GOALS AND OBJECTIVES:

At the completion of this section the student will be able to:

Analyze the gross and microscopic appearance of the specimens presented and discussed in the laboratory with emphasis on disorders related to:

1. Vulvar carcinoma
2. Cervical squamous intraepithelial neoplasia (low grade and high-grade)
3. Endometriosis and adenomyosis
4. Endometrial carcinoma (endometrioid type and serous type)
5. Leiomyoma (benign endometrial tumors)
6. Ovarian teratoma
7. Ovarian serous carcinoma

Relate the gross and microscopic appearance to the etiology, pathogenesis, clinical presentation and course of each condition illustrated.

Review the assigned cases on Aperio. For each condition discussed, review the clinical presentation, gross and microscopic features, pathogenesis and clinical course.

MANDATORY READING:

1. Robbins Pathologic Basis of Disease (9th edition)
   - Vulvar intraepithelial neoplasia and Vulvar Carcinoma, pages 997-999
   - Premalignant and malignant neoplasms of the cervix, pages 1002-1007 (including cervical intraepithelial neoplasia, cervical carcinoma and cervical cancer screening and prevention
   - Endometriosis and adenomyosis, pages 1010-1012
   - Malignant tumors of the endometrium (carcinoma of the endometrium) including type I (endometrial) carcinoma and type II (serous carcinoma), pages 1013-1018
   - Tumors of the myometrium (Leiomyomas and Leiomyosarcomas), page 1020-1021
   - Ovarian tumors (Epithelial tumors, Germ Cell tumors and Sex Cord Stromal Tumors), pages 1022-1034

2. Lectures:
   - Pathology of the Vulva, Vagina, Cervix, Endometrium, Myometrium.
   - Pathology of the Ovaries, fallopian tubes, and GTD
     - NOTE: Diseases of fallopian tubes and GTD will be presented in CPC-3
   - PAP smear/Cervical Cytology.

3. Papers:
1) VULVA: SQUAMOUS CELL CARCINOMA

CLINICAL HISTORY: A 60-year-old female presents with a long standing itching vulvar lump. Physical examination reveals an erythematous raised lesion covering the vulva and extending into the anal verge.

Clinical features relevant from this clinical history:

1. What are the risk factors associated with vulvar carcinoma? **HPV infection**
2. What are the premalignant lesions associated with “Basaloid and warty” carcinomas? **Vulvar Intraepithelial Neoplasia (VIN)**
3. What is the progression of “premalignant” to “malignant” vulvar HPV related carcinomas? **Low-grade dysplasia to moderate dysplasia to severe dysplasia to invasive carcinoma.**

SLIDE TO REVIEW: Aperio slide #813

ORIENTATION TO SLIDE: Multiple cross sections of vulvar resection.

ABNORMAL CHANGES: At medium power focus on the little fragment on top and follow the progression of non-invasive high-grade dysplasia on the left into invasive squamous carcinoma on the right. At high-power observe the HPV related changes consistent with koilocytosis. Dysplastic changes are “full-thickness” in this case. Use fragment #3 on bottom to compare normal vs. dysplastic.

Check list (have you seen the following structures):

- High-grade “full thickness” dysplasia
- Koilocytosis
- Invasive squamous carcinoma

4. What is the prognosis for patients with lesions less than 2 cm? (Robbins) **60-80%, 5-year survival with vulvectomy and lymphadenectomy**
5. What is the prognosis for larger lesions with lymph node involvement? (Robbins) **less than 10% 5-year survival.**

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Key Concepts

- Approximately 30% of vulvar cancers are caused by infection with high risk HPVs, principally HPV-16. These cancers develop from an in situ lesion termed **classic vulvar intraepithelial neoplasia** (classic VIN).
- Most vulvar cancers (70%) are not related to HPV and develop in a background of lichen sclerosus or squamous cell hyperplasia from the premalignant lesion called **differentiated vulvar intraepithelial neoplasia** (differentiated VIN).
2) CERVIX: DYSPLASIA (LOW-GRADE AND HIGH-GRADE)

CLINICAL HISTORY: A 22-year-old female was found to have an abnormal PAP smear (see pic)

Describe the abnormal changes for both patients:

Patient A: Koilocytic atypia. Includes nuclear enlargement, hyperchromasia (dark staining), presence of coarse chromatin granules, and variation of nuclear sizes and shapes. Cytoplasmic halos.

