

# PATHOLOGY OF THE OVARY AND CLINICAL CORRELATES

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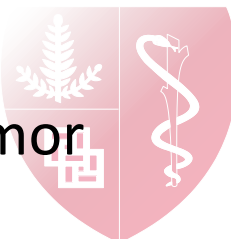


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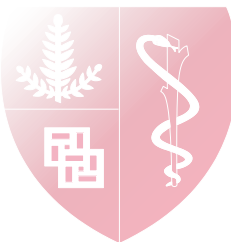
HHD Autumn 2015

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- At the conclusion of this session, students will
    - Be able to list the differential diagnosis of a pelvic mass in a woman of reproductive age
    - Be able to list the most important “can’t miss” diagnoses in a prepubertal child and postmenopausal woman
    - Be familiar with the natural history of surface epithelial malignancy, germ cell tumor, and sex cord stromal tumor
    - Be able to understand the concept of a tumor of low malignant potential (borderline tumor)
  - Ovarian Cancer, CA125, borderline tumor, germ cell tumor, sex cord stromal tumor

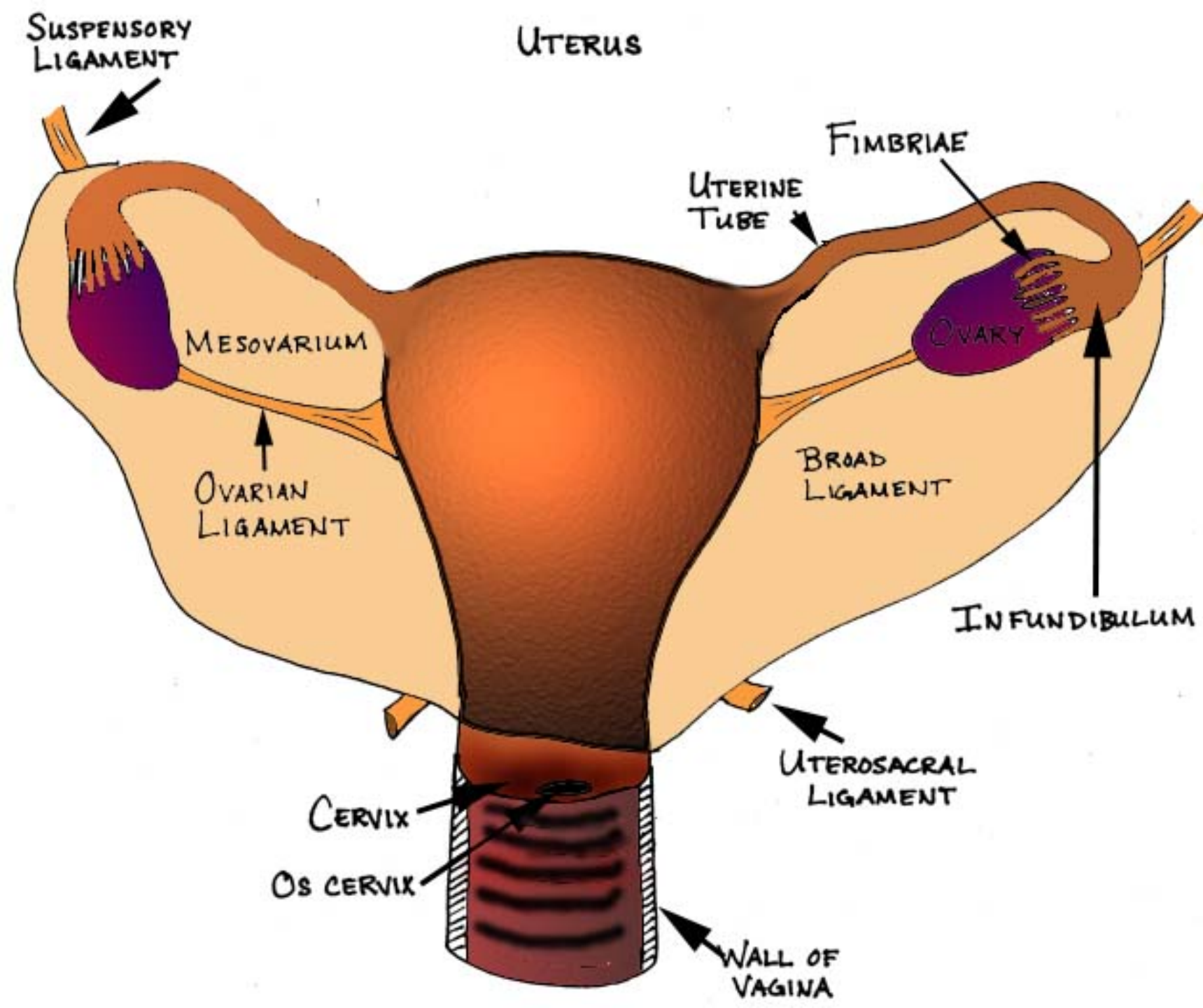


# OVARIAN ANATOMY AND HISTOLOGY

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# Pelvic Anatomy





# Ovarian Histology

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## 1. Surface epithelium and undifferentiated stroma

- Surface mesothelium but special properties
- Undifferentiated fibroblastic cells

## 2. Specialized ovarian stroma

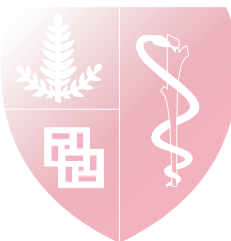
- Ovarian follicle: Endocrine organ each month
  - Granulosa cells
  - Theca cells

