 17 years, complained of primary amenorrhoea. Height 130 cm. Chromatin-negative; sex chromosome complement not determined. Note the short wide neck, barrel-shaped trunk, increased carrying angle, and the absence of secondary sex characters

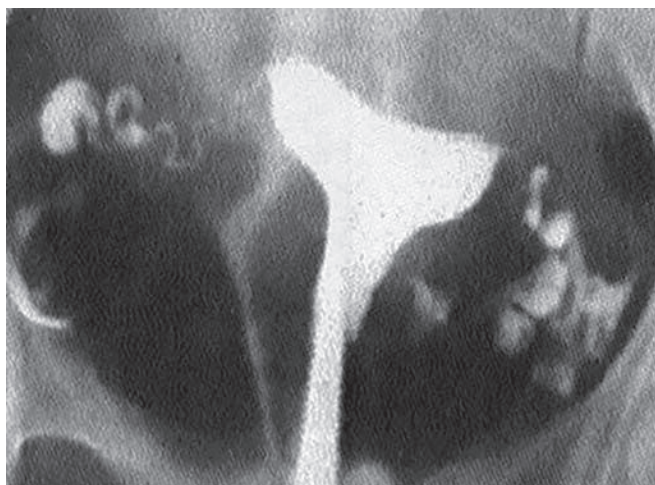


**Fig. 16:** Cryotherapy gun with probes of different size and shapes



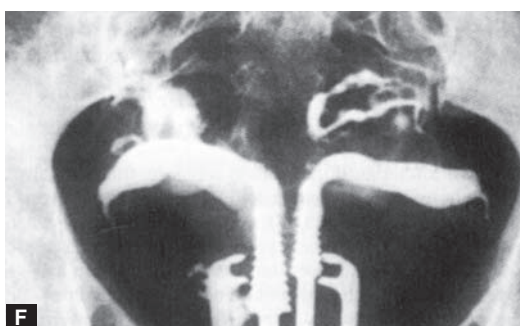
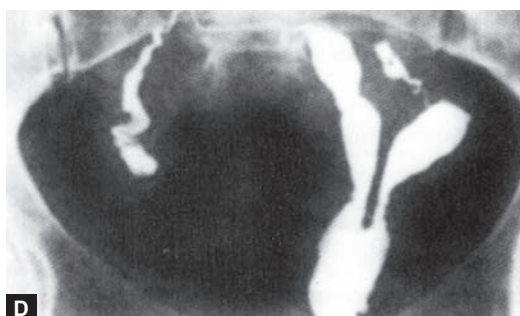
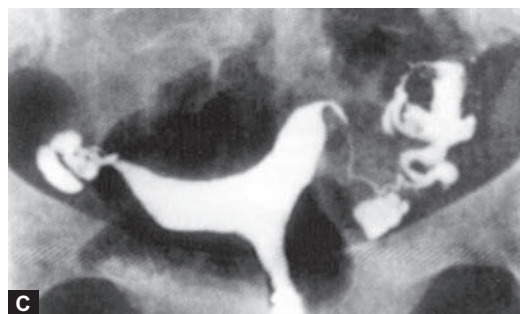
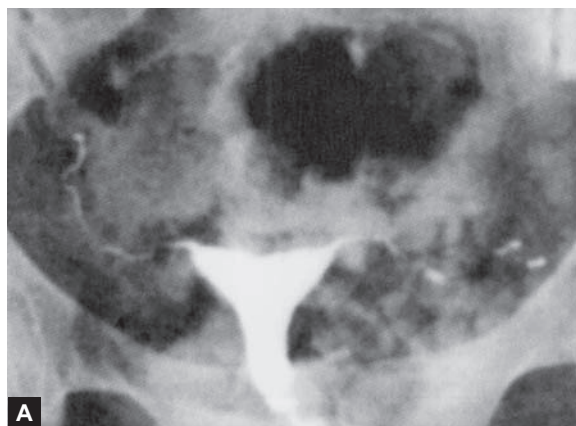
**Fig. 17:** Ultrasonography pictures of polycystic ovary

## IMPORTANT HSG'S IN GYNECOLOGY

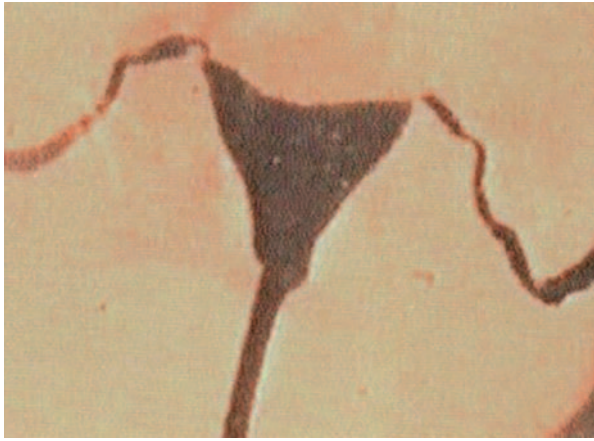


**Fig. 1:** Normal look of tubes at hysterosalpingography. Note way outline of tubes spill on both side

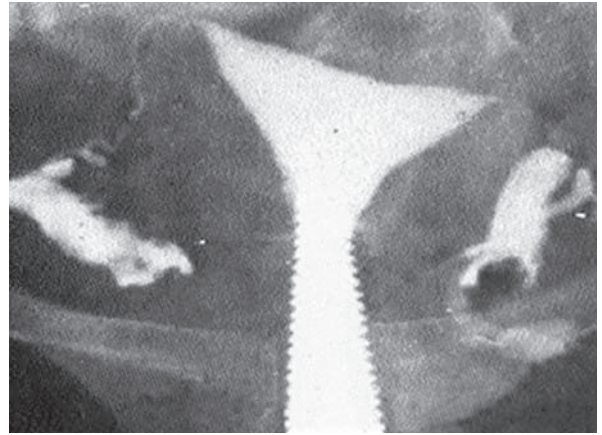
Courtesy: Dr Narayan M Patel, MD, DGO, FICS



**Figs. 2A to F:** Certain types of Mullerian duct malformation deformity revealed by hysterosalpingography. (A and B) Degrees of arcuate deformity, (C) A minor degree of bicornuate malformation; this type of radiograph is difficult to interpret because a similar picture can be produced by a fundal leiomyoma. (D) Septate uterus, (E) Uterus bicornis, (F) Uterus didelphys with a cannula in each cervix



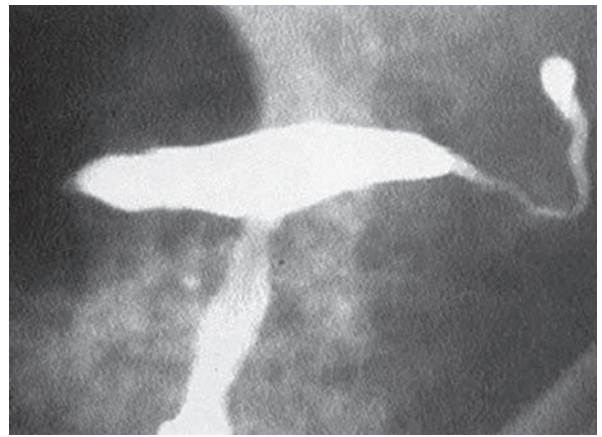
**Fig. 3:** Rigid pipe line tubes of proved Koch  
*Courtesy: Dr Narayan M Patel, MD, DGO, FICS*



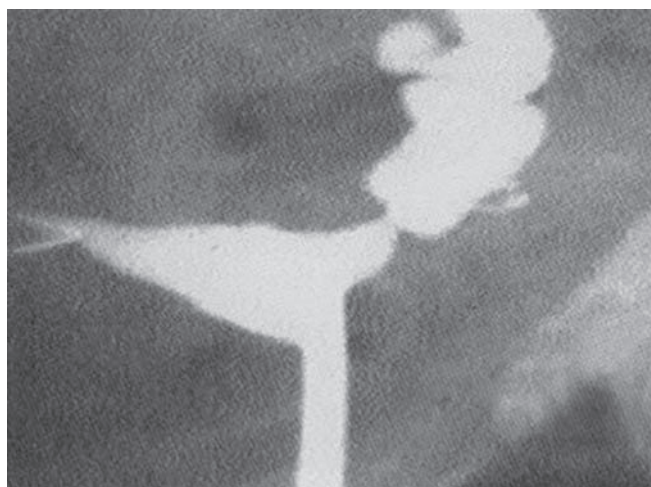
**Fig. 5:** Bilateral tobacco pouch appearance as described by Greenberg  
*Courtesy: Dr Narayan M Patel, MD, DGO, FICS*



**Fig. 4:** Bilateral hydrosalpinx. ATT given for 2 years  
*Courtesy: Dr Narayan M Pael, MD, DGO, FICS*

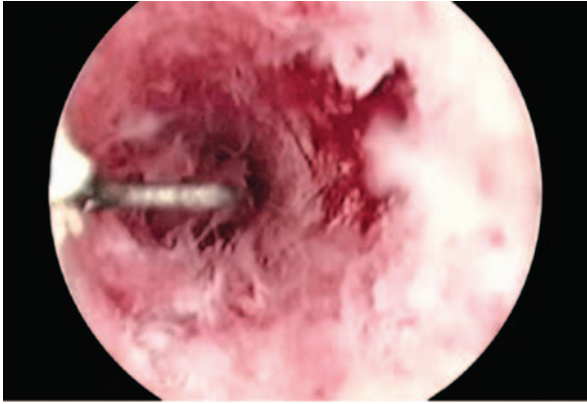


**Fig. 6:** Left tube appears as, if tubectomy has been doe. Look of a sperm head  
*Courtesy: Dr Narayan M Patel, MD, DGO, FICS*



**Fig. 7:** Left terminal hydrosalpingogram and right cornual block

## HYSTEROSCOPIC VIEW



**Fig. 1:** Dense intrauterine adhesions



**Fig. 2:** Hysteroscopic scissors for adhesiolysis



**Fig. 3:** Normalized cavity after adhesiolysis and estrogen therapy



# IMPORTANT PICTURES FOR PICTORIAL QUESTIONS

## A. INSTRUMENTS

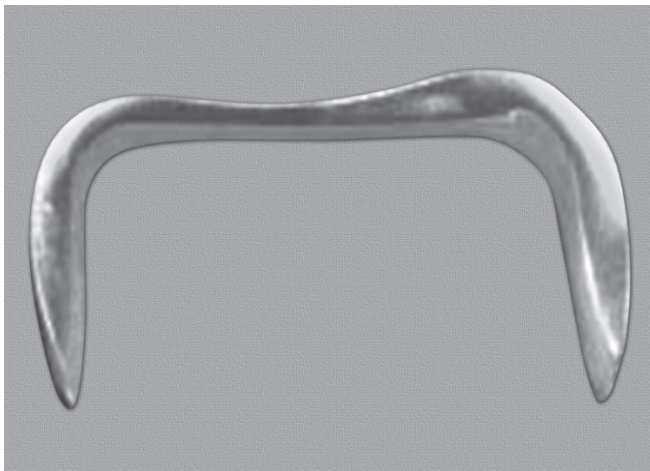
### SIM'S SPECULUM (FIG. 1)

*Material:* Stainless steel.