Patient B: Reduction in the amount of cytoplasm, increase in nucleus to cytoplasm ratio. Irregular “raisinoid” nuclear membrane, hyperchromasia (dark staining).

PAP diagnosis:

Patient A: Low grade squamous intraepithelial lesion (LSIL) - koilocytes

Patient B: High grade squamous intraepithelial lesion (HSIL)

Clinical features relevant from this clinical history:

1. What are the risk factors associated with genital HPV (refer to lecture)?
   - Multiple sexual partners, a male partner with multiple previous or current sexual partners, young age at first intercourse, high parity, persistent infection with a high oncogenic risk HPV, Immunosuppression, certain HLA types, use of oral contraceptives, use of nicotine.

2. What is the high peak age for HPV (refer to lecture)? 20’s due to sexual debut

3. What is the two-tier system used clinically for diagnosis and treatment of cervical dysplasia? LSIL and HSIL

4. What HPV types have been found in close to 100% of patients with HSIL? HPV 16 and 18

5. What are the PAP screening recommendations (refer to lecture)?
   - First PAP at 21 y/o or within 3 years of onset of sexual activity, and thereafter on annual basis.
   - After age 30, women who have had three consecutive normal cytology results may be screened every 2 to 3 years. (Lecture/Robbins)
6. What percentages of HPV lesions are cleared within 8 months? **50%**. What percentages are cleared within 2 years? **90%** (Lecture/Robbins)

7. Review Table 22-1, Classification Systems for squamous Cervical Precursor Lesions (page 1003, Robbins 9th edition).

<table>
<thead>
<tr>
<th>Dysplasia/Carcinoma in Situ</th>
<th>Cervical Intraepithelial Neoplasia (CIN)</th>
<th>Squamous Intraepithelial Lesion (SIL), Current Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild dysplasia</td>
<td>CIN I</td>
<td>Low-grade SIL (LSIL)</td>
</tr>
<tr>
<td>Moderate dysplasia</td>
<td>CIN II</td>
<td>High-grade SIL (HSIL)</td>
</tr>
<tr>
<td>Severe dysplasia</td>
<td>CIN III</td>
<td>High-grade SIL (HSIL)</td>
</tr>
<tr>
<td>Carcinoma in situ</td>
<td>CIN III</td>
<td>High-grade SIL (HSIL)</td>
</tr>
</tbody>
</table>

CIN, Cervical intraepithelial neoplasia; SIL, squamous intraepithelial lesion.

8. Review Figure 22-14: Spectrum of cervical intraepithelial neoplasia: normal squamous epithelium for comparison. *(page 1003, Robbins 9th edition)*

Both patients underwent colposcopy with biopsy of “suspicious” lesions as follows:

**SLIDE TO REVIEW**: Aperio slide # 866 (LSIL)

**ORIENTATION TO SLIDE**: Cross sections of cervical squamo-columnar junction mucosa.

**ABNORMAL CHANGES**: At medium power concentrate on the middle fragment. Observe the progression from normal squamous mucosa on the left to low-grade dysplasia on the right (above endocervical glands). Dysplasia in this case involves metaplastic glands. At high-power observe the superficial koilocytotic changes,
consistent with cells with bilobed to multilobed nucleus, irregular nuclear membranes and a perinuclear halo. Compare these cells to the PAP smear picture above.

SLIDE TO REVIEW:  Aperio slide # 868 (HSIL)

ORIENTATION TO SLIDE: Cross sections of cervical squamo-columnar junction mucosa.

ABNORMAL CHANGES: At medium power concentrate on the top fragment. Observe the dysplastic cells involving full mucosal thickness. Dysplastic cells have an enlarged irregular nucleus, high nuclear/cytoplasmic ratio and increased mitotic count. Compare these cells to the PAP picture above. In this slide you can also see low-grade changes, remember the progression from mild to moderate to high-grade dysplasia.

