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”
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 Gynec. 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


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

It would not be fair, therefore, to ignore the people who have played an important part in making me known as ‘Dr Sakshi Arora’ and to whom I am deeply grateful.

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# Contents

1. Anatomy of the Female Genital Tract .......................... 1
2. Reproductive Physiology and Hormones in Females .......... 19
3. Menopause and HRT ................................................. 44
4. PCOD, Hirsutism and Galactorrhea ............................ 52
5. Congenital Malformations ......................................... 68
6. Sexuality and Intersexuality ........................................ 82
7. Infections of the Genital Tract ..................................... 104
8. Urogynecology ......................................................... 125
9. Infertility ............................................................... 148
10. Contraception ......................................................... 176
11. Uterine Fibroid ......................................................... 220
12. Endometriosis and Dysmenorrhea ............................. 237
13. Disorders of Menstruation .......................................... 251
14. A. Gynecological Oncology: Uterine Cancer ................. 285
    B. Gynecological Oncology: CIN Cancer Cervix .......... 302
    C. Gynecological Oncology: Ovarian Tumors ............. 332
    D. Gynecological Oncology: Miscellaneous Tumors .... 368
15. Gynecological Diagnosis and Operative Surgery .......... 379
16. Miscellaneous Question Bank .................................... 390

## Latest Papers

- i. AIIMS Nov 2015 .................................................. 395
- ii. AIIMS May 2015 ................................................ 399
- iii. PGI May 2015 .................................................. 401
- iv. PGI Nov 2014 .................................................... 406

## Annexures

- Color Plates ............................................................ 407
<table>
<thead>
<tr>
<th>Symbols used in the book</th>
<th>Meaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>🌡️</td>
<td>Key points</td>
</tr>
<tr>
<td>🕵️‍♂️</td>
<td>Previously asked MCQs</td>
</tr>
<tr>
<td>🔄</td>
<td>Important concepts</td>
</tr>
<tr>
<td>📂</td>
<td>Definition</td>
</tr>
<tr>
<td>📘</td>
<td>Mnemonic</td>
</tr>
</tbody>
</table>
External Genital Organs (Syn: Vulva, Pudendum)

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

- **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.

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

**Important**

- 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**

<table>
<thead>
<tr>
<th>Anterior</th>
<th>Bladder (upper third)</th>
<th>Urethra (lower two-third)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posterior</td>
<td><strong>P</strong> = Pouch of douglas in the upper 1/3rd</td>
<td><strong>A</strong> = Ampulla of rectum in middle 1/3rd</td>
</tr>
<tr>
<td></td>
<td><strong>P</strong> = Perineal body in lower 1/3rd</td>
<td></td>
</tr>
<tr>
<td>Lateral</td>
<td><strong>Medicos</strong> = Mackenrodt’s ligament or pelvic cellular tissue</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Love</strong> = Levator ani muscle</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Books</strong> = Bulbocavernous muscle</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vestibular bulb</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bartholin’s glands</td>
<td></td>
</tr>
<tr>
<td></td>
<td>From above downwards</td>
<td></td>
</tr>
</tbody>
</table>

**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.

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

- Uterine vessels
- Mackenrodt’s ligament
- Ureter
- Vagina has inhabitant bacteria called **Doderlein’s bacteria** which is a lactobacilli and converts the glycogen present in vaginal epithelium into lactic acid 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.
Chapter 1  Anatomy of the Female Genital Tract

### Age and Vaginal pH

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

**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\(^9\). 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\(^9\).
- 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\(^9\).
- **Intermediate cells:** Which are predominant when there is progesterone predominance\(^9\), 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\(^9\).

### 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.
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 (uterovesical 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 and has complex racemose glands secreting alkaline mucus (pH 7.8). Portio vaginalis or exocervix is lined by nonkeratinized stratified squamous epithelium. The place where columnar epithelium gradually changes to squamous epithelium is called squamocolumnar junction/transformation zone.

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
- Where uterus and cervix meet

Anatomical Internal os
Where endometrial canal becomes cervical canal anatomically

Histological Internal os
Where histologically epithelium of uterus changes to epithelium of cervix

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.
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

**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:**
  - **Interstitium (Intramural):** 1.25 cm long and 1 mm diameter (narrowest part). It has no longitudinal muscles, only circular muscles are present and acts as anatomical sphincter.
  - **Isthmus:** 2.5 cm long and 2 mm in diameter (second narrowest part); acts as physiologic sphincter.
  - **Ampulla:** Widest and longest part (5 cm) and fertilization occurs here.
  - **Fimbria/infundibulum:** 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 whose function is not known. 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 / bulbourethral glands in males.
- They are 2 in number and of racemose type.
- 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.
- They are impalpable unless enlarged.
- The acini is lined by single layer of low columnar or cuboidal cells.
Bartholin’s duct is 2 cm long 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.

Duct is lined by multilayered columnar epithelium (not by transitional epithelium as is usually stated).

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 prostrate 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 L2 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 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.

Bartholin’s gland

Multilayered columnar cells (Not transitional)

Stratified squamous epithelium

Transitional epithelium

Columnar epithelium

High columnar epithelium

Squamous epithelium

Ciliated columnar epithelium

**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).
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- 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

<table>
<thead>
<tr>
<th>Visceral branches</th>
<th>Anterior division</th>
<th>Posterior division</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superior vesical</td>
<td></td>
<td>Nil</td>
</tr>
<tr>
<td>Obliterated umbilical</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inferior vesical</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Middle rectal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uterine</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parietal branches</th>
<th>Anterior division</th>
<th>Posterior division</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaginal</td>
<td></td>
<td>Iliolumbar</td>
</tr>
<tr>
<td>Obturator</td>
<td></td>
<td>Sacral</td>
</tr>
<tr>
<td>Inferior gluteal</td>
<td></td>
<td>Superior gluteal</td>
</tr>
<tr>
<td>Internal pudendal</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**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.
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, lliococcygeus, and coccygeous 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 pubovaginal 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 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 Ischiocavernous
  - Fibres of external anal sphincter.

**Broad Ligament**

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

**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 ligaments/Mackenrodt's ligaments/transverse cervical ligaments** that extends in fan-shaped manner from pelvic wall and inserted into the lateral supravaginal cervix.
Pubocervical ligament extend from arterolateral 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.
**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. Mackenrodt’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:  
   [I 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. Marsupilization  
    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

**Figure Based Questions**

**Fig. F1**  
Identify the structure ‘X’ shown in figure F1:  
   a. Fallopian tube  
   b. Round ligament  
   c. Ovarian ligament  
   d. Broad ligament

**Fig. F2**  
Identify the structure ‘X’ marked on the figure F1:  
   a. Fossa navicularis  
   b. Fourchette  
   c. Posterior commissure  
   d. Vestibule
### Chapter 1  Anatomy of the Female Genital Tract

#### NEW PATTERN QUESTIONS

20. With regards to labia majora all are correct except:
   a. Is homologous to scrotum in males
   b. Is supplied by branches of internal and external pudendal arteries
   c. Drains into superficial inguinal lymph nodes
   d. The broad ligament terminates at its anterior end

21. With regards to vagina all are correct except:
   a. Makes an angle of 45° with the horizontal in erect posture
   b. Looks like letter ‘H’ on cross section
   c. Vaginal axis lies parallel to the uterus and at right angles to the plane axis of inlet
   d. Is lined by stratified squamous epithelium

22. Vaginal defence is lost:
   a. Within 10 days of birth
   b. After 10 days of birth
   c. During pregnancy
   d. At puberty

23. Ovary is:
   a. Is attached to the posterior layer of the broad ligament by mesovarium
   b. Has hilus cells in the cortex
   c. Ovarian veins drain into inferior vena cava
   d. Is connected to the uterus by infundibulopelvic ligament

24. The fallopian tube:
   a. Is lined entirely by ciliated columnar epithelium
   b. Has a submucous layer
   c. Undergoes shedding during menstrual cycle
   d. Surrounded by peritoneum on all sides except along the line of attachment of mesosalpinx

25. All are true about the round ligament except:
   a. Measures 12 cm in length
   b. Is homologous to the gubernaculum testis
   c. Lies anterior to the obturator artery along its course
   d. Contains smooth muscles

26. All of the following are true with respect to ligation of internal iliac artery except:
   a. For hemostasis, anterior division is to be ligated
   b. Collateral circulation is established later between middle sacral and lateral sacral arteries
   c. Bleeding is always controlled with it
   d. The artery should be ligated and not transected

27. With regards to the nerve supply of pelvis all are correct except:
   a. The sensory component of pudendal nerve supplies the skin of vulva, clitoris, perineum and lower vagina
   b. The motor component of pudendal nerve supplies all the muscles of pelvic floor
   c. The anterior half of the vulva is supplied by ilioinguinal and genitofemoral nerves
   d. The posterior half of vulva is supplied by ilioinguinal nerve only

28. The triangular area bounded by clitoris, fourchette and labia minora is:
   a. Fossa navicularis
   b. Fourchette
   c. Vestibule
   d. Vulva

29. Fourchette is where:
   a. Both labia minora meet posteriorly
   b. Labia mionra and majora meet
   c. Distance between vulva and labia minora

30. Glands of litle are homologous to:
   a. Bartholin gland
   b. Cowper’s gland
   c. Skene glands
   d. Glands on labia

31. For hormonal study, sample should be taken from which wall of vagina:
   a. Anterior
   b. Posterior
   c. Lateral
   d. Any wall

32. Theoretically, Gonococcal vaginitis can be seen:
   a. In puberty
   b. In newborn females
   c. In reproductive age females
   d. Sex workers

33. Cervix: corpus ratio before puberty is:
   a. 1:2
   b. 2:1
   c. 1:3
   d. 3:1

34. Which ligament carries ovarian A in lateral wall:
   a. Ovarian ligament
   b. Suspensory ligament of ovary
   c. Broad ligament
   d. Round ligament

35. M/C site of ureteric injury during hysterectomy:
   a. Pelvic brin
   b. Where it is crossed by uterine artery.
   c. Where it enters the bsadder
   d. Where it is over obturator vessels
1. Ans. is d, i.e. Infundibulopelvic ligament  
   - 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  
   The cervix and all 4 fornices are related to  
   - *Uterine Vessels*  
   - *Mackenrodt’s ligament*  
   - *Ureter*  
   Posteriorly surrounding the pouch of douglas lie the uterosacral ligaments.  

3. Ans. is b, i.e. 4.5-5.5  
   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.**  

4. Ans. is b, i.e. Lactobacillus  
   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
   Let us analyze each option separately:
   **Option a:** It has mucus secreting glands – incorrect as
   No glands open into vagina\(^6\) and vaginal secretion is mainly derived from mucus discharge of cervix and partly from transudate through vaginal epithelium.\(^6\)
   • The vaginal mucosa is lined by stratified squamous epithelium.\(^6\)
   • 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\(^{st}\)/ed p 5

7. Ans. is b, i.e. Traverse labia from medial to lateral
   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 1/3rd 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 lymph nodes without metastasis in inguinal nodes.
   “From the upper 2/3rd of the left and right labia majora superficial lymphatics pass towards the symphysis and turn laterally to join the medial superficial inguinal nodes.”
   —CGDT 10\(^{th}\)/ed p 18
   Hence, they traverse labia from medial to lateral side.

8. Ans. is d, i.e. 1:2
   The relationship of the length of the cervix and that of the body of uterus varies with age.

<table>
<thead>
<tr>
<th>Age</th>
<th>Uterus to cervix ratio (Corpus / Cervix ratio)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before puberty</td>
<td>1:2</td>
</tr>
<tr>
<td>At puberty</td>
<td>2:1</td>
</tr>
<tr>
<td>In adults/Reproductive age</td>
<td>3:1 or 4:1</td>
</tr>
<tr>
<td>After menopause</td>
<td>Whole of uterus and cervix atrophy</td>
</tr>
</tbody>
</table>

9. Ans. is b, i.e. High columnar
   Read the text for explanation.

10. Ans. is a, i.e. Erosion of cervix
    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
    • Bartholin’s glands are pea sized oval glands in females homologous to Cowper’s Gland in male.\(^7\) / bulbo urethral glands in males.
    • The ducts of Bartholin gland is 2 cm long\(^7\) 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.\(^7\)
    • Duct as well gland is lined by multilayered columnar epithelium\(^7\) (Not by transitional epithelium as is usually stated).\(^7\)
    • Function of the gland is to produce abundant alkaline mucus during sexual excitement.

12. Ans. is a, i.e. Marsupilization

13. Ans. is c, i.e. Gonococcus
    Fluctuant non-tender swelling at the introitus suggests a diagnosis of Bartholin’s 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 develop 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 organism 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 2/3rd with posterior 1/3rd 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 15th/ed p 11
16. Ans. is b, i.e. 10–12 cm  Ref. Shaw 15th/ed p 11
   See the text for explanation
17. Ans. is c, i.e. Internal iliac artery  Ref. Shaw 14th/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 15th/ed p 91; Dutta Gynaec 6th/ed p35
   Development of vagina is composite, partly from the mullerian ducts (paramesonephric ducts) and partly from the urogenital sinus.

<table>
<thead>
<tr>
<th>Part of vagina</th>
<th>Development</th>
</tr>
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<tbody>
<tr>
<td>Upper 3/5ths</td>
<td>Mullerian ducts</td>
</tr>
<tr>
<td>Lower 1/5th</td>
<td>Urogenital sinus</td>
</tr>
<tr>
<td>Hymen</td>
<td>Junction of mullerian ducts and urogenital sinus</td>
</tr>
<tr>
<td>Epithelium of the vagina and portio vaginalis part of cervix</td>
<td>Endoderm of urogenital sinus</td>
</tr>
<tr>
<td>Fibromuscular layer of vagina</td>
<td>Mesoderm of fused caudal part of mullerian ducts</td>
</tr>
<tr>
<td>Vaginal introitus</td>
<td>Ectoderm of genital folds</td>
</tr>
</tbody>
</table>
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 Gynaec 6th/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 Gynaec 6th/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 Gynaec 6th/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 6th 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 T10 segment. Ovaries are sensitive to manual squeezing.

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

Ref. Dutta Gynae 6th 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).
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 6th 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 6th 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 | ← liolumbar |
| Middle sacral (aorta) → | with | ← Lateral sacral |
| Superior rectal (inferior mesenteric) → | with | ← Middle rectal |
| Ovarian (aorta) → | with | ← Uterine |

Bleeding does not 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
Both the motor and sensory part of the somatic supply to the pelvic organs are through:
- Pudendal nerve—S2, S3, S4.
- Ilio-inguinal nerve—L1, L2.
- Genital branch of genitofemoral nerve—L1, L2.
- 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 S3 and S4 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
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
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
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
Read the text for explanation.

34. Ans. is b, i.e. Suspensory ligament of ovary
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
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**.

**FSH acts on the granulosa cells**
- Releases estrogen
- Releases inhibin B (negative feedback on FSH)

**Proliferative effect on endometrium**
**Increases LH**
**Decreases FSH (negative feedback on FSH)**

**Sudden increase in LH called as LH surge**
- Ovulation occurs
- Corpus luteum is formed
- Corpus luteum releases
  - Mainly Progesterone
  - Leads to secretory changes in uterine endometrium and supports uterine endometrium
  - Leads to LH and FSH decrease
    - Negative feedback on GnRH
    - Progesterone decreases
    - Estrogen and inhibin decrease
    - FSH increases and new cycle begins

**Acts on theca cells to produce androgens**
- Undergo aromatization in granulosa cells
- Estrogen formed
- Inhibin A

**Corpus luteum**
- In non-pregnant state it is maintained by hormone LH
  - Life span = 10–12 days
- In pregnant state, corpus luteum is maintained by hormone hCG
  - Life span in pregnant state ≈ 10 weeks.

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 withdrawl bleeding.
**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 1st meiotic division and there is extrusion of 1st 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 26th day, i.e. 26 – 14 = 12th day.

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

- 1st sign of ovulation on endometrial biopsy is basal vacuolation.

**Line diagram showing Ovarian and Menstrual Cycle**

**Inhibin**

- Consists of 2 dissimilar peptides (called as α- and β- subunits). There are 2 forms of inhibin viz. inhibin A and inhibin B.
- In both of them α- subunit is identical, whereas β- 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

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

### Endometrium

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

### 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.
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 prostrate**: GnRH agonist are as effective as orchidectomy in Ca prostrate 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, Ganiirelix, 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.
Gonadotropin releasing hormone (GnRH)

<table>
<thead>
<tr>
<th>Agonists (every 90 minutes)</th>
<th>Antagonists (Daily administration)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulsatile (LH/FSH) ↑</td>
<td>↓ LH/FSH</td>
</tr>
<tr>
<td>Non-pulsatile (E/P/T) ↓</td>
<td>↓ E/P/T</td>
</tr>
<tr>
<td>Sex hormones (E/P/T) ↑</td>
<td>Used for:</td>
</tr>
<tr>
<td>- Anovulatory infertility</td>
<td>- Prostatic carcinoma</td>
</tr>
<tr>
<td>- Delayed puberty</td>
<td>- Endometriosis</td>
</tr>
<tr>
<td>- Fibroids</td>
<td></td>
</tr>
<tr>
<td>- Precocious puberty</td>
<td></td>
</tr>
</tbody>
</table>

Natural FSH and LH/Gonadotropins

- Released from anterior pituitary in a pulsatile manner.
- Produced by basophils
- FSH T½ = 3-4 hours
- LH T½ = 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
- Acts on pituitary to reduce secretion of FSH and brings about anovulation.

Key to Flowchart:

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

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:
↓ LH → Amenorrhea
↓ 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

<table>
<thead>
<tr>
<th>Composition</th>
<th>Estrogen</th>
<th>Progesterone</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$C_{18}$ compounds</td>
<td>Natural progesterone: $C_{21}$ compound Synthetic are $C_{19}$ steroids similar to androgens. Hence they have androgenic side effects. Remember: As generation increases $\Rightarrow$ androgenic side effects decrease and effect an lipid profile decreases</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Receptor</th>
<th>Estrogen receptor upregulate progesterone receptor</th>
<th>Intra cytoplasmic Progesterone receptor down regulate estrogen receptor</th>
</tr>
</thead>
</table>

| Source | 1. Granulosa cells ($E_2$) 2. Theca cells ($E_1$) (produce androgens which are converted to estrogen by enzyme aromatase in adipose tissue) 3. Placenta-(with the help of precursors obtained from fetus) ($E_3$ and $E_4$) 4. Corpus luteum ($E_2$) | 1. Corpus luteum 2. Placenta (with the help of maternal LDL) |

| State | Mostly present in bound form Only 1% free Mostly bound to sex hormone binding globulin (69%) and albumin (30%) | Mostly present in bound form Only 2% free Mostly bound to albumin and cortisol binding globulin |

| End product | Glucuronides (sulfonamides) | Pregnanediol |

| Effect on uterus | Proliferation of endometrium Growth of uterus in nonpregnant state | Secretory effect on endometrium Growth of uterus in pregnancy Smooth muscle relaxation during pregnancy |

| Effect on cervix | Cervical mucus is Copious Clear and watery Elastic (can be stretched between fingers-called as spinbarkeitt) Has increased water and electrolyte content, decreased protein content When dried and seen under microscop, shows a characteristic fern like pattern | Cervical mucus is Scanty Thick, tenacious Loses its stretchability (fractures on stretching, called as ‘tack’) Has increased protein content and decreased water and electrolyte On drying and seeing under microscope it loses its fern like pattern |

| Effect on vagina | Superficial cells predominate High karyopyknotic index | Intermediate cells predominate Low karyopyknotic index |

| Effect on fallopian tube | Increases motility Decreases secretion | Decreases motility Increases secretion |

| Effect on salt & water | Retention | Excretion |

*Contd...*
### Chapter 2  Reproductive Physiology and Hormones in Females

**Contd...**

<table>
<thead>
<tr>
<th><strong>Estrogen</strong></th>
<th><strong>Progesterone</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipid profile</td>
<td>Lipid profile</td>
</tr>
<tr>
<td>↑ HDL</td>
<td>↓ HDL</td>
</tr>
<tr>
<td>↑ TG</td>
<td>↓ TG</td>
</tr>
<tr>
<td>↓ LDL</td>
<td>↑ LDL</td>
</tr>
<tr>
<td>(cardio protective)</td>
<td></td>
</tr>
</tbody>
</table>

**Least**
- Ductular development
- Glandular development

**Effects on LH & FSH**
- At low conc → inhibits LH
- High conc: positive feedback on LH called as LH surge
- Inhibits GnRH
- At low conc: positive feedback on LH and FSH
- At high concentration negative feedback on LH
- Inhibits GnRH

**Other effects**
- Closure of epiphysis
- Procoagulant inhibits fibrinolysis
- Thermogenic-raises
- Basal body temperature by 0.2–0.5°C

**Estrogen**

- Natural
  - OE estradiol (E₂)
    - Most potent biologically active form of estrogen
    - Main form of estrogen during reproductive years
  - Estriol (E₃) Estetrol (E₃)
    - Produced by aromatization of androgens in ovary & peripheral sites like skin, muscle, and adipose tissue
    - 1/10⁶ as biologically active as E₂
    - Main form of estrogen in postmenopausal females
  - Steroidal estrogens
    - Ethinyl estradiol
    - Mestranol
  - Nonsteroidal estrogens
    - Diethyl stilbestrol (DES)
    - Hexestrol
    - Dienestrol
  - Conjugated estrogens
    - Conjugated equine estrogen (Premarin)
    - Estradiol valerate

**Progesterone**

- Natural
- Synthetic
- 1st generation (estranes–19 nortestosterone derivates)
  - Eg.: Nor ethindrone
  - Norethynodrel
  - Norethisterone acetate
- 2nd generation gonanes
  - Eg.: Levonorgestrel
  - Norethisterone
  - Norgestrel
- 3rd generation (least androgenic activity)
  - Eg.: Desogestrel
  - Gestodene
  - Norgestimate
- 4th generation (Antiandrogenic)
  - Eg.: Drospirenone
  - Dienogest
**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:**
  - 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**

<table>
<thead>
<tr>
<th>Estrogen</th>
<th>Commercial brand</th>
<th>Route of administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethinyl estradiol</td>
<td>Lynoral (.01 mg EE)</td>
<td>Oral</td>
</tr>
<tr>
<td>Ethinyl estradiol</td>
<td>Mixogen (EE 4.4 mg + Methyl testosterone 3.6 mg)</td>
<td>Oral/injectable</td>
</tr>
<tr>
<td>Ethinyl estradiol</td>
<td>Orgalutin (EE 0.5 mg + lynoetenol 2.5 mg)</td>
<td>Oral</td>
</tr>
<tr>
<td>Estradiol succinate</td>
<td>Evalon</td>
<td>Oral</td>
</tr>
</tbody>
</table>

**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 5th 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 IM. injection of 12.5 mg progesterone, oral micronized progesterone, or vaginal suppositories can be given.

Endometriosis: Progesterone induces a hyperprogesterogenic, 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. 17α 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 down-regulators (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.
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 2nd or 3rd 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 progesteronic.

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.
- Teratogenecity (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 globulin 1.1 free in females (2% in globular males)
- Receptors: Intra cytoplasmic
- Endproduct oxosteroid (keto steroid)

Testosterone
- Second most potent androgenic hormone (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 Albumen and six hormone binding globulin.
- 1% free in females (2% in males)
- Receptors–Intra cytoplasmic
- Ebdproduct–Oxosteroid (scetosteroid)
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.**

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.

<table>
<thead>
<tr>
<th>Antigonadotropic agent</th>
<th>Androgenic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acts on HPO axis and decreases frequency of GnRH pulses ↓ LH surge ↓ FSH surge (no change in basal gonadotropin levels) ↓ $\downarrow$ estrogen (endometrial atrophy) ↓ Pseudomenopause like state</td>
<td>As it decreases synthesis of sex hormone binding globulin hence level of free testosterone increases and thus it has virilising side effects</td>
</tr>
</tbody>
</table>

- It acts directly on ovaries and inhibits steroidogenesis.

**Danazol is used in**

<table>
<thead>
<tr>
<th>In females</th>
<th>In Breast for</th>
<th>In males</th>
</tr>
</thead>
</table>
| **Uterus :**  
  - Endometriosis (as it causes endometrial atrophy)  
  - DUB in old females  
  - Fibromyoma (to ↓ its size and vascularity)  
  - Infertility | **Cyclical mastalgia**  
  **Fibrocystic breast disease** | **Precocious puberty**  
  **Gynecomastia**  
  **Improves libido** |

Other use

In hereditary angioneurotic edema.

**Side Effects**

- It has androgenic side effects like acne, hirsutism, 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.

**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-α-hydroxylase and 17, 20-lyase.
- **5-α reductase inhibitors**: Most of the actions of testosterone are mediated by its conversion to DHT by 5-α reductase. Important amongst these are growth of prostate, male pattern baldness and hirsutism in females. Finasteride and dutasteride are 5-α 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.
- **Spironolactone**: It is an aldosterone antagonist that also competes with DHT for its receptor. It can be used for the treatment of 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.

**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:**

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

**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).
- 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 estrogentic effect.
Ovarian cycle

1. Which of the following is seen in the ovulatory phase? (AIIMS May 11)
   a. Stimulation of continuation of reduction division of oocytes
   b. Inhibin A is increased
   c. FSH increases steroid synthesis in granulosa cells
   d. Activin causes FSH to act on granulosa cells

2. In ovarian cycle increased levels of LH are due to: (AIIMS May 11)
   a. Increased Progesterone
   b. Increased Estrogen
   c. Increased FSH
   d. Increased Androgens

3. In 40 days of menstrual cycle the ovulation occurs at: [UP 03]
   a. 14th day
   b. 20th day
   c. 26th day
   d. 30th day

4. The ovarian cycle is initiated by: [DNB 96]
   a. FSH
   b. Estrogen
   c. LH
   d. Progesterone

5. The corpus luteum secretes: [DNB 04]
   a. Estrogens
   b. Progesterone
   c. Both
   d. None

6. 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]
   a. The involution of corpus luteum causes estradiol and progesterone levels to fall dramatically
   b. LH levels rise after ovulation
   c. Estradiol levels are not involved in the LH surge phenomenon
   d. Estradiol inhibits the induction of the progesterone receptor in the endometrium

7. Corpus luteum functions maximally without an implantation for ….. days: [PGI June 00]
   a. 9
   b. 12
   c. 6
   d. 15

8. Maximum function of corpus luteum occurs: [AIIMS Nov 03]
   a. At ovulation
   b. Before ovulation
   c. 3 days after ovulation
   d. 8-9 days after ovulation

9. 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]
   a. Anatomical asymmetry
   b. Difference in blood supply to both sides
   c. Right handedness is more common in population
   d. Some embryological basis

10. Ovulation occurs [AIIMS May 2013]
    a. Before LH surge
    b. After biphasic rise in body temperature
    c. After ripening of follicle by FSH
    d. Before estrogen peak

11. True about timing of LH surge: [PGI May 2013]
    a. Occur 12 hour before ovulation
    b. Occur 24 hour before ovulation
    c. Occur 12 hour after ovulation
    d. Occur 24 hour after ovulation
    e. Occur at time of ovulation

12. 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

13. Naturally occurring estrogens are: [PGI Dec 08]
    a. Estrone
    b. Estradiol
    c. Estriol
    d. Diethylstilbestrol
    e. Pregnanediol

14. The production of cervical mucus is stimulated by: [AIIMS Nov 02]
    a. Progesterone
    b. Estradiol
    c. Estriol
    d. Pregnenolone

15. Ferning of cervical mucus depends on: [DNB 96]
    a. Estrogen
    b. Progesterone
    c. LH
    d. FSH

16. 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

17. End product of progesterone metabolism found in urine is: [AIIMS May 2013]
    a. Pregnenolone
    b. 17-OH pregnanelone exerected in urine
    c. Pregnanediol
    d. Pregnanetriol

Clomiphene

18. Clomiphene citrate is: [AP 97]
    a. Antiandrogen
    b. Synthetic steroid
    c. Antiestrogen
    d. GnRH analogue

19. Clomiphene citrate is indicated in: [AI 98]
    a. Stein–Leventhal syndrome
    b. Ovarian cyst
    c. Asherman’s syndrome
    d. Carcinoma endometrium
Inhibin/Relaxin

29. Following are the features of inhibin except:
   [Karnataka 06]
   a. Non steroid 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, PGF2α 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. Terato genecity    d. Visual symptoms
40. Vaginal smear in old lady shows:
a. Atropic cells on smear
b. Basel 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 drag 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 in 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
1. **Ans. is a, i.e. Stimulation of continuation of reduction division of oocytes**


   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 I. Just before ovulation, the LH surge initiates the continuation of meiosis, forming secondary oocyte and 1st 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 8th 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 granulose 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 8th ed p 226.

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

   Ref. Shiela Balakrishnan 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 Balakrishnan 1st ed, p 34

3. **Ans. is c, i.e. 26th day**

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

   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

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

   Ref shaw 14th ed p 41, Dutta Gynaec 5th ed p 82

   As discussed in text –

   Ovarian cycle is initiated by FSH

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

   **FSH**

   i. It is the hormone which initiates ovarian cycle

   ii. 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.
Chapter 2  Reproductive Physiology and Hormones in Females

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

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

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

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

**Corpus luteum:** After ovulation, the ruptured Graafian follicle develops into corpus luteum.
   - Corpus luteum reaches its maximum maturity by 22nd day of cycle (Size = 2 cms or more), ovulation occurs on day 14, i.e. 8th days after ovulation corpus luteum reaches its maximum maturity.
   - Colour of corpus luteum in early stages is greyish yellow due to presence of lipids and later is distinctive yellow due to pigment carotene.
   - 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 luteui is maintained by hormone LH whereas in pregnant states by hormone hCG.
   - The corpus luteum rapidly declines 9–11 days after ovulation and starts forming corpus albicans if pregnancy doesnot 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 7th/ed p 121
   - If pregnancy occurs, hCG similar to LH stimulates corpus luteum to secrete progesterone. It’s growth reaches a peak at 8th 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

   - 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 venacava.
   - 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

    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**

**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**

- Day 1 — Follicles grow
- Day 14 — Corpus luteum formed
- Day 28 — Later half of cycle is called as secretory phase

Thus, hormonal levels coincide with ovarian cycle.

**Endometrial sampling**

- Day 1 — Main hormone estrogen which causes proliferative changes in endometrium
- Day 14 — Corpus luteum formed progesterone released
- Day 28 — Later half of cycle is called as secretory phase

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**

Vaginal squamous epithelium is composed of following types of cells—

<table>
<thead>
<tr>
<th>Type of Cells</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parabasal/basal cells</td>
<td>Which are predominant when there is no hormonal dominance.</td>
</tr>
<tr>
<td>Intermediate cells</td>
<td>Which are predominant when there is progesterone predominance i.e. in luteal phase/later half of menstrual cycle.</td>
</tr>
<tr>
<td>Superficial cells</td>
<td>Which are predominant 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.</td>
</tr>
</tbody>
</table>

**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

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

<table>
<thead>
<tr>
<th>Naturally occurring estrogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estradiol – Main estrogen during reproductive years.</td>
</tr>
<tr>
<td>Estrone (Produced by peripheral aromatization of androstenedione) – Main estrogen after menopause</td>
</tr>
<tr>
<td>Estriol (main source is placenta) – Main estrogen during pregnancy. It is a marker of fetomaternal-placental well being.</td>
</tr>
</tbody>
</table>

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

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, scarily, 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

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 antiovulatory effect so that it would not further inhibit ovulation.

Synthetic progesterones:

<table>
<thead>
<tr>
<th>Progesterone derivatives</th>
<th>19 Nortestosterone derivatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Have weak antiovulatory actions.</td>
<td></td>
</tr>
<tr>
<td>except chlormadinone acetate</td>
<td></td>
</tr>
<tr>
<td>e.g. : MDPA, Megestrol, Dydrogesterone, Hydroxy progesterone caproate, Nomegestrol</td>
<td></td>
</tr>
<tr>
<td>Have strong antiovulatory actions</td>
<td></td>
</tr>
<tr>
<td>e.g. Desogestrel, Norgestimate, Gestodene, Norethindrone, Norethisterone Norgesterel</td>
<td></td>
</tr>
</tbody>
</table>

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

See the text for explanation.

Clomiphene

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

Clomiphene is an antiestrogen.

<table>
<thead>
<tr>
<th>Category</th>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiestrogen/SERM</td>
<td>Clomiphene, Tamoxifen</td>
</tr>
<tr>
<td>Antiprogesterone</td>
<td>Mifepristone</td>
</tr>
<tr>
<td>Testosterone (Androgen derivative)</td>
<td>Danazol, Gestrinone</td>
</tr>
<tr>
<td>Antiandrogen</td>
<td>Cyproterone acetate, Spironolactone, Flutamide, Finasteride</td>
</tr>
</tbody>
</table>
19. Ans. is a, i.e. Stein-leventhal Syndrome
20. Ans. is a, b and c, i.e. All are correct options
21. Ans is a, i.e. Enclomiphen has antiestrogenic effect.


Let’s 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.

<table>
<thead>
<tr>
<th>Clomiphene binds and blocks estrogen receptors in hypothalamus (i.e. antiestrogen)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decrease in estrogen negative feedback</td>
</tr>
<tr>
<td>↓</td>
</tr>
<tr>
<td>Increase GnRH pulses</td>
</tr>
<tr>
<td>↓</td>
</tr>
<tr>
<td>Ovulation</td>
</tr>
</tbody>
</table>

Thus clomiphene is used for anovulation and is the DOC for PCOD patients.
Clomiphene is a racemic mixture of zuclomiphene enclomiphen. 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 14th ed p 64

Results:

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

Novak 14th ed p 1064; Shaw 14th ed p 284

Side effects:

Clomiphene and multiple pregnancy

“Multiple ovulation and multiple pregnancy in (case of clomiphene) is 10%.” .... Shaw 15th ed p 314.

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

– Leon speroff 8th ed p 1302

Novak 14th ed, p 1064 says— “Incidence of multiple pregnancies ranges from 6.25 to 12.3%.”

Jeffcoates 7th 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 8th 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 8th 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

Side effects of clomiphene:

Ref. Jeffcoates 7th ed p 105; Leon Speroff 7th ed p 1182
Ref. Textbook Gynecology Shaw 4th ed p 281
Chapter 2  Reproductive Physiology and Hormones in Females

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

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

Leon Speroff 7th 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
Read the text for explanation.

25. Ans. is b, i.e. Hyperprolactinemia
Read the text for explanation.

Danazol

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

27. Ans. is a, i.e Hirsutism
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
Read the text for explanation.

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
- Teratogenecity (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

Inhibin:
- Inhibin is a non-steroidal water soluble protein.
- It is secreted by Graffian follicle.
- 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.

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

• Relaxin is a peptide hormone. It is produced by the ovary to be specific by the corpus luteum of pregnancy. If corpus luteum is dominant and declines in the second trimester. This suggests a role in maintaining early pregnancy.
• It is not detected in men and non pregnant women.
• Levels of Relaxin rise during 1st trimester when corpus luteum is dominant and declines in the second trimester. This has no effect on prolactin secretion but enhances growth hormone secretion by the pituitary.

31. Ans. is d, i.e. Elevated and static level of estradiol is essential for ovulation

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 E₂. If for any reason the E₂ 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

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 inhibit 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/e p 35

33. Ans. is d, i.e. the peak steroid production is between 23-25th day.

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 F2α, estrogen and endothelin.

34. Ans. is b i.e. Aromatase

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

“Serum value of progesterone is less than 1ng/ml in follicular phase and 5-15 ng/ml mid luteal phase.”
Dutta Gynae 6/e p 75

Daily production, serum values and urinary excretion of hormones
### Chapter 2  Reproductive Physiology and Hormones in Females

**Hormones**

<table>
<thead>
<tr>
<th>Daily production</th>
<th>Follicular phase</th>
<th>At ovulation</th>
<th>Luteal phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estradiol (µg)</td>
<td>50</td>
<td>150–300</td>
<td>100</td>
</tr>
<tr>
<td>Progesterone (mg)</td>
<td>2–3</td>
<td></td>
<td>20–30</td>
</tr>
<tr>
<td><strong>Serum values</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estradiol (pg/mL)</td>
<td>50</td>
<td>300–600</td>
<td>150–200</td>
</tr>
<tr>
<td>Progesterone (ng/mL)</td>
<td>&lt;1</td>
<td>15–20</td>
<td>&gt;5</td>
</tr>
<tr>
<td>FSH (mIU/mL)</td>
<td>10</td>
<td>60</td>
<td>10</td>
</tr>
<tr>
<td>LH (mIU/mL)</td>
<td>5</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td><strong>Daily excretion</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total estrogen (µg)</td>
<td>10–25</td>
<td>35–100</td>
<td>25–75</td>
</tr>
<tr>
<td>Pregnanediol (mg)</td>
<td>&lt;1</td>
<td>3–6</td>
<td></td>
</tr>
</tbody>
</table>

36. **Ans. is b, i.e. Basal vacuolation**  
   Ref. Leon speroff 7th ed pp 120,190; Dutta Gynae 6th 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 21st day of the cycle.**

   Pseudostratification of nuclei is characteristic of proliferation phase but persists until active progesterone secretion begins. Hence, it is noted until 18th–19th 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 5th ed p 110  
   Read the text for explanation.

43. **Ans. is b, i.e. Estrogenic effect**  
   Ref. Taber’s Dictionary 19th 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).
The average age of menopause is 51 years with a normal range of 43–57 years. In India = 47 years.

### Menopausal Symptoms and Treatment

<table>
<thead>
<tr>
<th>Menopausal symptom</th>
<th>Description</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vasomotor symptoms:</strong></td>
<td>Hot flushes are <strong>the hallmark of menopause</strong>. 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 &amp; recur 5-10 times/day</td>
<td><strong>Hormone therapy</strong>&lt;sup&gt;1&lt;/sup&gt; (most effective). It should be given as a short-term therapy in minimum possible doses to women whose uterus is removed. Combined estrogen and progestin therapy&lt;sup&gt;2&lt;/sup&gt; is uterus is intact. Progesterin therapy&lt;sup&gt;2&lt;/sup&gt; (to be given in those women in whom estrogen is contraindicated). Tibolone&lt;sup&gt;2&lt;/sup&gt; (it is STEAR-selective tissue estrogen activity regulator, which has estrogenic, progestogenic, and androgenic properties). Non-hormonal prescription medicines: (not approved by FDA). Clonidine&lt;sup&gt;3&lt;/sup&gt; Selective serotonin reuptake inhibitor: paroxetine, fluoxetine. Serotonin and nor epinephrine&lt;sup&gt;2&lt;/sup&gt; reuptake inhibitor: venlafaxine&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Menopause</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ovarian failure</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Depletion of ovarian follicle</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Infertility</strong></td>
<td>Anovulation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>↓ Progesterone</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Amenorrhea</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Estradiol produced by ovary decreases. Esterone formed by conversion of androgen remains more or less normal. Main estrogen in menopausal females = Esterone. Overall = levels of estrogen ↓</td>
<td></td>
</tr>
<tr>
<td></td>
<td>↓ bone mass osteoporosis</td>
<td></td>
</tr>
<tr>
<td><strong>Senile vaginitis</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>1</sup> It is the hormone which initiates ovarian cycle.
<sup>2</sup> 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.
<sup>3</sup> 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.

<sup>Contd...</sup>
## Menopause and HRT

### Menopausal symptom

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Description</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hot flushes</td>
<td>Norepinephrine &amp; serotonin</td>
<td>Dopamine antagonist: Veralipride&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>are the neurotransmitters</td>
<td>Gabapentin&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>which trigger hot flushes</td>
<td>Bellergal (combination of ergotamines, phenobarbital and belladona, approved for the treatment of migraine).&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Main indication for prescribing HRT: is Hot flushes</td>
<td>Mirtazapine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Trazodone</td>
</tr>
<tr>
<td>Non-prescription medicines:</td>
<td></td>
<td>Isoflavones (100 mg/day)&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Soy products (60 g/d)&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Vitamin E (800 IU/day)&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

### Osteoporosis

- It is the single most important health hazard associated with menopause
- Osteoporosis is loss of bone strength resulting in an increased risk of fracture
- Diagnosis is made by determining bone mineral density (BMD) by dual energy X-ray absorptio metry (DEXA)
- BMD is best measured at hip is predictive of hip fracture and fracture at other sites
- M/c sites of fracture in osteoporotic women
  - Lumbar vertebrae
  - Wrist (distal radius)
  - Hip (femoral neck)

### Hormone therapy

- Combined estrogen & progestin therapy (if uterus is intact)
- Only estrogen (if female is hysterectomised)
- Tibolone (STEAR)
-Raloxifene (SERM)

### Non hormonal

- Bisphosphonates like Alendronates risedronate. It is the first line of treatment for osteoporosis
  - Calcium
  - Calcitonin
  - Vitamin D
  - Slow releasing sodium fluoride

### Senile vaginitis

- Dry vagina due to decreased estrogen
- Topical estrogen application

### Osteoporosis

#### Prevention

- Calcium 1200 mg/day
- Vitamin D, 800-1000 IU/day
- Regular weight bearing, muscle strengthening exercise
- Smoking cessation
- Moderate alcohol consumption

#### Treatment

- Treatment is given to all women ≥ 50 years old with any of the following:
  - Vertebral or hip fracture
  - T score ≤ −2.5 at the femoral neck or spine
  - T score between −1.0 and −2.5 at the femoral neck or spine & 10-year hip fracture risk ≥ 3%
  - Ten-year major osteoporosis related fracture probability ≥ 20%

- 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.

- Scores: It corresponds to the same measurements using women of same age as the reference

#### Normal bone T scores:

- 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.

**Raloxifene**

- Raloxifene is a *Selective Estrogen Receptor Modulator (SERM)*
- 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.
- 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.

**Side Effects**

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

**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 osteoporsis act by inhibiting osteoclast.

**Denosumab**
- Osteoclasts express a receptor called receptor for activated nuclear factor κ 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.

### Hormone Replacement Therapy (HRT)

<table>
<thead>
<tr>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Estrogen</strong></td>
</tr>
<tr>
<td>• Oral or transdermal</td>
</tr>
<tr>
<td>• Transdermal preferred for women with hypertriglyceridemia or impaired hepatic function</td>
</tr>
<tr>
<td>• Given alone in women who have undergone hysterectomy</td>
</tr>
<tr>
<td><strong>Progestin</strong></td>
</tr>
<tr>
<td>• Given in conjunction with estrogen for women with an intact uterus to decrease the risk of endometrial cancer.</td>
</tr>
</tbody>
</table>

**Side Effects of HRT**
- Abnormal uterine bleeding
- Mastodynia
- Edema, bloating, heartburn, and nausea
- Mood changes (due to progesterone component)

**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)
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 18th ed p 259*

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Uncertain risks</th>
<th>Definite risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Hip fracture</td>
<td>• Thromboembolic events (use of E+P not with E alone)</td>
<td>• Coronary heart disease(^2)</td>
</tr>
<tr>
<td>• Wrist fracture</td>
<td>• Dementia</td>
<td>• Breast cancer (use of E+P not with E alone)</td>
</tr>
<tr>
<td>• Vertebral fracture (i.e. osteoporosis)</td>
<td>• Endometrial cancer (use of E alone)</td>
<td>• Stroke(^2)</td>
</tr>
<tr>
<td>• Symptoms of menopause</td>
<td></td>
<td>• Ovarian cancer (E+P)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cholecystitis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Uncertain benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>• colorectal cancer</td>
</tr>
<tr>
<td>• diabetes mellitus</td>
</tr>
</tbody>
</table>

**LAST MINUTE REVISION**

- Increase in FSH is the *sine qua 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.
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

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

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

- Friends, Harrison 16\textsuperscript{th} ed p 30, 18\textsuperscript{th} ed p 3043; Williams Gynaec. 1\textsuperscript{st} ed p 494; Jefferis 6\textsuperscript{th} ed pp 105-106

- 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.

- 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 thrombembolism and cholecystitis.

- The WHI randomized controlled trial of combination hormone therapy versus placebo showed that hormone therapy did not prevent heart disease in healthy women, but instead it increased the risk of cardiovascular events in older women — Novak 15\textsuperscript{th} ed p 1242

3. Ans. is d, i.e Triglycerides

**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 lithogeneity of bile.

**Progesterone causes:**
- Plasma LDL ↑
- ↓ HDL

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

- 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\textsuperscript{rd} ed p 1124

- “Estrogen is important in maintaining bone mass primarily by retarding bone resorption.” — KDT 6\textsuperscript{th} 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

- During perimenopausal and postmenopausal period there is decrease in bone mass called as osteoporosis.

- Estrogen is used to prevent 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
   Alendronate, 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 at least 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:
   a. Calcium
   b. Vitamin D
   c. Calcitonin
   d. Slow releasing sodium fluoride.

7. Ans. is c, i.e. Reduces the incidence of venous thrombosis
   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 may also 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 14th ed p 1333

8. Ans. is c, i.e. Estrogen
   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 1st ed p 495; According to Jeffcoate 7th ed p 96

   All women who have intact uterus or even those who underwent hysterectomy for endometrial Cancer (Stage I), endometroid 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

10. Ans. is b, i.e. Raloxifene
   Raloxifene is a SERM. It does not decrease hot flushes and leg cramps, rather increases them.

11. Ans. is a, i.e. Thrombosis
   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.

<table>
<thead>
<tr>
<th>Hirsutism</th>
<th>Virilization</th>
<th>Hypertrichosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Excessive growth of androgen dependant sexual hair or male distribution of hair in females.</td>
<td>• 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.</td>
<td>• Excessive growth of nonsexual hair, i.e. lanugo hair</td>
</tr>
<tr>
<td>• Hair are coarse, dark and terminal hair</td>
<td></td>
<td>• Hair are soft and lightly pigmented</td>
</tr>
</tbody>
</table>

**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 age.

**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.

- **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.
Chapter 4  PCOD, Hirsutism and Galactorrhea

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.

**Algorithm for differential diagnosis of Hirsutism**

- Excessive hair growth
  - Normal deviation
  - Hirsutism
  - Hypertrichosis

- Virilization
  - No
  - Irregular menses
    - thyroid function tests
      - Abnormal: Treat dysfunction
        - Consider CAH, PCOS, anovulation
      - Normal: Consider Imaging of pituitary and ovaries
  - Normal menses
    - Serum testosterone
      - <200 ng/dL: Anovulation, Pelvic exam
      - >200 ng/dL: Image and consider surgical exploration
    - 17-OHP
      - <200 ng/dL: ACTH stimulation test
      - >200 ng/dL: Rules out adrenal hyperplasia/21 hydroxylase deficiency
  - Check DHEAS, testosterone, 17-OHP

- 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

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.
Polycystic Ovary Syndrome (PCOD)

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

Besides this – patients of PCOD/PCOS are:

- Obese—obesity is defined as BMI ≥ 30 kg/m²
- 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.

BMI (kg/m²) | Category
<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>&lt; 19</td>
</tr>
<tr>
<td>19.1-24.9</td>
</tr>
<tr>
<td>25-29.9</td>
</tr>
<tr>
<td>30-34.9</td>
</tr>
<tr>
<td>&gt; 35</td>
</tr>
</tbody>
</table>

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 –

Sr. fasting blood sugar
Sr. fasting insulin
< 4.5
Fasting serum insulin – > 25m IU/ml

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 | Insulin resistance
I | Acanthosis nigricans
R |
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.  

- 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 criteria being excluded (like cushing disease, adrenal hyperplasia)

**Management of PCOD**

Depends on the complain of the patient

<table>
<thead>
<tr>
<th>Complaint</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irregular periods</td>
<td>OCP’s</td>
</tr>
<tr>
<td>Obesity</td>
<td>Life style modifications</td>
</tr>
<tr>
<td>Insulin resistance</td>
<td>Metformin (Can be used in pregnancy also)</td>
</tr>
<tr>
<td>Hirsutism/ acne</td>
<td>OCP’s with cyproterone acetate</td>
</tr>
</tbody>
</table>

**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)

1st 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

2nd 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

**Hormonal changes in PCOS**

<table>
<thead>
<tr>
<th>Hormones Increased</th>
<th>Hormones Decreased</th>
</tr>
</thead>
<tbody>
<tr>
<td>Androgens (Testosterone, Androstenedione DHEAS)</td>
<td>Follicle stimulating hormone (FSH)</td>
</tr>
<tr>
<td>Luteinizing hormone (LH &gt; 10 IUI ml)</td>
<td>Progesterone (due to anovulation)</td>
</tr>
<tr>
<td>Estrogen (Estrone &gt; Oestradiol)</td>
<td>Sex hormone binding Globulin</td>
</tr>
<tr>
<td>Total Free Estrogen</td>
<td>HDL &amp; Apoprotein A-I</td>
</tr>
<tr>
<td>Insulin (&gt; 10 m IU / L due to insulin resistance)</td>
<td></td>
</tr>
<tr>
<td>Prolactin (in some patients)</td>
<td></td>
</tr>
<tr>
<td>LDL/cholesterol and triglycerides</td>
<td></td>
</tr>
</tbody>
</table>

**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**

<table>
<thead>
<tr>
<th>Normal</th>
<th>Increased</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCOS</td>
<td>pituitary or ovarian neoplasm</td>
</tr>
</tbody>
</table>
3rd line agents: GnRH agonist
a) Luprolide
b) Guserelin given in pulsatile manner
c) 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.

<table>
<thead>
<tr>
<th>Increase SHBG (Therefore, ↓ free Testosterone)</th>
<th>Decrease SHBG (Therefore, ↑ free Testosterone)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High estrogens like in OCP’s</td>
<td>PCOD (PCOS)</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Adrenal hyperplasia</td>
</tr>
<tr>
<td>Liver cirrhosis</td>
<td>Cushing syndrome</td>
</tr>
<tr>
<td>Elevated Thyroid Hormone</td>
<td>Growth hormone</td>
</tr>
</tbody>
</table>

Factors

<table>
<thead>
<tr>
<th>Ovary Related</th>
<th>Adrenal Related</th>
<th>Medications</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCOD (M/C)</td>
<td>Congenital adrenal hyperplasia</td>
<td>Acromegaly</td>
<td></td>
</tr>
<tr>
<td>Masculinizing tumors of ovary</td>
<td>Adrenal tumor</td>
<td>Hyperprolactinemia</td>
<td></td>
</tr>
<tr>
<td>Theca lutein cyst</td>
<td>Cushing syndrome</td>
<td>Hypothyroidism</td>
<td></td>
</tr>
<tr>
<td>Luteoma of pregnancy</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Medications that may cause hirsutism and / or hypertrichosis:

**Hirsutism**
- Anabolic steroids
- Danazol
- Metoclopramide
- Methylprednisolone
- Phenothiazines
- Progestins
- Reserpine
- Testosterone

**Hypertrichosis**
- Cyclosporine
- Diazoxide
- Hydrocortisone
- Minoxidil
- Pencillamine
- Phenytoin
- Psoralens
- Streptomycin
Medical Management of Hirsutism:

<table>
<thead>
<tr>
<th>Hormone profile</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated Testosterone (Ovary source)</td>
<td>Combined contraceptives (COCs containing drospirenone or desogestral or cyproterone acetate dianette)</td>
</tr>
<tr>
<td>Normal T and DHEA-S 3α-AG ↑ (idiopathic)</td>
<td>Anti-androgens</td>
</tr>
<tr>
<td>DHEA-S ↑, normal T</td>
<td>Dexamethasone</td>
</tr>
</tbody>
</table>

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 hypo-gonadotropic 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.
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. Amenorrhea
   b. Alopeica
   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. Oligomenorrhea and amenorrhea
   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:
    a. Persistently elevated LH (AIIMS Nov 08)
    b. Increased LH/FSH ratio
    c. Increased Dhea
    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:
    a. Menopausal Gonadotropin (PGI Dec 08)
    b. GnRH
    c. Spironolactone
    d. Hcg

14. A hirsuite 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:
    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 amenorrhea. Best investigation is: (AIIMS June)
    a. Testosterone estimation
    b. Dihydroepiandrosterone

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
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: (PGI June 99)
a. Hirsutism
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

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

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

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

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 oligomennorhea 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

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
- Androgenic alopecia. 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.

7. Ans. is a, i.e. 1–4 days
   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 6th ed p 205

8. Ans. is a, c and e, i.e. Oligomenorrhea and amenorrhoea; Innumerable cysts in ovary; and Theca cell hypertrophy
   Ref. Shaw 15th ed p 369-371
   • There is no doubt that PCOD causes oligomenorrhea/amenorrhoea, i.e. option ‘a’ is correct.
   • PCOS is seen in young females. Most common age affected is 15-25 years, 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. (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:
   • ≥ 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 14th ed p 1078-1079; Williams Gynaec 1st 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.

<table>
<thead>
<tr>
<th>Estrogen (in body has 3 forms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Oestradiol (E2)</td>
</tr>
<tr>
<td>Predominant estrogen in reproductive age group.</td>
</tr>
<tr>
<td>Most potent form E2 &gt; E1</td>
</tr>
<tr>
<td>2. Oestrone (E1)</td>
</tr>
<tr>
<td>Predominant estrogen following menopause</td>
</tr>
<tr>
<td>It is formed when androgens are converted to estrogen</td>
</tr>
<tr>
<td>3. Another form of estrogen is oestriol. Which is a metabolite of oestrogen. It is the predominant form in pregnancy</td>
</tr>
</tbody>
</table>

   In PCOS:
   “Patients with PCOS, E1, levels are increased E2 is at a follicular phase level.” — Novak 14th ed p 1078; 15th ed p 1079
   Therefore, in PCOS = E1 > E2, i.e. Reversal of E2 : E1 ratio.
   “Elevated androstenedione levels contribute to an increase in estrone levels through peripheral conversion.” — Williams Gynaec 1st ed p 386

   Warning: Do not go by what shaw’s 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

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 15th ed p 390 for option ‘a’

Rest all options have been explained earlier.

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

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.”

This is depicted clearly in the following graph from Leon Speroff 7th 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”

“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.”

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

<table>
<thead>
<tr>
<th>Prolactin levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are normal</td>
</tr>
<tr>
<td>PCOS / congenital adrenal hyperplasia should be considered</td>
</tr>
<tr>
<td>If elevated</td>
</tr>
<tr>
<td>Pituitary/ovarian neoplasm should be considered</td>
</tr>
</tbody>
</table>

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

Medical Treatment of Hirsutism
**Chapter 4  PCOD, Hirsutism and Galactorrhea**

**Treatment Category** | **Specific Regimens**
--- | ---
Weight loss | Oral contraceptives
Hormonal suppression | Medroxyprogesterone
Steroidogenic enzyme inhibitors | Gonadotropin-releasing hormone analogues
5α-reductase inhibitors | Glucocorticoids
Antiandrogens | Ketoconazole
Insulin sensitizer | Finasteride
Mechanical | Spironolactone

**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 bonding globilin), resulting in decreased free testosterone concentration.

   **“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.”**

ii. **Medroxy progesterone acetate: (MPA)**
   - ↓ GnRH production
   - ↓ FSH and ↓ LH
   - ↓ androgen and ↓ estrogen production by ovary
   - 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 Gnadotropin 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 1st 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 1st 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 4th ed p 491-492

v. **5α reductase inhibitor**:
   - Conversion of testosterone to dihydrotestosterone can be decreased by 5α 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:

<table>
<thead>
<tr>
<th>Depliation methods, i.e. hair removal above the skin surface e.g.</th>
<th>Epilation methods, i.e. methods which remove the entire hair shaft and root. In includes:</th>
</tr>
</thead>
<tbody>
<tr>
<td>– shaving</td>
<td>– plucking</td>
</tr>
<tr>
<td>– depilation creams</td>
<td>– waxing</td>
</tr>
<tr>
<td></td>
<td>– threading</td>
</tr>
<tr>
<td></td>
<td>– Thermal destruction using electrolysis or laser</td>
</tr>
</tbody>
</table>

**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 9th 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


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:**

<table>
<thead>
<tr>
<th>High androgenic bioactivity</th>
<th>Newer progestins with low androgenic bioactivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Norgestrel</td>
<td>• Desogestrel</td>
</tr>
<tr>
<td>• Norethindrone</td>
<td>• Gestodene</td>
</tr>
<tr>
<td>• Norethindrone acetate</td>
<td>• Norgestimate</td>
</tr>
<tr>
<td>• Drospirenone</td>
<td></td>
</tr>
</tbody>
</table>

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 10th ed p 937; Williams Gynae 1st ed p 387; Leon Speroff 7th 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 10th 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 1st ed p 387

16. Ans. is a, i.e. Ovarian disease

Ref. CGDT 10th ed p 937; Williams Gynae 1st 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


“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 1st 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 8th 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 7th ed p 484; Novak 1083 15th ed p 1085

<table>
<thead>
<tr>
<th>Chronic consequences of anovulation, PCOS</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑ Risk of cardiovascular disease</td>
</tr>
<tr>
<td>Infertility (Easily treatable)</td>
</tr>
<tr>
<td>↑ 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)</td>
</tr>
<tr>
<td>hirsutism</td>
</tr>
<tr>
<td>↑ risk of endometrial cancer and breast cancer</td>
</tr>
<tr>
<td>↑ risk of depression and mood disorders</td>
</tr>
<tr>
<td>↑ risk of metabolic X syndrome</td>
</tr>
</tbody>
</table>

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 women with PCOS.”

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 8th ed pp 508, 518, 519, 520; Williams Gynae 1st 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 let’s 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 8th 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 8th 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 8th 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 oligoovulation 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 androgen 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 (>12 in number, 2-9 mm in diam) are seen in one or both ovaries and ovarian volume is >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 do not establish and are not required for diagnosis of PCOS.”

Leon Speroff 8th 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 pathophysiology in already affected women by aggravating the degrees of insulin resistance and hyperinsulinemia.”

Leon Speroff 8th 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**


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 resistance 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 15th 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**


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 ≥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 gynaecology 15th ed p 371; Dutta Gynae 6th 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 61st 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 6th 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 7th 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 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 D2 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
- 2. Chin
- 3. Chest
- 4. Upper back
- 5. Lower back
- 6. Upper abdomen
- 7. Lower abdomen
- 8. Upper arms
- 9. Forearms
- 10. Thighs
- 11. Legs

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)

<table>
<thead>
<tr>
<th>BMI (kg/m2)</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;19</td>
<td>Underweight</td>
</tr>
<tr>
<td>19.1-24.9</td>
<td>Normal</td>
</tr>
<tr>
<td>25-29.9</td>
<td>Overweight</td>
</tr>
<tr>
<td>30-34.9</td>
<td>Obese</td>
</tr>
<tr>
<td>&gt;35</td>
<td>Morbidly obese</td>
</tr>
</tbody>
</table>
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

- Y chromosome is present/SRY region is present
- Bipotential gonads form Testis (7 weeks)
- Sertoli cells
  - Produce Mullerian inhibiting factor (also called as antimullerian factor) by 7 weeks
  - Regression of Mullerian ducts
  - Remnant of mullerian duct in males is – ‘appendix of testis’ and Prostatis utriculus
- Leydig cells
  - Testosterone (by 8 weeks)
  - Promotes growth of Wolffian duct – which forms the male internal genital organs viz.
- Enzyme 5-α reductase converts testosterone to dihydrotestosterone
  - Promotes the growth of external genitalia in males
  - Vas deferens, epididymis seminal vesicles.

In Females

- Y chromosome is absent
- SRY region is absent
- Gonads = Ovaries are formed (by 8–10 weeks)
  - Sertoli cells are absent
  - Leydig cells are absent
  - Testosterone is not converted into dihydrotestosterone

---

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 Turner’s 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.