*Sterilization:* Autoclaving and boiling.

#### Uses

- *Gynecologic*
  - Routine gynecological examination to visualize vagina and cervix
  - To collect discharge from posterior fornix
  - Hysterosalpingography (HSG)
  - Gynecological operations.
- *Obstetric*
  - Routine per speculum examination
  - Manual vacuum aspiration (MVA), first trimester medical termination of pregnancy (MTP)
  - Cervical cerclage
  - Diagnose and repair cervical tear.



**Fig. 1:** Sim's speculum

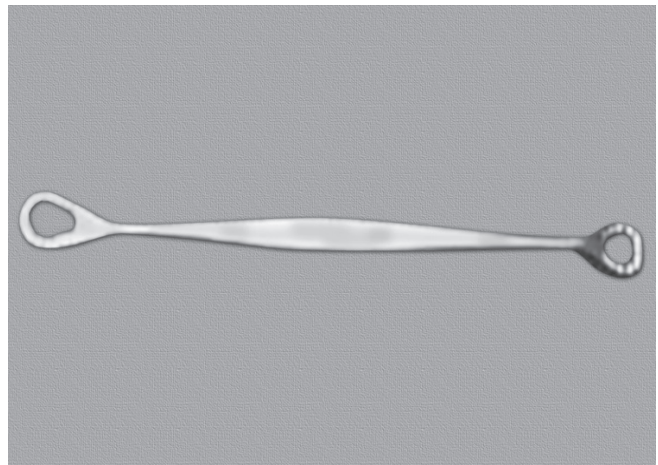
### SIM'S ANTERIOR VAGINAL WALL RETRACTOR (FIG. 2)

*Material:* Stainless steel.

*Sterilization:* Autoclaving and boiling.

#### Use

Along with Sim's speculum, to visualize cervix by retracting anterior vaginal wall.



**Fig. 2:** Sim's anterior vaginal wall retractor

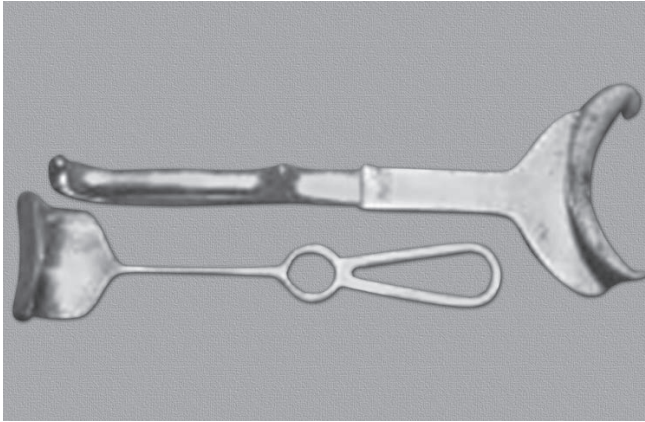
### DOYEN'S RETRACTOR (FIG. 3)

*Material:* Stainless steel.

*Sterilization:* Autoclaving.

#### Uses

- *Gynecologic*
  - Abdominal hysterectomy
  - Wertheim's hysterectomy
  - Tuboplasty
  - Sling operation
  - Purandare's cervicopexy
  - Exploratory laparotomy for ovarian tumors
  - Myomectomy.
- *Obstetric*
  - Cesarean section
  - Cesarean hysterectomy
  - Exploratory laparotomy for ruptured tubal ectopic pregnancy.



**Fig. 3:** Doyen's retractor

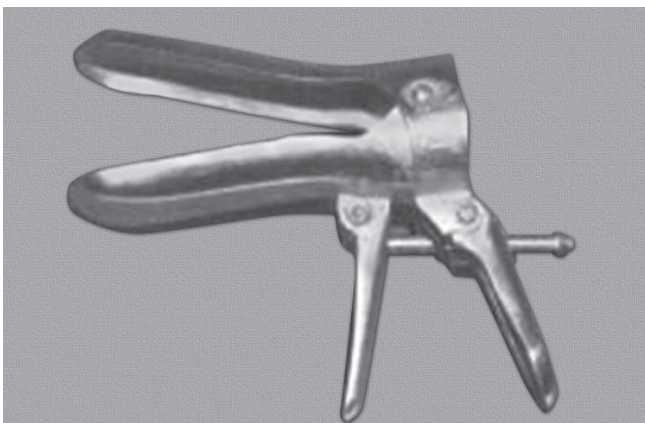
### CUSCO'S BIVALVED SELF-RETAINING VAGINAL SPECULUM (FIG. 4)

*Material:* Stainless steel.

*Sterilization:* Autoclaving and boiling.

#### Uses

- Routine per speculum examination in gynecology
- Colposcopy
- Endometrial biopsy
- Cervical punch biopsy
- Pap smear
- Insertion and removal of intrauterine contraceptive device (IUCO)
- Intrauterine insemination (IUI).



**Fig. 4:** Cusco's speculum

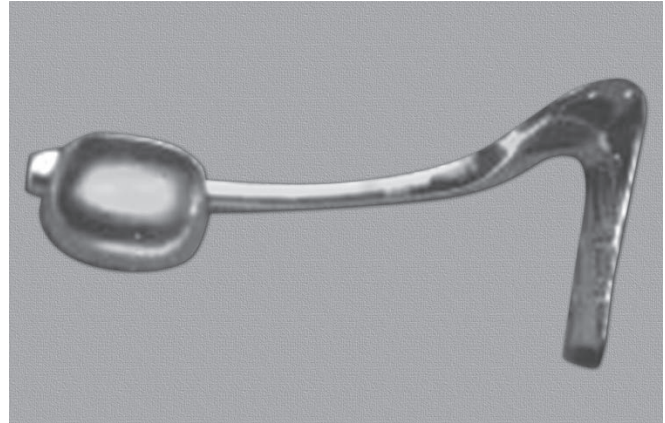
### AUVARD'S WEIGHTED SELF-RETAINING POSTERIOR VAGINAL SPECULUM (FIG. 5)

*Material:* Stainless steel.

*Sterilization:* Autoclaving.

#### Uses

- Vaginal hysterectomy
- Anterior colporrhaphy
- Kelly's repair
- Fothergill's/modified Fothergill's repair
- Vesicovaginal fistula repair
- Schauta's hysterectomy.



**Fig. 5:** Auvard's speculum

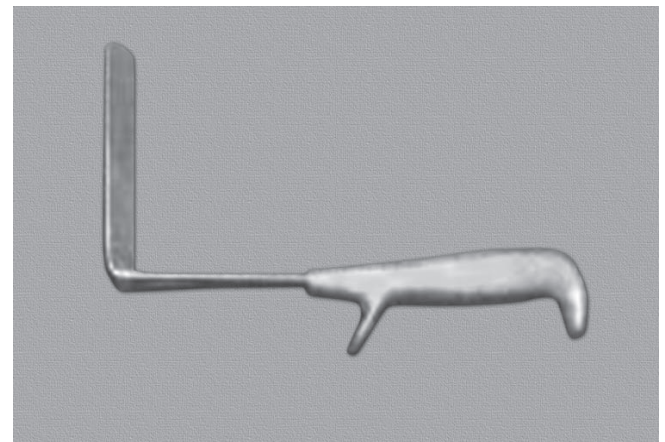
### LANDON BLADDER RETRACTOR (FIG. 6)

*Material:* Stainless steel.

*Sterilization:* Autoclaving and boiling.

#### Uses

- To retract the bladder away from cervix and uterus during vaginal hysterectomy. It is introduced into anterior pouch after the uterovesical fold of peritoneum has been opened
- To retract lateral and anterior vaginal walls during any vaginal operation .



**Fig. 6:** Landon bladder retractor

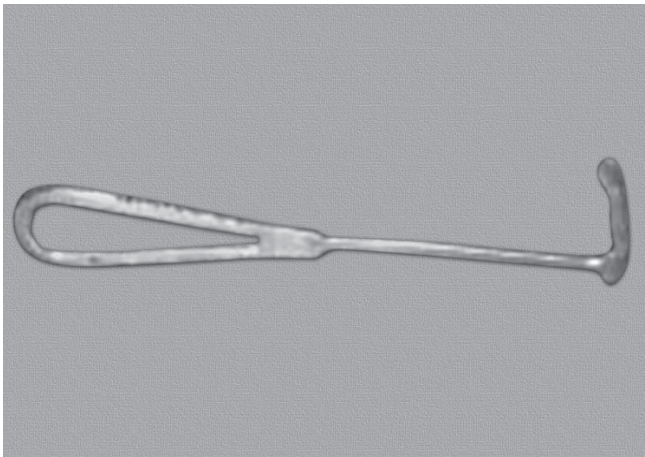
## RIGHT ANGLE RETRACTOR (FIG. 7)

*Material:* Stainless steel.

