GYNECOLOGIC EMERGENCIES

PAULA BILICA, DO FACOG
OBJECTIVES

MANAGEMENT OF ADNEXAL MASSES

MANAGEMENT OF ECTOPIC PREGNANCY

ABNORMAL PAP SMEAR – 2011 GUIDELINES

ABNORMAL UTERINE BLEEDING
Un.exam.Masses

Most arise from the ovary

can also arise from the uterus, bowel, retroperitoneum, or metastatic disease from breast or stomach

Can span all ages

Various etiologies

Ultimate diagnostic tool is histological examination

Prevalence varies (2.5*-8%**)

**Differential Diagnosis of Ovulary Masses**

<table>
<thead>
<tr>
<th>Extraovarian</th>
<th>Ovarian</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molar pregnancy</td>
<td>Simple or hemorrhagic physiologic cysts</td>
</tr>
<tr>
<td>Tubal pregnancy or TOA</td>
<td>Endometrioma</td>
</tr>
<tr>
<td>Ovarian cyst</td>
<td>Theca lutein cysts</td>
</tr>
<tr>
<td>Dermoid inclusion cyst</td>
<td>Benign, malignant, or borderline neoplasms (e.g. epithelial, germ cell, sex cord)</td>
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<tr>
<td>Unculated fibroid</td>
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<tr>
<td>Peritoneal abscess</td>
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<tr>
<td>Peritoneal abscess or tumor</td>
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<tr>
<td>Ulipian tube cancer</td>
<td>Metastatic carcinoma (e.g. breast, colon, endometrium)</td>
</tr>
<tr>
<td>Inflammatory or malignant bowel disease</td>
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<tr>
<td>Hydrosalpinx or pyosalpinx</td>
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<tr>
<td>Pyocele</td>
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<td>Hydrometrocolpos</td>
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<tr>
<td>Fetal kidney</td>
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<tr>
<td>Adnexal inclusion cyst</td>
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<tr>
<td>Ovarian inclusion cyst</td>
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<tr>
<td>Ovarian cyst</td>
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<tr>
<td>Ovarian neoplasm (e.g. epithelial, germ cell, sex cord)</td>
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<td></td>
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<tr>
<td>Metastatic carcinoma (e.g. breast, colon, endometrium)</td>
<td></td>
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</tbody>
</table>
### Table: Pathology Distribution Among Women Aged 27 to 59 (30% PMP)*

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brenner tumor</td>
<td>152</td>
</tr>
<tr>
<td>Serous cystadenoma</td>
<td>101</td>
</tr>
<tr>
<td>Mucinous cystadenoma</td>
<td>76</td>
</tr>
<tr>
<td>Teratoma</td>
<td>34</td>
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<tr>
<td>Hemorrhagic cyst</td>
<td>44</td>
</tr>
<tr>
<td>Ovarian cyst</td>
<td>22</td>
</tr>
<tr>
<td>Dermal cystadenoma</td>
<td>22</td>
</tr>
<tr>
<td>Sertoli-Leydig cell tumor</td>
<td>13</td>
</tr>
<tr>
<td>Brenner tumor</td>
<td>12</td>
</tr>
<tr>
<td>Brenner tumor</td>
<td>12</td>
</tr>
<tr>
<td>Hemorrhagic cyst</td>
<td>8</td>
</tr>
<tr>
<td>Ovarian cyst</td>
<td>8</td>
</tr>
<tr>
<td>Brenner tumor</td>
<td>4</td>
</tr>
<tr>
<td>Brenner tumor</td>
<td>2</td>
</tr>
<tr>
<td>Brenner tumor</td>
<td>2</td>
</tr>
<tr>
<td>Brenner tumor</td>
<td>122</td>
</tr>
<tr>
<td>Brenner tumor</td>
<td>19</td>
</tr>
</tbody>
</table>
The primary goals of diagnostic evaluation are to confirm that the adnexal mass is ovarian and to determine whether it is benign or malignant.”
Risk Factors for Ovarian Cancer

Family history
- breast, ovarian, colon

Self-history of cancer (e.g. gyn, breast, gastric)

Character of pain

Menstrual history

Gastrointestinal symptoms

Physical examination findings (e.g. ascites),
- complex/solid mass on ultrasound
Girls < 15 years old with an ovarian tumor have 6-11% risk of malignancy*

Overall risk increases with age after menarche (29-35% in PMP women with ovarian mass)**

character of Pain

New onset, mid-cycle pain in suggest physiologic cycle.
Immediate postcoital pain suggest ruptured cyst.
Dysmenorrhea/dyspareunia suggest endometriosis.
Abrupt severe pain with nausea/vomiting suggest ovarian torsion, degenerating fibroid or perforation.
Pain with fever suggests PID, appendicitis, or diverticulitis.

Chronic pain or bloating suggest ovarian neoplasm/fibroid.
Menstrual History

Don’t forget about ectopic pregnancies

Menorrhagia and dysmenorrhea occur with fibroids

PMB bleeding is common symptom of fallopian tube cancer; but fallopian tube cancer is a rare cause of PMB bleeding

Sex cord-stromal tumors and/or germ cell tumors are hormonally active

AUB, breast tenderness, hirsutism, sexual precocity
Gastrointestinal Symptoms

Non-specific GI complaints

- common manifestation of ovarian cancer in older women
- consider appendicitis in younger women
- diverticulitis to be considered in PMP women with LLQ pain with nausea/vomiting

- < 5% (age 40)
- 30% (age 60)
- 65% (age 85)
- 20% palpable mass
General considerations

- assess size, shape, and mobility
- empty bladder; fecal material can be mistaken for ovarian mass

*Normal ovaries in PMP women are usually not palpable*

- Cul-de-sac nodularity, shortened or tender terosacral ligaments, and lateral displacement of cervix

*Premenopausal state - consider endometriosis*
Cervical Exam Findings

Fibroids - characterized by an enlarged, mobile uterus with irregular contours

Tenderness upon palpation of adnexa suggest inflammatory process and/or ovarian neoplasm

Ovarian malignancy

irregularity

solid consistency

lack of mobility
Don’t forget to do a breast exam as the ovary can be a metastatic site.