9. How can you prevent HPV infections? Monogamous relationships, vaccination?
10. What would be the next step for the patient with a HSIL? Cone/LEEP biopsy

Check list (have you seen the following structures):

__ koilocytes
__ High grade dysplastic cells
3) UTERUS: ENDOMETRIOSIS/ ADENOMYOSIS

CLINICAL HISTORY: A 36-year-old female has a pelvic examination that reveals a symmetrically enlarged uterus, without apparent nodularity or a palpable mass. She has had menorrhagia and pelvic pain for several months. She had a normal, uncomplicated pregnancy 10 years ago. A serum pregnancy test result is negative.

Clinical features relevant from this clinical history:

1. Define endometriosis: **Endometriosis is the presence of endometrial tissue outside of the uterus.**
2. Define adenomyosis: **Presence of endometrial tissue within the uterine wall (myometrium).**
3. Describe the most common sites (in descending order) with endometriosis:
   - Ovaries
   - Uterine ligaments
   - Rectovaginal septum
   - Cul de sac
   - Pelvic peritoneum
   - Large and small bowel appendix
   - Mucosa of the cervix, vagina and fallopian tubes
   - Laparotomy scars
4. How do patients with endometriosis present? **Severe dysmenorrhea, dyspareunia (pain with intercourse) and pelvic pain due to the intrapelvic bleeding and perouterine adhesions. Pain on defecation indicates rectal wall involvement, and dysuria results from involvement of the serosa of the bladder.**
5. What are the consequences of endometriosis: **Infertility, dysmenorrhea (painful menstruation), pelvic pain and other problems.**
6. Describe the two major theories for the development of endometriosis:
   - The metastatic theory: endometrial tissue is implanted at abnormal locations. “retrograde menstruation”
   - The metaplastic theory: endometrium could arise directly from coelomic epithelium (mesothelium of pelvis or abdomen)
7. How does endometriosis look on laparoscopy: **red-blue to yellow brown appearance.**

GROSS:

8. What is the other name for cystic endometriotic ovaries? **Chocolate cysts.**

SLIDE TO REVIEW: Aperio slide #1123.

ORIENTATION TO SLIDE: Full thickness uterus section with endometrium on top and myometrium/serosa on bottom.
ABNORMAL CHANGES: At low power, observe the focus of endometrial glands and endometrial stroma within the myometrium. These “adenomyosis” foci look exactly like normal endometrium except the location is not the correct one. There are no signs of malignancy.

9. What components need to be present on histology for the diagnosis of endometriosis? Both endometrial glands and stroma need to be present.

Check list (have you seen the following structures):

__ Endometrial glands and endometrial stroma within myometrium
4) UTERUS: LEIOMYOMA

CLINICAL HISTORY: A 40-year-old woman has a feeling of pelvic heaviness. There is no history of abnormal bleeding. Her physician palpated an enlarged, nodular uterus on bimanual pelvic examination. A PAP smear was normal. Pelvic ultrasound is shown:

![Ultrasound Image]

A total abdominal hysterectomy is performed. See picture.

![Hysterectomy Image]

Clinical features relevant from this clinical history:

1. What are the most common symptoms associated with leiomyoma? Abnormal bleeding, compression of the bladder (urinary frequency), sudden pain if disruption of blood supply occurs, and impaired fertility. In pregnant woman: increase frequency of spontaneous abortion, fetal malpresentation, uterine inertia and postpartum hemorrhage.
2. Leiomyomata are tumors arising from the endometrium or myometrium or serosa? Myometrium
3. Describe the gross features of a typical leiomyoma. Sharply circumscribed, discrete, round, firm, gray-white tumors varying in size from small, barely visible nodules to massive tumors that fill the pelvis.

SLIDE TO REVIEW: Aperio slide # 1240.

ORIENTATION TO SLIDE: Cross section of leiomyoma. No normal myometrium is present.