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

Contd...
Remnants of wolffian duct (mesonephric duct) in females

<table>
<thead>
<tr>
<th>Part of wolffian duct</th>
<th>Remnant in females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pronephros</td>
<td>Hydatid of Morgagni or Kobelt tubercle</td>
</tr>
<tr>
<td>Mesonephros:</td>
<td>Epo-ophron or Organ of Rosenmuller</td>
</tr>
<tr>
<td>• Cranial end</td>
<td>Para-oophron</td>
</tr>
<tr>
<td>• Caudal end</td>
<td></td>
</tr>
<tr>
<td>WD proper</td>
<td>Gartner's duct</td>
</tr>
</tbody>
</table>

Descent of gonads

Both testis and ovary are formed in lumbar region of post-abdominal wall

- **Male**
  - During fetal life they gradually descend to the scrotum with the help of gubernaculum
  - Iliac fossa (3m)
  - Deep inguinal ring (7m)
  - Through inguinal canal (7m)
  - Scrotum (End of 8m)

- **Female**
  - Gubernaculum forms as in male which extends from the ovary to the labia majora.
  - It becomes attached to the developing uterus at its junction with uterine tube.
  - Part of gubernaculum that persists between ovary and uterus becomes ovarian ligament.
  - Part between uterus and the labium majus becomes round ligament of uterus.
  - Ovaries descend from lumbar to the true pelvis.

### 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.\(^{1}\)
- 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 5th month 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 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. 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

<table>
<thead>
<tr>
<th>Male development</th>
<th>Female development</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epididymis, vas deferens, and seminal vesicles</td>
<td>Remnant i.e. Gartner duct</td>
</tr>
<tr>
<td>Paradidymis</td>
<td>Epoophoron, and Paroophoron</td>
</tr>
<tr>
<td>Regresses-Remnant is Appendix of testes</td>
<td>Uterus, cervix, tubes, and upper vagina</td>
</tr>
<tr>
<td>Urinary bladder, urethra, prostate, prostatic utricle, and bulbourethral glands</td>
<td>Urinary bladder, urethra, paraurethral glands, Bartholin’s glands, and lower vagina</td>
</tr>
</tbody>
</table>

Contd...
### 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.

<table>
<thead>
<tr>
<th>Features of Gartner’s cyst</th>
<th>Cystocele</th>
</tr>
</thead>
<tbody>
<tr>
<td>➢ Rugosities of the overlying vaginal mucosa are lost</td>
<td>➢ Rugosities present</td>
</tr>
<tr>
<td>➢ Vaginal mucosa over it becomes tense and shiny</td>
<td>➢ Margins not well defined</td>
</tr>
<tr>
<td>➢ Margins are well defined</td>
<td>➢ Reducible</td>
</tr>
<tr>
<td>➢ Not reducible</td>
<td>➢ Impulse on coughing present</td>
</tr>
<tr>
<td>➢ No impulse on coughing</td>
<td></td>
</tr>
</tbody>
</table>

**ALSO KNOW**

**Anomalies caused by in utero exposure to Diethylstilbesterol (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.

### 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.  
- 40% septa are located in middle part.  
- 14% septa are located in lower part.  

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 mucolpos, and can present as:  
  - Abdominal tumour.  
  - Can compress the ureter resulting in hydroureter followed by hydronephrosis.  
  - Can compress the rectum resulting in obstipation/intestinal obstruction.
At Puberty

- Patient can present with primary amenorrhea (actually called as cryptomenorrhea as uterus menstruates normally but blood does not come out due to outflow tract obstruction).
- Secondary sexual characteristics are normal.
- Due to cryptomenorrhea, blood gradually collects and distends first the vagina (hematocolpos), then cervix, uterus (hematocervix and hematometra) and finally the tube (hematosalpinx). 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).
- Patient may complain of monthly cyclic pain (backache/lower abdomen pain).

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.

### Mullerian Duct Anomalies

<table>
<thead>
<tr>
<th>Anomaly</th>
<th>Defect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uterus Didelphys</td>
<td>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</td>
</tr>
<tr>
<td>Bicornuate uterus</td>
<td>In this condition only the lower part of the ducts fuse leaving the cornua separate, so always there is a single vagina</td>
</tr>
<tr>
<td>a. Uterus bicornis unicollis</td>
<td>Here vagina and cervix are fused, i.e. single vagina, single cervix but 2 uterus</td>
</tr>
<tr>
<td>b. Uterus bicornis bicollis</td>
<td>Here vagina is fused but cervix and uterus are not fused, i.e. single vagina, 2 cervix and 2 uterus</td>
</tr>
<tr>
<td>Septate / Subseptate uterus</td>
<td>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</td>
</tr>
<tr>
<td>Arcuate uterus</td>
<td>Here the fundal bulge of uterus does not develop after fusion of the ducts i.e. flat topped uterus</td>
</tr>
<tr>
<td>Unicornuate uterus</td>
<td>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</td>
</tr>
</tbody>
</table>

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 ≥ 3 abortions.

**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 (as 2/3rd of vagina is formed by Mullerian duct).

- Karyotype = 46 XX
- Phenotype = Female

**Associated Abnormalities**

- Renal anomalies (M/C Renal agenesis followed by horse-shoe shaped kidney)
- Skeletal abnormalities (most common - scoliosis).
- Cardiac abnormalities.

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.
- Secondary sexual characteristics are normal 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.
- P/V = Vagina is felt like a blind pouch and uterus is absent.
- “Although in MRKH fallopian tube should be absent, typically a part of the distal tube is present (distal 1/3rd present).” — William Gynae 1st ed p 416
- Findings are confirmed by USG.

**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.
- **Surgical management**: Vaginoplasty either by McIndoe reed procedure or Williams vaginoplasty 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.

**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 months. 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.
1. To diagnose uterus didelphys, procedure of choice is:
   a. Laparoscopy  
   b. IVP  
   c. HSG  
   d. USG  
   [AIIMS 92, AI 95]

2. The most important indication for surgical repair of a bicornuate uterus is:
   a. Infertility  
   b. Dysmenorrhea  
   c. Menorrhagia  
   d. Habitual abortion  
   [AIIMS Nov. 05]

3. Vaginal atresia is associated with:
   a. Uterine atresia  
   b. Exstrophy of bladder  
   c. Imperforate hymen  
   d. Ovarian atrophy  
   [AIIMS June 98]

4. Ideal age for repair of vaginal agenesis is:
   a. 6 months  
   b. 3 years  
   c. At puberty  
   d. Before marriage  
   [AIIMS 92]

5. Ovary develop from:
   a. Mullerian duct  
   b. Genital ridge  
   c. Genital tubercle  
   d. Mesonephric duct  
   e. Sinovaginal bulbs  
   [PGI June 02]

6. Diagnosis of septate uterus done by:
   a. USG  
   b. Uterine sound  
   c. Hysteroscopy  
   d. Hysterosalpingography  
   e. Laparoscopy  
   [PGI Dec 04]

7. MC congenital abnormality of uterus is:
   a. Uterus didelphys  
   b. Arcuate  
   c. Unicornuate  
   d. Septate  
   e. Bicornuate  
   [PGI Dec 05]

8. Transverse vaginal septum corresponds to:
   a. External os  
   b. Vesical neck  
   c. Bladder base  
   d. Hymen  
   e. Above the external meatus  
   [PGI Dec 04]

9. All of the following are features of mullerian agenesis except:
   a. 46 XX karyotype  
   b. Normal breast development  
   c. Absent vagina  
   d. Ovarian agenesis  
   e. XY phenotype  
   [PGI Dec 04]

10. True about MRKH syndrome:
    a. Absent uterus  
    b. Absent ovary  
    c. Absent vagina  
    d. XX phenotype  
    e. XY phenotype  
    [PGI May 2010]

11. Characteristic features of Rokitansky Kuster Hauser syndrome are all of the following except:
    a. Absent uterus  
    b. Absent vagina  
    c. Anovulation  
    d. 46 – XX  
    [AI 99; Delhi 05]

12. Rokitansky Kuster Hauser syndrome is associated with:
    a. Ovarian agenesis  
    b. Absent fallopian tube  
    c. Vaginal atresia  
    d. Bicornuate uterus  
    [AI 01]

13. In complete mullerian duct aplasia all of the following are likely to be absent except:
    a. Ovarian agenesis  
    b. Absent fallopian tube  
    c. Vaginal atresia  
    d. Bicornuate uterus  
    [AI 07]
14. Mayer Rokitansky Kuster Hauser syndrome consists of:
   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
   b. FSH receptor mutation
   c. Ovotesticular syndrome
   d. Mixed gonadal dysgenesis

16. Vaginal epithelium is derived from:
   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:
   a. Uterus didelphys
   b. Arcuate uterus
   c. Subseptate uterus
   d. Bicornuate uterus

18. Bicornuate uterus is due to:
   a. Incomplete fusion of uterine cavity
   b. Incomplete fusion of paramesonephric duct
   c. Incomplete fusion of mesonephric duct
   d. Incomplete formation of vagina

19. Unicollis bicornis means:
   a. Two uterine cavity with one cervix
   b. Single vagina with double uterus

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. Epophoron 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:
   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
Chapter 5  Congenital Malformations

ANSWERS

1. **Ans. is d, i.e. USG**  
   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 8th ed p 147

2. **Ans. is d, i.e. Habitual abortion**  
   Management: Bicornuate uterus requires surgical treatment only when it causes habitual abortions.  
   “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 7th 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 1st 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. These days hysteroscopic metroplasty is being done.

3. **Ans. is a, i.e. Uterine atresia**  
   Vaginal atresia is associated with uterine atresia and syndrome is called as Mayer Rokitansky Kuster Hauser syndrome (for details, see the preceding text).

**ANSWERS TO FIGURE BASED QUESTIONS**

F1. **Ans. is b, i.e Bicornuate uterus:**  
   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.

   ![Bicornuate vs Septate Uterus](image)

   Now as seen in F1:- Angle between the 2 horns is more than 60°, hence it is an HSG of bicornuate 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 hysteroscopic view of septate uterus.

F3. **Ans. is b, i.e. Bifid clitoris**  
   The genital tubercle is formed from two mesodermal bands which grows round from the dorsal aspect of the foetus in the 3rd 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 majora, absence of hair bearing skin of the pubes and a split pelvis.

F4. **Ans. is c, i.e. Arcuate uterus**  
   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.
4. Ans. is d, i.e. Before marriage

- 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

Male and female derivatives of embryonic urogenital structures.

<table>
<thead>
<tr>
<th>Part of female genital system</th>
<th>Originates from</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovary</td>
<td>Genital ridge</td>
</tr>
<tr>
<td>Fallopian tubes</td>
<td></td>
</tr>
<tr>
<td>Uterus</td>
<td>Mullerian/paramesonephric duct</td>
</tr>
<tr>
<td>Cervix</td>
<td></td>
</tr>
<tr>
<td>Upper part of vagina</td>
<td>Urogenital Sinus</td>
</tr>
<tr>
<td>Lower part of vagina</td>
<td></td>
</tr>
</tbody>
</table>

6. Ans. is a, b, c and e, i.e. USG; Uterine sound; Hysteroscopy; and Laparoscopy

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, there 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 Gynaec 1st 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.

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 Gynaec 1st 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 Gynaec. - I am including laparoscopy also in the correct options.

7. Ans. most probably d, i.e. Septate

Sorry for this one friends, 2 very reliable textbooks quote different incidences of different malformations.
### Chapter 5  Congenital Malformations

<table>
<thead>
<tr>
<th>Anomaly</th>
<th>Percentage</th>
<th>Anomaly</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bicornuate uterus</td>
<td>37%</td>
<td>Septate uterus</td>
<td>35%</td>
</tr>
<tr>
<td>Arcuate uterus</td>
<td>15%</td>
<td>Bicornuate uterus</td>
<td>26%</td>
</tr>
<tr>
<td>Incomplete septum</td>
<td>13%</td>
<td>Arcuate uterus</td>
<td>18%</td>
</tr>
<tr>
<td>Uterus didelphys</td>
<td>11%</td>
<td>Unicornuate uterus</td>
<td>10%</td>
</tr>
<tr>
<td>Complete septum</td>
<td>9%</td>
<td>Uterus didelphys</td>
<td>8%</td>
</tr>
<tr>
<td>Unicornuate uterus</td>
<td>4%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

8. **Ans. is a, i.e. External os**  
   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.
   - 40% septa were located in middle part.
   - 14% septa were located in lower part.

   *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**

   ![Mullerian agenesis/ MRKH syndrome diagram](image)

   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 15th ed p 95; Jeffcoate 7th 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

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.

<table>
<thead>
<tr>
<th>45 XO / 46 XY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streak</td>
</tr>
<tr>
<td>Gonads/ovary</td>
</tr>
<tr>
<td>↓ Formation of ipsilateral</td>
</tr>
<tr>
<td>Mullerian duct</td>
</tr>
<tr>
<td>Testis</td>
</tr>
<tr>
<td>↓ Formation of ipsilateral</td>
</tr>
<tr>
<td>Wolfian duct</td>
</tr>
</tbody>
</table>

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 Gynae 6/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 uterotubal 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/ed p 85; Jeffcoate 7/ed p 199; Williams Gynae 1/ed p 417

See the text for explanation.

20. Ans. is a, i.e. Short arm of Y chromosome

Ref. Textbook of Gynaec, Shiela Balakrishnan 1/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. Epoophoron and caudal end of wolffian duct

Epoophoron is cranial end of wolffian duct and not caudal.

22. Ans. is d, i.e. Gartner’s duct

Ref. Dutta Gynae 5/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

Diethylstilbestrol 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/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

**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

**Genes for male development**

<table>
<thead>
<tr>
<th>SRY gene</th>
<th>Master Gene for testis development</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOX 9</td>
<td>SRY &amp; SOX 9 induce testis to form</td>
</tr>
<tr>
<td></td>
<td>FGF-9 (chemotactic factor)</td>
</tr>
<tr>
<td></td>
<td>FGF-9 causes tubules from mesonepric duct to</td>
</tr>
<tr>
<td></td>
<td>penetrate gonodal ridge</td>
</tr>
<tr>
<td>SF1</td>
<td>It stimulates differentiation of sertole or leydig cells</td>
</tr>
</tbody>
</table>

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

“**Approximately 40% of patients with a unicornuate uterus will have a urinary tract anomaly (usually of kidney)**”

Ref: Leon speroff 8/e, page 146

27. Ans. is c, i.e. Septate

“The only form of malfusion deformity which may lower fertility significantly is a fully septate vagina.”

“Septate anomaly is the anomaly most highly associated with reproductive failure and obstetric complications including first and second trimester miscarriage, preterm delivery, fetal malpresentation, IUGR and infertility.”

Ref: Jefferies 8/e, page 188.
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 growth or growth spurt (1st sign)
- T = breast budding/Thelarche (1st visible sign of puberty)
- P = Development of pubic hair—Pubarche
- H = Increase in height/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

1st sign – Testicular growth

- Penile growth
- Pubarche
- Peak height velocity

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.

**Causes of hypogonadotropic hypogonadism**

- CNS abnormalities
  - Neoplasms of pituitary or hypothalamus
  - Postradiotherapy.
  - Infiltrative disorders like histiocytosis, sarcoidosis
- Isolated Gonadotropin deficiency
  - Kallmann syndrome
  - Late onset congenital adrenal hyperplasia
- Miscellaneous
  - Severe weight loss
  - Genetic factors like Prader-Willi syndrome/ Laurence Moon
  - Biedl syndrome
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 (Loss of one X chromosome is due to Non-dysjunction during meiosis, the X chromosome retained is maternal in origin in most cases).

Mosaics = 45 XO/46 XX or 45 XO/46 XY

Gonads: B/L Streak Gonads, (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 in constitutional delay, height is short, whereas in Kallmann syndrome, normal height is seen.

Turner syndrome is the most common chromosomal disorder in humans.

Presentation

Neonatal period
- Most of the fetuses with Turner Syndrome abort
- IUGR is seen
- After birth – babies have:
  - Lymphedema
  - Cystic hygroma
  - Shield-shaped chest
  - Cardiac problems:
  - M/C coarctation of aorta
  - Renal problems
  - M/C horse shoe-shaped kidney

At puberty
- Primary amenorrhea
- Secondary sexual characteristics are absent
- Short stature
- Widely spaced nipples
- Webbed neck
- Cubital valvus
- Short 4th metacarpal
- Micronathia
- Heart anomalies
- Renal anomalies

Adult life
- They are prone to:
  - Autoimmune disorders like Hashimoto’s thyroiditis, Addison’s disease
  - Hypertension
  - Diabetes
  - Thyroid problems
  - Colon cancer
  - Osteoporosis
Note: Intelligence is normal in patients of Turner's syndrome.
Management = Estrogen replacement therapy. Due to the potential risk of endometrial cancer with estrogen therapy, progesterone is given along with estrogen.

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.
- Frohlich syndrome: Hypogonadotropic 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.

Also know:
Male Turner Syndrome – Noonan syndrome:
- Autosomal dominant disorder
- Streak Gonads
- 46XY Karyotype
- Develop autoimmune thyroiditis
- Somatic defects resemble Turner Syndrome

Exceptions:
- Characteristic cardiac lesion is Pulmonary valve stenosis
- Mental Retardation present (Absent in Turner)

An Overview of Causes of Delayed Puberty

<table>
<thead>
<tr>
<th>FSH Level</th>
<th>Differential Diagnosis</th>
</tr>
</thead>
</table>
| High > 30 mIU/mL| - Gonadal dysgenesis syndromes: Turner syndrome, Swyer syndrome  
- Primary ovarian failure |
| Low < 10 mIU/mL | - Constitutional delay  
- Intracranial neoplasms  
- Isolated gonadotropin deficiencies  
- Hormone deficiencies  
- Kallmann’s syndrome  
- Prader-Willi syndrome  
- Laurence-Moon-Biedl syndrome  
- Chronic disease and malnutrition |
| Normal          | - Anatomic deformities result in normal development with primary amenorrhea  
- Imperforate hymen  
- Transverse vaginal septum  
- Mullerian agenesis |

Precocious Puberty

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.

Central/True precocious puberty (M/C)
- It is due to excessive GnRH, gonadotropins and sex hormones because of premature activation of hypothalamic-pituitary ovarian axis.
- Here breast development and pubic hair development both are seen.
- Cyclical vaginal bleeding is also seen.
- M/C cause is idiopathic
- DOC= GnRH analogues

Peripheral/Pseudo precocious puberty
- It is due to excessive sex steroid secretion from either adrenal gland or gonads and is independent of activation of HPO axis. Pubertal changes occur due to independent production of sex steroids, eg., ovarian tumor producing estrogen
- It can lead to breast development, sexual hair development but not to cyclical bleeding as menarche requires not only production of estrogen but also its withdrawal
- Management – treat the cause.
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.

**Causes of Central Precocious Puberty**

**Constitutional / Idiopathic**
- 80% cases

**Specific etiology**
- 20% cases

| Causes of Central Precocious Puberty | 
| --- | --- 
| **Congenital defect** | 
| - Hydrocephalus |
| **Tumors** | 
| - Astrocytoma |
| | 
| - Glioma |
| | 
| - Neurofibroma |
| | 
| - Ependymoma |
| | 
| - Pineal Tm |
| | 
| - Arachnoid cyst |
| | 
| - Hamartoma |
| **Acquired lesions** | 
| - Trauma/head injury |
| | 
| - Inflammation-meningitis, encephalitis |
| | 
| - Rickets |
| | 
| - Hypothyroidism |
| | 
| - Von Recklinghausen disease |

**Causes of Peripheral Precocious Puberty**

*Here hypothalamic pituitary ovarian axis is intact*

**Isosexual**
- A. Ovarian causes
  - Granulosa cell Tm
  - Theca cell Tm
- B. Adrenal cause
  - Feminizing adrenal neoplasia (generally adrenal causes lead to heterosexual puberty)
- C. Ectopic Gonadotropin production
  - Dysgerminoma
  - Choriocarcinoma
  - Hepatoblastoma
  - Secrete HCG
- D. Exogenous estrogen
  - In the form of OCP’s
  - Corticosteroid intake
- E. McCune-Albright syndrome

**Heterosexual**
- Congenital adrenal hyperplasia
- Ovarian/adrenal testosterone secreting tumors:
  - Androblastoma
  - Hilus cell Tm
  - Gynandroblastoma
  - Lipoid cell tumors
  - Exogenous androgen

**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**

<table>
<thead>
<tr>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ambiguous genitalia is due to androgen insensitivity or decreased androgen levels.</td>
<td>Ambiguous genitalia is due to exposure to an increased androgen levels in intrauterine life.</td>
</tr>
</tbody>
</table>

E.g.: M/c cause: Testicular feminisation syndrome
- 5-alpha reductase deficiency
- Congenital lipoid 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**

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

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 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 hypospadiasis, 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 disorder (if any couple has had one affected child, subsequent baby has 1 in 4 chance of having the same disability).

Pathology

Inherited enzyme error in the biosynthesis of cortisol

↓ Cortisol production

↓ Inhibition of ACTH and therefore ↑ACTH

Due to enzyme deficiency  
M/C = 21 hydroxylase others:  
- 11 hydroxylase deficiency  
- 3p hydroxysteroid deficiency

↓ Cortisol  
↓ aldosterone

↑ levels of 17 OH progesterone  
by alternate pathway forms  
↑ testosterone  
Virilisation

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.  
- Gonads = ovaries.  
- Uterus and vagina are present, as mullerian duct develops normally, but remain infantile therefore failure to menstruate.  
- Vulva and introitus are affected. There is clitoromegaly and the genital folds fuse to form penile urethra rather than labia minora. Labia majora are fused which appears like scrotum.
Heterosexual precocious puberty: Pubic hair and axillary hair appear and voice deepens by the age of 2-4 years. (since these characteristics are dependent on androgen).

Associated metabolic abnormalities (d/t decreased aldosterone): Hyponatremia, hyperkalemia and hypotension.

**Investigation**

- **USG:** shows presence of uterus, vagina, fallopian tubes and ovaries. (Thus, all patients are potentially fertile)
- **Sex chromatin study:** shows positive Barr body. (Note: whenever a child presents with ambiguous genitalia always do karyotyping)
- Serum 17 hydroxy progesterone is elevated (> 800ng/dl) and serum 17-ketosteroid is elevated.
- Level of serum 170HP < 200 ng/dl virtually rules out the diagnosis of CAH.
- Serum electrolyte studies show salt wasting.

**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 170HP < 200 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

**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.

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** so gonads will be testis. The testis are intra abdominal.

**Pathology**

There is resistance to androgen.
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).
- No uterus (therefore Primary amenorrhea) and a short vagina
- Scanty pubic and axillary hair
- Smooth and hairless skin

**Lab investigation:** To distinguish it from Mayer Rokitansky Kuster Hauser syndrome (Mullerian agenesis) do karyotyping.

**Findings in Gonadal Biopsy:**
- Seminiferous tubules are small and hyalinized.
- Spermatogenesis is absent.
- Leydig cells and sertoli cells are normal.

**Management**

**Let them be Females**

- The testis should be removed after puberty (16-18 years) as they have a high potential for malignant change, specially gonadoblastoma and dysgerminoma.
- Bilateral laparoscopic gonadectomy is the preferred procedure for removal of intra-abdominal testes.
- Estrogen therapy is desirable to prevent osteoporosis 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.

**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

In males with klinefelter syndrome:

- Damage to both seminiferous tubules and Leydig cells occurs
- Testis small and firm (< 3.5 cms)/seminiferous tubules functionless
- Testosterone levels are decreased
- Cryptorchidism and sterility
- Negative feedback on FSH and LH lost
- Males are under virilised/external genitalia hypoplastic
- Oligospermia or Azoospermia

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
- Mediastinal germ cell tumor
- SLE
- Oligospermia
- Antisocial mental disorder
- Breast CA
- Varicose legs
- Diabetes mellitus

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
1. The sequence of development of puberty in girls is:  
   a. Thelarche, Pubarche, Menarche  
   b. Pubarche, Thelarche, Menarche  
   c. Pubarche, Menarche, Thelarche  
   d. Menarche, Thelarche, Pubarche  

2. The first sign of puberty in girls is:  
   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?  
   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:  
   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 central precocious puberty is:  
   a. Exogenous gonadotrophins  
   b. Ethinyl estradiol  
   c. GnRH analogues  
   d. Ethinyl estradiol  

8. Gynaecomastia is seen in:  
   a. Secondary syphilis  
   b. Lepromatous leprosy  
   c. HIV  
   d. Klinefelter’s syndrome  

9. Gynaecomastia is seen in all of the following conditions except:  
   a. Prolactinoma  
   b. TSH secreting adenoma  
   c. HCG secreting tumor  
   d. estrogen secreting tumor  

10. During sexual differentiation in males:  
    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:  
    a. Placenta steroid sulfatase deficiency  
    b. Fetal aromatase deficiency  
    c. Wnt4 mutation  
    d. Congenital adrenal hyperplasia  

12. Most common cause of female pseudohermaphroditism is:  
    a. Virilizing ovarian tumor  
    b. Ovarian dysgenesis  
    c. Exogenous androgen  
    d. Congenital adrenal hyperplasia  

13. Female pseudohermaphroditism true is:  
    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:  
    a. Estrogens  
    b. Antiandrogens  
    c. ACTh  
    d. Cortisone  

15. Best prenatal treatment for CAH is:  
    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:  
    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:  
    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 nipples. Karyotype of the girl would be: (AIIMS May 2013)
   a. 45 XO  
   b. 46 XXY
   c. 46 xy  
   d. 46 xx
20. A 16-year-old girl with it 58 inches present with primary amenorrhea and rising FSH. The histological finding most consistent with her conditions is: (AIIMS Nov 2013)
   a. Low oocyte in ovary  
   b. Corpus luteum hemorrhage  
   c. Marfan syndrome  
   d. Pituitary apoplexy
21. A 17-year-old girl with amenorrhea, atrophied breast, hypoplastic uterus: (AIIMS Nov 09)
   a. Turner’s syndrome  
   b. Gonadal dysgenesis  
   c. Androgen insensitivity syndrome  
   d. 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)
   a. Turner’s syndrome  
   b. Mullerian agenesis  
   c. Testicular feminization syndrome  
   d. Premature ovarian failure
23. Androgen insensitivity syndrome true is: (AIIMS May 08)
   a. Phenotype may be completely female  
   b. Predominantly ovarian component in gonads  
   c. Always in female  
   d. Testes formed abnormally and receptors are normal
24. Which of the following statement is/are true regarding androgen insensitivity syndrome? (PGI Nov 2012)
   a. Absent vagina  
   b. Karyotype is XY  
   c. Karyotype is XY  
   d. Pubic hair is normally present  
   e. Breast development is normal
25. Regarding androgen insensitivity syndrome, which statement is/are true: (PGI May 2013)
   a. Genotype is 46 XX  
   b. Scanty pubic hair  
   c. Well developed female external genitalia  
   d. Uterus absent  
   e. Breast development is adequate
26. All are seen in testicular feminization syndrome except: (PGI June 99)
   a. 46XY  
   b. Primary amenorrhea  
   c. Short stature  
   d. 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)
   a. Testicular feminisation syndrome  
   b. Mullerian agenesis  
   c. Turner’s syndrome  
   d. Gonadal dysgenesis
28. All of the following statements about Androgen Insensitivity Syndrome are true except: (AI 08)
   a. Patients have an XY genotype  
   b. Pubic hair are abundant  
   c. Short vagina may be present  
   d. 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)
   a. Turner’s syndrome  
   b. Mullerian agenesis  
   c. STAR syndrome  
   d. Androgen insensitivity syndrome
30. Among the following which is a feature of testicular feminization syndrome: (PGI June 99)
   a. XX pattern  
   b. Commonly reared as male  
   c. Well formed female internal genitalia  
   d. High testosterone levels
31. In Testicular Feminization syndrome Gonadectomy is indicated: (UPSC 04)
   a. As soon as it is diagnosed.  
   b. At puberty  
   c. Only when malignancy develops in it  
   d. When hirsutism is evident
32. Pure gonadal dysgenesis will be diagnosed in the presence of: (AI 03)
   a. Bilateral streak gonads  
   b. Bilateral dysgenetic gonads  
   c. One side streak and other dysgenetic gonads  
   d. 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)
   a. Karyotyping  
   b. IVP  
   c. Gonadotrophin levels  
   d. Serum Prolactin
34. True about klinefelter syndrome: (PGI May 2010)
   a. XXY  
   b. XO  
   c. Male hypogonadism  
   d. Female hypogonadism  
   e. FSH
35. A patient of 47 XXY karyotype presents with features of hypogonadism; likely diagnosis is: (AI 01)
   a. Turner’s syndrome  
   b. Klinefelters syndrome  
   c. Edwards syndrome  
   d. Down syndrome
36. A girl has primary amenorrhea with normal ovaries, absent internal genitalia but normal external genitalia. Most probable diagnosis?: (AI 10)
   a. Mayer-Rokitansky-Kuster-Hauser syndrome  
   b. Turner’s syndrome  
   c. Noonan’s  
   d. 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)
   a. Turner’s syndrome  
   b. Mullerian agenesis  
   c. Klinefelter’s syndrome-XXY  
   d. Gonadal agenesis
38. Young male presents with delayed puberty with decreased FSH, LH, and testosterone. Which of the following is NOT possible? (AI 2012)
   a. Kallmann syndrome  
   b. Klinefelter’s syndrome  
   c. Constitutional delay  
   d. Dax-1 gene mutation

39. In which of the following conditions do the ovaries function normally? (AIIMS Nov 2011)
   a. Turner’s syndrome  
   b. Rokitansky-Kuster-Hauser syndrome  
   c. Androgen insensitivity syndrome  
   d. Swyer’s syndrome

40. A girl with normal stature and minimal or absent pubertal development is seen in: (AIIMS Nov 2014)
   a. Kallmann syndrome  
   b. Turner syndrome  
   c. Testicular feminization syndrome  
   d. Pure gonadal dysgenesis

NEW PATTERN QUESTIONS

41. Normal size but non functioning uterus is usually associated with:
   a. Stenosis of the external os  
   b. Uterine synechiae  
   c. Partial agenesis of the vagina  
   d. Complete absence of vagina

42. Exposure of a female fetus to androgen in early embryogenesis may arrest differentiation of:
   a. Mullerian ducts  
   b. Ovary  
   c. Urogenital sinus  
   d. Mesonephric ducts

43. Destruction of ovaries prior to 7th week following fertilization results in:
   a. Pseudohermaphroditism  
   b. Uterine agenesis  
   c. Masculinisation  
   d. None of the above

44. In testicular feminisation syndrome:
   a. Buccal smear is chromatin positive  
   b. Normal breast size is observed  
   c. Menstruation is scanty and infrequent  
   d. Familial incidence is recognised

45. Precocious puberty may be seen in all of the following conditions except:
   a. Granulosa – cell tumour  
   b. Head – injury  
   c. Corticosteroid intake  
   d. Hyperthyroidism

46. Precocious puberty associated with bony dysplasia and café au lait spots in skin is seen in:
   a. Frohlichs syndrome  
   b. Alports syndrome  
   c. McCune-Albright syndrome  
   d. Laurence-Moon-Biedl syndrome
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 1st/ed p 315; Novak 14th/ed p 992, 15th/ed p 993

In girls the sequence of development of puberty is (Mnemonic: GTPH in males).^\text{a}

\[ \begin{align*}
G &= \text{Growth spurt} \\
T &= \text{Breast development (Thelarche)}^\text{b} \\
P &= \text{Pubic hair development (Pubarche)}^\text{b} \\
H &= \text{Height increases; peak growth velocity attained} \\
\text{in males} &= \text{Menstruation starts (Menarche)}^\text{b} \\
\text{(Axillary hair develop after menstruation starts)}^\text{b}
\end{align*} \]

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


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%ed pp 1017, 1020; Textbook of Gynae shielabalakrishnan 1st/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 → Continous 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. Harrisons 18th ed p 2889, Schwartz 7th ed p 541
Ref. Schwartz 7th ed p 541; Behl 9th ed p 223

Gynaecomastia implies presence of female type mammary glands in male.

It can be:

<table>
<thead>
<tr>
<th>Physiological</th>
<th>Pathological</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonatal period</td>
<td></td>
</tr>
<tr>
<td>Adolescence</td>
<td>Senescence</td>
</tr>
<tr>
<td>12 and 15 years</td>
<td>50 and 70 years</td>
</tr>
<tr>
<td>Unilateral</td>
<td>Bilateral</td>
</tr>
</tbody>
</table>

Causes of Gynaecomastia:

I. Estrogen excess states:

A. Gonadal origin:

1. True hermaphroditism
2. Gonadal stromal (Nongerminal) neoplasm of testis:
   - Leydig cell (interstitial)
   - Sertoli cell
3. Germ cell tumours:
   - Choriocarcinoma
   - Seminoma, teratoma
   - Embryonal carcinoma

B. Nontesticular tumours:

1. Skin-nevus
2. Adrenal cortical Neoplasms
3. Lung carcinoma
4. Hepatocellular carcinoma

C. Endocrine disorders:

1. Hypothyroidism
2. Hyperthyroidism

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)
   b. Reifenstein syndrome, (XY)
   c. Rosewater, Gwinup, hamwi familial gynecomastia (XY)
   d. Kallman syndrome
   e. Kennedy disease with associated gynaecomastia
   f. Eunuchoidal males (Congenital anorchia)
   g. Hereditary defects of androgen biosynthesis
   h. ACTH deficiency

2. Secondary testicular failure:
   a. Trauma
   b. Orchitis: due to mumps and leprosy
   c. Cryptorchidism
   d. Irradiation
   e. Hydrocele
   f. Varicocele
   g. Spermatocoele

C. Renal failure

III. Drug related conditions that initiate gynecomastia

1. Estrogen
2. Digitalis
3. Spironolactone
4. Methyldopa
5. Captopril
6. Calcium Channel blocker
7. Cimetidine (high doses)
8. Ketoconazole
9. Tricyclic Antidepressant
10. Diazepam

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


As discussed earlier—

In males
In males—masculanization 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 masculanization is due to testosterone/dihydrotestosterone, therefore if it is deficient it will lead to undermasculanization 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 8th ed p 349; Dutta Gyne 6th 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.”

Ambiguity of sex at birth—"Cases of ambiguity of sex detected at birth are due to adrenogenital syndrome unless proved otherwise".

Ref. Dutta Gynae 6th ed p 404

12. Ans. is d, i.e. Congenital adrenal hyperplasia

Ref. Dutta Gynaec 4th ed p 404; Williams Gynaec 1st ed p 409; Novak 14th 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 Gynaec 6th ed p 440; William Gynaec 1st ed p 409; Shaw 15th ed p 113

In a female most common cause of ambiguous sex is congenital adrenal hyperplasia.

As discussed in preceeding 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 15th ed p 114; CGDT 10th ed p 120; Leon speroff 8th 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/m² 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

At 10 weeks do chorionic villi sampling or amniocentesis (later).

If fetus is affected female continue dexamethasone throughout pregnancy
If fetus is male/unaffected female discontinue dexamethasone

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 begining treatment in only those mothers with an affected female child.

16. Ans. is c, i.e. Anti mullerian hormone deficiency

Ref. Leon speroff 7th 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 17th ed p 2341; Jeffcoate 7th ed p 227; Shaw 15th ed p 110-111; Williams Gynaec 1st ed p 370

As discussed in proceeding text.

**TURNERS SYNDROME** (also called as *Gonadal Dysgenesis*)

- **Karyotype:** Most common = 45 XO
  - **Gonads:** B/L Streak Gonads (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

- 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 Turner 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

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:

<table>
<thead>
<tr>
<th>Turner’s syndrome</th>
<th>Mayer-Rokintansky-Kuster-hauser-syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secondary sexual characteristics are absent, i.e.</td>
<td>Secondary sexual characteristic present, i.e.</td>
</tr>
<tr>
<td>Breast will be atrophied</td>
<td>Breast will be formed</td>
</tr>
</tbody>
</table>

- In klinefelter syndrome – Gonada 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 8th/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 infantile and there is 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.

22. Ans. is c, i.e. Testicular feminization syndrome

When a female comes with a complaint of primary amenorrhea the first thing to do is see her secondary sexual characteristics:

- In Turner’s 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\textsuperscript{th} ed p 111-112; Williams Gynae 1\textsuperscript{st} 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—  
- 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\textsuperscript{th} ed p 111-2; Dutta Gynae 6\textsuperscript{th} ed p 424

Androgen insensitivity syndrome/Testicular Feminizing syndrome:

- Genotype: 46 XY
- They are males who are resistant to testosterone
- Internal genitilia 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


All options have been explained in detail in the preceding text, I dont 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

In Testicular Feminization Syndrome

- Genotype  -  46XY
- Gonads  -  Testis (intrabdominal)
- 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.

>"Laboratory evaluation demonstrates elevated LH levels, normal or slightly elevated testosterone levels, and a 46XY Karyotype."

- LH levels are high (due to insensitivity of pituitary and hypothalamus to testosterone) but FSH levels are Normal.

Ref. Harrison 17th/ed p 2344; Dutta Gynae 6th/ed p 443

31. Ans. is b, i.e. At puberty

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. 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 14th/ed p 1051, 15th/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.

Ref. Novak 14th/ed p 1051, 15th/ed p 1050

32. Ans. is a, i.e. Bilateral streak gonads

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 and genes which protect against streak gonads are on the long arms of XX or XY.
In genotype 46XX / 46XY

<table>
<thead>
<tr>
<th>If only short arm of X or Y are missing</th>
<th>If only long arms of X or Y are missing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical features of Turner's syndrome</td>
<td>Normal looking female (height is normal or may be increased) with bilateral streak gonads ↓ This is pure gonadal dysgenesis.</td>
</tr>
<tr>
<td>Seen but gonadal development is normal.</td>
<td>This is pure gonadal dysgenesis.</td>
</tr>
</tbody>
</table>

Mixed Gonadal dysgenesis. 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 or gonadoblastoma and Yolk sac tumor) if the owners karyotype contains a Y chromosome.

33. Ans. is a, i.e. Karyotyping

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).

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Mullerian Agensis</th>
<th>Androgen Insensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inheritance pattern</td>
<td>Sporadic</td>
<td>X-linked recessive</td>
</tr>
<tr>
<td>Karyotype</td>
<td>46,XX</td>
<td>46,XY</td>
</tr>
<tr>
<td>Breast development</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Axillary and pubic hair</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Uterus</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Gonad</td>
<td>Ovary</td>
<td>Testis</td>
</tr>
<tr>
<td>Testosterone</td>
<td>Female levels</td>
<td>Male levels</td>
</tr>
<tr>
<td>Associated anomalies</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

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

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

In males with klinefelter syndrome:

- Damage to both seminiferous tubules and Leydig cells occurs
- Testis small and Firm (< 3.5 cms)/seminiferous tubules functionless
- Testosterone levels are decreased

Negative feedback on FSH and LH lost

Males are under virilised/external genitalia hypoplastic

Oligosperma or Azoosperma

Cryptorchidism and sterility

FSH↑

Stimulate Leydig cells

Androstenedione raised

Peripheral converted to

Estrogen↑

Gynaecomastia

Length of arms and legs is increased

Ref. Jeffcoate 7th ed p 198; CGDT 10th ed p 931 Fig. 56-2

Ref. Leon speroff 8th ed p 1261-1262; Harrison 17th ed p 2340-42
36. Ans. is a, i.e. Mayer-Rokitansky-Kuster-Hauser syndrome
   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
   The questions clearly mentions:
   i. Phenotype of the patient is female: This rules out Kleinefelter syndrome (47 X XY) as in kenefelters 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 deficancy 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
   • 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 Klinefellers = Testosterone is decreased, which results in increase in LH and FSH.

39. Ans. is b, i.e. Rokitansky-Kuster-Hauser syndrome
   • 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 rokintansky 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”…

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
Let's 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
In partial 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.

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
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
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
In testicular feminization syndrome:
Genotype = 46 XY
• Hence boll 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 7th ed p 116-118
• Friend for the details on causes of precocious puberty kindly see the preceding text.
• Remember hypothyroidism and not hyperthyroidism causes precocious puberty.

Reason:

If precocious puberty is associated with delayed bone age it suggests primary hypothyroidism.

46. Ans. is c, i.e. McCune-Albright syndrome
Ref. Novak 15th ed p 1023
Precocious puberty with bony dysplasia and cafe au lait spots points towards incure in McCune-Albright syndrome as the diagnosis.

McCune-Albright Syndrome is characterised by the classic triad of polyostetic fibrous dysplasia of bone, irregular cafe 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 cafe 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
**Chapter 7**

**Infections of the Genital Tract**

### 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

<table>
<thead>
<tr>
<th>Organism</th>
<th>Bacterial vaginosis</th>
<th>Candidiasis</th>
<th>Trichomonas vaginitis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Alteration of vaginal flora; lactobacilli decrease whereas coccobacilli and Gardnerella increase</td>
<td>Candida albicans &gt; Candida galbreta &gt; Candida tropicalis</td>
<td>Trichomonas vaginalis (flagellated protozoa)</td>
</tr>
<tr>
<td>M/C</td>
<td>Most common vaginitis (overall)</td>
<td>M/C vaginitis in:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Pregnancy, diabetes</td>
<td>- Proverse frothy greenish yellow discharge</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Immunocompromised</td>
<td>- Urinary symptoms</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- OCP users, steroid users, antibiotic users</td>
<td>- Dysuria</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Dyspareunia</td>
</tr>
<tr>
<td>STD</td>
<td>Not an STD</td>
<td>Mostly not an STD</td>
<td>It is an STD</td>
</tr>
<tr>
<td>pH of discharge</td>
<td>&gt; 4.5</td>
<td>&lt; 4.5</td>
<td>5-6</td>
</tr>
<tr>
<td>M/C complaint</td>
<td>Foul smelling dirty white discharge</td>
<td>Intense pruritis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No inflammation-hence no itching</td>
<td>Curdy white discharge (or cottage cheese like discharge)</td>
<td></td>
</tr>
<tr>
<td>Signs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IOC</td>
<td>Saline microscopy</td>
<td>Saline microscopy</td>
<td>Saline microscopy</td>
</tr>
<tr>
<td></td>
<td>’Clue cells’, i.e. vaginal epithelial cells to which bacteria are adhered seen</td>
<td>pseudohyphae seen</td>
<td>typical motile flagellated trichomonas seen or motility seen</td>
</tr>
<tr>
<td>Gold standard investigation</td>
<td>Gram stain on gram staining Nugent scoring 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 ≥ 7 is consistent with bacterial vaginosis</td>
<td>Culture on sabouraud’s medium or Nickerson medium</td>
<td>Culture on—Feinberg-whittington media or Diamond media</td>
</tr>
<tr>
<td>Amine test/Whiff test, i.e.</td>
<td>Positive, i.e. on adding 10% KOH to discharge, fishy odour or amine like odour obtained.</td>
<td>Negative</td>
<td>Maybe positive/or negative</td>
</tr>
<tr>
<td>10% KOH added to discharge</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T/t = Nonpregnant females</td>
<td>Metronidazole (500 mg BD x 7 days) or clindamycin</td>
<td>Azole group of antifungals like fluconazole/miconazole which can be applied topically or given orally (150 mg, single dose)</td>
<td>Metronidazole (2 gm single dose oral)</td>
</tr>
<tr>
<td>Pregnancy = DOC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Metronidazole (250 mg TDS x 7 days) To be avoided in first trimester</td>
<td>Topical azole antifungals To be avoided in first trimester</td>
<td>Metronidazole (250 mg TDS x 7 days)</td>
</tr>
<tr>
<td>Simultaneous treatment of</td>
<td>Not needed as BV is not an STD</td>
<td>If partner has symptoms then treatment needed</td>
<td>Always done as Trichomonas vaginalis is an STD</td>
</tr>
<tr>
<td>male partner</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Gonorrhea
- 2nd M/C cause of PID
- Caused by Gram negative diplococcus N: Gonorrhea
- Associated with trichomonas or chlamydia infection in 60% cases
- M/C route of spread: Ascending infection along with sperms
- M/C site affected: endocervix and Bartholin’s gland
- Symptoms: – Purulent vaginal discharge
  – Dysuria and frequency
  – No pruritus unless it is associated with trichomonas infection
- Diagnosis—Nucleic acid amplification testing (NAAT) of urine or endocervical discharge is done.
- Gold standard—culture in Thayer Martin media.
- Test for cure—Not done routinely.
- DOC: Penicillin (4.8 mega units of procaine penicillin). In areas of resistance—ciprofloxacin (500 mg) and ofloxacin (400 mg).
- 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
- DOC in pregnancy—Injection Ceftriaxone 125 mg single dose or oral cefixime 400 mg, single dose.

## Chlamydia
- Most common cause of PID
- Caused by chlamydia trachomatis (D-K serotype) an obligate intracellular parasite
- Associated with Gonorrhea infection
- M/C route of spread: Ascending infection along with sperms
- M/C site affected-endocervix, urethra and Bartholin’s gland: Like Gonococcus—stratified squamous epithelium is resistant to chlamydia also.
- Symptoms: It is insidious in onset
  – Mostly asymptomatic
  – May present with mucopurulent discharge
  – Dysuria and frequency of micturition with bacteriuria < 10^5 organisms/ml of urine is pathognomic of chlamydia infection in young sexually active females.
- Diagnosis—Nucleic acid amplification testing (NAAT) of urine or endocervical discharge is done.
- Gold standard—culture in McCoy lines
- Test for cure not done routinely
- DOC: Azithromycin 1 gm single dose or Amoxicillin 500 mg TDS x 7 days
- DOC in pregnancy—Azithromycin 1 gm single dose or amoxicillin 500 mg TDS x 7 days

## Condyloma Acuminata (Genital Warts)
- Most common viral STI
- Causative agent: HPV (human papilloma virus)
- >200 types 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.

---

**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.

**M/C cause of PID—chlamydia**

- 80% of women having Chlamydia are asymptomatic; 50% of women having gonococcal infection are asymptomatic.

- Test of cure for C. trachomatis and N. gonorrhoea is not routinely indicated. Repeat testing done 3 weeks after treatment is recommended for pregnant women only.
Chapter 7  Infections of the Genital Tract

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 dichloroacetic 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)

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. Primay 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 umblication
- 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.
Pelvic Inflammatory Disease (PID)

KNOW IN-DEPTH

Organisms Causing PID

<table>
<thead>
<tr>
<th>Primary</th>
<th>Secondary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlamydia (M/C)</td>
<td>E. coli</td>
</tr>
<tr>
<td>Gonococci</td>
<td>Group B Streptococcus</td>
</tr>
<tr>
<td>Mycoplasma</td>
<td>Klebsiella</td>
</tr>
<tr>
<td></td>
<td>Anaerobes</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Outpatient Treatment</th>
<th>Inpatient Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Patient should have oral therapy for 14 days</td>
<td>• Regimen A</td>
</tr>
<tr>
<td>• Regimen A</td>
<td>– Cefotaxime/cefotetan 2 g IV every 6 hours for 2–4 days PLUS</td>
</tr>
<tr>
<td>– Levofloxacin 500 mg (or ofloxacin 400 mg BD) PO once daily with or without</td>
<td>– Doxycycline 100 mg PO for 14 days</td>
</tr>
<tr>
<td>– Metronidazole 500 mg PO BID</td>
<td>• Regimen B</td>
</tr>
<tr>
<td>• Regimen B</td>
<td>– Clindamycin 900 mg IV every 8 hours PLUS</td>
</tr>
<tr>
<td>– Ceftriaxone 250 mg IM single dose PLUS</td>
<td>– Gentamicin 2 mg/kg IV (loading dose), followed by 1.5 mg/kg IV (maintenance dose) every 8 hours</td>
</tr>
<tr>
<td>– Doxycycline 100 mg PO BID with or without</td>
<td>• Alternative Regimen</td>
</tr>
<tr>
<td>– Metronidazole 500 mg PO BID for 14 days</td>
<td>– Levofloxacin 500 mg IV once daily with or without</td>
</tr>
<tr>
<td></td>
<td>– Metronidazole 500 mg IV every 8 hours</td>
</tr>
</tbody>
</table>

Broad spectrum antibiotic coverage (cefotaxime/cefofetin) 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. Extranatal 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.
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.

<table>
<thead>
<tr>
<th>Sites of Genital TB</th>
<th>% involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tubes</td>
<td>90–100%</td>
</tr>
<tr>
<td>Uterus</td>
<td>50–60%</td>
</tr>
<tr>
<td>Ovaries</td>
<td>20–30%</td>
</tr>
<tr>
<td>Vagina and Vulva</td>
<td>1–2%</td>
</tr>
</tbody>
</table>

Menstrual problems occurring in TB patients:
M/C menstrual complain oligomororrhea/Amerorrhea 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

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

Infertility results from tubal as well as endometrial disease. The tubes may be patent on HSG but there is functional loss.
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

```
1 for histopathological examination
1 for Culture in LJ medium
1 for PCR
```

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 – Gonorrhea
- M/c site for asymptomatic Gonorrhea 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 of gonorrhea 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.
The diagnosis of bacterial vaginosis was made based upon all of the following findings on microscopy except:

a. Abundance of gram variable coccobacilli  
b. Absence of lactobacilli  
c. Abundance of polymorphs  
d. Present of clue cells

7. In hysterosalpingography, fallopian tubes are seen beaded in appearance with clubbing of fimbrial end and ampulla. Most likely cause is:

a. Tuberculosis  
b. Candidiasis  
c. Chlamydia  
d. Gonococcus

8. 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?

a. Chancroid  
b. Herpes  
c. Syphilis  
d. Malignancy

9. A 25-year-old female with history of multiple contacts presenting with growth on vulva, the probable diagnosis is:

a. Condyloma accuminata  
b. Verruca plana  
c. Verruca vulgaris  
d. Condyloma lata

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:

a. Premetharin cream 1%  
b. Malathion 0.5%  
c. Overnectin  
d. Petroleum jelly

F2. Identify the lesion in the figure. All of the following drugs can be used in this condition except:

a. Imiquimod  
b. Podophyllin  
c. Methotrexate  
d. Trichlorocetic acid
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:
   a. Pseudomonas
   b. Staphylococcus
   c. Chlamidia
   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:
   a. IV antibiotics (broad spectrum)
   b. Drainage of TO mass
   c. Abdominal hysterectomy
   d. Laparoscopic exploration

14. Nongonococcal urethritis is caused by:
   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:
   a. Flagellated parasite (PGI June 05)
   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:
   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?
   a. Mycobacterium can be grown from menstrual blood (PGI Dec 01)
   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:
   a. Endocervix (AI 97)
   b. Vagina
   c. Urethra
   d. Fornix

26. Gonococcal vaginitis occurs in:
   a. Adults
   b. Children
   c. Infants
   d. Adolescents (TN 2007)

27. Which of the following cannot be detected by wet film?
   a. Candida
   b. Trichomonas
   c. Chlamydia
   d. Bacterial vaginosis (Delhi 08)

28. The most sensitive method for detecting cervical chlamydia trachomatis infection is:
   a. Direct fluorescent antibody test (AI 04)
   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)
   a. Culture on chocholate agar supplemented with hemin
   b. Culture on McCoy cells
   c. Culture on a bilayer human blood agar
   d. Culture on Vero cell lines

30. Drug of choice for Chlamydia in pregnancy: (AI 10)
   a. Doxycycline
   b. Tetracycline
   c. Erythromycin
   d. Penicillin

31. A woman presents with a thick curdy-white vaginal discharge. The best treatment for her is: (AI 00)
   a. Miconazole
   b. Metronidazole
   c. Nystatin
   d. Doxycycline

32. Creamy fishy odor is caused by: (AI 09)
   a. Trichomonas
   b. Gardnerella
   c. Candida
   d. Chlamydia

33. A lady presented with creamy white vaginal discharge with fishy odor, drug of choice is: (AIIMS May 09)
   a. Doxycycline
   b. Ofloxacin
   c. Metronidazole
   d. Clindamycin

34. Most common site for genital tuberculosis is: (AI 98)
   a. Ovary
   b. Uterus
   c. Cervix
   d. Fallopian tube

35. Most common route of transmission of endometrial tuberculosis is: (AIIMS June 98)
   a. Direct local spread
   b. Lymphatic spread
   c. Retrograde spread
   d. Hematogenous

36. The most common cause of tubal block in India is: (AI 06)
   a. Gonorrhoea infection
   b. Chlamydia infection
   c. Tuberculosis
   d. Bacterial vaginosis

37. Salpingitis/Endosalpingitis is best confirmed by: (AI 08)
   a. Hysteroscopy and laparoscopy
   b. X-ray
   c. Hysterosalpingography
   d. Sonosalpingography

38. A 19-year-old girl with painless ulcer in labia majora with everted margins: (AIIMS May 2013)
   a. Treponema pallidum
   b. Chlamydia
   c. Gonorrhoea
   d. Herpes genital ulcer disease

39. Which of the following is true with regards to genital tuberculosis?
   a. Ovarian involvement can occur without tubal affection
   b. Infertility is mainly due to anovulation
   c. Acid fast bacilli is identified in 100% cases of tubercular endometritis
   d. A negative Mantoux test reasonably excludes tuberculosis

40. The following statements are related to tubercular salpingitis except:
   a. The abdominal ostium may be patent with eversion of fimbriae
   b. The early lesion may be confused with adenocarcinoma on histology
   c. Genital tuberculosis is always secondary and the tubes are invariably the primary sites
   d. Salpingitis isthmic nodosa is the exclusive pathology to tuberculosis

41. True statement about female genital tuberculosis:
   a. Genital tract involvement results from lymphatic spread
   b. Premenstrual histopathological examination is diagnostic
   c. Polymerase chain reaction (PCR) techniques have got higher sensitivity in detection
   d. Reproductive outcome following antituberculous chemotherapy is satisfactory

42. The risk factors of acute pelvic inflammatory disease (PID) are the following except:
   a. Menstruating teenagers who have multiple sex partners
   b. IUD users
   c. Women with monogamous partner who had vasectomy
   d. Previous history of acute PID

43. The following are the primary sites of acute gonococcal infection except:
   a. Urethra
   b. Bartholin’s gland
   c. Skene’s gland (paraurethral glands)
   d. Ectocervix

44. Ulceration of the vulva is commonly seen in all except:
   a. Bacterial vaginosis
   b. Syphilis
   c. Chancroid
   d. Behçet’s disease

45. Regarding bacterial vaginosis, all are true except:
   a. Homogeneous vaginal discharge with pH 5.0 to 6.0
   b. Positive KOH — With fishy odour
   c. Positive clue cells in 100% of cases
   d. 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 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.

---

1. Ans. is a, i.e. Echinococcus

Classification of sexually transmitted disease

<table>
<thead>
<tr>
<th>Bacterial</th>
<th>Viral</th>
<th>Protozoa</th>
<th>Fungal</th>
<th>Ectoparasites</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neisseria gonorohoea</td>
<td>Herpes 1 – 2</td>
<td>Entamoeba histolytica</td>
<td>Candida</td>
<td>Phthirus pubis</td>
</tr>
<tr>
<td>Chlamydia trachomatis</td>
<td>Hepatitis B</td>
<td>Giardia</td>
<td></td>
<td>Sarcoptes scabei</td>
</tr>
<tr>
<td>Treponema pallidum</td>
<td>HIV</td>
<td>Molluscum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemophilus ducreyi</td>
<td>Molluscum</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mycoplasma hominis</td>
<td>25%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ureaplasma urealyticum</td>
<td>80%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calymmatobacterium granulomatis</td>
<td>liquid nitrogen</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shigella species</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group B streptococcus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bacterial vaginosis</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Campylobacter spp.</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
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).

3. **Ans. is d, i.e. Trichomonas vaginalis**

Strawberry vagina or angry-looking vagina is seen in case of Trichomonas infection.

4. **Ans. is b, i.e. Hypertension**

**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**

“Clue cells are the most reliable indicator of bacterial vaginosis. The positive predictive value of this test for the presence of BV is 95%.”

**Microscopy in Bacterial vaginosis shows:**

- Clue cells\(^1\) seen in wet mount
- ↑ number of Gardnerella vaginalis\(^2\)
- ↓ number of lactobacilli\(^3\)
- ↓ leukocytes (conspicuously absent)\(^4\)/polymorphs absent

Clue cells are vaginal epithelial cells to which bacteria are adhered.

7. **Ans. is a, i.e. Tuberculosis**

**HSG findings in case of tuberculosis:**

- Rigid non-peristaltic pipe like tube called as *lead pipe appearance.*\(^9\)
- *Beading of tube and variation in filling density.*\(^9\)
- Elongated and distended tube with everted fimbrae and patent abdominal ostium called as ‘tobacco pouch’ appearance.\(^3\)
- Calcification of tube.\(^5\)
- Bilateral cornual block.\(^9\)
- Vascular or lymphatic intravasation of dye.\(^6\)
- Tubal diverticula and/or fluffiness of tubal outline.\(^9\)
- Uterine cavity—irregular outline, honeycomb appearance or presence of uterine synechiae (*Asherman’s syndrome*).\(^9\)

**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. Chancre

Painless well-defined ulcers with firm base should raise the suspicion of chancre.

(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).

**Chancre** 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

Painless well-defined ulcers with firm base should raise the suspicion of chancre.

**Condyloma accuminata:**
- It is a **sexually transmitted disease** caused by HPV 6, 16, and 18.
- Warts are seen on the vulval area.
- Warts are common in the regions affected most directly by coitus i.e. posterior fourchette and lateral areas of vulva. These verrucous growths may coalesce to form large cauliflower growths.
- Condyloma is associated with vulval, vaginal, and cervical cancers.
- Diagnosis is by colposcopy which shows raised patches of aceto-white epithelium with speckled appearance.

**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
  - Podofilox
  - Imiquimod
  - Trichloroacetic acid: 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.
Lets also rule out other options.

- **Verrucous plana:**
  - Hands and face are the most common site, warts are not seen in genital area.
  - It is usually seen in children.
  - Sometimes it can also occur in young women, but then face is the most common site involved.

- **Verruca vulgaris:**
  - Here also the site of warts is different; usually affected areas are exposed parts of the body, hand, feet, nails, arms, and legs, face, and scalp.

- **Condyloma lata:**
  - Is the growth seen on genitalia in secondary syphilis.
  - The presence of these lesions without any other features of syphilis is very unlikely.

10. Ans. is a, i.e. Metronidazole and fluconazole

**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 manageents 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. Thee include detection of vaginal discharge abdominal pain, cervical motion tenderness, bilateral adnexal 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

**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.

**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

**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

**Non gonococcal urethritis is caused by:**
- Chlamydia trachomatis (30 – 40%)
- Mycoplasma genitalium
• 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.

Gonorrhea infection is caused by Neisseria gonorrhoeae—a gram-negative diplococci.
Incubation period = 3–7 days

Clinical features in adults

– 50 percent of patients with Gonorrhoea are asymptomatic
– Asymptomatic gonorrhoea in females is due to infection of endocervix.

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”


Signs:

• Labia are swollen and look inflammed.
• Cervicitis with a mucopurulent cervical discharge.
• Bartholin glands are enlarged and tender.
• On squeezing the ducts: purulent exudate escapes.

Complications-PID, Fitz-Hugh-Curtis syndrome and septicia.

Diagnosis: Secretions from the urethra, Bartholin’s gland and endocervix are collected for Gram staining and culture.

Treatment: Single dose ceftriaxone and azithromycin or you can give doxycycline 100 mg twice daily x 7 days for chlamydia

17. Ans. is a, d and e, i.e. Flagellated parasite, Pruritus, and Sexually transmitted disease

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

Trichomonas vaginalis has not been associated with infertility.

Infact Jeffcoate’s 7th 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 urealyticum

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.”


Effect of Trichomonas on Pregnancy Outcome

“Pregnant women with Trichomonas vaginitis are at increased risk for premature rupture of membranes and preterm delivery.”