- 50-90% of metastasis to the ovary originate from the GI tract or breast.

## Associated with BRCA1 & BRCA2 mutations*

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Estimated Lifetime Risk in BRCA1 Mutation carriers</th>
<th>Estimated Lifetime Risk in BRCA2 Mutation carriers</th>
<th>Lifetime Risk in General Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>47 to 66%</td>
<td>40 to 57%</td>
<td>12.5%</td>
</tr>
<tr>
<td>Bilateral Breast</td>
<td>Up to 65%</td>
<td>Up to 50%</td>
<td>~1% per year</td>
</tr>
<tr>
<td>ovarian</td>
<td>35 to 46%</td>
<td>13-23%</td>
<td>1.5%</td>
</tr>
<tr>
<td>ovarian tubal</td>
<td>Not increased</td>
<td>Not increased</td>
<td>5%</td>
</tr>
<tr>
<td>prostate</td>
<td>Elevated</td>
<td>35 to 40%</td>
<td>15%</td>
</tr>
<tr>
<td>Prostate Cancer</td>
<td>0.2 to 2.8%</td>
<td>3.2 to 12%</td>
<td>0.1%</td>
</tr>
<tr>
<td>colorectal</td>
<td>&lt;10%</td>
<td>&lt;10%</td>
<td>1.3%</td>
</tr>
</tbody>
</table>

Most will be Benign...

Series of 129 women with breast cancer subsequently diagnosed with adnexal mass (but no evidence of disseminated disease)*

88% - benign adnexal cysts
5% - tumors of low malignant potential
5% - epithelial ovarian cancer
2% - metastatic breast cancer

Ultrasound Examination

The most valuable diagnostic study in the
<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity/Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bimanual exam</td>
<td>45/90</td>
</tr>
<tr>
<td>Ultrasound morphology</td>
<td>86-91/68-83</td>
</tr>
<tr>
<td>MRI</td>
<td>91/87</td>
</tr>
<tr>
<td>CT</td>
<td>90/75</td>
</tr>
<tr>
<td>PET</td>
<td>67/79</td>
</tr>
<tr>
<td>CA 125 (using &gt;35 U/mL)</td>
<td>78/78</td>
</tr>
</tbody>
</table>

Symptomatic and asymptomatic patients

Premenopausal and postmenopausal patients

Authors concluded that:

“all diagnostic modalities showed trade-offs between sensitivity and specificity, but did not provide sufficient detail on relevant characteristics of study populations to allow confident estimation of the optimum diagnostic strategy.”

Nevertheless, these modalities can be used to categorize some adnexal masses with confidence.
Ovarian Ultrasound Characteristics

Normal Ovary measures:

3.5 x 2.0 x 1.5 cm (premenopausal)
1.5 x 0.7 x 0.5 cm (PMP 2-5 years)

*PMP ovary > 2X size of contralateral ovary is considered suspicious for malignancy*

Normal physiologic follicles < 2.5 cm

*Unilocular cyst size does not correlate well with malignancy*

*Large multilocular cysts and solid tumors are more likely malignant*
Ultrasound

Simple cysts, hemorrhagic cysts, endometriomas, and dermoids often have characteristic ultrasound features that are highly predictive of the histologic diagnosis.

Series of 173 consecutive surgeries* for adnexal masses:

- 51% - specific dx could not be made
- 42% - correct specific dx made
- 7% - incorrect diagnosis made

Sensitivity/specificity - 92/97% (endometrioma); 90/98% (dermoid cyst)
A normal appearing left ovary containing a single anechoic clear cyst which is consistent with a follicle. A small amount of ovarian tissue is identified surrounding the follicle as indicated by the arrow.
Normal left ovary with two follicles that are shown by the arrows. The follicles are circular anechoic structures within the substance of the hypoechoic ovarian tissue.

- Solitary, thin walled, unilocular, usually < 8-10 cm.
Corpus luteum cysts can look more complex than follicular cysts. In this case, ultrasonography reveals a central blood clot within the cyst.
emorrhagic Cyst with Color Doppler

Transvaginal ultrasound image of the right adnexa showing an organized hemorrhagic cyst of the right ovary viewed with color Doppler imaging. The hemorrhagic cyst is primarily cystic due to significant retraction of the clot (long arrow). No blood flow is demonstrated using color Doppler imaging within the cyst itself. Some normal appearing blood flow is shown in the ovarian tissue (short arrow).
Acute Hemorrhagic Cyst

- Transvaginal ultrasound image of a hemorrhagic ovarian cyst. This mass has the typical appearance with internal echoes, some of which have a reticular pattern of fine linear to curvilinear echoes, thought to be due to fibrin strands.
Pelvic ultrasonography shows multiple ovarian cysts (ring of black circles on right, < 1cm) that are suggestive, although not diagnostic, of polycystic ovary syndrome.
Polycystic Ovarian Syndrome

- Classic phenotype is woman who is hirsute, obese, and anovulatory.

- Rotterdam criteria
  - >12 follicles/ovary
  - 2-9 mm diameter
  - Increased ovarian volume (>10 mL) calculated as \(0.5 \times \text{width} \times \text{length} \times \text{thickness}\)
Fibroids clinically apparent in ~25% of reproductive-aged women

Pedunculated fibroids can be confused with an ovarian neoplasms

Sarcomatous degeneration is rare (0.4-1.4%)*

A rapid increase in size should raise concern in the peri- or postmenopausal woman

uterine Leiomyomata

Intraoperative photograph of multiple uterine tumors.
Endometrioma

Growth of ectopic endometrial tissue

Patients typically complain of: pelvic pain/dysmenorrhea/dyspareunia

Homogenous low to medium level echoes in a cystic mass (i.e. complex mass on US)