ABNORMAL CHANGES: Tumor composed of whorled bundles of smooth muscle. The individual muscle cells are uniform in size and shape and have a characteristic oval nucleus. Mitotic figures are uncommon.
4. What histologic features will make you think of the possibility of leiomyosarcoma? **Nuclear atypia, highly anaplastic, mitosis, necrosis.**

5. What clinical features will guide you towards leiomyoma vs leiomyosarcoma? **Post-menopausal old female.**

6. How common are leiomyosarcomas in comparison with leiomyomata? **Uncommon, while fibroids are the most common tumor in females.**

   Check list (have you seen the following structures):
   
   __ Spindle cells with ovoid nuclei

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**Key Concepts**

- Endometrial stromal tumors include stromal nodules, low-grade stromal sarcomas, and high-grade stromal sarcomas.
  - Stromal nodules are benign, well-circumscribed tumors.
  - Low-grade stromal sarcomas resemble stromal nodules, but infiltrate into the surrounding myometrium. They are associated with fusion of the \( JAZF1 \) gene and various polycomb factor genes, usually \( SUZ12 \).
  - High-grade stromal sarcomas show marked atypia and are associated with other gene fusions.
  - Both low- and high-grade stromal sarcomas are prone to late recurrences.

- Leiomyomas are common benign smooth muscle tumors that cause significant morbidity and are often associated with \( MED12 \) mutations.

- Leiomyosarcomas (malignant smooth muscle tumors) are uncommon, highly malignant myometrial tumors that usually arise de novo.
5) ENDOMETRIUM: ENDOMETRIAL ADENOCARCINOMA (ENDOMETRIOID TYPE, Type I Robbins)


Clinical features relevant from this clinical history:

1. Age presentation: **Post-menopausal women (55-65 y/o)**
2. Clinical presentation: **Post-menopausal bleeding**
3. Risk factors for endometrioid type carcinoma: **unopposed estrogen (obesity, diabetes, hypertension, infertility)**
4. What is the precursor lesion of this type of carcinoma? **Endometrial hyperplasia**
5. What mutated gene has been identified in 30% to 80% of endometrioid carcinomas and in approximately 20% of endometrial hyperplasias? **PTEN**
6. What other mutations, molecular changes have been found to be associated with endometrioid carcinoma

- **PIK3CA 40%** (not present on hyperplasias, these findings suggest a role on invasive carcinoma).
- **KRAS 25%**
- **Loss of function mutations in ARID1A**: of interest ARID1A is also frequently mutated in ovarian endometrioid and clear cell carcinomas, tumors that arise within endometriosis.
- **Defects involving DNA mismatch repair genes** are found in about 20% of sporadic tumors and are prevalent in endometrial carcinomas arising in women from families with HNPCC.

7. Review Table 22-4 from Robbins.
8. What screening test is currently available for early detection of endometrial carcinoma? **There is no currently available screening test for carcinoma of the endometrium. Fortunately, postmenopausal bleeding often leads to early detection, and cures are possible in most patients.**

9. What is the clinical presentation of a patient with hyperplasia/carcinoma? **Post-menopausal bleeding, uterine enlargement.**
After a malignant diagnosis was rendered on biopsy, patient undergoes hysterectomy showing the following GROSS findings:

10. Describe gross findings on endometrial hyperplasia/carcinoma: **It can be a localized polypoid tumor or a diffuse tumor involving the endometrial surface.**

**SLIDES TO REVIEW:** Aperio slide # 860

**ORIENTATION:** Full thickness uterus section with endometrium on top and myometrium/serosa on bottom.

**ABNORMAL CHANGES:** At low power observe the increased endometrial thickness (use histology normal from last year for comparison if necessary). At high power tumor has a preserved glandular architecture with little or no intervening stroma, “back to back glands”. The majority of the tumor is glandular with less than 5% having a solid growth (FIGO grade 1). At high-power glands are crowded with more than 2 cell layers and individual cells have an enlarged elongated nucleus with moderate atypia and a few mitoses. Tumor is confined to the uterus and involves less than 50% of myometrial thickness.

