Female Genital Tract: Ovary

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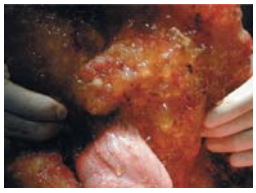
IU Health Bloomington hospital
Depart. Pathology

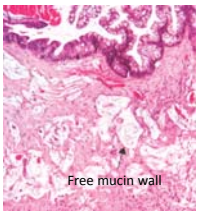
Ovary

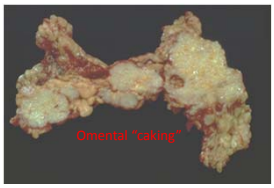
- Ovarian ca accounts for 3% of all ca's.
- Fifth MCC of death due to ca in women.
- Most are detected b/c of ascitis when the tumor has already spread beyond the ovary (peritoneal spread).
- Pseudomyxoma peritonei: extensive mucinous ascitis, cystic epithelial implants peritoneal surfaces/adhesions.
  - Can cause death due to GI obstruction
  - Once thought to originate from ovary, NOW we think of appendiceal primary.

Pseudomyxoma peritonei

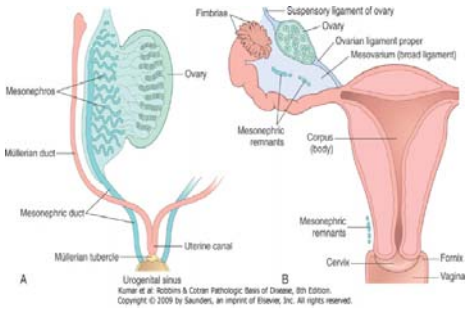
- Massive overgrowth gelatinous metastatic tumor originating ovary/or appendix.





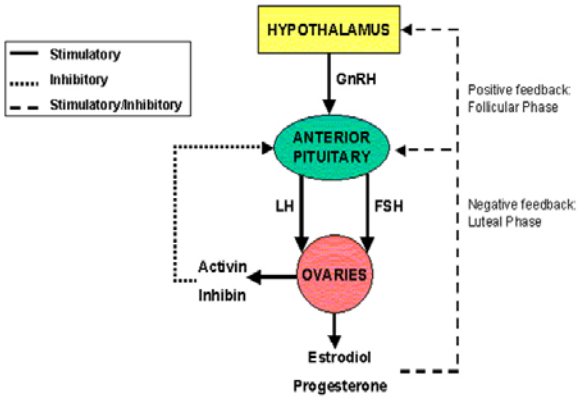


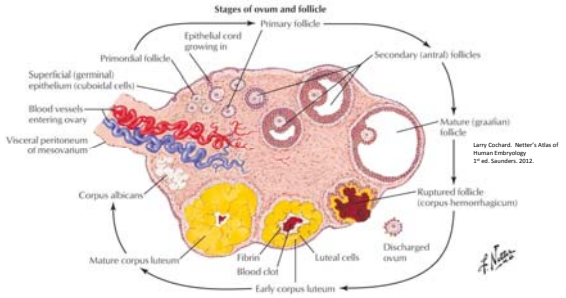
Embryology of female lower genital tract



3 main histologic compartments:

1. Surface mullerian epithelium
2. Germ cells
3. Sex cord-stromal cells



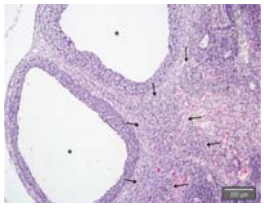


Nonneoplastic cysts

- Cystic follicle cyst:
  - Originate unruptured graafian follicles or in follicles that have ruptured and immediately sealed.