- may have thick walls
- multilocular

“chocolate cyst”
A transvaginal ultrasound image of the right adnexa showing an endometrioma of the right ovary. The cystic nature of the endometrioma is indicated by post-cyst enhancement (long arrow). The homogeneous echotexture of the cyst contents, "ground-glass" appearance) is characteristic of an endometrioma (short arrow).
Transvaginal ultrasound image of the left adnexa showing a tuboovarian abscess. A complex solid and cystic mass is identified in the left adnexa. A large cyst identified by the long arrow. A tubular fluid collection with low level echoes is shown by the short arrow.
Tuboovarian Abscess

Intraoperative photograph of a left tuboovarian abscess with surgical intervention.
Malignancy rate ascertained from a mixed study of pre and postmenopausal women undergoing US*:

- 0.3% (1/296) unilocular cysts were malignant
- 8% (20/229) multilocular cysts
- 36% (147/209) multilocular solid tumors
- 39% (31/80) solid tumors

Terroid Cyst

Benign germ cell tumor; bilateral in 10-15%

Most common ovarian tumor in 2nd/3rd decades of life

Varying densities due to presence of:

- sebaceous material
- bone
- adipose tissue, and/or hair
Benign cystic teratoma (dermoid tumor) of the right ovary. The complex nature of this small tumor is demonstrated. The long arrow indicates the solid hyperechoic echogenic portion with shadowing of the ultrasound beam distal to the echogenic portion. The short arrow demonstrates the anechoic cystic portion with post cyst enhancement of the ultrasound beam.
Benign cystic teratoma (dermoid tumor) of the left ovary is indicated by the arrow. The complex nature of this tumor is demonstrated with both hypoechoic and hyperechoic echogenic areas intermixed. The similarity to surrounding bowel and overlying abdominal wall can make this tumor difficult to visualize. The margins are measured with the electronic calipers.
Benign Teratoma

Intraoperative photograph of a benign teratoma.
Serous Cystadenoma with Septations

Transvaginal ultrasound image of the left ovary showing a serous cystadenoma of the left ovary. A multiseptated (arrows) cystic structure is noted in the left adnexa. The anechoic cystic areas have no solid areas nor areas of nodularity. Ovarian tissue seen surrounding the cystic mass (arrowhead).
allograft component that is not hyperechoic and is often nodular or villary

- Irregular thick (>2 to 3 mm) septations, if present, that are thick (>2 to 3 mm)

- Doppler demonstration of flow in the solid component

- Presence of ascites

- Peritoneal masses, enlarged nodes, or matted bowel

Ovarian Cancer

Cross intraoperative photograph of an enlarged, solid mass.
Malignant Ovarian Mass

- Ultrasound image of complex, malignant ovarian mass (arrow)
Ovarian Cancer

- Transvaginal ultrasound image of the left ovary showing ovarian cancer. The left ovarian mass is primarily solid as indicated by the long arrow. A small cystic portion is demonstrated by the short arrow.
Ovarian Cancer

Ovarian mass in a PMP woman should be considered malignant until proven otherwise.”

Majority are derived from coelomic epithelium

papillary serous cystadenocarcinoma is the most common

Mean age 50-60 years

Constitutional symptoms are associated with advanced disease

EX findings usually include

pleural effusions

abd distension with ascites
Surgical specimen of a left fallopian tube carcinoma.
Ultrasound reveals a sausage-shaped structure in the adnexa (arrow) consistent with a fallopian tube carcinoma. Neovascularization Doppler flow not uncommon.
Doppler color flow imaging can be helpful in differentiating malignant vs benign masses. Malignancies are rich in neovascularization, showing lower resistive & pulsatile indices. Benign cysts show no vascularization. Meta-analyses (Kinkel 2000)* concluded that gray-scale ultrasound imaging combined with color Doppler imaging was superior than each assessment alone.
Transvaginal ultrasound image of ovarian cancer of the left ovary. The ovarian mass is 4.7 cm and primarily solid as indicated by the long arrow. Color Doppler imaging demonstrates blood flow within the solid portion of the ovarian mass (short arrow). Almost no normal ovary is visible in the image.
Laboratory Studies

Beta hCG - exclude pregnancy

CBC - leukocytosis could indicate infectious etiology (e.g. PID and/or TOA)

Tumor markers - not diagnostic, but if elevated can help characterize the ovarian neoplasm*

most useful for follow-up of patients treated for ovarian cancer (i.e. tumor recurrence, evaluate response to treatment)**

A 125 Tumor Marker

Serum glycoprotein (normal < 35 U/mL)

Elevated in ~80% of women with ovarian ca*

Average sensitivities: 50% (Stage I); 90% (Stage N)

Non-specific in both benign & malignant conditions

*can be elevated in 1% healthy women

Kast RC, et al. A radioimmunoassay using a monoclonal antibody titer to monitor the course of epithelial ovarian cancer.
<table>
<thead>
<tr>
<th>Gynecologic Conditions</th>
<th>Nongynecologic Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epithelial ovarian and endometrial cancers</td>
<td>Liver disease &amp; cirrhosis</td>
</tr>
<tr>
<td>Fallopian tube cancers and germ cell tumors</td>
<td>Colitis</td>
</tr>
<tr>
<td>Adenocarcinoma of the cervix</td>
<td>CHF</td>
</tr>
<tr>
<td>Sertoli-Leydig cell tumors of the ovary</td>
<td>Diabetes</td>
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<tr>
<td>Adenomyosis</td>
<td>Lupus</td>
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<tr>
<td>Benign ovarian neoplasms</td>
<td>Mesothelioma</td>
</tr>
<tr>
<td>Endometriosis</td>
<td>Pericarditis</td>
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<tr>
<td>Functional ovarian cysts</td>
<td>Polyarteritis nodosa</td>
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<tr>
<td>Leiomyomata</td>
<td>Postoperative period</td>
</tr>
<tr>
<td>Meig’s Syndrome</td>
<td>Previous irradiation</td>
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<tr>
<td>Menstruation</td>
<td>Renal disease</td>
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<tr>
<td>Pregnancy</td>
<td>Sarcoidosis</td>
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<tr>
<td>Ovarian hyperstimulation</td>
<td>Tuberculosis</td>
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<tr>
<td>Pelvic inflammation</td>
<td>Pleural effusion</td>
</tr>
<tr>
<td>Ascites</td>
<td>Breast &amp; Lung cancer</td>
</tr>
<tr>
<td>Colon &amp; pancreas cancer</td>
<td></td>
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</tbody>
</table>
Serves as a baseline study; GYN-ONC consultation is recommended. 