*Sterilization:* Autoclaving and boiling.

### Uses

- To retract abdominal wall during tubal ligation
- To retract bladder and posterior vaginal wall during hysterectomy
- To retract bladder during abdominal hysterectomy.



**Fig. 7:** Right angle retractor

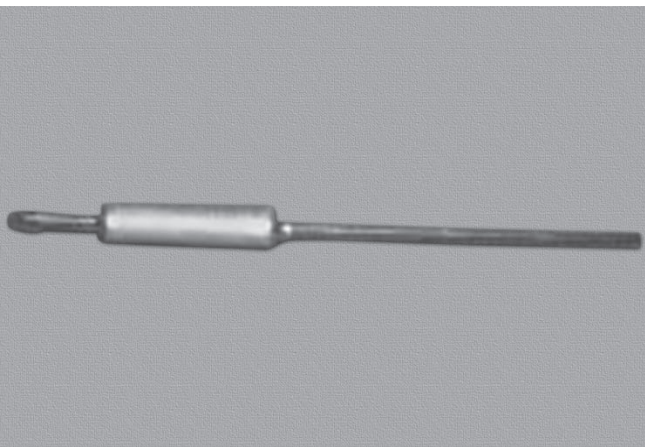
## FLUSHING CURETTE (FIG. 8)

*Material:* Stainless steel.

*Sterilization:* Autoclaving and boiling.

### Use

Dilatation and evacuation operation.



**Fig. 8:** Flushing curette

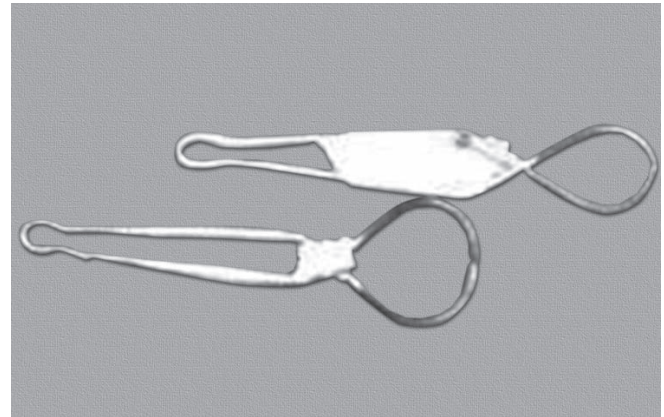
## TOWEL CLIP (FIG. 9)

*Material:* Stainless steel.

*Sterilization:* Autoclaving and boiling.

### Uses

- For draping
- Can be used for hemostasis.



**Fig. 9:** Towel clip

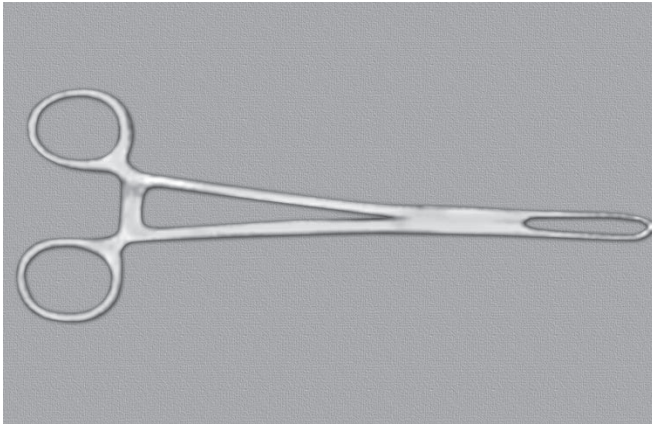
## ALLIS TISSUE-HOLDING FORCEPS (FIG. 10)

*Material:* Stainless steel.

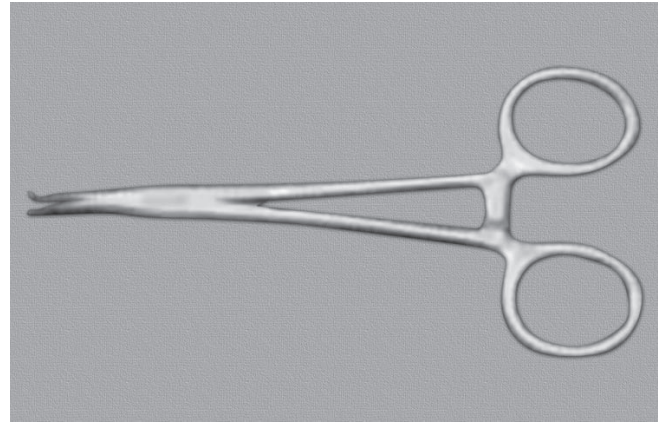
*Sterilization:* Autoclaving and boiling.

### Uses

- *General:* To hold the rectus sheath while opening and closing abdominal wall
- *Gynecologic:* To hold the edges of vagina
  - In anterior colporrhaphy, enterocele repair, colpoperineorrhaphy
  - In vaginal hysterectomy, abdominal hysterectomy
  - Fothergill's repair
  - Repair of vesicovaginal/rectovaginal fistula
  - To hold the cervix
  - Abdominal hysterectomy
  - To hold the lips of pediatric cervix
  - To hold the uterus
  - Vaginal and abdominal hysterectomy, myomectomy, utriculoplasty
  - Marchetti test for detection of stress urinary incontinence.
- *Obstetric*
  - In lower segment cesarean section (LSCS) to hold angles of uterine incision
  - For correction of acute inversion of uterus.



**Fig. 10:** Allis tissue holding forceps



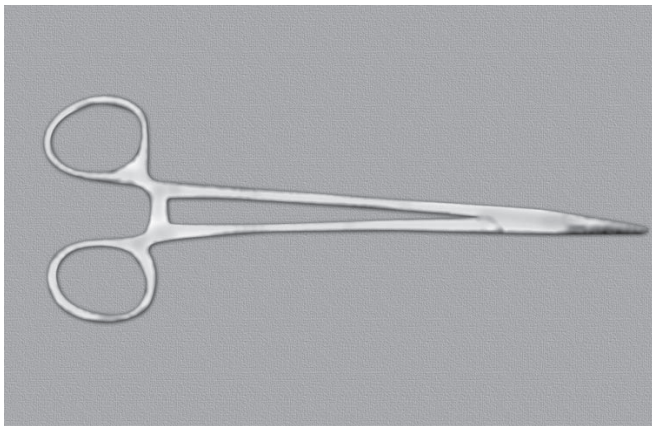
**Fig. 12:** Curved artery forceps

### NEEDLE HOLDER (FIG. 11)

*Material:* Stainless steel.  
*Sterilization:* Autoclaving.

#### Use

To hold needle during suturing.



**Fig. 11:** Needle holder

### ARTERY FORCEPS (FIG. 12)

*Material:* Stainless steel.  
*Sterilization:* Autoclaving.

#### Uses

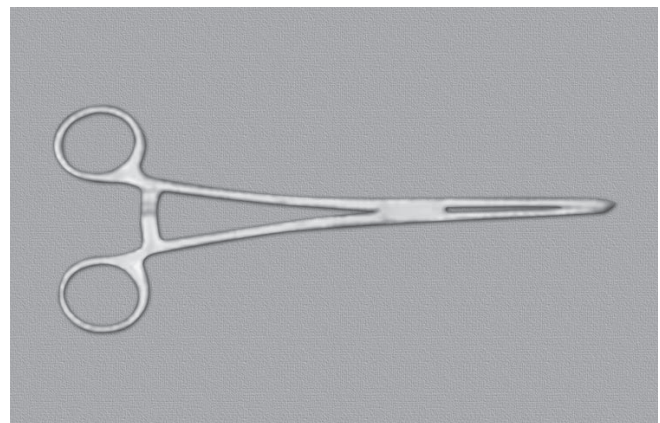
- For hemostasis
- Holding structures like peritoneum, rectus sheath, vessels, muscles, etc. during any operative procedure
- For suture removal
- Can be used for clamping placenta after delivery of baby

### SPONGE-HOLDING FORCEPS (FIG. 13)

*Material:* Stainless steel.  
*Sterilization:* Autoclaving and boiling.

#### Uses

- General
  - Painting and preparing parts preoperatively
  - Swab out cavities like vagina and pelvic cavity
- Gynecologic
  - For applying pressure over deep bleeding points during pelvic surgery
  - To check hemostasis of stumps during vaginal hysterectomy
  - For packing away omentum and intestines out of pelvis in gynecological operations
- Obstetric
  - To hold lips of pregnant cervix during tightening of as
  - For diagnosis and repair of cervical tear
  - Swab out blood in uterine cavity.



**Fig. 13:** Sponge-holding forceps

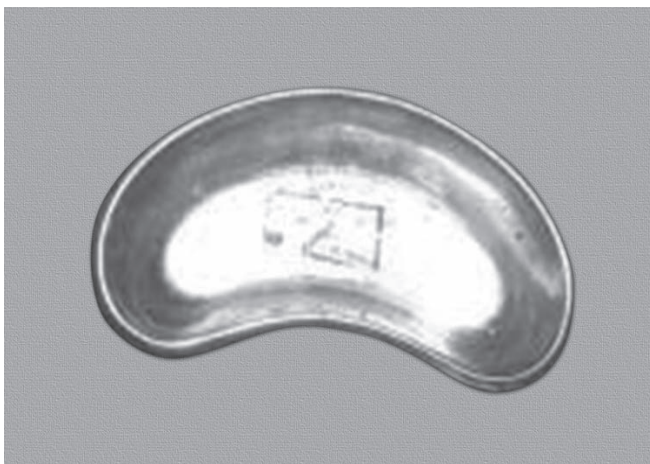
## KIDNEY TRAY (FIG. 14)

*Material:* Stainless steel.

*Sterilization:* Autoclaving and boiling.