  Multiple; considered normal

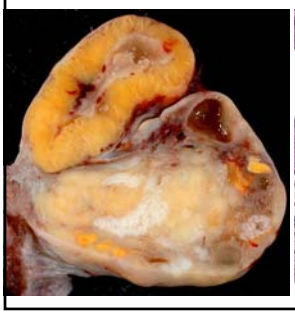
Follicle cyst

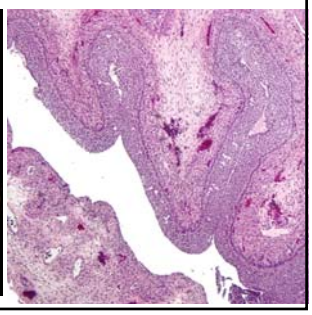


Nonneoplastic cysts

- Granulosa luteal cysts (corpora lutea)
  - Normally present
  - Grossly lined by rim bright yellow tissue containing luteinized granulosa cells.
  - Sometimes hemorrhagic/fibrosis; differential from endometriotic cysts.

Corpus luteal cyst





Polycystic ovary

Stein-Leventhal syndrome
Anovulatory hyperandrogenism

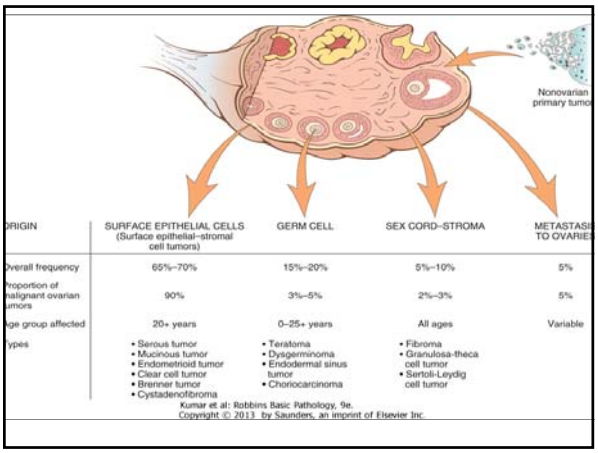
String of pearls

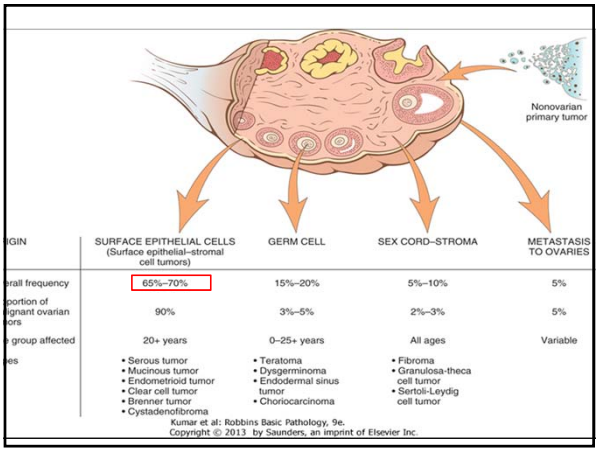
- Ovaries are 2X nml size
- Gray-white outer cortex w/subcortical cysts
- Microscopically, hyperplasia of theca interna (follicular hyperthecosis).

- Affects 3-6% reproductive-age women
- Numerous cystic follicles
- Persistent anovulation, obesity (40%), hirsutism (50%), and rarely virilism

Classification ovarian tumors

- Surface epithelium (derived from coelomic epithelium)
- Germ cells (which migrate from yolk sac to ovary)
- Stroma (including sex cords)
- Metastatic



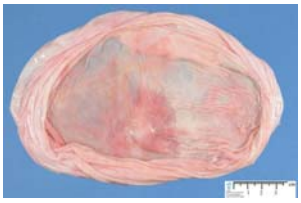


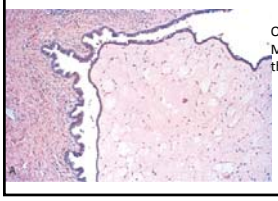
Torsion of ovary

Surface epithelial tumors: 3 histologic subtypes

- Serous
  - Benign
  - Borderline
  - malignant
- Mucinous
  - Benign
  - Borderline
  - malignant
- Endometroid

Two different types based on pathogenesis:
1. Those that arise in association with borderline tumors
2. Those that arise as "de novo" carcinomas.

