Pathology of the Female Genital Tract

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Dr. Mohammad Arafa
Department of Pathology
Faculty of Medicine
Mansoura University
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Recognize aetiology, pathogenesis, clinical features, diagnosis of common and life threatening illness affecting the body and each of its major organ systems, presenting throughout the age spectrum including inflammatory, neoplastic and degenerative lesions of the female genital tract.

**Infections of the Female Genital Tract**

**Common infections of the female genital tract**

<table>
<thead>
<tr>
<th>Organism</th>
<th>Source</th>
<th>Vulva</th>
<th>Vagina</th>
<th>Cervix</th>
<th>Corpus</th>
<th>Adnexa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herpesvirus</td>
<td>STD</td>
<td>Genital warts, intrapithelial neoplasia, invasive carcinoma</td>
<td></td>
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<tr>
<td>Molluscum contagiosum</td>
<td>STD</td>
<td>Molluscum lesions</td>
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<tr>
<td>HPV</td>
<td>STD</td>
<td>Genital warts, intrapithelial neoplasia, invasive carcinoma</td>
<td></td>
<td>Follicular cervicitis, endometritis, salpingo-oophoritis</td>
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<tr>
<td>Chlamydia trachomatis</td>
<td>STD</td>
<td>Skene gland adenitis</td>
<td>Vaginitis in</td>
<td>Acute cervicitis</td>
<td>Acute endometritis and salpingitis</td>
<td></td>
</tr>
<tr>
<td>Neisseria gonorrhoeae</td>
<td>STD</td>
<td>Enogenous Vulvovaginitis</td>
<td></td>
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<td></td>
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<tr>
<td>Candida</td>
<td></td>
<td>Vulvovaginitis</td>
<td></td>
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</tr>
<tr>
<td>Trichomonas</td>
<td>STD</td>
<td>Vulvovaginitis</td>
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</table>

**Pelvic Inflammatory Disease (PID)**

*Definition:* Ascending infection that begins in the vulva or vagina and spreads upward to involve most of the structures in the female genital system.

*Etiology:* *Gonococcus* is the common cause of PID. Others include *Chlamydia* infection and puerperal infections (*staphylococci, streptococci, coliform bacteria, and Clostridium perfringens*).

This results in pelvic pain, adnexal tenderness, fever, vaginal discharge, tubal scarring, infertility and intestinal obstruction.
Benign exophytic lesions of the vulva
Condyloma Accuminata which is virus related (low risk HPV). Squamous cell papilloma is not of viral origin.

Squamous lesions
Squamous cell carcinomas are, in a proportion of cases, related to (high risk HPV). They are preceded by a precursor lesion (vulvar intraepithelial neoplasia, VIN).

Glandular lesions
Benign tumour arising from modified apocrine sweat glands (papillary hydradenoma). Adenocarcinomas are also reported.

Malignant melanoma

VAGINA

Tumours
Squamous cell carcinoma: These tumours are related to (high risk HPV) and are preceded by a precursor lesion (vaginal intraepithelial neoplasia, VaIN).
Clear cell carcinoma: This is a variant of adenocarcinoma. It is preceded by a precursor lesion (vaginal adenosis) which is an area of vaginal mucosa not covered by squamous epithelium. The condition is uncommon but is seen in up to 90% of patients exposed in utero to DES.

Embryonal rhabdomyosarcoma (sarcoma botryoides): This tumour is uncommon occurring chiefly in girls from birth to adolescence (90% of cases occur under 5 years of age). Grossly, it occurs in submucosa, pushes the normal vaginal epithelium in front it and appears as a large polypoid, reddish, soft mass. Microscopically, it consists of malignant embryonal cells (small cells with oval nuclei showing criteria of malignancy) in a myxoid stroma that contains also striated muscle and smooth muscles. It is the least malignant of rhabdomyosarcomas.

CERVIX
Inflammations (Acute and chronic cervicitis)
* Some degree of cervical inflammation may be found in virtually all women, and it is usually of little clinical consequence.
* Infections by gonococci, chlamydiae, mycoplasmas, and herpes simplex virus may produce significant acute or chronic cervicitis.
* Important is to identify their association with upper genital tract disease, complications during pregnancy, and sexual transmission.
* Cervical inflammation produces reparative and reactive changes of the epithelium.