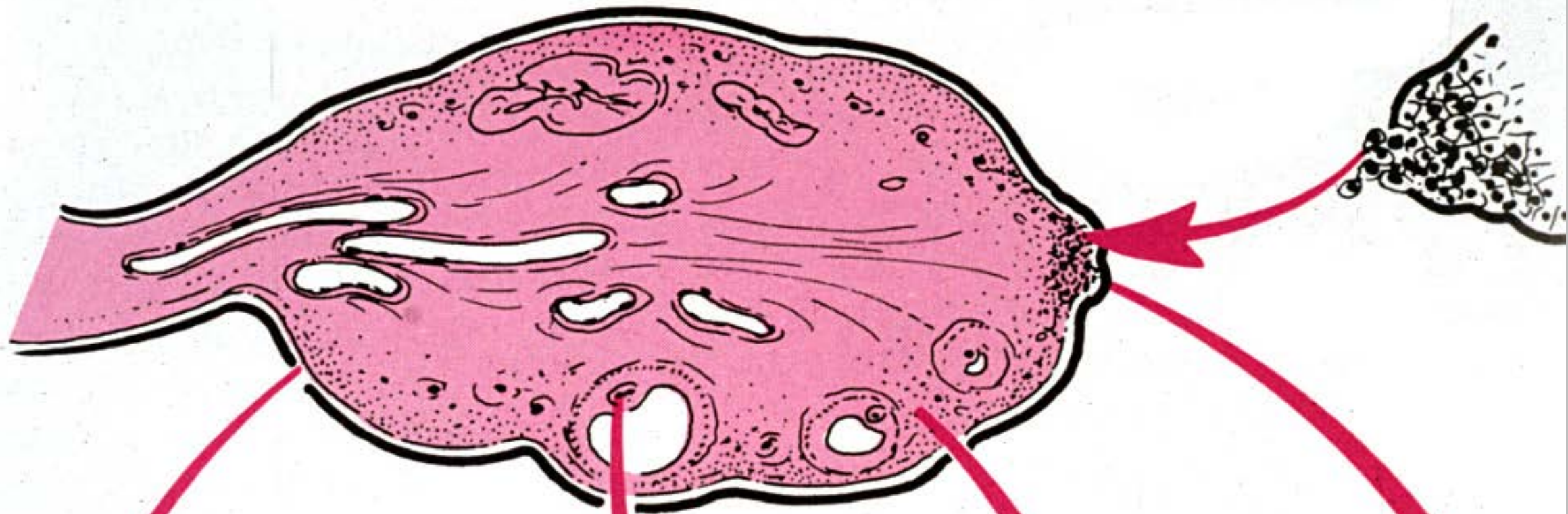
## 3. Germ cells

- Migrate from the yolk sac
- Midline location of extragonadal germ cell tumor
- Arrested in the first meiotic division