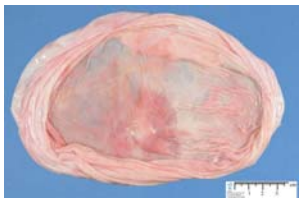
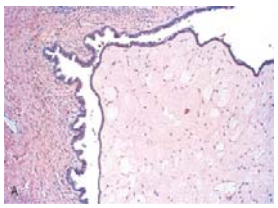




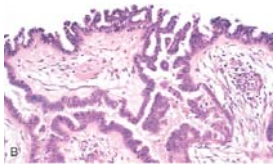
Origin of tumors: transformation coelomic epithelium
Mechanism :invaginations of surface epithelium that lose its connection to the surface.

Ovarian serous cystadenoma

- Serous MC, lined by tall, columnar, ciliated and nonciliated epithelial cells.
- Account for 40% of all ovarian ca.
- Risk factors: nulliparity, family history, and heritable mutations (BRCA1, BRCA2); reduced tubal ligation and oral contraceptives.
- Estimated risk in BRCA1,2 is 20-60% by the ripe old age of 70
- Some people have classified in low-grade/high grade:
  low gd: KRAS, BRAF
  high gd: p53
- Recent studies: BRCA1,2 arise from fimbriated ends of fallopian tubes.

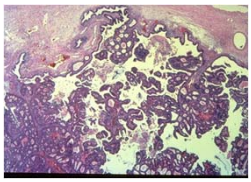
Serous tumor of low malignant potential

- Cyst cavity lined by delicate papillary tumor growths.
- Bilateral tumors common (30%)

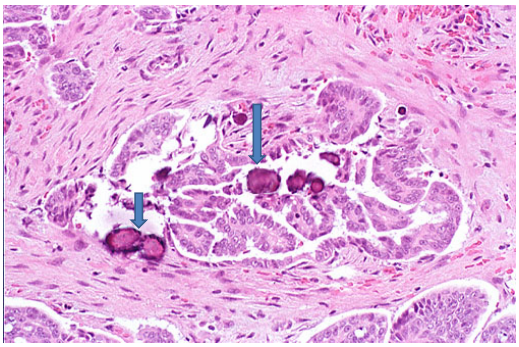
- Borderline tumors show increased architectural complexity and epithelial cell stratification.

Serous cystadenocarcinoma

- Invasion underlying stroma.
- Bilateral tumors 66%.
- Borderline/malignant involve (originate from) surface ovary.

Serous adenocarcinoma with psammoma bodies

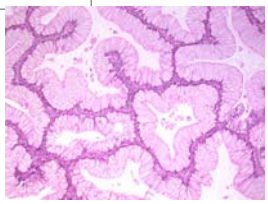


Mucinous cystadenoma

- Less common than serous tumors, 30% of all ovarian tumors in middle adult life.
- Only 15% of these are malignant.
- Risk factors: smoking (not for serous).
- Consistent KRAS proto-oncogene mutation (found in 85% of malignant tumors).
- Rarity of surface involvement
- Less frequently bilateral.
- They can be HUGE!!
- Multiloculated tumors with mucin, tall columnar epithelium w/apical mucin and absence of cilia.

Ovarian mucinous cystadenoma

- Multicystic appearance, delicate septa, mucin within cysts

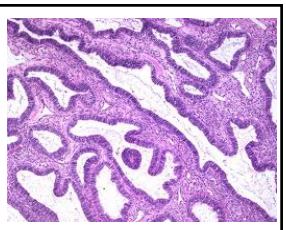
Mullerian mucinous cystadenoma

- Benign/borderline tumor arising from endometriosis.
- Looks like endometrial or cervical epithelium.