With regards to detecting malignant disease*:

Not a useful diagnostic test in premenopausal women

- sensitivity/specificity/PPV: 50-74%/26-92%/5-67%

More useful in postmenopausal women

- sensitivity/specificity/PPV: 69-87%/81-100%/73-100%
## Serum Markers in Malignant Germ Cell Tumors of the Ovary

<table>
<thead>
<tr>
<th>Histology</th>
<th>AFP</th>
<th>hCG</th>
<th>LDH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysgerminoma</td>
<td>-</td>
<td>+ / -</td>
<td>+</td>
</tr>
<tr>
<td>Yolk sac tumor</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Mature teratoma</td>
<td>+ / -</td>
<td>-</td>
<td>+ / -</td>
</tr>
<tr>
<td>Mixed germ cell tumor</td>
<td>+ / -</td>
<td>+ / -</td>
<td>+ / -</td>
</tr>
<tr>
<td>Choriocarcinoma</td>
<td>-</td>
<td>+</td>
<td>+ / -</td>
</tr>
<tr>
<td>Embryonal CA</td>
<td>+ / -</td>
<td>+</td>
<td>+ / -</td>
</tr>
<tr>
<td>Polyembryoma</td>
<td>+ / -</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>

**Legend:**
- **AFP:** alpha fetoprotein
- **hCG:** human chorionic gonadotropin
- **LDH:** lactate dehydrogenase
Recurrence rate is high*

Diagnostic accuracy**

- 235 cystic ovarian lesions
- 56% devoid of dx cells
- sensitivity/specificity 35-83/$\sim$100%

Rupture of cyst contents

- potential dissemination of malignant cells

pproach to Management
Do Intervene or Not?
Based on Age, Symptoms, Pelvic, US, Lab Findings

Consider the following:

- **Risk of malignancy** *(poor prognosis with late diagnosis)*
- **Risk of rupture** *(spillage of irritants and/or malignant cells)*
- **Risk of torsion** *(may lead to ovarian necrosis/oophorectomy)*

- The risks & benefits of surgery with respect to future fertility *(chicken or the egg?)*
Simple cysts < 10 cm size can be followed*

*Observational series

60% will resolve over the course of several cycles

OCPs may prevent formation of new cysts

in general, formulations > 35 mcg of estrogen resulted in fewer follicular cysts and ovulatory cycles**

**Observational series


Women with cysts > 10 cm and those with findings suspicious for malignancy require surgical exploration.

Findings” can include:

- sonographic appearance
- no change or increase in size
- very elevated CA 125 (>200 U/mL)

Ascites, suspicion for metastatic dz, or fam hx of first degree relative with ovarian or breast cancer.

regnancy

Guidelines do not change (except OCPs are not given)

Surgical exploration in the second trimester does not appear to be associated with a significantly increased risk of pregnancy or fetal complications*

Management tends to be more aggressive since risk for malignancy is higher

Largest study to date included 2763 PMP women diagnosed with 3259 simple cysts <10 cm, with serial sonograms every 3-6 months*

69.4% spontaneous resolution rate over a mean f/u of six years

10 diagnosed with ovarian cancer

- 7/10 had additional abnormal US findings
- 2/10 developed ovarian cancer after cyst had resolved on interval US
- 1/10 developed ovarian cancer in contralateral ovary
Follow-up with serial US and CA 125 appropriate if all criteria met:

- simple unilateral ovarian cyst on US and Doppler imaging
- asymptomatic
- normal pelvic exam
- normal cervical cytology and CA 125**

No consensus on maximum cyst size for expectant management although 5-10 cm has been commonly reported.
Refer to GYN Oncologist if:

- Symptomatic cyst
- Cyst > 5 cm (commonly used threshold)**
- CA 125 > 35 U/mL
- Ascites
- Metastatic suspicion
- Hereditary predisposition to breast/ovarian cancer in a first-degree relative
### Guidelines for Referral of Pelvic Mass to a Gyn Oncologist*

<table>
<thead>
<tr>
<th>Premenopausal Women (refer if any are present)</th>
<th>Postmenopausal Women (refer if any are present)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA 125 &gt; 200 U/mL</td>
<td>CA 125 &gt; 35 U/mL</td>
</tr>
<tr>
<td>Ascites</td>
<td>Ascites</td>
</tr>
<tr>
<td>Abdominal / distant metastases</td>
<td>Nodular or fixed pelvic masses</td>
</tr>
<tr>
<td>Fam Hx breast or ovarian ca in a first degree relative</td>
<td>Fam Hx breast or ovarian ca in a first degree relative</td>
</tr>
</tbody>
</table>

*G Committee Opinion: No.280, December 2002. The role of the generalist obstetrician-gynecologist*
SS. et al. Validation of referral guidelines for women with pelvic masses. Obstet Gynecol 2005; 105:

<table>
<thead>
<tr>
<th>Study Measures Questions</th>
<th>Premenopausal Group</th>
<th>Postmenopausal Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capture rate of ovarian cancer</td>
<td>70%</td>
<td>94%</td>
</tr>
<tr>
<td>PPV</td>
<td>33.8%</td>
<td>59.5%</td>
</tr>
<tr>
<td>NPV</td>
<td>&gt;90%</td>
<td>&gt;90%</td>
</tr>
</tbody>
</table>

Sensitivity 92-98% (late stage ca); 56% (premenopausal women with early stage disease); 80% (postmenopausal women with early stage disease)**
Abnormal PAP Smears
Cervical Cancer Screening

Etiology

Screening Guidelines

Review changing guidelines and reason for changes

Reporting of results: Bethesda 2001 guidelines

Treatment

Assess knowledge
Why Screen for Cervical Cancer?