## 4. Other

- **Metastasis**



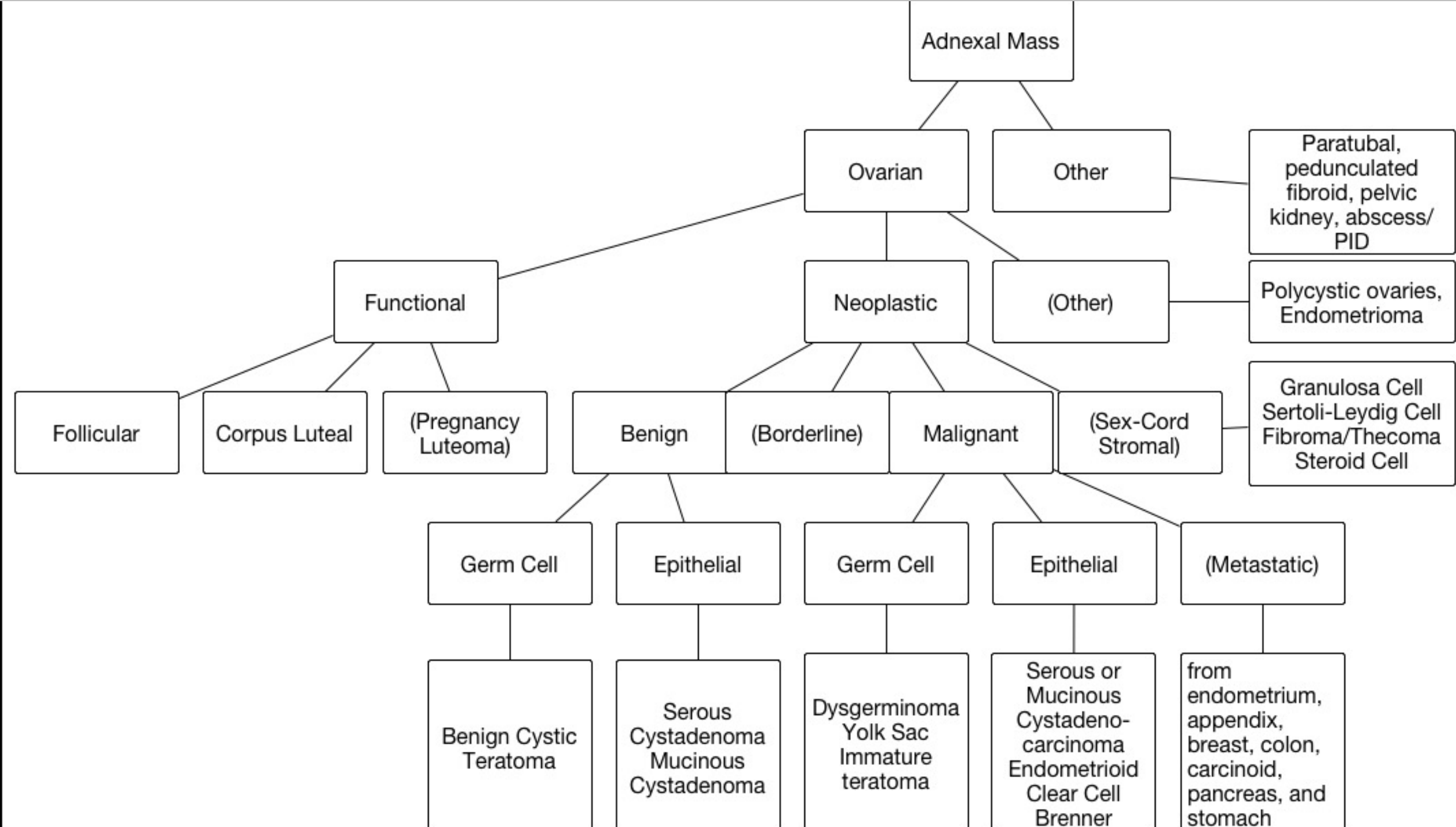


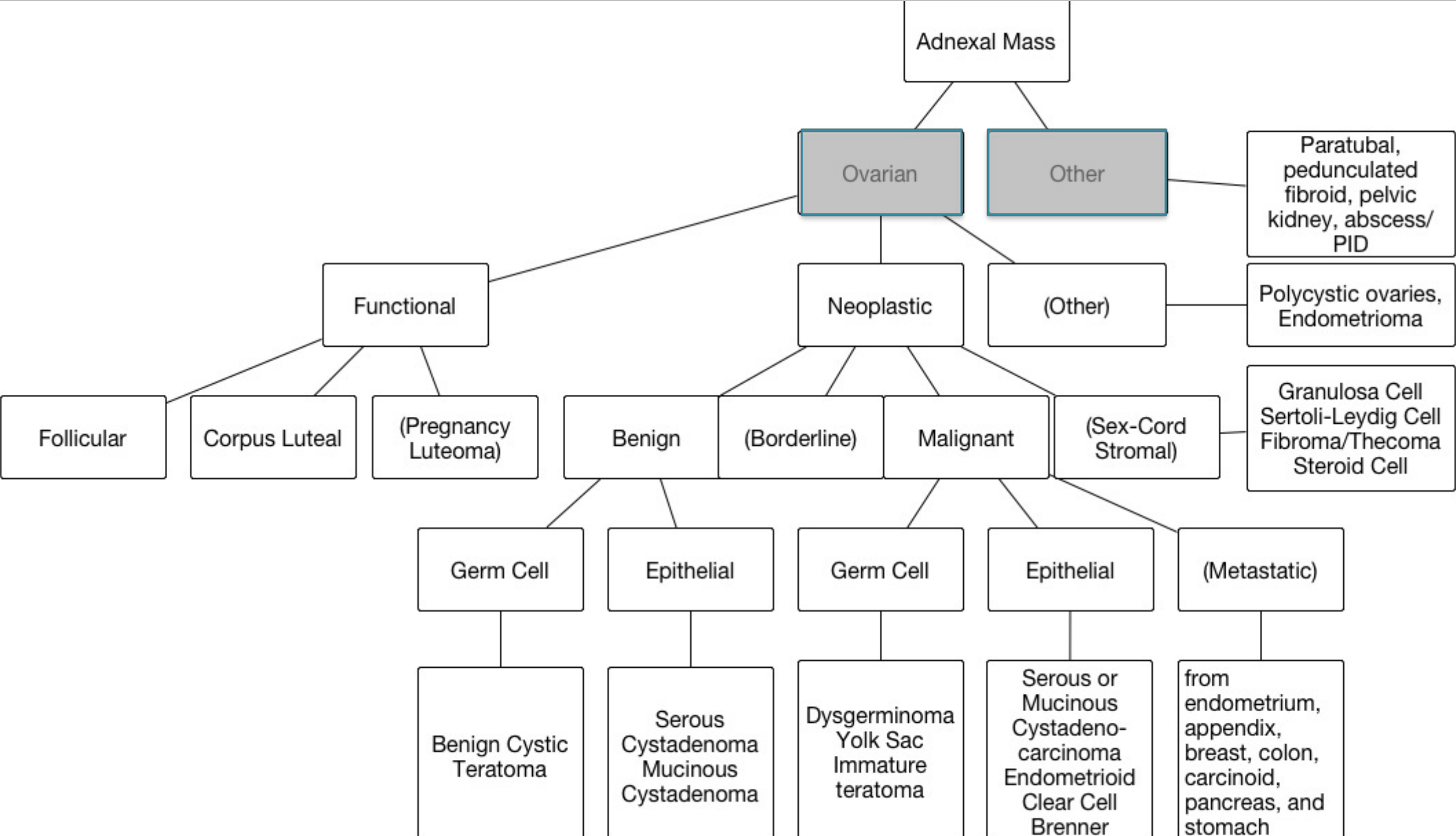
Surface epithelial cells  
(common epithelial tumors)