Endocervical Polyps
* Cervical polyps are benign exophytic growths that usually arise from the endocervix.
* They can cause irregular vaginal bleeding.
* Polyps are soft, almost mucoid, lesions composed of a loose fibrous stroma containing dilated, mucus-secreting endocervical glands, often accompanied by inflammation.

Premalignant and Malignant Neoplasms
One of the commonest cancer in females specially in developing countries. The age peak of incidence for cervical carcinoma is 45 years.

Pathogenesis:
* Persistent infection with oncogenic high risk HPVs (subtypes 16 and 18) are currently considered to be the single most important factor in cervical oncogenesis.
* HPVs infect immature basal cells of the squamous epithelium in areas of epithelial breaks, or immature metaplastic squamous cells present at the squamocolumnar junction.
* Integration of HPV DNA interferes with the p53 and RB genes.
* Other risk factors include multiple sexual partners, immunosupression and smoking.
Precancerous lesions:

*Cervical Intraepithelial Neoplasia (CIN) is the precancerous lesion of cervical squamous cell carcinoma. It is classified as CIN1, CIN2 or CIN3 according to the upward extension of the abnormal cells in the epithelium. CIN3 is the most severe where the atypical cells involve the whole thickness of the epithelium.

*Adenocarcinoma insitu (AIS) is the precancerous lesion for invasive adenocarcinoma.

Cervical carcinoma:
The most common types of cervical carcinomas are squamous cell carcinoma (80% of cases) and adenocarcinoma (15% of cases).

*Grossly: Exophytic or infiltrative

*Microscopically: Squamous cell carcinomas either keratinizing or nonkeratinizing. Adenocarcinomas are characterized by formation of glandular structures. Other types include adenosquamous carcinoma and neuroendocrine carcinoma.

*Staging:
Stage 0: Carcinoma in Situ (CIN III)
Stage I: Carcinoma confined to the cervix.

NB. Stage I carcinoma with stromal invasion no deeper than 3 mm and no wider than 7 mm is called microinvasive carcinoma.
Stage II: Carcinoma extends beyond the cervix but not to the pelvic wall. Carcinoma involves the vagina but not the lower third.

Stage III: Carcinoma extends to the pelvic wall. Carcinoma involves the vagina but not the lower third of the vagina.

Stage IV: Carcinoma has extended beyond the true pelvis or has involved the mucosa of the bladder or rectum. This stage also includes cancers with metastatic dissemination.

*Prognosis: Because of screening programs, most of patients are discovered in early stages. Patients with stage IV cancer die as a consequence of local extension of the tumor (e.g., into and about the urinary bladder and ureters, leading to urethral obstruction, pyelonephritis, and uremia) rather than distant metastases.

**Body of UTERUS and ENDOMETRIUM**

**Abnormal Uterine Bleeding**

The causes of abnormal bleeding from the uterus are many and vary among women of different age groups. In some instances, bleeding is the result of a well-defined organic abnormality, such as chronic endometritis, submucosal leiomyomas, endometrial polyp or endometrial neoplasms. However, the largest single group encompasses functional disturbances (dysfunctional uterine bleeding) due to abnormalities in the menstrual cycle or systemic diseases.
Inflammation

ACUTE ENDOMETRITIS
Acute endometritis is uncommon and limited to bacterial infections arising after delivery or miscarriage. Retained products of conception are the usual predisposing factors. Curettage and antibiotic are sufficient therapy. Progression of the inflammation leads to puerperal sepsis.