Most common gynecological cancer in U.S.

Approx 11,000 new cases diagnosed yearly in U.S.

High mortality if not diagnosed

Asymptomatic stage can last 1-20 years

Test is inexpensive

50% of cervical carcinoma in US occur in women who have never had pap smear
Human Papillomavirus (HPV)

Responsible for 5% of all cancers worldwide

- 100% of cervical cancer
- 90% of anal cancer
- 40% of penile, vaginal, and vulvar cancer
- 35% of oropharyngeal cancer
When should we start screening?

2009 ACOG recommendations

- Age 21 irrespective of the age of onset of sexual activity
- Most cytological abnormalities in adolescents and young women spontaneously regress
- Delaying screening until age 21 avoids unnecessary procedures
How often should we screen?

Every 2 yrs for women age 21-29

Women 30 or greater with 3 consecutive normal PAP smears can extend to 3yr intervals (based on risk factors)
When should we stop screening?

ACOG

ACS
Should we screen after hysterectomy?

If hysterectomy for benign condition and no history of abnormal PAP smears, no further screening required.

Continue with yearly PAP smears in patients with prior CIN 2, CIN 3, or cervical cancer.
Exceptions to screening guidelines

Risk factors such as HIV, immunosuppression

DES exposure in utero

Women treated in the past for CIN 2, CIN 3, or cervical cancer
Homosexual patients

Reliable history of no vaginal intercourse or non-penetrating sexual contact ever in their lifetime

Women who have been immunized against HPV 16 and 18
Provided by PAP smear

Candida infection
Trichomonas
Actinomyces infection
Bacterial Vaginosis
Atrophy
Endometrial cells in women >40
Inflammation
# Cervical Dysplasia Terminology

<table>
<thead>
<tr>
<th>CYTOLOGY</th>
<th>HISTOLOGY</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-US Atypical squamous cells of undetermined significance</td>
<td>Atypia or metaplasia</td>
</tr>
<tr>
<td>C-H Atypical squamous cells – cannot exclude high grade SIL</td>
<td></td>
</tr>
<tr>
<td>SIL Low-grade squamous intraepithelial lesion</td>
<td>CIN 1 = Mild dysplasia</td>
</tr>
<tr>
<td>s-SIL High grade squamous intraepithelial lesion</td>
<td>CIN 2 = Moderate dysplasia</td>
</tr>
<tr>
<td>C Atypical glandular cells</td>
<td>CIN 3 = Severe dysplasia</td>
</tr>
</tbody>
</table>

CIN 1 = Mild dysplasia
CIN 2 = Moderate dysplasia
CIN 3 = Severe dysplasia
Reflex HPV testing in patients < 30. (If > 30 test at initial screening)

- If POS → Refer for colposcopy
- If NEG → Repeat both PAP and HPV in one year
- If either HPV POS or ASCUS or > on repap → Refer for colposcopy
Atypical Glandular Cells (AGC)

- More likely to be associated with both squamous and glandular abnormalities than ASCUS
- Increased risk of cancer diagnosis
- Refer for colposcopy and endometrial biopsy
Who needs referral for colposcopy?

- ASCUS with POS HPV
- ASC-H
- LGSIL
- HGSIL
- AGC

- Also need endometrial biopsy
When to start screening and how often

- Age 21 regardless of sexual history
- Age 21-29 every 2yrs
- Age >30 every 3yrs
PV Screening

PAP and HPV combination testing: sensitivity 100%

- Can be used for women >30 in combination with PAP smear
- If NEG for HPV and normal PAP risk to develop CIN 2/3 in 3 yrs <1%
- If PAP smear NEG and HPV POS repeat both in one year
Ectopic Pregnancy
Definition

An ectopic pregnancy is a pregnancy that develops at any site other than the endometrium. Hemorrhage from an EP is still the leading cause of pregnancy related maternal death in the first trimester and accounts for 4-10% of all pregnancy related deaths.
Incidence Rate of Ectopic Pregnancy

Per 1000 Reported Pregnancies

4.5

20.0
Safer to Have an Ectopic Now?

- Incidence Rate of Ectopic Pregnancies
- Fatality Rate of Ectopic Pregnancies

Per 1000 Reported Pregnancies

- 1970: Incidence 35.5, Fatality 4.5
- 1987: Incidence 16.8, Fatality 3.8
- 1992: Incidence 20.0, Fatality 3.0

90% decrease in fatalities
Risk Factors*

- Prior ectopic pregnancy (OR 9.3-47 with 10-30% recurrence)
- H/O tubal ligation (OR 3.0-139; 25-50% if tubal failure)
- Infertility (OR 1.1-28)
- Prior PID (OR 2.1-3.0)
- Smoking (OR 2.3-3.9)

*Risk directly related to number smoked/day; 4-fold increased risk with >30/day

*Reprinted with permission from Fertil Steril 1997;68:525-531
And Yet More Risk Factors...**

- IUDs (*OR 1.1-45*)
- Progestin only contraception
- DES exposure (*OR 2.4-13*)
- Pelvic inflammation (*e.g. endometriosis*)?
- SIN (*salpingitis isthmica nodosa*)
Epiphititis Isthmica Nodosa with hyperplasia of the muscularis and a gland lumen which can produce multiple small nodular swellings in the tubal wall.
Where Do Ectopics Occur?

- 97% Ampullary (>80%)
- 0.5% Ovarian
- 0.1% Tubal
- 4% Interstitial/Cornual
- ~.03% Abdominal
3D US image of a heterotopic pregnancy

3D US image of a cervical ectopic pregnancy
Where in the Tube?