Check list (have you seen the following structures):

__ glandular tumor with “back to back” glands
__ minimal (less than 5%) solid growth
__ less than 50% of myometrial invasion

11. Review the FIGO classification of endometrial tumors *(Figure 22-25, page 1016, Robbins 9th edition).*
Endometrioid adenocarcinomas demonstrate glandular growth patterns resembling normal endometrial epithelium. There are three histologic grades: **well differentiated** (grade 1) (Fig. 22-25A), composed almost entirely of well-formed glands; **moderately differentiated** (grade 2) (Fig. 22-25C), showing well-formed glands mixed with areas composed of solid sheets of cells, which by definition make up 50% or less of the tumor; and **poorly differentiated** (grade 3) (Fig. 22-25D), characterized by greater than 50% solid growth pattern. Well differentiated tumors may be distinguished from hyperplasias by lack of intervening stroma.

Up to 20% of endometrioid carcinomas contain foci of squamous differentiation. Squamous elements may be histologically benign-appearing when they are associated with well-differentiated adenocarcinomas. Less commonly, moderately or poorly differentiated endometrioid carcinomas contain squamous elements that appear frankly malignant. Current classification systems grade the carcinomas based on glandular differentiation alone and ignore areas of solid squamous differentiation.

**G1. Well-differentiated adenocarcinoma, less than 5% solid growth.**

**G2 Moderately differentiated adenocarcinoma with partly (less than 50%) solid growth.**

**G3 Poorly differentiated adenocarcinoma with a predominantly solid growth (greater than 50%)**

12. Review endometrial carcinoma staging *(Figure 22-25, Page 1017, Robbins 9th edition)*.

Pathologic staging of both type I and II endometrial adenocarcinoma and malignant mixed müllerian tumors (described later) is as follows:

- **Stage I**—Carcinoma is confined to the corpus uteri itself.
- **Stage II**—Carcinoma involves the corpus and the cervix.
- **Stage III**—Carcinoma extends outside the uterus but not outside the true pelvis.
- **Stage IV**—Carcinoma extends outside the true pelvis or involves the mucosa of the bladder or the rectum.
6) ENDOMETRIUM: ENDOMETRIAL ADENOCARCINOMA (NON-ENDOMETRIOID TYPE, SEROUS CARCINOMA, Type II Robbins)

CLINICAL HISTORY: A 76-year-old female (post-menopausal female) presents with an episode of vaginal bleeding. On pelvic examination her uterus appears enlarged. The cervix is normal. An ultrasound reveals a fungating mass within the posterior fundus. Patient undergoes curettage.

Clinical features relevant from this clinical history:

1. Age presentation: old women (decade later than type I carcinoma).
2. Clinical presentation: same as endometrioid post-menopausal vaginal bleeding.
3. Are these tumors less common or more common than endometrioid carcinomas: less common.
4. What is the precursor lesion of this type of carcinoma? Endometrial intraepithelial carcinoma.
5. What is the most frequent alteration (mutation) present on these tumors: p53.
6. What is the prognosis of this cancers (in comparison with endometrioid adenocarcinoma) Less than 50% survival after 3 years.

SLIDES TO REVIEW: Aperio slide # 1242

ORIENTATION: Multiple fragments of tumor.

ABNORMAL CHANGES: At medium power observe the papillary architecture of this tumor. Fibrovascular cores are lined by malignant cells with marked cytologic atypia, with high nuclear to cytoplasmic ratio, atypical mitosis and prominent nucleoli.

A p53 was performed (not shown) and was interpreted as “strong nuclear staining”.

Check list (have you seen the following structures):

__ papillary architecture
__ highly atypical cells
Key Concepts

Endometrial Carcinoma

- Endometrial carcinoma is the most common malignancy of the female genital tract.
- There are two major types of endometrial carcinoma: type I and type II. Type I tumors are low-grade and usually indolent; type II tumors are high-grade aggressive tumors and have a poor prognosis.
- Endometrioid (type I) carcinoma is often preceded by atypical hyperplasia and commonly has mutations in the PTEN, PIK3CA, KRAS, and ARID1A genes.
- Serous (type II) carcinoma is associated with serous endometrial intraepithelial carcinoma and the most common mutations are in TP53. TP53 mutations are also found in precursor lesions.
- Stage remains the most important factor in outcome; serous tumors are much more likely to present at advanced stage and have a decidedly worse prognosis.
- Malignant mixed müllerian tumors (MMMTs) are carcinosarcomas that resemble endometrial carcinoma genetically and have poor outcomes with current therapies.
7) OVARY: MATURE TERATOMA

CLINICAL HISTORY: A 24-year-old female presents with a unilateral 7cm adnexal mass. Abdominal ultrasound shows a cystic mass with calcifications.