CHRONIC ENDOMETRITIS
This can be presented with bleeding, pain, discharge and infertility. The inflammation is characterized by the presence of plasma cells. Chronic inflammation of the endometrium occurs in patients suffering from chronic PID, in postpartum or post-abortion patients with retained gestational tissue, in women with intrauterine contraceptive devices and in women with tuberculosis, either from miliary spread or, more commonly, from drainage of tuberculous salpingitis.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Puberty</td>
<td>Precocious puberty (hypothalamic, pituitary, or ovarian origin)</td>
</tr>
<tr>
<td>Adolescence</td>
<td>Anovulatory cycle, coagulation disorders</td>
</tr>
<tr>
<td>Reproductive age</td>
<td>Complications of pregnancy (abortion, trophoblastic disease, ectopic pregnancy)</td>
</tr>
<tr>
<td></td>
<td>Organic lesions (leiomyoma, adenomyosis, polyps, endometrial hyperplasia, carcinoma)</td>
</tr>
<tr>
<td></td>
<td>Anovulatory cycle</td>
</tr>
<tr>
<td></td>
<td>Ovulatory dysfunctional bleeding (e.g., inadequate luteal phase)</td>
</tr>
<tr>
<td>Perimenopausal</td>
<td>Anovulatory cycle</td>
</tr>
<tr>
<td></td>
<td>Irregular shedding</td>
</tr>
<tr>
<td></td>
<td>Organic lesions (carcinoma, hyperplasia, polyps)</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>Organic lesions (carcinoma, hyperplasia, polyps)</td>
</tr>
<tr>
<td></td>
<td>Endometrial atrophy</td>
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</tbody>
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## Endometriosis and Adenomyosis

<table>
<thead>
<tr>
<th>Definition</th>
<th>External endometriosis</th>
<th>Adenomyosis</th>
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</thead>
<tbody>
<tr>
<td><strong>Definition</strong></td>
<td>Presence of endometrial tissue (glands and intervening stroma) outside the uterus.</td>
<td>Presence of endometrial tissue (glands and stroma) in the myometrium of uterine wall.</td>
</tr>
<tr>
<td><strong>Site</strong></td>
<td>ovaries, uterine ligaments, recto-vaginal septum, cul de sac, pelvic peritoneum, GI tract, mucosa of cervix, vagina, fallopian tube and laparotomy scar.</td>
<td>Myometrium of body of uterus</td>
</tr>
<tr>
<td><strong>Pathogenesis</strong></td>
<td>Suggested theories are: 1- Regurgitation theory: during menstruation, viable endometrial fragments pass via fallopian tube to implant on the peritoneum (retrograde menstruation). 2-Metaplastic (differentiation) theory: endometrial metaplasia of serosal cells (derived from coelomic epithelium) leads to peritoneal lesions. 3-Vascular and lymphatic dissemination theory: explains extra pelvic and L.N. involvement.</td>
<td>Abnormal growth activity of the endometrium, the basal zone of endometrium dips into the adjacent myometrium.</td>
</tr>
</tbody>
</table>
| **Grossly** | * Hemorrhagic lesions (as the endometrial tissue undergoes cyclic menstrual bleeding forming areas of old and recent hemorrhage.). It excites excessive fibrous tissue around them. | *The uterus is symmetrically enlarged and the uterine wall is thickened  
*The lesions form dark red foci |

*Ovarian endometriosis (chocolate cysts) which appear in one or both ovaries as multiple small cysts or a large single cyst with dark red brown
altered blood content.
*The blood may organize leading to fibrous adhesion with surroundings.

| M/E | Lesion originally consists of endometrial glands and stroma with hemosiderin.
*However, cyclic menstrual bleeding of lesion obscures its structural detail.
*Eventually fibrosis and hemosiderin laden macrophage. |

Nests of endometrial glands and stroma in myometrium between muscle bundles.

### Endometrial Hyperplasia

Increased proliferation of the endometrial glands relative to the stroma, resulting in an increased gland-to-stroma ratio when compared with normal proliferative endometrium. It is an important cause of abnormal uterine bleeding.

*Causes:* The condition is related to prolonged unopposed estrogen stimulation (repeated anovulatory menstrual cycles, obesity, estrogen secreting tumors and polycystic ovarian disease).

*Grossly:* Increased endometrial thickness.

*Microscopically:* Based on architectural (simple or complex) and cytologic features (with or without atypia), endometrial hyperplasia is divided into four major categories:

1. **Simple hyperplasia without atypia** (also known as cystic or mild hyperplasia) is characterized by glands of various sizes and irregular shapes with cystic dilatation. These lesions uncommonly progress to adenocarcinoma (approximately 1%).
2. **Simple hyperplasia with atypia** is uncommon. There is cytologic atypia within the glandular epithelial cells (e.g. loss of polarity and prominent nucleoli). Approximately 8% of such lesions progress to carcinoma.
3. **Complex hyperplasia without atypia** (also known as adenomatous hyperplasia) shows an increase in the number and size of endometrial glands, marked gland crowding, and branching of glands. This class of lesions has about a 3% progression to carcinoma.