Ovarian mucinous cystadenocarcinoma

- Areas of solid growth grossly
- Similar morphology to cervical or intestinal epithelium.
- Abundant glandlike or papillary growth with nuclear atypia and stratification, necrosis.(Looks like colon ca)

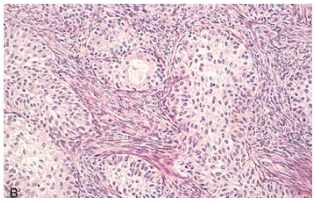
Endometrioid tumors (cystadenoma/borderline)



- 40% are bilateral.
- Low grade tumors glandular patterns
- 5-year survival for stage 1 is 75%

- Benign endometriod tumors are called endometriod adenofibromas.
- Account for 20% of all ovarian ca's.
- Characterized by tubular glands looking like endometrium.
- Can arise from endometriosis, 15-20% (usually borderline)
- Interestingly 15-30% can be accompanied by endometrial ca
- Mutations PTEN tumor suppresor gene and in p53, KRAS, B-catenin oncogenes, as well as microsatellite instability.

Brenner tumor



- Classified as adenofibromas in which the epithelial component consists
- of nests of transitional-type epithelial cells.
- Stroma composed of plump fibroblasts.
- Usually unilateral.
- Range from 1-30 cm in size, can be b9, borderline or malignant.

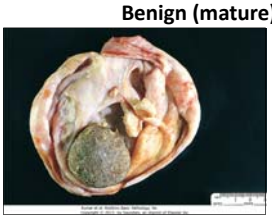
Germ cell tumors constitute 15-20% of all ovarian tumors, most are benign cystic teratomas.

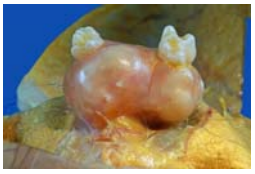
Teratomas divided in 3 categories:
1. Immature (malignant)
2. mature (benign)
3. monodermal or highly specialized

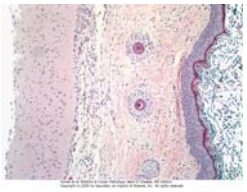
Benign (mature) cystic teratoma

- Most are cystic, also called dermoid cysts.
- Young women
- Can be incidental or cause paraneoplastic syndrome
- Bilateral 10-15% of cases
- Characteristically unilocular, contains hair, sebaceous material, sometimes teeth, thyroid, cartilage, and neural tissue.
- **About 1% can undergo malignant transformation (MC SCC).**

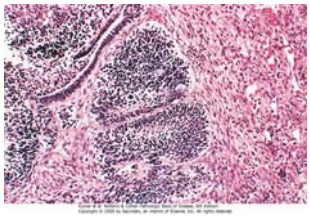
Benign (mature) cystic teratoma





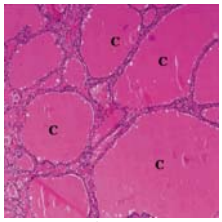


Malignant (immature) teratoma



- Specialized teratoma includes struma ovarii and carcinoid.
- Can cause hyperthyroidism, and 5-hydroxytryptamine

Struma ovarii

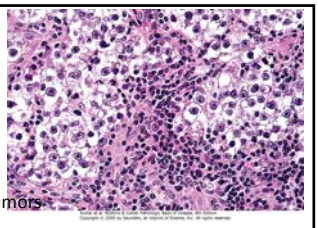


- Prepuberal young women.
- Tumors are bulky, solid, w/areas necrosis and hemorrhage.
- These should have a histologic grade, based on
- Immature neuroepithelium.
- Grow rapidly, stage 3 gets chemo
- Most recurrences occur within 2 yrs

(so if your disease free for this time it carries a excellent cure rate)

Germ cell tumors

Dysgerminoma

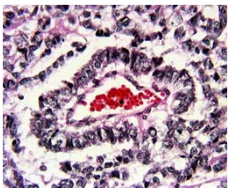


- "Seminoma counterpart"
- 50% of malignant germ cell tumors (but only 2% of all tumors)
- 2-3rd decade
- All malignant, 80%unilateral
- Express Oct3-4, Nanog, C-KIT (c-kit useful diagnostic/therapeutic ma
- Grossly solid tumors soft fleshy looking
- Composed large vesicular cells w/clear cytoplasm
- Cells well defined boundaries, infiltration of lymphocytes.
- Responsive to chemo!!
- Survival 80%