– Novak 14th ed p 544
As far as abortions is concerned—
Organisms which have been associated with sporadic abortions are:
- *Chlamydia trachomatis*
- *Ureoplasma ureolyticum*
- *Mycoplasma hominis*
- *Toxoplasma gondii*
- *Listeria monocytogenes*
- *Camphylobacter*
- *Herpes virus*
- *Cytomegalovirus*

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.


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 15th ed p 131; Dutta Gynae 6th 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)
- Grayish white homogeneous discharge
- An amine smell with or without potassium hydroxide (positive whiff test)
- Presence of clue cells (20% of cells)

Clue cells are epithelial cells of the vagina that get their distinctive stippled appearance by being covered with bacteria. They are a sign of bacterial vaginosis, 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 15th ed p 156-58; Jeffcoate 7th 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 7th ed p 327

23. Ans. is c, i.e. ESR – 10 mm/hour

- 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 9th ed pp 678, 679; Dutta Gynecology 6th ed p 126

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 5th ed p 143, 8th ed p 147; CGDT 10th ed p 671, 672

There are 2 important points which we should be remembered about gonorrhoea infection.
- Squamous epithelium is resistant to gonococcal 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 gonoccal infection, Chlamydia trachomatis)
- 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

Chlamydia Infections

“Except in highly sophisticated centres, the detection of Cl. trachomatis is difficult by wet film.”
• Polymerase and ligase chain reactions are fast, highly sensitive and specific (96%) and now considered gold standard in the laboratory diagnosis.

Note: Ref. Harrison 18th 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

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 McCoy 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

In non pregnant females – DOC for Chlamydia = Azithromycin

Treatment of chlamydia infection during pregnancy

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Drug and Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preferred choice</td>
<td>Azithromycin (1 g) as a single dose</td>
</tr>
<tr>
<td></td>
<td>Amoxicillin (500 mg) orally 3 times a day × 7 days</td>
</tr>
</tbody>
</table>

“Azithromycin is the first-line treatment and has been found to be safe and efficacious in pregnancy.” – Williams Obs 23rd ed p 124

But since azithromycin is not given in the options, the next best option is Amoxicillin (penicillin).

Harrison 18th 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

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 or Candida glabrata.
- Antibiotic treatment needs to be prolonged (Fluconazole 150 mg weekly x 6 months or ketoconazole/Itroconazole 100 mg daily x 6 months).
- Simultaneous treatment of male partner.
- Patients on prolonged therapy should have their LFT monitored.

32. Ans. is b, i.e. Gardnerella

33. Ans. is c, i.e. Metronidazole

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.

**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**

**Reasons for infertility:**
- Tubal blockage
- Even if tubes are patent infertility is due to loss of tubal function.
- Tubercular endometritis causes infertility due to uterine scarring resulting in destruction of endometrium
- 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**

37. **Ans. is a, i.e. Hysteroscopy and laparoscopy**

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.

**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

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 adressesons in endometrial cairty

**Option c:** Acid fast bailli is identified in 1007 cases of TB endometritis incorrect

**Option d:** A negative mantoux test reasonably excludes TB correct

Ref. Dutta Gynae 6th ed p 140

40. Ans. is d, i.e. Salpingitis isthmica nodosa is the exclusive pathology to tuberculosis

- 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 tuber first size in the isthmic part near the uterine cornu, it is called as salpingitis isthmic 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

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

Women with monogamous partner who had vasectomy is a protective factor for PID and not risk factor
Risk factors of PID

- Menstruating teenagers.
- Multiple sexual partners.
- Absence of contraceptive pill use.
- Previous history of acute PID.
- IUD users.
- Area with high prevalence of sexually transmitted diseases.

Protective factors of PID

Contraceptive practice
- Barrier methods, specially condom, diaphragm with spermicides
- Oral steroidal contraceptives have got two preventive aspects.
  - Produce thick mucus plug preventing ascent of sperm and bacterial penetration
  - Decrease in duration of menstruation, creates a shorter interval of bacterial colonization of the upper tract.
- Monogamy or having a partner who had vasectomy.

Others
- Pregnancy
- Menopause
- Vaccines: Hepatitis B, HPV

43. **Ans. is d, i.e. Ectocervix**

Ref. Dutta Gynae 6th ed p 147

Ectocervix is covered by squamous epithelium and squamous epithelium is resistant to Gonococcal infection

Primary genital sites of involvement of gonorrhea

- Endocervix
- Urethra
- Skene’s gland
- Bartholin’s gland

44. **Ans. is a, i.e. Bacterial vaginosis**

**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>
<thead>
<tr>
<th>Table: Ulcers of the Vulva</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>STD related</strong></td>
</tr>
<tr>
<td>Syphilis</td>
</tr>
<tr>
<td>Herpes genitalis</td>
</tr>
<tr>
<td>Chancroid</td>
</tr>
<tr>
<td>Granuloma inguinale</td>
</tr>
<tr>
<td>Lymphogranuloma venerum</td>
</tr>
</tbody>
</table>

**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 6th ed p 152

We have discussed BV in detail.

Clue cells are diagnostic but about 40% patients may not have clue cells.
Pelvic Relaxation/Prolapse

Supports of Uterus

Primary Supports

| a. Mechanical support | • Uterine axis
| | • Angle of anteversion (angle between cervix and vagina)
| | • Angle of anteflexion (angle between cervix and uterus)
| b. Muscular or active support | • Pelvic diaphragm (formed by levator ani muscle)
| | • Perineal body
| | • Urogenital diaphragm (superficial and deep transverse perinei muscles)
| c. Fibromuscular support | • Pubocervical ligament
| | • Transverse cervical ligament (cardinal ligament/Mackenrodt’s ligament)
| | • Uterosacral ligament

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 anteflexed position and prevent it from descending through the urogenital diaphragm.

<table>
<thead>
<tr>
<th>Acquired</th>
<th>Congenital</th>
</tr>
</thead>
</table>
| • Menopause
| • Spina bifida occulta
| • Repeated child birth
| • Neurological disorders viz Ehler Danlos syndrome, Marfans syndrome
| • Traumatic deliveries
| • Iatrogenic trauma like in case of vaginal hysterectomy, vulvectomy
| • Faulty birth practices
| • Increased intra-abdominal pressure like in COPD, constipation, obesity
| • Precipitate labor

Classification of Prolapse

<table>
<thead>
<tr>
<th>Vaginal prolapse</th>
<th>Uterine prolapse</th>
</tr>
</thead>
</table>
| **A. Anterior vaginal wall:**
| Upper two thirds – cystocele/cystourethrocele
| Lower one third – urethrocele |
| Shaw’s classification (old classification):
| 1° – descent of the cervix to the vagina
| 2° – descent of the cervix to the introitus
| 3° – descent of the cervix outside the introitus.
| Procidetia: all of the uterus outside the introitus. |

Normally uterus remains in anteverted and anteflexed 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.

Edwardian's hernia is a rare type of hernia in the female genital tract. It is most commonly seen in the posterior vaginal wall and is caused by a congenital defect in the peritoneum. It is characterized by a mass protruding through the posterior vaginal wall duringVaginal prolapse.

The only true hernia of the pelvis is an ENTEROCELE and Rectocele because peritoneum herniates with the small bowel.
Vaginal prolapse (Fig. 8.1) | Uterine prolapse
---|---

**B. Posterior vaginal wall:**
- Upper one third – enterocoele (pouch of Douglas herniates)
- Middle one third – rectocele.
- Lower one third – Lax perineum

**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 while the patient performs valsala. 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.

**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

<table>
<thead>
<tr>
<th>Level</th>
<th>Structures included</th>
<th>Defect can lead to</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level I</td>
<td>Cardinal and uterosacral ligament</td>
<td>Uterine prolapse vault</td>
</tr>
<tr>
<td>Level II</td>
<td>Paravaginal attachments (pelvic fascia and superior fascia of levator ani)</td>
<td>Anterior and posterior vaginal wall prolapse</td>
</tr>
<tr>
<td>Level III</td>
<td>Perineal body, levator ani muscle, urogenital diaphram (They support distal 1/3 of vagina and introitus)</td>
<td>Anterior and posterior wall prolapse</td>
</tr>
</tbody>
</table>

**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).
- 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 not due to friction created by rubbing of the prolapsed parts with the thigh.
> **Treatment of decubitus ulcer:** Reduction of the prolapse part into the vagina and daily packing with glycerine and acriflavine. Acriflavine is an antiseptic agent while glycerine is a hygroscopic agent.

> Cancer of cervix or vagina is rarely seen, even in untreated cases of prolapse.

**Management of Prolapse**

**Vaginal Prolapse**

- Repair of cystocele & urethrocele
- Repair of lax perineum & rectocele
- Repair of enterocele

**Anterior colporrhaphy** – In this procedure layers of vaginal muscularis & pubocervical fascia are plicated. Success rate 30-40%

**Posterior Colpoperineorrhaphy** – Here para rectal & rectovaginal fascia are plicated over rectal wall. M/c complication – dyspareunia

**Abdominal repair:** Mosowitz repair (done by placing concentric purse string sutures around the cul de sac) Halbar repair (obliterates cul de sac via longitudinally placed sutures between the uterosacral ligaments)

**Vaginal repair** – McCall culdoplasty

**Uterine Prolapse**

Management depends on age and parity of the female—

- In a Young Nulliparous female or any female who desires future pregnancy/congenital prolapse
- Female <40 years and does not desire future pregnancy but wants to retain menstrual function
- Female >40 years and does not desire future pregnancy and does not want to retain menstrual function
- Female > 60 years and medically unfit for hysterectomy
- Prolapse during pregnancy/puerperium

- Sling surgery or cervicopexy
- Manchester operation (Fothergills operation)
- Ward Mayo’s vaginal hysterectomy
- Le Forts repair Dani’s repair
- Ring pessary

**Details of Prolapse Surgeries**

**Abdominal Sling Surgeries**

<table>
<thead>
<tr>
<th>Purandare Sling/ cervicopexy</th>
<th>Shirodkar Sling</th>
<th>Composite/Virkud Sling</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Sling made of fascia lata used</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• It is type of <strong>static sling</strong> which aims at strengthening the uterosacral. Mersilene tape is attached anteriorly to posterior surface of cervix and posteriorly to anterior longitudinal ligament in front of Sacral promontory.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• This surgery has drawback mainly on left side because tape has to pass below the mesentery of sigmoid colon to reach the sacral promontory.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• 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).</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**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 Marfans 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%).

Contd…
Contd…

<table>
<thead>
<tr>
<th>Purandare Sling/cervicopexy</th>
<th>Shirodkar Sling</th>
<th>Composite/Virkud Sling</th>
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</thead>
<tbody>
<tr>
<td><strong>Drawback:</strong></td>
<td></td>
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<td>• Injury to sigmoid colon,</td>
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<tr>
<td>• Intestinal obstruction</td>
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<tr>
<td>• Injury to ureter</td>
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<tr>
<td>• Haemorrhage from</td>
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</tr>
<tr>
<td>• Injury to genitofemoral</td>
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<tr>
<td>• Injury to sigmoid colon,</td>
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<tr>
<td>• Injury to genitofemoral</td>
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</tbody>
</table>

**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 6th 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° 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

<table>
<thead>
<tr>
<th>Patient is fit for abdominal surgery</th>
<th>In obese, elderly patients, not fit for abdominal surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transabdominal sacral colpopyx (Mesh is attached to the vault and sacral promontory).</td>
<td>Transvaginal sacrospinous ligament fixation/colpopyx can be done.</td>
</tr>
<tr>
<td>It is the Gold Standard Surgery for vault prolapse</td>
<td>A special instrument: Miya Hook is used for the surgery.</td>
</tr>
<tr>
<td>Recurrence rate—3%.</td>
<td></td>
</tr>
</tbody>
</table>

### 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 reposition 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 childbirth 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 reposited*
- 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 of delivery as there is always the possibility of recurrence of prolapse.
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 1st trimester
- Following vaginal delivery-after 24 hours
- Following cesarean section-after 24 hours

**Limitations of Kegel’s exercises**
- Kegels 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

**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

<table>
<thead>
<tr>
<th></th>
<th>Vesicovaginal Fistula</th>
<th>Ureterovaginal Fistula</th>
<th>Urethrovaginal Fistula</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>M/C</strong></td>
<td>VVF is the m/c urinary fistula</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| **Etiology**             | In developing countries – Obstructed labor  
It is due to ischemic necrosis, so develops 3–5 days 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 | Continuous 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** | **Technique:** Layer technique/ Latzko repair (for post hysterectomy VVF repair)  
chassar moir technique  
**Time of surgery:** 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 urethro vaginal 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).

<table>
<thead>
<tr>
<th>Observation</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper most swab soaked with urine but unstained with dye</td>
<td>Ureterovaginal fistula&lt;sup&gt;0&lt;/sup&gt;</td>
</tr>
<tr>
<td>Upper and lower swab remain dry but the middle swab soaked with dye</td>
<td>Vesicovaginal fistula&lt;sup&gt;0&lt;/sup&gt;</td>
</tr>
<tr>
<td>The upper two swab remain dry but lower one soaked with dye</td>
<td>Urethrovaginal fistula&lt;sup&gt;0&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

**Most Common in Fistulae**

<table>
<thead>
<tr>
<th>Most Common Fistula</th>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>MC urinary fistula</td>
<td>Vescovaginal&lt;sup&gt;0&lt;/sup&gt;</td>
</tr>
<tr>
<td>MC cause of VVF in India</td>
<td>Obstructed labour&lt;sup&gt;0&lt;/sup&gt;</td>
</tr>
<tr>
<td>MC cause of Uretero Vaginal Fistula</td>
<td>Injury to ureter after gynecological operation&lt;sup&gt;0&lt;/sup&gt; especially Wertheim's hysterectomy&lt;sup&gt;0&lt;/sup&gt;</td>
</tr>
<tr>
<td>MC cause of Vesico Vaginal fistula</td>
<td>Cesarean section&lt;sup&gt;0&lt;/sup&gt;</td>
</tr>
<tr>
<td>MC cause of Recto Uterine fistula</td>
<td>Cesarean perineal tear&lt;sup&gt;0&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

**Hot Topic**

**Menouria**
- It is seen in uterovesical fistulae<sup>0</sup>, i.e. fistula connecting uterus to bladder (Fig. 8.3).
- Usually follows cesarean section<sup>0</sup>
- The patient complains of hematuria/passage of menstrual discharge via urethra at the time of menstruation. Patient does not have urinary incontinence.<sup>0</sup>
- As is obvious 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>0</sup>
The presence of the fistula can be demonstrated by hysterography (but not by cystography) and cystoscopy. Treatment is by abdominal repair. Another important cause of cyclical hematuria is endometriosis of bladder.

**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**

<table>
<thead>
<tr>
<th>Sympathetic</th>
<th>Parasympathetic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Via T10 – L2/ L3</td>
<td>Via S2 – S4</td>
</tr>
<tr>
<td>Neurotransmitter – Norepinephrine</td>
<td>Neurotransmitter-acetyl choline that acts via muscarinic receptors in bladder.</td>
</tr>
<tr>
<td>• α receptor – located on urethra (close urethra and ↑ urine storage and continence)</td>
<td>• Contracts detrusor muscle</td>
</tr>
<tr>
<td>• β receptor - located mainly on bladder (↓ tone of bladder and urethra and promote storage of urine). (The somatic supply to bladder is mainly by pudendal nerves.)</td>
<td>• Relaxes urethra</td>
</tr>
</tbody>
</table>

**Types of Urinary Incontinence**

<table>
<thead>
<tr>
<th>Stress urinary incontinence</th>
<th>Urge urinary incontinence</th>
<th>Mixed incontinence</th>
<th>Functional incontinence</th>
<th>Bypass incontinence</th>
</tr>
</thead>
<tbody>
<tr>
<td>It is involuntary escape of urine when intra abdominal pressure is increased as in sneezing or coughing or laughing.</td>
<td>Involuntary leakage accompanied by or immediately preceded by the urge to void.</td>
<td>Both SUI and urge incontinence together</td>
<td>It is associated with cognitive, psychological or physical impairment that makes it difficult to reach the toilet.</td>
<td>May be caused by urogenital fistula or any congenital abnormality</td>
</tr>
<tr>
<td>It is the most common variety of urinary incontinence.</td>
<td>Involuntary detrusor muscle contractions are typically the cause of urge incontinence.</td>
<td></td>
<td>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</td>
<td></td>
</tr>
</tbody>
</table>

**Stress Urinary Incontinence (SUI)**

M/C type of urine incontinence in women accounting for 50-70% of cases.
**SUI Can Be Due To**

<table>
<thead>
<tr>
<th>Bladder Neck Descent (Including urethral hypermobility) (75–80%)</th>
<th>Intrinsic Sphincter Defect (20–25%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>It occurs due to loss of integrity of the fibromuscular tissue that supports the bladder neck &amp; urethra</td>
<td>It is diagnosed when the sphincter mechanism is compromised and fails to close the urethrovaginal junction. These patients are severely incontinent.</td>
</tr>
</tbody>
</table>

**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 urethro – vesicle angle.

**Management**

- **1st line of mgt:** Pelvic floor exercise i.e. Kegel’s exercises.

- **Definitive management:** Surgical management.

**Earlier concept:**

- i. For bladder neck descent (urethral hypermobility): Surgery done was colposuspension.

- ii. For intrinsic sphincter defect: Surgery done was pubovaginal sling surgery, e.g. aldridge, McGuire sling.

**Current principle:** These days – these surgeries have been replaced by minimally invasive synthetic midurethral slings—TVT and TOT.

<table>
<thead>
<tr>
<th>TVT</th>
<th>TOT</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Tension-free vaginal table)</td>
<td>(Tension free obturator tape)</td>
</tr>
<tr>
<td>• Both are vaginal surgeries</td>
<td>• Both are day care surgeries</td>
</tr>
<tr>
<td>• Both are day care surgeries</td>
<td>• In both surgeries, midurethra is suspended</td>
</tr>
</tbody>
</table>

**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

**Marshall-Marchetti-Krantz procedure for treating SUI is Osteitis pubis.**
**Tension Free Slugs**

<table>
<thead>
<tr>
<th>TVT</th>
<th>TOT</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Devised by Nelson in 1998</td>
<td>• Devised by Delorne in 2001</td>
</tr>
<tr>
<td>• A mersilene tape is passed vaginally in a U-shaped manner under midurethra to either sides</td>
<td>• A multifilament polypropylene tape is passed through obturator foramen</td>
</tr>
<tr>
<td>• Retropubic space of retzius is entered, chances of bladder injury present</td>
<td>• Retropubic space is not entered: ( \therefore ) Less complications</td>
</tr>
</tbody>
</table>
| • Complications:  
  – Injury to bladder  
  – Retropubic hematoma  
  – Sling erosion  
  – Overactive bladder | • Cystoscopy done at the end of procedure  
  • Preferred method |

**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
- 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.

**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 elastomer
- Inverted 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.

**Must rule out neurological cause for urge incontinence**
- Multiple sclerosis
- Slipped disc
- Diabetes mellitus

**Fig. 8.5: Intriol**

**Fig. 8.6: Continence guard**
1. A 30 years old multipara has uterine prolapse, the management of choice is: (AIIMS Nov 99)
   a. Fothergill’s repair
   b. Fothergill’s repair with tubal ligation
   c. Sling operation
   d. Vaginal hysterectomy

2. A 28-year-old female P3, has IIInd degree of utero-vaginal prolapse. The management of choice is:
   a. Fothergill’s repair (AIIMS Dec 97)
   b. Wertheim’s hysterectomy
   c. Perineal exercises x 3 month
   d. Vaginal hysterectomy with vault repair

3. A lady with prolapsed uterus after Fothergill’s repair will complain of following except:
   a. First trimester abortion  (AIIMS Nov 00)
   b. Cervical dystocia
   c. Premature labour
   d. Premature rupture of membrane

4. Fourteen weeks pregnancy with third degree prolapse. Best management will be: (AIIMS Dec 98)
   a. Sling surgery
   b. Foot end elevation
   c. Ring Pessary
   d. No treatment

5. Most common cause of vesicovaginal fistula in India is: (AIIMS Nov 02)
   a. Gynae surgery
   b. Irradiation
   c. Obstructed labour
   d. Trauma

6. Kamla, a 48-years-old lady underwent hysterectomy. On the seventh day, she developed fever, burning micturation and continuous urinary dribbling. She can also pass urine voluntarily. The diagnosis is: (AIIMS May 01)
   a. Vesico vaginal fistula
   b. Urge incontinence
   c. Stress incontinence
   d. Uretero-vaginal fistula

7. Post partum VVF is best repaired after: (AIIMS 87)
   a. 6 weeks
   b. 8 weeks
   c. 3 months
   d. 6 months

8. Ureter is identified at operation by: (AIIMS 96)
   a. Rich arterial plexus
   b. Peristaltic movement
   c. Relation to lumber plexus
   d. Accompanied by renal vein

9. **Version I**
   Most important structure preventing uterine prolapse is: (PGI 88)
   a. Round ligament
   b. Broad ligament
   c. Cardinal ligament
   d. Uterosacral ligament

   **Version II**
   All of the following are classified as primary supports of uterus except:
   a. Transcervical ligament
   b. Pubocervical ligament
   c. Uterosacral ligament
   d. Broad ligament

---

**FIGURE BASED QUESTIONS**

**F1.** The instrument used in figure F1 is used to measure:
   a. Urethrovescical angle
   b. Angle of arteflexion
   c. Angle of Anteversion
   d. Angle of vagina with horizontal

**F2.** The instrument shown in figure F2 is used for:
   a. Kegel’s exercise
   b. Retroversion
   c. Prolapse
   d. Measuring rectal pressure

**F3.** The pessary shown in Figure F3 is used for:
   a. Prolapse of uterus
   b. Stress urinary incontinence
   c. Retroversion of uterus
   d. Inversion of uterus
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:
   a. Nulliparous  (PGI Dec 03)
   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. Cystocoele  
   b. Procidentia  
   c. Rectocoele  
   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:  (Delli 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. Uterocevrical 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. Enterocoele  
   b. Subacute intestinal obstructions  
   c. Cliterar 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 procidentia. 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 colpexy  
   b. Sacrospinous ligament fixation  
   c. Le forts repair  
   d. Anterior colporrhaphy
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:
   a. VVF  
   b. Stress incontinence  
   c. Urethrocoele  
   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. Uretero – 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. Ureterovaginal  
   b. Vesico-vaginal  
   c. Vesico-uterine  d. Uretero-uterine
29. Multi para With LSCS, Presents With Cyclical Hematuria, Diagnosis can be: (PGI Dec 08)
30. Patient of rectovaginal fistula should be initially treated with: (AI 05)
31. The recommended non surgical treatment of stress incontinence is: (AI 09)
   a. Pelvic Floor Muscle Exercises  b. Bladder Training  c. Electrical stimulation  d. Vaginal cone/weights
32. Kelly’s plication operation is done in: (PGI June 05)
   a. Stress incontinence  b. Rectal prolapse  c. Urinary incontinence  d. Uterine prolapse
33. Bonney’s test demonstrates:
   a. Stress urinary incontinence  b. Urge incontinence  c. Overflow  d. All of the above
34. Version I
   Which of the following surgeries for stress incontinence has highest success rate: (AI 2011)
   a. Bursch colposuspension  b. Pereyra sling  c. Kelly’s stitch  d. Tension free vaginal tape (TVT)
   Version II
   Among the surgeries to correct SUI, the long-term success rate is maximum with: (AI 2002, 2011)
35. Site of placement of tension free vaginal tapes in stress urinary incontinence: (PGI May 2013)
   a. At ureterovaginal junction  b. At urethrovaginal junction  c. At upper part of urethra  d. At middle part of urethra  e. 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?
37. A woman treated for infertility, presents with 6 week amenorrhea with urinary retention. The most likely etiology is: (AI 00)
   a. Retrotverted uterus  b. Pelvic hematocoele  c. Impacted Cervical Fibroid  d. Carcinoma Cervix
38. Childbirth trauma leading to urine incontinence is seen least in females with:
39. Ureterovaginal fistula should best be treated by:
   a. Ureteroneocystostomy  b. End-to-end anastomosis through an ureteric catheter  c. Implantation into colon  d. Ileal conduit
40. Accidental injury of the ureter during abdominal operation should be managed by all except:
   a. Deligation  b. End-to-end anastomosis through an ureteric catheter  c. Implantation into the bladder  d. Colonic implantation
41. In anterior colporrhaphy, the best method of suture apposing the vaginal flaps is:
   a. Interrupted  b. Continuous  c. Interlocking  d. Interrupted mattress
42. Regarding the sling procedure for Urodynamic Stress Incontinence (USI):
   a. Tension-free vaginal tape (TVT) elevates the bladder neck to a retropubic position
   b. TVT is an autologous sling material
   c. Intrinsic sphincter deficiency is an indication
   d. Success rate of TVT is low than other retropubic procedures
43. Complications of sling procedures (TVT) for USI are all except:
   a. Injury to bladder and wound haematoma
   b. Sling erosion particularly with polytetrafluoroethylene (Goretex)
   c. Overactive bladder in about 7% cases
   d. Obturator nerve injury is about 10%
44. Urinary symptoms of procidentia:
   a. Frequency of micturition  b. Retention of urine  c. Stress incontinence  d. All of the above
45. Enterocele formation is a common complication of:
   a. Suburethral sling surgery  b. TVT  c. Bursch colposuspension  d. TOT
46. Baldy webster operation is done in case of:
   In case of:
47. In Baden Walker Halfway system of classification of prolapse, the reference point is:
A. Ans. is b, i.e. Fothergill’s repair with tubal ligation

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.”

Thus in question 1 answer is fothergill’s repair with tubal ligation

B. Ans. is a, i.e. Fothergill’s repair

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.

Thus in question 1 answer is fothergill’s repair with tubal ligation

C. Ans. is c, i.e. First trimester abortion

In fothergills repair ceroidial abortion 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

**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.

D. Ans. is c, i.e. Ring pessary

Other indications of Ring pessary:

• 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.

**Note:** Pessaries are of two varieties: Supportive pessary eg – Ring pessary

Space occupying pessary eg – Gelhorn pessary.

E. Ans. is c, i.e. Retroversion of uterus

The pessary shown in F 3 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.
5. Ans. is c, i.e. Obstructed labour

“In developing countries, 90% of genitourinary fistulas arise from obstetric trauma, specifically from prolonged or obstructed labour.” —William Gynae 1st/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. 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 be abdominal and vaginal.” —Williams Gynae 1st/ed p 573

Extra Edge:

<table>
<thead>
<tr>
<th>Most common in fistulae</th>
<th>MC urinary fistula</th>
<th>Vesicovaginal³</th>
</tr>
</thead>
<tbody>
<tr>
<td>MC cause of VVF in india</td>
<td></td>
<td>Obstructed labour²</td>
</tr>
<tr>
<td>MC cause of Uretero Vaginal Fistula</td>
<td></td>
<td>Injury to ureter after gynaecological operation² especially Wertheim’ hysterectomy²</td>
</tr>
<tr>
<td>MC cause of Vesico Uterine fistula</td>
<td>Cesarean section²</td>
<td></td>
</tr>
<tr>
<td>MC cause of Recto Vaginal fistula</td>
<td>Cesarean perineal tear²</td>
<td></td>
</tr>
</tbody>
</table>

6. Ans. is d, i.e. Ureterovaginal fistula

- 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.⁰
- 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 7th/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 incontinence, 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

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 months⁰ for all tissue inflammation to subside. If one attempt fails to heal fistula, second attempt is done after 3 months.⁰
- 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.

Post-operative Management—
- Continuous bladder drainage for 14 days.
- 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.

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/st 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

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

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.”

Thus answer to Q9 version 1 is both cardinal ligament and uterosacral ligament.

10. Ans. is b, i.e. Venous congestion

“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 patients 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

*Fothergill’s repair/Manchester operation*

“It is suitable for women under 40 years who are desirous of retaining their menstrual and reproductive function.”

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 2nd 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).

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 gynaecological 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 Mackenrodt’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.**


As explained in preceeding 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 colporhaphy 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 7th ed p 855; Dutta Gynae 6th ed p 410

Important gynecological causes of acute retention:—

<table>
<thead>
<tr>
<th>Period of life</th>
<th>Associated disorders</th>
<th>Provisional diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postmenarchal</td>
<td>Primary amenorrhea</td>
<td>Primary amenorrhea</td>
</tr>
<tr>
<td>Childbearing period</td>
<td>Short period of secondary amenorrhea; Menorrhagia; No menstrual abnormality; Irregular bleeding with pain; Irregular bleeding with fever</td>
<td>Retroverted gravid uterus; Uterine fibroid impacted in POD; Impacted ovarian tumor, cervical or broad ligament fibroid; Pelvic hematocoele; Pelvic abscess</td>
</tr>
</tbody>
</table>

Besides the above causes Jeffcoate 6th 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 15th ed p 345-7; Jeffcoate 7th 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)._
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
- 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 case of infertility. Surgical correction of the retroversion should result in conception.
- Abortion: can cause abortion between 10th to 14th 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
  - Baldy webster operation

16. Ans. is a, i.e. Cystocele
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 14th ed p 898
Anterior organ prolapse is cystocele

17. Ans. is a, i.e. Prolapse Uterus
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
Example: Already explained in preceding text.

19. Ans. is c, i.e. Shirodkar’s abdominal sling
   - 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
   - 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. Enterocele
As discussed in preceeding text enterocele 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
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:**

- 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** – Jeffrey 7th/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**

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 anaesthesist will not agree to give anaesthesia.

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 colpocleisis**

**Vault Prolapse:**

- It is a long complication of hysterectomy and refers to prolapse of the vaginal stump left behind after performing hysterectomy.

<table>
<thead>
<tr>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient is fit for abdominal surgery</td>
</tr>
<tr>
<td>Trans abdominal sacral colpocleisis (Mesh is attached to the vault and sacral promontory).</td>
</tr>
</tbody>
</table>

24. **Ans. is c, i.e. Foley’s catheterisation**

“Urine culture is mandatory before surgery and infection should be treated. The urine is collected by Catheterization.”

– Shaw 14th/ed p 167

In VVF

“Preoperative collection is best to be done through ureteric catheterization.”

– Dutta 5th/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 5th/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**


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**

Methods for repairing VVF:

- Layer Technique
- Latzko procedure (for fistulas following hysterectomy)
- Chassar moir technique

Ref. Shaw 15th/ed p 186-7; Dutta Gynaec 6th/ed pp 421, 423
27. Ans. is b, i.e. Uretero-vaginal fistula

Ref. Dutta Gynae 6th ed p 420; Shaw 15th 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).

<table>
<thead>
<tr>
<th>Observation</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Upper most swab soaked with urine but unstained with dye</td>
<td>Ureterovaginal fistula?</td>
</tr>
<tr>
<td>2. Upper and lower swab remain dry but the middle swab soaked with dye</td>
<td>Vesicovaginal fistula?</td>
</tr>
<tr>
<td>3. The upper two swab remain dry but lower one soaked with dye</td>
<td>Urethrovaginal fistula?</td>
</tr>
</tbody>
</table>

28. Ans. is c, i.e. Vesico-uterine

Ref. Shaw 15th ed p 188; Jeffcoate 7th ed p 266

29. Ans. is b and c, i.e. UVF, and bladder endometriosis

The condition of cyclical passage of menstrual blood in urine is called as menouria.

Menouria:
- It is seen in uterovesical fistulae
- Usually follows cesarean section
- The patient complains of hematuria/ passage of menstrual discharge via urethra at the time of menstruation. Patient does not have urinary incontinence.
- Mensouria is seen when uterovesical fistula opens into the uterus above the isthmus.
- The presence of the fistula can be demonstrated by hysterography (but not by cystography) and cystoscopy.
- Treatment is by abdominal repair.
- Another Important cause of cyclical hematuria is endometriosis of bladder.

30. Ans. is a, i.e. Colostomy


Rectovaginal fistula is a communication between the epithelium lined 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:

<table>
<thead>
<tr>
<th>Congenital</th>
<th>Acquired</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Due to congenital abnormalities</td>
<td>- Trauma</td>
</tr>
<tr>
<td></td>
<td>- Inflammatory bowel disease</td>
</tr>
<tr>
<td></td>
<td>- Irradiation</td>
</tr>
<tr>
<td></td>
<td>- Neoplasia</td>
</tr>
<tr>
<td></td>
<td>- Infection</td>
</tr>
<tr>
<td></td>
<td>- Other causes</td>
</tr>
</tbody>
</table>

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.  

**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 5th ed p 586; Novak 14th ed p 875; Williams Gynae 1st ed p 525-6; Textbook of Gynae Sheila Balakrishnan 1st ed p328

The most recommended non surgical treatment for stress incontinence is pelvic floor muscle exercise.

“The most recommended non surgical treatment for stress incontinence is pelvic floor muscle exercise.”

- Novak’s 14th ed p 875; Dewhurst 10th 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*\textsuperscript{th} ed p 174; *Textbook of Gynae Shiela Balakrishnan 1*\textsuperscript{st} ed p 330

Kelly’s plication/Kelly’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*\textsuperscript{th} 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 a 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)**


**Version II**

**Ans. is a, i.e. Burch’s colposuspension**  
Ref. *Telinde 9*\textsuperscript{th} 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 choose it.

So in version II- Answer is Burch colposuspension  
*Telinde 9*\textsuperscript{th} ed p 1050-6.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Long-term success rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burch's colposuspension</td>
<td>89.5</td>
</tr>
<tr>
<td>Stamey's repair</td>
<td>85</td>
</tr>
<tr>
<td>Kelly's repair</td>
<td>50–60</td>
</tr>
<tr>
<td>Aldridge Repair</td>
<td>85</td>
</tr>
</tbody>
</table>

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 sons) 2007/440

35. **Ans. is d, i.e. At middle part of urethra**  
Ref. *Shaw 15*\textsuperscript{th} ed p 193-194; *Dutta gynae 6*\textsuperscript{th} ed p 404

Read the text for explanation.

36. **Ans. is d, i.e. Osteitis pubis**  
Ref. *Telinde 9*\textsuperscript{th} ed pp 1057-8; *Textbook of Gynae, Shiela Balakrishnan 1*\textsuperscript{st} 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 complaint 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*\textsuperscript{th} ed p 299

So Option “a” is ruled out

**Option “b” Pelvic hematocoele**

"Pelvic hematocoele is formed in a patient complaining of 6 weeks amenorrhea in case of ectopic pregnancy.”  
— *Jeffcoate 6*\textsuperscript{th} ed p 212
Though pelvic hematocele 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\textsuperscript{th} 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\textsuperscript{th} 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 pevis.

39. Ans. is a, i.e. Ureteroneocystostomy
Ref. Dutta Gynae 6\textsuperscript{th} 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
See previous question
Ref. Dutta Gynae 6\textsuperscript{th} ed p 427

41. Ans. is a, i.e. Interrupted
Ref. Dutta Gynae 6\textsuperscript{th} 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.
Let 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 autologus sling material. Autologus 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. Jeffwates 8/e, page 803
Complications of TVT are:
• Injury to bladder
• Retropubic hematoma
• Sling erosion
• Overactive bladder.

44. Ans. is d, i.e. All of the above
Ref. Dutta Gynae 6\textsuperscript{th} ed p 208
All the urinary symptoms given in the options can occur in case of prolapse.
“Retention of urine may rarely occur.”
Ref. Dutta Gynae 6\textsuperscript{th} ed p 208

45. Ans. is c, i.e. Burch’s colposuspension
Ref. Dutta Gynae 6\textsuperscript{th} ed p 404
Enterocele formation occurs with Bursch colposuspension.

46. Ans. is b, i.e. Retroversion of uterus
Ref. Jeffcoates 8/e, page 274.

Surgeries for Retroversion
• Baldy webster operation
• Modified Gilliam’s operation
• Laparoscopic ventrosuppression
Since round ligament helps to keep uterus in antverted position in all these surgeries, round ligaments are tightened.

47. Ans. is a, i.e. Hymen
(Ref. Jeffcoates 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.
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Percent</th>
<th>Basic Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male factors</td>
<td>30</td>
<td>Semen analysis</td>
</tr>
<tr>
<td>Tubal/uterine/peritoneal factors</td>
<td>25</td>
<td>HSG, laparoscopy, chromoperturbation</td>
</tr>
<tr>
<td>Anovulation/ovarian factors</td>
<td>25</td>
<td>BBT chart, midluteal progesterone level, endometrial biopsy, luteinizing hormone testing</td>
</tr>
<tr>
<td>Cervical factors</td>
<td>10</td>
<td>Postcoital test</td>
</tr>
<tr>
<td>Unexplained infertility</td>
<td>10</td>
<td>All of the above</td>
</tr>
</tbody>
</table>

### 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
Infertility

WHO Semen Analysis

1992 guidelines

<table>
<thead>
<tr>
<th>Parameter</th>
<th>1992 guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>2 ml</td>
</tr>
<tr>
<td>Sperm concentration</td>
<td>20 million/ml</td>
</tr>
<tr>
<td>Sperm motility</td>
<td>50% progress</td>
</tr>
<tr>
<td>or &gt; 25% rapidly</td>
<td></td>
</tr>
<tr>
<td>progressive</td>
<td></td>
</tr>
<tr>
<td>Morphology (Strict Criteria)</td>
<td>&gt; 15% normal</td>
</tr>
<tr>
<td>WBC</td>
<td>&lt; 1 million/ml</td>
</tr>
<tr>
<td>Immuno bead</td>
<td>&lt; 10% coated with</td>
</tr>
<tr>
<td>or mixed antiglobulin</td>
<td>antibodies</td>
</tr>
<tr>
<td>reaction test</td>
<td></td>
</tr>
</tbody>
</table>

Male Infertility

Common Causes

- Pretesticular
  - Endocrine
  - Gonadotropin deficiency
  - Thyroid dysfunction
  - Hyperprolactinaemia
  - Psychosexual
  - Impotence
  - Erectile dysfunction
  - Drugs
  - Antihypertensives
  - Antipsychotics
  - Genetic
  - 47 XXY (Klinefelter)
  - Y chromosome deletions
- Testicular
  - Immotile cilia syndrome
  - Cryptorchidism
  - Infection (mumps orchitis)
  - Toxins (drugs, radiation)
  - Primary testicular failure
  - Sertoli cell-only syndrome
  - Oligoasthenoteratozoospermia
- Post-testicular
  - Obstruction of efferent duct
  - Congenital
  - Absence of vas deferens
  - Young’s syndrome
  - Acquired infection
  - Tuberculosis, gonorrhoea
  - Surgical
  - Vasectomy
  - Others
  - Ejaculatory failure
  - Bladder neck surgery
  - Retrograde ejaculation

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)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>WHO 2010</th>
<th>WHO 1999</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>≥ 1.5 mL</td>
<td>≥ 2 mL</td>
</tr>
<tr>
<td>pH</td>
<td>7.2–7.8</td>
<td></td>
</tr>
<tr>
<td>Viscosity</td>
<td>&lt; 3 (scale 0–4)</td>
<td></td>
</tr>
<tr>
<td>Sperm concentration</td>
<td>15 million/mL</td>
<td>≥ 20 million/mL</td>
</tr>
<tr>
<td>Total sperm count</td>
<td>39 million/ ejaculate</td>
<td>≥ 40</td>
</tr>
<tr>
<td>Motility</td>
<td>Progressive motility = 32%</td>
<td>≥ 25%</td>
</tr>
<tr>
<td>Total motility</td>
<td>≥ 40</td>
<td>≥ 50%</td>
</tr>
<tr>
<td>Morphology</td>
<td>Normal forms 4%</td>
<td>≥ 14</td>
</tr>
<tr>
<td>Viability</td>
<td>Living 58%</td>
<td>≥ 75</td>
</tr>
<tr>
<td>Leucocytes</td>
<td>Less than 1 million/mL</td>
<td></td>
</tr>
<tr>
<td>Round cells</td>
<td>&lt; 5 million/mL</td>
<td></td>
</tr>
<tr>
<td>Sperm agglutination</td>
<td>&lt; 10% spermatozoa with adherent particles</td>
<td></td>
</tr>
</tbody>
</table>
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 / oligospermia – Decreased sperm number < 20 million/ml
- Asthenozoospermia / asthenospermia – Decreased sperm motility
- Teratozoospermia – Increased abnormal forms of sperm
- Oligoasthenoteratozoospermia – All sperm variables abnormal
- Azoospermia – No sperm in semen
- Aspermia – No ejaculate (ejaculation failure)
- Leucocytospermia – Increased white cells in semen
- Necrozoospermia – All sperms non-viable or non-motile

- 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 oligospermia 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.
Chapter 9 Infertility

<table>
<thead>
<tr>
<th>Cause</th>
<th>Lab Test</th>
</tr>
</thead>
</table>
| **Pretesticular cause**-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 |
| **Testicular cause**-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. |
| **Post testicular cause** 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).

**Management Options in Male Infertility**

Mild oligospermia = IUI (Intrauterine insemination)

**Severe Oligospermia**

- Hypergonadotropic hypogonadism (↑FSH & ↑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.

**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.
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

**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)
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%).

- 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
- Percutaneous Epididymal Sperm aspiration: PESA
- Testicular sperm extraction: TESE
- Percutaneous Testicular sperm fine needle aspiration: TESA (also called Fine Needle Aspiration FNA).

**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.

**TESA**
- 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).

**MESA**
- 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 anesthesis).
  - 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.

**PESA**
- Percutaneous epididymal sperm aspiration can also be used in cases of Post testicular azoospermia but it is a blind procedure. Bleeding, epididymal injury and postsurgical fibrosis can occur.

**TESE**
- Indicated in men with testicular azoospermia or gonadal failure.
**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 amenorrhea, 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/M²) 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 amenorrhea 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

Diagnosis of Ovulation

Indirect

Direct

Conclusive

Laparoscopy

Pregnancy

Basal Body Temperature
In ovulatory cycle, there is a biphasic pattern of temperature variation. At the time of ovulation, BBT is raised to 0.5 to 1°F. The rise sustains throughout the 2nd half of the cycle and falls two days prior to the next period - called biphasic pattern. In pregnancy, rise of temperature is sustained. In anovulatory cycle - No Rise of temperature through-out the cycle.

Cervical Mucus Study
Under the influence of oestrogen, cervical mucus shows ferning or stretchability (spinbarkeit). After ovulation, progesterone causes loss of ferning and stretchability. Persistence of ferning/spinbarkeit beyond 22 days means anovulation.

Vaginal Cytology
Maturation index shifts to left under the effect of progesterone after ovulation.

Hormonal Estimation
- 
- 
-  
-  
- 

Endometrial Biopsy
It should be done in premenstrual phase day of regular cycle. In case of irregular cycles it is done within 24 hours of the period 2 samples should be taken one for HPE and other for means ovulation has accrued. AFB. Secretory endometrium ovulatory. Proliferative endometrium anovulatory cycle.

USG
Serial sonography can precisely measure the size of Graafian follicle, and thus the exact time of ovulation. Features of recent ovulation are collapsed follicle and some fluid in pouch of Douglas.

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.
- Dose = 50–250 mg. However, the US FDA-approved maximum dose for clomiphene citrate is 100 mg
- Clomiphene blocks “Estrogen” receptors → increase FSH from pituitary → growth of follicles
- Thus it can be used only in patients with intact hypothalamic −pituitary ovarian axis
- 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 inhibit 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 inhibit 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.
Chapter 9  Infertility

### 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.
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.
- In women desiring reversal of tubal sterilization with poor prognosis for recanalization.
- Ovarian failure and Diminished ovarian reserve: Here IVF is performed using donor oocytes.
- 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.
- 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.
- 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.
- 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
- Unexplained infertility

Since, we have to choose one option: Tubal pathology i.e. option ‘a’ is the best option.

**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.

<table>
<thead>
<tr>
<th>Quality of cervical mucus: (under the influence of estrogen)</th>
<th>Number of motile sperms/HPF:</th>
<th>Motility of sperms:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preovulatory cervical mucus is clear, watery, abundant and stretchable (spin barkeit &gt; 8 – 10 cm) with good tertiary ferning and low cellularity. Characteristic of Progesterone stimulated mucus: – Thick &amp; opaque – Lacks ferning – Breaks (tacks) on stretching</td>
<td>Atleast 15 – 20 motile sperms/HPF should be seen.</td>
<td>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 immobile.</td>
</tr>
</tbody>
</table>

**Prerequisites for the test:**

- Abstinence of 2 days
- Intercourse to be performed 2 - 12 hours before the test
- No use of lubricant

**Tests for studying sperm function**

- Sperm Penetration assay
- Miller kurzrok test
- Hypoosmotic swelling test: Test for studying tail function.
- Hemizona Test: Test for studying the ability of sperm to bind to human zona pellucida.

**Also Know**

- Tests for studying sperm penetration

**Confirmatory tests for detecting antisperm**

- Sperm agglutination test
- MAR (mixed agglutination reaction) Test.
- Immunobead test
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. Gonorrhea  
   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

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 clomiphene 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 cornu diagnosed on hysterosalpingography. Next step in treatment is: (AIIMS Nov 2011)
   a. IVF
   b. Laparoscopy and hysteroscopy
   c. Tuboplasty
   d. Hydrotubation

Female Infertility: Cervical Cause

19. Post coital test detects all of the following except: (AIIMS May 01)
   a. Fallopian tube block
   b. Cervical factor abnormality
   c. Sperm count
   d. Sperm abnormality

20. Postcoital test (PCT) is done for: (PGI June 05)
   a. Cervical receptivity
   b. Sperm motility
   c. Absolute sperm count
   d. Viable sperm count
   e. Endometrial function

21. Cervical hostility is tested by following except: (PGI Dec 97)
   a. Spinnbarkeit
   b. Postcoital test
   c. Miller kuzrole test
   d. Keller test

22. Postcoital test showing non motile sperms in the cervical smear and Motile sperms from the posterior fornix suggests: (UPSC 97)
   a. Faulty coital practice
   b. Immunological defect
   c. Hypospadias
   d. Azoospermia

23. Treatment for Cervical infertility can be all except: (Delhi 99)
   a. Condom for 3 month
   b. IUI
   c. Gamete Intrafallopian transfer
   d. 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)
   a. Weight gain
   b. Less exercise
   c. Vegetarian diet
   d. Weight loss

Male Infertility

25. According to WHO criteria, the minimum normal sperm count is: (AIIMS May 03)
   a. 10 million/ml
   b. 20 million/ml
   c. 40 million/ml
   d. 60 million/ml

26. Which is a not an essential criteria according to WHO for normal semen analysis:
   a. Sperm count > 20 million/ml (AIIMS Nov 07)
   b. Volume > 1 ml
   c. Sperm with normal morphology (strict criteria) > 15%
   d. Motility > 25% with rapidly progressive motility

27. WHO definition of normal sperm count: (PGI Dec 05)
   a. 10 million/ml
   b. 20 million/ml
   c. 40 million/ml
   d. 50 million/ml
   e. 60 million/ml

28. Aspermia is the term used to describe: (AI 05)
   a. Absence of semen
   b. Absence of sperm in ejaculate
   c. Absence of sperm motility
   d. 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)
   a. Normospermia
   b. Oligospermia
   c. Azoospermia
   d. Aspermia

30. Which of the following is true about obstructive azoospermia: (AI 09)
   a. ↑ FSH and ↑ LH
   b. Normal FSH and normal LH
   c. ↑ LH, Normal FSH
   d. ↑ 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)
   a. MAL descended testis
   b. Klinefelter’s syndrome
   c. Kallmann’s syndrome
   d. VAS obstruction

32. In azoospermia, the diagnostic test which can distinguish between testicular failure and obstruction of Vas deferens is: (UPSC 04)
   a. Estimation of FSH level
   b. Estimation of testosterone level
   c. Karyotyping
   d. 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:
   a. Prostatic infection
   b. Mumps orchitis
   c. Block in efferent duct system
   d. 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)
   a. Testicular FNAC
   b. Ultrasound for obstruction
   c. Local palpation of vas
   d. Karyotyping
IUI

35. Intrauterine insemination means implantation of:
   (PGI June 05)
   a. Semen  b. Washed semen
   c. Million of sperm  d. Fertilized ova

IVF

36. In vitro fertilization is indicated in:
   (AIIMS Dec 97)
   a. Tubal pathology  b. Uterine dysfunction
   c. Ovarian pathology  d. Azoospermia

37. Aspiration of sperms from testes is done in:
   (AI 07)
   a. TESA  b. MESA
   c. ZIFT  d. GIFT

38. In semen banks, semen is preserved at low temperature using:
   (JIPMER 81; DNB 90)
   a. Dry ice  b. Deep freeze
   c. Liquid nitrogen  d. Liquid air

39. Which is not an assisted reproduction technique:
   (AI 95)
   a. GIFT  b. ZIFT
   c. IVF and ET  d. Artificial insemination

40. Ovulation can be diagnosed by all except:
    (AIIMS Dec 97)
    a. Measuring day 14 serum progesterone
    b. Rise in basal body temperature in the second half of cycle
    c. Study of cervical mucus
    d. Endometrial histology

41. Indications of intrauterine insemination (IUI) are all except:
    a. Hostile cervical mucus
    b. Unexplained infertility
    c. Oligoasthenospermia
    d. Luteal Phase defect

42. In which case homologous artificial insemination is used in females:
    a. Hormonal disturbance
    b. Tubal block
    c. Cervical factor
    d. All of the above

43. Artificial insemination with husband’s semen is indicated in all the following situations, except:
    a. Oligospermia
    b. Impotency
    c. Antisperm antibodies in the cervical mucous
    d. Azoospermia

44. The major contribution to the human seminal fluid is from:
    a. Testes
    b. Seminal vesicles
    c. Prostate
    d. Bulbourethral and urethral glands

45. Absent fructose content in the seminal fluid suggests:
    a. Congenital absence of seminal vesicle
    b. Partial duct obstruction
    c. None
    d. Both
1. Ans. is a, i.e. One year
   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.
   • Infertility:
     - Primary : When no previous pregnancies have occurred.
     - Secondary : When a prior pregnancy although not necessary although not necessary a live birth, has occurred.
   Ref. Shaw 15th ed p 200

2. Ans. is a, b, c and d, i.e. Fibroid uterus; Endometriosis; Adenomyosis; and PID

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. It includes:
   Anovulation / Dysovulation:
   • Like in case of hypothalamic dysfunction, Kallmann syndrome
   • Hyperprolactinemia (due to drugs, pituitary adenoma)
   • Primary hypothyroidism
   • PCOS
   • 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
     - Gonococcal
     - Chlamydial
     - Tuberculous
   • 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).
   • Intruterine adhesions (Asherman’s syndrome)
   • Endometrial polyps
   • Leiomyomas (most common with sub mucus variety)
   • Chronic endometritis (TB)
   • 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/c, 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; Gonorrhea; and Mycoplasma

PID resulting in salpingitis is an important cause of infertility.

Infertility from PID can occur due to following organisms:

- a. Chlamydia
- b. Gonorrhea
- c. Tuberculosis
- d. Mycoplasma (Specifically ureoplasma)
- e. Schistosoma

Certain Infections cause Intrauterine synechiae or asheman syndrome thus leading to infertility like:

4. Ans. is b, i.e. Anovulation

“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.”

- 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

- 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 is either due to blockage of fallopian tube or due to loss of tubal function even if tubes are patent.

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.”

6. Ans. is d, i.e. Mycobacterium tuberculosis

The following findings on hysterosalpingogram strongly suggest tubercular salpingitis:
- A rigid nonperistaltic pipe like tube, called lead pipe appearance
- Beading and variation in filling density
- Calcification of the tube
- Cornual block
- A jagged fluffiness of the tubal outline
- Vascular or lymphatic intravasation of the dye
- 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

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.”

Most common etiology is: D and C done for post partum haemorrhage.

Other Etiologies:
- D and C done:
  - After previous elective pregnancy termination.
For missed abortion
For hydatidiform mole
After cesarean section

As a postoperative complication of:
- Abdominal/hysteroscopic myomectomy
- Metroplasty
- Septoplasty
- Uterine artery embolisation for the treatment of uterine fibroids
- Chronic infection-like genital tuberculosis and Schistosomiasis 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 conceives, 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 the method of choice for diagnosis and treatment.

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 is 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 14th ed p 1225, 15th ed p 1161
Read the preceding text for explanation

9. Ans. is c, i.e. 20 – 22 days
Ref. Shaw 15th ed p 215; Dutta Gynaec 5th/ed p 229
Endometrial biopsy should be taken in premenstrual phase 1 – 2 days before the onset of menstruation (Shaw 14th ed p 193-194) or on 21-23 day (Dutta Gynaec 5th/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:

<table>
<thead>
<tr>
<th>Test</th>
<th>Time</th>
<th>Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tests for Documenting Ovulation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Basal Body Temp</td>
<td>Throughout cycle</td>
<td>Biphasic pattern</td>
</tr>
<tr>
<td>2. Cervical mucus</td>
<td>Day 12 – 14</td>
<td>Cervical mucus is clear watery, stretchability present, ferning present.</td>
</tr>
<tr>
<td></td>
<td>Day 21 – 23</td>
<td>Cervical mucus is thick, viscid, tack present ferning absent.</td>
</tr>
<tr>
<td>3. Vaginal cytology</td>
<td>Day 12 – 14</td>
<td>Estrogen dominated smears – clear, discrete confined, polygonal,</td>
</tr>
<tr>
<td></td>
<td>Day 21 – 23</td>
<td>supercial cells (predominant cells)</td>
</tr>
<tr>
<td>4. Endometrial Biopsy</td>
<td>Day 24 – 26</td>
<td>Secretory Endometrium (Confirming ovulation)</td>
</tr>
<tr>
<td>5. Serum Progesterone</td>
<td>D8 and D21</td>
<td>D – 8 &lt; 1 ng/ml</td>
</tr>
<tr>
<td></td>
<td></td>
<td>D – 21 &gt; 6.5 ng/ml</td>
</tr>
<tr>
<td>6. Follicular Monitoring</td>
<td>D10 – D14</td>
<td>Follicle is measured by USG.</td>
</tr>
<tr>
<td>7. Laparoscopy</td>
<td>Secretory phase</td>
<td>Recent corpus luteum is directly seen</td>
</tr>
<tr>
<td><strong>TESTS FOR TUBAL PATENCY:</strong> <em>(Or for any Tubal Pathology):</em> viz</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insufflation test</td>
<td>(Mid follicular phase) Day 6 – Day 11 (not performed later so that if Pregnancy has occurred &amp; zygote formed it is not disrupted &amp; not</td>
<td></td>
</tr>
<tr>
<td>HSG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sonohysterosalpingography</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fallopscopy</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TESTS FOR CERVICAL FACTOR:</strong> viz</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Post coital test</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Immunological tests</td>
<td></td>
<td>Done just before ovulation (as cervical mucus is most</td>
</tr>
<tr>
<td>• Miller kurzrok test</td>
<td></td>
<td>Receptive for sperm at that time).</td>
</tr>
</tbody>
</table>

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

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

Most commonly used drugs for ovulation induction:
1. Clomiphene citrate (CC)
2. Letrozole
3. Gonadotropins

Ref. Shaw 15th ed p 215
Ref. Williams Gynae 1st ed p 450-452; Novak, 14th ed p 1210-1213
12. Ans. is b, i.e. Clomiphene citrate

Extra Edge:

<table>
<thead>
<tr>
<th>Condition</th>
<th>TOC</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Asherman syndrome</td>
<td>hysteroscopic adhesiolysis with IUCD insertion</td>
</tr>
<tr>
<td>• Stein-Leventhal syndrome</td>
<td>Clomiphene citrate</td>
</tr>
<tr>
<td>• Post pill amenorrhea</td>
<td>Clomiphene citrate</td>
</tr>
<tr>
<td>• Ovulation induction in-patient</td>
<td>Clomiphene citrate</td>
</tr>
<tr>
<td>who bleed in response to progestin challenge</td>
<td></td>
</tr>
<tr>
<td>• For ovulation induction in patient with hypogonadotropic amenorrhea</td>
<td>HMG (Human menopausal gonadotropin)</td>
</tr>
<tr>
<td>(Progestin challenge –ve)</td>
<td></td>
</tr>
<tr>
<td>• Ovulation induction in-patient with primary ovarian failure</td>
<td>Steroid/IVF with donor oocyte</td>
</tr>
</tbody>
</table>

13. Ans. is d, i.e. Hyperstimulation syndrome

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
- FSH/LH (MC)
- GnRH

**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
- Increased clotting
- Depletion of Na+ and albumin
- Third space fluid accumulation manifested by ascites and hydrothorax.

**Clinical features:**

a. Related to third space fluid accumulation.
   i. Abdominal distension (ascites) leading to abdominal discomfort and respiratory difficulty.
   ii. Hydrothorax (in severe cases).

b. Related to decreased intravascular volume.
   i. Decreased urinary output
   ii. Hypovolemia
   iii. Finally renal impairment.

c. Because of hypercoagulable state patient may present with venous thrombosis.

d. Because of excessive ovarian response to stimulation.
   i. Size of ovaries increases
   ii. Ovaries are palpable on P/V
   iii. 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

- **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

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
- No anesthesia is required for tube testing
- **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 / CO₂ Insufflation test (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

18. Ans. b, i.e. Laparoscopy and hysteroscopy

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 7th 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 8th 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”

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 periodnemal 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

20. Ans. is a, i.e. Cervical receptivity

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.
- If 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 what so ever 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.¹
– Intercourse to be performed 2–12 hours before the test.²
– No use of lubricant.³

<table>
<thead>
<tr>
<th>Assessment and Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality of cervical mucus:</td>
</tr>
<tr>
<td>Preovulatory cervical mucus (under the influence of estrogen) is clear, watery, abundant and stretchable (spinbarkeit &gt; 8 – 10 cm) with good tertiary ferning and low cellularity. Characteristic of Progesterone stimulated mucus:</td>
</tr>
<tr>
<td>• Thick &amp; opaque</td>
</tr>
<tr>
<td>• Lacks ferning</td>
</tr>
<tr>
<td>• Breaks (tacks) on stretching</td>
</tr>
</tbody>
</table>

In Q. 20 – I am not including other options because actually-
”It does not give much information on sperm count, motility and morphology.” … Novak 14th ed p 1220

21. Ans. is d, i.e. Keller test
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
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 antispem antibodies are present in the cervix, i.e immunological defect seen.

23. Ans. is d, i.e. Clomiphene citrate
Cervical factor infertility can be due to abnormal or deficient mucus
i. Infection
ii. Prior cervical surgery
iii. Use of antiestrogens (e.g. clomiphene citrate) for ovulation induction (so clomiphene is a cause of cervical factor infertility rather than management)
iv. 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 antispem 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.


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:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>1992 Guidelines</th>
<th>2010 Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>2 ml</td>
<td>&gt; 1.5 ml</td>
</tr>
<tr>
<td>Sperm concentration</td>
<td>20 million/ml</td>
<td>&gt; 15 million/ml</td>
</tr>
<tr>
<td>Sperm motility or &gt; 25% rapidly progressive</td>
<td>50% progressive</td>
<td>&gt; 32% progressive</td>
</tr>
<tr>
<td>Morphology (Strict Criteria)</td>
<td>&gt; 15% normal forms</td>
<td>&gt; 4% normal forms</td>
</tr>
<tr>
<td>WBC</td>
<td>&lt; 1 million/ml</td>
<td>&lt; 1 million/ml</td>
</tr>
<tr>
<td>Immunobead or mixed anti globulin reaction test</td>
<td>&lt; 10% coated with antibodies</td>
<td>&lt; 50%</td>
</tr>
</tbody>
</table>

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.