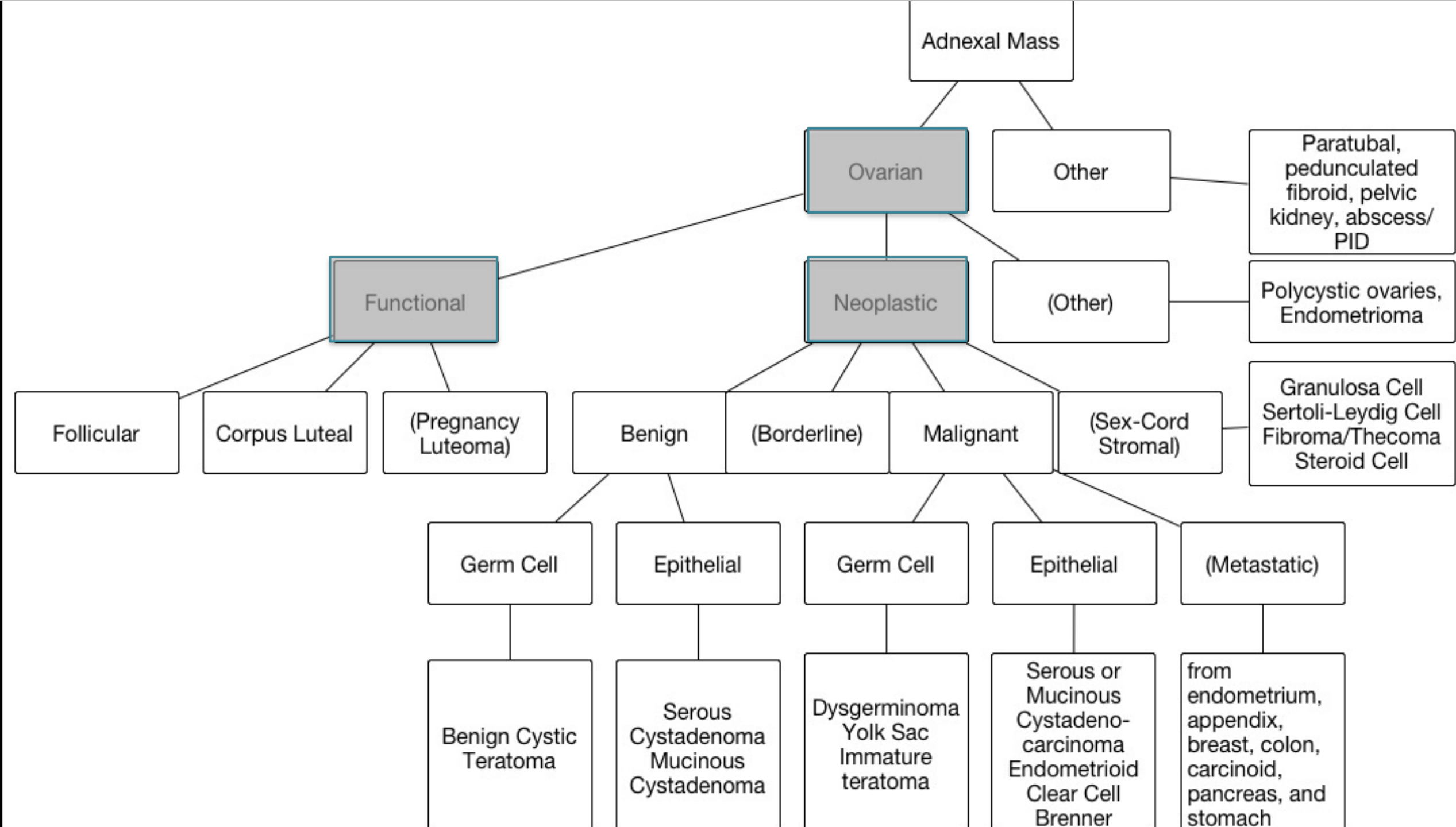
Germ cell

Sex cord-stroma

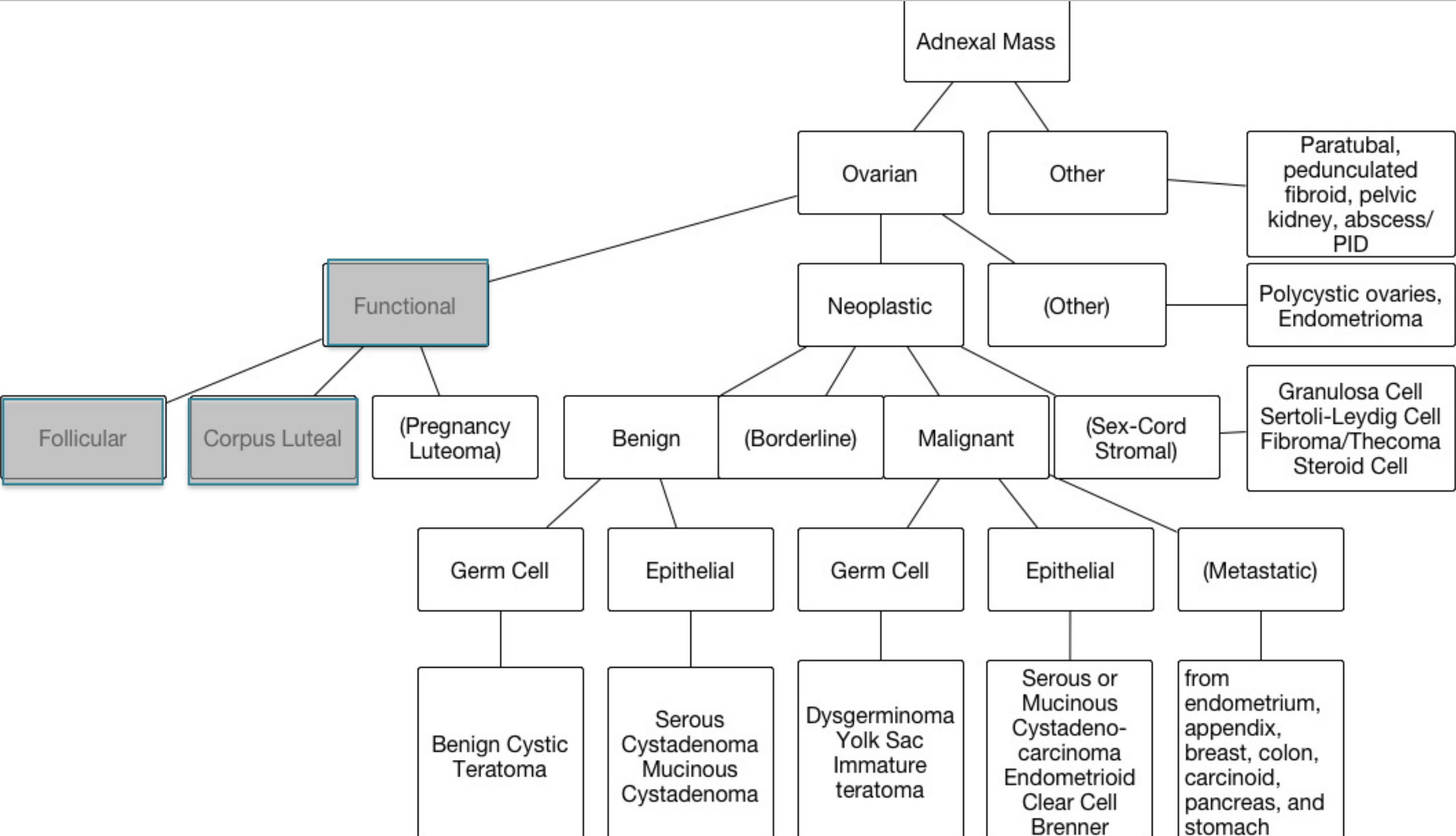
Metastasis  
to ovary

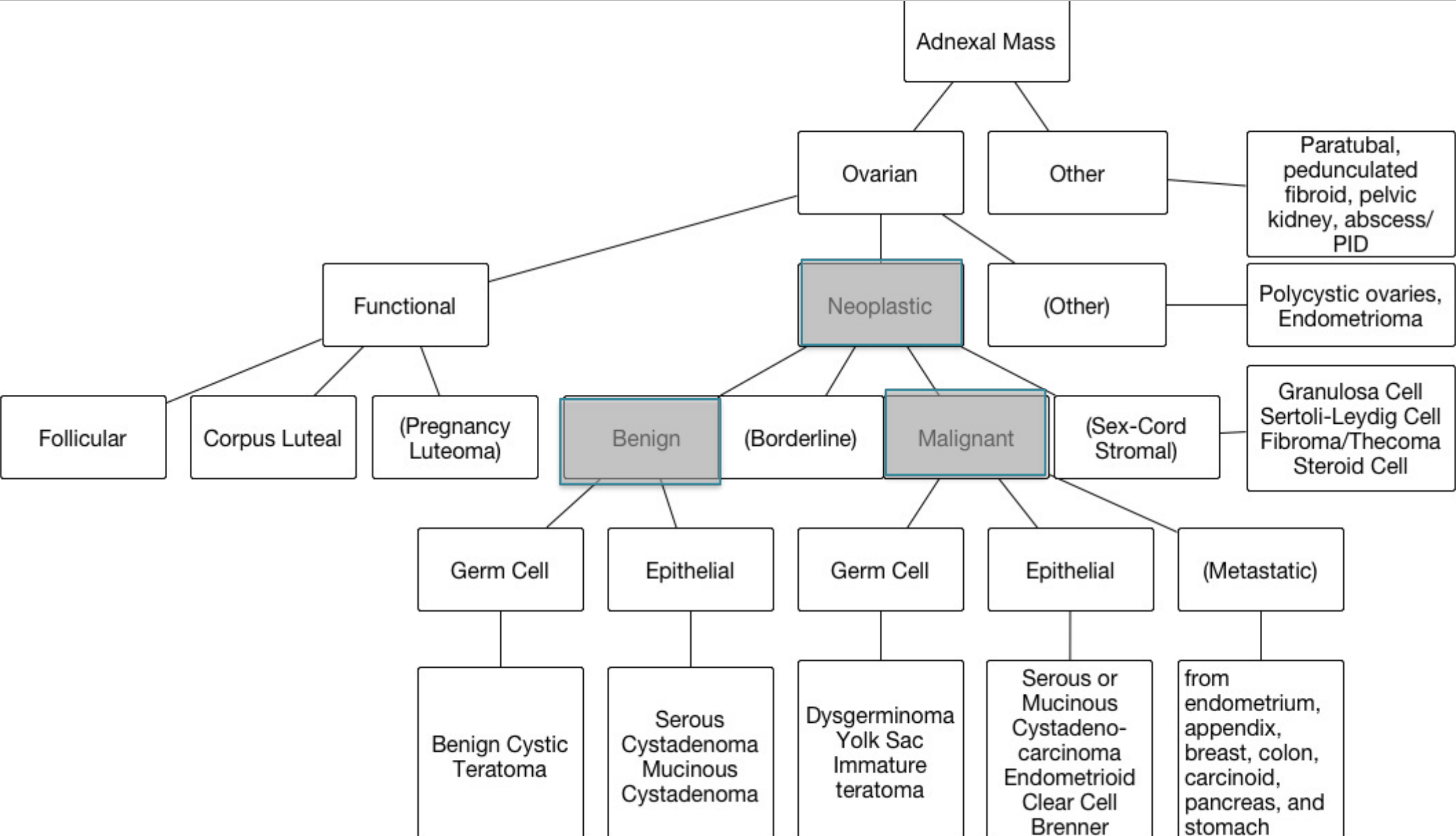


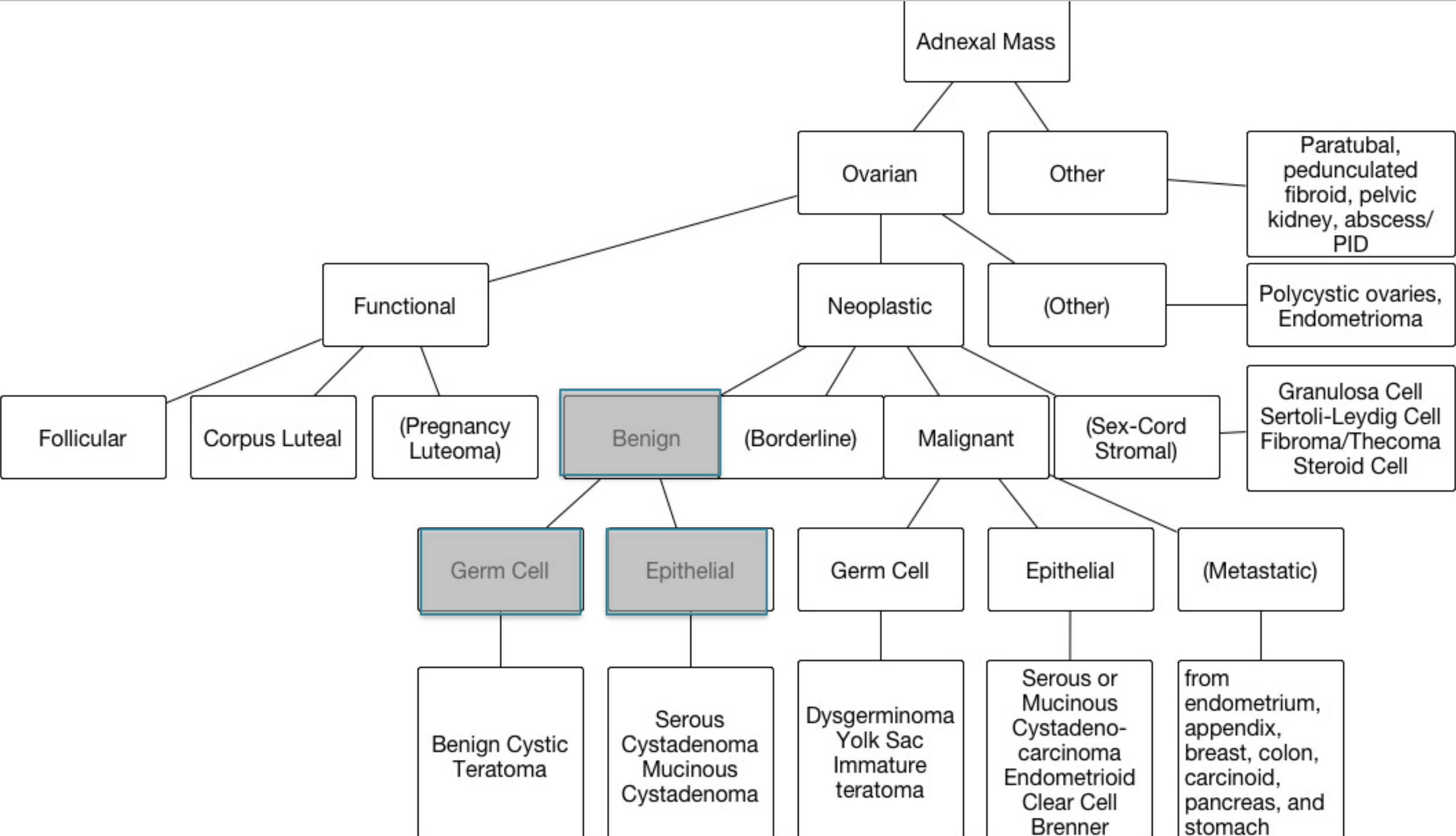




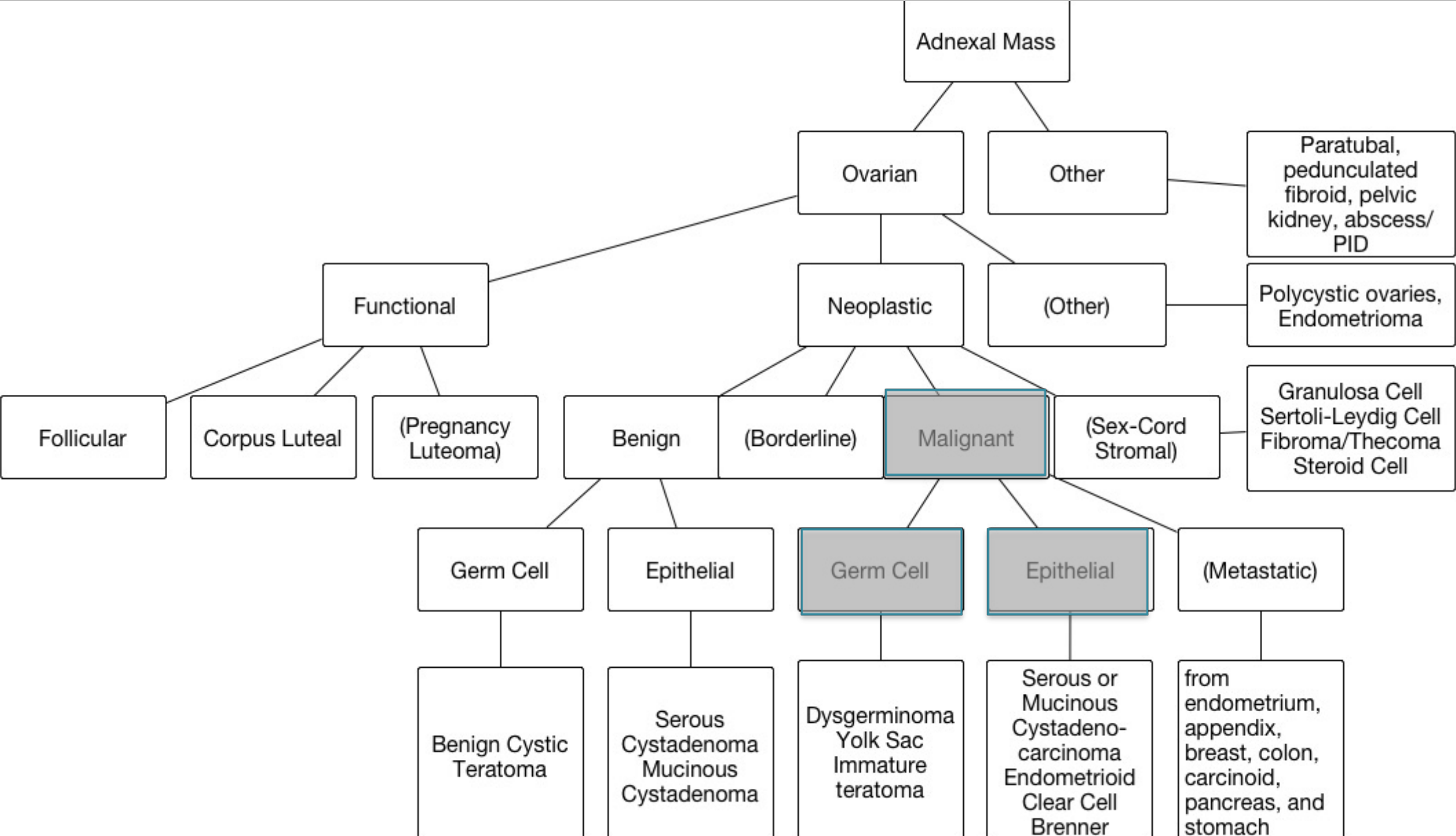












# PELVIC MASSES AND ABNORMAL OVARIES

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- Not all pelvic masses are ovarian
- Ovarian masses vary by reproductive age