Figure 18-21

Germ cell tumors

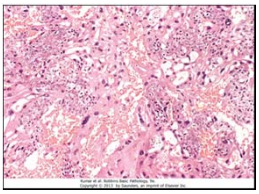
Yolk sac (endodermal sinus) tumor



- Rare; children or young women
- Grow rapidly /aggressive
- Derived from malignant germ cells along extra-embryonic yolk sac lineage.
- Schiller-Duval body: glomerulus-like structure composed of central blood vessel enveloped by germ cells within a space lined by germ cells.
- α-fetoprotein & alpha1-antitripsin
- Before chemo, used to be fatal with 2 years.Yikes!

Germ cell tumors

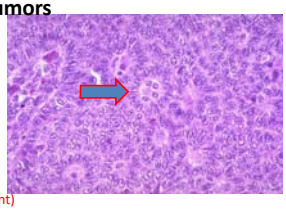
Choriocarcinoma



- Most coexist with other germ cell tumors
- Ovarian primaries aggressive; met through bloodstream to lungs, liver, bone.
- Syncytiotrophoblasts
- Cytotrophoblasts
- High levels β-hCG(establish dx or detecting recurrences).
- Unresponsive to chemo and often fatal

Ovarian sex cord-stromal tumors

- Derived from ovarian stroma, which in turn comes from sex cords of the embryonic gonad.

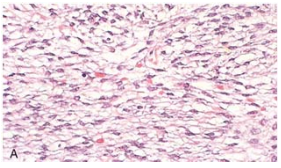


Granulosa cell tumor

- 5% of all ovarian tumors
- 2/3 postmenopausal women but any age
- Estrogenic (precocious sexual development)
- Call-Exner bodies: gland like structure filled with acidophilic material recall immature follicle
- Composed entirely granulosa or granulosa/theca cells.

Ovarian sex cord-stromal tumors

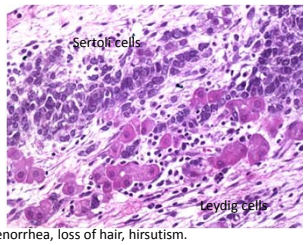
Fibroma-thecoma



- Composed of fibroblasts (fibromas) or plump spindle cells w/lipid droplets (thecom
- Meigs syndrome: Ovarian tumor,hydrothorax and ascitis
- Unilateral 90%, solid, spherical, or slightly lobulated, encapsulated gray white mass
- Genesis unknown
- Association w/ basal cell nevus syndrome
- If malignant (high mitosis) we call it fibrosarcoma

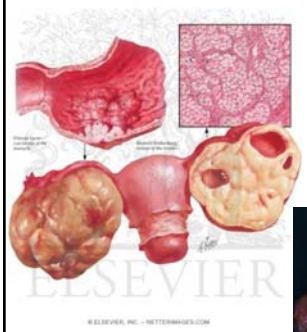
Ovarian sex cord-stromal tumors

Sertoli-Leydig cell tumor



- Androgenic: atrophy breasts, amenorrhea, loss of hair, hirsutism.
- Occur in women all ages, more so 2-3rd decade
- Unilateral
- Cut surface gray to golden brown
- Tubules composed of Sertoli cells or Leydig cells interspersed with stroma.
- Poorly differentiated tumors can have sarcomatous pattern
- Recurrence <5%

Krukenberg tumor



Classic example of metastatic GI signet ring ca to bilateral ovaries, usually stomach

Clinical course, detection and prevention

- Lower abdominal pain, enlargement, GI complaints, urinary frequency, dysuria, pelvic pressure.
- Massive ascitis, wl, cachexia (malignant tumors seed the peritoneum)
- Usually go undiagnosed until they are large, and no longer confined to the ovary.
- Early diagnosis, prevention are top priorities
  - CA125 80% serum; useful for moniter disease
  - Can give false elevations with peritoneal irritation
  - Osteopontin newer, can be used in detection.
- Mets can involve liver, lungs, and GI tract.
- Pts with BRCA mutations standard to perform prophylactic salpingo-oophorectomy.