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

29. Ans. is b or a, i.e. Oligospermia or Normospermia

The semen analysis of the patient shows:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>1992 Guidelines</th>
<th>2010 Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sperm count is 15 million/ml.</td>
<td>Normal should be at least 20 million/ml</td>
<td>&gt; 15 million/ml</td>
</tr>
<tr>
<td>PH = 7.5</td>
<td>(N = &gt; 7.2)</td>
<td>&gt; 7.2</td>
</tr>
<tr>
<td>Volume = 2 ml</td>
<td>N = at least 2 ml</td>
<td>&gt; 1.5 ml</td>
</tr>
<tr>
<td>Morphology = 60% normal</td>
<td>N = 15% (strict criteria)</td>
<td>&gt; 4 % (strict criteria)</td>
</tr>
<tr>
<td>Motile = 60%</td>
<td>N = &gt; 50% motile</td>
<td>&gt; 32 % motile</td>
</tr>
</tbody>
</table>

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*/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.

<table>
<thead>
<tr>
<th>Cause</th>
<th>Example</th>
<th>Lab tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pretesticular cause</td>
<td>Kallmann syndrome</td>
<td>LH is decreased,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>FSH is decreased,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Testosterone decreased</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Testicular volume decreased</td>
</tr>
<tr>
<td>Testicular cause</td>
<td>Varicocele, orchitis, trauma, torsion,</td>
<td>Testosterone decreased so negative feedback</td>
</tr>
<tr>
<td></td>
<td>klunefelter syndrome</td>
<td>on FSH is lost,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>so FSH is increased.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Testicular volume is decreased.</td>
</tr>
<tr>
<td>Post testicular cause/</td>
<td>Obstruction, Kartagener syndrome,</td>
<td>FSH is normal</td>
</tr>
<tr>
<td>obstructive azoospermia</td>
<td>Post vasectomy, Congenital B/L absence of</td>
<td>LH is normal</td>
</tr>
<tr>
<td></td>
<td>vas deferens</td>
<td>Testosterone is normal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Testicular volume is normal</td>
</tr>
</tbody>
</table>

33. **Ans. is c, i.e. block in the efferent duct system.**  
*Ref: Leon speroff 7*/ed p 1135-1140*

<table>
<thead>
<tr>
<th>Condition</th>
<th>Semen Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostatic Infection</td>
<td>Sperrms will be present, Increased</td>
</tr>
<tr>
<td>Mumps Orchiditis</td>
<td>WBC levels-purulent semen</td>
</tr>
<tr>
<td>Block in efferent duct</td>
<td>Oligo, astheno and teratospermia</td>
</tr>
<tr>
<td></td>
<td>Azoospermia, presence of fructose, and sperms seen</td>
</tr>
<tr>
<td></td>
<td>on testicular biopsy system</td>
</tr>
</tbody>
</table>

34. **Ans. is b, i.e. Ultrasound for obstruction**  
*Ref. Reproductive medicine secrets by Peter Chan 1*/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*/ed p 214; Clinical Endocrinology & Infertility by Leon Speroff 7*/ed p 1216; John Hopkins manual of obs and gynae 4*/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**
• **Unexplained infertility**

37. **Ans. is a**, i.e. TESA

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
- Percutaneous epididymal sperm aspiration: PESA
- Testicular sperm extraction: TESEx
- Percutaneous testicular sperm fine needle aspiration: TESAx

**The choice of the method depends on:**
1. The underlying diagnosis,
2. Whether goal of the procedure is diagnostic or therapeutic
3. 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

**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:
- I2-Propanediol (Iodine)
- Glycerol
- dimethyl sulphoxide (DMSO) with sucrose.

**They are then stored in liquid nitrogen till required.**

- 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

**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**

<table>
<thead>
<tr>
<th>Method</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVF - ET</td>
<td>In vitro fertilization and embryo transfer</td>
</tr>
<tr>
<td>GIFT</td>
<td>Gamete intra fallopian transfer</td>
</tr>
<tr>
<td>ZIFT</td>
<td>Zygote intra-fallopian transfer</td>
</tr>
<tr>
<td>POST</td>
<td>Peritoneal oocyte and sperm transfer</td>
</tr>
<tr>
<td>SUZI</td>
<td>Subzonal insemination</td>
</tr>
<tr>
<td>ICSI</td>
<td>Intra-cytoplasmic sperm injection</td>
</tr>
</tbody>
</table>

40. **Ans. is a**, i.e. Measuring day 14 serum progesterone

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

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, 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
   The seminal vesicle contributes 60% and prostate about 30% of the seminal fluid.  
   Ref. Dutta Gynae 6th ed p 232

45. Ans. is d, i.e. Both
   Absent fructose content in the seminal fluid suggests congenital absence of seminal vesicle or portion of the ductal system or both.  
**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.

1. **Rhythm method/calendar method:**
   - It is based on ogino knaus theory which states ovulation occurs on day 14 ± 2 in a female with a regular 28 days cycle (i.e. avoid sex between 12th and 16th 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)

2. **Symptothermal method**

3. **Withdrawal/Coitus Interruptus**

**Characteristics of an Ideal Contraceptive:**
- Safe, effective, inexpensive, reversible, simple to use, independent of coitus, long lasting and requires minimal medical supervision.

**Fig. 10.1:** The Calendar (Rhythm) Method
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.

**Mucus Pattern**

<table>
<thead>
<tr>
<th>Flow</th>
<th>Dry Mucus</th>
<th>Tacky</th>
<th>Cloudy</th>
<th>Wet and sloppy Mucus Days</th>
<th>Cloudy</th>
<th>Tacky</th>
<th>Dry Mucus</th>
<th>Flow</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unsafe</td>
<td>Safe</td>
<td>Unsafe</td>
<td>Days</td>
<td>Unsafe</td>
<td>Safe</td>
<td>Unsafe</td>
<td>Safe</td>
<td>Unsafe</td>
</tr>
</tbody>
</table>
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

Frequent intense suckling
↓ prolactin released
Disrupts secretion of GnRH
↓
Interferes with release of LH and FSH
↓
Disrupts follicular development
↓
Anovulation and amenorrhea.

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

- 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 deducting 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)**

<table>
<thead>
<tr>
<th>Contraception</th>
<th>Perfect use rate</th>
<th>Typical use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implants</td>
<td>0.5%</td>
<td>.05%</td>
</tr>
<tr>
<td>Sterilization</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>0.1%</td>
<td>0.15%</td>
</tr>
<tr>
<td>Female</td>
<td>0.5%</td>
<td>0.5%</td>
</tr>
<tr>
<td>IUCD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mirena</td>
<td>0.2%</td>
<td>0.2%</td>
</tr>
<tr>
<td>CuT</td>
<td>0.6%</td>
<td>0.8%</td>
</tr>
</tbody>
</table>

**WHO category 2 (user dependent)**

<table>
<thead>
<tr>
<th>Contraception</th>
<th>Perfect use rate</th>
<th>Typical use</th>
</tr>
</thead>
<tbody>
<tr>
<td>OCP’s</td>
<td>0.3%</td>
<td>8.7%</td>
</tr>
<tr>
<td>Vaginal ring</td>
<td>0.3%</td>
<td>8%</td>
</tr>
<tr>
<td>Transdermal path</td>
<td>0.3%</td>
<td>8%</td>
</tr>
<tr>
<td>DMPA</td>
<td>0.3%</td>
<td>3%</td>
</tr>
<tr>
<td>Diaphragm</td>
<td>20%</td>
<td>20%</td>
</tr>
<tr>
<td><strong>Sponge</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nulliparous</td>
<td>9</td>
<td>16</td>
</tr>
<tr>
<td>Parous</td>
<td>26</td>
<td>32</td>
</tr>
<tr>
<td>Condom</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2</td>
<td>16</td>
</tr>
<tr>
<td>Female</td>
<td>5</td>
<td>21</td>
</tr>
</tbody>
</table>

**Note:** Least failure rate is with perfect use. If in question nothing is mentioned take it as Typical use.

**Barrier Methods**

<table>
<thead>
<tr>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Condoms</td>
<td>• Female condoms (Femshield)</td>
</tr>
<tr>
<td></td>
<td>• Today contraceptive/vaginal sponge</td>
</tr>
<tr>
<td></td>
<td>• Vaginal diaphragm/cervical cap</td>
</tr>
</tbody>
</table>

**Note:** Spermicidal agents like nonoxynol octoxynol and menfegol are added to any of the above barrier methods to increase its effectiveness.
Also Know

Natural membrane condoms/Lamb skin condoms
These condoms are usually made from lamb cecum and can have pores up to 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.

Male Condoms/French Letters

**Types:**
- Latex
- Vylex
- Polyurethane
- Polyisoprene
- Natural membrane condoms

**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, gonorrhea, 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.
Chapter 10  Contraception

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 presents 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.

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

Spermicides

- Spermicidal agents are chemical agents with 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) - Octoxyynol
  - Menfegol - Enzyme inhibiting agents
  - Benzalkonium chloride.
- 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.
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.

- Advantage 24 is a new contraceptive gel which contains nonoxynol.

Today/Vaginal Sponge

- 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 7th 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.

Oral Contraceptives

Mechanism of action

<table>
<thead>
<tr>
<th>Prevention of ovulation</th>
<th>Prevention of fertilization</th>
<th>Interference with Implantation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progestin reduces frequency of LH secretory pulses, while estrogen primarily reduces FSH secretion.</td>
<td>Thick cervical mucus, hostile to sperms may inhibit fertilization.</td>
<td>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.</td>
</tr>
<tr>
<td>Both synergise each other to inhibit midcycle LH surge.</td>
<td>Uterine and tubal contractions may be modified to disfavor fertilization.</td>
<td></td>
</tr>
<tr>
<td>As a result, follicles fail to develop and rupture and ovulation does not occur.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Compositions Chart

- **Mala D**
  - EE = 30 mcg
  - LNG = 0.15 mg
  - (Available in market @ Rs. 3/- per pkt.)
- **Mala N**
  - EE = 30 µg
  - Levo norgestrel = 0.15 mg
  - (Available at Govt. health facilities free of cost). Both of them have 7 tables of ferrous fumarate
- **Loette**
  - EE 20 mcg
  - LNG 0.1 mg
  - (Available in market @ Rs. 3/- per pkt.)
- **Femilon**
  - Desogestrel 0.15 mg
  - EE 0.1 mg
  - LNG 0.15 mg
  - (Available at Govt. health facilities free of cost)
Chapter 10 Contraception

OCPs Can Be

<table>
<thead>
<tr>
<th>Monophasic</th>
<th>Biphasic</th>
<th>Triphasic</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Have same estrogen (E) and progesterone (P) in 21 tablets.</td>
<td>• First 10 pills have one dosage</td>
<td>• First 7 pills have same dosage (EE - 30 mcg, LNG - 50 mcg)</td>
</tr>
<tr>
<td></td>
<td>• Next 11 pills have some other E and P dosage</td>
<td>• Next 7 have another dosage (EE - 40 mcg, LNG - 75 mcg) and last 7 have yet another dosage (EE - 30 µg, LNG - 125 mcg)</td>
</tr>
</tbody>
</table>

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 low dose → EE = 0.020 mg (20 mcg)

The M/c estrogen used in OCP’s is ethinyl estradiol.

Progesterones in OCPs

<table>
<thead>
<tr>
<th>Generation</th>
<th>Progesterone</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st generation – (Estranes derived from Testosterone)</td>
<td>Norethisterone, Norethindrone, Norethynodrel, lynestrenol</td>
<td>Used in pills with ≥ 50 mcg of EE</td>
</tr>
<tr>
<td>2nd generation</td>
<td>Levonorgestrel, Norgestrel</td>
<td>Levonorgestrel is the M/c used progesterone in OCPs</td>
</tr>
<tr>
<td>3rd generation (Gonanes)</td>
<td>Desogestrel (active from 3-keto DSG), Gestodene, Norgestimate</td>
<td>Benefits given below</td>
</tr>
<tr>
<td>4th generation</td>
<td>Drospirenone, Dienogest, nomegestrol</td>
<td>Useful in women with hirsutism, acne, and those who have fluid retention after taking OCP and in treating PMS, PMDD</td>
</tr>
</tbody>
</table>

Benefit of 3rd generation Progesterone

Desogestrel/Gestodene/Norgestimate

↑ Sex hormone binding globulin
Less break through bleeding
Do not increase body weight
Slightly ↑ ed chances of venous thromboembolism (+/-)
↓ free testosterone concentration (i.e. ↓ ed androgenic effects)
↓ Acne
↓ Hirsutism (therefore useful in PCOD patients)
Favourable lipid profile/ lipid friendly
Decreased premenstrual syndrome

Tumors and OCPs—

Tumors associated with OCP use
1. Cervical cancer (adenocarcinoma)
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
- Fibroid uterus (Progesterone only pills)
- Ovarian cysts

183
**Benign Disease of Genital Tract**

- Benign breast diseases
- Endometriosis (if used continuously)
- PID (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:  

- 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
Mitr 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**

<table>
<thead>
<tr>
<th>Missed 1 or 2 pills</th>
<th>Missed 3 or more of these 14 pills</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Take 1 pill as soon as remembered</td>
<td>• Take 1 as soon as remembered</td>
</tr>
<tr>
<td>• Take all others as usual</td>
<td>• Take the others of this row, one each day, then start a new pack (throw away the last row of this pack)</td>
</tr>
<tr>
<td>If missed any of these 7 pills</td>
<td>• Use condoms for 7 days</td>
</tr>
<tr>
<td>• Throw the missed pills and takes others as usual</td>
<td></td>
</tr>
</tbody>
</table>

**OCPs are the contraceptive of choice**

- In newly married couples staying together.
- After evacuation of molar pregnancy.
- Women wanting to space their pregnancy.
- 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.

**Other Combined (E + P) Contraceptives**

<table>
<thead>
<tr>
<th><strong>Transdermal patch called as ortho Vera</strong></th>
<th><strong>Vaginal ring called as Nuva ring</strong> (Launched in India in November 2009) (Fig. 10.8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>P = Norgestimate</td>
<td>P = Etonorgestrel (active metabolite of desogestrel)</td>
</tr>
<tr>
<td>E = Ethinyl estradiol</td>
<td>E = Ethinyl estradiol (Releases 15 µg EE and 120 µg ENG)</td>
</tr>
<tr>
<td>• Applied weekly to anybody location for 3 weeks followed by 1 week patch free withdrawal bleeding week</td>
<td>• Placed in vagina for 3 weeks and removed for 1 week</td>
</tr>
<tr>
<td></td>
<td>• Made of diethyl polysiloxane</td>
</tr>
<tr>
<td></td>
<td>• Can be removed for upto 3 hours daily including during intercourse. If ring is out of vagina for &gt; 3 hours backup method required.</td>
</tr>
</tbody>
</table>

**Other Rings**

- Silastic vaginal rings (SVR) containing levonorgestrel and releasing 20 mcg of LNG daily.
- Nestorone –150 mcg progesterone + 15 mcg EE₂
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%

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

<table>
<thead>
<tr>
<th>In regular cycles</th>
<th>Amenorrhea</th>
<th>During lactation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recent WHO recommendations suggest POP should be started within 1st five days of menstrual cycle without need of additional contraception (preferably 1st day).</td>
<td>Start any time after being sure that there is no pregnancy (Additional protection or abstinence from sex being advised for the first 48 hours)</td>
<td>As per CDC guidelines it can be stated any time after delivery according to WHO it is started after 6 weeks</td>
</tr>
</tbody>
</table>

➢ Traditional progesterone only pill should be taken every day without break and at the same time. 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)

Failure rate of POPs

Breast feeding women
• Typical use – 1/1HMY
• Perfect use – 0.3/1HMY
Nonbreast feeding women
• Typical use – 3-10/1HMY
• Perfect use – 0.3/1HMY

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 velarate 5 mg
Marvelon – Desogestrol 150 mcg + EE 30 mcg
Femovan – Gestodene 75 mcg + EE 35 mcg
Anafertin – Dihydroprogesterone 150 mg + testosterone enanthate 5 mg

Suited ideally for—
• Lactating women
• Sickle cell anemia (best contraceptive)
• Seizure disorder (raises seizure threshold)

Only POP available in India = cerazette (0.075 mg desogestrel)
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\(^2\) (Most common side effect) Park 20\(^{th}\)/ed p 434
- Occasional phase of amenorrhea\(^2\)
- Weight gain\(^2\)
- Prolonged infertility after its use\(^2\) (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**

<table>
<thead>
<tr>
<th>Norplant I (Fig. 10.9)</th>
<th>Norplant II/Jadelle</th>
<th>Implanon (Fig. 10.10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>It has 6 rods containing 36 mg of Levonorgestrel each</td>
<td>It has 2 rods each containing 75 mg of LNG and releases the drug at the same dose as norplant 1</td>
<td>It has a single rod 4 cms in size containing 68 mg of 3 ketodesogestrel (etonorgestrel). It is 4 cm long</td>
</tr>
<tr>
<td>Replaced after 5 years</td>
<td></td>
<td>Most popular implant these days.(^2)</td>
</tr>
<tr>
<td>It is 3 cm long</td>
<td></td>
<td>Replaced after 3 years.(^2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Releases 60 mcg of hormone per day</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Doesnot decrease bone mineral density.</td>
</tr>
</tbody>
</table>

**Note:** Now implanon has been replaced by Nexplanon which has same characteristic like implanon.

**Mechanism of Action**

<table>
<thead>
<tr>
<th>Norplant</th>
<th>Implanon</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thickening of cervical mucus(^2)</td>
<td>Main mechanism is ovulation inhibition(^2) (Remember - newer progestin only pills containing desogestrel also have ovulation inhibition as their main mechanism).</td>
</tr>
<tr>
<td>Suppressing the LH surge and causing either anovulatory cycles or luteal insufficiency(^2)</td>
<td>Rest of the mechanism is same as Norplant</td>
</tr>
<tr>
<td>Causes endometrial atrophy(^2)</td>
<td></td>
</tr>
</tbody>
</table>
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 days–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.
- Can be used by lactating females.
- 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)**
- GTB library (GTB is Guru Tegh Bahadur Hospital in Delhi).
  - G – Undiagnosed Genital bleeding
  - T – Active Thrombophlebitis or Thromboembolic disease
  - B – Known or suspected Breast cancer
  - Library – 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—

<table>
<thead>
<tr>
<th>Generation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>First generation IUDs</td>
<td>These are inert or non-medicated devices. e.g. Lippe’s loop.</td>
</tr>
<tr>
<td>Second generation IUDs</td>
<td>It consists of copper or silver containing IUDs e.g. T Cu-220 C, T Cu 380- Ag, Nova T, Multiload Cu 250/375</td>
</tr>
<tr>
<td>Third generation IUDs</td>
<td>This consists of hormone releasing IUDs. E.g. Progestasert, Mirena.</td>
</tr>
</tbody>
</table>

**Mechanism of Action of IUCD**

<table>
<thead>
<tr>
<th>Nonmedicated IUCD</th>
<th>Cu containing IUCD</th>
<th>Progestin releasing IUCD</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 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.</td>
<td>• Elute copper which bring about enzymatic and metabolic changes in the endometrial tissue &amp; also produce changes in cervical mucus and endometrial secretions.</td>
<td>• They cause decidualization with atrophy of endometrial glands, therefore inhibit implantation.</td>
</tr>
<tr>
<td></td>
<td>• It provokes uterine contractility &amp; increases tubal peristalsis.</td>
<td>• Alter cervical Mucus causing inhibition of sperm penetration and capacitation.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• In 40% cases ovulation is also inhibited.</td>
</tr>
</tbody>
</table>
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 year
- 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 mm³ 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 mm² copper wire on vertical stem and two 33 mm² 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.
Newer IUCDs

Cu Safe 300: has 300 mm² 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 mm² 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
- 2nd 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—peurperal 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 15th/ed p 224)

Mnemonic: Please Don’t Try to Put Condom

Relative contraindications of IUCD

- Distortions of uterine cavity due to congenital malformations on fibroid
- 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.
Decrease pelvic infection rates.
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 oligomenorrhoea which are common in first 3-4 months of use
Amenorrhoea (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 Levonorgestrel. One new pill available world wide but not in India is Ella - 30 mg of ulipristal.
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.

a. 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
b. Irving method—Ligating and burying the proximal tubal end in serosa of posterior uterine wall.
   Failure Rate = 1 in 1000 surgeries.
c. Uchida technique—No Failure Rate in 19000 surgeries
d. Fimbriectomy/kroeners technique—Very high failure rate 2–3 in 100 surgeries
e. Madlener technique—High failure rate-0.3–2 in 100 surgeries
Chapter 10 Contraception

193

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
   - Done using laparoscope.
   - It is a safe and effective method.
   - **It should not be done concurrently with 2nd trimester MTPs and in post-partum period.**
   - The patient is laid in lithotomy position and with a help of verses needle (introduced at an angle of 45°) pneumoperitoneum is created.
   - The gas used is CO₂ (M/C)
   - 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.
   - The methods of occlusion used during laparoscopy are

   ![Mechanical occlusion diagram]

   - Yoon falope ring/sialistic band
   - Clips
   - Spring-loaded Hulka-clemens clips
   - Silicon titanium clip (fl ishie clip)

   **Note:** In this method, a clip is placed on the isthmus of the uterus – 2–3 cm away from the uterus. It leads to minimum 4–5 mm damage to the tube. It is suitable for young females who may need reversal or after abortion when tubes are edematous.

   ![Methods with good chances of recanalization]
   - Laparoscopic clips (best)
   - Laparoscopic - yoon Falope ring/band
   - Pomeroy and Uchida methods
   - Lowest with cautery.

   ![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 mesosalpinx are not unduly disturbed.

3. Hysteroscopic tubal ligation: Can be done using cautery - 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**

<table>
<thead>
<tr>
<th>Method</th>
<th>Failure Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pomeroy's method</td>
<td>0.4%</td>
</tr>
<tr>
<td>Modified pomeroy</td>
<td>0.2%</td>
</tr>
<tr>
<td>Madlener</td>
<td>7%</td>
</tr>
<tr>
<td>Irving</td>
<td>Very low failure rate</td>
</tr>
<tr>
<td>Uchida</td>
<td>Very low failure rate</td>
</tr>
<tr>
<td>Laparoscopic sterilization</td>
<td>0.2–1.3%</td>
</tr>
<tr>
<td>Hysteroscopic tubal block</td>
<td></td>
</tr>
<tr>
<td>Cauterization</td>
<td>30%</td>
</tr>
<tr>
<td>Sclerosants</td>
<td>15%</td>
</tr>
</tbody>
</table>

![Falope rings introduced by yoon in 1974]
**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
- Adnexal 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**

<table>
<thead>
<tr>
<th>Sterilization procedure</th>
<th>Term pregnancy (range %)</th>
<th>Ectopic pregnancy (range %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spring-loaded clip</td>
<td>88 (75–100)</td>
<td>2 (0.4)</td>
</tr>
<tr>
<td>Ring occlusion (silastic bands)</td>
<td>75 (44–95)</td>
<td>2 (0–4)</td>
</tr>
<tr>
<td>Pomeroy ligation</td>
<td>59 (45–70)</td>
<td>2 (0–3)</td>
</tr>
<tr>
<td>Electrocoagulation</td>
<td>43 (26–58)</td>
<td>5 (0–9)</td>
</tr>
</tbody>
</table>

*Note:* Most suitable for reversal is clips followed by silastic bangs/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 deference.
- 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 (vasovasotommy) 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 known

Centchroman

- It is a synthetic NON-Steroidal (ormiloxifene) contraceptive.
- A tablet of 30 mg started on 1st day of menstruation and taken twice weekly for (12 weeks or 3 months), and weekly thereafter (t½ - 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.
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.
1. Which of the following is correct for the calculation of pearl index: \( \frac{\text{No. of accidental pregnancies} \times 1200}{\text{No. of patient observed} \times \text{months of use}} \) 
   a. \( \frac{\text{No. of accidental pregnancies} \times 1200}{\text{No. of patient observed} \times \text{months of use}} \) 
   b. \( \frac{\text{No. of patient observed} \times 2400}{\text{No. of accidental pregnancies} \times 1200} \) 
   c. \( \frac{\text{No. of patient observed} \times 2400}{\text{No. of accidental pregnancies}} \) 
   d. \( \frac{\text{No. of accidental pregnancies} \times 1200}{\text{No. of patient observed}} \)

2. Pearl’s index indicates: 
   a. Malnutrition 
   b. Population 
   c. Contraceptive failure 
   d. LBW 
   e. IUGR

3. Contraceptive methods with failure rate <5: 
   a. Copper - T 
   b. Vaginal sponge 
   c. Condom 
   d. OCP 
   e. Tubectomy

4. Reversible methods of contraception are: 
   a. Female sterilization 
   b. OCP 
   c. IUCD 
   d. Barrier 
   e. Depot injection

5. Date of birth of billionth baby is: 
   a. May 11, 2011 
   b. May 11, 2000 
   c. April 11, 2000 
   d. April 11, 2011

6. Which natural family planning method is based on ogino knauss theory: 
   a. BBT method 
   b. Rhythm method 
   c. Lactational anerorrhea 
   d. Withdrawl method

7. Which of the following statements about calendar method (Rhythm method) is false: 
   a. Abstinence is needed for only a few days in a month 
   b. It is associated with no costs 
   c. Safe period can also be observed using temperature rhythm or mucous method 
   d. Ectopic pregnancy is a reported complication of calendar method

8. Rise in body temperature after ovulation is due to: 
   a. Estrogen 
   b. Progesterone 
   c. LH 
   d. FSH

9. Billing’s method of contraception refers to: 
   a. Monitoring BBT 
   b. Cervical mucus method 
   c. Rhythm method 
   d. Coitus interruptus method

10. Not a barrier contraceptive: 
    a. Diaphragm 
    b. Centchroman 
    c. Condom 
    d. Today

**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: 
   a. It contains norelgestromin and ethyl estradiol. 
   b. A single patch to be used for 3 weeks 
   c. A single patch to be used for 1 week 
   d. Compliance is good with the patch

**F2.** Figure F2 shows a popular method of performing sterilization. Regarding this technique true statements is: 
   a. Is performed with absorbable suture material 
   b. Is performed using permanent suture 
   c. Includes crushing the fallopian tube 
   d. Is irreversible
11. Which one of the following is not a correct statement regarding the use of condom:
   (LIPSC 07)
   a. Air should be squeezed out of tip
   b. It should be tested by inflating
   c. It should be unrolled on erect penis
   d. 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:
   (LIPSC 02)
   a. Increased monilial infection of vagina
   b. Premature ejaculation
   c. Contact dermatitis
   d. Retention of urine

13. All are contraindications of diaphragm except: (LIP 05)
   a. Multiple sex partners
   b. Recurrent UTI
   c. Uterine prolapse
   d. Herpes vaginitis

14. Contraceptive vaginal foam tablet “today” contains:
   a. Nonoxynol 9
   b. Octoxynol 9
   c. Menfegol
   d. None of the above

15. Spermicidal jelly acts through:
   (AIIMS Dec 98)
   a. Acrosomal enzyme
   b. Cervical enzyme alteration
   c. Glucose uptake inhibition by sperms
   d. Disruption of cell membrane

16. Spermicidal agents are:
   (PGI June 06)
   a. Nonoxynol
   b. Menfegol
   c. Progestasert

17. All of the following mechanisms of action of oral contraceptive pills are true, except: (AI 06)
   a. Inhibition of ovulation
   b. Prevention of fertilization
   c. Interference with implantation of fertilized ovum
   d. Interference with placental functioning

18. Version I
   Amount of estrogen in low dose oral contraceptive pills:
   (AIIMS Nov 01)
   a. 30 µg
   b. 40 µg
   c. 50 µg
   d. 20 µg

19. Version II
   Minimum effective dose of ethinyl estradiol in combination oral pills is:
   (AIIMS May 04)
   a. 20 µg
   b. 35 µg
   c. 50 µg
   d. 75 µg

20. Third generation oral contraceptive pills containing norgestimate and gestodene along with estrogens:
   a. Are more lipid friendly
   b. Decreases the risk of venous thromboembolism
   c. Increase the risk of breakthrough bleeding
   d. Are not used for emergency contraception

21. Norgestimate OCP’s have the following advantage except:
   a. Reduces venous thrombosis
   b. Is cheaper than standard OCP’s
   c. Reduces acne and hirsutism
   d. Useful in heart disease

22. The progesterone component of OCP acts by:
   a. Preventing ovulation
   b. Inhibiting implantation
   c. Bringing about alterations in cervical mucus
   d. All of the above

23. Amount of estrogen in Mala D is:
   (LIP 00)
   a. 30 µg
   b. 50 µg
   c. 10 µg
   d. 80 µg

24. Which of the following OCP’s have the least amount of estrogen:
   a. Mala N
   b. Triquilar
   c. Femilon
   d. Novelon

Benefits of OCP’s

25. Oral contraceptive pills decrease incidence of all of the following conditions except:
   (AI 99)
   a. Salpingitis
   b. Hepatic adenoma
   c. Ovary CA
   d. Fibroadenosis

26. Use of OCP’s are known to protect against following malignancies except:
   (AIIMS Nov 02)
   a. Ovarian carcinoma
   b. Endometrial carcinoma
   c. Uterine sarcoma
   d. Carcinoma cervix

27. Use of oral contraceptives decreases the incidence of all of the following except:
   (AIIMS May 05)
   a. Ectopic pregnancy
   b. Epithelial ovarian malignancy
   c. Hepatic adenoma
   d. Pelvic inflammatory disease

28. Non contraceptive use of OCPs are all except:
   (AI 07)
   a. Ca endometrium
   b. Ca breast
   c. Rheumatoid arthritis
   d. Endometriosis

29. OCP gives protection against following cancers:
   (PGI June 06)
   a. Endometrial
   b. Ovary
   c. Cervix
   d. Breast
   e. Liver

Side Effects of OCPs

30. OCP’s cause all except:
   (AIIMS Dec 98)
   a. Dysmenorrhea
   b. Mastalgia
   c. Nausea
   d. 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: (AIIMS May 03)
   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 treatmen of menohorrhegia

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. Polymenorrhea
   d. Amenorrhea

51. Mirena is: (AIIMS May 05)
   a. Used in abortions
   b. Antiprogesterone
   c. Progestosterone IUCD
   d. Hormonal implant
52. Use of Levo-Norgestrel releasing, IUCD is helpful in all of the following conditions except: (AIIMS Nov 02)
   a. Menorrhagia
   b. Dysmenorrhea
   c. Premenstrual symptoms
   d. Pelvic inflammatory disease

53. Benefits of LNG IUCD: (PGI Dec 09)
   a. Endometriosis
   b. Fibroid uterus
   c. PID
   d. Contraception
   e. Extraterine endometriosis

54. True about Mirena: (PGI Nov 2012)
   a. Progestrone containing IUCD
   b. Contain desogestrol
   c. Causes endometrial hyperplasia
   d. Decreases menstrual blood flow

55. Which of the following statements is incorrect regarding levonorgestrel releasing intrauterine contraceptive devices: (AI 06)
   a. There is increased incidence of menorrhagia
   b. This system can be used as hormone replacement therapy
   c. This method is useful for the treatment of endometrial hyperplasia
   d. Irregular uterine bleeding can be a problem initially

56. All of the following mechanisms might account for a reduced-risk of upper genital tract infection in users of progestin – releasing IUDs, except: (AI 06)
   a. Reduced retrograde menstruation
   b. Decreased ovulation
   c. Thickened cervical mucus
   d. Decidual changes in the endometrium

57. Contraceptive LNG-IUD (levonorgesterol intra-uterine device) has the cumulative pregnancy rate at 5 years of:
   a. 0.5
   b. 1.0
   c. 1.5
   d. 2.0

IUCDs

58. Characteristics of an ideal candidate for copper-T insertion include all of the following except: (AIIMS May 05)
   a. Has born at least one child
   b. Is willing to check IUD tail
   c. Has a history of ectopic pregnancy
   d. Has normal menstrual periods

59. Mechanism by which IUCD does not act: (AIIMS Dec 98)
   a. Chronic endometrial inflammation
   b. Increase the motility of tubes
   c. Inducing endometrial atrophy
   d. Inhibition of ovulation

60. All IUCD’s are changed every 4–5 year except: (AIIMS Dec 97)
   a. Cu 280
   b. Cu 320
   c. Multiload devices
   d. Progestasert

61. Among of following IUCD’s which has life span for 10 years:
   a. CuT380A
   b. CuT200
   c. Nova T
   d. Multiload

62. Composition of Nova - T: (PGI June 05)
   a. Copper and Silver
   b. Copper and aluminium
   c. Copper only
   d. Copper and selenium
   e. Copper and molybdenum

63. A lady with IUCD becomes pregnant with tail of IUCD being seen, next course of action is: (PGI Dec 98)
   a. MTP
   b. Remove the IUCD
   c. Continue the pregnancy
   d. 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:
   a. Leave the IUD in place without any other treatment
   b. Remove the IUD to decrease the risk of malformations
   c. Remove the IUD to decrease the risk of infection
   d. 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:
   a. Hysteroscopy
   b. No need of removal (wait and watch)
   c. IUCD hook
   d. Laparoscopy

66. Absolute contraindication for IUCD includes all of the following except: (AI 97)
   a. Undiagnosed vaginal bleeding
   b. Suspected pregnancy
   c. Congenital malformation of uterus
   d. PID

67. Absolute contraindication of IUCD is: (AIIMS Dec 97)
   a. Endometriosis
   b. Iron deficiency anemia
   c. Dysmenorrhea
   d. Pelvic tuberculosis

68. Contraindications of IUCD:
   a. Undiagnosed vaginal bleeding
   b. PID
   c. Smoking
   d. Obesity
   e. Diabetes

69. Contraindication of IUCD: (PGI Dec 04)
   a. Oligomenorrhea
   b. PID
   c. Uterine malformation
   d. Controlled diabetes
   e. Previous cesarean section

70. Contraindication of IUCD: (PGI Dec 04)
   a. Oligomenorrhea
   b. PID
   c. Uterine malformation
   d. Controlled diabetes
   e. Previous ectopic pregnancy
Chapter 10  Contraception

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? (AIIMS Dec 98)
   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. Irving’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. Isthumo-isthmic anastomosis  
   b. Isthumo-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. Dyspareunia

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:
   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: 
   a. Barrier method  
   b. IUCD  
   c. OCP  
   d. DMPA

(AIIMS May 2011)

94. Ideal contraceptive for lactating mother is:  
   a. Barrier method  
   b. Combined OCP  
   c. Lactational amenorrhoea  
   d. Progesterone only pill

(AIIMS May 2011)

95. Peritoneum is opened in all of the following sterilization procedures except:  
   a. Mini lap  
   b. Laparoscopy  
   c. Vasectomy  
   d. Transvaginal tubectomy

(AP 97)

96. Contraceptive to be avoided in epilepsy:  
   a. OCP  
   b. Condom  
   c. IUCD  
   d. Mirena

(AIIMS May 2011)

NEW PATTERN QUESTIONS

97. The following are true related with regards to vasectomy except:  
   a. Leads to immediate sterility  
   b. Failure rate is 0.1%  
   c. Involves ligation and division of spermatic cord  
   d. Partner (wife may be given DMPA for 3 months

98. The following are the contraindications of tubal reconstructive surgery except  
   a. Length of tube <4 cms  
   b. Patients over 30 years of age  
   c. Pelvic tuberculosis  
   d. Reversal done after 5 years of sterilization

99. The intra-abdominal pressure during laparoscopy should be set between:  
   a. 5–8 mm Hg  
   b. 10–15 mm Hg  
   c. 20–25 mm Hg  
   d. 30–35 mm Hg

100. A 30-year-old P,L, wants contraception for 6 months. She has dhymenorrhea and is a known case of complicated migraine. On USG, uterus has multiple fibroids. Contraception of choice is:  
   a. Cu T 200  
   b. OC pills  
   c. Vaginal diaphragm  
   d. Tubal sterilization

101. A 28-year-old P,L, 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:  
   a. Hysteroscopy  
   b. No need removal (wait and watch)  
   c. IUCD hook  
   d. Laparoscopy

102. All of the following are contraceptive implants except:  
   a. Norplant  
   b. Implanon  
   c. Jadelle  
   d. Mesigyna

103. Least failure in sterilization occurs with:  
   a. Falope ring  
   b. Bipolar cautery  
   c. Unipolar cautery  
   d. Hulka clip

104. All of the following are LARC methods except:  
   a. IUCD  
   b. DMPA  
   c. POPs  
   d. Implanon

105. Preferred method of contraception in family for a female with H/O ovarian cancer:  
   a. POP  
   b. Cu IUCD  
   c. OCP  
   d. Barrier method
Chapter 10  Contraception

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

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 deducting 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

See the text for explanation.

4. Ans. is b, c, d and e, i.e. OCP; IUCD; Barrier, and Depot injection

Methods of contraception (can be classified as)

- **Temporary methods** (used to postpone pregnancy or space births)
  - Barrier method
  - Natural contraception
  - Oral contraceptive pills
  - Injectables
  - Implants
  - Devices like IUCD’s
- **Permanent methods** (Surgical methods arm is to purposefully and permanently destroy the Reproductive capacity of an individual)
  - Permanent method
  - In female
    - Tubectomy
  - In male
    - Vasectomy

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
   Discussed in preceding text in detail

Barrier Methods

10. Ans. is b, i.e. Centchroman
    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 6th ed p 82; Leon Speroff 7th ed p 998

12. Ans. is c, i.e. Contact dermatitis
    Ref. Shaw 15th 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 gonorrhea, 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 15th 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.

Contradications 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
    TODAY: It contains 1 gm of NONOX Y NOL-9
    Ref. Shaw 14th ed p 203
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

“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
  - Benzalkonium chloride.

Ref. Shaw 15th ed p 224

• 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.

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.

OCPs

17. Ans. is d, i.e. Interference with placental functioning

Ref. KDT 6th 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. 6th ed p 543; Novak 14th ed pp 268, 277

Version II

Ans. is a, i.e. 20 µg

Ref. Dutta Obs. 6th ed p 542; Shaw 15th ed p 231

Friends, I had a tough time in finding answers to these questions.

“Low dose pills have estrogen less than 50 mcg.”

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.”

It further says (Novak 14th 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 6th 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 7th ed p 802; Dutta Gynaec 6th ed p 465; SK Chaudhary 7th 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 9th ed pp 723-725

22. Ans. is d, i.e. all of the above

    Ref. SK Chaudhary 7th 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 6th ed p 543

24. Ans. is c, i.e. Femilon

<table>
<thead>
<tr>
<th>Commercial name</th>
<th>Composition Progestin (mg)</th>
<th>Estrogen (µg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Mala N (Distributed free of cost by govt. of India)</td>
<td>Levo norgestrel 0.15</td>
<td>Ethinyl estradiol 30</td>
</tr>
<tr>
<td>2. Mala D</td>
<td>D-levo Norgestrel 0.15</td>
<td>Ethinyl estradiol 30</td>
</tr>
<tr>
<td>3. Femilon</td>
<td>Desogestrel 0.15</td>
<td>Ethinyl estradiol 20</td>
</tr>
<tr>
<td>4. Loette</td>
<td>Levonorgestrel 0.1 mg</td>
<td>Ethinyl estradiol 20</td>
</tr>
</tbody>
</table>

   • Eg’s of very low dose OCP’S are femilon and Loette
   • Triphasic/Triquilar
   • Days: 1.6, 7-11, 12-21
   • Contain EE + LNG

Benefits of OCPs

25. Ans. is b, i.e. Hepatic adenoma


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
• Fibroid uterus (Progestosterone only pills)
• Ovarian cysts
• Benign breast diseases

Benign disease of genital tract
• Endometriosis (if used contenterously)
• PID (here Salpingitis)
• Ectopic pregnancy (as it decreases incidence of PID)

They decrease ovulation thus, are helpful in
• Dysmenorrhea, premenstrual tension and Mittlescherz syndrome.
• By decreasing blood loss they are helpful in menorrhagia and polymenorrhea.
• Acne and hirsutism (especially those containing desogesterel)

OCP’s are also beneficial in:
• DUB
• Hormone therapy for hypothalamic amenorrhea
• Prevention of menstrual porphyria.

26. Ans. is d, i.e. Carcinoma cervix
Ref. Dutta Obs 6th ed p 545; Shaw 14th ed p 208; Harrison 17th 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.

<table>
<thead>
<tr>
<th>Tumors associated</th>
<th>OCPs</th>
<th>Provides protection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical cancer</td>
<td></td>
<td>Ovarian tumors/cysts</td>
</tr>
<tr>
<td>Hepatic cancer</td>
<td></td>
<td>Uterine tumor</td>
</tr>
<tr>
<td>Pituitary adenoma</td>
<td></td>
<td>Benign breast disease</td>
</tr>
<tr>
<td>Breast cancer</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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 metaanalysis 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 6th ed p 315; Jeffcoat 7th 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 6th ed p 545; Shaw 14th ed p 208

OCP’s have antiovulatory effect and by virtue of this property, relieve dysmenorrhea (rather than causing it), premenstrual tension and Mittlescherz syndrome.

Side effects of OCPs are:

<table>
<thead>
<tr>
<th>Nonserious side effects</th>
<th>Side effects which appear later</th>
<th>Serious side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea, vomiting</td>
<td>Weight gain</td>
<td>Leg vein/Pulmonary Thrombosis</td>
</tr>
<tr>
<td>Headache (Migraine may be precipitated)</td>
<td>Chloasma</td>
<td>Coronary Artery</td>
</tr>
<tr>
<td>Break through bleeding/spotting</td>
<td>Pruritis vulva</td>
<td>Cerebral Artery Thrombosis</td>
</tr>
<tr>
<td>Breast discomfort/Mastalgia</td>
<td>Carbohydrate intolerance</td>
<td>Hypertension</td>
</tr>
<tr>
<td></td>
<td>Mood swing</td>
<td>Increased MI and stroke</td>
</tr>
<tr>
<td></td>
<td>Abdominal distension</td>
<td>Cholestatic Jaundice</td>
</tr>
<tr>
<td></td>
<td>Monilial Vaginitis</td>
<td>and Gall bladder stone</td>
</tr>
<tr>
<td></td>
<td>Corneal edema and irritation</td>
<td></td>
</tr>
</tbody>
</table>
Cancers related to OCP use:
- Carcinoma cervix
- Hepatic adenoma
- Pituitary adenoma (+/-)
- Breast cancer (+/-)

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 7th 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

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 9th 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 13th ed p 259; 14th 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 7th 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 Chlamydia 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.”

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’

So, now we can be sure that the answer is Chlamydia endocervicitis.

Also know:

Infections and Oral contraception:

<table>
<thead>
<tr>
<th>Use of OCP is associated with</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased risk of infection</td>
</tr>
<tr>
<td>Candida (Moniliasis)</td>
</tr>
<tr>
<td>Chlamydia</td>
</tr>
<tr>
<td>Urinary tract infections</td>
</tr>
</tbody>
</table>

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 7th ed p 906
Contraindications of OCPs:

**Absolute contraindications include:**

- Known or suspected Breast cancer
- Severe Hypertriglyceridemia/Hypercholesteremia
- (Undiagnosed Abnormal) Vaginal bleeding
- Smokers over the age of 35 years
- Thrombophlebitis/Thromboembolic disorders, (present H/O, past H/O, family H/O) Cerebral and Cardiac disease
- Pregnancy
- Hypertension (Moderate to severe)
- Markedly Impaired Liver function/infective hepatitis
- Diabetes mellitus with vascular disease
- 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**  
Patient taking OCP’s and presenting with abdominal pain and psychiatric problem, diagnosis is undoubtedly acute intermittent porphyria as OCP’s can precipitate porphyria.

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**  
Interactions of OCP’s with other Drugs.

Drug Interaction

- Rifampicin
- Carbamazepine
- Phenytin
- Antifungals like Griseofulvin, Ketoconazole, Itraconazole
- Ampicillin
- Tetracycline

**Drugs reducing the effectiveness of OCP**

<table>
<thead>
<tr>
<th>Drugs reducing the effectiveness of OCP</th>
<th>Drugs which increase the plasma level of steroids of OCP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifampicin&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Ascorbic acid</td>
</tr>
<tr>
<td>Carbamazepine&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Acetaminophen</td>
</tr>
<tr>
<td>Phenytin</td>
<td></td>
</tr>
<tr>
<td>Antifungals like Griseofulvin</td>
<td>Induce synthesis of cytochrome P450 enzymes in liver.</td>
</tr>
<tr>
<td>Ketoconazole</td>
<td></td>
</tr>
<tr>
<td>Itraconazole</td>
<td></td>
</tr>
<tr>
<td>Ampicillin</td>
<td>Kill gut bacteria and cause hydrolysis of steroid glucuronides in intestine.</td>
</tr>
<tr>
<td>Tetracycline</td>
<td></td>
</tr>
</tbody>
</table>

42. **Ans. is a, i.e. Gossypol**  

**Gossypol**

- It is a male contraceptive pill which contains Disequilterpene aldehyde
- 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 bucolate injectable

Progestosterone 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”.

Progestosterone only pills

Mechanism of action of POP’s is mainly on cervical mucus—

“All Estrogen free pills except the newer desogesterel 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.
• Main progestogen used are:
  – Norethisterone 350 mcg
  – Norgestrel 75 mcg
  – Levonorgestrel 30 mcg
• Their main mechanism of action (as discussed earlier) is thickening of cervical mucus.
  – 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/ed p 922

I have already discussed minipill/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/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

**Chapter 10  Contraception**

**DMPA** i.e. *depot medroxyprogesterone acetate (depot provera)* and *Neten* are progesterone only injectable contraceptives

DMPA is discussed in detail in preceding text:

49. **Ans. is a, i.e. Irregular bleeding**  
Ref. Dutta Obs 6th 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.**

<table>
<thead>
<tr>
<th>Composition</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Lunelle/cyclofem</td>
<td>25 mg DMPA + 5 mg estradiol cypionate Monthly injection</td>
</tr>
<tr>
<td>• Mesigyna</td>
<td>50 mg NET-EN + 5 mg estradiol valerate Monthly injection</td>
</tr>
</tbody>
</table>

50. **Ans. is b, i.e. Metrorrhagia**  
Ref. Novak 14th 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:**

<table>
<thead>
<tr>
<th>Norplant I</th>
<th>Norplant II/Jadelle</th>
<th>Implanon</th>
</tr>
</thead>
<tbody>
<tr>
<td>• It has 6 rods containing 36 mg of Levonorgestrel each</td>
<td>• It has 2 rods each containing 75 mg of LNG and releases the drug at the same dose as norplant I</td>
<td>• It has a single rod containing 68 mg of 3 keto-desogestrel (etinorgestrel)</td>
</tr>
<tr>
<td>• Replaced after 5 years</td>
<td></td>
<td>• Most popular implant these days.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Replaced after 3 years.9</td>
</tr>
</tbody>
</table>

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 15th ed p 228  
Mirena is a progesterone IUCD. It contains 52 mg levonorgesterol, 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. 6th ed p 537; Clinical Gynaecologic Endocrinology and Infertility by Leon Speroff 7th 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  
LNG - IUD has a pregnancy rate of 0.2 100 women years (HWY) (here nearest is 0.5 so that is the answer).  
Ref. Leon Speroff 7th ed p 981

IUCDs

58. Ans. is c, i.e. Has history of ectopic pregnancy  
Ref. Parks 20th 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.
  - 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 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 15th ed p 229; Leon Speroff 7th ed p 980

**Mechanism of Action Of IUCD:**

<table>
<thead>
<tr>
<th>Non medicated IUCD</th>
<th>Cu containing IUCD</th>
<th>Progestin releasing IUCD</th>
</tr>
</thead>
</table>
| 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  
It provokes uterine contractility and increases tubal peristalsis. | Elute copper which bring about enzymatic and metabolic changes in the endometrial tissue & also produce changes in cervical mucus and endometrial secretions. | They cause decidualization with atrophy of endometrial glands, therefore inhibit implantation  
Alter cervical mucus causing inhibition of sperm penetration and capacitation.  
In 40% cases, ovulation is also inhibited. |

“**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 7th 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 15th ed p 227

61. Ans. is a, i.e. CuT380A

Most of the IUCDs have an average life span of 3 years.

Exceptions are:

- Nova T/ Multiload 375/Levonova
- CuT 380 A (also known as Paragard)
- Progestasert
- CuT200 B
- Levonorgestrel containing IUCD can be used for: (Mirona)

- 5 years
- 10 years – Distributed free of cost
- 1 year
- 4 years, in US and 3 years in India and in European countries.
- 7–10 years, but is approved for 5 years

Ref. Shaw 15th ed p 227; Novak 14th ed p 263

62. Ans. is a, i.e. Copper and silver

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.

Ref. Shaw 15th ed p 227

63. Ans. is b, i.e. Remove the IUCD

64. Ans. is c, i.e. Remove the IUD to decrease the risk of infection


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 1st ed p 120

Ref. SK Chaudhary 7th 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

Lost/Misplaced IUCD

Do USG (to localize the lost IUCD)

Within uterine cavity
- Hysteroscopic removal (best)
- IUCD hook

In abdominal cavity
- Laparoscopy
- Laparotomy (if dense adhesions present)

Ref. Shaw 15th ed p 227

66. Ans. is c, i.e. Congenital malformation of uterus

Ref. Shaw 15th ed p 228

67. Ans. is d, i.e. Pelvic tuberculosis

Ref. Shaw 15th ed p 228
68. Ans. is a and b, i.e. Undiagnosed vaginal bleeding and PID  

Ref. Park 20th ed p 427; Shaw 15th ed p 228; Novak 15th ed p 224

Absolute contraindications of IUCD/WHO Category 4

| Please | Puerperal sepsis/Pregnancy |
| Don’t  | DUB                        |
| Try to | Gestation of trophoblastic disease |
| Put    | current PID/STD or within the past 3 months puerperal sepsis |
| Condom | Cancer cervix |
|        | Cancer endometrium |

Mnemonic: Please Don’t Try to Put Condom

Relative contraindications of IUCD

- Distortions of uterine cavity due to congenital malformations, fibroid
- Wilson disease
- Scard 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

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 7th ed p 988

“IUCDs-They are the contraceptive method of choice in woman with either type I or type II diabetes.”

— Curren 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 maintainence and no drug interaction.”

— Curren Concept in Contraception and Women Health, p 97

Leon Speroff 7th ed p 985 also supports the use of IUCD’s in HIV infected females.

71. Ans. is b, i.e. Bleeding

Complication of IUCD

- M/C complication–Bleeding
- II 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 actinomycetes.
- 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

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 7th ed pp 925-926

“Contrary to popular belief, it is not an abortifacient i.e. will not act after implantation has occured.”

— 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. 6th ed p 549; Leon Speroff 7th 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

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.  

Drugs used for Emergency contraception

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. OCP's (Morning after pill)</strong></td>
<td><strong>Yuzpee’s method</strong> 2 tablets of ovral (EE=50 mg and Levonorgestrel .25 mg) followed by 2 tablets 12 hours later. <strong>Remember</strong> 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.</td>
</tr>
<tr>
<td><strong>2. Levonorgestrel alone—Most appropriate drug/progestrone for Emergency contraception — (3rd most effective)</strong></td>
<td>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 E pill under the National Family Welfare Programme. Other brands available are: I pill/ Ecee2/unwanted 72. It is the drug of choice for emergency contraception.</td>
</tr>
<tr>
<td><strong>3. Copper Intrauterine device, (2nd most effective)</strong></td>
<td>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.</td>
</tr>
<tr>
<td><strong>4. Mifepristone/RU-486</strong></td>
<td>A single dose of 10 mg given as soon as possible is effective in preventing 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).</td>
</tr>
<tr>
<td><strong>5. Centchroman</strong></td>
<td>2 tablets (60 mg) to be taken twice at an interval of 12 hours within 24 hours of intercourse.</td>
</tr>
<tr>
<td><strong>6. Ulipristal—(most effective)</strong></td>
<td>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.</td>
</tr>
</tbody>
</table>

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 7th 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

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 14th ed p 213 says
“The tables can be offered up to 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 8th ed p 1042

According to current concepts in contraception and women health also -

Emergency contraception can be given up to 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

Methods of contraception (can be classified as)

<table>
<thead>
<tr>
<th>Temporary methods (used to postpone or space births)</th>
<th>Permanent methods (Surgical methods aim is to purposefully and permanently destroy the Reproductive capacity of an individual)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Barrier method</td>
<td>Female</td>
</tr>
<tr>
<td>• Natural contraception</td>
<td>Male</td>
</tr>
<tr>
<td>• Oral contraceptive pills</td>
<td>Tubectomy</td>
</tr>
<tr>
<td>• Injectables</td>
<td>Vasectomy</td>
</tr>
<tr>
<td>• Implants</td>
<td></td>
</tr>
<tr>
<td>• Intrauterine devices like Copper T, Levonorgestrel IUCD’s</td>
<td></td>
</tr>
</tbody>
</table>

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 Shaw which says some of these methods are reversible, it does not mean they are not permanent methods.

79. Ans. c, i.e. Essure

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

Hysteroscopic tubal occlusion is done by 2 methods and both these methods have high failure rates.

<table>
<thead>
<tr>
<th>Hysteroscopic tubal occlusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cauterization (Failure rate 30%)</td>
</tr>
<tr>
<td>Sclerosants (Failure rate 15%)</td>
</tr>
<tr>
<td>• Due to high failure rate these methods are obsolete now</td>
</tr>
</tbody>
</table>

81. Ans. is d, i.e. Laparoscopic tubal ligation with clips

Reversal of tubal ligation

<table>
<thead>
<tr>
<th>Sterilization procedure</th>
<th>Term pregnancy (range %)</th>
<th>Ectopic pregnancy (range %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spring-loaded clip</td>
<td>88 (75–100)</td>
<td>2 (0.4)</td>
</tr>
<tr>
<td>Ring occlusion (silastic bands)</td>
<td>75 (44–95)</td>
<td>2 (0–4)</td>
</tr>
<tr>
<td>Pomeroy ligation</td>
<td>59 (45–70)</td>
<td>2 (0–3)</td>
</tr>
<tr>
<td>Electrocoagulation</td>
<td>43 (26–58)</td>
<td>5 (0–9)</td>
</tr>
</tbody>
</table>

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

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

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 7th ed p 825

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 mesosalpinx are not unduly disturbed.

87. Ans. is b, i.e. 0.1%

Read the text for explanation

88. Ans. is b, i.e. No sperms in ejaculate

Sterility does not occur immediately after vasectomy. Sperms remain in the semen for 15–20 ejaculation, 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

90. Ans. is d, i.e Condom

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 20th ed p 425

• Combined oral contraceptive pills are contraindicated in a woman with cardiac disease.

• IUCD is carefully considered in a cardiac and diabetic woman because of the possibility of pelvic infection.

• 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 in the puerperium under local anesthesia through abdominal root by minilap technique

• If the heart is not well compensated, the husband is advised for vasectomy.

91. Ans. is b, i.e. Condom

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 14th 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

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 ager 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 7th 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 responses 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.
- If 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 15th 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 8th ed p 1026; text book of gynecology, sheila bala krishnan 1st 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 8th ed p 1026

Epilepsy/seizure disorder is a relative contraindication for the use of OCP’s as antiepileptic drugs like phenytoin, carbamezapine 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


- Vasectomy consists of dividing and excising a part of vas deferens (with spermatic cord).
- It leads to permanently ending fertility fo 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 6th 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 7th ed p 209-211

During laparoscopy, pneumoperitoneum is created with CO₂ or nitrous oxide. CO₂ is preferred because N₂O can cause explosion in presence of volatile anesthetic drugs. About 2 litres of gas is introduced at 10 mgHg. 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 7th 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 7th 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 1st 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 7th ed p 842; 8th ed p 926

Female tubal sterilization methods-10 year cumulative failure rates:

<table>
<thead>
<tr>
<th>Method</th>
<th>Failure Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unipolar cauterisation</td>
<td>0.75%</td>
</tr>
<tr>
<td>Postpartum tubal excision</td>
<td>0.75%</td>
</tr>
<tr>
<td>Silastic ring/fallope ring</td>
<td>1.77</td>
</tr>
<tr>
<td>Interval tubal exclusion</td>
<td>2.01</td>
</tr>
<tr>
<td>Bipolar coagulation</td>
<td>2.48</td>
</tr>
<tr>
<td>Hulka - clemens clips</td>
<td>3.65</td>
</tr>
</tbody>
</table>

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

Ref. Leon Speroff 7th ed p 842; 8th ed p 926

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.
Fibroids

- Fibroids are the most common benign solid tumors in females. It is the most common pelvic tumor.
- Most common age group affected is 35–45 years.
- Fibroids are most commonly seen in nulliparous female.
- Locations of fibroid is described as follows (Fig. 11.1):
  - Intramural/interstitial: grow within the myometrial wall (M/C) 75%
  - Submucous: grow toward the uterine cavity 15%
  - Subserous: grow outward toward the peritoneal surface 5%
  - Most common is cervical fibroid

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
- 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
- Intramural/interstitial (75%) followed by submucous (15%) and subserous (10%)
- Submucous fibroid
- Interstitial (Intramural)
- Submucous
- Posterior cervical
- Large pedunculated subserous fibroid
- Subserous fibroid
- Menorrhagia
- Fundal fibroid
- Menorrhagia
- Submucous fibroid
- Submucous fibroid
- Cervical fibroid
- Fibroid polyp
- Subserous 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
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.
- Most fibroids are slow growing.

Degenerations/Secondary Changes in a Fibroid

<table>
<thead>
<tr>
<th>Avoid</th>
<th>Red</th>
<th>Hot</th>
<th>Fatty</th>
<th>Meat of Chicken</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrophy</td>
<td>Red degeneration</td>
<td>Hyaline degeneration (MC)</td>
<td>Fatty degeneration or calcification</td>
<td>Cystic degeneration</td>
</tr>
</tbody>
</table>

(Mnemonic: Avoid red hot fatty meat of chicken)

Red Degeneration of Fibroid (also called as Carneous Degeneration)
- It is seen mostly during pregnancy, especially mid pregnancy-2nd trimester (But can occur at other times as well and in nonpregnant females also).
- It is an aseptic condition.
- The myoma suddenly becomes acutely painful, enlarged and tender.
- Patient presents with: Acute abdominal pain, Vomiting, Malaise, Slight fever.
- Lab investigations: Moderate leukocytosis, Raised esr.

Pathological changes in the tumor
- Fibroid becomes soft, necrotic or homogenous especially in its center.
- It is stained Salmon pink, or red (due to diffusion of blood pigments from the thrombosed vessels).
- It has a fishy odor (due to secondary infection with coliform organisms)
- Histologically: There is evidence of thrombosis in some vessels.
- Pathogenesis: There is subacute necrosis of the myoma caused by an interference in blood supply (aseptic infarction).

Management
- Conservative management
- Patient is advised rest
- Analgesics are given to relieve the pain.
- The acute symptoms subside in 3–10 days and pregnancy proceeds uneventfully.
- Diagnosis is by ultrasound.

Differential Diagnosis
- Appendicitis, twisted ovarian cyst, pyelitis and accidental hemorrhage.

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.\(^2\)
- The malignant process begins from the center.\(^2\)
- M/c in submucous followed by intramural fibroid.\(^2\)
- Diagnosis is made by histological examination of the removed myoma.\(^2\)
- 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%.

**Symptoms of Fibroid**
- Mostly fibroids are asymptomatic\(^2\) (M/C presentation)
- Most common symptom — Menstrual disturbances\(^2\)
- Most common menstrual disturbance: Progressive menorrhagia\(^2\) (seen in 30% cases).
  - Other Menstrual Symptoms:
  - Metrorrhagia\(^2\) – (Continuous and irregular bleeding)\(^2\)
  - Causes:
    - Ulceration of submucous fibroid or polyp.\(^2\)
    - Sarcomatous change in leiomyoma.\(^2\)
  - Dysmenorrhea – congestive\(^2\) as well as spasmodic\(^2\) type seen.
- Pressure symptoms
  - Infertility: As a sole cause, fibroid is responsible for < 3% cases of infertility.
  - Causes:
    - Fibroid hinders with the ascent of the sperm.\(^2\)
    - Interferes with implantation of fertilized ovum.\(^2\)
    - Can cause associated disturbance in ovulation\(^2\)
  - 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.
Chapter 11 Uterine Fibroid

- **Pain:** A fibroid usually does not cause pain.
  - **Causes:**
    - Malignancy
    - It is being extruded from body as a polyp
    - Associated endometriosis
    - Torsion of a pedunculated fibroma
    - Degeneration

  **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.)
  - 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

**Management of Fibroids**

**Indications for Operating an Asymptomatic Fibroid:** — Jeffcoate 7th ed, p 496

- Fibroids larger than 12–14 weeks pregnancy.
- Rapidly growing fibroids.
- Subserous and pedunculated fibroid prone to torsion.
- If it is likely to complicate a future pregnancy
- If there is doubt about its nature
- Unexplained infertility and unexplained recurrent abortion.