4. **Complex hyperplasia with atypia** shows cytologic atypia in addition to the architectural complexity. Approximately 29% of such lesions progress to carcinoma. About 1/4 of the patients has concurrent malignancy.

**Malignant tumours of the Endometrium**

Endometrial carcinoma is the most common cancer of the female genital tract and accounts for 7% of all invasive cancer in women. Carcinoma of the endometrium is uncommon in women younger than 40 years of age. The peak incidence is in 55 to 65 year-old women.

*Pathogenesis:* Clinicopathologic studies and molecular analyses support the classification of endometrial carcinoma into two broad categories, referred to as type I (about 80% of cases) and type II (about 20% of cases).
*Precancerous lesions: *Type I carcinoma: atypical endometrial hyperplasia (also known as *endometrial intraepithelial neoplasia, EIN*) has high risk of progression.

*Type II* carcinoma: a precursor surface endometrial lesion is called *Endometrial intraepithelial carcinoma, EIC* (also known as *minimal serous carcinoma*).  

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<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Type I</th>
<th>Type II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>55–65 yr</td>
<td>65–75 yr</td>
</tr>
</tbody>
</table>
| Clinical setting | Unopposed estrogen  
Obesity  
Hypertension  
Diabetes | Atrophy  
Thin physique |
| Morphology     | Endometrioid | Serous  
Clear cell  
Mixed müllerian tumor |
| Precursor      | Hyperplasia | Endometrial intraepithelial carcinoma |
| Molecular genetics | PTEN | p53 |
| Behavior       | Indolent  
Spreads via lymphatics | Aggressive  
Intraperitoneal and lymphatic spread |
*Grossly*: Polypoid or invasive. Type II tends to be more bulky and diffuse.

*Microscopically*: **Type I** is usually of endometrioid histology (tumour resembling endometrial glands). According to the degree of glandular differentiation, endometrioid carcinoma is graded into GI (less than 5% solid areas), GII (less than 50% solid areas) and GIII (more than 50% solid areas). Carcinomas with squamous differentiation are common. **Type II** is usually of serous histology (similar to its ovarian counterpart).

*Staging:

Stage I: Carcinoma is confined to the corpus uteri itself.

Stage II: Carcinoma has involved the corpus and the cervix.

Stage III: Carcinoma has extended outside the uterus but not outside the true pelvis.

Stage IV: Carcinoma has extended outside the true pelvis or has obviously involved the mucosa of the bladder or the rectum.

*Prognosis*: Because of abnormal (postmenopausal) uterine bleeding, most tumours (specially type I) are detected in early stages.

### Tumours of the Myometrium

**Leiomyoma**

Commonly called fibroid, this is the commonest tumour in women.

*Aetiology*: The tumour is linked to prolonged hyperestrinism. This is evidenced by more occurrences in nullipara than multiparous women, being more during reproductive period and tendency to regress after menopause.

* Site*: Commonly arise in the body of uterus and rarely in cervix. Most tumours arise within the wall of the uterus (intramural). As the tumour increases in size it may
project in the uterine cavity under the endometrium (submucous) or projects to outside under the peritoneum (subserous).

*Grossly:*

- **Number:** they are frequently multiple (but may be single).
- **Size and shape:** rounded masses vary in size, pseudocapsulated. (It surrounded by false capsule of compressed uterine muscle and interstitial tissue).
- **A submucous leiomyoma** bulges into uterine cavity causing expansion and distortion. The covering endometrium is stretched thinned. The tumour may become pedunculated and protrude through cervix into vagina.
- **A subserous leiomyoma** may become pedunculated and adheres to surrounding organs where it may take its blood supply after it separated from his pedicle It is called. (parasitic fibroid)
- **Consistency:** firm and somewhat elastic
- **Cut surface:** paler than surrounding myometrium with solid whorly appearance.

*Microscopically:* Interlacing bundles of smooth muscle cells running alternating with fibroblasts. The muscle cells are long spindled with rounded ends, abundant
cytoplasm and short rod-shaped nuclei. The fibroblasts are spindled with tapering ends, scanty cytoplasm and long flat nuclei.