Table 14.4 Causes of Pelvic Mass by Approximate Frequency and Age

Infancy	Prepubertal	Adolescent	Reproductive	Perimenopausal	Postmenopausal
Functional cyst	Functional cyst	Functional cyst	Functional cyst	Fibroids	Ovarian tumor (malignant or benign)
Germ cell tumor	Germ cell tumor	Pregnancy	Pregnancy	Epithelial ovarian tumor	Functional cyst
		Benign cystic teratoma/other germ cell tumors	Uterine fibroids	Functional cyst	Bowel, malignant tumor or inflammatory
		Obstructing vaginal or uterine anomalies	Epithelial ovarian tumor		Metastases
		Epithelial ovarian tumor			

**“Can’t  
Miss”  
Disagnoses**

Hillard, Benign Diseases of the Female Reproductive Tract in Berek & Novak’s Gynecology, 15<sup>th</sup> Ed.

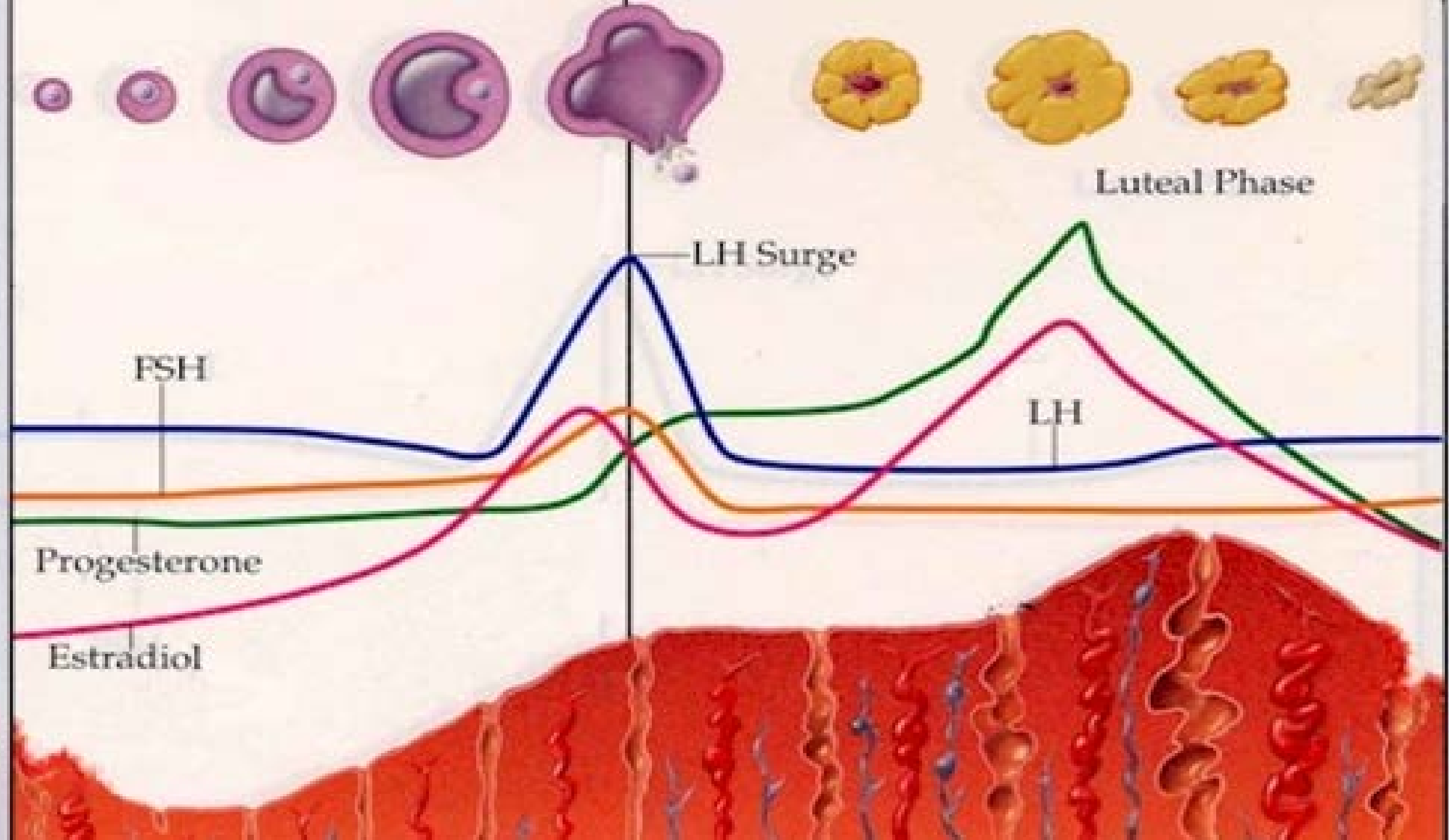


# Mechanism of Ovarian Symptoms

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- Chronic
  - Mass effect—Pressure (early satiety, bladder or rectal pressure, palpable mass )
- Acute Pain—Assess in relation to menstrual cycle
  - Hemorrhage into cyst cavity (Corpus Luteum CL cyst)
  - Hemorrhage into peritoneal cavity—Hemoperitoneum
  - Torsion
- Endocrine
  - Hyperestrogenic symptoms (precocious puberty; AUB)--RARE
  - Hyperandrogenic symptoms (Hirsutism, virilization)--COMMON