— Dutta Gynaec 4th ed p 264

- Uncertain diagnosis: If patient is symptomatic decide whether you give medical treatment or surgical treatment.

**Indications of Medical Management:**

- To treat anemia and recover hemoglobin levels before surgery.
- To reduce the size of large fibroid and facilitate surgery.
Treatment of women approaching menopause to avoid surgery.

In women with medical contraindication to surgery or those who are postponing surgery.

For preservation of fertility in women with large myomas before conservative surgery like myomectomy.

**Indications of Surgical Management**

Fibroids causing any symptoms like

- Menorrhagia or pressure symptoms like urinary retention (by a cervical or broad ligament fibroid) or chronic pelvic pain with 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.

**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

- **U**: Ulipristone
- **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**

- **Surgical Management**
  
  - Uterus conserving surgery
  - Remove the uterus
    
    - Myomectomy
    - Hysterectomy
Some Specific Indications for Hysterectomy

- In patients > 40 years of age.
- Multiparous women.
- If fibroid is associated with malignancy.
- During myomectomy, if their is uncontrolled hemorrhage or other surgical difficulty.

Myomectomy

- Myomectomy is specifically indicated in an infertile woman or woman desirous of bearing child and wishing to retain the uterus.
- **Prerequisites:** Anemia should be corrected.
  - All other causes of infertility should be excluded.
  - Male factor infertility should be ruled out (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.
  - Hysteroscopy or hysterosalpingography (HSG) should be done to detect a fibroid encroaching the uterine cavity or a polyp or tubal block.

Time of Myomectomy

- It should be performed in immediate postmenstrual phase to reduce blood loss during surgery.
- It should not be performed during pregnancy and at the time of cesarean section.
- Route of myomectomy
  - Laparoscopic
  - Abdominal
  - Hysteroscopic

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)
- Multiple tiny fibroids scattered through the uterine wall.
- Infected fibroid
- Pelvic or endometrial TB
- During pregnancy on following section

Hysterectomy for fibroids can be done by
- Abdominal route
- Vaginal route–done, if size of uterus is < 12 weeks in size

Myomectomy

Myomectomy is the enucleation of myomata from the uterus leaving behind a potentially functioning organ capable of future reproduction.

Instrument used to decrease blood loss during myomectomy: Bonney’s myomectomy clamp.

**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.
- Bonney’s hood technique: is done in interstitial fibroid on the fundal posterior wall.
Results (Important)
- Pregnancy rate following myomectomy: 40–60%
- Recurrence rate: 30–50%
- Persisting menorrhagia: 1–5%
- 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
- **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 alcohol or gel foam. 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 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 decease blood cans during surgery or can be used alone for therapeutic purpose.

Results
These patients experience:
- Lowered fertility rate
- Risk of placental insufficiency
- Uterine rupture in subsequent pregnancy 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 ≥ 57°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 cm from semi surface

**Extra edge**

**FIGO Fibroid Classification**

<table>
<thead>
<tr>
<th>FIGO Leiomyoma Classification System</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>SM-Submucosal</td>
<td>Pedunculated intracavitary</td>
<td>&lt; 50% intramural</td>
<td>≥ 50% intramural</td>
<td>Contacts endometrium; 100% intramural</td>
<td>Intramural</td>
<td>Subserosal ≥ 50% intramural</td>
<td>Subserosal &lt;50% intramural</td>
<td>Subserosal pedunculated</td>
<td>Other (specify e.g. cervical, parasitic)</td>
</tr>
<tr>
<td>O-Other</td>
<td>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</td>
<td>Submucosal and subserosal, each with less than half the diameter in the endometrial and peritoneal cavities, respectively.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Fig. 11.2: FIGO Classification of fibroids**
FIGURE BASED QUESTIONS

F1. Identify the fibroid based on FIGO classification:
   a. Type 3
   b. Type 4
   c. Type 5
   d. Type 7

F2. Identify the instrument:
   a. Myoma clamp
   b. Myoma screw
   c. Uterine manipulator
   d. IUCD removing hook

F3. Identify the instrument shown in Figure F3
   a. Bonneys myoma screw
   b. Bonneys myoma clamp
   c. Cervical occlusion clamp
   d. Uterus holding forcep

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. Amenorrhea
   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: (LIP 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

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

22. All are prerequisites for myomectomy except:
   a. Husband’s 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 morcellement
   c. Hysteroscopy
   d. All of the above
ANSWERS TO FIGURE BASED QUESTIONS

F1. Ans. is c i.e. Type 5  
   The fibroid shown is the figure is subserosal with 50% intramural component. Hence it is type 5.  
   Ref. Novaks Gynae 15/e p445

F2. Ans. is b i.e. Myoma screw  
   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.)  
   Ref. Dutta Gyane 6/e p635

F3. Ans. is d i.e. Bonneys myoma clamp  
   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.  
   Ref. Dutta Gyane 6/e p635

ANSWERS

1. Ans. is b, i.e. Squamous metaplasia  
   Fibromyoma can have following complications and degenerative changes:

<table>
<thead>
<tr>
<th>Complications</th>
<th>Changes/Degenerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Torsion</td>
<td>• Avoid</td>
</tr>
<tr>
<td>• Hemorrhage</td>
<td>• Red</td>
</tr>
<tr>
<td>• Infection</td>
<td>• Hot</td>
</tr>
<tr>
<td>• Ascites, pseudo-Meig’s syndrome (Produced by pedunculated subserous fibroid)</td>
<td>• Fatty</td>
</tr>
<tr>
<td>• Malignant change (rarest)</td>
<td>• Meat</td>
</tr>
<tr>
<td></td>
<td>• Of chicken</td>
</tr>
<tr>
<td>(Mnemonic: Avoid Red hot fatty meat of chicken)</td>
<td>= Atrophy</td>
</tr>
<tr>
<td></td>
<td>= Red degeneration</td>
</tr>
<tr>
<td></td>
<td>= Hyaline degeneration (MC)</td>
</tr>
<tr>
<td></td>
<td>= Fatty degeneration or calcification</td>
</tr>
<tr>
<td></td>
<td>= Myxomatous degeneration</td>
</tr>
<tr>
<td></td>
<td>= Cystic degeneration</td>
</tr>
</tbody>
</table>

   Also know:  
   • Most common degeneration: Hyaline degeneration.  
   • Degeneration starts from the central part, as fibroid is lined by a pseudocapsule. The blood vessels supplying the  
     fibroid lie in the pseudocapsule. 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.  
   • Most uncommon (rarest) change in fibroid is malignant change/sarcomatous change. It occurs in 0.5% cases of  
     fibroid.

2. Ans. is c, i.e. Red degeneration of fibroid  
   Ref. Shaw 15%ed p 355; Dutta Obs 6%ed p 314; High Risk Pregnancy 2%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  
   • Patient is pregnant  
   • Pain in abdomen at 28 weeks (preterm labor is where labor starts before the 37 th completed weeks. The lower limit is 28  
     weeks in developing countries and 20 weeks in developed countries  

   Points against  
   • Preterm labor is diagnosed  
   • When there are regular uterine contractions. (Not acute pain) With or without pain at least in every 10 minutes.  
   • Dilatation of cervix is > 2 cm  
   • Effacement of cervix = 80%  
   • Length of cervix as measured by TVS < 2.5 cm and funneling of the internal OS.  
   • Pelvic pressure backache, vaginal discharge, or bleeding. None of the above criteria are being fulfilled  

   Contd....
Chapter 11 Uterine Fibroid

Option “b” Torsion of fibroid

<table>
<thead>
<tr>
<th>Points in favor</th>
<th>Points against</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Patient has fibroid (Though no mention has been made whether it is pedunculated or not, Remember torsion is seen in subserous pedunculated myomas)</td>
<td></td>
</tr>
<tr>
<td>• Patient is complaining of acute pain in abdomen</td>
<td></td>
</tr>
<tr>
<td>• Torsion is not associated with fever and leukocytosis</td>
<td></td>
</tr>
</tbody>
</table>

Option “d” Infection of fibroid

<table>
<thead>
<tr>
<th>Points in favor</th>
<th>Points against</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Presence of fibroid (Remember: Infection is common in submucous fibroids)</td>
<td></td>
</tr>
<tr>
<td>• Fever</td>
<td></td>
</tr>
<tr>
<td>• Leukocytosis</td>
<td></td>
</tr>
<tr>
<td>• Acute pain in abdomen (Infection of fibroid will not cause acute pain in abdomen).</td>
<td></td>
</tr>
<tr>
<td>• Infection of fibroid occurs following abortion or labor (Here patient is pregnant but there is no history of abortion or labor)</td>
<td></td>
</tr>
<tr>
<td>• Infection causes blood stained discharge (Not seen in this patient)</td>
<td></td>
</tr>
</tbody>
</table>

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.
• The myoma suddenly becomes acutely painful, enlarged, and tender.
• Patient presents with: - Acute abdominal pain - Vomiting - Malaise - Slight fever

Lab investigations: Show moderate leukocytosis and raised ESR

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

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).

• 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

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. 6th 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.”

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 15th ed pp 360-2; Jeffcoate 7th ed pp 497-9; Dutta Gynae 5th ed pp 269-73

6. Ans. is a, i.e. Myomectomy  
Ref. Shaw 15th ed p 360; Jeffcoate 7th 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
- Chronic lower abdomen pain

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 15th 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.

8. Ans. is b, i.e. Subserous  
Ref. Dutta Gynae 6th ed p 265

“Calcareaous 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 5th ed p 265

Ref. Jeffcoate 7th ed p 490

9. Ans. is a, i.e. Endometriosis  

Diseases commonly associated with leiomyomas are:
- Follicular cysts of ovary
- Endometrial hyperplasia
- Endometrial cancer
- Endometriosis

- 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 amenorrhea (so obviously amenorrhea is not correct).

Now coming to the last option – Tamoxifen.

Tamoxifen causes Endometrial hyperplasia and Endometrial cancer, not Fibromyoma.

10. Ans. is a, i.e. Analgesics  

Management of red degeneration of fibroid.
- Patient is managed conservatively.
• Patient is put to bedrest and given analgesics (to relieve the pain), sedatives, and if required, antibiotics.
• 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.

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)
USG: Ultrasound is the most readily available, least costly imaging technique to diagnose fibroid. It checks the number, location, and size 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.
Ulterine Curettage: It can also help in diagnosis of submucous fibroid by feeling of a bump during curettage.
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

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 1st 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  
   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/ed p 205

   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/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/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  
   As discussed earlier, fibroids are estrogen dependant tumors$^0$ and don’t have a true capsule but a pseudo capsule$^0$.
   • 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  
   • 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/ed p163

19. Ans. is a, i.e. Amenorrhea  
   Fibroids do not lead to amenorrhea, they lead to menorrhagia/metrorrhagia

20. Answer is a, i.e. Frequency of urine  
   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  
   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**

   **Prerequisites for myomectomy:** Anemia should be corrected.\(^9\)
   - All other causes of infertility should be excluded.\(^9\)
   - Male factor infertility should be ruled out.\(^9\) (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.\(^9\)
   - Hysteroscopy or HSG: To detect a fibroid encroaching the uterine cavity or a polyp or tubal block.\(^9\)

23. **Ans. is d, i.e. Placenta previa**

   Thus, placenta previa is not a complication of fibroid → Abruptio placenta is a complication.

24. **Ans. is a, i.e. Mucous polyp**

   - M/C uterine polp 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**

   **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 prudside)
   - Use of vasoconstrictive agents mainly vasopressin intraoperatively
   - Use of vctor 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**

   The M/C investigation done to diagnose/detect fibroids is USG “USG is an useful diagnostic tool to confirm its diagnosis”.\(^9\)
   - 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  
   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 on via estrogen” Dutta Gynae 6th/ed p 272. Hence option d is correct.

28. Ans. is d, i.e. All of the above

<table>
<thead>
<tr>
<th>Polyp</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endometrial polyp</td>
<td><strong>Hysteroscopy and resection (best)</strong></td>
</tr>
<tr>
<td></td>
<td>Removal by ovum forcep</td>
</tr>
<tr>
<td></td>
<td>Incase of recurrence and, if family completed—</td>
</tr>
<tr>
<td></td>
<td>uterine curettge hysterectomy</td>
</tr>
<tr>
<td>Cervical polyp</td>
<td><strong>Twisting of the pedicle</strong></td>
</tr>
<tr>
<td>Big fibroid in vagina</td>
<td>• Removal of polyp by morcellation</td>
</tr>
<tr>
<td></td>
<td>• If associated with inversion enucleate</td>
</tr>
</tbody>
</table>

Ref. Dutta Gynae 6th/ed p 272, 287, 288
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 embryonal 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

**Risk Factors**
- Family history (7–10 fold increased risk if affected 1st degree relative)
- Obstructive anomalies of genital tract (earlier onset)
- Nulliparity
- High socioeconomic status due to late marriage and late childbirth
- In utero exposure to DES
- Hormone – estrogen dependant condition

**Protective Factors**
- Regular exercise
- Smoking
- Pregnancy
Scar Endometriosis is seen in
- Hysterotomy scar
- Classical cesarean section scar
- Myomectomy scar
- Ventrofixation scar
- Scar involving section of fallopian tube operation.

Pathology

<table>
<thead>
<tr>
<th>Peritoneum</th>
<th>Peritoneal cavity</th>
<th>Ovary</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Earliest lesion is red petechial</td>
<td>- Contains yellowish brown fluid which</td>
<td>- Characteristic chocolate cyst (True cyst</td>
</tr>
<tr>
<td>lesion later becoming cystic,</td>
<td>has prostaglandin responsible for pain</td>
<td>with columnar lining epithelium.</td>
</tr>
<tr>
<td>dark brown or blue black in</td>
<td>of endometriosis</td>
<td>Beneath the epithelium are pseudo-xanthoma</td>
</tr>
<tr>
<td>appearance called as</td>
<td></td>
<td>cells which are brown colored due to</td>
</tr>
<tr>
<td>powder-burn appearance/</td>
<td></td>
<td>ingested hemosiderin pigment</td>
</tr>
<tr>
<td>gunshot appearance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Presence of defects in</td>
<td></td>
<td></td>
</tr>
<tr>
<td>peritoneum (usually scarring</td>
<td></td>
<td></td>
</tr>
<tr>
<td>overlying implants) is called</td>
<td></td>
<td></td>
</tr>
<tr>
<td>as Allen-Masters syndrome</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

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.

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-CR-125 levels are raised in endometriosis.
- Monocyte chemotatic 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

A.

Management of pain

Mainly-Medical management

Surgery—Done only if medical management fails
- Adhesiolysis
- Fulguration of implants
- Presacral neurectomy
- Hysterectomy

Minimal/Mild disease 🛡️
DOC = NSAID (if only pain)
OCPs (Pain with menstrual complaint)

Moderate/severe disease 🔧
DOC = GnRH agonist (continuous)
1st drug to start: Progesterone
(it causes decidualization of implants)

B. Management of Infertility

- In minimal/mild endometriosis the cause of infertility is ovarian, either oogenesis is defective on 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 INF is the management

Management of Endometrioma

Laparoscopic management of the endometroma is the preferred management

Recent Advances

- 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.

Adenomyosis

Adenomyosis is a condition where there is ingrowth of endometrium (both gland + stroma) directly into the myometrium. Earlier it was called endometriosis interna.
**Age group**: Elderly patients > 40 years

**Parity**: Multiparous

**Symptoms**: Most common symptom: Menorrhagia

2nd most common symptom: Dysmenorrhea

Presenting feature: Menorrhagia and citalies Dysmenorrhea

**On per vaginal examination**: Symmetrical enlargement of uterus (not more than 12–14 weeks of pregnancy), 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) 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.

<table>
<thead>
<tr>
<th>Primary/Spasmodic</th>
<th>Secondary/Congestive</th>
</tr>
</thead>
<tbody>
<tr>
<td>• No pelvic pathology is responsible for the pain</td>
<td></td>
</tr>
<tr>
<td>• Mostly seen in adolescents</td>
<td></td>
</tr>
<tr>
<td>• M/C in affluent society</td>
<td></td>
</tr>
<tr>
<td>• Almost always confined to ovulatory cycle, hence pain appears within 6 months–1 year after onset of menarche (when cycles become ovulatory)</td>
<td></td>
</tr>
<tr>
<td>• Pain appears within 2 years of menarche</td>
<td></td>
</tr>
<tr>
<td>• Pain appears on 1st day of menstrual period and usually lasts for 12 hours.</td>
<td></td>
</tr>
<tr>
<td>• Pain never persists beyond 48 hours</td>
<td></td>
</tr>
<tr>
<td>• Pain is spasmodic and confined to lower abdomen. May radiate to back and medial aspect of thigh</td>
<td></td>
</tr>
<tr>
<td>• Systemic discomfort present</td>
<td></td>
</tr>
<tr>
<td>• Pain is usually cured after 24 years of age and following pregnancy and delivery.</td>
<td></td>
</tr>
<tr>
<td>• Pain is due to presence of pelvic pathology.</td>
<td></td>
</tr>
<tr>
<td>• Pain seen years after menarche (mostly in parous females)</td>
<td></td>
</tr>
<tr>
<td>• Can be seen in anovulatory cycles also</td>
<td></td>
</tr>
<tr>
<td>• Patients mainly complain of deep seated pelvic pain. Pain is dull, situated in back and front without any radiation</td>
<td></td>
</tr>
<tr>
<td>• No systemic discomfort seen</td>
<td></td>
</tr>
<tr>
<td>• Pain appears 3–5 days prior to the period and is relieved with the start of the period.</td>
<td></td>
</tr>
</tbody>
</table>

Contd...
Primary/Spasmodic | Secondary/Congestive
--- | ---
Treatment of spasmodic dysmenorrhea-
1. Prostaglandin synthetase inhibitor-M/C used drug.
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.
3. Surgery – rarely required e.g.  
   - Dilatation of cervical canal
   - Paracervical block.
   - Presacral neurectomy (LPSN) and uterosacral nerve ablation (LUNA)
| Important causes are  
- PID  
- Endometriosis  
- Adenomyosis  
- IUCD in uterus  
- Uterine fibroid  
- Polyps  
- Cervical stenosis  
- Congenital malformation of uterus like bicornuate uterus
| Management: Treatment of the underlying cause.

**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.
- Pain is usually situated in the hypogastrium or to one iliac fossa.
- Pain is usually located on one side and does not change side according to which ovary is ovulating.
- Nausea and vomiting is conspicuously absent.
- It rarely lasts for more than 12 hours.
- It may be associated with slight vaginal bleeding or mucoid discharge.
- The probable factors are:
  - Increased tension of graffian follicle just prior to rupture.
  - Peritoneal irritation by follicular fluid following ovulation.
  - Contraction of tubes and uterus.

**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):
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 (PNS)

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

<table>
<thead>
<tr>
<th>Conservative Measures</th>
<th>Inhibition of Ovulation</th>
<th>Medications directed at symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Elimination of caffeine from diet</td>
<td>• Oral contraceptives (especially drospirenone containing)</td>
<td>• For fluid retention: diuretics</td>
</tr>
<tr>
<td>• Smoking cessation</td>
<td>• GnRH agonist</td>
<td>• For pain: prostaglandin synthetase</td>
</tr>
<tr>
<td>• Counselling, emotional support</td>
<td></td>
<td>• For mastalgia: evening primrose oil and pyridoxine</td>
</tr>
<tr>
<td>• Low-fat, high-fiber diet, and essential fatty acids in diet.</td>
<td></td>
<td>• For anxiety/depression: SSRI like fluoxetine and preferred Tricyclic antidepressants can also be used.</td>
</tr>
<tr>
<td>• Regular exercise</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Adequate sleep</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Stress reduction</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
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 3rd or 4th decade  
   b. Premenstrual spotting  
   c. Endometrial sarcoma is most common malignancy associated with it  
   d. True cyst  
   e. 1st 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:  
   (AIIMS Dec 97)
   a. Medroxyprogesterone acetate  
   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

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:  
   a. Bromocriptine  
   b. Ibuprofen  
   c. Mefenamic acid  
   d. 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:  
   a. Endometriosis  
   b. Dysmenorrhea  
   c. Pelvic tuberculosis  
   d. Mittelschmerz

18. Which of the following is NOT to be given in cyclic mastalgia is:  
   a. Evening primrose oil  
   b. Danazol  
   c. Tamoxifen  
   d. Estrogen

19. Which of the following modalities have shown best result for pre menstrual syndrome?  
   a. SSRI  
   b. Progesterone  
   c. Oestrogen  
   d. Anxiolyties
ANSWERS

1. Ans. is c, i.e. Contains clear fluid

   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 (Option “d”).
   - Can also involve lungs and pleura (Option “b”).
   - In endometriosis ovary contains tarry dark brown fluid (due to presence of blood pigments like hemosiderin) and cul de sac has yellow brown fluid. Clear fluid is not seen anywhere, So, Option “c” is incorrect.

2. Ans. is a, b, d and e, i.e. Most common in 3rd or 4th decade; premenstrual spotting; and true cyst; and 1st degree relative seen

   As discussed in the preceding text-
   i. Endometriosis occurs most commonly in 3rd or 4th 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

   Chocolate cysts of ovary:
   • They are true cysts
   • The cysts enlarge with cyclic bleeding. The serum gets absorbed in between periods and the content inside becomes chocolate, tarry brown in color.
   • Histology
     – Lining epithelium is columnar epithelium.
     – 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

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
     – HCG therapy
     – Hydatidiform Mole
     – Choriocarcinoma
   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

   “Deep penetrating endometriosis is a form of the disease which was described by Koninck’s group. These lesions can extend 10 mm or more down from the peritoneal surface and the deeper lesions appear to have a closer association with pain than infertility, whereas less deep lesions have a closer association with infertility than pain.”

   Dysmenorrhea:

   “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 Cramer 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 7th 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 14th ed p 1144, 15th ed p 512

5. Ans. is b, i.e. Endometrioma

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

<table>
<thead>
<tr>
<th>↑ CA-125</th>
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</thead>
<tbody>
<tr>
<td>Neoplastic conditions</td>
</tr>
<tr>
<td>-------------------------------</td>
</tr>
<tr>
<td>Gynecological</td>
</tr>
<tr>
<td>Ovarian cancer (nonmucinous)</td>
</tr>
<tr>
<td>Endometrial cancer</td>
</tr>
<tr>
<td>Tubal cancer</td>
</tr>
<tr>
<td>Non-gynecological</td>
</tr>
<tr>
<td>Lung cancer</td>
</tr>
<tr>
<td>Breast cancer</td>
</tr>
<tr>
<td>Ca Pancreas</td>
</tr>
<tr>
<td>Colon cancer</td>
</tr>
</tbody>
</table>

- 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 14th 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 Gynaec, Sheila Balakrishnan 1st 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

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
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


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 7th 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
- Classical cesarean section
- Myomectomy
- Ventrofixation
- Following operations for section of fallopian tube
- Following operations for removal of pelvic endometriosis
- Episiotomy

11. Ans. is e, i.e. All of the above

Ref. Shaw 15th 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.

<table>
<thead>
<tr>
<th>Theory</th>
<th>Proposed by</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sampson’s implantation theory</td>
<td>Sampson</td>
<td>Endometriosis occurs as a result of reflux of menstrual endometrium through the fallopian tubes and its subsequent implantation.</td>
</tr>
<tr>
<td>Coelomic metaplasia</td>
<td>Meyer and Ivanoff</td>
<td>Endometriosis arises as a result of metaplastic changes in embryonal cell rests of embryonic mesothelium, which are capable of responding to hormone stimulation.</td>
</tr>
<tr>
<td>Metastatic theory</td>
<td>Halban</td>
<td>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.</td>
</tr>
<tr>
<td>Histogenesis by induction</td>
<td></td>
<td>Proposes that an endogenous (undefined) biochemical factor can induce undifferentiated peritoneal cells to develop into endometrial tissue.</td>
</tr>
</tbody>
</table>

12. Ans. is a, i.e. Laparoscopy


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
- Serous or clear vesicles
- White plaques/scarring
- Yellowish brown discoloration of peritoneum
- Sub ovarian adhesions
- 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 1st ed p 235; Bijoy Sree Sen Gupta 2nd 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 2nd/ed p 138

According to William’s Gynae 1st/ed p 239 –

“Hysterectomy with bilateral oopherectomy 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  
   As discussed in text - *adenomyosis is a condition where there is ingrowth of endometrium (both gland + stroma) directly into the myometrium.* Earlier it was called as Endometriosis interna
   It is more common in Multiparous 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  
   Spasmodic dysmenorrhea is another name for primary dysmenorrhea. (i.e. no pelvic pathology is responsible for pain)
   **Characteristics of spasmodic dysmenorrhea**
   - 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 4th/ed p 172, 5th/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 preceeding text.
18. Ans. is d, i.e. Estrogen
Mastalgia is painful breast:
It can be:

<table>
<thead>
<tr>
<th>Cyclical</th>
<th>Non-cyclical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mostly seen in young women</td>
<td>Mostly seen in older women</td>
</tr>
<tr>
<td>It occurs for a few days before menstruation</td>
<td>May be a symptom of breast carcinoma, cyst Tietze syndrome (Chest wall pain)</td>
</tr>
<tr>
<td>It is usually bilateral diffuse and most severe during luteal phase of menstrual cycle</td>
<td>It has no relation to menstrual cycle</td>
</tr>
<tr>
<td></td>
<td>It is often focal.</td>
</tr>
</tbody>
</table>

Treatement of Mastalgia

- **Cyclical**
  - Examination
    - Mild (requires assurance & observation)
    - Moderate (requires treatment)
      - Analgesic or Evening Primrose oil 3g (having gamma linoleic acid or Efamast)
    - No improvement
      - Danazol 100 mg bid
    - No response or Severe mastalgia
      - GnRH analogue Goserelin 3.6 mg monthly injection
      - Testosterone undecanoate 40 mg bid
      - GnRH agonist

- **Non-cyclical (rule out cancer)**
  - Tietze syndrome NSAIDs, anaesthetic + steroid injection
  - Investigation (cancer)
    - Treat
      - Bromocriptine 2.5 mg bid

19. Ans. is a, i.e. SSRI

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:**

<table>
<thead>
<tr>
<th>Conservative measures</th>
<th>Inhibition of ovulation</th>
<th>Medications directed at symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elimination of caffeine from diet</td>
<td>Oral contraceptives (especially drospirenone containing)</td>
<td>For fluid retention: diuretics</td>
</tr>
<tr>
<td>Smoking cessation</td>
<td>GnRH agonist</td>
<td>For pain: Prostaglandin synthetase</td>
</tr>
<tr>
<td>Counselling, emotional support</td>
<td></td>
<td>For mastalgia: evening primrose oil and pyridoxine</td>
</tr>
<tr>
<td>Low-fat, high-fiber diet and essential fatty acids in diet</td>
<td></td>
<td>For anxiety/depression: SSRI like fluoxetine preferred</td>
</tr>
<tr>
<td>Regular exercise</td>
<td></td>
<td>Tricyclic antidepressants can also be used</td>
</tr>
<tr>
<td>Adequate sleep</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stress reduction</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
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 15th 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, verlaflaxine), administered daily or only during the luteal phase”

— Leon speroff 8th ed p 578

“SSRIs are the most effective pharmacologic treatment for moderate to severe PMS and PMDD”

— Johns Hopkins Manual of Obs and Gynae 4th ed p 462

Remember: The most significant side effect of SSRI is sexual dysfunction including decreased libido and anorgasmia.
Amenorrhea

**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**

<table>
<thead>
<tr>
<th>Congenital</th>
<th>Acquired</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imperforate hymen (M/c cause)</td>
<td>Cervical stenosis following:</td>
</tr>
<tr>
<td>Transverse vaginal septum</td>
<td>• Amputation</td>
</tr>
<tr>
<td></td>
<td>• Cauterization</td>
</tr>
<tr>
<td></td>
<td>• Conization</td>
</tr>
</tbody>
</table>

**Pathology**

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 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 in turn originate from ovary.
- The maturation of follicular apparatus is guided by gonadotropins–FSH and LH (released by pituitary).
- The secretion of these hormones is in turn 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)

<table>
<thead>
<tr>
<th>Compartment I (Disorders of outflow tract/ uterus)</th>
<th>Mullerian Anomalies(^a) (2(^{nd}) M/C cause of primary amenorrhea)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Androgen insensitivity syndrome (Testicular feminization syndrome)(^a)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Compartment II (Disorders of Ovary)</th>
<th>Gonadal dysgenesis (M/C cause of Primary Amenorrhea)(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Turners syndrome: 45XO(^a)</td>
</tr>
<tr>
<td></td>
<td>Pure gonadal dysgenesis: 46 XX(^a)</td>
</tr>
<tr>
<td></td>
<td>Swyers syndrome: 46 XY(^a)</td>
</tr>
<tr>
<td></td>
<td>Savage syndrome: Resistant ovary syndrome</td>
</tr>
</tbody>
</table>

Contd…
Chapter 13  Disorders of Menstruation

Contd…

| Compartment III (Disorders of Anterior Pituitary) | Neoplasia  
| Prolactinomas\(^\circ\)/Craniopharyngiomas\(^\circ\)  
| Hypopituitary states – Simmond’s disease\(^\circ\)/ Chiari  
| Frommel syndrome\(^\circ\)  
| Forbes Albright syndrome (Not very important) |

| Compartment IV (Disorders of CNS) | Kallmann syndrome\(^\circ\) (Amenorrhea + Anosmia)  
| Adrenal hypoplasia |

The details of Mullerian agenesis (MRKH syndrome), testicular feminizing syndrome, and Turners syndrome have been dealt in previous chapters.

Secondary Amenorrhea

M/c cause of Primary Amenorrhea – Turner syndrome  
2nd M/c cause – MRKH syndrome  
3rd M/c cause – Testicular feminizing syndrome/Androgen insensitivity syndrome

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
Asherman’s syndrome is amenorrhea due to intrauterine synechiae formation. M/C cause of Asherman’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 honeycombed appearance.
**Management**
Hysteroscopic adhesiolysis followed by insertion of CuT to prevent reformation of synechiae and cyclical estrogen and progesterone.

### Important causes of Secondary Amenorrhea (Compartment wise)

<table>
<thead>
<tr>
<th>Compartment I (Disorders of outflow tract/uterus)</th>
<th>Compartment II (Disorders of Ovary)</th>
<th>Compartment III (Pituitary)</th>
<th>Compartment IV (Hypothalamus)</th>
</tr>
</thead>
<tbody>
<tr>
<td>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.</td>
<td>Ovary Tumor – Masculinizing tumors/PCOD</td>
<td>Hyperprolactinemia/prolactin tumor/prolactinoma</td>
<td>GnRH deficiency</td>
</tr>
<tr>
<td>Asherman’s syndrome&lt;sup&gt;2&lt;/sup&gt; Following excessive curettage or endometrial tuberculosis</td>
<td>Trauma – Surgical extirpation/Radiotherapy</td>
<td>Insufficiency as in Simmond’s disease, Sheehan’s syndrome</td>
<td>Vigorous exercise/excessive stress</td>
</tr>
<tr>
<td>V V F (cause unknown)</td>
<td>Infections – Mumps, Tuberculosis rarely pyogenic infections</td>
<td>Empty sella syndrome</td>
<td>Weight loss</td>
</tr>
<tr>
<td></td>
<td>Premature ovarian failure</td>
<td>Infiltrative disease</td>
<td>Eating disorders – anorexia and Bulimia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Tumor (including craniopharyngioma, germinoma, endodermal sinus tumor, eosinophilic granuloma, and glioma)</td>
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<td></td>
<td></td>
<td></td>
<td>Radiation</td>
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<td></td>
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<td></td>
<td>Pseudocyesis</td>
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<td></td>
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<td></td>
<td>Infection (TB)</td>
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<td></td>
<td>Infiltrative disease (sarcoidosis)</td>
</tr>
</tbody>
</table>

Besides these some other causes of secondary amenorrhea are
- Pregnancy-M/C cause of secondary amenorrhea
- Hypothyroidism<sup>2</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 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**
- Failure of lactation after delivery (due to ↓ Prolactin)
- Secondary amenorrhoea (↓ LH, ↓ FSH)
- Loss of libido
- Increased sensitivity to cold (hypothyroidism) (↓ TSH)

**Signs**
- Absence of axillary sweating
- Loss of axillary and pubic hair
- Decrease in skin pigmentation
- Anemia due to lack of pituitary erythropoietic factor
- Weakness, lethargy
- Hypothyroidism and hypothermia
- Hypoglycemia (due to decreased insulin tolerance)
- All genital organs show atrophy, uterus is smaller than in postmenopausal women as there is decrease in FSH, LH and estrogen although dormant ovaries retain their ova till menopause.

**Lab Investigation**
Most common is prolactin deficiency along with decreased levels of FSH, LH, TSH, ACTH, oestrogens, and urinary 17-keto steroids.

**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 amenorrhoea for at least 3 months with raised FSH, raised FSH/LH ratio and low E₂ levels in women under 40 years of age.

**Work up for a case of Secondary Amenorrhea**

<table>
<thead>
<tr>
<th>Urine pregnancy test</th>
<th>TSH</th>
<th>Prolactin/Imaging of Sella</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>Increased</td>
<td>Increased</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Hypothyroidism</td>
<td>Pituitary adenoma</td>
</tr>
<tr>
<td>Negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Progesterone challenge test³</td>
</tr>
</tbody>
</table>

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.
Withdrawal bleeding present
(For withdrawal bleeding to occur uterus should be primed with estrogen)

Inference:
- Sufficient estrogen is present i.e.
  - Functional ovary (Compartment II normal)
  - Intact hypothalamic pituitary compartment (compartment III and IV normal)
  - Normal uterus and outflow tract (compartment I normal)
- Defect: Anovulation (like in PCOS)
- LH/FSH estimation (LH >10 mIU/mL or LH:FSH = 3:1)

Proceed to
Estrogen/Progestrone challenge test

Method: 1.25 mg conjugated estrogen or 2 mg estradiol is given daily for 21 days and Medroxy progesterone acetate added for last 5 days.

Withdrawal bleeding absent

Inference:
- Defect in compartment I systems (viz endometrium or outflow tract)

Asherman’s syndrome

Assessment of serum FSH/LH

Normal FSH = 5 – 20 IU/L with ovulatory mid cycle peak about 2 times the base level.
LH = 5 – 20 IU/L with ovulatory midcycle peak about 3 times the base level.

High LH/FSH (LH>40 & FSH > 20)
Hypergonadotropic state
- In postmenopause
- Ovarian failure

Low LH & FSH (both < 5 IU/L)
Hyponadotropic state

Pituitary dysfunction
Hypothalamic dysfunction

To differentiate between the two

GnRH dynamic test

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.

Rise of LH & FSH
Hypothalamic disorder

No Rise of LH & FSH
Pituitary dysfunction

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

- Estrogen withdrawal
- Anovulation Coagulopathies
- Infections
- Complications of pregnancy
- Anovulation
- Polyps and myomas
- Endometrial hyperplasia
- Cervical/endometrial cancer
- Foreign body
- Trauma
- Infection
- Ovarian tumor
- Sarcoma botryoides
- Anovulation
- Hormonal contraception
- Complications of pregnancy
- Infections
- Endocrine disorders
- Polyps and myomas
- Vaginal/endometrial atrophy
- Hormone therapy
- Endometrial cancer

Type of DUB

DUB is of two types:
1. Anovulatory (80%)
2. Ovulatory (20%)

Anovulatory (80%):
- Threshold bleeding of puberty menorrhagia
- Metropathia hemorrhagica\(^6\)/cystic glandular hyperplasia\(^6\)
- Premenopausal DUB (Atrophy of endometrium).

Ovulatory (20%):
- Irregular ripening\(^6\) of corpus luteum
- Irregular shedding\(^6\) of corpus luteum/Halban’s disease
- IUCD insertion
- Following sterilization operation.

Algorithm of Diagnostic Rules in DUB

Management options in different age groups

<table>
<thead>
<tr>
<th>Age group</th>
<th>Investigations</th>
<th>Treatment</th>
</tr>
</thead>
</table>
| I Puberty menorrhagia   | Rule out bleeding disorders by coagulation studies, CBC, platelet count, TSH levels, USG | • Reassurance
<p>|                          |                 | • Psychological support         |
|                         |                 | • Correction of anemia         |
|                         |                 | Non hormonal T/t:              |
|                         |                 | – NSAID’s - mefenamic acid      |
|                         |                 | – Antifibrinolytics - Tranexamic acid |</p>
<table>
<thead>
<tr>
<th>Age group</th>
<th>Investigations</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>progestin therapy</td>
<td>Note: These 2 investigations USG &amp; TSH should be done in all groups.</td>
<td>Puberty menorrhagia (DUB)</td>
</tr>
<tr>
<td></td>
<td>If female has been sexually active.</td>
<td>Acute episode Norethisterone 5 mg TDS</td>
</tr>
<tr>
<td></td>
<td>• During pregnancy test</td>
<td>Maintainence therapy (MPA 10–20 mg/day)</td>
</tr>
<tr>
<td></td>
<td>• Cultures for gonorrhea, Trichomonas, and Chlamydia testing</td>
<td>• Responsive</td>
</tr>
<tr>
<td></td>
<td>Investigation never done in this age group</td>
<td>• Unresponsive</td>
</tr>
<tr>
<td></td>
<td>• P/V examination</td>
<td>Continue MPA for 2–3 cycles from D5-D25</td>
</tr>
<tr>
<td></td>
<td>• Dilatation and curettage</td>
<td>Conjucted estrogen 20–40 mg IV every 6–8 hours</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Responsive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• D &amp; C</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Biopsy</td>
</tr>
</tbody>
</table>

- In patients with von Willebrand’s disease, Desmopressin is the DOC
- In young sexually-active females, Levonorgestrel IUCD-Mirena can also be used.

### II Reproductive age
- (In this age group, it is necessary to rule out pregnancy complications, fibroids, polyps and premalignant conditions like endometrial hyperplasia and CIN)

<table>
<thead>
<tr>
<th>Investigations</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH</td>
<td>Mgt</td>
</tr>
<tr>
<td>USG</td>
<td>1. Antifibrinolytic drugs like tranexamic acid</td>
</tr>
<tr>
<td>UPT</td>
<td>2. Prostaglandin synthetase inhibitor—mefenamic acid</td>
</tr>
<tr>
<td>Endometrial sampling (by dilatation and curettage/hysteroscopy and biopsy)</td>
<td>3. <strong>To stop bleeding:</strong> Norethisterone preparations (5 mg TDS x 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)</td>
</tr>
<tr>
<td>Papsmear</td>
<td>4. <strong>Cyclic Therapy</strong></td>
</tr>
<tr>
<td>Colposcopy</td>
<td>a. <em>In ovular bleeding where patient does not want pregnancy:</em> Any <strong>low dose combined oral pills</strong> 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 hypothalamo-pituitary axis more effectively and has contraceptive benefits also. “Treatment with an estrogen progestin contraceptive is the better choice for those who likely still ovulate or want to avoid pregnancy.” — Leon Speroff 8th/ed p 607</td>
</tr>
<tr>
<td></td>
<td>b. <em>In ovular bleeding, where the patient wants pregnancy or in cases of irregular shedding or irregular ripening of the endometrium:</em> Dydrogesterone 1 tab (10 mg) daily or twice a day from 15th to 25th day may cure the state.</td>
</tr>
<tr>
<td></td>
<td>c. <em>In anovulartony bleeding:</em> Cyclic progestogen prepa ration of <strong>medroxyprogesterone acetate (MPA)</strong> 10 mg or norethisterone 5 mg is used from 5th to 25th day of cycle for 3 cycles.</td>
</tr>
</tbody>
</table>

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Cont'd…
### Continuous progestins Therapy
Continuous progestins also inhibit pituitary gonadotropin secretion and ovarian hormone production. Continuous therapy can be in the form of oral therapy or Mirena.

- **Medroxyprogesterone acetate**: 10 mg thrice daily is given and treatment is usually continued for at least 90 days.
- **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. “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

5. **GnRH agonist** 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.

6. **Danazol**: 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.

7. **Mifepristone (RU 486)**: It is an anti-progesterone (19 norsteroid). It inhibits ovulation and induces amenorrhea and reduces myoma size

### Surgical methods

8. **Dilatation and Curettage** 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.

9. **Endometrial ablation**

   - It is an alternative to hysterectomy in those reproductive age females who donot desire future pregnancy.

10. **Hysterectomy** is generally not required in this age group but in older age group.

### Perimenopausal/ post menopausal age

- **Always rule out cancers first in Perimenopausal age-M/C cause after ruling out cancers is anovulatory**

<table>
<thead>
<tr>
<th>Age group</th>
<th>Investigations</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Never wait and watch Histopathological diagnosis should be made</td>
<td><strong>Continuous progestins Therapy</strong></td>
</tr>
<tr>
<td></td>
<td>• Do hysteroscopy and biopsy along with papsmear and colposcopy.</td>
<td>Continuous progestins also inhibit pituitary</td>
</tr>
<tr>
<td></td>
<td>• Fractional curettage is preferred to blind D and C.</td>
<td>gonadotropin secretion and ovarian hormone</td>
</tr>
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<td></td>
<td></td>
<td>production. Continuous therapy can be in the</td>
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<tr>
<td></td>
<td></td>
<td>form of oral therapy or Mirena.</td>
</tr>
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<td>III Perimenopausal</td>
<td>• Medroxyprogesterone acetate 10 mg thrice daily is given and treatment is</td>
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<tr>
<td>post menopausal</td>
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9. **Endometrial ablation**

   - It is an alternative to hysterectomy in those reproductive age females who donot desire future pregnancy.

10. **Hysterectomy** is generally not required in this age group but in older age group.
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 Asherman’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

Uses of Progesterone in DUB

<table>
<thead>
<tr>
<th>Progesterones – Used</th>
<th>For stopping acute episode of bleeding</th>
<th>For maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Norethisterone</td>
<td>MPA</td>
</tr>
<tr>
<td></td>
<td>Cyclically</td>
<td>Continuously</td>
</tr>
<tr>
<td></td>
<td>If the patient has ovular bleeding</td>
<td>If the patient has anovular bleeding</td>
</tr>
<tr>
<td></td>
<td>Any low dose OCP is given from day 5 to day 25 for 3 consecutive cycles. (It reduces menstrual blood loss by 50% &amp; serves as a contraceptive also). Or If the patient wants pregnancy or in case of irregular shedding or irregular ripening of endometrium. Progesterone dydrogesterone is given from day 15 to day 25.</td>
<td>MPA (10 mg) /norethisterone (5 mg) is given from day 5 to day 25</td>
</tr>
<tr>
<td></td>
<td>MPA is given 10 mg thrice daily for at least 90 days. It suppresses the endometrium &amp;</td>
<td></td>
</tr>
</tbody>
</table>

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 up to 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 up to a depth of 4–5 mm using laser, roller ball, thermal balloon, microwave, is an effective method. Resection of endometrium up to 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**

![Diagram](image)

**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.\(^Q\)
- Some glands are small and some large giving appearance of “swiss cheese”.\(^Q\)
- Glands are empty and lined by columnar epithelium.
- Secretory changes are absent.\(^Q\) (no cork screw glands seen)
- Follicular cysts containing estrogen present on ovaries.

**Signs and Symptoms:** 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).

<table>
<thead>
<tr>
<th>Normal Menstruation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cycle interval</td>
</tr>
<tr>
<td>Menstrual flow</td>
</tr>
<tr>
<td>Menstrual blood loss</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Classification of AUB (FIGO-2011)</th>
<th>Nonstructural systemic causes (COEIN)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structural causes (PALM)</td>
<td></td>
</tr>
<tr>
<td>• Polyp</td>
<td>AUB–P</td>
</tr>
<tr>
<td>• Adenomyosis</td>
<td>AUB–A</td>
</tr>
<tr>
<td>• Leiomyoma</td>
<td>AUB–L</td>
</tr>
<tr>
<td>– Submucosal myoma</td>
<td>AUB–L SM</td>
</tr>
<tr>
<td>– Other myoma</td>
<td>AUB–LO</td>
</tr>
<tr>
<td>• Malignancy and hyperplasia</td>
<td>AUB–M</td>
</tr>
<tr>
<td></td>
<td>Coagulopathy</td>
</tr>
<tr>
<td></td>
<td>Ovulatory dysfunction</td>
</tr>
<tr>
<td></td>
<td>Endometrial</td>
</tr>
<tr>
<td></td>
<td>Iatrogenic</td>
</tr>
<tr>
<td></td>
<td>Not yet identified</td>
</tr>
</tbody>
</table>

### 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.
Chapter 13  Disorders of Menstruation

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:
   a. Non-functioning uterus
   b. Non-functioning ovaries
   c. Normal female karyotype
   d. Normal secondary sexual characteristics

Fig. F1

QUESTIONS

1. 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)
   a. Mayer Rockitansky Kuster Hauser syndrome
   b. Testicular feminization syndrome
   c. Imperforate hymen
   d. Asherman’s syndrome

2. The commonest cause of primary amenorrhea is:
   (AIIMS Nov. 03)
   a. Genital tuberculosis
   b. Ovarian dysgenesis
   c. Mullerian duct anomalies
   d. Hypothyroidism

3. Which is not primary amenorrhea?
   (AI 09/AI 2011/AIIMS May 2010)
   a. Sheehan’s syndrome
   b. Kallmann’s syndrome
   c. Mayer Rokitansky Koster Hauser syndrome
   d. Turner syndrome

4. A woman has 2 kids. She presents with galactorrhoea and amenorrhea for 1 year. The most probable diagnosis is:
   (AIIMS May 02)
   a. Pregnancy
   b. Pituitary tumor
   c. Sheehan’s syndrome
   d. Metastasis to pituitary from other carcinoma

5. Mrs. Sinha having her youngest child of 6 years age presents to her family physician with complaints of pruritis vulvae and amenorrhea. 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:

   a. Cortisol  b. Insulin  c. Ethinyl estradiol  d. Thyroid extract

6. Hypothalamic amenorrhea is seen in:
   (AIIMS Nov. 01)
   a. Asherman syndrome
   b. Stein-leventhal syndrome
   c. Kallmann syndrome
   d. Sheehan’s syndrome

7. Primary amenorrhoea with anosmia is seen in:
   (AIIMS June 00)
   a. Kallmann syndrome
   b. Laurence Moon Biedl syndrome
   c. Foster – Kennedy syndrome
   d. Sheehan’s syndrome

8. A 19-year-old patient complains of primary amenorrhea. She had well developed breast and pubic hair but on examination there was absence of uterus and vagina. Likely diagnosis is:
   (AIIMS Nov 2010)
   a. XYY
   b. Mullerian agenesis
   c. Gonadal dysgenesis
   d. Klinefelter syndrome

9. 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)
   a. Panhypopituitarism
   b. Polycystic ovarian disease
   c. Exogenous estrogen administration
   d. Premature menopause

10. A 30-year-old woman para 2+0, hypertension have menorrhagia. Which is best treatment for her?
    (AIIMS May 2011)
    a. Combined pills  b. Mirena  c. Hysterectomy  d. 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)
   a. Histopathology  b. Hysterectomy  c. Progesterone  d. OCP

12. Raja Devi 45 years old women present with history of poly-menorrhea for last six months. The first line of management is: (AI 02)

13. In a 45 years old lady with DUB for 6 months duration best line of management is: (AIIMS June 00)
   a. Progesterone for 6 months  b. OCP for 6 months  c. Dilation and curettage  d. Hysterectomy

14. Commonest cause of post menopausal bleeding in India is: (AI 07; AIIMS May 07)
   a. Ca endometrium  b. Ca cervix  c. Ca vulva  d. Ovarian tumour


16. Primary Amenorrhea: (PGI Dec 08)
   a. Absence of Menarche by 14 years without secondary sexual characters  
   b. Absence of Menarche by 16 years with secondary sexual characters  
   c. Absence of secondary sexual characters by years

17. Causes of secondary amenorrhea are: (PGI June 01)
   d. Thyroiditis  e. PCOD

18. Lady recovered from severe PPH, complains of failure of lactation and menstruation, which of the following can be seen: (PGI Dec 08)
   a. Increased Excretion of Na+  b. Retention of Water  
   c. Increased Prolactin  d. Increased GnRH  e. Increased TSH

19. A patient with amenorrhea had bleeding after giving a trial of progesterone. This implies: (PGI Dec 01)
   a. Sufficient estrogen  b. Sufficient progesterone  c. Normal ovarian function  
   d. Intact endometrium  e. Intact pituitary axis

20. Positive progesterone challenge test in a patient of secondary amenorrhea, seen in: (PGI June 04)
   a. Asherman Syndrome  b. Endometrial TB  c. Hypopituitarism  
   d. Premature ovarian failure  e. PCOD

21. Withdrawal bleeding with progesterone seen in otherwise amenorrheic woman due to: (PGI Dec. 97)
   a. Hypogonadotrophic hypogonadism  b. Anovulation  
   c. Ovarian failure  d. TB endometritis

22. In a case of secondary amenorrhea who fails to get withdrawal bleeding after taking E and P, the fault lies at the level of: (PGI June 05)

23. Child with primary amenorrhea with negative progesterone challenge test but positive combined progesterone and estrogen test. Diagnosis may be: (PGI June 07)
   a. Mullerian agenesis  b. PCOD  c. Asherman syndrome  d. Prolactinoma

24. Average blood loss in normal menstruation:
   a. 50 mL  b. 80 mL  c. 100 mL  d. 120 mL  e. 10 mL

25. Menorrhagia is defined as blood loss per vagina more than: (AIIMS Nov. 99)
   a. 80 mL  b. 110 mL  c. 150 mL  d. 50 mL

26. Polymenorrhoea Means: (PGI Dec 08)
   a. Menses < 21 days  b. Menses >35 days  c. Painful menses  d. DUB

27. Initial evaluation in adolescent with abnormal uterine bleeding: (PGI June 05)
   a. Haemogram  b. Platelet count  c. USG  d. D & C  e. Examination under anesthesia
28. Most common cause of puberty menorrhagia:  
(PGI June 07)  
a. Anovulation  
b. Malignancy  
c. Endometriosis  
d. Bleeding disorder  
29. Puberty menorrhagia is treated by:  
(PGI June 02)  
a. Progesterone  
b. Progesterone and estrogen  
c. GnRH analogues  
d. Danazol  
e. Surgery  
30. Causes of dysfunctional uterine bleeding can be:  
(PGI Dec. 01)  
a. Uterine polyp  
b. Fibroid  
c. Granulosa cell tumour  
d. Irregular ripening of endometrium  
e. Irregular shedding of endometrium  
31. The most common histological finding of endometrium in DUB is:  
(PGI June 99)  
a. Hypertrophic  
b. Hyperplastic  
c. Cystic glandular hyperplasia  
d. Dysplastic  
32. Treatment of DUB in young female is:  
(PGI 95)  
a. Hormones  
b. Radiotherapy  
c. D & C  
d. Hysterectomy  
33. Treatment for 32 years old multipara with dysfunctional uterine bleeding (DUB) is:  
(PGI Dec 00)  
a. Progesterone  
b. Danazol  
c. Prostaglandins  
d. Endometrial ablation  
e. Hysterectomy  
34. A 45-year-old female presenting with dysmenorrhea and menorrhagia most probably has:  
(PGI Dec 97)  
a. DUB  
b. Endometriosis  
c. Fibroid  
d. Endometrial Ca  
35. All are causes of postmenopausal bleeding except:  
(PGI Dec 00)  
a. Carcinoma in situ of cervix  
b. Ca. endometrium  
c. Ca. ovary  
d. Ca. fallopian tube  
36. Post-menopausal bleeding is associated with all except:  
(PGI Dec 04)  
a. Ca cervix  
b. CIN  
c. Ca ovary  
d. Endometrial Ca  
e. 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)  
a. Assess for H/o HRT  
b. Hysterectomy  
c. PAPs smear  
d. Endometrial biopsy  
e. DUB  
38. Evaluation of a patient with post menopausal bleeding is done by:  
(PGI June 05)  
a. Pap smear  
b. USG  
c. Endometrial biopsy  
d. Dilatation & curettage  
39. Cryptomenorrhoea occurs due to:  
(AI 95)  
a. Imperforate hymen  
b. Asherman’s syndrome  
c. Mullerian agenesis  
d. 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)  
a. Menopause  
b. Pituitary tumor  
c. Sheehan’s syndrome  
d. 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)  
a. Pituitary adenoma  
b. Craniopharyngioma  
c. Sheehan’s syndrome  
d. Pinealoma  
42. In a woman presenting with amenorrhea headache, blurred vision and galactorrhea appropriate investigation:  
(AI 97)  
a. Prolactin levels  
b. LH  
c. FSH  
d. HCG  
43. A middle aged female presents with increasing visual loss, breast enlargement and irregular menses. Investigation of choice would be:  
(AI 97)  
a. S. calcitonin  
b. S. prolactin  
c. S. hemoglobin concentration  
d. S. calcium  
44. Primary amenorrhoea with absent uterus, normal breasts and scanty pubic hair is seen in:  
(AI 2010)  
a. Mayer Rokitansky Kuster hauser Syndrome  
b. Turner Syndrome  
c. Noonan Syndrome  
d. 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)  
a. Ovarian failure  
b. Uterine Synechiae  
c. Pregnancy  
d. Pituitary failure  
46. Lactational amenorrhoea is due to:  
a. Prolactin induced inhibition of GnRH  
b. Prolactin induced inhibition of FSH  
c. Oxytocin induced inhibition of GnRH
47. All of the following conditions are associated with primary amenorrhea except:  
   (AI 97)  
   a. Testicular feminization syndrome  
   b. Stein-Leventhal syndrome  
   c. Turner’s syndrome  
   d. Mayer Rockitansky Kuster Hauser Syndrome

48. The most common cause of secondary amenorrhea in India is:  
   (AI 05)  
   a. Endometrial tuberculosis  
   b. Premature ovarian failure  
   c. Polycystic ovarian syndrome  
   d. Sheehan’s syndrome

49. Evidence based treatment for menorrhagia is all except:  
   (AI 09/AIIMS May 2010)  
   a. OCPS  
   b. Progesterone for three months cyclically  
   c. Tranexamic acid  
   d. 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)  
   a. Blood loss of more than 80 ml  
   b. Cycle duration is more than 35 days or less than 21 days  
   c. Bleeding period lasting 7 days or more  
   d. 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:  
   a. Increased estrogen  
   b. Decreased receptors of progesterone  
   c. Decreased receptors of estrogen  
   d. Pituitary imbalance of hormones

54. Halban’s disease is due to:  
   a. Persistent corpus luteum  
   b. Deficient corpus luteum  
   c. Persistent trophoblast  
   d. 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:  
   a. Normal  
   b. Hyperplastic with Swiss-Cheese pattern  
   c. Nonsecretory  
   d. Atrophic

58. Most common cause of menorrhagia in childbearing period:  
   a. Fibroid  
   b. Dysfunctional uterine bleeding  
   c. Pelvic endometriosis  
   d. Adenomyosis

59. Primary amenorrhoea is most commonly associated with:  
   a. Developmental defect of the genital tract  
   b. Tuberculosis  
   c. Endocrine disorders  
   d. Chromosomal abnormality

60. Dysfunctional uterine bleeding is commonly met in all except:  
   a. Adolescence  
   b. Following childbirth  
   c. Premenopausal period  
   d. Postmenopausal period

61. Withdrawal bleeding following administration of progestogen in a case of secondary amenorrhoea indicates all except:  
   a. Absence of pregnancy  
   b. Production of endogenous estrogen  
   c. Endometrium is responsive to estrogen  
   d. Defect in pituitary gonadal axis

62. The following are the features of anovular menstruation except:  
   a. The only symptom may be failure of conception  
   b. It is usually associated with painless periods  
   c. May be associated with premenstrual syndrome  
   d. May be associated with DUB

63. Anita 15-year-old, complains of heavy periods mmHg. All of the following investigations are indicated, except:  
   a. S. TSH  
   b. Platelet count  
   c. Bleeding and clotting time  
   d. Estradiol levels

64. Period of amenorrhoea followed by massive bleeding is seen in premenopausal women with:  
   a. Irregular ripening  
   b. Irregular shedding  
   c. Metropathia hemorrhagica  
   d. All of the above

65. The investigation of choice in a 55-year-old postmenopausal women who has presented with postmenopausal bleeding is:  
   a. Pap smear  
   b. Fractional curettage  
   c. Transvaginal ultrasound  
   d. 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 15th 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 7th ed p 420; Shaw 15th ed p 284
   • Most common cause of Primary Amenorrhea = Gonadal dysgenesis\textsuperscript{9}/ovarian dysgenesis
   • 2nd most common cause of Primary Amenorrhea = Mullerian agenesis (Mayer Rokitansky Kuster Hauser Syndrome).\textsuperscript{9}
   “Mullerian agenesis is a relatively common cause of primary amenorrhea, more frequent than congenital androgen insensitivity and second only to gonadal dysgenesis.”
   – Leon Speroff 7th ed p 420
   • 3rd most common cause is testicular feminizing syndrome.

3. Ans. is a, i.e. Sheehan’s syndrome
   Ref. Shaw 14th 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 14th ed pp 1104, 1109; Harrison 17th ed pp 2205-2206; Williams Gynae 1st 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.

<table>
<thead>
<tr>
<th>Microadenomas</th>
<th>Macroadenomas</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 cm in diameter\textsuperscript{2}</td>
<td>&gt; 1 cm in diameter\textsuperscript{2}</td>
</tr>
<tr>
<td>Female–male ratio = 20:1\textsuperscript{2}</td>
<td>Female–male ratio = 1:1\textsuperscript{2}</td>
</tr>
<tr>
<td>5% of microadenomas progress to macroadenomas.</td>
<td>Prolactin levels &gt; 100 μg/L</td>
</tr>
<tr>
<td>30% resolve spontaneously</td>
<td></td>
</tr>
</tbody>
</table>

Presentation:
   Women present with:
   • Galactorrhea\textsuperscript{2}  
   • Features of hypogonadism: (as prolactin inhibits GnRH)
   • Amenorrhea\textsuperscript{2} / Oligomenorrhea
   • Delayed puberty, Anovulation
   • Infertility\textsuperscript{2}

   Men present with:
   • Impotence
   • Loss of libido
   • Infertility.

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 hypoestrogenemia 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

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
  - 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 6th 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.

Replacement therapy with appropriate hormones including corticosteroid and thyroid are needed

6. Ans. is a, i.e. Kallmann Syndrome

**Let’s 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)

**Let’s 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).

Also know:

**Kallmann syndrome may be associated with:**
- Optic atrophy
- Color blindness
- Nerve deafness
- Cleft palate
- Renal anomalies
- Cryptorchidism
- Neurologic abnormalities
Males with Kallmann syndrome present with:
- Delayed puberty
- Micropenis
- Anosmia

Females present with:
- Primary amenorrhea
- Failure of secondary sexual development
- Anosmia.

Management: Cyclical estrogen/progesterin therapy or gonadotropins.

Extra Edge:
Other congenital hypothalamic syndromes leading to Amenorrhea are:
- Prader willi syndrome
- Laurence Moon Biedl syndrome
- Septo-optic dysplasia
- Frohlich’s syndrome.