### Uses

- To collect and hold urine
- To hold swabs for painting before any operation
- To collect placenta after delivery of baby
- To collect blood in ruptured ectopic pregnancy
- To collect vomitus



**Fig. 14:** Kidney tray

## KOCHER'S CLAMP (FIG. 15)

*Material:* Stainless steel

*Sterilization:* Autoclaving and boiling

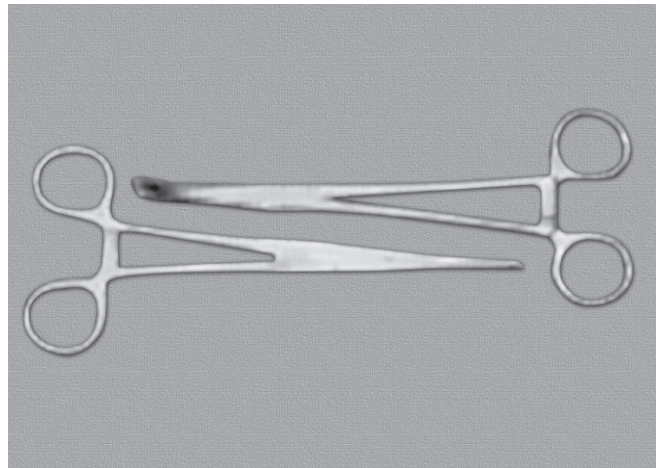
The blades may be curved or flat or straight. One blade has a longitudinal ridge which fits in a longitudinal groove on the other blade. It has transverse serrations on its blade.

### Uses

#### Hysterectomy

To damp the uterosacral ligaments, uterine blood vessels and the cornual structures or the infundibulopelvic ligaments in vaginal hysterectomy.

- Oophorectomy for ovarian cysts or tumors
- Removal of pedunculated leiomyomatous polyps
- Salpingectomy for tubal ectopic gestation
- Cesarean hysterectomy
- Clamping the umbilical cord of the newborn
- Artificial low rupture of membranes
- To hold the uterus during abdominal hysterectomy.



**Fig. 15:** Kocher's clamp

## TENACULUM (FIG. 16)

*Material:* Stainless steel.

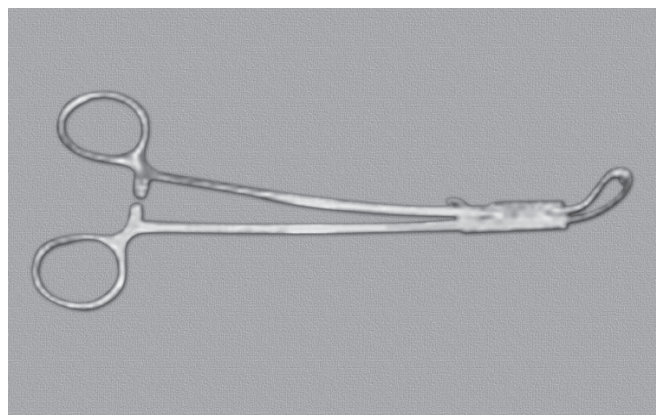
*Sterilization:* Autoclaving and boiling.

### Use

- To hold the lips of nulliparous cervix
- To hold cervical stump in subtotal hysterectomy.

### Special Use

- Hysterosalpingography
- Chromopertubation test
- Rubin's test.



**Fig. 16:** Tenaculum

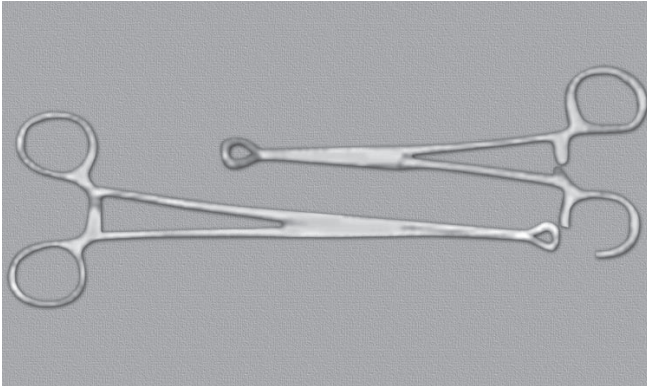
## BABCOCK FORCEPS (CURVED AND STRAIGHT) (FIG. 17)

*Material:* Stainless steel.

*Sterilization:* Autoclaving and boiling.

### Uses

- To hold tubular structures like:
  - Fallopian tubes in tubal sterilization, ruptured tubal ectopic pregnancy
  - Round ligaments
  - Ureters in Wertheim's hysterectomy
  - Vas in vasectomy
  - Appendix and cecum in appendicectomy.



**Fig. 17:** Straight Babcock forceps

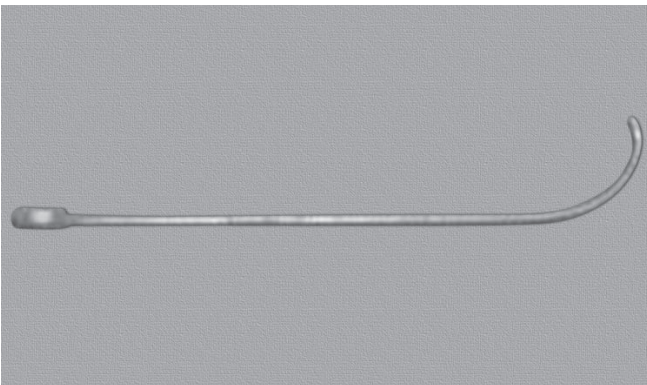
### BLADDER SOUND (FIG. 18)

*Material:* Stainless steel.

*Sterilization:* Autoclaving and boiling.

### Uses

- To define the limits of bladder during operation
- To confirm a suspected bladder injury during vaginal hysterectomy
- To determine length and direction of vesicovaginal fistulae
- To sound a calculus or foreign body in the bladder
- To differentiate bladder or urethral diverticulum from anterior vaginal wall cyst.



**Fig. 18:** Bladder sound

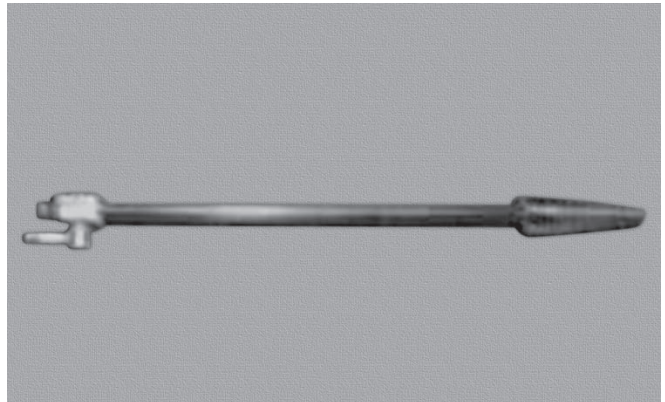
### LEECH WILKINSON CANNULA (FIG. 19)

*Material:* Stainless steel.

*Sterilization:* Autoclaving and boiling.

### Uses

- Hysterosalpingography
- Chromopertubation test in laparoscopy
- Hydrotubation.



**Fig. 19:** Leech Wilkinson cannula

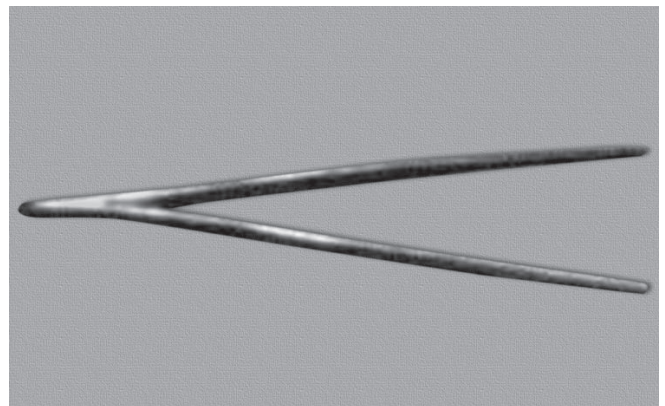
### PLAIN FORCEP (FIG. 20)

*Material:* Stainless steel.

*Sterilization:* Autoclaving and boiling.

### Uses

- To hold thin delicate structures such as peritoneum
- Muscles, vessels, thin fascia, intestinal wall, bladder wall, etc.
- During suture removal
- Packing abdominal cavity during abdominal operations.



**Fig. 20:** Plain forcep

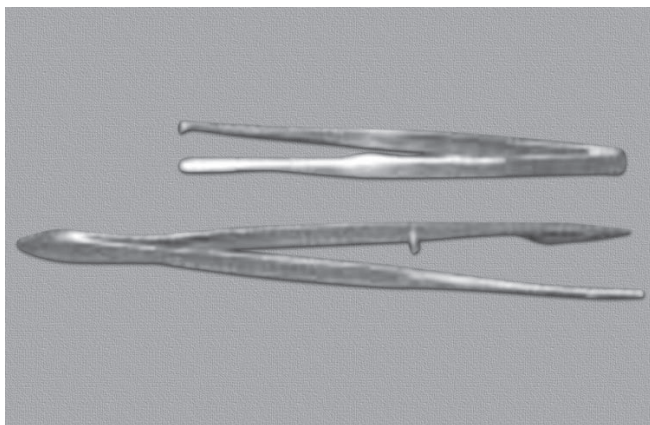
## TOOTH FORCEP (FIG. 21)

*Material:* Stainless steel.

*Sterilization:* Autoclaving and boiling.

### Uses

- To hold tough structures like:
  - Tendon
  - Fascia
  - Skin
  - Rectus sheath
  - Uterine wall, etc.
- Can be used for hemostasis.



**Fig. 21:** Tooth forcep

## HEGAR DILATOR (FIG. 22)

*Material:* Stainless steel.

*Sterilization:* Autoclaving and boiling.