Secondary changes include hyaline degeneration, cysts, fatty degeneration, myxomatous degeneration, necrosis and calcification. Red degeneration (hemorrhagic infarction) occurs particularly during pregnancy. It is caused by vascular obstruction by thrombosis, or uterine contraction. The affected part is necrotic and stained with blood.

*Complications:
1- Abnormal uterine bleeding.
2- Infertility due to prevention of implantation of fertilized ovum.
3- Risk of abortion.
4- Interfere with child birth.
5- Iron deficiency anemia
6- Malignant transformation to Leiomyosarcoma (rare, 1%).

**Leiomyosarcoma:**

These uncommon malignant neoplasms arising de novo from the myometrium. Leiomyosarcomas grow within the uterus and invade the uterine wall. It may be polypoid masses that project into the uterine lumen. On histologic examination, they show atypia, increased mitotic figures, and coagulative necrosis.
OVARIES

Ovarian Tumors

There are numerous types of ovarian tumors. Ovarian cancer accounts for 3% of all cancers in females.

Benign tumors occur mostly in young women between (20-25 years old). Borderline tumors occur at slightly older ages. Malignant tumors are more common in older women (45-65 years old).

Most malignant ovarian cancers are detected when they have spread beyond the ovary, therefore, they account for a considerable number of deaths from cancer of the female genital tract.

<table>
<thead>
<tr>
<th>Type</th>
<th>Percentage of Malignant Ovarian Tumors</th>
<th>Percentage That Are Bilateral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serous</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benign (50%)</td>
<td></td>
<td>25</td>
</tr>
<tr>
<td>Borderline (15%)</td>
<td></td>
<td>30</td>
</tr>
<tr>
<td>Malignant (25%)</td>
<td>45</td>
<td>65</td>
</tr>
<tr>
<td>Mucinous</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benign (80%)</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Borderline (10%)</td>
<td></td>
<td>10</td>
</tr>
<tr>
<td>Malignant (10%)</td>
<td>6</td>
<td>&lt;5</td>
</tr>
<tr>
<td>Endometrioid carcinoma</td>
<td>20</td>
<td>40</td>
</tr>
<tr>
<td>Undifferentiated carcinoma</td>
<td>10</td>
<td>—</td>
</tr>
<tr>
<td>Clear cell carcinoma</td>
<td>6</td>
<td>40</td>
</tr>
<tr>
<td>Granulosa cell tumor</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Teratoma</td>
<td></td>
<td>15</td>
</tr>
<tr>
<td>Benign (96%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malignant (4%)</td>
<td>1</td>
<td>Rare</td>
</tr>
<tr>
<td>Metastatic</td>
<td>6</td>
<td>&gt;60</td>
</tr>
<tr>
<td>Others</td>
<td>3</td>
<td>—</td>
</tr>
</tbody>
</table>

(I) TUMORS OF SURFACE (MÜLLERIAN) EPITHELIUM
The most widely accepted theory for the derivation of surface epithelial tumors is the transformation of coelomic epithelium. This view is based on the embryologic pathway by which the müllerian ducts are formed from the coelomic epithelium and evolve into serous (tubal), endometrioid (endometrial), and mucinous (cervical) epithelia present in the normal female genital tract.

These tumours have similar manifestations of abdominal pain and enlargement. High serum CA125 is present in many patients. Torsion of the pedicle of large tumours leads to acute abdomen.

(1) **Serous Tumours:**

They account for 30% of all ovarian tumors.

*Pathogenesis:* The low-grade tumors arising in serous borderline tumors with only rare mutations in p53. In contrast, the high-grade tumors have a high frequency of mutations in the p53 gene.

*Grossly:* They are cystic lesion (cystadenoma) with smooth surface and serous fluid contents. Intarcystic papillary projections may be present (papillary cystadenoma). The outer surface of cystadenocarcinomas may show, in addition, nodules and outward papillary projections. Bilaterality is common in serous tumours.

*Microscopically:* Benign lesions are lined by a single layer of tall, columnar, ciliated epithelial cells, occasionally forming microscopic papillae. Malignant tumours have multilayered epithelium with many papillae, solid areas and stromal invasion.
Psammoma bodies are present. *Borderline* tumours show some of features of carcinomas but without stromal invasion.

(2) **Mucinous Tumours:**

They account for 25% of all ovarian neoplasms.