What clinical features are relevant from this clinical history?

1. What percentage of ovarian neoplasms are germ cell tumors? 20-50%
2. What percentage of germ cell tumors are teratomas? 90%
3. What percentages of teratomas are malignant? 1%
4. What percentages of teratomas are bilateral? 10-15%
5. Name the other germ cell tumors? Dysgerminoma, Embryonal carcinoma, yolk sac carcinoma, choriocarcinoma.

The ovary is resected, with the GROSS features depicted below:

6. Describe the gross presentation/appearance of these lesions: Cystic structure. The cyst wall is composed of squamous epithelium, hair shafts, and sebaceous glands. Cystic contents include, hair, bone, cartilage, and brain.

7. Teratomas are almost pathognomonic on gross examination, why do pathologist sample them thoroughly? To look for immature components/malignancy.

SLIDES TO REVIEW: Aperio slide # 727

ORIENTATION TO SLIDE: Two sections of ovarian tumor. Normal ovarian parenchyma is shown on the left.
ABNORMAL CHANGES: At low and medium power observe a tumor containing skin, sebaceous glands, cartilage, respiratory mucosa and bone. No immature elements (immature brain, bone or cartilage) suggestive of malignancy are present.

Check list (have you seen the following structures):

___ Tumor containing skin, sebaceous glands, cartilage, respiratory mucosa and bone.

8. What is “Struma ovary”? monodermal teratoma, only one component: thyroid tissue
8) OVARY: SEROUS CARCINOMA

CLINICAL HISTORY: A 58-year-old woman presented with a **complain of abdominal pain**. A **mass** was found on pelvic examination and her **serum CA-125 level was 1,080 U/ml**. The right oophorectomy specimen consisted on a 13x11x6 cm **solid and cystic mass**.

Clinical features relevant from this clinical history:

1. This neoplasm derives from which of the following (surface epithelium vs germ cell vs sex cord stroma)? **surface epithelium**
2. Clinical presentation: **unfortunately, usually asymptomatic**.
3. Risk factors associated with development of ovarian serous carcinomas: **Nulliparity, family history and heritable mutations**.
4. Describe the relationship of BRCA 1 and BRCA 2 with ovarian serous carcinoma: **Risk of ovarian cancer in women with BRCA1 or BRCA2: 20% to 60% by the age of 70 years. Almost all reported cases of ovarian carcinomas arising in women with BRCA1 or BRCA2 mutations are high-grade serous carcinoma and commonly have p53 mutations.**
5. What is the prognosis for serous carcinoma? **For tumors confined to the ovaries 70 %, for tumors involving the peritoneum 25% (but majority of patients present with tumor beyond peritoneum).**

GROSS:

6. **How do these tumors look grossly? Cystic cavity lined by delicate papillary tumor growth.**
7. **What percentage of tumors are bilateral? 20% of serous cystadenomas, 30% of borderline and 66% of serous carcinomas.**

SLIDES TO REVIEW: Aperio slide #1210

ORIENTATION TO SLIDE: 3 sections of cystic tumor.

ABNORMAL CHANGES: At medium power observe a tumor invading into the ovarian stroma. Tumor cells show marked nuclear atypia, pleomorphism, atypical mitotic figures and multinucleation. At medium power observe concentric calcifications (psammoma bodies).