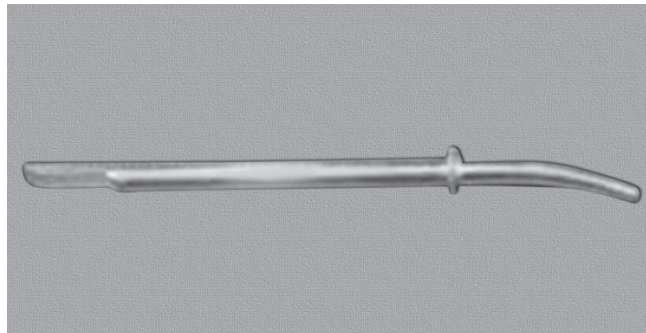
It is a solid rod-curved near the tip and tapering towards the tip. The curve is shallow and the dilating portion is within terminal 1.5 cm of the dilator.

### Uses

For the rapid dilatation in:

- Prior to endometrial curettage
- Prior to suction aspiration for first trimester MTP
- Prior to suction evacuation of mole
- Removal of endometrial polyp, placental polyp, leiomyomatous polyp
- Hysteroscopy
- Amputation of cervix, Fothergill's operation, following cervical conization
- Cervical stenosis

- Application of intrauterine radiotherapy
- Primary dysmenorrhea
- Diagnosis of incompetent os.



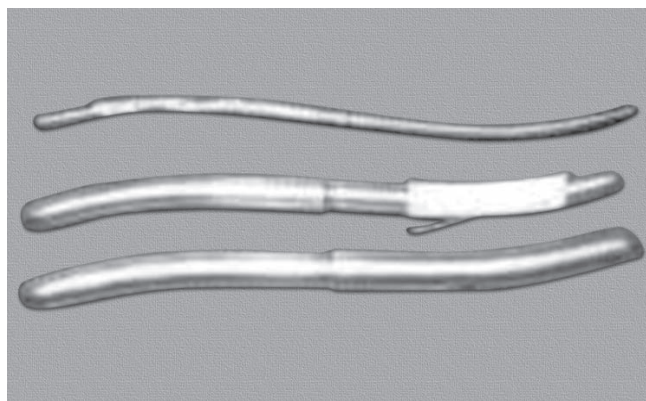
**Fig. 22:** Hegar dilator

## FENTON DILATOR (FIG. 23)

It is similar to Hegar dilator except for two important differences – it is more tapering and hollow inside.

### Use

Same as that of Hegar dilator.



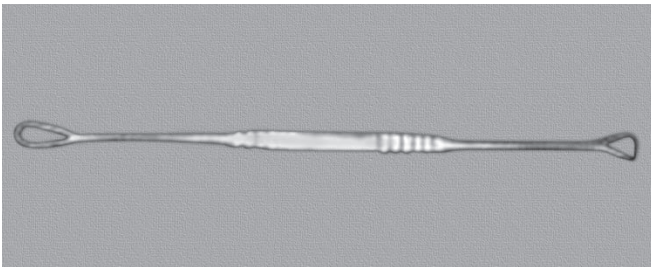
**Fig. 23:** Fenton dilator

## UTERINE CURETTE (FIG. 24)

### Uses

- Gynecological uses
  - Diagnostic
    - Primary or secondary infertility for ovulation detection
    - Tuberculous endometritis
    - Abnormal uterine bleeding
    - Endometrial hyperplasia/endometrial carcinoma

- Carcinoma cervix
- Secondary amenorrhea
- Postmenopausal bleeding
- o Therapeutic
  - Dysfunctional uterine bleeding (DUB)
- Asherman's syndrome
- To remove embedded intrauterine device (IUD)
- Obstetrical uses:
  - o MTP, check curettage
  - o Blunt curettage in abortions
  - o Secondary persistent pulmonary hypertension (PPH), subinvolution.



**Fig. 24:** Sharp and blunt curette

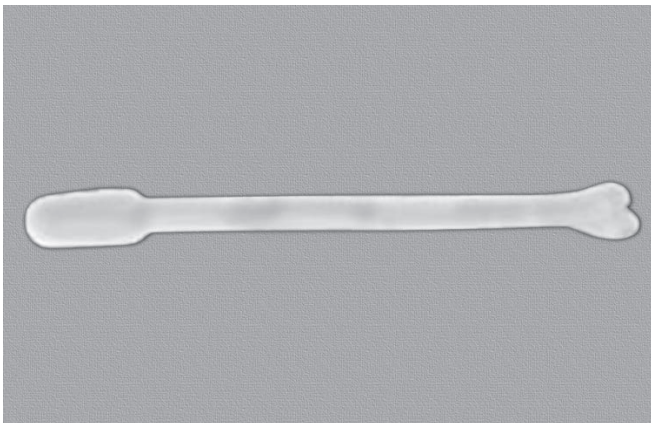
### AYRE'S WOODEN SPATULA (FIG. 25)

*Material:* Wood.

*Sterilization:* Dry heat.

#### Uses

- Pap smear
- To take surface biopsy in obvious cases of carcinoma cervix
- Hormonal cytology
- Cervicovaginal smear
- Buccal smear.



**Fig. 25:** Ayre's wooden spatula

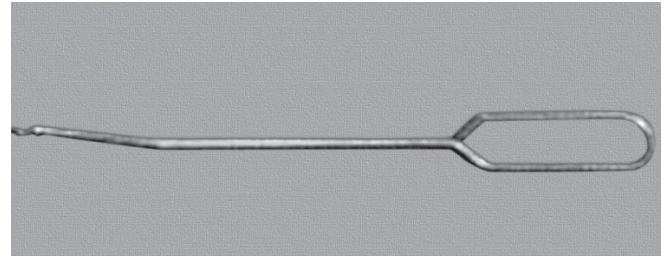
### IUCD REMOVING HOOK (FIG. 26)

*Material:* Stainless steel.

*Sterilization:* Autoclaving and boiling.

#### Uses

- Removal of an embedded IUD from the uterine cavity
- Removal of tubal prosthesis from the uterine cavity.



**Fig. 26:** IUCD removing hook

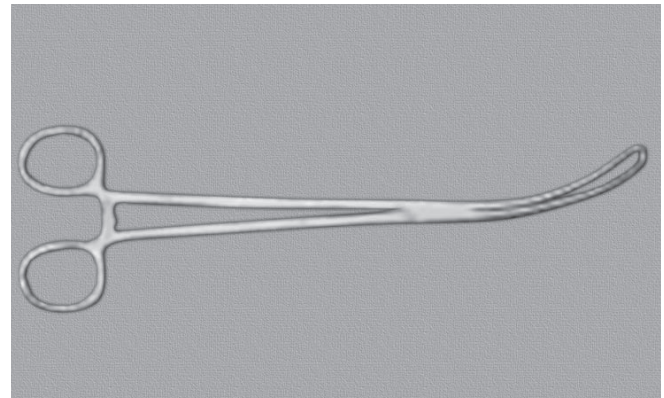
### VULSELLUM (FIG. 27)

*Material:* Stainless steel.

*Sterilization:* Autoclaving and boiling.

#### Uses

- Anterior lip held in:
  - o Endometrial biopsy
  - o IUCD insertion
  - o Intrauterine insemination
  - o Vaginal hysterectomy
  - o Cauterization of cervix and cervical biopsy.
- Posterior lip held in:
  - o Colorpuncture for suspected ruptured ectopic pregnancy
  - o Culdoscopy
  - o Posterior colpotomy.



**Fig. 27:** Vulsellum



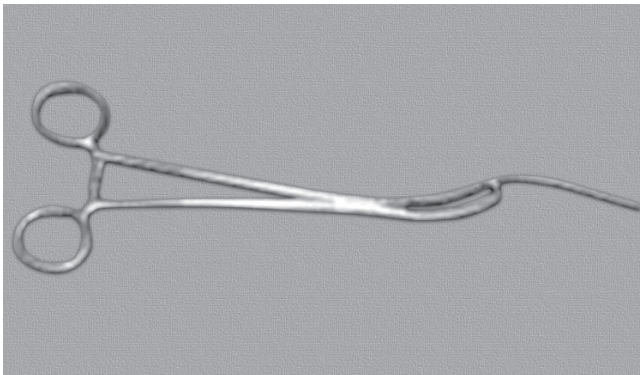
## HULKA UTERINE MANIPULATOR (FIG. 28)

*Material:* Stainless steel.

*Sterilization:* Autoclaving and boiling.

### Uses

- It is used to elevate and manipulate position of uterus for following:
  - Laparoscopic sterilization
  - Sterilization by minilaparotomy
  - Visualization of pelvic structures by laparoscopy.



**Fig. 28:** Hulka uterine manipulator

## VITTOON UTERINE MANIPULATOR (FIG. 29)

*Material:* Stainless steel.

*Sterilization:* Autoclaving and boiling.

### Uses

Same as that of Hulka uterine manipulator.



**Fig. 29:** Vitoon uterine manipulator

## DREW-SMYTHE CATHETER (FIG. 30)

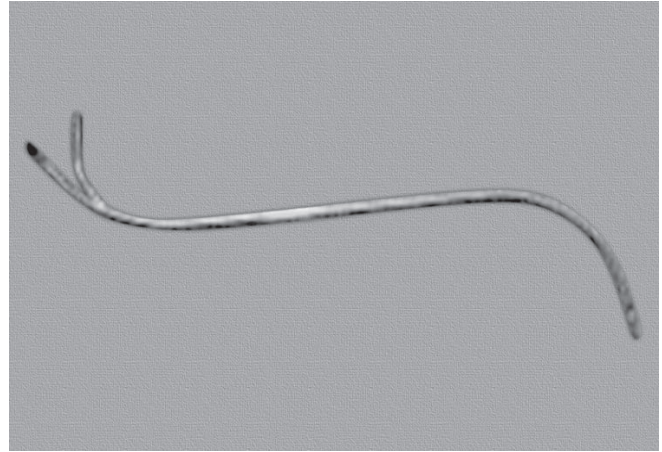
*Material:* Stainless steel.

*Sterilization:* Autoclaving and boiling.