- Morula implants in oviduct
- Trophoblast invades and grows within lumen or between lumen of tube and peritoneal covering
- Retroperitoneal tubal hemorrhage is mainly extraluminal
<table>
<thead>
<tr>
<th>Symptom</th>
<th>Patients w/ Symptoms (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>90-100</td>
</tr>
<tr>
<td>Amenorrhea</td>
<td>75-95</td>
</tr>
<tr>
<td>Vaginal bleeding</td>
<td>50-80</td>
</tr>
<tr>
<td>Dizziness / Fainting</td>
<td>20-35</td>
</tr>
<tr>
<td>Pregnancy Symptoms</td>
<td>10-25</td>
</tr>
<tr>
<td>Passage of tissue</td>
<td>5-10</td>
</tr>
</tbody>
</table>

*Weckstein LN, Boucher AR et al: Accurate diagnosis of early ectopic*
Keep in mind, over 50% of women are asymptomatic before tubal rupture and don’t have an identifiable risk factor for an ectopic pregnancy.*
### Signs of an Ectopic Pregnancy*

<table>
<thead>
<tr>
<th>Sign</th>
<th>Patients with signs (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adnexal tenderness</td>
<td>75-90</td>
</tr>
<tr>
<td>Abdominal tenderness</td>
<td>80-90</td>
</tr>
<tr>
<td>Adnexal mass*</td>
<td>50</td>
</tr>
<tr>
<td>Uterine enlargement</td>
<td>20-30</td>
</tr>
<tr>
<td>Orthostatic symptoms</td>
<td>10-15</td>
</tr>
<tr>
<td>Fever</td>
<td>5-10</td>
</tr>
</tbody>
</table>

What is the Differential Diagnosis of an Ectopic Pregnancy?

- Abortion (Miscarriage)
- Ruptured CL Cyst
- Appendicitis
- Degenerating Fibroid
- Adnexal Torsion
- GTD
- Salpingitis
- DUB
- Endometriosis
Delayed diagnosis increases morbidity!
If a woman of childbearing age presents with abdominal and/or pelvic pain, abnormal uterine bleeding, and a positive hCG, she has an ectopic pregnancy until proven otherwise.
When is Ultrasound Helpful?

- Definitive if yolk sac or embryo with cardiac activity is identified either in the tube or uterus*

- In conjunction with hCG titers, US can be helpful in confirming an IUP

*Detected in less than 50% of cases, however.
Specific US Findings of an Ectopic Pregnancy

- Tubal ring (seen ~ of the time)
- 1-3 cm mass
- 2-4 mm concentric echogenic rim
- Hypoechoic center
Nonspecific US Findings of an Ectopic Pregnancy

- Pseudosac
- Free fluid in cul-de-sac
- Simple free fluid and an empty uterus:
  - *sensitivity - 63%
  - *specificity - 69%

Pseudogestational Sac

Don’t Be Fooled!

• Usually a single hyperechoic layer, irregular borders and centrally located

• Present in 20-40% of ectopic pregnancies

• Absence of low-resistance endometrial arterial flow on color Doppler
However...

Hyperechoic fluid and/or large amounts of free fluid are more suggestive of an ectopic pregnancy.
Ultrasound Findings

Ultrasound showing uterus and tubal pregnancy

Same image -
Uterus outlined in red,
uterine lining in green,
ectopic pregnancy in yellow.
Fluid within uterus in blue -
“pseudosac”
Ultrasound Findings

Same case.
Detailed view of ectopic

Same image -
Tubal pregnancy circled in red, 4.5mm fetal pole in green, yolk sac in blue
• Color Doppler can identify 1/65 ectopics not picked up on grey scale (Pelleritto, 1992)

• Vascular flow around an ectopic pregnancy is directly proportional to the amount of viable trophoblastic tissue present

Blood flow in the fallopian tube with an ectopic pregnancy is 20-45% higher than the normal
Very Rare Case of a Heterotopic Pregnancy

What is the incidence?*

1/30,000 - spontaneous pregnancies
1/100 to 1/3000 - ART

Molloy D et al. Multiple ciated pregnancy after in vitro fertilization and gamete
Case of a Cornual Ectopic Pregnancy

- EP
- distance 1.4mm from myometrium
- distance 1.4mm from serosa (<5mm)
- note eccentric location "high in the fundus"
Beta Subunit of hCG

- Glycoprotein produced by trophoblastic tissue
  *alpha subunit similar to LH/FSH/TSH*

- Beta subunit is unique to hCG

- Measured 8-12 days after fertilization

- Mean plasma concentration usually lower for an EP compared to a viable IUP*

C, et al. Human chorionic gonadotropin profile for women with ectopic preg
  Citalipram L868-107-535
Study of hCG Levels in 47 Ectopics*

<table>
<thead>
<tr>
<th>Peak hCG Level</th>
<th>% of Ectopics</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1000</td>
<td>45%</td>
</tr>
<tr>
<td>1000-3000</td>
<td>21%</td>
</tr>
<tr>
<td>3000-5000</td>
<td>15%</td>
</tr>
<tr>
<td>5000-10,000</td>
<td>10%</td>
</tr>
<tr>
<td>&gt;10,000</td>
<td>9%</td>
</tr>
</tbody>
</table>

*Daus et al., Journal of Reproductive Medicine, Feb 1989*
• Serial hCG testing performed q 48 hours

• Rate of hCG doubling decreases every 1.5 days in early pregnancy to every 3.5 days towards 7 weeks ega*

• 66% or greater increase is normal in ~85% of cases

• Caveat ~6-17% EPs have normal doubling times

Kadar N, Bohrer M et al. The discriminatory human chorionic gonadotropin
<table>
<thead>
<tr>
<th>Sampling Interval (Days)</th>
<th>Increase in hCG (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>29</td>
</tr>
<tr>
<td>2</td>
<td>66</td>
</tr>
<tr>
<td>3</td>
<td>114</td>
</tr>
<tr>
<td>4</td>
<td>175</td>
</tr>
<tr>
<td>5</td>
<td>255</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Trend of hCG Levels</th>
<th>% of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Falling</td>
<td>57</td>
</tr>
<tr>
<td>Abnormally Rising</td>
<td>36</td>
</tr>
<tr>
<td>Normally Rising</td>
<td>6.4</td>
</tr>
</tbody>
</table>

*Daus et al. Journal of Reproductive Medicine, Feb 1989, p 162*
Standards of Testing

• Quantitation is complicated by existence of multiple ref. standards for hCG assay

• 10-15% interassay variability among laboratories*

• defined as the serum hCG level above which a gestational sac should be visualized by ultrasound examination if an intrauterine pregnancy is present.*
  • 1500-2000 IU/L (transvaginal)
  • 6500 IU/L (transabdominal)
“Setting the DZ threshold at 2000 IU/L instead of 1500 IU/L minimizes the risk of interfering with a viable IUP, if present, but increases the risk of delaying diagnosis of an ectopic pregnancy.” *

Should You Check Serum Progesterone Levels?