Check list (have you seen the following structures):

- Nest of tumor cells within ovarian stroma
Slides are available at Aperio at http://aperio.ad.tamhsc.edu

User name: student1 (or 2/3/4 depending on your working station number)

PW: tamhsc2 (or 2/3/4 depending on your working station number)

- Pathology course
- GYN lab

**APERIO SLIDES**

Aperio #813: Vulva SCC
Aperio #866: Cervix, LSIL
Aperio #868: Cervix, HSIL
Aperio #1123: Uterus, endometriosis
Aperio #1211: Uterus, adenomyosis
Aperio #1240: Uterus, leiomyoma
Aperio #860: Endometrium adenocarcinoma (endometrioid type)
Aperio #1242: Endometrium, serous carcinoma
Aperio #727: Ovarian germ cell, teratoma
Aperio #859: Fallopian tube, ectopic pregnancy
Aperio #1210: Ovarian surface, serous carcinoma
Tumor: carcinoma vs sarcoma vs melanoma
Name the two types of vulvar squamous carcinomas and the age at presentation:

- HPV related: Basaloid carcinomas, younger age (reproductive)
- Non-HPV related: Keratinizing Squamous Carcinomas, older women (7 decade)

Describe lesions (benign and malignant that can present with “leukoplakia”):
Lichen sclerosus (thin epidermis), Lichen simplex chronicus (thick epidermis), vulvar carcinomas
Name the cell finding caused by HPV virus (yellow arrow): **Koilocytosis**

Diagnosis: **Low grade squamous dysplasia, CIN-I**

What HPV serotype will most likely be positive on the above case: **HPV 6, 11, 16, 18**

A. Cytology (PAP smear) preparation

B. Biopsy

What is the preferred method used for screening in US: **PAP smear, Thin prep**

What patients should go to colposcopy: **HSIL or high risk serotypes**

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Diagnosis: **HSIL, CIN-III**

Is PAP smear image on right or left: **right**

What is the HPV serotype most likely associated with this findings: **HPV 16, 18, 31, 33**

What is the next step on management for this patient: **LEEP, Cone**
Diagnosis: adenomyosis
Age of presentation: reproductive age
Clinical: infertility, dysmenorrhea (painful menses), pelvic pain

Diagnosis: Leiomyomas (fibroids)
Age of presentation: Childbearing age
Clinical presentation: abnormal uterine bleeding, infertility and a pelvic mass
Can you generate a diagnosis based on image alone? ______

What information is missing to differentiate benign vs malignant process? _____

Choose the best classification for the above tumor:

- Endometrioid type, Type I Robbins
- Non-endometrioid type, Type II Robbins

Which type is associated with estrogen exposure? ____________________________

- No, the image (gross and micro) can be compatible with hyperplasia or carcinoma (need to see invasion into myometrium)

- Age/clinical presentation: Could this be endometriosis for example.... YES, it is a possibility. If post-menopausal bleeding then think hyperplasia/carcinoma

- Endometrioid type, Type I Robbins (see picture from Dr. Jimenez lecture)

Endometrial carcinoma

1. **ENDOMETRIOID TYPE** (Type I Robbins): ESTROGEN (55-65 y/o), associated with hyperplasia

1. **NON-ENDOMETRIOID** (Type II Robbins), including
   - serous, clear cell and mixed Müllerian tumor:
     - Not related to estrogen exposure
     - Older females, 65-75 y/o
     - Mutation of the p53 tumor suppressor gene
     - Poor prognosis
Diagnosis: **Endometrial serous carcinoma**
Is this tumor associated with estrogen exposure? **NO**
What is the approximate age for the above patient? **75 (older than endometrioid)**
What mutation is frequently present on this tumor? **p53**
What is the prognosis? **poor**

Age at presentation: **0-25%**
What is the most frequent germ cell tumor: **Teratoma**
What percentage become malignant: **1%**
Name all the germ cell tumors: **Teratoma, dysgerminoma, endodermal sinus tumor, choriocarcinoma**
Diagnosis: **Malignant serous carcinoma of ovary**

Name the structure on the yellow arrow: **psammoma bodies (concentric calcifications)**. Not specific for malignancy.

Common mutations on this tumors: **KRAS, BRAF, p53**

Name all the “surface epithelial tumors”, described on Robbins: **Serous tumor, Mucinous tumor, Endometrioid tumor, Clear cell tumor, Brenner tumor, Cystadenofibroma**