7. Ans. is a, i.e. Kallmann Syndrome

Friends, you know the answer to this question quite well. Here I would like to point out that in solving PGMEE 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:
- Obesitas
- 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

In the question a 19 year old girl is presenting with primary amenorrhea, she has well developed breast and public hair but on examination uterus and vagina are absent. Since her breast and public 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 XXY (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 public hair development, no usable vagina and have no symptoms or signs of cryptomenorrhea because the rudimentary uteri contain no functional endometrium.”

– Leon sperooff 8th/ed p 455

9. Ans. is d, i.e. Premature menopause

- Premature menopause is defined as secondary amenorrhea before 40 years of age, due to ovarian failure. It is clinically defined as secondary amenorrhea for at least 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.
Our answer is further supported by the following lines -
In future, if she desires pregnancy, she may get mirena removed.
Thus, Mirena serves 2 purposes in this female-
1. Controls bleeding
2. 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.”
“Heavy menstrual bleeding that does not 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.”
11. Ans. is a, i.e. Histopathology
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 ≤ 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. It 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 ≥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 9th ed p 629; Jeffcoate 7th 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 will 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 dys synchronous cycles as the cause before hormone therapy is started.”

“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 Shila Balakrishnan 1st 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 Shila Balakrishnan 1st 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 7th 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 6th 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 7th 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 2nd ed p 156-157; Shaw 15th ed p 392; Jeffcoate 7th 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 2nd 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 15th ed pp 1256, 427

In 15/2 two different tables are given on two different pages. I am giving both of them here.

<table>
<thead>
<tr>
<th>Table 35.3, p 1256</th>
<th>Cause</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endometrial atrophy (MC)</td>
<td>60 – 80%</td>
<td>Exogenous estrogens</td>
</tr>
<tr>
<td>Estrogen Replacement therapy</td>
<td>15 – 25%</td>
<td>Atrophic endometritis/vaginitis</td>
</tr>
<tr>
<td>Endometrial Polyps</td>
<td>2 – 12%</td>
<td>Endometrial cancer</td>
</tr>
<tr>
<td>Endometrial hyperplasia</td>
<td>5 – 10%</td>
<td>Endometrial or cervical polyps</td>
</tr>
<tr>
<td>Endometrial cancer</td>
<td>60 – 80% 10%</td>
<td>Endometrial hyperplasia</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 14.16, p 427</th>
<th>Cause</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

15. Ans. is d, i.e. Cypionate acetate

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 8th 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.

**Progestrone** 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 Cypionate 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 cypionate 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 cypionate 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

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 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

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 Gynaec p 365
Important causes of Secondary Amenorrhea (Compartment wise)

**Compartment I**
(Disorders of outflow tract/uterus)
- 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.
- *Asherman’s syndrome*²
  Following excessive curettage or endometrial tuberculosis
- V V F (cause unknown)

**Compartment II**
(Disorders of Ovary)
- Ovary Tumor – masculinizing tumors/
- Trauma – surgical expiration/radiotherapy
- Infections – mumps, tuberculosis rarely pyogenic infections
- Premature ovarian failure

**Compartment III**
(Pituitary)
- Hyperprolactinemia
- Insufficiency as in Simmond’s disease, Sheehan’s syndrome
- Empty sella syndrome
- Infiltrative disease

**Compartment IV**
(Hypothalamus)
- GnRH deficiency
- Vigorous exercise/Excessive stress
- Weight loss
- Eating disorders – anorexia and Bulimia
- Tumor (including craniopharyngioma, germinoma, endodermal sinus tumor, eosinophilic granuloma, and glioma)
- Radiation
- Pseudocyesis
- Infection (TB)
- Infiltrative disease (sarcoidosis)

Besides these some other causes of secondary amenorrhea are:
a. Pregnancy-M/C cause of secondary amenorrhea
b. Hypothyroidism (V.Imp. cause, should be ruled out in every case).
c. Hyperprolactinemia
d. Diabetes
e. Tuberculosis
f. Renal disease/Liver disease
g. Addison’s disease/Cushing’s syndrome/Acromegaly
h. Drugs (phenothiazines, reserpine, antidepressants, OCPs).
i. Malabsorption syndrome
j. 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⁺

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 Gynaec 5/e ed p 447, 6/e ed p 469; Leon Speroff 7/e ed pp 404-409
20. Ans. is e, i.e. PCOD

21. Ans. is b, i.e. Anovulation  
   Ref. Dutta Gynae. 5th ed p 447; Williams Gynae 1st 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 hypothalamic-pituitary 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° amenorrhea is polycystic ovarian disease.

22. Ans. is d, i.e. Endometrium  
   Ref. Dutta Gynae 5th 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

<table>
<thead>
<tr>
<th>Withdrawal bleeding occurs</th>
<th>No withdrawal bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Means endometrium and outflow tract are normal and if provided</td>
<td>Means their is a defect in endometrium</td>
</tr>
<tr>
<td>by normal hormonal levels, results in menstruation.</td>
<td>or outflow tract (As despite normal hormonal sequence no bleeding occurs).</td>
</tr>
<tr>
<td>Defect lies in production of estrogen i.e. either in ovary\hypothalamus</td>
<td></td>
</tr>
</tbody>
</table>

23. Ans. is d, i.e. Prolactinoma
   Ref. Dutta Gynae 6th 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., component I
     system (uterus, endometrium and outflow tract) is normal if properly stimulated by estrogen which rules out nullerian
     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 14th ed p 461; Shaw 15th ed p 283

25. Ans. is a, i.e. 80 mL
   Ref. Shaw 15th ed p 283

26. Ans. is a and d, i.e. Menses <21 days; and DUB
   Shaw 15th ed p 283
   • A normal menstrual cycle lasts from 21 – 35 days, with 2 – 6 days of flow and an average blood loss of 20 to 60 mL.
   • 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.
   Irregularities in Normal Menstrual Cycle:

<table>
<thead>
<tr>
<th>Definitions of Menstrual cycle irregularities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oligomenorrhea</td>
</tr>
<tr>
<td>Polymenorrhea</td>
</tr>
<tr>
<td>Menorrhagia</td>
</tr>
<tr>
<td>Metrorrhagia</td>
</tr>
<tr>
<td>Menometrorrhagia</td>
</tr>
<tr>
<td>Hypomenorrhea</td>
</tr>
<tr>
<td>Intermenstrual bleeding</td>
</tr>
</tbody>
</table>

Note: Polymenorrhea, irregular ripening and irregular shedding of endometrium are forms of ovulatory DUB.

   Dutta Gynae 6th ed p 187

27. Ans. is a, b and c, i.e. Haemogram; Platelet count; and USG
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%ed p 302; Novak 15%ed pp 394-397; Dutta Gynae 6%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:**

![Diagram of Menorrhagia](image)

**Causes of puberty menorrhagia:**
- Most common cause - anovulation
- Indirect most common cause – Bleeding disorders - blood dyscrasias and coagulation disorders.

**Management protocol of puberty menorrhagia**

- **Heavy bleeding continues**

  - Admit for investigation
    - Hb%
    - Peripheral blood film
    - Platelet count
    - Clotting factors study
    - Ultrasonography for any pelvic pathology
    - Thyroid profile in suspected cases
    - Blood transfusion, if required

  - Puberty menorrhagia (DUB)
    - Acute episode Nor ethisterone 5 mg TDS
    - Maintenance therapy (MPA 10–20 mg/day)

  - Responsive
    - Continue MPA for 2–3 cycles from D5–D25
  - Unresponsive
    - Conjugated estrogen 20–40 mg IV every 6–8 hours

  - Responsive
    - Unresponsive
      - Replace therapy with combined oral pills containing 50 μg of estrogen

  - Secondary to
    - Thyroid dysfunction
    - ITP
    - Leukemia
    - Von Willebrand's disease
    - Anatomical disorders
    - Pregnancy complications

**Appropriate therapy**
Remember
- In DUB– Progesterone of choice:
  (i) For acute bleeding–Norethisterone
  (ii) For maintenance purpose–DMPA
- In patients with von Willebrand’s 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 intruterine clots are seen on USG (as the cause of bleeding) to rule out endometrial tuberculosis.” – Novak 15th 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 14th 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 14th ed p 454, 15th ed p 397

30. Ans. is d and e, i.e. Irregular ripening of endometrium; and Irregular shedding of endometrium

Ref. Shaw 15th 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/cystic glandular hyperplasia
- Premenopausal DUB (Atrophy of endometrium).

Ovulatory (20%):
- Irregular ripening of corpus luteum
- Irregular shedding of corpus luteum
- IUCD insertion
- Following sterilization operation.

31. Ans. is b, i.e. Hyperplastic

Endometrial pattern in DUB
- Normal secretory endometrium = 60%
- Hyperplastic endometrium = 30%
- Irregular shedding = 10%
- Atrophic pattern

Since normal secretory endometrium is not given in options so, we will see 2nd most common which is hyperplastic endometrium.

32. Ans. is a, i.e. Hormones

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 α-ethyl 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 15th ed p788; Williams Gynaec 1st 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 does not return future pregnancy -we can do endometrial ablation.

“Heavy menstrual bleeding that does not 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 15th 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 15th ed pp 302-303

Well friends, here we will have to weigh each option one by one.

Option “a”: DUB

• 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.

“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.”

— Jefcoate 7th 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 15th 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 15th ed p 418; Jefcoate 7th ed p 508

35. Ans. is a, i.e. Carcinoma in situ of cervix

36. Ans. is b, i.e. CIN


Postmenopausal bleeding is defined as bleeding which occurs after 12 months amenorrhea in a middle aged women.

Causes of Post Menopausal Bleeding:

- Exogenous estrogen (HRT)
- Vaginitis - tubercular, candida, chlamydia, senile
- Endometrial hyperplasia
- Cervical cancer
- Uterine sarcoma
- DUB - ovolatroy/anovulatory ulcer/Foreign body
- Bleeding from urethra, bladder, rectum which is mistaken for vaginal bleeding.

- Endometritis - tubercular, senile pyometra & hemometra
- Endometrial/cervical polyp
- Endometrial cancer (correct option)
- Ovarian cancer (correct option)
- Fallopian tube carcinoma
- Injuries - direct trauma / Decubitus

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 profuens). 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 10th 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 10th ed pp 577-578; Novak 15th ed p 427, 1256

- Postmenopausal bleeding is more likely to be caused by pathological disease than 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:**

![Abnormal bleeding diagram](image)
39. Ans. is a, i.e. Imperforate hymen  
- 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:

<table>
<thead>
<tr>
<th>Congenital</th>
<th>Acquired</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imperforate hymen (commonest)</td>
<td>Cervical stenosis following:</td>
</tr>
<tr>
<td>Transverse vaginal septum</td>
<td>• Amputation</td>
</tr>
<tr>
<td>Atresia of upper third vagina &amp; cervix</td>
<td>• Cauterization</td>
</tr>
<tr>
<td></td>
<td>• Conization</td>
</tr>
<tr>
<td></td>
<td>• ‘Radium’ treatment for malignant conditions</td>
</tr>
</tbody>
</table>

40. Ans. is c, i.e. Sheehan’s syndrome  
- Pituitary adenoma and craniopharyngioma: Ref. Dutta Gynaec 6th ed p 450; Shaw 15th ed pp 96-97

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 due to spasm in its arterioles occurring at the time of severe hemorrhage or shock, complicating childbirth.

Clinical Features: Symptoms
- Failure of lactation after delivery
- Secondary amenorrhea
- Loss of libido
- Increased sensitivity to cold (hypothyroidism)

Always Remember:

41. Ans. is a, i.e. Pituitary adenoma  
- Ref. Novak 14th ed pp 1104,1109; Harrison 17th ed pp 2205-2206; Williams Gynaec 1st 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 17th 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 17th 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 14th ed p 1104

So, pituitary adenoma is more common than craniopharyngioma and this confirms our answer.

42. Ans. is a, i.e. Prolactin levels  

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)
- TSH (as patients with hypothyroidism have elevated TRH which acts to stimulate the release of prolactin)
- X Ray skull (shows space occupying lesion)
- MRI
- Contrast enhanced CT.
43. Ans. is b, i.e. S. prolactin

A middle aged female is presenting with:
- Increasing visual loss
- Breast enlargement
- Irregular menses
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 ammenorrhoea, galactorrhea, and hyperprolactinemia

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.

45. Ans. is b, i.e. Uterine Synechiae

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
- Incase 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 synechiae (Asherman’s Syndrome). Thus, the most probable diagnosis is uterine synechiae.

Remember
Hyperprolacrtinemia leads to decreased levels of FSH.

46. Ans. is a, i.e. Prolactin induced inhibition of GnRH

- 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 (by inhibiting synthesis of progesterone and by changing testosterone/dihydropyestosterone ratio i.e. increasing local antiestrogen concentrations) to produce lactational amenorrhea and anovulation.

The principle of GnRH suppression by prolactin is reinforced by the demonstration that, treatment of amenorrheic, lactating women with pulsatile GnRH, fully restores pituitary secretion and normal ovarian cyclic activity.

47. Ans. is b, i.e. Stein–Leventhal syndrome

The Stein–Leventhal Syndrome also known as Polycystic Ovarian Disease (PCOD) is an important cause of Secondary Amenorrhea in young women. Testicular Feminizing syndrome, Turner's syndrome and Mayer Rokitansky Kuster Hauser syndrome are causes of Primary amenorrhea.

48. Ans. is a, i.e. Endometrial tuberculosis

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 amenorrhea.

49. Ans. is d, i.e. Ethamsylate

Ref. Williams Gynaec 1st/ed p 187

50. Ans. is b, i.e. Clomiphene

Ref. Dewhurst's textbook of Obst & Gynaec. 7th/ed p 401; Gynaecology by Soutter – Stanton 2nd/ed p 435; Shaw 12th/ed p 242

Medical Management of Menorrhagia:

<table>
<thead>
<tr>
<th>A. Prostaglandin synthetase inhibitor</th>
<th>B. Antifibrinolytic</th>
<th>C. Hormones</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mefenamic Acid</td>
<td>Tranexamic acid</td>
<td>Progestogens</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Estrogen</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OCP’s</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Danazol/Gestrinone (androgen)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>GNRH analogues</td>
</tr>
</tbody>
</table>

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 dysmenorrhea
- **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 Gynaec 1st/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 became the mainstay in the management of DUB in all age groups and practically replaced the isolated use of oestrogens and androgens."

– Dutta Gynaec 5th/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 amenorrhea.

**Gestrinone** can also be used like Danazol.

**Mifepristone:** It is an antiprogestosterone. It inhibits ovulation and induces amenorrhea but is not commonly used for DUB (this drug is not mentioned in Williams Gynaec for management of DUB)

**Gonadotropin Releasing hormone agonists (GnRH agonist):** Its subtherapeutic doses decrease the blood loss whereas therapeutic doses produce amenorrhea.

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 Gynaec. specifically says:
    "Because of its inconsistent efficacy, in United States ethamsylate doesn't have a clinical role the treatment of menorrhagia."

– Williams Gynaec 1st/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.

<table>
<thead>
<tr>
<th>Normal Menstruation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cycle interval</td>
</tr>
<tr>
<td>Menstrual flow</td>
</tr>
<tr>
<td>Menstrual blood loss</td>
</tr>
</tbody>
</table>

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 etiologic 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.

<table>
<thead>
<tr>
<th>Classification of AUB (FIGO-2011)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structural causes (PALM)</td>
</tr>
<tr>
<td>• Polyp</td>
</tr>
<tr>
<td>• Adenomyosis</td>
</tr>
<tr>
<td>• Leiomyoma</td>
</tr>
<tr>
<td>– Submucosal myoma</td>
</tr>
<tr>
<td>– Other myoma</td>
</tr>
<tr>
<td>• Malignancy and hyperplasia</td>
</tr>
</tbody>
</table>

52. Ans. is d, i.e. Intramural fibroid

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.

<table>
<thead>
<tr>
<th>Causes of Ayclical bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>• DUB - usually during adolescence, following childbirth and abortion and preceding menopause</td>
</tr>
<tr>
<td>• Submucous fibroid</td>
</tr>
<tr>
<td>• Uterine polyp</td>
</tr>
<tr>
<td>• Carcinoma cervix and endometrial carcinoma</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Causes of Contact bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Carcinoma cervix</td>
</tr>
<tr>
<td>• Mucous polyp of cervix</td>
</tr>
<tr>
<td>• Vascular ectopy of cervix specially during pregnancy, pill use</td>
</tr>
<tr>
<td>• Infection: chlamydial, tubercular</td>
</tr>
<tr>
<td>• Cervical endometriosis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Causes of Intermenstrual bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Urethral caruncle</td>
</tr>
<tr>
<td>• Ovular bleeding</td>
</tr>
<tr>
<td>• Breakthrough bleeding in pill users</td>
</tr>
<tr>
<td>• IUCD in utero</td>
</tr>
<tr>
<td>• Decubitus ulcer</td>
</tr>
</tbody>
</table>

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

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**  
**Halban’s disease:**
- Rare, self-limiting process.
- Also called irregular shedding.
- It is due to persistent corpus luteum 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. Pregnanediol 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.
  - 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 pregnanediol <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. Progestogen**  
**As discussed in the preceding text metropathica hemorrhagica is a type of anovulatory DUB, hence logically speaking it should be best treated by progestogen 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**  
**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**
- Already explained, see Ans 31 for explanation.

58. **Ans. is b, i.e. Dysfunctional uterine bleeding**

**Common causes of menorrhagia:**
- Dysfunctional uterine bleeding
- Fibroid uterus
- Adenomyosis
- Chronic tubo-ovarian mass

59. **Ans. is d, i.e. Chromosomal abnormality**  
**As discussed earlier:**
- M/C cause of primary amenorrhea is Turner’s 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**  
**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 6th 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 6th 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 6th ed p 188-189  
Discussed in detail in preceding text.

65. **Ans. is b, i.e. Fractional curettage**  
Ref. Dutta Gynae 6th 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.
Endometrial Hyperplasia

It represents a spectrum of morphological and biological alteration of endometrium (both in glands and stroma), ranging from an exaggerated physiological state to carcinoma in situ. They are clinically important because:
- They cause abnormal bleeding.
- Either precede or occur simultaneously with endometrial carcinoma.

Types of Endometrial Hyperplasia

<table>
<thead>
<tr>
<th>Simple</th>
<th>Complex</th>
</tr>
</thead>
</table>
| It results from circumstance in which there is prolonged, increased oestrogen production:  
  i. Follicular cysts of ovary  
  ii. PCOD  
  iii. Granulosa and Theca cell tumours of ovary  
  iv. HRT  
  In perimenopausal age they are associated with glucose intolerance. | Less obviously connected with increased estrogen  
  Mostly, cause is unknown  
  Can be associated with:  
  - PCOD  
  - Glucose Intolerance |

Pathology
- Glands are large, cystic with increased glands/stromal ratio
- Scanty mitosis
- Glands lined by columnar epithelium
- Stroma is sparsely cellular
- Glands number is increased, size is increased and Glands are thrown into folds (over crowding of glands)
- Numerous mitosis
- Glands are lined by stratified squamous epithelium
- Stroma is densely cellular

Chances of Progression to Carcinoma

<table>
<thead>
<tr>
<th>Type of hyperplasia</th>
<th>Progression to cancer</th>
</tr>
</thead>
</table>
| Simple without atypia | 1%  
| Complex without atypia | 3%  
| Simple with atypia | 8%  
| Complex with atypia | 29–30% |

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:
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
Family history
Has Hypertension
O Obesity
L Late menopause/Early menarche
D Diabetes
A Atypical endometrial hyperplasia
U Unopposed estrogen or increased estrogen in body as in : HRT, Fibroid, PCOD and Feminizing ovarian tumours
N Nulliparity
T Therapy: Tamoxifen Therapy and Radiation Therapy
I H/O infertility/menstrual irregularity
S 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 (HNPPC) 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
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:

<table>
<thead>
<tr>
<th>Features</th>
<th>Type I (Endometrioid) (80%)</th>
<th>Type II (Nonendometrioid) (20%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unopposed estrogen</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Menopausal status</td>
<td>Pre-and perimenopausal</td>
<td>Postmenopausal</td>
</tr>
<tr>
<td>Hyperplasia</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Race</td>
<td>White</td>
<td>Black</td>
</tr>
<tr>
<td>Grade</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Myometrial invasion</td>
<td>Minimal</td>
<td>Deep</td>
</tr>
<tr>
<td>Specific subtypes</td>
<td>Endometrioid, Adeno CA grade 1,2</td>
<td>Serous, clear cell, Adeno CA-grade 3</td>
</tr>
<tr>
<td>Behavior</td>
<td>Stable</td>
<td>Aggressive</td>
</tr>
<tr>
<td>Associated gene</td>
<td>pTEN/Kras</td>
<td>p53</td>
</tr>
</tbody>
</table>

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.
% of patients of postmenopausal bleeding with endometrial CA-10%.

M/C cause of postmenopausal bleeding—senile endometritis.
M/C cancer causing of PMB-In India-Ca cervix.

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 (hydrorrhea).
  - 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.
  - 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 their 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).
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 paraaortic 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**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Tumor confined to uterus</td>
</tr>
<tr>
<td></td>
<td>A = only endometrium involved</td>
</tr>
<tr>
<td></td>
<td>B = &lt; 50% of myometrium involved</td>
</tr>
<tr>
<td></td>
<td>C = ≥ 50% of myometrium involved</td>
</tr>
<tr>
<td>II</td>
<td>Tumor involves cervix</td>
</tr>
<tr>
<td></td>
<td>A = Glands involved</td>
</tr>
<tr>
<td></td>
<td>B = Stroma Involved</td>
</tr>
<tr>
<td>III</td>
<td>Local spread</td>
</tr>
<tr>
<td></td>
<td>A = Serosa/adenexa/positive peritoneal cytology</td>
</tr>
<tr>
<td></td>
<td>B = Vaginal metastasis</td>
</tr>
<tr>
<td></td>
<td>C = Pelvic &amp; paraaortic lymph nodes involved</td>
</tr>
<tr>
<td>IV</td>
<td>Metastases</td>
</tr>
<tr>
<td></td>
<td>A = Regional metastasis (Bladder/Bowel, involved)</td>
</tr>
<tr>
<td></td>
<td>B = Distant metastasis including abdominal metastases and inguinal lymph node metastasis</td>
</tr>
</tbody>
</table>

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.
In all gynaecological cancers FIGO staging system is being followed except in cancer vulva where both FIGO and TNM staging can be done.

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.
- Tumor histology:
  - Clear cell carcinoma
  - Papillary serous carcinoma
  - Squamous carcinoma.
- Adenocarcinoma grade III
- More than half of the myometrium involved.
- Tumour extends to isthmus-cervix
- Extraterine disease.
- Tumor size > 2 cms.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>Cancer confined to uterus and anything &lt; 50% of myometrium.</td>
</tr>
<tr>
<td>IB</td>
<td>Cancer confined to uterus but 50% or more of myometrium involved.</td>
</tr>
<tr>
<td>II</td>
<td>Endocervical stroma involved. Note endocervical glandular involvement is non-considered stage I.</td>
</tr>
<tr>
<td>IIIA</td>
<td>Tumor invades serosa or adnexa. Positive cytology has to be reported separately without changing the stage.</td>
</tr>
<tr>
<td>IIIB</td>
<td>Vaginal and/or parametrical involvement</td>
</tr>
<tr>
<td>IIIC1</td>
<td>Metastasis to pelvic lymph node</td>
</tr>
<tr>
<td>IIIC2</td>
<td>Metastasis to Para-aortic lymph node.</td>
</tr>
<tr>
<td>IV</td>
<td>No change</td>
</tr>
</tbody>
</table>

**Spread**
- Most common mode of spread is direct extension.
- 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.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA grade 1 and 2</td>
<td>Surgery = (TAH) + (BSO) + LN dessection (pelvic lymphadenectomy) if Tm size is &gt; 2 cms. (No other postoperative therapy required).</td>
</tr>
<tr>
<td>IA grade III and IB (all grades)</td>
<td>Surgery = TAH + BSO + Pelvic and paraaortic lymphadenectomy followed by radiotherapy (after 4-6 weeks)</td>
</tr>
<tr>
<td>II</td>
<td>Modified radical hysterectomy</td>
</tr>
<tr>
<td>III and stage IV</td>
<td>Debulking surgery followed by chemotherapy and radiotherapy</td>
</tr>
</tbody>
</table>

**Choice of Radiotherapy**

<table>
<thead>
<tr>
<th>Radiation Type</th>
<th>Used in</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaginal Vault Radiation</td>
<td>Grade 3 tumor and Lymph vascular space invasion</td>
</tr>
<tr>
<td>Whole Pelvis External Beam Radiation</td>
<td>Extrapelvic disease including adnexital spread, parametrical involvement and pelvic lymph node metastases, in absence of extrapelvic disease</td>
</tr>
<tr>
<td>Extended field radiation including entire pelvis, common iliac lymph nodes and para aortic lymph nodes</td>
<td>Endometrial cancer with positive para aortic lymph nodes</td>
</tr>
</tbody>
</table>

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 15th ed p 1278

### 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 endometrioid 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**

<table>
<thead>
<tr>
<th>Endometrial Stromal Sarcoma (ESS)</th>
<th>Leiomyosarcoma</th>
<th>Carcinosarcoma (Mixed Mullerian Tumor)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arises from stromal cells</td>
<td>Occurs when fibroid becomes malignant (0.1 – 0.5%) fibroids undergo malignancy</td>
<td>M/c variety</td>
</tr>
<tr>
<td>Least aggressive of the sarcomas</td>
<td>M/c age = 43–53 years</td>
<td>M/c age = 62 years</td>
</tr>
<tr>
<td>M/c age = Perimenopausal and postmenopausal females</td>
<td>Differentiating feature of leiomyosarcomas is &gt; 10 mitosis 10 high power fields.</td>
<td>M/c - post menopausal bleeding</td>
</tr>
<tr>
<td></td>
<td></td>
<td>M/c mode of spread - Blood borne</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Most aggressive sarcomas</td>
</tr>
<tr>
<td></td>
<td>No whorled apperance and no capsule</td>
<td>M/c type of cells seen MMT are spindle cells.</td>
</tr>
</tbody>
</table>

**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.

salpingoopherectomy) 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:

<table>
<thead>
<tr>
<th>Stage</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>Tumor limited to uterus &lt; 5 cm</td>
</tr>
<tr>
<td>IB</td>
<td>Tumor limited to uterus &gt; 5 cm</td>
</tr>
<tr>
<td>IIA</td>
<td>Adnexal involvement</td>
</tr>
<tr>
<td>IIB</td>
<td>Tumor extends to extraterine pelvic tissue</td>
</tr>
<tr>
<td>IIIA</td>
<td>Tumor invades one site of abdominal tissue</td>
</tr>
<tr>
<td>IIIB</td>
<td>Tumor invades more than one site of abdominal tissue</td>
</tr>
<tr>
<td>IIIC</td>
<td>Metastasis to pelvic and/or para-aortic lymph nodes</td>
</tr>
<tr>
<td>IVA</td>
<td>Tumor invades bladder and/or rectum</td>
</tr>
<tr>
<td>IVB</td>
<td>Distant metastasis</td>
</tr>
</tbody>
</table>

### 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.
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:  
   (AI 03, 02)  
   a. Obesity  
   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:  
   (JIPMER 03)  
   a. Adenocarcinoma  
   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:
   a. Para-aortic      b. Presaral
   c. Inferior mesenteric  d. Inguinal
   (AIIMS 97)

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:
   a. Stage IIIA       b. Stage IIIC
   c. III C1           d. Stage IVB
   (AIIMS Nov 2010)

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?
   a. III A           b. III B
   (May 2012)        c. III C1        d. III C2

21. Stage III B endometrial Ca—true is:
   a. Vaginal metastasis
   b. Lymph node metastasis
   c. Bowel involvement
   d. Lung metastasis
   e. Serosa involved
   (PGI June 08, Dec. 06)

22. Stage-IIIB endometrial carcinoma true is/are:
   a. Vaginal metastasis
   (PGI June 09)
   b. Lymph node metastasis (paraaortic)
   c. Pelvic lymph node involvement
   d. Positive peritoneal cytology
   e. Rectal invasion

23. Choice of adjuvant treatment for endometrial carcinoma stage I A grade I is:
   a. Radiotherapy
   b. Chemotherapy
   c. Chemotherapy + Radiotherapy
   d. No treatment
   (AI 04)

24. The following are indications for postoperative radiotherapy in a case of carcinoma endometrium except:
   a. Myometrial invasion of more than half thickness
   b. Positive lymph nodes
   c. Endocervical involvement
   d. Tumor positive for estrogen receptors
   (AIIMS 04, 05)

25. Indication for radiotherapy in carcinoma endometrium include all except:
   a. Pelvic node involvement
   b. Deep myometrial involvement
   c. Enlarged uterine cavity
   d. Poor differentiation
   (AIIMS Nov. 07)

26. Indication of adjuvant radiotherapy in Ca endometrium is/are:
   a. Cervical involvement
   b. Lymph node involvement
   c. Carcinoma in situ
   d. Papillary serous tumor
   e. Estrogen receptor positive

27. Which of the following direct lymph node dissections in endometrial carcinoma?
   a. Penetration into half of myometrium
   b. Clear cell carcinoma
   c. Fundal involvement d. Peritoneal metastasis
   e. 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?
   a. Body habitus
   b. Level of CA–125
   c. Nutritional status
   d. Histologic type of tumor
   (AI 04)

29. Following can cause endometrial cancer: (AP 2008)
   a. Metropathia hemorrhagica
   b. Gynandroblastoma
   c. Dysgerminoma
   d. All of the above

30. A female patient has adenocarcinoma uterus along with sarcoma of uterus. It is known as:
   a. Homologous sarcoma
   b. Sarcoma uterus
   c. Mixed Mullerian carcinogenesis
   d. Heterologous sarcoma

31. All are true regarding sarcoma botryoides except:
   a. Seen in vagina
   b. Grape like clusters are seen
   c. Seen in elderly women
   d. It is an adenocarcinoma
   e. Familial incidence is common
   (PGI 01)

32. True statement regarding sarcoma botryoides:
   a. Involvement of vagina
   b. Grape like growth seen
   c. Common in old age
   d. Malignant
   (PGI May 2010)

33. Primary carcinoma body of the uterus may be of following types except:
   a. Adenocarcinoma
   b. Adenosquamous carcinoma
   c. Clear cell type
   d. Large cell keratinising type

34. The following are precursors of endometrial carcinoma except:
   a. Atypical adenomatous hyperplasia
   b. Atrophic endometrium
   c. Adenocarcinoma in situ
   d. Cystic hyperplasia

NEW PATTERN QUESTIONS
1. Ans. is d, i.e. Complex hyperplasia with atypia
2. Ans. is d, i.e. 28%
3. Ans. is c, i.e. 1% Choice: 

   Ref. Jeffcoate 7th ed p 422-3; Novak 14th ed p 1346; 15th ed p 1252-3; Williams Gynae 1st 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 without 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:

<table>
<thead>
<tr>
<th>Type of hyperplasia</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple without atypia</td>
<td>1%&lt;sup&gt;Q&lt;/sup&gt;</td>
</tr>
<tr>
<td>Complex without atypia</td>
<td>3%&lt;sup&gt;Q&lt;/sup&gt;</td>
</tr>
<tr>
<td>Simple with atypia</td>
<td>8%&lt;sup&gt;Q&lt;/sup&gt;</td>
</tr>
<tr>
<td>Complex with atypia</td>
<td>29–30%&lt;sup&gt;Q&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

   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>Q</sup>

4. Ans. is c, i.e. PCOD

   Ref. Jeffcoate 7th 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

   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 1st 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 7th 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


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:

<table>
<thead>
<tr>
<th>Family</th>
<th>Family history</th>
</tr>
</thead>
<tbody>
<tr>
<td>Has</td>
<td>Hypertension</td>
</tr>
<tr>
<td>O</td>
<td>Obesity</td>
</tr>
<tr>
<td>L</td>
<td>Late menopause/early menarche</td>
</tr>
<tr>
<td>D</td>
<td>Diabetes</td>
</tr>
<tr>
<td>A</td>
<td>Atypical endometrial hyperplasia</td>
</tr>
<tr>
<td>U</td>
<td>Unopposed estrogen or increased estrogen in body as in: HRT, Fibroid, PCOD and Feminizing ovarian tumour</td>
</tr>
<tr>
<td>N</td>
<td>Nulliparity</td>
</tr>
<tr>
<td>T</td>
<td>Therapy: tamoxifen therapy and radiation therapy</td>
</tr>
<tr>
<td>I</td>
<td>H/o infertility/menstrual irregularity</td>
</tr>
</tbody>
</table>

**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


**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 7th ed p 504, Dutta Gynaec 5th 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**  
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\textsuperscript{th} ed p 503-5; Shaw 15\textsuperscript{th} ed pp 417 for option a, 418 for option b, 416 for option c & option d; Novak 14\textsuperscript{th} ed p 1345, 15\textsuperscript{th} 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\textsuperscript{th} ed p 1545, Table 42.3.2; Dutta Gynae 4\textsuperscript{th} ed p 334; Novak 14\textsuperscript{th} ed p 1354; Williams Gynae 1\textsuperscript{st} ed p 969

**Endometrial cancers can be histologically classified as:**

<table>
<thead>
<tr>
<th>Features</th>
<th>Type I (Endometrioid)</th>
<th>Type II (Nonendometrioid)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unopposed estrogen</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Menopausal status</td>
<td>Pre-and perimenopausal</td>
<td>Postmenopausal</td>
</tr>
<tr>
<td>Hyperplasia</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Race</td>
<td>White</td>
<td>Black</td>
</tr>
<tr>
<td>Grade</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Myometrial invasion</td>
<td>Minimal</td>
<td>Deep</td>
</tr>
<tr>
<td>Specific subtypes</td>
<td>Endometrioid</td>
<td>Serous and clear cell</td>
</tr>
<tr>
<td>Behavior</td>
<td>Stable</td>
<td>Aggressive</td>
</tr>
</tbody>
</table>

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.

14. **Ans. is b, i.e. Fractional curettage**  
Ref. Devita cancers-8\textsuperscript{th} ed p 1546; Jeffcoate 7\textsuperscript{th} ed p 509; Novak 14\textsuperscript{th} ed p 1350; 15\textsuperscript{th} ed p 1257-8; Bijoy Sree Sen Gupta 2\textsuperscript{nd} ed p 616-7; Dutta Gynae 5\textsuperscript{th} 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

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)”.

“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\textsuperscript{th} 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.”

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.

<table>
<thead>
<tr>
<th>Remember:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• First investigations in case of endometrial cancer – Endometrial aspiration biopsy.</td>
</tr>
<tr>
<td>• Best investigation for diagnosing endometrial cancer – Hysteroscopy and biopsy.</td>
</tr>
</tbody>
</table>

15. Ans. is b, i.e. Ib

FIGO stating and revised FIGO staging has been given in the preceeding 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

In general inguinal lymph node metastasis are very frequently asked in exams–

<table>
<thead>
<tr>
<th>Remember:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• In ca endometrium–Inguinal LN are involved in stage IV B</td>
</tr>
<tr>
<td>• In ca ovary–Inguinal LN are involved in stage III C</td>
</tr>
<tr>
<td>• In ca cervix–Lymph nodes rarely involved–Inguinal LN</td>
</tr>
<tr>
<td>• In vulva cancer–Sentinel lymph nodes, i.e., first lymph nodes involved are–inguinal lymph node.</td>
</tr>
</tbody>
</table>

17. Ans. is a, b, c and d, i.e. Vaginal metastasis; Para aortic lymph node involvement; Pelvic lymph node involvement; and Peritoneal involvement

Kindly see FIGO staging given in preceeding text.

18. Ans. is c, i.e. Inferior mesenteric

| Lymphatic drainage of uterus: . . . Lymph nodes involved in ca endometrium. . . . BDC Vol II, 3rd 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
The lady in above question has cancer spread to inguinal lymph nodes i.e. stage IVB.

20. Ans. is b, i.e. III B
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
Before answering these questions I want all of you to quickly revise staging of Ca Endometrium.
- Vaginal metastasis means stage IIIB
- 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
As discussed in preceeding 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

<table>
<thead>
<tr>
<th>Indications of adjuvant radiotherapy:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Extauterine extension.</td>
</tr>
<tr>
<td>• Lower uterine or cervical involvement.</td>
</tr>
<tr>
<td>• Papillary serous or clear cell histology.</td>
</tr>
<tr>
<td>• Poor histologic differentiation (Grade III).</td>
</tr>
<tr>
<td>• Myometrial penetration greater than 1/2 of thickening.</td>
</tr>
<tr>
<td>• Pelvic node involvement.</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Indications for lymph node (pelvic and Para-aortic) dissection in endometrial cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Tumour histology:</td>
</tr>
<tr>
<td>• Clear cell carcinoma</td>
</tr>
<tr>
<td>• Papillary serous carcinoma</td>
</tr>
<tr>
<td>• Squamous carcinoma</td>
</tr>
<tr>
<td>2. Adenocarcinoma (endometriod) III.</td>
</tr>
<tr>
<td>3. More than half of myometrial invasion</td>
</tr>
<tr>
<td>4. Isthmus- cervix extension</td>
</tr>
<tr>
<td>5. Extrauterine disease.</td>
</tr>
<tr>
<td>6. Tumor size &gt; 2 cm</td>
</tr>
</tbody>
</table>

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%/ed p 1358
28. Ans. is d, i.e. Histologic type of tumor. Ref. John Hopkins Manual of Obs & Gynae 4\textsuperscript{th}ed p 564; Novak 15\textsuperscript{th}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.”

**Prognostic factors in endometrial adenocarcinoma**
- Most important prognostic factor is lymph node metastasis.\(^O\)
- Age at diagnosis (older the patient poorer the prognosis).\(^O\)
- Stage of the disease.\(^O\)
- Histologic type (endometrioid adenocarcinoma have good prognosis, clear cell carcinoma have poor prognosis).\(^O\)
- Histologic grade.\(^O\)
- Myometrial penetration (Increasing depth of invasion is associated with increasing likelihood of extraperitoneal spread and recurrence).
- Extension to cervix.
- 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.
Role of Peritoneal cytology on prognosis is controversial.

29. Ans. is a, i.e. Metropathia hemorrhagica Ref. Shaw 14\textsuperscript{th}ed p 340, 341, 338; Dutta Gynae 5\textsuperscript{th}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.
- Gynandroblastoma is a virilising tumor which secretes androgens (not estrogens) and so does not lead to endometrial cancer
- Dysgerminoma is a neutral tumor which does not secrete either male or female sex hormones but secretes placental alkaline phosphatase, LDH and BHCG and therefore does not lead to endometrial cancer.

30. Ans. is c, i.e. Mixed Mullerian carcinogenesis

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.\(^O\)
- Most common symptom of uterine sarcoma is bleeding.
- Surgery is main stay of treatment followed by chemotherapy.

Also know:
Heterologous tumors: If sarcomas 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\textsuperscript{th}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\textsuperscript{st}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.”
- “Sarcoma botryoides are usually seen in patients who are younger than 5 years of age.”

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 cyclophasphamide 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**
Microscopically, endometrial carcinoma may be of following varities:
- 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**
**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.
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, shape, and polarity.
- Have altered nucleo-cytoplasmic ratio (N/C ratio is increased).
- Have large, irregular hyperchromatic nuclei with marginal condensation of chromatin material.
- 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.

<table>
<thead>
<tr>
<th>WHO</th>
<th>CIN</th>
<th>Description</th>
<th>Bethesda classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild dysplasia</td>
<td>CIN I</td>
<td>Dysplastic cells seen in lower 1/3 of epithelial lining of cervix</td>
<td>LSIL&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Moderate dysplasia</td>
<td>CIN II</td>
<td>Dysplastic cells seen in 2/3 of epithelial lining of cervix</td>
<td>HSIL&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Severe dysplasia</td>
<td>CIN III</td>
<td>Dysplastic cells seen in more than 2/3 of epithelial lining of cervix</td>
<td>HSIL&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Carcinoma in situ</td>
<td></td>
<td>Dyplastic cells seen full thickness but basement membrane is intact</td>
<td>HSIL&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

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).
> 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.
- No Nuclear atypia.
- Do not transform into malignant cells.
- 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
  - Multiple sex partners
  - Multiparity
  - Poor personal hygiene
  - Poor socioeconomic status
- Smoking *(predisposes to squamous cell CA)*.
- Immunosuppressed individuals
- Women on OCP 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.
Polymerase chain reaction (PCR) or southern blot or hybrid capture technique is used for HPV DNA detection.

**Rate of Progression of CIN**

<table>
<thead>
<tr>
<th>Rate of Progression</th>
<th>CIN I</th>
<th>CIN II</th>
<th>CIN III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regression to normal</td>
<td>60%</td>
<td>40%</td>
<td>30%</td>
</tr>
<tr>
<td>Persistence</td>
<td>30%</td>
<td>35%</td>
<td>50%</td>
</tr>
<tr>
<td>Progression to CIN III</td>
<td>10%</td>
<td>20%</td>
<td>—</td>
</tr>
<tr>
<td>Progression to cancer</td>
<td>&lt;1%</td>
<td>5%</td>
<td>20%</td>
</tr>
</tbody>
</table>

**Epidemiology of CIN**

**Age**

<table>
<thead>
<tr>
<th>CIN</th>
<th>M/c in 20–30 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ca in situ</td>
<td>30–35 years.</td>
</tr>
<tr>
<td>Ca cervix</td>
<td>Bimodal peak</td>
</tr>
<tr>
<td></td>
<td>1st peak seen at 35–39 years.</td>
</tr>
<tr>
<td></td>
<td>2nd peak seen at 55–60 years.</td>
</tr>
</tbody>
</table>

**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.

- 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

Management Strategies of Various Cytological Abnormalities

Depending on the Report of pap smear, which is a cytological report, further investigations are done:

<table>
<thead>
<tr>
<th>Pap smear report</th>
<th>Next step</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal/reactive/infective</td>
<td>Resume pap smear as per ACOG guidelines</td>
</tr>
<tr>
<td>ASCUS</td>
<td>Options are:</td>
</tr>
<tr>
<td></td>
<td>• Repeat pap smear after 6 months</td>
</tr>
<tr>
<td></td>
<td>• If female is ≥30 years, do HPV-DNA testing</td>
</tr>
<tr>
<td></td>
<td>• If pap smear report this time is ≥ASCUS or if HPV-DNA testing is positive—colposcopy is done</td>
</tr>
<tr>
<td></td>
<td>• Best method of following ASCUS is immediate colposcopy (biopsy)</td>
</tr>
<tr>
<td>LSIL</td>
<td>• Colposcopy (Gold standard) ± endocervical curettage</td>
</tr>
<tr>
<td></td>
<td>• If lesion is visible—punch biopsy</td>
</tr>
</tbody>
</table>

Contd...
Pap smear report

<table>
<thead>
<tr>
<th>Pap smear report</th>
<th>Next step</th>
</tr>
</thead>
<tbody>
<tr>
<td>HSIL</td>
<td>• Colposcopy (Gold standard) ± endocervical curettage • If lesion is visible—punch biopsy</td>
</tr>
</tbody>
</table>

Definitive Diagnostic Procedures for CIN

<table>
<thead>
<tr>
<th>Colposcopy</th>
<th>Cone biopsy</th>
<th>Punch biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Done to confirm findings of abnormal pap smear when lesion is not visible.</td>
<td>Done to confirm findings of colposcopy if there is a discrepancy in pap smear result and colposcopy.</td>
<td>Done to confirm findings of abnormal pap’s when lesion is visible.</td>
</tr>
</tbody>
</table>

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
- To obtain directed biopsies
- Conservative therapy under colposcopy guidance
- For follow up of cases treated conservatively

... *Shaw 14th ed p 362*
Absolut 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 spaghetti like configuration. (They suggest early stromal invasion).

**Result** - Colposcopy report is a histopathology report

![Colposcopy](image)

**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.

![Cone biopsy](image)

**Indications of Cone biopsy**

<table>
<thead>
<tr>
<th>Diagnostic</th>
<th>Therapeutic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Limits of the lesion can not be visualised with colposcopy</td>
<td>Cancer in situ in young females</td>
</tr>
<tr>
<td>The squamocolumnar junction is not seen at colposcopy</td>
<td>Cancer cervix Stage 1A1 in young females</td>
</tr>
<tr>
<td>Endocervical curettage is positive in HSIL</td>
<td></td>
</tr>
<tr>
<td>Microinvasive carcinoma or adenocarcinoma in situ is suspected based on biopsy, colposcopy or cytology results</td>
<td></td>
</tr>
<tr>
<td>Lack of correlation between cytology, biopsy and colposcopy results</td>
<td></td>
</tr>
</tbody>
</table>

Cone biopsy can lead to incompetent os and subsequent recurrent second trimester abortions.
Complications of Cone Biopsy

- Bleeding\(^\text{Q}\) (M/C complication)
- Infection\(^\text{Q}\)
- Cervical stenosis\(^\text{Q}\)
- Incompetent os\(^\text{Q}\)

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 HPV) as one of the three vaccines for preventive HPV.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Bivalent (2V HPV)</th>
<th>Quadrivalent (4V HPV)</th>
<th>9 Valent (9V HPV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brand name</td>
<td>Cervarix</td>
<td>Gardasil</td>
<td>Gardasil-9</td>
</tr>
<tr>
<td>HPV subtypes</td>
<td>16, 18</td>
<td>6, 11, 16, 18</td>
<td>6, 11, 16, 18, 31, 33, 45, 52, 58</td>
</tr>
<tr>
<td>Protects against</td>
<td>CIN, Ca cervix</td>
<td>Anogenital warts, CIN, Ca cervix</td>
<td>Anogenital warts CIN, Ca cervix, vulva intraepithelial neoplasia, vaginal intraepithelial neoplasia</td>
</tr>
<tr>
<td>Manufacturer</td>
<td>GlaxoSmithKline</td>
<td>Merck &amp; Co</td>
<td>Merck &amp; Co</td>
</tr>
<tr>
<td>Manufacturing</td>
<td>Trichoplusia insect line infected with L1 encoding baculovirus</td>
<td>Saccharomyces cerevisiae expressing L1</td>
<td>Saccharomyces cerevisiae expressing L1</td>
</tr>
<tr>
<td>Adjuvant</td>
<td>500 mcg aluminium hydroxide with monophosphoryl</td>
<td>225 mcg Al(OH)(\text{PO}_4)</td>
<td>500 mcg Al(OH)(\text{PO}_4)</td>
</tr>
<tr>
<td>Dose</td>
<td>0.5 ml</td>
<td>0.5 ml</td>
<td>0.5 ml</td>
</tr>
<tr>
<td>Administration</td>
<td>1/m</td>
<td>1/m</td>
<td>1/m</td>
</tr>
<tr>
<td>Administered to</td>
<td>Only females</td>
<td>Both males and females</td>
<td>Both males and females</td>
</tr>
<tr>
<td>males or females</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age in females Ideal age range</td>
<td>11-12 years</td>
<td>11-12 years</td>
<td>11-12 years</td>
</tr>
<tr>
<td></td>
<td>9-26 years</td>
<td>9-26 years</td>
<td>9-26 years</td>
</tr>
<tr>
<td>Age in males Ideal age range</td>
<td>x</td>
<td>11-12 years</td>
<td>11-12 years</td>
</tr>
<tr>
<td></td>
<td>9-26 years</td>
<td>9-15 years—FDA approved</td>
<td>9-26 years—ACIP recommendation</td>
</tr>
</tbody>
</table>

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%.
Chapter 14B  Gynecological Oncology: CIN Cancer Cervix

Criteria for employing ablative methods for treating CIN:
- Entire lesion should be visualised within the transformation zone (TZ)
- No evidence of microinvasion or macroinvasion.
- No endocervical glandular involvement
- No discrepancy in cytology, colposcopy and biopsy report.

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.

Definitive Treatment

Options

<table>
<thead>
<tr>
<th>Ablative methods</th>
<th>Surgical Excisional methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cryosurgery</td>
<td>Large loop excision of transformation zone (LLETZ) or loop electroexcisional procedure (LEEP)</td>
</tr>
<tr>
<td>Laser ablation or vaporization</td>
<td>Conization</td>
</tr>
<tr>
<td></td>
<td>Hysterectomy</td>
</tr>
</tbody>
</table>

Aim: To destroy the entire transformation zone of the cervix (upto a depth of 6–8 mm from the surface).

Major disadvantage is follow up with histopathological examination, is not possible after the procedure as SCJ recedes into the endocervix.

Comparison of Ablative Techniques for Managing CIN

Ablative techniques for CIN management

<table>
<thead>
<tr>
<th>Cryotherapy</th>
<th>CO₂ Laser</th>
</tr>
</thead>
<tbody>
<tr>
<td>Destroys the surface epithelium of cervix by crystallising intracellular water.</td>
<td>Best method to treat CIN I/II if it extends to vaginal fornices.</td>
</tr>
<tr>
<td>Aim should be to produce an ice ball that extends 5-10 mm beyond the margin of lesion.</td>
<td></td>
</tr>
<tr>
<td>Temp = −22°C Agent used = N₂O or CO₂</td>
<td>Depth of destruction = 7 mm.</td>
</tr>
<tr>
<td>Depth of destruction = 5 mm. (Method = freeze – thaw – freeze = 3 min- 5 min- 3 min).</td>
<td></td>
</tr>
<tr>
<td>Aim should be produced.</td>
<td></td>
</tr>
<tr>
<td>Can be used only if, lesion is on ectocervix. (Not on endocervix.)</td>
<td>Major advantage: It can be used if vaginal extension of CIN is present.</td>
</tr>
<tr>
<td>No evidence of microinvasive/invasive cancer.</td>
<td>No evidence of microinvasive invasive cancer.</td>
</tr>
<tr>
<td>Vagina is not involved.</td>
<td></td>
</tr>
<tr>
<td>Postoperative complication M/C vaginal discharge cervical stenosis or cervical dystocia (uncommon)</td>
<td>No vaginal discharge</td>
</tr>
</tbody>
</table>

Fig. 14B.3: Cryosurgery probe
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 up to 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.

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 lessons 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 Gynaec. p 541)
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.
### Histology

<table>
<thead>
<tr>
<th>Squamous cell carcinoma (Epidermoid carcinoma)</th>
<th>Adenocarcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Accounts for 80% of carcinoma cervix²</td>
<td>• Accounts for 20% of carcinoma cervix²</td>
</tr>
<tr>
<td>• Arises from squamocolumnar junction²</td>
<td>• Arises from endocervix²</td>
</tr>
<tr>
<td>• Squamous cell carcinoma can be further classified as:</td>
<td>• M/C in young females</td>
</tr>
<tr>
<td>Large cell Keratinizing type (M/C)</td>
<td>• Recently increased in incidence because of use of OCP, Progesterone pills for long time.</td>
</tr>
<tr>
<td>Large cell non Keratinizing type</td>
<td>• 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.</td>
</tr>
<tr>
<td>Small cell Worst prognosis</td>
<td></td>
</tr>
<tr>
<td>Ca Verrucous Ca associated with HPV-6²</td>
<td></td>
</tr>
<tr>
<td>Slow growing, locally invasive neoplasm.³</td>
<td></td>
</tr>
<tr>
<td>Radical resection is the mainstay of therapy. It resembles condyloma acuminata.</td>
<td></td>
</tr>
</tbody>
</table>

#### 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. The odour is caused by infection of necrotic tissue with saprophytes.

**Symptoms of Advanced Stage**

- Deep pelvic pain² 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:
  - Hardness²
  - Friability²
  - Fixation²
  - Bleeds on touch²

**Complications**

Mnemonic: Private FUND

---

² M/C cause of death in patients of Ca cervix is renal failure.
³ IInd M/C common cause of death is haemorrhage.

... Jeffcoates 7th ed p 472
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 does not change the stage of cancer.

- **Lymphatic spread**: The lymph nodes involved in cancer cervix are:

<table>
<thead>
<tr>
<th>Primary group</th>
<th>Secondary group</th>
</tr>
</thead>
<tbody>
<tr>
<td>H = Hypogastric</td>
<td>Common iliac</td>
</tr>
<tr>
<td>O = Obturator</td>
<td>Para aortic</td>
</tr>
<tr>
<td>P = Presacral and parametrial</td>
<td>Inguinal</td>
</tr>
<tr>
<td>E = External iliac</td>
<td></td>
</tr>
</tbody>
</table>

- **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.

<table>
<thead>
<tr>
<th>Physical examination</th>
<th>Radiological studies</th>
<th>Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palpate lymph node</td>
<td>Chest X-ray</td>
<td>Biopsy</td>
</tr>
<tr>
<td>Examine vagina</td>
<td>Skeletal X Ray</td>
<td>Conisation</td>
</tr>
<tr>
<td>Bimanual rectovaginal examination</td>
<td>IVP</td>
<td>Endocervical Curettage</td>
</tr>
<tr>
<td></td>
<td>Barium enema</td>
<td>Colposcopy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hysteroscopy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cystoscopy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Proctoscopy</td>
</tr>
</tbody>
</table>

**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
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

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>No change</td>
</tr>
<tr>
<td>IIA</td>
<td>Without parametrial involvement is further divided into-</td>
</tr>
<tr>
<td></td>
<td>A1 Tumor size &lt; 4 cms size</td>
</tr>
<tr>
<td></td>
<td>A2 Tumor size ≥ 4 cms size</td>
</tr>
<tr>
<td>IIB</td>
<td>No change</td>
</tr>
<tr>
<td>III/IV</td>
<td>No Change.</td>
</tr>
</tbody>
</table>

**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 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
   - ERBT 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:

<table>
<thead>
<tr>
<th>Location</th>
<th>Point A</th>
<th>Point B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location</td>
<td>2 cm above and 2 cm lateral to external os</td>
<td>2 cm above and 5 cm lateral to external os</td>
</tr>
<tr>
<td>Structure present</td>
<td>Paracervical/parametrical lymph node</td>
<td>Obturator lymph node</td>
</tr>
<tr>
<td>Dose of radiation</td>
<td>8000 cGy or 80 Gy</td>
<td>6000 cGy or 60 Gy</td>
</tr>
</tbody>
</table>

- ABS criteria (American Brachytherapy Society):
  - Point A: Early stage - Dose 80-85 Gy
    - Locally advanced - stage (≥ 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.
### Stagewise Management of Ca Cervix

<table>
<thead>
<tr>
<th>Stage</th>
<th>Management</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage IA1</td>
<td><strong>No lymphovascular space invasion</strong>&lt;br&gt;Young female - conization&lt;br&gt;Older female - simple hysterectomy with bilateral salpingo-oophorectomy&lt;br&gt;&lt;b&gt;In case of LVSI&lt;/b&gt;&lt;br&gt;Young females - Radical Trachelectomy and pelvic lymphadenectomy&lt;br&gt;Older females - Simple or Wertheim’s hysterectomy with pelvic lymphadenectomy</td>
<td>Pelvic lymphadenectomy is not needed as &lt;1% chances of pelvic node metastasis&lt;br&gt;No postoperative management</td>
</tr>
<tr>
<td>Stage IA2</td>
<td><strong>Family not complete</strong>&lt;br&gt;Radical trachelectomy and pelvic lymphadenectomy&lt;br&gt;&lt;b&gt;Family complete&lt;/b&gt;&lt;br&gt;Wertheim’s hysterectomy (Type II) with pelvic lymphadenectomy</td>
<td>Incidence of nodal metastasis—3 to 8%&lt;br&gt;Postoperative management given if intermediate or high-risk factors present</td>
</tr>
<tr>
<td>Stage IB1</td>
<td><strong>Family not complete</strong>&lt;br&gt;If size of tumor &lt; 2 cms, radical trachelectomy, pelvic lymphadenectomy and para aortic LN sampling&lt;br&gt;&lt;b&gt;Family complete&lt;/b&gt;&lt;br&gt;Wertheim’s hysterectomy (Type II) with pelvic and para aortic lymphadenectomy</td>
<td>Postoperative management given if intermediate or high-risk factors present</td>
</tr>
<tr>
<td>Stage IB2 and IIA</td>
<td><strong>Both options</strong>&lt;br&gt;• Primary chemoradiation (better)&lt;br&gt;• Surgery: Type III radical hysterectomy, pelvic lymphadenectomy and para aortic lymphadenectomy</td>
<td>Postoperative management given</td>
</tr>
<tr>
<td>Stage IIB-IIIB</td>
<td>Chemoradiation</td>
<td>Cisplatin used as radiosensitizer</td>
</tr>
<tr>
<td>Stage IV</td>
<td>CT and palliative pelvic radiation therapy</td>
<td></td>
</tr>
</tbody>
</table>

**Post Operative Management of Cancer Cervix**

Once surgery is performed in cancer cervix, patient is reassessed for the presence or absence of risk factors:

<table>
<thead>
<tr>
<th>Intermediate Risk factors</th>
<th>High Risk Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Large tumor size</td>
<td>• Positive or close margins</td>
</tr>
<tr>
<td>• Cervical stromal invasion to middle or deep one third (&gt; 1 cms)</td>
<td>• Positive lymph nodes</td>
</tr>
<tr>
<td>• Lymph vascular space invasion</td>
<td>• Microscopic parametrial involvement</td>
</tr>
</tbody>
</table>
Comparison Between Surgery and Radiotherapy for Management of Cancer Cervix

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Radiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survival</td>
<td>85%</td>
</tr>
<tr>
<td>Serious complications</td>
<td>Urological fistulas 1-2%</td>
</tr>
<tr>
<td></td>
<td>Intestinal and urinary strictures and fistulas 1.4–5.3%</td>
</tr>
<tr>
<td>Vagina</td>
<td>Initially shortened but may lengthen with regular intercourse</td>
</tr>
<tr>
<td></td>
<td>Fibrosis and possible stenosis, particularly in postmenopausal patients</td>
</tr>
<tr>
<td>Ovaries</td>
<td>Can be conserved</td>
</tr>
<tr>
<td></td>
<td>Destroyed</td>
</tr>
<tr>
<td>Chronic effects</td>
<td>Bladder atony in 3%</td>
</tr>
<tr>
<td></td>
<td>Radiation fibrosis of bowel and bladder in 6–8%</td>
</tr>
<tr>
<td>Surgical mortality</td>
<td>1%</td>
</tr>
<tr>
<td></td>
<td>1% (from pulmonary embolism during intracavitatory therapy)</td>
</tr>
</tbody>
</table>

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.