- Limited clinical use
- Unlike hCG, progesterone levels are not dependent on gestational age
  - < 15 ng/ml ~ 14% ectopic risk
  - 20-25 ng/ml ~ 4% ectopic risk
  - > 25 ng/ml ~ 2% ectopic risk

*Gelder MS, et al. Use of a single random serum progesterone value as a...
The Future?

• Vascular Endothelial Growth Factor (VEGF)
  • found to be higher in EPs compared to normal IUPs or arrested IUPs*
  • at cut-off level of 200 pg/mL
  • sensitivity - 60%
  • specificity - 90%
  • PPV - 86%
Role of D&C

- Tissue diagnosis can be helpful when
  - serum hCG above DZ
  - gestational age > 38 days
  - absence of IUP via transvaginal US
  - No chorionic villi = presumptive diagnosis of ectopic pregnancy*

*More rarely - GTD, nongestational choriocarcinoma, or an embryonal cell tumor may be the cause.
Ria's-Stella Reaction

- Atypical endometrial changes of secretory cells with 4 key features:
  - hypertrophy, hyperchromatism, pleomorphism, & increased mitosis

- Previously thought to be unique to ectopics*
Histologic study of endometrium in 84 women diagnosed with ectopic pregnancies*

- Secretory Endometrium: 20%
- Decidual Reaction: 20%
- Proliferative Endometrium: 40%
- Arias-Stella Reaction: 20%
“Sometimes the only thing keeping you from a diagnosis is the anterior abdominal wall”
Ectopic Pregnancy (unruptured)
Management Options

• Stable patient
• Serial quantitative hCG testing*
• Transvaginal ultrasound*
• Serum progesterone?
• D&C
• Medical vs. Surgical treatment

*Sensitivity 97% Specificity 95% - Ankum WM, et al. Transvaginal sonography and human chorionic adotropin measurements in suspected ectopic pregnancy: a detailed analyses of a diagnostic approach
Management Options

- Unstable patient
- Qualitative hCG*  
- Transvaginal ultrasound*
- Culdocentesis?  
- Surgical treatment*
Surgical Options

• Nearly all ruptured ectopic pregnancies require surgical treatment
  • Radical operation - salpingectomy
  • Conservative operation* - linear salpingostomy or segmental resection

*Preferred approach when all things considered equal. IUP rate higher (61 & 33% respectively), although risk of recurrent ectopic pregnancy is higher (15 & 10% respectively)**
Linear Salpingostomy (Laparoscopy/Laparotomy)

- Method of choice for tubal ectopics
- Best for ampullary (not isthmic) ectopics less than 4 cm in size
- Use microsurgical techniques
Linear Salpingostomy

Incision already made; ectopic exposed

Ectopic teased out & irrigated; incision
chorionic villi seen in a background of hemorrhage (red center) next to a portion of gestational sac (pink)
Visualizaion of the tubal epithelium and under stroma.
Embryo of tubal pregnancy seen inside the tubal gestational sac. Some trophoblastic villi are also seen.

*From H. Allen of Clinical Gynecologic Oncology, 1982,*
Think Salpingectomy if:

- Uncontrolled bleeding
- Recurrent ectopic in the same tube
- Severely damaged tube
- Large tubal pregnancy (i.e. > 5 cm)
- Women who have completed childbearing
Other Techniques
(Pending circumstances, conservative surgery is usually advised)

<table>
<thead>
<tr>
<th>Ectopic Location</th>
<th>Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isthmic</td>
<td>Partial salpingectomy/LS*</td>
</tr>
<tr>
<td>Fimbrial</td>
<td>Fimbriectomy/LS*</td>
</tr>
<tr>
<td>Cornual</td>
<td>MTX/IR/Wedge resection/TAH*</td>
</tr>
<tr>
<td>Cervical</td>
<td>MTX/KCI/IR/TAH*</td>
</tr>
<tr>
<td>Ovarian</td>
<td>Partial resection/oophorectomy</td>
</tr>
</tbody>
</table>
Following Beta-hCGs

• POD 1 beta declines > 50%*

• Target or goal
  • level < 5% of preoperative value
  • higher value calls for repeat measurements q weekly
  • follow until < 10 mIU/mL

References:
Sorfer SD et al. Postoperative day 1 serum human chorionic gonadotropin level as a predictor of persistent ectopic pregnancy after conservative surgical management.
1982 - Tanaka et al. reported successful use of MTX for sole treatment of an unruptured interstitial pregnancy

1983 - Miyazaki et al. reported first series of successful treatment of small unruptured ectopic pregnancies with MTX
Folinic acid antagonist that inhibits dihydrofolic acid reductase which inhibits DNA synthesis, repair, and cellular replication.
How Effective is MTX?

- Median success rate is 84% associated with single-dose MTX regimen.

- Largest study involved 120 women with an overall success rate of 94% with 25% requiring more than one dose of MTX.