It is S-shaped and has a side opening to drain liquor amnii. It has a spring loaded stylet with a blunt tip.

### Uses

- High amniotomy
- To drain a hydrocephalic head through a spina bifida, in case of a breech delivered up to the head.



**Fig. 30:** Drew-Smythe catheter

## FLUSHING CANNULA (FIG. 31)

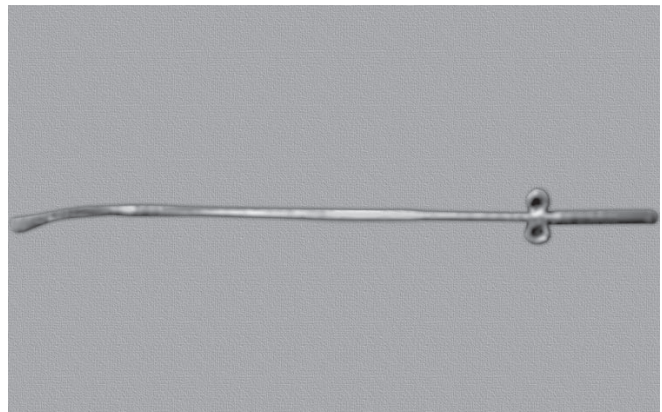
*Material:* Stainless steel.

*Sterilization:* Autoclaving and boiling.

### Uses

Used for suction to keep the operating field dry during operation in narrow field, for example:

- Tuboplasty
- Repair of vesicovaginal fistula and rectovaginal fistulae.



**Fig. 31:** Flushing cannula

## OVUM FORCEPS (FIG. 32)

Designed by Haywood Smiths.

### Parts

#### Blades

- Blades are spoon-shaped, fenestrated and have blunt ends
- Longitudinal fenestrations can hold good amount of tissue.

#### Lock

- It is absent .
  - Anything held in blades is firmly caught but not nipped and so no crushing.
  - Ovum forceps is differentiated from sponge holding forceps by following points:
    - It has no lock
    - It has no serrations
- Catch lock is absent so less chances of injury to intra-abdominal structures.

### Uses

- Evacuation of products of conception in abortion and vesicular mole.
- Evacuation of products of conception in secondary PPH.

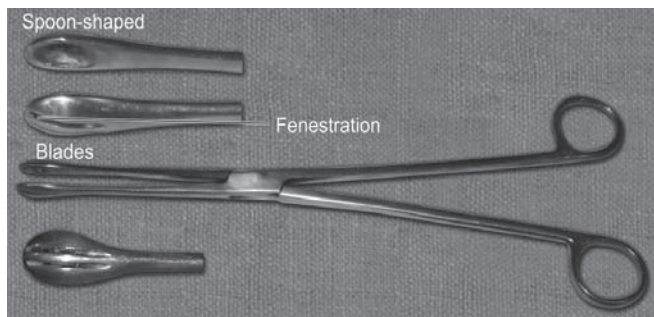


Fig. 32: Haywood Smiths ovum forceps

## KARMAN CANNULA (FIG. 33)

A long tubular structure made of plastic or metal.

- Types: Rigid or flexible
- Sizes: 4-12 mm
- Parts
  - *Distal end*: Double whistle at the terminal end.
  - *Proximal end*: Fixes into syringe.

- Superior overhanging edge acts as a curette.

The number of cannula corresponds to diameter of cannula in millimeters. A plastic cannula is preferred because it is less traumatic, transparent and disposable.

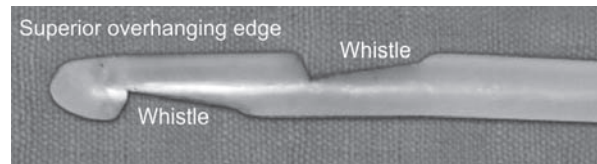


Fig. 33: Karman cannula

## KARMAN MENSTRUAL REGULATION SYRINGE (MR SYRINGE) (FIG. 34)

Used for aspiration of uterine contents within 42 days of missed period.

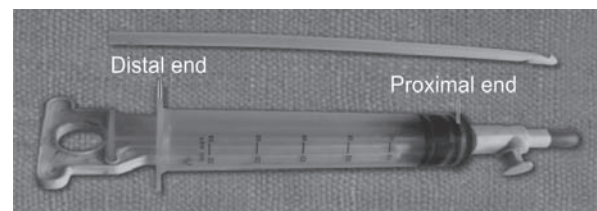


Fig. 34: MR syringe

## MANUAL VACUUM ASPIRATION SYRINGE (MVA SYRINGE) (FIG. 35)

For aspiration of uterine contents till 12 weeks. Superior version of MR is MVA.

WHO recommends MVA a procedure of choice before 10 weeks and safely up to 12 weeks.

### Syringe

60 mL syringe capable of creating vacuum of 650 mm (65 cm) of Hg. It has a barrel and a piston. There is a pressure controlled valve system. When the lock is pressed and piston pulled out a negative pressure is created in syringe.

### Uses of Cannula

- Medical termination of pregnancy (MTP)
- Sand E in incomplete abortion, missed abortion
- Sand E in molar pregnancy
- Cannula is used in draining (SF after craniotomy in hydrocephalus/dead baby
- Endometrial aspiration for endometrial pathology.

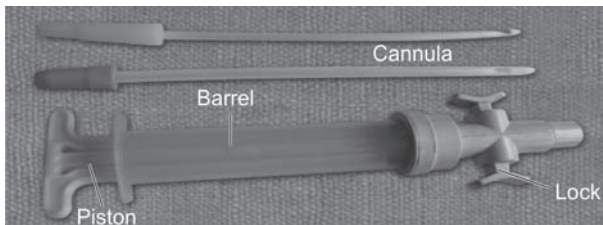
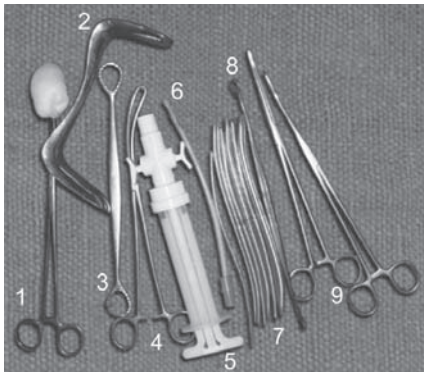


Fig. 35: MVA instruments

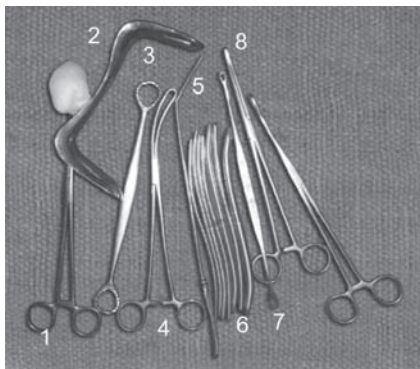
### Instrument Tray for MTP (Fig. 36)



1. Sponge holder for cleaning	2. Speculum
3. Anterior vaginal wall retractor	4. Vulsellum
5. Manual vacuum aspiration (MVA) syringe	6. Cannula
7. Hegar's dilators	8. Uterine curette
9. Sponge holder	

Fig. 36: MTP set

### Instrument Tray for D and C (Fig. 37)



1. Sponge holder for cleaning	2. Speculum
3. Anterior vaginal wall retractor	4. Vulsellum
5. Uterine sound	6. Hegar's dilators
7. Uterine curette	8. Sponge holder

Fig. 37: D and C set

### LAMINARIA TENT (FIG. 38)

Made up of hygroscopic material derived from the stems of seaweed called *Laminaria japonica*. It swells up by absorbing fluid (hygroscopic) and is a slow dilator of cervix.

#### Parts

- Stem is 5.5-6 cm
- Small, medium, large sizes are available according to the diameter
- A string is looped through one end and tied to gauze for easy removal (Fig. 38).
- Two or three tents can be introduced side by side, if required into the cervical canal.
- Tents swell up 3-5 times of their size after absorbing secretions of cervical canal in 12-24 hours and dilate cervix.
- Sterilized by dipping in absolute alcohol.

#### Uses

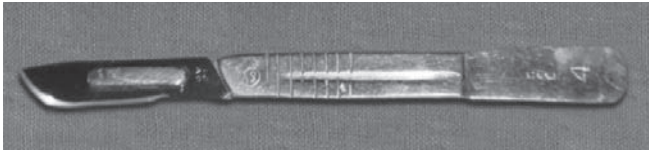
- First and second trimester pregnancy termination
- Expulsion of Poe in missed abortion, incomplete abortion
- Induction of labor.



Fig. 38: Laminaria tent

### BARD PARKER'S KNIFE (FIG. 39)

- Popularly known as surgeon's knife.
- It has a straight handle with a notch. Different sizes of blades can be attached with different sizes of handles. Larger sizes of blades are used for larger tissues and incisions. Smaller sizes of blades are used for finer incisions (Fig. 39).
- The no. 10 scalpel blade is the most commonly used size. Acute angle of no. 11 blade is used for giving stab incisions for drains and in draining abscesses, e.g. Bartholin's abscess.



**Fig. 39:** Handle with blade

### **BONNEY'S MYOMECTOMY CLAMP (FIG. 40)**

- Designed by Victor Bonney
- It is used to reduce intraoperative blood loss in operations.

#### **Parts**

##### **Blades**

- These are at an angle of 120° to the shaft
- It has overlapping transverse bar dividing it into two compartments
- There is a rubber tubing in anterior half of the compartment which prevents trauma to the structures.

##### **Shaft**

##### **Handle**

- Handle has two pairs of finger grips (Fig. 40)
- Distal finger grip is used for applying and removing the instrument
- Proximal finger grip can open up the instrument wider in bulky uterus.