**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.
8. Pap smear of Lelawati 45 years female shows CIN grade III. Which of the following is the next step in management:
   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:
   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:
    a. Parametrial invasion
    b. Abnormal pap smear
    c. Endometrial Ca
    d. Endocervical curettage positive
    e. Clear cell Ca

11. Therapeutic conisation is indicated in:
    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:
    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:
    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:
    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:
    a. Hysterectomy
    b. Laser coagulation
    c. Cryoablation
    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:
    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 outpatient 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 presents 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. Microinvasive 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)
   a. Common at squamocolumnar junction
   b. CT scan is mandatory for staging
   c. Post coital bleeding is a common symptom
   d. 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)
   a. Obturator LN  b. External iliac LN
   c. Inguinal LN   d. Femoral LN  e. Hypogastric LN

42. LN involved in cervical cancer: (PGI Dec. 05)
   a. Inguinal LN  b. Obturator LN
   c. Hypogastric LN  d. External Iliac LN
   e. Femoral LN

43. Best treatment of carcinoma in situ of cervix: (PGI 98)
   a. Simple hysterectomy
   b. Conization
   c. Laser
   d. Cryosurgery
   e. All

44. A 42-year-old female P3 + 0 + 0 + 3 is found to have carcinoma in situ. Best treatment would be: (AI 97)
   a. Hysterectomy
   b. Wertheim’s hysterectomy
   c. Conisation
   d. Wait and watch

45. In microinvasive cervical cancer, most common treatment is: (PGI 97)
   a. Conization
   b. Laser
   c. Simple hysterectomy
   d. Radical hysterectomy

46. False statement about treatment of Ca cervix: (PGI June 05)
   a. Radiotherapy is helpful in all stages
   b. Prognosis of surgery good if done in early stages
   c. When radiotherapy is given, para-aortic LN should be included
   d. Chemotherapy is reserved for late stages
   e. 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)
   a. Chemotherapy
   b. Radiotherapy
   c. Chemoradiation
   d. Follow-up

48. Treatment of Ca cervix stage IB includes: (PGI Nov 10)
   a. Surgery
   b. Chemotherapy
   c. Radiotherapy
   d. Cryotherapy
   e. Leep

49. Treatment of stage Ila cervical cancer includes: (PGI Nov 12)
   a. Radical hysterectomy
   b. Radical hysterectomy with pelvic lymph node dissection
   c. Total abdominal hysterectomy with B/L salpingo oopherectomy
   d. Chemoradiation

50. Treatment of stage III B carcinoma cervix is: (AIIMS Nov 2010/AIIMS May 2012 Nov 2012)
   a. Wertheim procedure
   b. Schauta’s procedure
   c. Chemotherapy
   d. Intracavitary brachytherapy followed by external beam RT

51. True statement regarding Ca cervix involving parametrium but not pelvic involvement: (PGI May 2010)
   a. Stage II A
   b. Stage II B
   c. Radiotherapy should be given
   d. Hysterectomy can be useful
   e. Staging should be done after cystoscopy

52. Cervical cone biopsy in a case of carcinoma cervix causes all, except: (AIIMS May 94)
   a. Bleeding
   b. Cervical stenosis
   c. Infection
   d. 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)
   a. Surgery plus chemotherapy
   b. Radiotherapy plus chemotherapy
   c. Chemotherapy
   d. Radiotherapy plus HPV vaccine

54. All are signs of inoperabilty of carcinoma of cervix except:
   a. Cervix of cervix and parametrum to lateral pelvic wall
   b. Presence of extrapelvic metastasis
   c. Involvement of bladder
   d. 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:
   a. Uteroseval and uterovesical ligament
   b. Pelvic LN
   c. Both ovaries
   d. Upper third of vagina

56. Point B in the treatment of carcinoma cervix receives the dose of:
   a. 7000 cGy
   b. 6000 cGy
   c. 5000 cGy
   d. 10,000 cGy

57. HPV triage strategy includes all except:
   a. Conventional pap smear
   b. Liquid based cytology
   c. Hybrid capture 2 for HPV DNA
   d. Colposcopy

58. M/C site of metastasis of Ca cervix is:
   a. Lymph node
   b. Lungs
   c. Bone
   d. 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
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 15th ed p 400; Novak 14th 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 Chalmydia 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.”

Ref. Novak 14th ed p 1404

2. Ans. is d, i.e. 5%

Rate of progression of CIN

<table>
<thead>
<tr>
<th></th>
<th>CIN I</th>
<th>CIN II</th>
<th>CIN III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regression to Normal</td>
<td>60%</td>
<td>40%</td>
<td>30%</td>
</tr>
<tr>
<td>Persistence</td>
<td>30%</td>
<td>35%</td>
<td>50%</td>
</tr>
<tr>
<td>Progression to CIN III</td>
<td>10%</td>
<td>20%</td>
<td></td>
</tr>
<tr>
<td>Progression to cancer</td>
<td>&lt; 1%</td>
<td>5%</td>
<td>20%</td>
</tr>
</tbody>
</table>

Ref. CGDT 10th ed p 840, Table 50.2

3. Ans. is a, i.e. Breaking of basement membrane

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, shape and polarity.
- Have altered nucleo-cytoplasmic ratio (N/C ratio is increased).
- Have large, irregular hyperchromatic nuclei with marginal condensation of chromatin material.
- 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.

Ref. Robbin’s 7th ed p 1076, Shaw 15th ed p 400

<table>
<thead>
<tr>
<th>Classification system</th>
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<tbody>
<tr>
<td>WHO</td>
</tr>
<tr>
<td>Mild dysplasia</td>
</tr>
<tr>
<td>Moderate dysplasia</td>
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<tr>
<td>Severe dysplasia</td>
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</tbody>
</table>

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

In Bethesda system:
LSIL = CIN 1
HSIL = CIN 2, CIN 3/Ca in situ

Ref. Shaw 15th ed p 400

5. Ans. is a, i.e. gonorrhea

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 trichomoniases 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.

Ref. Novak 15th ed p = ?
6A. Ans. is c, i.e. Cervical polyp  
Ref. Novak 14th/ed p 576

6B. Ans. is a, i.e. Condyloma  
Ref. Novak 14th/ed p 576

6C. Ans. is a, i.e. Upper 2/3rd endocervix  
Ref. Novak 14th/ed p 576

6D. Ans. is a and c, i.e. Suspicious pap smear; and Suspected invasive carcinoma  
Ref. Shaw 15th/ed p 403; CGDT 10th/ed p 837; Williams Gynae 1st/ed p 630

See the preceding text for explanation.

7. Ans. is c, i.e. conization  

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 visualize upper part of endocervix.

8. Ans. is c, i.e. Colposcopy directed biopsy  
Ref. CGDT10th/ed p 837, 841; Harrison 17th/ed p 608; Williams Gynecology 1st/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  

Cone biopsy or conization is both diagnostic as well as therapeutic procedure

<table>
<thead>
<tr>
<th>Indications of Cone biopsy</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diagnostic</strong></td>
<td><strong>Therapeutic</strong></td>
</tr>
<tr>
<td>- Limits of the lesion cannot be visualised with colposcopy.</td>
<td>- Ca in situ in young females</td>
</tr>
<tr>
<td>- The squamocolumnar junction is not seen at colposcopy</td>
<td>- Cancer cervix stage 1A1 in young females (microinvasive cancer)</td>
</tr>
<tr>
<td>- In endocervical curettage histological findings are positive for CIN - II or CIN - III, CA in situ</td>
<td></td>
</tr>
<tr>
<td>- Micro Invasive carcinoma or adenocarcinoma in situ is suspected based on biopsy, colposcopy or cytology results</td>
<td></td>
</tr>
<tr>
<td>- Lack of correlation between cytology, biopsy &amp; colposcopy results.</td>
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</table>

Complications of cone biopsy

- Bleeding  (M/C complication)
- Infection
- Cervical stenosis
- Incompetent os

12. Ans. is b, i.e. Colposcopy  
Ref. Jeffcoate 7th/ed p 410-1; Dutta Gynae. 4th/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 be 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 7th/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 at least 12 weeks postpartum.
- Management:
  - Thermal cauterization
  - Cryosurgery
  - Laser vaporisation

**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/e p 837, 841 fig. 50-6; Williams Gynaec 1/e 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 Lugol’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.  
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 may be the case with adenocarcinoma, — cervical conisation may be necessary.

15. **Ans. is a, i.e. Hysterectomy**  
*Ref. Shaw 15/e p 405; Jeffcoate 7/e p 421; Novak 14/e 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/e p 635; Novak 14/e p 582, 583; Devita 8/e 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/e 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/e 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/e p 582.*  
“LEEP is now considered the preferred treatment for non invasive squamous lesions”  
*Devita 8/e p 1506.1*  
So our answer is Colpscopy 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 lets 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/e 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 CO2 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 8th 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 the 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

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

21. Ans. is a, i.e. Colposcopy biopsy

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:

Post coital bleeding / irregular bleeding/ Abnormal cervical cytology smear, i.e. abnormal pap smear. Do perspeculum examination

If lesion is visible

Punch Biopsy

Colposcopy and biopsy and endo cervical curetage

If Negative, go for colposcopy and directed biopsies

Still no diagnosis can be established

Cone

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.

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
  - Multiple sex partners
  - Multiparity
  - Poor personal hygiene
  - Poor socioeconomic status
- Smoking
- Immunosuppressed individuals
- Women on OCP, 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
31. Ans. is a, and b, i.e. Type 16; and Type 18
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 15th ed p 400; Novak 14th ed p 564; Williams Gynae 1st 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
   “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, strainning at stool or trauma.”... Jeffcoate 7th ed p 471
“[For those with symptoms, however, early stage cervical cancer may create a watery, blood tinged vaginal discharge. Intermittent vaginal bleeding that follows coitus or douching may also be noted.]”... Williams Gynae. 1st 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 8th 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
         • Ca cervix has bimodal peak - first at 35-39 years and second at 60-64 years.
35. Ans. is b, i.e. Uremia
   Ref. Jeffcoate 7th 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
Staging Procedures in Ca cervix (As recommended by FIGO).

<table>
<thead>
<tr>
<th>Physical examination</th>
<th>Radiological studies</th>
<th>Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palpate lymph node</td>
<td>Chest X-ray</td>
<td>Biopsy</td>
</tr>
<tr>
<td>Examine vagina</td>
<td>Skeletal X Ray</td>
<td>Conisation</td>
</tr>
<tr>
<td>Bimanual recto vaginal examination</td>
<td>IVP</td>
<td>Endocervical Curettage</td>
</tr>
<tr>
<td></td>
<td>Barium enema</td>
<td>Colposcopy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hysteroscopy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cystoscopy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Proctoscopy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mnemonic: BS, C Exam</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B = Biopsy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C = Conization</td>
</tr>
<tr>
<td></td>
<td></td>
<td>S = 4 types of scope’s Exam</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Endocervical curettage</td>
</tr>
</tbody>
</table>

Note: USG, CECT, MRI, PET, Laparoscopy, 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
   As discussed in the staging given in preceeding 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 > 5mm and size of lesions 4 cms.

   Read the text for explanation.

40. Ans. is b, i.e. CT scan is mandatory for staging

   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.

<table>
<thead>
<tr>
<th>Squamous cell carcinoma (Epidermoid carcinoma)</th>
<th>Adenocarcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accounts for 80% of carcinoma cervix*</td>
<td>Accounts for 20% of carcinoma cervix*</td>
</tr>
<tr>
<td>Arises from squamocolumnar junction*</td>
<td>Arises from Endocervix*</td>
</tr>
</tbody>
</table>

   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.

   As 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

   “Carcinoma in situ (stage 0) can be managed successfully by cone biopsy or by abdominal hysterectomy.”

43. Ans. is a and b, i.e. Simple hysterectomy; and Conization

44. Ans. is a, i.e. Hysterectomy

   “Carcinoma in situ (stage 0) can be managed successfully by cone biopsy or by abdominal hysterectomy.”

45. Ans. is c, i.e. Simple hysterectomy

   A micro invasive carcinoma is one in which stromal invasion is < 5 mm from the base and lateral spread < 7mm with no vascular or lymphatic involvement (Stage Ia of Ca cervix)\*.

   Microinvasive Ca can be further subdivided as:

   Stage Ia,
   Lesion with invasion< 3 mm
   Risk of nodal metastasis <1%
   
   If patient is young/ desires fertility
   Conization\*  
   
   If patient does not desires fertility
   Simple hysterectomy/ Type I hysterectomy/ vaginal hysterectomy

   Stage Ia,
   Lesion with invasion 3-5 mm
   Risk of nodal metastasis is >5%
   
   If patient has not completed family
   Radical trachelectomy + pelvic lymphadenectomy
   
   If patient has completed family
   Modified radical hysterectomy* + Pelvic lymph adenectomy
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

I have discussed management of cancer cervix in detail in preceeding 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 lymphnodes. 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.”

**Note:**

- IOC to know whether para-aortic lymph nodes are evolved 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 2A -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.”

47. Ans. is d, i.e. Follow-up

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

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.

As discussed in the preceeding 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 IIIB: Radiotherapy should be given; Staging should be done after cystoscopy.

Cancer cervix involving the parametrium but not the pelvis refers to stage II B (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/ Wertheim’s 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 15th ed pg 406; Jeffcoate 7th ed p 421; Williams Gynae 1st ed p 635
Complications of Cone biopsy are:

- Hemorrhage
- Sepsis (infection)
- Cervical stenosis
- Pregnancy complications which include:
  - Mid trimester abortions
  - Preterm labour
  - Cervical dystocia

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\textsuperscript{nd} ed p 787; Novak 14\textsuperscript{th} 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)

55. Ans. is c, i.e. Both ovaries

Ref. Textbook of Gynaecology sheila Balakrishnan 1\textsuperscript{st} 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\textsuperscript{th} ed p 1428; John Hopkins manual of obs and cynae 4\textsuperscript{th} ed p 554

Two important points in the radiotherapy of cancer cervix are

<table>
<thead>
<tr>
<th>Location</th>
<th>Structure present</th>
<th>Dose of radiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 cm above and 2 cm lateral to external os</td>
<td>Paracervical/parametrial lymph node</td>
<td>7000-8000 cGy</td>
</tr>
<tr>
<td>2 cm above and 5 cm lateral to external os</td>
<td>Obturator lymph node</td>
<td>4000-6000 cGy</td>
</tr>
</tbody>
</table>

57. Ans. is a, i.e. Conventional pap smear

Ref. Dutta Gynae 6\textsuperscript{th} ed p 323-4

HPV triage strategy includes:

- Pap smear test—by liquid based thin layer cytology
- Hybrid capture 2 for detecting HPV DNA

This triage strategy can detect CIN II and III lesions effectively and reduces the load of coloscopy clinic.

58. Ans. is b, i.e. Lungs

Ref. Dutta Gynae 6\textsuperscript{th} ed p 346

Metastasis to distant organs is 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 Ila — 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 after the staging so Answer remains is Stage 11a.

60. **Ans. is c, i.e. State 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 11 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 tracheectomy and pelvic lymph adenectomy can be done for stage IIA disease**

For stage Ia, surgery of choice is conization in young females and simple hysterectomy in older females. Radical hysterectomy is not done in stage Ia (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 tracheectomy 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 tracheectomy 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 tracheectomy are:** (i) preservation of fertility, (ii) early stage disease (stage IA1, A2, IB1), (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 tracheectomy is not done in stage IIA disease

62. **Ans. is d, i.e. In younger age group, radiotherapy is preferred**

As explained in the text, in younger age group we prefer surgery with preservation of ovaries and not radiotherapy
Ultrasound Characteristics of Benign vs Malignant Ovarian Tumors

<table>
<thead>
<tr>
<th>Physical examination</th>
<th>Benign tumor</th>
<th>Malignant tumor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mobility</td>
<td>Mobile</td>
<td>Fixed, large and multiloculated</td>
</tr>
<tr>
<td>Consistency</td>
<td>Cystic</td>
<td>Solid or firm</td>
</tr>
<tr>
<td>Laterality</td>
<td>Unilateral</td>
<td>Bilateral</td>
</tr>
<tr>
<td>Cul-de-sac</td>
<td>Smooth on P/V examination</td>
<td>Nodular on P/V examination</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Radiography</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Size</td>
<td>Usually &lt; 10 cm size</td>
<td>Any size</td>
</tr>
<tr>
<td>Septations</td>
<td>&lt; 2 mm thickness</td>
<td>Multiple septations &gt; 3 mm in size</td>
</tr>
<tr>
<td>Calcification</td>
<td>Seen in teratoma</td>
<td>Usually absent</td>
</tr>
<tr>
<td>Omental caking</td>
<td>Absent</td>
<td>Seen</td>
</tr>
<tr>
<td>Ascites</td>
<td>Absent</td>
<td>Present</td>
</tr>
</tbody>
</table>
| Intraoperative       | Unilateral cyst with no adhesion | Solid areas with adhesion, rupture may occur.
|                     | Capsule intact | Capsule is breached |

Physiological/Functional Cysts

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
<th>Presentation</th>
<th>Ultrasound/Cytology</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follicular cyst</td>
<td>Follicle fails to rupture during ovulation</td>
<td>Usually asymptomatic</td>
<td>4–8 cm mass, unilocular, lined with granulosa cells</td>
<td>If &lt;6 cm, wait 6 weeks then re-examine as cyst usually regresses with next cycle</td>
</tr>
<tr>
<td></td>
<td></td>
<td>May rupture, bleed, tort, infarct causing pain ± signs of peritoneal irritation</td>
<td></td>
<td>OCP (ovarian suppression) – will prevent development of new cysts</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Treatment usually laparoscopic</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Painful, multiloculated, or partially solid masses warrant surgical exploration</td>
</tr>
<tr>
<td>Lutein cyst</td>
<td>Corpus luteum fails to regress after 14 days, becoming cystic or hemorrhagic</td>
<td>More likely to cause pain than follicular cyst</td>
<td>Larger and firmer than follicular cysts</td>
<td>Same as for follicular cysts</td>
</tr>
<tr>
<td></td>
<td></td>
<td>May delay onset of next period</td>
<td>Show a cob web like appearance</td>
<td></td>
</tr>
<tr>
<td>Theca-lutein cyst</td>
<td>Due to atretic follicles stimulated by abnormal β-hCG levels</td>
<td>Associated with molar pregnancy, ovulation induction with clomiphene pregnancy</td>
<td>Conservative</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Cyst will regress as β-hCG levels fall</td>
<td></td>
</tr>
</tbody>
</table>

Risk of malignancy index (RMI)

RMI = U × M × 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

Contd...
### Benign Ovarian Tumors

- **Benign epithelial tumors = M/C = 80%**
  - Serous cystadenoma = M/C but overall, M/C benign tumor is dermoid cyst.
  - Mucinous cystadenoma
  - Endometroid 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

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
<th>Presentation</th>
<th>Ultrasound/Cytology</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luteoma of pregnancy</td>
<td>• Usually bilateral</td>
<td>• Associated with multiple pregnancy</td>
<td>• Same as for theca-lutein</td>
<td>• Regresses postpartum</td>
</tr>
<tr>
<td></td>
<td>• Due to prolonged elevation of $\beta$-hCG</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### 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)
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.\(^9\)
- Most common benign neoplasm diagnosed during pregnancy.\(^9\)
- Most common germ cell tumor.\(^9\)
- 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.\(^9\)
  - 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.
- 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.

**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 differentiated 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**

- 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**

<table>
<thead>
<tr>
<th>Depends on the size of cyst</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 5 cm</td>
</tr>
<tr>
<td>Wait and watch</td>
</tr>
</tbody>
</table>

- Solid areas
  - Operate in second trimester (14-20 weeks)
- Clear
  - Wait and watch

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 females (> 65 IU/mL)
4. Acute complication of ovarian cyst.
5. For diagnostic purpose.

- **Ovarian cyst**
  - **Premenopausal**
    - 3-5 cms
      - Wait and watch
    - 5-7 cms
      - Serial USG’s at 3, 6, 12 weeks
    - > 7 cms
      - Surgery
  - **Postmenopausal**
    - Measure CA125 levels
      - Normal
      - Elevated
        - Size of cyst < 7 cms
          - Surgery correlative of size
        - Size of cyst ≥ 7 cms
          - Wait and watch
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
  - Caicasions
  - 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.

- **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

<table>
<thead>
<tr>
<th>Ovarian Cancer</th>
<th>Arises from</th>
<th>Types</th>
<th>Age Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epithelial</td>
<td>Coelomic epithelium</td>
<td>Serous, Mucinous</td>
<td>Peri/postmenopausal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Endometrioid</td>
<td>(45 + years)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clear cell, Brenner</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Undifferentiated</td>
<td></td>
</tr>
<tr>
<td>Sex cord stromal</td>
<td>Gonadal stromal</td>
<td>Granulosa cell tumor, Sertoli-Leydig tumor</td>
<td>Reproductive</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(20 – 40 years)</td>
</tr>
<tr>
<td>Germ cell tumors</td>
<td>Primitive germ cells</td>
<td>Dysgerminoma, Endodermal sinus tumor,</td>
<td>Prepubertal-pubertal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Embryonal, Teratoma, Chorio carcinoma</td>
<td>(15–20 years)</td>
</tr>
<tr>
<td>Others</td>
<td>Metastatic</td>
<td>Krukenberg</td>
<td></td>
</tr>
</tbody>
</table>

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
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 16th ed p 554

<table>
<thead>
<tr>
<th>Benign gynaecological condition</th>
<th>Malignant condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy</td>
<td>Endogenous – Endometrial Ca</td>
</tr>
<tr>
<td>PID</td>
<td>Pneumocystis – Pancreas Ca</td>
</tr>
<tr>
<td>Endometriosis</td>
<td>Carinii – Colon Ca</td>
</tr>
<tr>
<td>Uterine fibroid</td>
<td>Causes – Cervix Ca</td>
</tr>
<tr>
<td>About 1% of normal females</td>
<td>T – Fallopian tubes Ca</td>
</tr>
<tr>
<td><strong>Mnemonic:</strong> CA - 125 is raised in pregnant patient with endometrial fibroid B and PID</td>
<td>B – Breast Ca</td>
</tr>
<tr>
<td></td>
<td>Of – Ovarian epithelial Ca (MC cause)</td>
</tr>
<tr>
<td></td>
<td>Lung – Lung Ca</td>
</tr>
<tr>
<td></td>
<td><strong>Mnemonic:</strong> Endogenous Pneumocystis Carinii Causes TB Of Lungs</td>
</tr>
</tbody>
</table>

- 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)**

<table>
<thead>
<tr>
<th>STAGE I: Tumor confined to ovaries</th>
<th>OLD</th>
<th>NEW (2014)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>Tumor limited to 1 ovary, capsule intact, no tumor on surface, negative washings/ascites.</td>
<td>IA</td>
</tr>
<tr>
<td>IB</td>
<td>Tumor involves both ovaries otherwise like IA</td>
<td>IB</td>
</tr>
<tr>
<td>IC</td>
<td>Tumor involves 1 or both ovaries with any of the following: capsule rupture, tumor on surface, positive washings/ascites.</td>
<td>IC</td>
</tr>
<tr>
<td></td>
<td>IC1</td>
<td>Surgical spill (Intra operative capsule rupture)</td>
</tr>
<tr>
<td></td>
<td>IC2</td>
<td>Capsule rupture before surgery or tumor on ovarian surface.</td>
</tr>
<tr>
<td></td>
<td>IC3</td>
<td>Malignant ascites or peritoneal washings.</td>
</tr>
</tbody>
</table>

**Stage II: Tumor involves 1 or both ovaries with pelvic extension (below the pelvic brim) or primary peritoneal cancer**

<table>
<thead>
<tr>
<th>OLD</th>
<th>NEW</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIA Extension and/or implant on uterus and/or Fallopian tubes</td>
<td>IIA Extension and/or implant on uterus and/or Fallopian tubes</td>
</tr>
<tr>
<td>IIB Extension to other pelvic intraperitoneal tissues</td>
<td>IIB Extension to other pelvic intraperitoneal tissues and pelvic nodes.</td>
</tr>
<tr>
<td>IIC IIA or IIB with positive washings as cites</td>
<td></td>
</tr>
</tbody>
</table>

**Tumor markers in ovarian cancers**

<table>
<thead>
<tr>
<th>Ovarian Tumor</th>
<th>Tumor Marker</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epithelial ovarian tumors</td>
<td></td>
</tr>
<tr>
<td>Serous variety</td>
<td>CA 125</td>
</tr>
<tr>
<td>Mucinous variety</td>
<td>Ca 19 – 9, CEA</td>
</tr>
<tr>
<td>Serous and mucinous</td>
<td>OCCA, OCA</td>
</tr>
<tr>
<td>Endodermal sinus/Yolk sac tumor</td>
<td>AFP</td>
</tr>
<tr>
<td>Choriocarcinoma</td>
<td>HCG</td>
</tr>
<tr>
<td>Dysgerminoma</td>
<td>LDH, Alkaline phosphatase</td>
</tr>
<tr>
<td>Granulosa cell tumor</td>
<td>Inhibin</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>OLD</th>
<th>NEW</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIIA</td>
<td>IIIA (Positive retroperitoneal lymph nodes and/or microscopic metastasis beyond the pelvis.)</td>
</tr>
<tr>
<td>Microscopic metastasis beyond the pelvis.</td>
<td>IIIA1  Positive retroperitoneal lymph nodes only</td>
</tr>
<tr>
<td></td>
<td>IIIA 1(i)  Metastasis ≤ 10 mm</td>
</tr>
<tr>
<td></td>
<td>IIIA 1(ii)  Metastasis &gt; 10 mm</td>
</tr>
<tr>
<td></td>
<td>IIIA2  Microscopic extrapelvic (above the brim) peritoneal involvement ± positive retroperitoneal lymph nodes</td>
</tr>
<tr>
<td>IIIIB</td>
<td>IIIB  Microscopic extrapelvic ≤ 2 cm ± positive retroperitoneal lymph nodes</td>
</tr>
<tr>
<td>Macroscopic, extrapelvic, peritoneal metastasis ≤ 2 cm in greatest dimension.</td>
<td></td>
</tr>
<tr>
<td>IIIC</td>
<td>IIIC  Microscopic extrapelvic, peritoneal metastasis &gt; 2 cm ± positive retroperitoneal lymph nodes</td>
</tr>
<tr>
<td>Macroscopic, extrapelvic, peritoneal metastasis &gt; 2 cm in greatest dimension and/or regional lymph node metastasis.</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>OLD</th>
<th>NEW</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV</td>
<td>IV A  Pleural effusion with positive cytology</td>
</tr>
<tr>
<td>Distant metastasis excluding peritoneal metastasis. Includes hepatic parenchymal metastasis.</td>
<td>IVB  Hepatic and/or splenic parenchymal metastasis, metastasis to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside of the abdominal cavity)</td>
</tr>
</tbody>
</table>

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)
Management of Epithelial Ovarian Tumors

In ovarian cancers similar to endometrial cancer – staging is surgical i.e. hysterectomy with bilateral salpingo oopherectomy 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

<table>
<thead>
<tr>
<th>Stage</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low malignant potential tumors</td>
<td>Surgical staging. No postoperative treatment required</td>
</tr>
<tr>
<td>Stage I (A or B) Grade I and II</td>
<td>Surgical staging. No postoperative treatment required. Note: In a young woman who wishes to preserve fertility if intraoperative findings are consistent with stage I, unilateral salpingo oopherectomy may be performed. The uterus and the contralateral ovary can be removed later when the patient has completed child bearing.</td>
</tr>
<tr>
<td>Stage I (A or B) Grade III and all grades of Stages IC and II</td>
<td>Surgical staging followed by three to six cycles of chemotherapy postoperatively.</td>
</tr>
<tr>
<td>Advanced ovarian cancer – Stage III/IV</td>
<td>Cytoreduction or debulking surgery followed by six cycle of platinum based chemotherapy (carboplatin + paclitaxel preferred) each cycle given after 3 weeks.</td>
</tr>
</tbody>
</table>

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.
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 isalate feature.

Mnemonic : YES PCT

Y - Yolk sac Tumor (Endodermal sinus Tm)
E - Embryonal carcinoma
S - Seminoma ≈ Dysgerminoma
P - Polycystic ovarian disease
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 (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 pathognomic finding is Schiller - Duval bodies 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

- M/c malignant GCT
- Most radiosensitive
- Best prognosis amongst all germ cell tumors
- Worst prognosis in germ cell tumors is with endodermal sinus tumor.

Endodermal Sinus Tumor/Yolk Sac Tumor

Endodermal sinus tumour / Yolk sac tumor:

- 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 pathognomic finding is Schiller - Duval bodies 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 of ovary.
- They are the most common ovarian malignancy detected during pregnancy.
- Primarily affect young women (average age of incidence is 20 years).
- Usually unilateral 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.
- Pathologically it is a solid neoplasm with areas of softening 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).
- 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 phosphate, which are used as tumour marker of dysgerminoma.
Chapter 14C  Gynecological Oncology: Ovarian Tumors

- 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 overran 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**

<table>
<thead>
<tr>
<th>Granulosa stromal cell tumour</th>
<th>Androblastoma</th>
<th>Gynandroblastoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Granulosa cell tumour</td>
<td>• Sertoli cell tumour</td>
<td></td>
</tr>
<tr>
<td>• Tumours in thecoma fibroma group</td>
<td>• Sertoli leydig cell tumour</td>
<td></td>
</tr>
<tr>
<td>– Thecoma</td>
<td>• Leydig cell tumour</td>
<td></td>
</tr>
<tr>
<td>– Fibroma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>– Unclassified</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**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.
If it occurs

<table>
<thead>
<tr>
<th>Before puberty</th>
<th>Reproductive age</th>
<th>Postmenopausal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Precocious puberty</td>
<td>Initially it leads to amenorrhoea (Due to suprathreshold level of estrogen) f/b prolonged bleeding (similar to metropathia hemorrhagica).</td>
<td></td>
</tr>
</tbody>
</table>

- Most common symptoms are: Menometrorrhagia and post menopausal bleeding.

**Pathology**
- They are low grade malignancies.
- Almost always unilateral (B/L in < 2%)
- Encapsulated tumours and have smooth surface.

**On microscopy:** Granulosa cells exhibit coffee bean nucleus and call exner bodies.

**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.

<table>
<thead>
<tr>
<th>Women of reproductive age stage IA</th>
<th>Postmenopausal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unilateral salpingo-oophorectomy</td>
<td>TAH + BSO.</td>
</tr>
</tbody>
</table>

**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.

### Masculanising Tumors

<table>
<thead>
<tr>
<th>Arrhenoblastoma/Androblastoma Hlius cell Tm</th>
<th>Adrenal cortical Tm/Lipoid cell Tm of ovary</th>
<th>Gynandroblastoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Affect child bearing age group (10–35 years)</td>
<td>Seen in postmenopausal females</td>
<td>Combination of granulosa cell tumour &amp; arrheno blastoma</td>
</tr>
<tr>
<td>It includes:</td>
<td>Characterised by presence of Reinke’s crystals</td>
<td></td>
</tr>
<tr>
<td>• Sertoli Cell Tumor (SCT)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Leydig cell Tumor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Sertoli – Leydig cell Tumor</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**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 amenorrhoa
  - flattening of breast
  - increased hair growth – hirsutism
- 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

<table>
<thead>
<tr>
<th>First Type</th>
<th>Second Type (Krukenberg Tumour)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• They are metastatic tumors from Intestine, Gall bladder, pancreas, corpus, and cervix</td>
<td></td>
</tr>
<tr>
<td>• They are most commonly bilateral</td>
<td></td>
</tr>
<tr>
<td>• They have irregular surface</td>
<td></td>
</tr>
<tr>
<td>• The method of ovarian infiltration is by surface implantation or retrograde implantation</td>
<td></td>
</tr>
<tr>
<td>• They are metastatic tumors from stomach (70%), large bowel (15%) and breast (6%)</td>
<td></td>
</tr>
<tr>
<td>• They are always bilateral.</td>
<td></td>
</tr>
<tr>
<td>• They have a smooth surface which may be slightly bossed.</td>
<td></td>
</tr>
<tr>
<td>• Always arise by retrograde lymphatic spread.</td>
<td></td>
</tr>
</tbody>
</table>

### 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* 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
- Have smooth surface
- 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
- Have waxy consistency

### Histological Characteristics of Ovarian Tumors

<table>
<thead>
<tr>
<th>Feature</th>
<th>Associated tumour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Call exner bodies &amp; coffee bean nuclei</td>
<td>Granulosa cell tumour</td>
</tr>
<tr>
<td>Schiller duval bodies</td>
<td>Endodermal sinus tumor</td>
</tr>
<tr>
<td>Reinke’s crystal</td>
<td>Hilus cell tumour</td>
</tr>
<tr>
<td>Psammoma bodies</td>
<td>Serous epithelial tumours</td>
</tr>
<tr>
<td>Walthard cell nest</td>
<td>Brenner tumour</td>
</tr>
<tr>
<td>Signet ring cell</td>
<td>Krukenberg tumour</td>
</tr>
<tr>
<td>Hobnail cell</td>
<td>Clear cell tumour</td>
</tr>
<tr>
<td>Large polygonal cell with lymphocytic infiltration and fibrous septa</td>
<td>Dysgerminoma</td>
</tr>
<tr>
<td>Skin, teeth, cartilage</td>
<td>Teratoma</td>
</tr>
</tbody>
</table>
### Tumor Markers of Ovarian Neoplasm

<table>
<thead>
<tr>
<th>Epithelial cell Tumor-Serous variety</th>
<th>CA 125</th>
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</thead>
<tbody>
<tr>
<td>• Mucinous variety-Ca 19-9, CEA</td>
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<tr>
<td>• Both serous and mucinous variety-</td>
<td>OCCA, OCA</td>
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<tr>
<td>Germ cell Tumors</td>
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<tr>
<td>(In individual tumors see flow chart given below)</td>
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<tr>
<td>Granulosa cell tumor</td>
<td>Inhibin</td>
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</tbody>
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#### 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 Tumors-Stage 1A in young female
- Borderline Tumors

#### Diagram

- **Primordial Germ cell**
  - **Dysgerminoma**
    - AFP - nt
    - HCG - nt
    - LDH + nt
    - PLAP + nt
  - **Embryonal carcinoma**
    - AFP + HCG +
  - **Extra embryonic differentiation**
  - **Embyronic differentiation**
  - **Troplast**
  - **Yolk sac**
  - **Immature teratoma**
    - AFP - nt
    - HCG - nt
  - **Endodermal sinus tumor**
    - AFP (+), HCG (-)
  - **Mature teratoma**
    - AFP - nt
    - HCG - nt
General

1. All of the following are known risk factors for the development of ovarian carcinoma except: (AIIMS 03)
   a. Family history of ovarian carcinoma
   b. Use of oral pills
   c. Use of Clomiphene
   d. BRCA - 1 positive individual
2. 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)
   a. Use of oral contraceptive pills
   b. Screening with transvaginal ultrasound
   c. Screening with CA - 125
   d. Prophylactic oophorectomy
3. Most common ovarian tumor in less than 20 years is: (AIIMS 97)
   a. Epithelial tumour
   b. Germ cell tumour
   c. Metastatic tumour
   d. Sexcord stromal tumour
4. Which of the following is the most radiosensitive ovarian tumors? (AIIMS 97)
   a. Dysgerminoma
   b. Dermoid cyst
   c. Serous cystadenoma
   d. Endodermal sinus tumour
5. MC ovarian tumour in younger age group or M/C malignant Tm in young age group: (PGI June 05/04)
   a. Dysgerminoma
   b. Dermoid
   c. Mucinous cystadenoma
   d. Fibroma
   e. Granulosa cell tumour
6. All of the following are true about Borderline tumors except:
   a. 10% of all epithelial tumours are borderline.
   b. They have a good prognosis.
   c. Metastases are common
   d. Absence of stromal invasion
7. According to WHO classification of ovarian tumours, Brenner tumor of ovary belongs to:
   a. Epithelial tumours
   b. Sex cord stromal tumours
   c. Germ cell tumours
   d. Metastatic tumours
8. Ovarian tumours are commonly arise from: (UP 05)
   a. Stroma
   b. Surface epithelium
   c. Germinal epithelium
   d. Endoderm
9. True about Brenner tumor: (PGI 03)
   a. Usually bilateral
   b. Resembles fibroma
   c. Accounts for 20% of all ovarian tumors
   d. Common in postmenopausal age group
10. 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)
    a. Serial Ca-125 measurement and follow-up
    b. Hysterectomy and bilateral pingo oophorectomy
    c. Hysterectomy + Radiotherapy
    d. Radiotherapy
11. Chemotherapeutic drug effective in the treatment of epithelial ovarian cancer is: (Karn 02)
    a. Carboplatin
    b. Paclitaxel
    c. Cyclophosphamide
    d. Methotrexate karnataka

Epithelial Cell Tumors

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   b. Surface epithelium
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    c. Cyclophosphamide
    d. Methotrexate karnataka

Sex Cord Tumors

12. Which of the following are masculinizing tumors of the ovary? (AI 97)
    a. Granulosa cell tumor
    b. Dysgerminoma
    c. Dermoid Cyst
    d. Arrhenoblastoma
13. Which of the following is correct regarding granulosa cell tumour of ovary? (AIIMS 96)
    a. Common in puberty
    b. Associated with Ca endometrium
    c. Malignant change occur rarely
    d. It is bilateral
14. True about granulosa cell tumours: (PGI Dec 05)
    a. MC malignant tumour of ovary
    b. It secretes hormones
    c. Associated with endometrial hyperplasia
    d. 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 form 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

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 sono graphic 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

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 x 6 x 6 cm in size. Ultrasonography reveals solid structures in the mass. Her serum biomarkers such as AFP, fO-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

### 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
55. A lady with CA ovary in follow-up with raised CA 125 level, next step: \( \text{(AIIMS May 08)} \)
   a. CT 
   b. PET 
   c. MRI 
   d. Clinical exam and serial follow up of CA 125

56. Placental alkaline phosphatase is marker of: \( \text{(PGI 96)} \)
   a. Theca cell tumor 
   b. Teratoma 
   c. Choriocarcinoma 
   d. Dysgerminoma

57. Marker for granulosa cell tumor: \( \text{(AIIMS May 08)} \)
   a. CA 19-9 
   b. Ca 50 
   c. Inhibin 
   d. Teratoma

58. All of the following ovarian tumours usually occur bilaterally, except: \( \text{(AIIMS 95)} \)
   a. Metastatic mass 
   b. Dysgerminoma 
   c. Cyst adenoma of ovary 
   d. Dermoid cyst

59. Bilateral germ cell tumour is: \( \text{(AIIMS May 07)} \)
   a. Dysgerminoma 
   b. Immature teratoma 
   c. Embryonal cell carcinoma 
   d. Endodermal sinus tumour

60. Which ovarian tumor is likely to involve the opposite ovary by metastasis? \( \text{(AI 96)} \)
   a. Granulosa cell tumor 
   b. Dysgerminoma 
   c. Gynandroblastoma 
   d. Endodermal sinus tumor

61. Surgical staging of ovarian Ca all done except: \( \text{(AI 09)} \)
   a. Peritoneal washing 
   b. Peritoneal biopsy 
   c. Omental biopsy 
   d. 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? \( \text{(AI 03)} \)
   a. Stage II b 
   b. Stage III a 
   c. Stage III b 
   d. Stage III c

63. Bilateral ovarian cancer with; capsule breached; ascites positive for malignant cells. Stage is: \( \text{(AI 01; AIIMS 07)} \)
   a. I 
   b. II 
   c. III 
   d. IV

64. A 55-year-old female patient has carcinoma ovary with bilateral involvement with ascitic fluid in the abdomen. The stage is: \( \text{(AIIMS 99)} \)
   a. II 
   b. III 
   c. IV 
   d. IC 
   e. Dysgerminoma

65. What is the stage of ovarian Ca with superficial liver metastasis with B/L ovarian mass? \( \text{(PGI Dec 06)} \)
   a. Stage I 
   b. Stage II 
   c. Stage III 
   d. Stage IV 
   e. Ca in situ

Ovarian Cysts and Their Management

66. Which ovarian cyst does not undergo malignancy? \( \text{(AIIMS 92)} \)
   a. Mucinous 
   b. Papillary 
   c. Dermoid 
   d. Granulosa Theca

67. All are true about serous cystadenoma of the ovary except: \( \text{(LP 04)} \)
   a. Bilateral 
   b. Unilateral 
   c. Concentric calcification 
   d. Multiloculated, sticky, gelatinous fluid

68. A 35-year-old patient on USG shows 3 × 4 cm clear ovarian cyst on right side. Next line of management is: \( \text{(PGI Dec 08)} \)
   a. Laparoscopy 
   b. OC pills 
   c. Wait and watch 
   d. 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:
   a. USG guided ovarian tapping \( \text{(AI 2007)} \)
   b. Wait and watch 
   c. Surgery 
   d. OC pills x three cycles.

Pregnancy and Cysts

70. Most common ovarian tumour in pregnancy is: \( \text{(AIIMS 96)} \)
   a. Mucinous cyst adenoma 
   b. Dermoid cyst 
   c. Metastasis 
   d. Dysgerminoma

71. Which of the following ovarian tumor is most prone to undergo torsion during pregnancy? \( \text{(AI 06)} \)
   a. Serous cystadenoma 
   b. Mucinous cystadenoma 
   c. Dermoid cyst 
   d. Theca lutein cyst

72. A 15 cms X 15 cms ovarian cyst has been diagnosed in an 8 weeks pregnant lady. Further Management includes: \( \text{(PGI Nov 10)} \)
   a. Only follow up without surgical intervention 
   b. Laparotomy at 14-16 weeks 
   c. Cesarean delivery and ovariotomy at term 
   d. Surgery after delivery 
   e. Immediate operation
73. Which is/are used in management of stage III ovarian cancer:
   a. Debulking
   b. Mantle field irradiation
   c. Abdomino-pelvic radiotherapy is very effective
   d. Chemotherapy
   e. Cytoreduction

NEW PATTERN QUESTIONS

74. Lutein cysts are associated with all except:
   a. Gestational trophoblastic tumours
   b. Clomiphene administration
   c. Bilaterality
   d. Use of OCP’s

75. The following statements are related to Krukenberg tumour except:
   a. It is always secondary
   b. The most common primary site is pylorus of the stomach
   c. The tumour is bilateral
   d. ‘Signet ring’ looking cells are characteristic

76. Sex cord stromal tumours of the ovary include all except:
   a. Luteomas
   b. Gynandroblastomas
   c. Sertoli-Leydig cell tumours of the ovary
   d. Theca-fibroma

77. True regarding neoplasms of the ovary are:
   a. Stromal invasion is commonly present in ovarian tumours of borderline malignancy
   b. Lymphocytic infiltration is characteristic to dysgerminoma
   c. Presence of ascites and pleural effusion in Brenner tumour indicates poor prognosis
   d. 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:
   a. USG guided ovarian tapping
   b. Wait and watch
   c. Surgery
   d. OCP
1. Ans. is b, i.e. Use of oral pills

See the text for explanation.

2. Ans. is d, i.e. Prophylactic oophorectomy

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 1st 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 1st 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

4. Ans. is a, i.e. Dysgerminoma

“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.”

“Dysgerminomas are the most common malignant germ cell tumours of the ovary and have been considered the female equivalent of seminoma.”

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.
- Most common malignant tumour of ovary – Serous cystadenocarcinoma.
- Most common benign tumour of ovary (overall) – Dermoid cyst.
- Most common benign epithelial tumor of ovary – Serous cystadenoma.
- 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 bilateral- 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 24th 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)
• Tumour with lymphocytic infiltration: – Dysgerminoma.

5. Ans. is a, i.e. Dysgerminoma
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.
- **Mucinous 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
See the text for exploration.

7. Ans. is a, i.e. Epithelial tumours

Cancer of Ovary

<table>
<thead>
<tr>
<th>Ovarian Cancer</th>
<th>Arises from</th>
<th>Types</th>
<th>Age Group</th>
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<tbody>
<tr>
<td>Epithelial</td>
<td>Coelomic epithelium</td>
<td>Serous, mucinous endometrioid clear cell, Brenner undifferentiated</td>
<td>Premenopausal (45 + years)</td>
</tr>
<tr>
<td>Sex cord stromal</td>
<td>Gonadal stromal</td>
<td>Granulosa cell tumor, Sertoli-Leydig tumor</td>
<td>Reproductive (20 – 40 years)</td>
</tr>
<tr>
<td>Germ cell tumors</td>
<td>Primitive germ cells</td>
<td>Dysgerminoma, endodermal sinus tumor, embryonal, teratoma, choriocarcinoma</td>
<td>Prepubertal-pubertal (15–20 years)</td>
</tr>
<tr>
<td>Others</td>
<td>Metastatic</td>
<td>Krukenberg</td>
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8. **Ans. is b, i.e. Surface epithelium**

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**

*Brenner tumour is also called as Transitional cell tumour:*
- It is a rare epithelial neoplasm of ovary resembling fibroma.
- It is an essentially benign tumour.
- Tumour is generally seen in women around menopause and is generally unilateral.
- Cause menopausal bleeding and Pseudomeig syndrome (ascites and hydrothorax).
- Malignant change is very rare.
- Histologically it shows walthard cell rests of transitional cells, cells have coffee bean nuclei, cut section is gritty.

10. **Ans. is a, i.e. Serial Ca-125 measurement and follow-up**

Here the patient is 25 years old nullipara and cystectomy sample shows serous cystadenocarcinoma - Probably the disease is limited to the ovary removed, hence to be called stage la. 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\textsuperscript{th} ed p 1479-1480; 15\textsuperscript{th} ed p 1371

11. **Ans. is a and b, i.e. Carboplatin; and Paclitaxel**

**Role of Chemotherapy in Epithelial ovarian tumors**

<table>
<thead>
<tr>
<th>In early stage (Stage I)</th>
<th>In advanced stages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk patients No adjuvant therapy required.</td>
<td>Combination chemotherapy: intraperitoneal cisplatin and paclitaxel or I.V. carboplatin &amp; paclitaxel are the treatments of choice for patients with advanced disease.</td>
</tr>
<tr>
<td>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</td>
<td>In patients who cannot tolerate combination chemotherapy, single agent, I.V. administered carboplatin can be given.</td>
</tr>
</tbody>
</table>

**Recommendations for therapy –** 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.

<table>
<thead>
<tr>
<th>In patients who have hypersensitivity to paclitaxel or carboplatin alternative drugs used are:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Docetaxel</td>
</tr>
<tr>
<td>Liposomal doxorubicin</td>
</tr>
<tr>
<td>Topotecan</td>
</tr>
<tr>
<td>Etoposide</td>
</tr>
</tbody>
</table>

12. **Ans. is d, i.e. Arrhenoblastoma**

*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**

*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
- **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** (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\textsuperscript{th} 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 14th/ed p 1520 - 1521, 15th/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 14th/ed p 1523, 15th/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 2nd/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 10th/ed p 875; Devita 7th/ed p 1391; Novak 14th/ed p 1506; 15th/ed p 1394; Williams Gynae 1st/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 cysts (Benign in nature).
• Most common malignant GCT – Dysgerminoma.
• Second most common malignant GCT – Endodermal sinus Tumor. (Yolk Sac tumor)
• Most common benign Tumor of ovary – Dermoid cyst
   ... Williams Gynae 1st/ed p 214; Merck manual online medical library on Internet; Jeffcoate 7th/ed p 531

18. Ans. is a, i.e. Unilateral
   Ref. Shaw 15th/ed p 378; CGDT 9th/ed p 937

19. Ans. is a and b, i.e. Radiosensitive; and Most common malignant germ cell tumor
   Ref. Shaw 15th/ed p 378

20. Ans. is a, d and e, i.e. Blood spread seen; Bleomycin, etoposide and cisplatin given; and Radiosensitive
   Ref. Novak 14th/ed p 1508-9, 1511,15th/ed p 1395-1397

Dysgerminoma:
• Commonest malignant germ cell tumour of ovary.
  They are the most common ovarian malignancy detected during pregnancy.
  Primarily affect young women (average age of incidence is 20 years) and not postmenopausal females.
  Usually unilateral 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 due to degeneration.
  “Consistency is fleshy”
  ... CGDT 10th/ed p 875
  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. 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

**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

**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

**Dermoid cyst:** Dermoid cyst is a benign teratoma.
- It is most common benign tumour of ovary in reproductive age group. 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.**
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 Gynae 1\textsuperscript{st} ed p 742; Jeffcoates 7\textsuperscript{th} ed p 541; Novak 15\textsuperscript{th} 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. (M/C, being Dysgerminoma, 2nd M/C Immature teratoma)
- Tumour is highly malignant and is most rapidly growing tumour of whole body.
- Histologically the pathognomic finding is Schiller - Duval bodies\textsuperscript{9} 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\textsuperscript{th} ed p 425-6

27. Ans. is b, i.e. Krukenberg tumor

Ref. Shaw 15\textsuperscript{th} ed p 425-6; CGDT 10\textsuperscript{th} 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\textsuperscript{9} i.e. carcinoma cells pass from the stomach to the superior gastric lymphnode which also receive lymphatics from ovary.

**Characteristics of Krukenberg Tumour:**
1. Always bilateral\textsuperscript{9}
2. Have smooth surface\textsuperscript{9}
3. No tendency to form adhesions
4. Freely mobile
5. No infiltration through the capsule.
6. Histologically tumour has signet ring cells in the background of myxomatous stroma.
7. They retain the shape of normal ovary.\textsuperscript{9}
8. Have waxy consistency.\textsuperscript{9}

28. Ans. is c, i.e. Oesophagus

Ref. Novak 14\textsuperscript{th} 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.

<table>
<thead>
<tr>
<th>Gynaecologic</th>
<th>Gastrointestinal tract</th>
<th>Breast</th>
<th>Lymphoma and Leukemia</th>
<th>Melanoma</th>
<th>Carcinoid Tm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tubes (13%)</td>
<td>Stomach</td>
<td></td>
<td>(Most common)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endometrium</td>
<td>(Characteristic Krukenberg tumour)</td>
<td></td>
<td>Burkitt’s lymphoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervix (Rare &lt; 1%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colon</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small intestine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Appendix</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**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\textsuperscript{th} ed p 543; Novaks 15\textsuperscript{th} 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  
**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  

**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 15th/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.

**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

“A benign cystic teratoma is the most common neoplasm to undergo torsion, and it to the M/C benign tumor diagnosed during pregnancy.”

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

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.
- Mucocele 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

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.

39. Ans. is c, i.e. Staging

“FIGO staging is based on finding at surgical exploration.”

“Whenever malignancy is suspected, a staging laparotomy should be carried out.”

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 assess 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

<table>
<thead>
<tr>
<th>Feature</th>
<th>RMI 1 Score</th>
<th>RMI 2 Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrasound features:</td>
<td>0 = None</td>
<td>0 = None</td>
</tr>
<tr>
<td>* Multilocular cyst</td>
<td>1 = One abnormality</td>
<td>1 = One abnormality</td>
</tr>
<tr>
<td>* Solid areas</td>
<td>3 = Two or more abnormalities</td>
<td>4 = Two or more abnormalities</td>
</tr>
<tr>
<td>* Bilateral lesions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Ascites</td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Intra-abdominal metastases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Premenopausal</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Ca 125 U/ml</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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:

\[ \text{RMI score} = \text{Ultrasound score} \times \text{Menopausal score} \times \text{Ca 125 level in U/mL} \]

- 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

- Malignant ovarian tumour are often bilateral solid and present with ascites.”

Omental caking on CT is also a sign of malignancy.

<table>
<thead>
<tr>
<th>Physical examination</th>
<th>Benign tumour</th>
<th>Malignant tumour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mobility</td>
<td>Mobile</td>
<td>Fixed, large and multiloculated</td>
</tr>
<tr>
<td>Consistency</td>
<td>Cystic</td>
<td>Solid or firm</td>
</tr>
<tr>
<td>Laterality</td>
<td>Unilateral</td>
<td>Bilateral</td>
</tr>
<tr>
<td>Cul-de-sac</td>
<td>Smooth on P/V examination</td>
<td>Nodular on P/V examination</td>
</tr>
</tbody>
</table>

Radiotherapy

<table>
<thead>
<tr>
<th>Size</th>
<th>Usually &lt; 10 cm size</th>
<th>Any size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Septations</td>
<td>&lt; 2 mm thickness</td>
<td>Multiple septations &gt; 3 mm in size</td>
</tr>
<tr>
<td>Calcification</td>
<td>Seen in teratoma</td>
<td>Usually absent</td>
</tr>
<tr>
<td>Omental caking</td>
<td>Absent</td>
<td>Seen</td>
</tr>
<tr>
<td>Ascites</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Intra operative</td>
<td>Unilateral cyst with no adhesion</td>
<td>Solid areas with adhesion, rupture</td>
</tr>
<tr>
<td></td>
<td>Capsule intact</td>
<td>may occur.</td>
</tr>
</tbody>
</table>

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).

Also know:

Pelvic Mass Evaluation: Criteria for Gynecologic Oncology Referral

<table>
<thead>
<tr>
<th>Premenopausal women</th>
<th>Postmenopausal women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very elevated CA-125 (&gt;200 U/mL)</td>
<td>Elevated CA-125</td>
</tr>
<tr>
<td>Ascites</td>
<td>Ascites</td>
</tr>
<tr>
<td>Evidence of abdominal or distant metastasis</td>
<td>Evidence of abdominal or distant metastasis</td>
</tr>
<tr>
<td>Family history of one or more first degree relatives with ovarian or breast cancer</td>
<td>Family history of one or more first degree relatives with ovarian or breast cancer</td>
</tr>
<tr>
<td>Nodular or fixed pelvic mass</td>
<td>Nodular or fixed pelvic mass</td>
</tr>
</tbody>
</table>

41. Ans. is b and c, i.e. Septations; and Bilaterality

42. Ans. is c, i.e. Papillary vegetation

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**  
   "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\textsuperscript{st} 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, ache 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**  
   **An ovarian mass with radio opaque shadow on X-ray points towards dermoid cyst as the diagnosis.**

   **Causes of Pelvic Calcification are:**
   1. Fibroids: popcorn type
   2. Dermoid cyst: it is the commonest ovarian mass to calcify
   3. Other ovarian masses: cystadenoma / carcinoma, fibromas
   4. Pseudomyxoma peritonei
   5. Fallopian tube calcification (rare): suggest TB
   6. Uterine i.e. endometrial calcification from chronic endometritis.

45. **Ans. is a, i.e. Dysgerminoma**  
   **M/C tumor in young females is- Germ cell tumor**

   **Hence in this female it could either be a dysgerminoma, endodermal sinus tumor or malignant terotoma, 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\textsuperscript{th} ed p 1394, 14\textsuperscript{th} ed p 1505; Shaw 14\textsuperscript{th} ed p 338

46. **Ans. is b, i.e. Krukenberg tumor**

   Already explained.

47. **Ans. is d, i.e. Hilus cell tumor**

48. **Ans. is a, i.e. Schiller-duval bodies**

   **Call exner bodies are small cyst like spaces found in cases of granulosa cell tumour.**

<table>
<thead>
<tr>
<th>Feature</th>
<th>Associated tumour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Call exner bodies &amp; coffee bean nuclei</td>
<td>Granulosa cell tumour</td>
</tr>
<tr>
<td>Schiller duval bodies</td>
<td>Endodermal sinus tumor</td>
</tr>
<tr>
<td>Reinek’s crystal</td>
<td>Hilus cell tumour</td>
</tr>
<tr>
<td>Psammoma bodies</td>
<td>Serous epithelial tumours</td>
</tr>
<tr>
<td>Walthard cell nest</td>
<td>Brenner tumour</td>
</tr>
<tr>
<td>Signet ring cell</td>
<td>Krukenberg tumour</td>
</tr>
<tr>
<td>Hobnail cell</td>
<td>Clear cell tumour</td>
</tr>
<tr>
<td>Large polygonal cell with lymphocytic infiltration and fibrous septa</td>
<td>Dysgerminoma</td>
</tr>
<tr>
<td>Skin, teeth, cartilage</td>
<td>Teratoma</td>
</tr>
</tbody>
</table>
49. Ans. is c, i.e. Serum lactic dehydrogenase

50. Ans. is b, i.e. LDH

“Unlike other germ cell tumour dysgerminoma is not associated with raised AFP and rarely increase HCG; however placental alkaline phosphate and lactate dehydrogenase are commonly produced by dysgerminomas and may be useful in monitoring the disease.”

51. Ans. is a, i.e. CA - 125

CA 125 is tumour marker of epithelial cell neoplasm (not for germ cell tumour).

52. Ans. is a, i.e. Carcinoma ovary

53. Ans. is c, i.e. Ovarian Ca

54. Ans. is c, i.e. Epithelial cell carcinoma of ovary

- 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:

<table>
<thead>
<tr>
<th>Benign condition</th>
<th>Malignant condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy</td>
<td>Endogenous</td>
</tr>
<tr>
<td>PID</td>
<td>Pneumocystis</td>
</tr>
<tr>
<td>Endometrioses</td>
<td>Carinii</td>
</tr>
<tr>
<td>Uterine fibroid</td>
<td>Causes</td>
</tr>
<tr>
<td>About 1% of normal females</td>
<td>T</td>
</tr>
</tbody>
</table>

Mnemonic: CA - 125 is raised in pregnant patient with endometrial fibroid and PID

Mnemonic: 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\textsuperscript{th} 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.
  \begin{itemize}
  \item If CA 125 levels decreases after treatment - It indicates response to treatment.
  \item If CA 125 levels increase after treatment - It indicates relapse after treatment.
\end{itemize}

- 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:
  \begin{itemize}
  \item 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.)
\end{itemize}

56. **Ans. is d, i.e. Dysgerminoma**

Ref. Novak 14\textsuperscript{th} ed p 1505

Placental alkaline phosphatase and LDH are tumour markers of dysgerminoma.

57. **Ans. is c, i.e. Inhibin**

Ref. William Gynae 1\textsuperscript{st} ed p 747

<table>
<thead>
<tr>
<th>Ovarian Tumor</th>
<th>Tumor Marker</th>
</tr>
</thead>
<tbody>
<tr>
<td>– Epithelial ovarian tumors</td>
<td>CA 125</td>
</tr>
<tr>
<td>Serous variety</td>
<td>Ca 19 – 9, CEA</td>
</tr>
<tr>
<td>Mucinous variety</td>
<td>OCCA, OCA</td>
</tr>
<tr>
<td>Serous and mucinous</td>
<td></td>
</tr>
<tr>
<td>– Endodermal sinus/Yolk sac tumor</td>
<td>AFP</td>
</tr>
<tr>
<td>– Chorio carcinoma</td>
<td>HCG</td>
</tr>
<tr>
<td>– Dysgerminoma</td>
<td>LDH, Alkaline phosphatase</td>
</tr>
<tr>
<td>– Granulosa cell tumor</td>
<td>Inhibin</td>
</tr>
</tbody>
</table>

58. **Ans. is d, i.e. Dermoid cyst**

Ref. Williams Gynae 1\textsuperscript{st} ed p 741

59. **Ans. is a, i.e. Dysgerminoma**

Ref. Jeffcoate 6\textsuperscript{th} ed p 522; Novak 14\textsuperscript{th} ed p 1519, 1517, 1514

“**Dysgerminomas are the only germ cell malignancy with a significant rate of bilateral involvement 15 to 20%.”**

**Remember**

A “**Funda”** - 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 tumour as I have said is U/L in 100% cases so it is ruled out, Dysgerminoma is bilateral in 15–20% cases.

**Embryonal cell carcinoma**

- The primary lesions tend to be large, and about two thirds are confined to one ovary at the time of diagnosis.

**In Q 59**-

Endodermal sinus tumour as I have said is U/L in 100% cases so it is ruled out, Dysgerminoma is bilateral in 15–20% cases.

**Embryonal cell carcinoma**

- The primary lesions tend to be large, and about two thirds are confined to one ovary at the time of diagnosis.

**Answer 60**

Ref. Shaw 15\textsuperscript{th} ed p 379-80

“**The metastasis of granulosa cell tumour is interesting because the opposite ovary first become involved, then metastasis develop in the lumbar 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:

<table>
<thead>
<tr>
<th>Incidence</th>
<th>Granulosa cell tumour</th>
<th>Theca cell tumour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Occurs at any age but most common after 40 years.</td>
<td>Occur after menopause</td>
</tr>
<tr>
<td>Presentation</td>
<td>In prepubertal girls it leads to precocious puberty, hypertrophy of breast.</td>
<td>Usually presents as postmenopausal bleeding.</td>
</tr>
<tr>
<td></td>
<td>In adults – leads to amenorrhoea followed by prolonged bleeding (metropathia hemorrhagica)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>In postmenopausal women – Causes Postmenopausal bleeding</td>
<td></td>
</tr>
<tr>
<td>Metastases to opposite ovary first is characteristic feature.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Remember:
- Both these tumors cause endometrial hyperplasia and so, risk of carcinoma endometrium is increased.
- 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.
- Both these tumors can cause pseudomeig syndrome.

61. Ans. is c, i.e. Omental biopsy

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

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 6th ed p 276 which says.