*Stovall TG, Ling FW. Single-dose methotrexate: an expanded clinical use.*
## Indications for MTX*

<table>
<thead>
<tr>
<th>Absolute Indications</th>
<th>Relative Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemodynamically stable</td>
<td>Unruptured Mass &lt; 3.5cm</td>
</tr>
<tr>
<td>Future fertility desired</td>
<td>No fetal cardiac activity</td>
</tr>
<tr>
<td>Compliant patient</td>
<td>Beta hCG &lt; 6,500 mIU/ml</td>
</tr>
<tr>
<td>Normal liver/kidney fxn</td>
<td></td>
</tr>
<tr>
<td>Absent chorionic villi*</td>
<td></td>
</tr>
</tbody>
</table>

*Stovall TG, Ling FW. Single-dose methotrexate: an expanded
MTX Single Dose Protocol

Day 0
Beta-hCG
BUN/creatinine
LFTs/CBC
ABO & Rh

Day 4
Beta-hCG

Day 7
Beta-hCG
BUN/creatinine
LFTs/CBC

Values WNL & criteria met

Administer MTX 50mg/m²

Remember:
Stop folic acid and PNVs

Laparoscopy/Laparotomy
or
Repeat MTX

<15% decline in Beta-hCG from day 4 to day 7

<25% decline in Beta-hCG from day 0 to day 7

ITX Side Effects

- Nausea/vomiting
- Stomatitis
- Diarrhea
- Gastric distress
- Rare neutropenia and alopecia
- Pneumonitis
Over 60% of patients who receive MTX on day 0 will experience an increase in abdominal pain between days 3-7 as well as bleeding/spotting. These symptoms/signs could also represent a ruptured ectopic.
### Comparing MTX to Surgery

<table>
<thead>
<tr>
<th></th>
<th>MTX</th>
<th>Tube-Sparing Laparoscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resolution Rate (%)</td>
<td>87</td>
<td>91</td>
</tr>
<tr>
<td>Complication Rate (%)</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>Cost ($)</td>
<td>477</td>
<td>4102</td>
</tr>
</tbody>
</table>

Future Fertility

- Multiple factors affect future pregnancies such as:
  - age, parity, condition of tubes, infertility history, contraception etc.

- In general the IUP rate in patients with previous full-term pregnancies 60-80%

- Rate is ~40% if nulliparous
Future Fertility Rates

- After One Ectopic & Tubal Sparing Surgery
- After One Ectopic & Other Tube Abnormal

% IUP | % Recurrent Ectopic | % Infertility
---|---------------------|------------------
60  | 50                  | 20               
50  | 50                  | 15               
30  | 30                  | 25               

Diagnosis of Ectopic pregnancy*

- Giving MTX without visual and/or histologic confirmation of an ectopic pregnancy

- Why?
  - Attempt to simplify management
  - Save time & expense
  - Avoid risks associated with surgery
• Retrospective cohort study @ University of Pennsylvania 2002; 113 patients reviewed*

• Recommended D&C; confirm dx before tx

• Why?

  • Presumptive dx of ectopic pregnancy was inaccurate 40% of the time

  • Diagnostic accuracy of US limited, especially when hCG below DZ
• MTX alone never studied as a treatment for nonviable pregnancies

• Side effects reported in ~40% of patients

• Legal implications; teratogenic effects

• Falsely perceived success of treatment of women with true ectopics

• False diagnosis may impact future care
To D&C or Not?

Food for thought...

• Decision analyses comparing cost/complication rates*
  • no significant benefit of one approach over the other
  • negligible side effects of one dose of MTX

All Rh negative, unsensitized women with an ectopic pregnancy should receive Rh immunoglobulin (RhoGAM™).
Ectopic Pregnancy

The Take Home Points

• Leading cause of pregnancy-related death during first trimester

• Diagnosis & treatment before tubal rupture decreases risk of death

• Early detection may allow for medical treatment
ABNORMAL UTERINE BLEEDING
Common in women of all ages

~5% of women of reproductive age seek help annually

Life phase determines most likely cause

Take time to properly assess the problem

Work-up and treat in rational manner
Common Causes

- Pregnancy
- Hormonal/Dysfunctional
- Anatomic
- Coagulopathy/bleeding disorder
Characterize menses
Age, parity, past pregnancies, sexual history, contraception, past gynecologic problems, medications
Personal or family history of bleeding disorder
Symptoms of thyroid disease
History of liver disease
Physical Exam

Orthostatic VS if indicated by HX

Pelvic exam

Skin – ecchymoses, hirsutism

Thyroid gland

Liver and assoc stigmata

Signs of virulization
CBC with Plts
Urine beta-hCG
TSH
LFTs, coagulation studies
Coagulation profile
GC, Chlamydia
Free testosterone, DHEA-S
FS
Reproductive Age

Rule out pregnancy

Genital tract lesion

Enlarged uterus

  • Sono for anatomic cause
If not pregnant and normal exam: most likely hormonal

Determine ovulatory status

Treatment usu. hormonal
Assess for secondary hypothalamic disorder
Check TSH
Test for PCOS if indicated
Consider chronic anovulation
Address underlying disorder

Treat with monthly OCPs or progesterone withdrawal

- Regulate cycles and protect against endometrial CA
Ovulatory Bleeding

- Usually underlying prostaglandin imbalance
- Much less common 5-10%
- Structural lesions
- Systemic disease
  - Liver dz, remal failure bleeding disorder
Ovulatory Bleeding

>35 EMB

TSH

Metabolic labs

TVUS

Consider sonohysterogram

Hysteroscopy – “Gold Standard”
5-10% endometrial carcinoma

EMB/TVUS

DDX: endometrial hyperplasia, cervical cancer, cervicitis, atrophic vaginitis/endometrium, submucosal fibroids, endometrial polyps, endometrial cancer
Treatment: Acute Bleeding

Conjugated estrogen x 21d

IV estrogen for severe bleeding

High dose OCP: 1qid x 4d tapering dose
Surgical Treatment

Therapeutic D&C
Fastest method to stop bleeding in unstable patients

Endometrial ablation – if fertility not desired

Hysterectomy
Abnormal uterine bleeding is very common.
Life phase and detailed menstrual history are key.
Employ rational evaluation and treatment strategy.
Ovulatory Bleeding

Empiric Treatment

- NSAIDS
- Cyclic OCP’s
- Progesterone IUD
- Tranexamic acid
dolescents

Usually anovulation due to immature hypothal-pit axis

Rule out pregnancy

Consider bleeding disorder

Observe or Rx with cyclic OCP’s
THANK YOU

• ANY QUESTIONS?