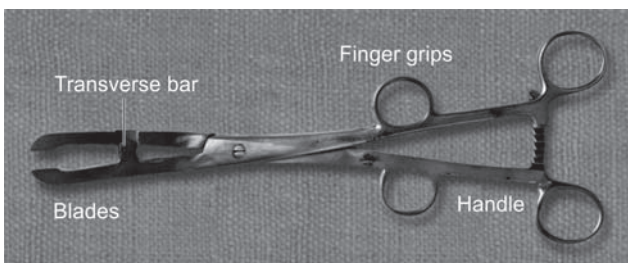
#### **Uses**

To control bleeding during operation of:

- Myomectomy
- Hysterotomy
- Metroplasty.

Use has become less because myoma can be removed by latest methods:

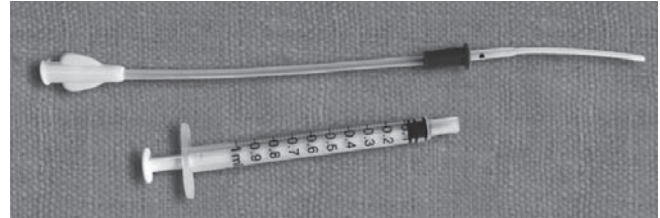
- Laparoscopic myomectomy
- Motorized morcellation
- Mini lap incision.



**Fig. 40:** Bonney's myomectomy clamp

### **INTRAUTERINE INSEMINATION CANNULA (FIG. 41)**

It is a thin flexible catheter which is placed in uterine cavity for intrauterine insemination (IUI).



**Fig. 41:** Intrauterine insemination cannula

### **CERVICAL PUNCH BIOPSY FORCEPS (FIG. 42)**

It is a strong instrument.

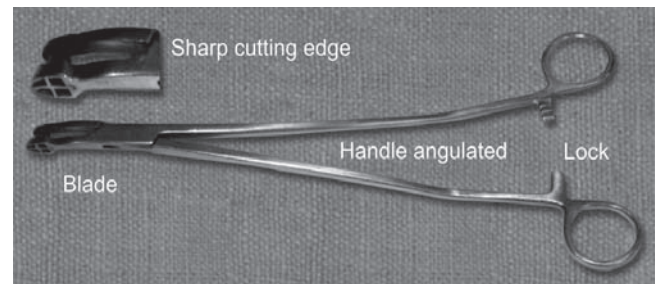
#### **Parts**

##### **Blade**

- There are two blades
- Smaller blade has sharp cutting edge and fits into larger blade (Fig. 42)
- Specimen is held in it like a basket.

##### **Handle**

- Handle is angulated to avoid obstruction of field of vision.



**Fig. 42:** Cervical punch biopsy forceps

### **CRYOMACHINE (FIG. 43)**

Used for cryosurgery (Syn:cryocautery/cryotherapy) which is an ablative method used to eliminate cervical intraepithelial lesion.

Compressed gas creates extremely cold temperature that necroses cervical epithelium. As compressed gas expands it drains heat away from cervical epithelium and causes destruction of cell by crystallization of intracellular fluid.

## Parts

*Cryoprobe:* Tip is made of silver or copper and is in contact with surface of cervix.

## Refrigerating Gas Cylinder

i. *Nitric oxide:* Most common gas which is used.

Probe temperature can reach (-65°C)

ii. *CO<sub>2</sub>:* Temperature (-60°C)

iii. *Freon:* Temperature (-60°C)

Cryogun is attached with connecting tube to a cylinder of refrigerating gas, i.e. nitrous oxide cylinder with pressure gauge.

Pressure of at least 20 pounds is required.

## Patient Evaluation

- CIN is confirmed by colposcopy/cervical biopsy and there should be no evidence of invasive cancer.
- Woman should not be pregnant or recently delivered.
- The entire lesion is located in ectocervix with no extension in endocervix and vagina.
- The lesion is visible in its entire extent and does not extend more than 2-3 mm into the endocervical canal.
- The lesion should be adequately covered by the largest cryoprobe and lesion should extend less than 2 mm beyond the cryoprobe.

## Technique

- *Informed consent:* Preferred postmenstrual and generally no analgesia is required. Dorsal lithotomy position.
- *Cryoprobe placement:* Appropriate probe is placed firmly on cervix to cover transformation zone and lesion.
- *Ice ball formation:* Gas tank valve is opened and pressure of 20 pounds is created. The trigger is squeezed and gas forms a layer called 'ice ball' on cervix (Fig. 43).
- The portion of ice ball in which temperature falls below -20°C is called "lethal zone".
- This zone extends from center of cryoprobe to a point 2 mm inside outer ice ball edge. Cells reduced to -20°C (or one minute or more undergo cryonecrosis).
- When cryotherapy is performed the ice ball is allowed to enlarge until it reaches a mark 7 mm distal to probe margin.

- This ensures freezing depth of 7 mm, (i.e. 5 mm lethal zone). A depth of 5 mm is sufficient to treat endocervical glandular crypt involvement of most lesions.
- *Caution:* Cryoprobe should not contact the vaginal side walls. If it happens gas delivery is stopped. Allow probe warming.

Single freeze	3 Min	5 Min	
		(Freeze)	(Thaw)
Double freeze	3 Min	5 Min	3 Min
(Preferred)	(Freeze)	(Thaw)	(Freeze)



Fig. 43: Cryomachine

## COLPOSCOPE (FIG. 44)

A binocular microscope to study the epithelium of lower anogenital tract under illumination and magnification.

It was introduced by Hans Hinselmann in 1927.

For details refer to Chapter 148 of the guide.

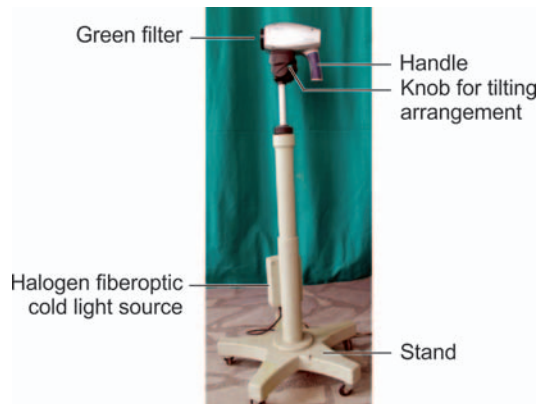
## Technique of Colposcopy

- Informed consent.
- *Position:* Lithotomy.
- No P/V examination. Cervix is exposed with bivalve speculum and inspect cervix and vagina.
- Colposcope is focused on external os at a distance of 20 cm.
- Magnification taken is 6x-15x.
- Pap smear is taken, if required.
- Purpose of colposcopy is to identify SC1 (Fig. 44), detect suspicious area, take direct biopsy.
- Saline technique physiological saline is applied with cotton swab 2" x 2" before application of acetic acid and Lugol iodine. This helps in removing the cervical mucus and studying the subepithelial vascular pattern.
- Green filter to study vascular pattern. Blood vessels appear black (Fig. 44).

- Application of acetic acid 3-5% acetic acid is applied with cotton balls held by sponge holder.

*Principle:* Acetic acid precipitates protein (clumps nuclear chromatin) and abnormal epithelium appears white called acetowhite (AW) change (Fig. 44).

- Application of Schiller's iodine (Lugol iodine test) (Fig. 44).



**Fig. 44:** Colposcope

Normal epithelium is mahogany or black due to glycogen content.

Dysplastic epithelium is mustard or saffron yellow because it is glycogen free.

Iodine uptake is only in glycogen containing squamous epithelium as iodine is glycolytic.

- Endocervical curettage and biopsy is taken, if it is required.

- Findings are documented satisfactory or unsatisfactory (if SCJ is seen or not).

- Normal findings:

- Normal columnar epithelium is red grape-like.
- Normal squamous epithelium is homogeneous gray.

- Insignificant findings:

- Acetowhite epithelium is shiny or semi transparent.
- Borders are not sharp.
- *Vessels:* Fine punctuation, fine mosaic, ICD (intercapillary distance) is short.

- Abnormal findings significant:

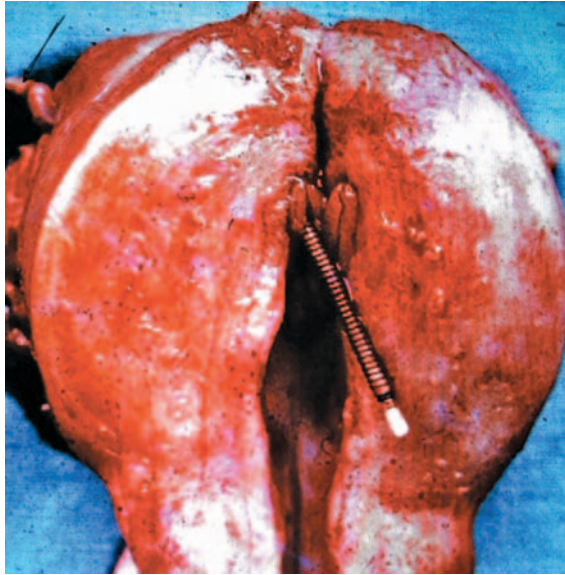
- Dense acetowhite area with sharp border. Appears faster and lasts longer (Fig. 44).
- Vessels are dilated, irregular or coiled (coarse punctuation and mosaic) atypical vessels.
- Intercapillary distance is more.

### Advantages

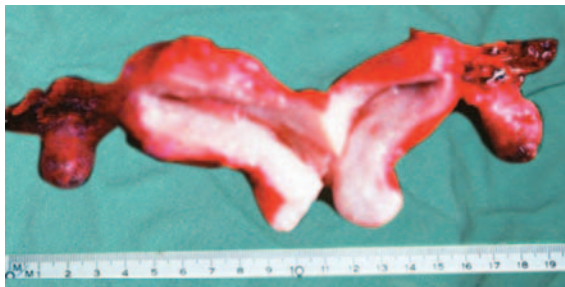
- Colposcopy can locate abnormal areas so that selected biopsy can be taken
- Unnecessary biopsy can be avoided, if findings are normal
- Colposcopy can reduce size of biopsy and conization
- Therapeutically colposcopic ablative techniques can be done in preinvasive cancer of cervix and vagina.