63. Ans. is a, i.e. Stage I

64. Ans. is d, i.e. Stage Ic

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

- Superficial liver metastasis is included in Stage III.
- Metastasis to liver parenchyma is included in Stage IV.

66. Ans. is None

Rate of malignant transformation of different tumors:
- Serous cystadenoma – 25%-40%
- Granulosa cell tumor – 50%
- Mucinous cystadenoma – 5%-10%
- Dermoid – 1.7%-2%

In ovarian cysts: “The risk of malignancy is maximum with serous cystadenoma (40%) and least with dermoid cyst (1-2%).”

Note: M.C malignancy seen with dermoid cyst is squamous carcinoma.

67. Ans. is d, i.e. Multiloculated, sticky, gelatinous fluid

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 3rd, 4th and 5th 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

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 donot hasten the resolution of existing cyst

69. Ans. is c, i.e. Surgery

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

72. Ans. is b, i.e. Laparotomy at 14–16 weeks

“Dysgerminomas are the most common malignant tumor diagnosed during pregnancy but overall most common is dermoid cyst.”

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.**

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/m²) and carboplatin (400 mg/m²) 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**

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**

- Krukenberg tumor is generally a metastatic tumor to the ovary. But “krukenberg tumor may be a primary tumor”

- 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**

**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
In postmenopausal women with unilocular cyst measuring 8–7 or less with normal several CA125 levels, expectant management is acceptable.
Vulva

Premalignant Lesions of Vulva

- VIN
- Lichen sclerosis
- Paget’s disease
- Squamous hyperplasia/hyperplastic dystrophy
- Bowen disease erythroplasia of queyrat

Classification of Epithelial Vulvar Diseases

<table>
<thead>
<tr>
<th>Non-neoplastic epithelial disorders of skin and mucosa</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Lichen sclerosis</td>
<td></td>
</tr>
<tr>
<td>Squamous hyperplasia (earlier called as hyperplastic dystrophy)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mixed neoplastic and non-neoplastic epithelial disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraepithelial neoplasia</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Squamous intraepithelial neoplasia</th>
<th>Nonsquamous intraepithelial neoplasia</th>
</tr>
</thead>
<tbody>
<tr>
<td>VIN 1</td>
<td>Paget’s disease</td>
</tr>
<tr>
<td>VIN 2</td>
<td>Tumor of melanocyte and Noninvasive</td>
</tr>
<tr>
<td>VIN 3</td>
<td></td>
</tr>
<tr>
<td>VIN 1</td>
<td></td>
</tr>
</tbody>
</table>

Invasive tumors

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
- CO₂ 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.

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.
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 lymphode 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 ≤ 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 inguinofermoral 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 until the superficial layer of urogenital fascia.
In modified radical/radical vulvectomy - dissection done until the deep fascia of urogenital diaphragm, i.e. the perineal membrane.
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.

Vaginal cancer staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Vaginal intraepithelial neoplasia (VAIN)</td>
</tr>
<tr>
<td>I</td>
<td>Carcinoma limited to the vaginal wall.</td>
</tr>
<tr>
<td>II</td>
<td>Carcinoma extending beyond the vagina, but not extending to the pelvic side walls.</td>
</tr>
<tr>
<td>III</td>
<td>Carcinoma extends up to the pelvic walls.</td>
</tr>
<tr>
<td>III</td>
<td>Carcinoma extending beyond the true pelvis or involving the bladder and/or rectum, or evidence of distal metastasis.</td>
</tr>
</tbody>
</table>

Management

- Stage I – Tumor involving upper 1/3rd vagina – Radical hysterectomy + Radical vaginectomy + bilateral pelvic lymphadenectomy
- Tumor involving lower 1/3rd 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 1/3rd 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 I b 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 cancer
    c. Vulval cancer
    d. Vaginal cancer

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

18. Most common recurrence sites or metastatic sites of malignancy following pelvic surgery are all except: *(PGI 99)*
    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: *(AIIMS May 08)*
    a. Labia majora
    b. Labia minora
    c. Prepuce of the clitoris
    d. Bartholin’s gland

### New Pattern Questions

18. Most common recurrence sites or metastatic sites of malignancy following pelvic surgery are all except: *(AIIMS May 93)*
    a. Carcinoma cervix — Lateral pelvic wall and central pelvis
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19. The most common site of vulval cancer: *(AIIMS May 93)*
    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:
   a. Common to those whose mothers were given diethylstilbestrol during early pregnancy
   b. Vaginal adenosis may progress to this condition
   c. The middle one-third is the commonest site
   d. May be multicentric and may involve even the cervix as well

21. The following primary tumours are common in the vulva except:
   a. Adenocarcinoma
   b. Basal cell carcinoma
   c. Choriocarcinoma
   d. Squamous cell carcinoma

22. All of the following statements hold true for melanoma of vulva except:
   a. It is the 2nd M/C vulval cancer
   b. M/C site is labia majora
   c. May arise from junctional nevus
   d. Has a poor prognosis
Chapter 14D  Gynecological Oncology: Miscellaneous Tumors

ANSWERS

1. Ans. is a, i.e. Squamous cell carcinoma

2. Ans. is c, i.e. III

**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**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Vaginal intraepithelial neoplasia (VAIN)</td>
</tr>
<tr>
<td>Stage I</td>
<td>Carcinoma limited to the vaginal wall.</td>
</tr>
<tr>
<td>Stage II</td>
<td>Carcinoma extending beyond the vagina, but not extending to the pelvic side walls.</td>
</tr>
<tr>
<td>Stage III</td>
<td>Carcinoma extends up to the pelvic walls.</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Carcinoma extending beyond the true pelvis/or involving the bladder and/or rectum, or evidence of distal metastasis.</td>
</tr>
</tbody>
</table>

3. Ans. is b, i.e. Condylomata acuminata

Verrucous carcinoma is variant of squamous cell carcinoma of cervix.
“Verrucous carcinomas may resemble giant condyloma acuminatum, are locally invasive and rarely metastasise.”

Condylomata acuminata is an STD (due to HPV 6 and HPV 11 infection) and has a verrucous appearance.

4. Ans. is d, i.e. HPV 6

“Low Risk HPV types 6 and 11 cause nearly all genital warts.”

**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, polyphitic 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 cavitational ultrasonic surgical aspiration.

**Medical Management of Genital Warts:**

- Topical 5-percent imiquimod cream (immunomodulator)
- Podophyllin (antimitotic agent)
- Trichloroacetic acid (proteinolytic agent)
- Bichloroacetic acid (proteinolytic 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

**Premalignant lesion of vulva:**
- Vulvar intraepithelial neoplasia VIN (most common)
- Chronic vulvar dystrophies
- Lichen sclerosis
- Erythroplasia of Queyrat

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

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:

<table>
<thead>
<tr>
<th>Non-neoplastic epithelial disorders of skin and mucosa</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Lichen sclerosis</td>
</tr>
<tr>
<td>• Squamous hyperplasia (earlier called as hyperplastic dystrophy)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mixed neoplastic and non-neoplastic epithelial disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraepithelial neoplasia</td>
</tr>
<tr>
<td>• VIN 1</td>
</tr>
<tr>
<td>• VIN 2</td>
</tr>
<tr>
<td>• VIN 3</td>
</tr>
<tr>
<td>• VIN 1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Non-squamous intraepithelial neoplasia</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Paget’s disease</td>
</tr>
<tr>
<td>• Tumor of melanocyte, Noninvasive</td>
</tr>
</tbody>
</table>

“The malignant potential of the non-neoplastic epithelial disorders is low but patients with lichen sclerosis and concomitant hyperplasia may be at high risk.”

So I am taking option “a” and “c” as correct.

Condyloma acuminiata (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 veneral granulomas and vulvar warts with 20-30 years standing.”

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 leison 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.

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

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 viurses - HIV, HPV, HSV-II).
• Most common site – Labia majora (Anterior 2/3rd) followed by clitorus and labia minora.
• Associated with cervical cancer in 20% cases.
• Presents with pruritus and visible leison. All though pain, bleeding and ulceration also may be the initial complain.
• 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.

**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
   - Radiotherapy is recommended in advanced stages of Ca cervix i.e. stage IIB onwards.
   - 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.
   - Vaginal squamous cell Ca is only moderately sensitive to irradiation.
   - In all advanced cases exenteration operation is done.
   - 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.

9. Ans. is b, i.e. 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.
   - Secretes estrogen
   - Secretes estrogen
   - Secretes androgens

10. Ans. is a, i.e. Carcinoma endometrium

11. Ans. is a, i.e. Carcinoma vulva

Pyometra is collection of pus or mixture of pus and blood within the uterus.

**Causes:**
- Most common cause: *carcinoma endometrium.*
- 2nd most common cause: *semale endometritis.*

**Other causes:**
- Congenital atresia of the vagina/cervix.
- Stenosis of cervix/vagina following:
  - Operations
  - Burns
  - Radiotherapy
  - Senile
  - Tuberculous
  - Puerperal
- Endometritis:
- Carcinoma:
  - Ca endometrium (most common)
12. Ans. is a, i.e. Watery discharge P/V

- 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

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 CIN1I, CIN1II and ca in situ.

14. Ans. is c, i.e. Vulval ca

- 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.

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.

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

Treatment of leukoplakia:

<table>
<thead>
<tr>
<th>Treatment of the cause</th>
<th>General treatment</th>
<th>Empirical measures (when cause can not be treated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia correction</td>
<td>Sedatives - to prevent scratching and to ensure sleep</td>
<td>Corticosteroids (mainstay of therapy)³</td>
</tr>
<tr>
<td>Folic acid and vit B12 (given in case of deficiency)</td>
<td>Cold cream application</td>
<td>Estrogens and testosterone⁴</td>
</tr>
<tr>
<td>Treatment of candidiasis</td>
<td>Washing with 1% sodium bicarbonate</td>
<td>Local analgesia</td>
</tr>
<tr>
<td></td>
<td>Use of loose and light cotton underclothing</td>
<td>Division of cutaneous nerves; nerve block</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cod liver oil or cream of zinc oxide &amp; olive oil</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Local applications</td>
</tr>
<tr>
<td></td>
<td></td>
<td>For refractory lesion intralesional injection of triamcinolone acetonide may be tried.</td>
</tr>
</tbody>
</table>
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.

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

<table>
<thead>
<tr>
<th>Screening test</th>
<th>Disease screened</th>
</tr>
</thead>
<tbody>
<tr>
<td>Papanicolaou (Pap’s) smear</td>
<td>Cervical cancer</td>
</tr>
<tr>
<td>Mammography</td>
<td>Breast cancer</td>
</tr>
<tr>
<td>CA-125</td>
<td>Ovarian cancer</td>
</tr>
</tbody>
</table>

**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.

<table>
<thead>
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</tr>
</thead>
<tbody>
<tr>
<td>Papanicolaou (Pap’s) smear</td>
<td>Cervical cancer^2</td>
</tr>
<tr>
<td>Mammography</td>
<td>Breast cancer^2</td>
</tr>
<tr>
<td>Bimanual oral examination</td>
<td>Oral cancer^2</td>
</tr>
<tr>
<td>ELISA</td>
<td>HIV^2</td>
</tr>
<tr>
<td>Urine for sugar, Random blood sugar</td>
<td>Diabetes mellitus^2</td>
</tr>
<tr>
<td>AFP</td>
<td>Developmental anomalies in fetus^2</td>
</tr>
<tr>
<td>DRE + PSA</td>
<td>Prostate cancer^2</td>
</tr>
<tr>
<td>Fecal occult blood test</td>
<td>Colorectal cancer^2</td>
</tr>
<tr>
<td>CA-125</td>
<td>Ovarian cancer^2</td>
</tr>
</tbody>
</table>

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^th ed p 360, 354,376

**Endometrial cancer/cancer body uterus**

**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**

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, urethral 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

**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

**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

**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

**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

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.
1. Hysteroscopy means visualization of:  
   a. Genital tract  
   b. Fallopian tube  
   c. Uterine cavity  
   d. Cervix  
   e. Abdominal cavity  

2. For hysteroscopy, following are/is used:  
   a. Distilled Water  
   b. Air  
   c. Glycine  
   d. CO$_2$

3. Hysteroscopy can diagnose all, except:  
   a. Asherman’s syndrome  
   b. Septate uterus  
   c. Adenomyosis  
   d. TB endometritis

4. Hysteroscopy is used in all EXCEPT:  
   a. Uterine synechiae  
   b. Abnormal vaginal bleeding  
   c. Infertility  
   d. Recurrent still birth and abortions

5. Asherman’s syndrome can be diagnosed by all except:  
   a. Hysterosalpingography  
   b. Saline sonography  
   c. Endometrial culture  
   d. Hysteroscopy

6. Best gas used for creating pneumoperitoneum at laparoscopy is:  
   a. N$_2$  
   b. O$_2$  
   c. CO$_2$  
   d. N$_2$O

7. Laparoscopy is best avoided in patients with:  
   a. Hypertension  
   b. Diabetes  
   c. Obesity  
   d. COPD

8. Laparoscopy is contraindicated in:  
   a. Ectopic pregnancy  
   b. PID  
   c. Endometriosis  
   d. Peritonitis

9. A 26-year-old female with 3 living issues having cervical erosion which bleeds to touch, diagnosis can be done by:  
   a. Pap smear  
   b. Excision biopsy  
   c. Hysteroscopy  
   d. Colposcopy

10. Occurrence of ovulation is indicated by:  
    a. LH  
    b. FSH  
    c. Estradiol  
    d. Progesterone  
    e. Cortisol

11. Time of ovulation is detected by:  
    a. Urine LH  
    b. Urine FSH  
    c. Urine HCG  
    d. Serum Estradiol  
    e. BBT

12. Which of the following methods for assessment of female infertility during a menstrual cycle can best predict timing of ovulation:  
    a. BBT  
    b. Fern Test  
    c. Spin Barkeit Phenomenon  
    d. Hormonal Study

13. Best indicator of ovarian reserve is:  
    a. FSH  
    b. Estradiol  
    c. LH  
    d. FSH/LH Ratio

14. Goniometer is used for:  
    a. Amount of vaginal secretions  
    b. To measure width of genital hiatus  
    c. Gonococcal colony count  
    d. Urethrovesical angle

15. Feature of post ovulatory endometrium on ultrasound is:  
    a. Single hyperechoic thin line  
    b. Three line sign  
    c. Prominent halo  
    d. Prominent posterior enhancement

16. Luteal phase defect is best diagnosed by:  
    a. Serum progesterone levels  
    b. Endometrial biopsy  
    c. Basal body temperature  
    d. Ultrasonography

17. Chassarmoir surgery is done in case of:  
    a. Uterine inversion  
    b. VVF repair  
    c. Ureterovesical fistula repair  
    d. Retroverted uterus

18. All of the following are advantages of vaginal hysterectomy over abdominal hysterectomy except:  
    a. Better tolerated by elderly and obese patients  
    b. Lesser risk of postoperative thromboembolism  
    c. Other visceral structures can be easily visualized  
    d. Corrects prolapse of other organs
19. Maximum chances of ureteric injury are with:  
   a. TAH 
   b. Wertheims hysterectomy 
   c. Anterior colporrhaphy 
   d. Vaginal hysterectomy

20. Transcervical endometrial resection (TCRE) is used in:  
   a. Endometriosis  
   b. DUB  
   c. Carcinoma endometrium  
   d. Submucous fibroid 

NEW PATTERN QUESTIONS

21. Cryosurgery is effective in all except:  
   a. Chronic cervicitis  
   b. Squamous intraepithelial lesion (SIL)  
   c. Condyloma acuminate  
   d. Cases with severe dysplasia or CIS lesion 

22. Regarding outpatient hysteroscopy all are correct except:  
   a. Abnormal uterine bleeding is an indication  
   b. Normal saline as distension medium can be used  
   c. It is less accurate than saline infusion sonography (SIS)  
   d. It is not reliable to exclude endometrial carcinoma 

23. To minimize ureteric damage, the following preoperative and operative precautions may be taken except:  
   a. Cystoscopy  
   b. Direct visualization during surgery  
   c. Ureter should not be dissected off the peritoneum for a long distance  
   d. 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:  
   a. In cases with müllerian agenesis  
   b. In virgin females  
   c. To differentiate rectocele from enterocele  
   d. For staging of ovarian malignancy 

25. The advantages of cryosurgery over electrocauterization are all except:  
   a. Less discomfort to the patient  
   b. Postoperative bleeding is much less  
   c. Postoperative vaginal discharge is also much less  
   d. Cervical stenosis is extremely rare 

26. Position of the patient should be as described except:  
   a. Diagnostic laparoscopy — Trendelenburg with about 30° tilt  
   b. Colposcopy — Lithotomy  
   c. Transvaginal sonography in gynecology — Lithotomy with full bladder  
   d. Hysteroscopy — Lithotomy 

27. Absolute contraindications of laparoscopy are:  
   a. Diaphragmatic hernia  
   b. Generalized peritonitis  
   c. Patient on anticoagulant therapy  
   d. Previous incomplete laparoscopy 

28. As regards the use of laser in gynecology, all are correct except:  
   a. Management of CIN, VIN, VAIN  
   b. Laser laparoscopy for ectopic pregnancy  
   c. Laser hysteroscopy for presacral neurectomy  
   d. 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 CO₂
3. Ans. is c, i.e. Adenomyosis


- Hysteroscopy is the endoscopic technique of visualizing the interior of uterus directly.
- 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 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 CO₂, 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 – CO₂
Most common media used for therapeutic purpose – Glycine

Contraindication:
- Infection (except in case of misplaced IUCD)
- Pregnancy
- Genital malignancy

Diagnostic Indications of hysteroscopy:
Friends, let’s 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.
- Any uterine synechiae (as in Ashermann syndrome).
- Misplaced IUCD.
- Submucous fibroid

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.
- Pregnancy related conditions like : Molar tissue or products of conception.

Besides these hysteroscopy is also indicated in:
- Unexplained abnormal uterine bleeding
- Premenopausal
- Postmenopausal
- Selected infertility cases: In case of
  - Abnormal HSG
  - Unexplained infertility
- Recurrent spontaneous abortion
  - The therapeutic indications of hysteroscope are (here also don’t mug up, just try to understand them).
  - To excise uterine septum
  - To lyse adhesions in Ashermann’s syndrome
  - To retrieve lost IUCD
  - Hysteroscopic myomectomy
  - Polypectomy
  - Endometrial ablation for menorrhagia
  - Tubal occlusion for control of fertility
  - Intratubal ballooning in tubal blockage
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."

Also know:

| Technique for visualization of | \[ | \] |
|-------------------------------|-------------------------------|
| Cervix | Colposcopy |
| Fallopian tube | Salpingoscopy |
| – To see its mucosa | Falloscopy |
| – To see its lumen | Laparoscopy |

4. Ans. is d, i.e. Recurrent still birth and abortions

Hysteroscopy is used undoubtedly in:

- Uterine synechiae i.e. Ashermann syndrome - Hysteroscopy is the gold standard technique for diagnosing uterine synechiae (Ashermann 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)".
- 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."

But hysteroscopy is not useful in recurrent still births.

5. Ans. is c, i.e. Endometrial culture

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
- Abortion
- Diagnosis:
  - 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. CO₂
7. Ans. is d, i.e. COPD
8. Ans. is d, i.e. Peritonitis

Important points to remember on laparoscopy:
- CO₂ is currently the insufflation gas of choice for laparoscopy. It fulfills most of the requirements for an ideal insufflation gas, being colorless, nonflammable and rapidly excreted from the circulation. Other alternative is N₂O: But it is expensive, less soluble in blood and supports combustion.
- Instrument used for creating pneumoperitoneum is veress needle.
- It should be inserted at an angle of 45 degrees to the spine.
- Flow rate of CO₂ 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.

Ref. Williams Gynae 1st/ed p 932, COGDT 10th/ed p 801-2

<table>
<thead>
<tr>
<th>Absolute</th>
<th>Relative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intestinal obstruction</td>
<td>Previous periumbilical surgery</td>
</tr>
<tr>
<td>Generalized peritonitis</td>
<td>Cardiac or pulmonary disease</td>
</tr>
<tr>
<td>Massive hemorrhage</td>
<td>Shock</td>
</tr>
<tr>
<td>Cancer involving anterior abdominal wall</td>
<td></td>
</tr>
</tbody>
</table>

Contraindications of laparoscopy

Additional factors weighing against performing laparoscopy surgery are:
- Extremes of weight.
- Intrauterine pregnancy after first or early 2nd trimester.
- Presence of large mass. i.e. abdominal tumor, large uterus
- IBD (inflammatory bowel disease)
- Known severe intraperitoneal adhesions.
- Umbilical hernia and diaphragmatic hernia.

9. Ans. is a, b and d, i.e. Pap smear; Excision biopsy; and Colposcopy

Cervical erosion (ectopy) is condition where the squamous epithelium of ectocervix is replaced by columnar epithelium of endocervix.

Etiology:

<table>
<thead>
<tr>
<th>Congenital</th>
<th>Acquired Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hormonal</td>
<td></td>
</tr>
<tr>
<td>During pregnancy</td>
<td>Chronic cervicitis</td>
</tr>
<tr>
<td>In pill users</td>
<td></td>
</tr>
</tbody>
</table>

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.

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.”

“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.”

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

   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 7th 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


   “Ovarian reserve refers to the size of the non-growing or resting, primordial follicle population which presumably determines the number of growing follicles and the quality or reproductive potential of their oocytes.”

   ... Novak 14th 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:

<table>
<thead>
<tr>
<th>Serum day 3 FSH and estradiol levels</th>
<th>Clomiphene citrate challenge test</th>
<th>Serum Inhibin B</th>
<th>TVS</th>
</tr>
</thead>
<tbody>
<tr>
<td>• An elevated baseline FSH on day 3 indicates decreased ovarian reserve due to aging of ovaries</td>
<td>• This test helps to detect those cases of decreased ovarian reserve which show normal day 3 FSH.</td>
<td>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.</td>
<td>Assesses atrial follicle number &amp; ovarian size</td>
</tr>
<tr>
<td>• FSH &gt; 40 mIU and serum estradiol indicates absence of ovarian follicles.</td>
<td>• It measures serum FSH &amp; estradiol on day 3 &amp; again on day 10 after administering clomiphene citrate (100 mg) from D5 to D9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Serum FSH is the best predictor of ovarian reserve</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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/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.

<table>
<thead>
<tr>
<th>AMH levels (ng/ml)</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.0–6.8</td>
<td>Optimal fertility</td>
</tr>
<tr>
<td>2.2–4.0</td>
<td>Satisfactory fertility</td>
</tr>
<tr>
<td>0.3–2.2</td>
<td>Low fertility</td>
</tr>
<tr>
<td>&lt;0.3</td>
<td>Very low fertility</td>
</tr>
<tr>
<td>&gt;6.8</td>
<td>High levels (PCOS and granulosa cell tumor)</td>
</tr>
</tbody>
</table>
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 1st 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
  Three line sign.

- **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
  Loss of three line sign
  Prominent posterior enhancement

16. Ans. is b, i.e. Endometrial biopsy
   Ref. Shaw 14th ed p 30-1; Dutta Gynae 5th ed p 230; Novak 15th 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

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Done in</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Kelly stitch/Boney’s Test/ Marshall Marchetti Krantz Surgery</td>
<td>Stress Urinary Incontinence</td>
</tr>
<tr>
<td>2. Chassar Moir Technique/Latzko technique/layer technique</td>
<td>VVF Repair</td>
</tr>
<tr>
<td>3. Boari Flap Technique</td>
<td>Urethrovaginal Fistula repair</td>
</tr>
<tr>
<td>4. Purandare Sling/Fothergill’s Repair/Manchester Repair/Ward Mayo Hysterectomy/ Lefort’s Colpocleisis</td>
<td>Prolapse Uterus</td>
</tr>
<tr>
<td>5. Strassman Unification Surgery</td>
<td>Bicornuate/Didelphic uterus (Indication for operation, if bicornuate or didelphic uterus lead to &gt;3 Abortion)</td>
</tr>
<tr>
<td>6. Hysteroscopic Septal Resection (M/c done), Jones/Thompkins/ Williams metroplasty</td>
<td>Septate Uterus</td>
</tr>
<tr>
<td>7. McIndoe Vaginoplasty</td>
<td>MRKH Syndrome/Vaginal agenesis (Best time to perform this surgery is just before/just after marriage)</td>
</tr>
<tr>
<td>8. Mc Donald/Shirodkar Cerclage</td>
<td>Incompetent Internal os</td>
</tr>
<tr>
<td>9. Baldy Webster operation, Modified Gilliams operation, Laparoscopic ventrosuspension</td>
<td>Retroversion of the uterus</td>
</tr>
<tr>
<td>10. Hautains Operation (via abdominal route), Spinellis operation (via vaginal route)</td>
<td>Inversion of uterus</td>
</tr>
</tbody>
</table>

18. Ans. is c, i.e. other visceral structures can be easily visualized

Vaginal Hysterectomy

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Can be done in obese patients</td>
<td>• Exploration of abdominal organs and pelvic organs cannot be done</td>
</tr>
<tr>
<td>• Less postoperative complications</td>
<td>• Tubo-ovarian pathologies cannot be simultaneously dealt</td>
</tr>
<tr>
<td>• Less morbidity and mortality</td>
<td>• Difficult to perform if uterus is &gt;12 weeks size and if pelvic adhesions are present</td>
</tr>
<tr>
<td>• Less postoperative pain</td>
<td>• Concurrent surgical procedures cannot be done</td>
</tr>
<tr>
<td>• Less hospital stay</td>
<td></td>
</tr>
<tr>
<td>• No abdominal scar</td>
<td></td>
</tr>
<tr>
<td>• Early resumption of day to day activities</td>
<td></td>
</tr>
</tbody>
</table>

19. Ans. is b, i.e. Wertheims hysterectomy

<table>
<thead>
<tr>
<th>Terminology</th>
<th>Structures Removed</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Total hysterectomy /Simple Hysterectomy</td>
<td>Whole uterus+ whole of cervix (TAH; Type I hysterectomy)</td>
</tr>
<tr>
<td>• Pan hysterectomy</td>
<td></td>
</tr>
<tr>
<td>• Modified radical hysterectomy/Wertheim’s hysterectomy (Type II hysterectomy)</td>
<td>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</td>
</tr>
<tr>
<td>• Radical/Modified Wertheims hysterectomy</td>
<td>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</td>
</tr>
<tr>
<td>• Extended Radical hysterectomy (Type IV)</td>
<td>Radical hysterectomy + 3/4th of vagina+ Periureteral tissue + Superior vesical artery.</td>
</tr>
</tbody>
</table>

- 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 5th 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 up to 1.6% for laparoscopic cases and to as high as 30% for some older series of Wertheim’s Radical Hysterectomies.”... CGDT 10th ed p 779

**Also know**

Piver Rutledge classification of types of hysterectomy

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type I</td>
<td>Total Abdominal Hysterectomy.</td>
</tr>
<tr>
<td>Type II</td>
<td>Wertheim's hysterectomy</td>
</tr>
<tr>
<td>Type III</td>
<td>Radical hysterectomy/ Meigs hysterectomy</td>
</tr>
<tr>
<td>Type IV</td>
<td>Extended radical hysterectomy</td>
</tr>
<tr>
<td>Type V</td>
<td>Complete pelvic extenteration</td>
</tr>
</tbody>
</table>

20. **Ans. is b i.e. DUB**

Ref. Shaw 15th ed pg -305; Bijoy Sree Sen Gupta 2nd ed p 151 - 152; Williams Gynae 1st 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 synchiae → 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 endometrium, 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:** ... Williams Gynae 1st ed p 188
  - 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

21. **Ans. is d, i.e. Case with severe dysplasia or CIS lesion**

Ref. Dutta Gynae 6th 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°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 far 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**

**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**
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**

**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.
1. CA 125 is elevated in all except:  
   a. Tuberculosis  b. Endometriosis  
   c. Ovarian tumor  d. Polycystic ovarian disease  

2. A 21-year-old unmarried woman has premenstrual fullness of breast and pain, the likely diagnosis is:  
   a. Galactocele  b. Fibroadenosis  
   c. Fibroadenoma  d. Mastitis  

3. Corpus luteum cyst occurs due to:  
   a. HCG  b. HPL  
   c. Estrogen  d. Progesterone  

4. In those mammals which are seasonal breeder, the females are receptive only once in a year; the cycle is termed as:  
   a. Follicular  b. Estrous  
   c. Menstrual  d. Luteal  

5. Which of the following is true regarding precocious puberty?  
   a. Sexual maturity is attained early  
   b. Mental function is increased  
   c. No reproductive function  
   d. Body proportions are enlarged  

6. Menstruation is defined as precocious if it starts before the child reaches the age of:  
   a. 8 years  b. 10 years  
   c. 14 years  d. 20 years  

7. Primary peritonitis is more common in females because:  
   a. Ostia of fallopian tubes communicate with abdominal cavity  
   b. Peritoneum overlies the uterus  
   c. Rupture of functional ovarian cysts  
   d. None of the above  

8. Postmenopausal estrogen production is due to:  
   a. Peripheral aromatization of androstenedione  
   b. Adrenal – direct production  
   c. Ovarian tumor  
   d. Ovary testosterone secretion  

9. 40 years female, mass in pelvis detected clinically, following investigations should be done except:  
   a. CT  b. Laparoscopy  
   c. Pap smear  d. USG  

10. A female presents to gynecological OPD with complain of cyclical pain, dyspareunia and infertility. The best investigation to establish the diagnosis would be:  
   a. TVS  b. Diagnostic laparoscopy  
   c. Hormonal study  
   d. Aspirate from the pouch of Douglas  

11. These are the names with associated conditions—match the following:  
   a. Henry Turner  1. Repair of bladder fistula  
   b. John Tanner  2. Primary amenorrhea with delayed secondary sex characters  
   c. Marion Sims  3. Surgery for carcinoma cervix  
   d. Joe Meige  4. Staging of puberty changes  

12. Causes of vulval pain are due to all except:  
   a. Neuralgia of the genitofemoral nerve  
   b. Herpes  
   c. Vulval vestibulitis syndrome  
   d. Lichen sclerosus  

13. Match the names associated in the treatment of stress incontinence:  
   a. Osteitis pubis  1. Raj and Stamey  
   c. Cystoscopy  3. Aldridge sling  
   d. Cystourethroplasty  4. Howard Kelly  

14. Match the following appropriately:  
   a. Asherman’s syndrome  1. Chronic pelvic pain  
   b. Rokitansky-Küster-Hauser syndrome  2. Secondary amenorrhea  
   c. Toxic shock syndrome  3. Primary amenorrhea  
   d. Ovarian remnant syndrome  4. Menstruation and use of tampons
1. Ans. is d, i.e. Polycystic ovarian disease (PCOD)

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

<table>
<thead>
<tr>
<th>Neoplastic conditions</th>
<th>Non-neoplastic/Benign conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gynecological</td>
<td></td>
</tr>
<tr>
<td>Ovarian cancer (nonmucinous)</td>
<td></td>
</tr>
<tr>
<td>Endometrial cancer</td>
<td></td>
</tr>
<tr>
<td>Tubal cancer</td>
<td></td>
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<tr>
<td>Non-gynecological</td>
<td></td>
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<tr>
<td>Lung cancer</td>
<td></td>
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<tr>
<td>Breast cancer</td>
<td></td>
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<tr>
<td>Ca Pancreas</td>
<td></td>
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<tr>
<td>Colon cancer</td>
<td></td>
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<tr>
<td>Endometriosis</td>
<td></td>
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<tr>
<td>Peritoneal inflammation, including PID</td>
<td></td>
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<tr>
<td>Tuberculosis</td>
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<tr>
<td>Hemorrhagic ovarian cysts</td>
<td></td>
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<tr>
<td>Liver disease</td>
<td></td>
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<tr>
<td>Leiomyoma</td>
<td></td>
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<tr>
<td>Pregnancy</td>
<td></td>
</tr>
<tr>
<td>Physiological</td>
<td></td>
</tr>
<tr>
<td>Menstruation</td>
<td></td>
</tr>
</tbody>
</table>

2. Ans. is b, i.e. Fibroadenosis

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

Lutein cysts of ovary

Granulosa lutein cyst
- Functional, non neoplastic enlargement of the ovary.
- Persistent corpus luteum cyst may cause local pain, tenderness or delayed menstruation
- Cysts are often palpable clinically
- Usually resolve spontaneously

Theca lutein cyst
- They are associated with trophoblastic disease, chorionic gonadotrophin therapy (HCG) & clomiphene therapy
- They are bilateral and filled with straw coloured fluid.
- They resolve spontaneously after elimination of the H mole, therapeutic curettage, destruction of choriocarcinoma or discontinuation of gonadotropin therapy

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  

**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

6. Ans. is b, i.e. 10 years

**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

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

- 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.
- Main estrogen in pregnancy is oestriol.

9. Ans. is b, i.e. Laparoscopy

**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.**

<table>
<thead>
<tr>
<th>Conditions diagnosed as a pelvic mass in women of reproductive age:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Full urinary bladder</td>
</tr>
<tr>
<td>- Sharply anteflexed or retroflexed uterus</td>
</tr>
<tr>
<td>- Ovarian or adnexal masses</td>
</tr>
<tr>
<td>- Functional cysts</td>
</tr>
<tr>
<td>- Inflammatory masses</td>
</tr>
<tr>
<td>- Tubo-ovarian masses</td>
</tr>
<tr>
<td>- Diverticular abscess</td>
</tr>
<tr>
<td>- Appendiceal abscess</td>
</tr>
<tr>
<td>- Paraovarian or paratubal cysts</td>
</tr>
<tr>
<td>- Intraligamentous myomas</td>
</tr>
<tr>
<td>- Urachal cyst</td>
</tr>
<tr>
<td>- Pregnancy (with or without concomitant leiomyomas) / ectopic pregnancy</td>
</tr>
<tr>
<td>- Matted bowel loops &amp; omentum</td>
</tr>
<tr>
<td>- Peritoneal cyst</td>
</tr>
<tr>
<td>- Stool in sigmoid colon</td>
</tr>
<tr>
<td>- Neoplastic tumors:</td>
</tr>
<tr>
<td>- Benign</td>
</tr>
<tr>
<td>- Malignancy</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Less common conditions that must be excluded:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Pelvic kidney</td>
</tr>
<tr>
<td>- Carcinoma of the colon, rectum and appendix</td>
</tr>
<tr>
<td>- Carcinoma of the fallopian tube</td>
</tr>
<tr>
<td>- Retroperitoneal tumors (anterior sacral meningocele)</td>
</tr>
<tr>
<td>- Uterine sarcoma or other malignant tumors.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Investigations to done:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Complete pelvic examination including rectovaginal examination</td>
</tr>
<tr>
<td>- Lab investigation - complete hemogram, ESR, test of stool or occult blood</td>
</tr>
<tr>
<td>- Pap smear</td>
</tr>
<tr>
<td>- Urine pregnancy test</td>
</tr>
</tbody>
</table>
• 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

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. 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

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
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 Gonorrhea
   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
1. **Ans. is b i.e. PreMenstrual Tension**  
   See Q. 52 of chapter 10 for Explanation  
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.

3. **Ans. is b i.e. Can be fertile with ovum donation**  
   *Ref. Shaw’s Textbook of Gynecology 15/e p145*

---

**EXPLANATIONS**

**1. Ans. is b i.e. PreMenstrual Tension**  
   *Ref. Williams Obstetrics 24/e p701*

**2. Ans. is c i.e. 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

5. Ans. is a i.e. Endometrial polyp
   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
   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
   See chapter 10 for details

8. Ans. is a i.e. Serum FSH > 40
   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
   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
    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.
1. A 18-year-old girl presented to the gynecology OPD with amenorrhea. 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. Methyline 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 variies
   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**
   See Ans. 22, Chapter 6 of the guide

2. **Ans. is a i.e. Ureterovaginal fistula**
   The site of the fistula can be determined by the complaint and also by Methyline Blue 3 Swab test.

<table>
<thead>
<tr>
<th>Complaint</th>
<th>Urogenital fistula</th>
</tr>
</thead>
<tbody>
<tr>
<td>• H/O normal voiding + Continuous dribbling of urine from vagina</td>
<td>Ureterovaginal fistula</td>
</tr>
<tr>
<td>• Continuous dribbling of urine from vagina but no normal voiding</td>
<td>Vesicovaginal fistula</td>
</tr>
<tr>
<td>• No continuous leakage but when patient urinates, urine comes out from urethra and vagina</td>
<td>Urethrovaginal fistula</td>
</tr>
</tbody>
</table>

For details of methylene blue 3 swab test-Refer chapter 8 of the guide.

<table>
<thead>
<tr>
<th>Observation</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper most swab soared with urine (yellow) but not with dye. Remaining 2 swabs unstained</td>
<td>Ureterovaginal fistula</td>
</tr>
<tr>
<td>Upper and lower remain dry but middle swab soaked with dye. The upper two swabs remain dry but lower soared with dye</td>
<td>Vesicovaginal fistula</td>
</tr>
</tbody>
</table>
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 Sha’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, Krukenburg 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%

<table>
<thead>
<tr>
<th>Semen characteristics</th>
<th>WHO 1999</th>
<th>WHO 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume (ml)</td>
<td>≥ 2</td>
<td>≥ 1.5</td>
</tr>
<tr>
<td>Sperm count (10^6/mL)</td>
<td>≥ 20</td>
<td>≥ 15</td>
</tr>
<tr>
<td>Total sperm count (10^9)</td>
<td>≥ 40</td>
<td>≥ 39</td>
</tr>
<tr>
<td>Total motility (%)</td>
<td>≥ 50</td>
<td>≥ 40</td>
</tr>
<tr>
<td>Progressive motility (%)</td>
<td>≥ 25%</td>
<td>≥ 32%</td>
</tr>
<tr>
<td>Vitality (%)</td>
<td>≥ 75</td>
<td>≥ 58</td>
</tr>
<tr>
<td>Morphology (%)</td>
<td>14</td>
<td>≥ 4</td>
</tr>
</tbody>
</table>
1. All are true about polycystic ovarian disease (PCOD) except:
   a. Testosetrone > 2 ng/ml
   b. Infertility
   c. High FSH/LH ratio
   d. ↑ Insulin level
   d. ↑E_2/oestrone(E_1)ratio

2. Not true about Endometriosis:
   a. Sampson gave implantation theory
   b. Cause infertility
   c. Laproscopy 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. ~ 0.05% 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 abot 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 pili:
   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
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**

   **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**
   - The age of the husband should not ordinarily be less than 225 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 r 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.

5. **Ans. is a, and e i.e. > 50% Testosterone secreted from ovary, and daily production of testosterone is 0.2–0.3% mg**

   **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
   - 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)
   - Timing of insertion:
     1. Interval insertion - Insertion-6 weeks after parturition or MTP or abortion
     2. Insertion immediately after delivery or 1st 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 2nd trimester abortion - Insertion should be done after uterine involution
     6. Post cortisol insertion - As an emergency contraceptive

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.
   - Many women can be prescribed hormonal contraception without clinical breast and pelvic examination (Thus, option ‘a’ is incorrect)
   - 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, palpation 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 xanthosis
   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**
   - 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 mcg/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**

    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.**

For details of dysgerminoma — see chapter 14c of the guide

12. **Ans is a and c, i.e. Legs are more in length than trunk and gynaeromastia.**

13. **Ans is b, c and d i.e. Fractional cumettage, aspiration cytology from uterus and hysteroscopy and biopsy.**

**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.
Klinefelter syndrome

Genotype = 47 XXY

M/c cause of primary testicular failure

- Testes — small, firm and damage to Leydig cells and Sertoli cells cryptorchidism

- Undervirilized
  - Testosterone converts to estrogen
  - leads to gynecomastia

- Length of arms and legs is increased

↓ Sperm count

↓ Testosterone

↑ LH and FSH

Using TESE — (Normal pregnancies have been achieved in congenital or acquired testicular failure post chemotherapy, azoospermia and Klinefelter syndrome)

Fertility can be achieved by IVF or ICSI following retrieval of sperms using TESE

- Long repetitive CAG sequences—called Polymorphism
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)
   For details see chapter 14A of the guide

2. Ans. is b, c and d i.e T. Vaginals is a flagellated protozoa, metronidazole is used for treatment, and strawberry cervix.
   Infection in genital tract may be responsible for sporadic abortion but its relation to recurrent abortion is inconclusive.

3. Ans. is b, d and e i.e. LNG containing IUD, suppression of endometrium and no significant effect on ovaries
   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
   Absolute - Periperal Sepsis, pregnancy
   Don’t- DUB
   Try to- Gestational Trophloptic 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

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
   All the options have been explained earlier in the guide
Annexures

Annexure 1

Lining of Female Genital Tract

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

Blood Supply of Genital Tract

<table>
<thead>
<tr>
<th>Organ</th>
<th>Supplied By</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uterus</td>
<td>Uterine artery (branch of ant. div. of internal iliac artery) and ovarian artery.</td>
</tr>
<tr>
<td>Cervix</td>
<td>Descending cervical artery (branch of uterine artery).</td>
</tr>
<tr>
<td>Vagina</td>
<td>Vaginal artery (Separate branch of int. iliac artery or may come from uterine artery), branches of int. pudendal, middle and inferior rectal arteries.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Organ</th>
<th>Supplied By</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovary</td>
<td>Ovarian artery (branch of aorta).</td>
</tr>
<tr>
<td>Vulva</td>
<td>Internal pudendal artery (terminal branch of int. iliac artery).</td>
</tr>
</tbody>
</table>

Annexure 2

Lymphatic Drainage of Female Genitalia

<table>
<thead>
<tr>
<th>Organ</th>
<th>Lymphatic drainage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovaries</td>
<td>Para–aortic lymph node (lateral aortic nodes)</td>
</tr>
<tr>
<td>Fallopian Tube</td>
<td>Along ovarian lymphatic</td>
</tr>
<tr>
<td></td>
<td>Along cornua</td>
</tr>
<tr>
<td></td>
<td>Lateral aortic lymph node</td>
</tr>
<tr>
<td></td>
<td>Superficial inguinal lymph node</td>
</tr>
<tr>
<td>Uterus</td>
<td>Lateral aortic lymph node</td>
</tr>
<tr>
<td></td>
<td>External iliac lymph node</td>
</tr>
<tr>
<td></td>
<td>Superficial inguinal lymph node (along round ligament)</td>
</tr>
<tr>
<td></td>
<td>H – Hypogastric lymph node/internal iliac</td>
</tr>
<tr>
<td></td>
<td>O – Obturator lymph node</td>
</tr>
<tr>
<td></td>
<td>P – Presacral lymph node and parametrial lymph node (sentinel lymph node)</td>
</tr>
<tr>
<td></td>
<td>E – External iliac lymph node</td>
</tr>
</tbody>
</table>

(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. 1st lymph node involved in cancer cervix–parametrial lymph node or paracervical lymph node (also called as ureteric lymph node).  

Contd...
Self Assessment & Review: Gynecology

Organ | Lymphatic drainage
--- | ---
**Vagina:**
- Upper part
- Middle part
- Lower
  - Same like cervix.
  - Internal iliac lymph node.
  - Superficial inguinal lymph node.

**Vulva**
- Superficial inguinal lymph node (sentinel lymph node)
- Deep inguinal lymph node
- Internal iliac nodes

**Clitoris**
- Superficial + deep inguinal lymph node.
- The anterior most lymph node of deep inguinal group is called as lymph node of cloquet/ Rosenmuller lymph node

Annexure 3

**pH of vagina at different ages:**

<table>
<thead>
<tr>
<th>Age</th>
<th>Vaginal pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborn infants</td>
<td>Between 4–5</td>
</tr>
<tr>
<td>6 weeks old child</td>
<td>6–8</td>
</tr>
<tr>
<td>Puberty</td>
<td>Charges from alkaline to acidic</td>
</tr>
<tr>
<td>Reproductive age group</td>
<td>4–5.5</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>3.5–4.5</td>
</tr>
<tr>
<td>Menstruation</td>
<td>6–8</td>
</tr>
<tr>
<td>Menopause</td>
<td>6–8</td>
</tr>
</tbody>
</table>

Annexure 4

**Some Important Measurements**

<table>
<thead>
<tr>
<th>Structure</th>
<th>Measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isthmus which forms lower uterine segment</td>
<td>5–6 mm $^\circ$</td>
</tr>
<tr>
<td>Female urethra</td>
<td>35–40 mm $^\circ$</td>
</tr>
<tr>
<td>Posterior vaginal wall</td>
<td>11.5 cm</td>
</tr>
<tr>
<td>Anterior vaginal wall</td>
<td>9 cm</td>
</tr>
<tr>
<td>Uterus (Nulliparous)</td>
<td>8 cm × 6 cm × 4 cm</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Structure</th>
<th>Measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervix</td>
<td>2.5–3.5 cm</td>
</tr>
<tr>
<td>Ovary</td>
<td>3 × 2 × 1 cms</td>
</tr>
<tr>
<td>Fallopian tube</td>
<td>10–12 cm</td>
</tr>
<tr>
<td>Mature ovum</td>
<td>120–140 microns</td>
</tr>
<tr>
<td>Mature/ripe graafian follicle</td>
<td>5–8 mm</td>
</tr>
<tr>
<td>Just before ovulation site of graafian follicle</td>
<td>16–24 mm ($\approx$ 20 mm)</td>
</tr>
</tbody>
</table>

**Some important angles to remember:**
- Angle of anteflexion (angle between cervix and uterus) | 120–130$^\circ$ |
- Angle of anteversion (angle between cervix and vagina) | 90$^\circ$ |
- Urethrovesical angle | 100$^\circ$ |
## Annexure 5
### Male and female derivatives of embryonic urogenital structures

<table>
<thead>
<tr>
<th>Embryonic structures</th>
<th>Male</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Labioscrotal swelling</td>
<td>Scrotum&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Labia majora&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Genital folds</td>
<td>Ventral aspect of penis</td>
<td>Labia minora</td>
</tr>
<tr>
<td>Genital tubercle&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Penis&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Clitoris&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Urogenital sinus</td>
<td>Urinary bladder</td>
<td>Urinary bladder</td>
</tr>
<tr>
<td></td>
<td>Urethra except navicular fossa</td>
<td>Urethral and paraurethral glands</td>
</tr>
<tr>
<td></td>
<td>Prostate gland</td>
<td>Lower part of Vagina</td>
</tr>
<tr>
<td></td>
<td>Prostatic utricle</td>
<td>Bartholin’s glands</td>
</tr>
<tr>
<td></td>
<td>Bulbourethral glands</td>
<td></td>
</tr>
<tr>
<td>Paramesonephric duct/ Mullerian duct</td>
<td>Appendix of testes</td>
<td>Hydatid of Morgagni, uterus, cervix, fallopian tubes, upper part of vagina</td>
</tr>
<tr>
<td>Mesonephric duct/Wolffian duct</td>
<td>Ductus epididymis</td>
<td>Duct of epoophoron</td>
</tr>
<tr>
<td></td>
<td>Seminal vesicles</td>
<td>Gartner’s cyst</td>
</tr>
<tr>
<td>Mesonephric tubules</td>
<td>Ductus efferentes</td>
<td>Epoophoron (cranial end)</td>
</tr>
<tr>
<td></td>
<td>Paradidymis</td>
<td>Paroophoron (caudal end)</td>
</tr>
<tr>
<td>Genital ridge</td>
<td>Testis</td>
<td>Ovary</td>
</tr>
</tbody>
</table>

## Annexure 6
### Origin of female genital tract

<table>
<thead>
<tr>
<th>Part of female genital system</th>
<th>Originates from</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovary</td>
<td>Genital ridge</td>
</tr>
<tr>
<td>Fallopian tubes</td>
<td>Mullerian/paramesonephric duct</td>
</tr>
<tr>
<td>Uterus</td>
<td>Mullerian/paramesonephric duct</td>
</tr>
<tr>
<td>Cervix</td>
<td>Mullerian/paramesonephric duct</td>
</tr>
<tr>
<td>Upper part of vagina</td>
<td>Urogenital Sinus</td>
</tr>
<tr>
<td>Lower part of vagina</td>
<td>Urogenital Sinus</td>
</tr>
</tbody>
</table>

## Annexure 7
### Culture Media and DOC of Various Organism
#### Culture Medium

<table>
<thead>
<tr>
<th>Organism</th>
<th>Culture Medium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trichomonas</td>
<td>Feinberg-Whittington media/Diamond media</td>
</tr>
<tr>
<td>Candida</td>
<td>Sabouraud’s media</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>McCoy cells/HeLa cells</td>
</tr>
<tr>
<td>TB</td>
<td>LJ media/Bactec</td>
</tr>
</tbody>
</table>

#### DOC

<table>
<thead>
<tr>
<th>Condition</th>
<th>Drug of choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trichomonas vaginitis</td>
<td>Metronidazole (2 g single dose)</td>
</tr>
<tr>
<td>Nonpregnant</td>
<td>Metronidazole in 2&lt;sup&gt;nd&lt;/sup&gt; &amp; 3&lt;sup&gt;rd&lt;/sup&gt; trimester</td>
</tr>
<tr>
<td>Pregnant</td>
<td></td>
</tr>
<tr>
<td>Candidiasis</td>
<td>Antifungals</td>
</tr>
<tr>
<td>Bacterial vaginosis</td>
<td></td>
</tr>
<tr>
<td>HSV</td>
<td>Acyclovir or Fancyclovir</td>
</tr>
</tbody>
</table>

Contd...
Contd...

<table>
<thead>
<tr>
<th>Condition</th>
<th>Drug of choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Syphilis</td>
<td>Benzathine penicillin</td>
</tr>
<tr>
<td>Chancroid</td>
<td>Azithromycin or Ceftriaxone or Erythromycin</td>
</tr>
<tr>
<td>Granuloma Inguinale/Donovanosis caused by <em>Calymmatobacterium</em> (<em>Klebsiella</em>) <em>granulomatis</em></td>
<td>Doxycycline or Azithromycin Ciprofloxacin or Erythromycin</td>
</tr>
<tr>
<td><strong>Gonococcal infection:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Uncomplicated:</strong> Nonpregnant</td>
<td>Single dose = Ceftriaxone + Azithromycin or Doxycycline (100 mg B/D × 7 days)</td>
</tr>
<tr>
<td></td>
<td>Ceftriaxone or Cefixime.</td>
</tr>
<tr>
<td></td>
<td>If patient is allergic to cephalosporin → Spectinomycin</td>
</tr>
<tr>
<td></td>
<td><strong>Note:</strong> for Gonococcal endocarditis antimicrobials should be continued for 4 weeks &amp; for meningitis 10–14 days</td>
</tr>
<tr>
<td>Pregnant</td>
<td></td>
</tr>
<tr>
<td>Chlamydia</td>
<td>I&lt;sup&gt;st&lt;/sup&gt; Choice</td>
</tr>
<tr>
<td>Non pregnant</td>
<td>Single dose = Azithromycin + contact tracing</td>
</tr>
<tr>
<td></td>
<td>2nd choice = Doxycycline or Erythromycin</td>
</tr>
<tr>
<td></td>
<td>I&lt;sup&gt;st&lt;/sup&gt; Choice</td>
</tr>
<tr>
<td></td>
<td>Azithromycin or Amoxicillin</td>
</tr>
<tr>
<td></td>
<td>2nd choice = Erythromycin</td>
</tr>
<tr>
<td>Pregnant &amp; young children</td>
<td></td>
</tr>
<tr>
<td>Health care worker's choice</td>
<td></td>
</tr>
<tr>
<td>Scabies</td>
<td>Lindane</td>
</tr>
<tr>
<td>Non pregnant</td>
<td>10% Crotamine lotion cream or 5% Permethrin cream</td>
</tr>
</tbody>
</table>

**Annexure 8**

**Clinical Features of Genital Ulcers**

- **Genital ulcers**
  - **Number**
    - Single
    - Multiple
      - Probably syphilis (Chancre = manifestation of 1<sup>st</sup> syphilis)
      - Herpes
      - Chancroid

- **Edges**
  - Raised edges
  - Erythematous
  - Undermined
    - Syphilis
    - Herpes
    - Chancroid

- **Base**
  - Smooth, nonpurulent nonerythematous
    - Syphilis
  - Erythematous Nonvascular
    - Herpes
  - Purulent & bleeds on touch
    - Chancroid

- **Induration**
  - Firm
    - Syphilis
  - Undermined
    - Chancroid
Annexure 9

Types of Hysterectomies and Structures Removed

<table>
<thead>
<tr>
<th>Hysterectomy</th>
<th>Structure Removed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple Hysterectomy/Total abdominal hysterectomy/Extrafascial hysterectomy/Type I hysterectomy</td>
<td>Uterus + Cervix</td>
</tr>
<tr>
<td>Wertheim’s hysterectomy/Modified Radical hysterectomy (Type II hysterectomy)</td>
<td>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</td>
</tr>
<tr>
<td>Radical hysterectomy/Type III hysterectomy/Meigs hysterectomy</td>
<td>Uterus + cervix + 2 cms of vagina (upper 1/3) + whole of cardinal and uterosacral ligament + whole of uterine artery + pelvic lymphadenectomy</td>
</tr>
<tr>
<td>Type IV hysterectomy</td>
<td>Same like Type III but upper 3/4 of vagina removed + periureteral tissues + superior vesical artery</td>
</tr>
<tr>
<td>Type V hysterectomy (Rarely done)</td>
<td>Same like Type IV + distal ureter and bladder also removed</td>
</tr>
</tbody>
</table>

Annexure 10

Pearl Index: WHO category 1 (user independent)

<table>
<thead>
<tr>
<th>Contraception</th>
<th>Perfect use rate</th>
<th>Typical use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implants</td>
<td>0.5%</td>
<td>0.05%</td>
</tr>
<tr>
<td>Sterilization</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>0.1%</td>
<td>0.15%</td>
</tr>
<tr>
<td>Female</td>
<td>0.5%</td>
<td>0.5%</td>
</tr>
<tr>
<td>IUCD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mirena</td>
<td>0.2%</td>
<td>0.2%</td>
</tr>
<tr>
<td>CuT</td>
<td>0.6%</td>
<td>0.8%</td>
</tr>
</tbody>
</table>

WHO category 2 (user dependent)

<table>
<thead>
<tr>
<th>Contraception</th>
<th>Perfect use rate</th>
<th>Typical use</th>
</tr>
</thead>
<tbody>
<tr>
<td>OCP's</td>
<td>0.3%</td>
<td>8.7%</td>
</tr>
<tr>
<td>Vaginal ring</td>
<td>0.3%</td>
<td>8%</td>
</tr>
<tr>
<td>Transdermal path</td>
<td>0.3%</td>
<td>8%</td>
</tr>
<tr>
<td>DMPA</td>
<td>0.3%</td>
<td>3%</td>
</tr>
<tr>
<td>Diaphragm</td>
<td>20%</td>
<td>20%</td>
</tr>
<tr>
<td><strong>Sponge</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nulliparous</td>
<td>9</td>
<td>16</td>
</tr>
<tr>
<td>Parous</td>
<td>26</td>
<td>32</td>
</tr>
<tr>
<td>Condom</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2</td>
<td>16</td>
</tr>
<tr>
<td>Female</td>
<td>5</td>
<td>21</td>
</tr>
</tbody>
</table>
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); M: Gellhorn Flexible (Silicone); O: Ring with Support (Silicone); P: Ring with 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); 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)

**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

**Figs. 15A and B:** Klinefelter’s syndrome. Man aged 28 years, married but infertile and complaining of gynaecomastia. 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. 16:** Cryotherapy gun with probes of different size and shapes

**Fig. 17:** Ultrasonography pictures of polycystic ovary
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 malfusion 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. 4: Bilateral hydrosalpinx. ATT given for 2 years
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. 6: Left tube appears as, if tubectomy has been done. Look of a sperm head
Courtesy: Dr Narayan M Patel, MD, DGO, FICS

Fig. 7: Left terminal hydrosalpingogram and right cornual block
Fig. 1: Dense intrauterine adhesions

Fig. 2: Hysteroscopic scissors for adhesiolysis

Fig. 3: Normalized cavity after adhesiolysis and estrogen therapy
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.

Along with Sim's speculum, to visualize cervix by retracting anterior vaginal wall.

![Sim's speculum](Fig. 1: Sim's speculum)

**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.

![Sim's anterior vaginal wall retractor](Fig. 2: Sim's anterior vaginal wall 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).

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.

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.
**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](image)

**FLUSHING CURETTE (FIG. 8)**

*Material:* Stainless steel.
*Sterilization:* Autoclaving and boiling.

**Use**
Dilatation and evacuation operation.

![Fig. 8: Flushing curette](image)

**TOWEL CLIP (FIG. 9)**

*Material:* Stainless steel.
*Sterilization:* Autoclaving and boiling.

**Uses**
- For draping
- Can be used for hemostasis.

![Fig. 9: Towel clip](image)

**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, enterocoele repair, colpoperineorrhaphy
  - Invaginal 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.
NEEDLE HOLDER (FIG. 11)

Material: Stainless steel.
Sterilization: Autoclaving.

Use
To hold needle during suturing.

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.

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
**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

---

**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.

**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.

---

**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.

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.

LEECH WILKINSON CANNULA (FIG. 19)

Material: Stainless steel.
Sterilization: Autoclaving and boiling.

Uses

- Hystersalpingography
- Chromopertubation test in laparoscopy
- Hydrotubation.

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.
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
  - Therapeutic
    - Dysfunctional uterine bleeding (DUB)
- Asherman's syndrome
- To remove embedded intrauterine device (IUD)
- Obstetrical uses:
  - MTP, check curettage
  - Blunt curettage in abortions
  - Secondary persistent pulmonary hypertension (PPH), subinvolution.

### 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](image)

### 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](image)

### VULSELLUM (FIG. 27)

**Material:** Stainless steel.
**Sterilization:** Autoclaving and boiling.

**Uses**
- Anterior lip held in:
  - Endometrial biopsy
  - IUCD insertion
  - Intrauterine insemination
  - Vaginal hysterectomy
  - Cauterization of cervix and cervical biopsy.
- Posterior lip held in:
  - Colorpuncture for suspected ruptured ectopic pregnancy
  - Culdoscopy
  - Posterior colpotomy.

![Fig. 27: Vulsellum](image)
**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](image)

**VITOON UTERINE MANIPULATOR (FIG. 29)**

*Material:* Stainless steel.
*Sterilization:* Autoclaving and boiling.

**Uses**
Same as that of Hulka uterine manipulator.

![Fig. 29: Vitoon uterine manipulator](image)

**DREW-SMYTHE CATHETER (FIG. 30)**

*Material:* Stainless steel.
*Sterilization:* Autoclaving and boiling.

**Uses**
- It is S-shaped and has a side opening to drain liquor amnii. It has a spring loaded stylet with a blunt tip.

![Fig. 30: Drew-Smythe catheter](image)

**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](image)
**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.

**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](image)

**KARMAN MENSTRUAL REGULATION SYRINGE (MR SYRINGE) (FIG. 34)**

Used for aspiration of uterine contents within 42 days of missed period.

![Fig. 34: MR syringe](image)

**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. 32: Haywood Smiths ovum forceps](image)
**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

**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.

**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.
**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.

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**INTRAUTERINE INSEMINATION CANNULA (FIG. 41)**

It is a thin flexible catheter which is placed in uterine cavity for intrauterine insemination (IUI).

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**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.

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**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 necrosis 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. *CO₂*: 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.

<table>
<thead>
<tr>
<th>Single freeze</th>
<th>3 Min (Freeze)</th>
<th>5 Min (Thaw)</th>
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</table>

![Fig. 43: Cryomachine](image)

**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).

**Principles:**
- 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.

**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.

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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

**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. 8:** Bicornuate uterus

**Fig. 9:** Hysterosalpingogram showing normal uterine cavity with bilateral hydrosalpinx

**Fig. 10:** Hysterosalpingogram showing uterovesical fistula