*Grossly:* Compared to serous tumours, mucinous neoplasms tend more to be unilateral and larger. They appear as multiloculated cystic tumors (mucinous cystadenoma) filled with sticky, gelatinous fluid. Rupture of the cyst may lead to pseudomyxoma peritonei.

*Microscopically:* Benign lesions are lined by tall columnar non-ciliated epithelium with apical mucin similar to intestinal or cervical epithelium. Malignant tumours usually have intestinal-type epithelium and show solid areas, necrosis and stromal invasion. Borderline tumours show some of features of carcinomas but without stromal invasion.

(3) **Endometrioid Tumours:** Most are malignant. Many cases occur in the setting of concurrent endometriosis.

(4) **Clear cell adenocarcinoma:** Uncommon, show cells with clear cytoplasm.

(5) **Brenner's tumour:** Most are benign. They consist of rounded islands of transitional epithelium embedded in dense fibrous stroma.
(II) GERM CELL TUMORS

1) Undifferentiated germ cell neoplasm (Dysgerminoma)
Uncommon malignant non functioning neoplasm occurs in children and young adults. Microscopically, it is similar to seminoma of testis.

2) Differentiated along embryonic pathway (Teratoma):

1) Mature teratoma: It is usually cystic (dermoid cyst) and benign.

2) Immature teratoma: It is predominantly solid and malignant.
3) Monodermal teratoma: Characterized by one sided development. Examples are struma ovarii (only thyroid tissue) and some cases of mucinous cystadenoma (G.I.T. epithelium).

(3) Differentiated germ cell tumours along extra embryonic pathway
1) Choriocarcinoma: Differentiation towards trophoblasts. It secretes HCG hormones.
2) Endodermal sinus tumour: Differentiation towards yolk sac. It secretes α fetoprotein.

(III) SEX CORD STROMAL TUMORS
These neoplasms are derived from the ovarian stroma, which in turn is derived from the sex cords of the embryonic gonad. Because the gonadal mesenchyme produces structures of specific cell type in both male (Sertoli and Leydig) and female (granulosa and theca) gonads, tumors resembling all of these cell types can be identified in the ovary. Moreover, because some of these cells normally secrete estrogens (granulosa and theca cells) or androgens (Leydig cells), their corresponding tumors may be either feminizing (granulosa–theca cell tumors) or masculinizing (Leydig cell tumors).

(1) Differentiated along female line:

a- Granulosa cell tumour: low grade malignant tumour secretes estrogen

b- Theca cell tumour (thecoma): benign tumour, mostly mixed with fibroma (fibrothecoma). May secrete oestrogen but, mostly are hormonally inactive.

(2) Differentiated along male line (Androblastoma, Arrhenoblastoma):
These may be sertoli cell tumour (secretes estrogen), leydig cell tumour (secrets androgen) or combination of them. The majority are benign.

(3) Mixed male and female differentiation (Gynandroblastoma):
Contain elements of granulosa, theca, sertoli and leydig tumours. It produces both hormones.

(4) Differentiated along stromal cell line (Fibroma):

May be presented as a pure fibroma or mixed with thecoma (fibrothecoma). Meig's syndrome is the association of ovarian fibroma with hydrothorax and ascitis.

(IV) UNCLASSIFIED TUMOURS

Lymphomas, Hemangiomas, Lipomas, Leiomyomas,…etc…

(V) METATATIC TUMOURS

The ovary is a common site for metastatic tumors..

- These tumours are usually bilateral. They reach both ovaries by transcoelomic spread, blood spread, retrograde lymphatic spread or direct spread. Site of primaries include uterus, G.I.T, gall bladder, pancreas, and lung.

- Krukenberg tumour is bilateral ovarian secondaries showing signet ring cells scattered in fibrous stroma. The primary is present in G.I.T, mainly stomach.

Non Neoplastic Cysts of the Ovary

1- Follicular cysts: Extremely common finding. They are <2cm, lined by follicular cells, and filled with clear fluid. They commonly originate in unruptured graafian follicles.

2- Corpus luteum cysts: Dilatation of degenerated corpus luteum. Usually single and filled with blood.

3- Polycystic ovary (stein- leventhal syndrome): Affects women inreproductive age and is in the form of bilateral multiple small cystic follicles with cortical fibrosis.
Oligomenorrhea, hirsutism and infertility are presenting symptoms. The condition is related to disturbance in androgen synthesis.