*Source of Figures 1 to 44:* Principles and Practice of Obstetrics and Gynecology for Postgraduates. Instruments in Obstetrics and Gynecology, Jaypee Brothers Medical Publishers (P) Ltd. Narendra Malhotra, PK Shah, Hema Divakar (Eds). Instruments in Obstetrics and Gynecology, P 1258.

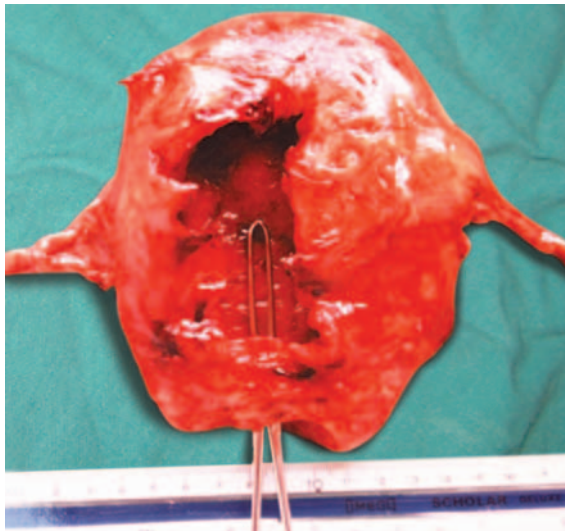
## B. SPECIMENS



**Fig. 1:** Copper T in uterine musculature



**Fig. 2:** Double uterus (cut specimen)



**Fig. 3:** Hysterectomy for classical scar rupture



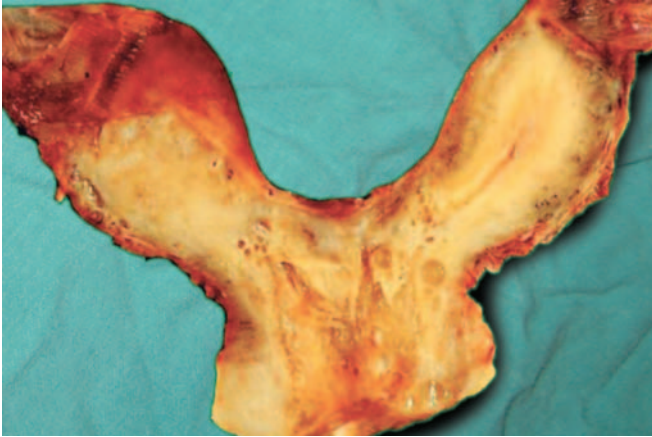
**Fig. 4:** Specimen showing submucous fibroid



**Fig. 5:** Procidentia



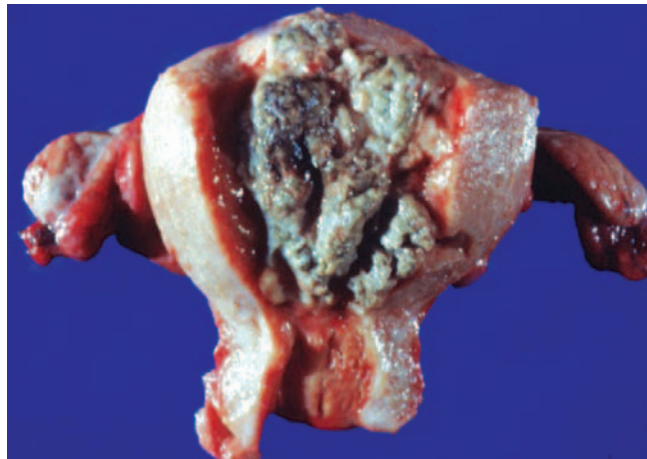
**Fig. 6:** Specimen showing ovary with multiple follicular cysts



**Fig. 7:** Bicornuate uterus with single cervix



**Fig. 8:** Carcinoma of vulva

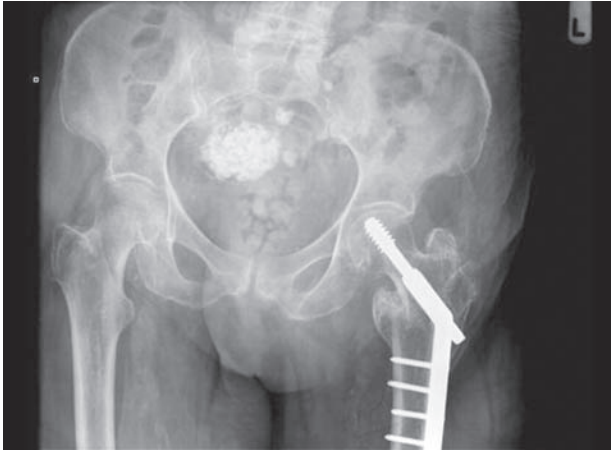


**Fig. 9:** Endometrial adenocarcinoma

Source of Figures 1 to 9: *Principles and Practice of Obstetrics and Gynecology for Postgraduates. Instruments in Obstetrics and Gynecology*, Jaypee Brothers Medical Publishers (P) Ltd. Narendra Malhotra, PK Shah, Hema Divakar (Eds). Specimens in Obstetrics and Gynecology, P 1287.



## C. RADIOLOGY IN GYNECOLOGY



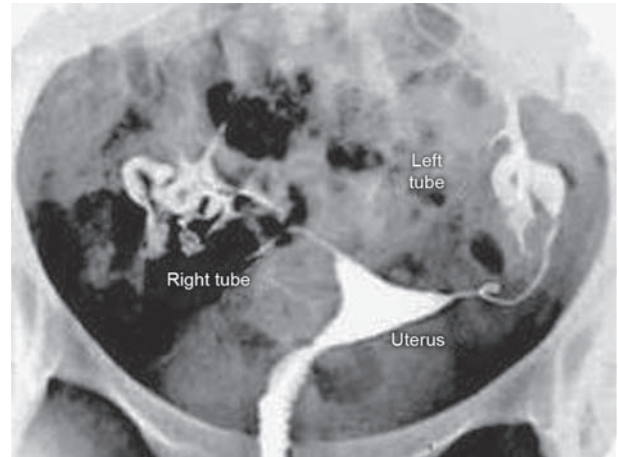
**Fig. 1:** Calcified uterine fibroid



**Fig. 2:** Plain abdominal radiograph with a tooth like opacity projected over the left sacroiliac joint (arrow)



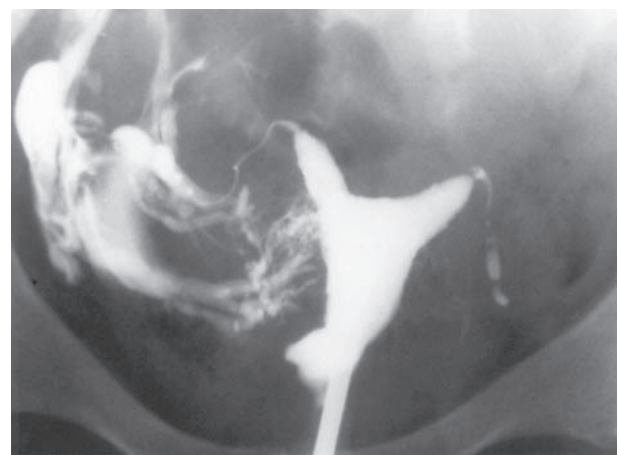
**Fig. 3:** Plain radiograph of pelvis showing Cu-T in pelvis



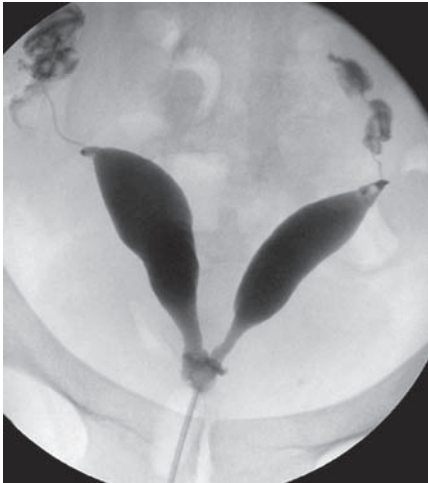
**Fig. 4:** Hysterosalpingogram showing visualization of normal uterine cavity with normal visualization of both fallopian tubes and spilling, also seen venous intravasation



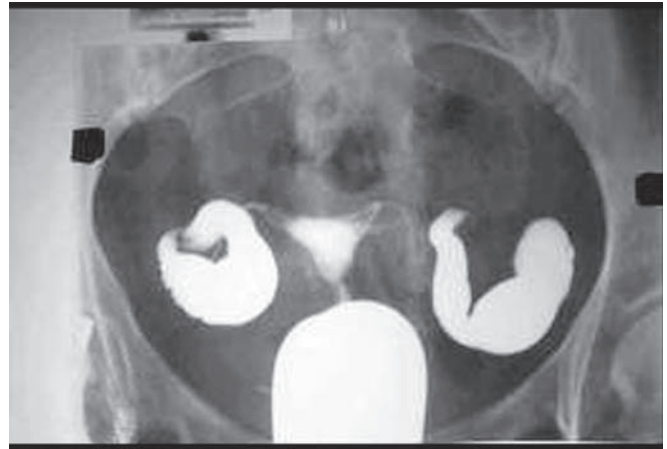
**Fig. 5:** Hysterosalpingogram showing unicornuate uterus



**Fig. 6:** Arcuate uterus



**Fig. 7:** Uterus didelphys



**Fig. 9:** Hysterosalpingogram showing normal uterine cavity with bilateral hydrosalpinx



**Fig. 8:** Bicornuate uterus



**Fig. 10:** Hysterosalpingogram showing uterovesical fistula

Source of Figures 1 to 10: Principles and Practice of Obstetrics and Gynecology for Postgraduates. Instruments in Obstetrics and Gynecology, Jaypee Brothers Medical Publishers (P) Ltd. Narendra Malhotra, PK Shah, Hema Divakar (Eds). Obstetrics and Gynecology, P 1299.