**FALLOPIAN TUBES**

**Inflammations**

In *suppurative salpingitis*, gonococcus accounts for more than 60% of cases. These tubal infections are a part of pelvic inflammatory disease. *Tuberculous salpingitis* is more common in parts of the world where tuberculosis is prevalent and is an important cause of infertility.

**Tumors**

Tumors of the fallopian tube are uncommon. Primary adenocarcinoma of the fallopian tubes is rare. A precursor lesion (*tubal intraepithelial carcinoma, TIC*) has been identified.

**GESTATIONAL TROPHOBLASTIC DISEASES**

**Hydatiform (vesicular) Mole**

Hydatidiform mole is characterized histologically by cystic swelling of the chorionic villi, accompanied by variable trophoblastic proliferation. Risk is highest at either extreme of reproductive years.

**A- Complete Hydatiform mole:**

- Due to fertilization of dead ovum. (46XX or 46XY karyotyping)
**Grossly:** The uterus is more enlarged than the duration of pregnancy. It is filled with a mass that resembles a punch of grape. It is formed of clusters of variable sized vesicles (2mm- 3cm) thin walled and translucent, (filled with translucent fluid) and separated by delicate fibrous bands. No trace of embryo, amniotic sac or umbilical cord (i.e. lack of contents of conception).

**Microscopically:**

- No fetus or normal placenta.
- Abnormal chorionic villi showing hydropic degeneration of the villous connective tissue core which is avascular. They are covered by hyperplastic chorionic trophoblasts (cytotrophoblast and syncytiotrophoblast) with varying degree of cell proliferation and atypia.

**Prognosis:** 80% are benign, 15% become invasive mole and 5% pass into choriocarcinoma.

***(B) Partial Hydatidiform mole:***

- It occurs in normal pregnancy but in fetus that is abnormal. (69XXY karyotyping)

**Grossly:** Normal placenta with only few abnormal chorionic villi with grape like mass. Abnormal fetus is seen.
**Microscopically:** Odema of some chorionic villi with focal slight trophoblastic proliferation.

**Prognosis:** It rarely passes to choriocarcinoma.

**(C) Invasive mole (chorioadenoma destruens):**

It complicates complete mole which becomes more invasive to myometrium and blood vessels. The tumour may be perforated. Spread to distant sites as lungs and brain could occur. The prognosis is intermediate between hydatiform mole and choriocarcinoma. Distant lesions may regress after removal of uterine invasive mole. Chemotherapy cures most cases.

**Choriocarcinoma**

Gestational choriocarcinoma is a malignant neoplasm of trophoblastic cells derived from a previously normal or abnormal pregnancy, which can even include extrauterine ectopic pregnancy. Choriocarcinoma is rapidly invasive and metastasizes widely, but once identified responds well to chemotherapy.

**Incidence:** 50% arise in hydatidiform moles, 25% in previous abortions, approximately 22% in normal pregnancies, with the remainder occurring in ectopic pregnancies. Very rarely, a nongestational choriocarcinoma may develop from germ cells in the ovaries or the mediastinum.

**Grossly:** Uterus is enlarged. The tumour appears as large mass distending uterine cavity and invading the uterine wall. It is yellowish white, soft, friable, fleshy, very hemorrhagic, and necrotic.
Microscopically: Tumour tissue consists of malignant cytotrophoblasts and syncytiotrophoblasts which do not keep their normal relation but occurs as separate large sheets. The cytotrophoblasts (Langhan's cells) are large, polygonal and cubical with cell boundaries and large hyperchromatic nuclei. The syncytiotrophoblasts appear in the form of cytoplasmic masses (with no cellular boundaries) containing scattered malignant darkly stained nuclei. The tumour has little or no stroma and the tumour sheets are present in a pool of blood. Excessive necrosis is present as well as inflammation. No intact chorionic villi present.

Spread: Widespread metastases are characteristic. Frequent sites of involvement are the lungs (50%) and vagina (30% to 40%), followed in descending order of frequency by the brain, liver, and kidney.

Clinical features: Choriocarcinoma presents with uterine bleeding, rising titre of HCG hormone in blood and urine (higher than with hydatiform mole). Chemotherapy produce high percent cure rate. Spontaneous disappearance of tumour may occur due to immune reaction.