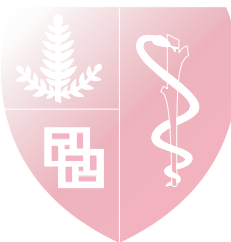


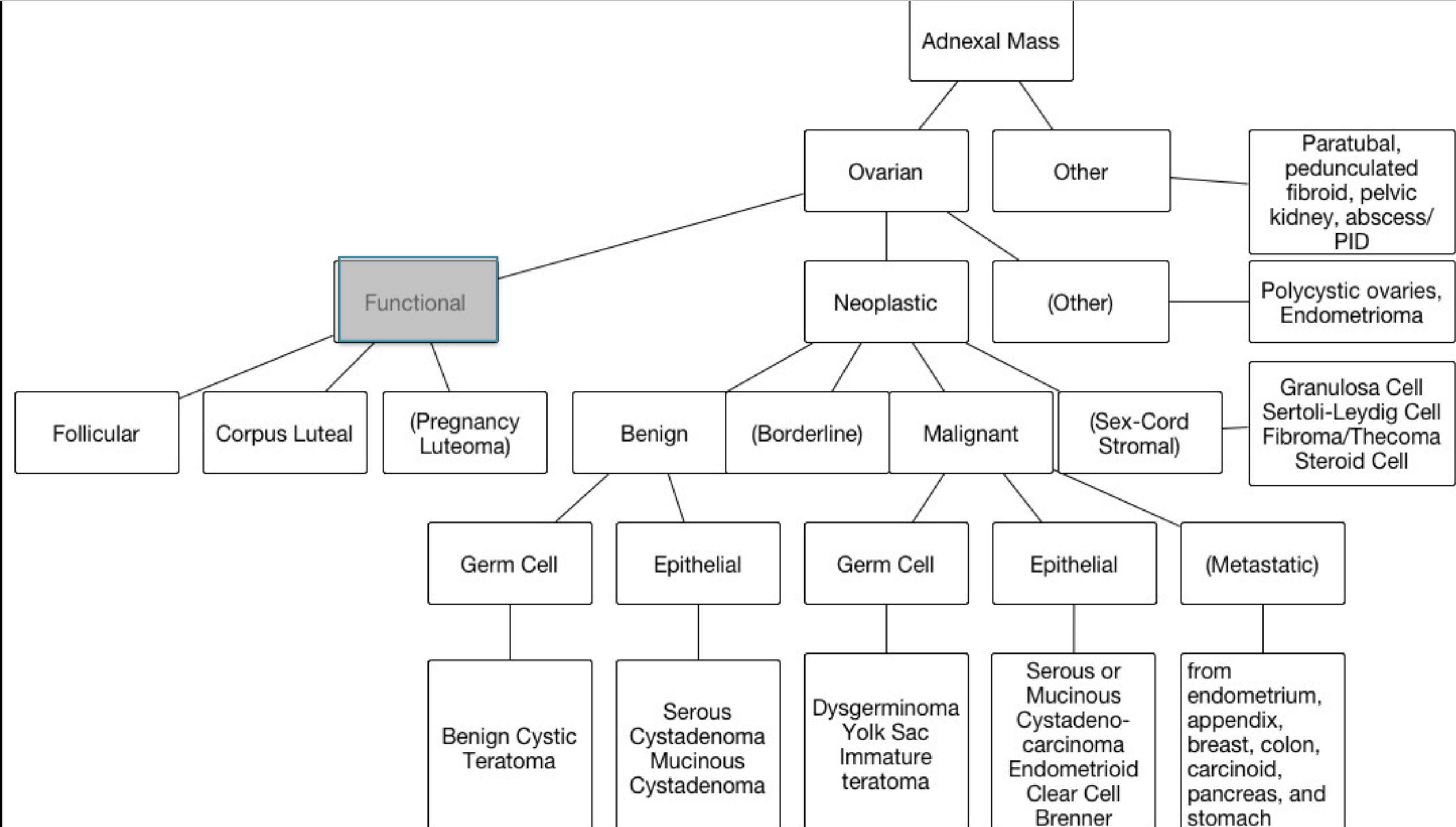


# MOST COMMON OVARIAN MASSES/CYSTS)

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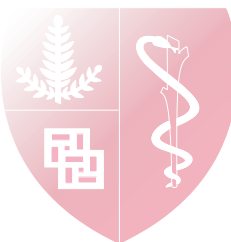
- Functional Ovarian Cysts
  - Follicular Cyst
    - <3 cm = Cystic Follicle
  - Corpus Luteum Cyst
  - Pregnancy Luteoma





# FUNCTIONAL OVARIAN CYSTS

- Exaggeration of physiologic function
  - Cystic follicle (first half of cycle) becomes follicular cyst if  $>3\text{cm}$  in diameter
  - Cystic corpus luteum becomes corpus luteum cyst (second half of cycle)
  - NOT a neoplasm
  - Resolve over time without intervention

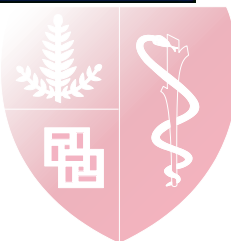




# FUNCTIONAL OVARIAN CYSTS

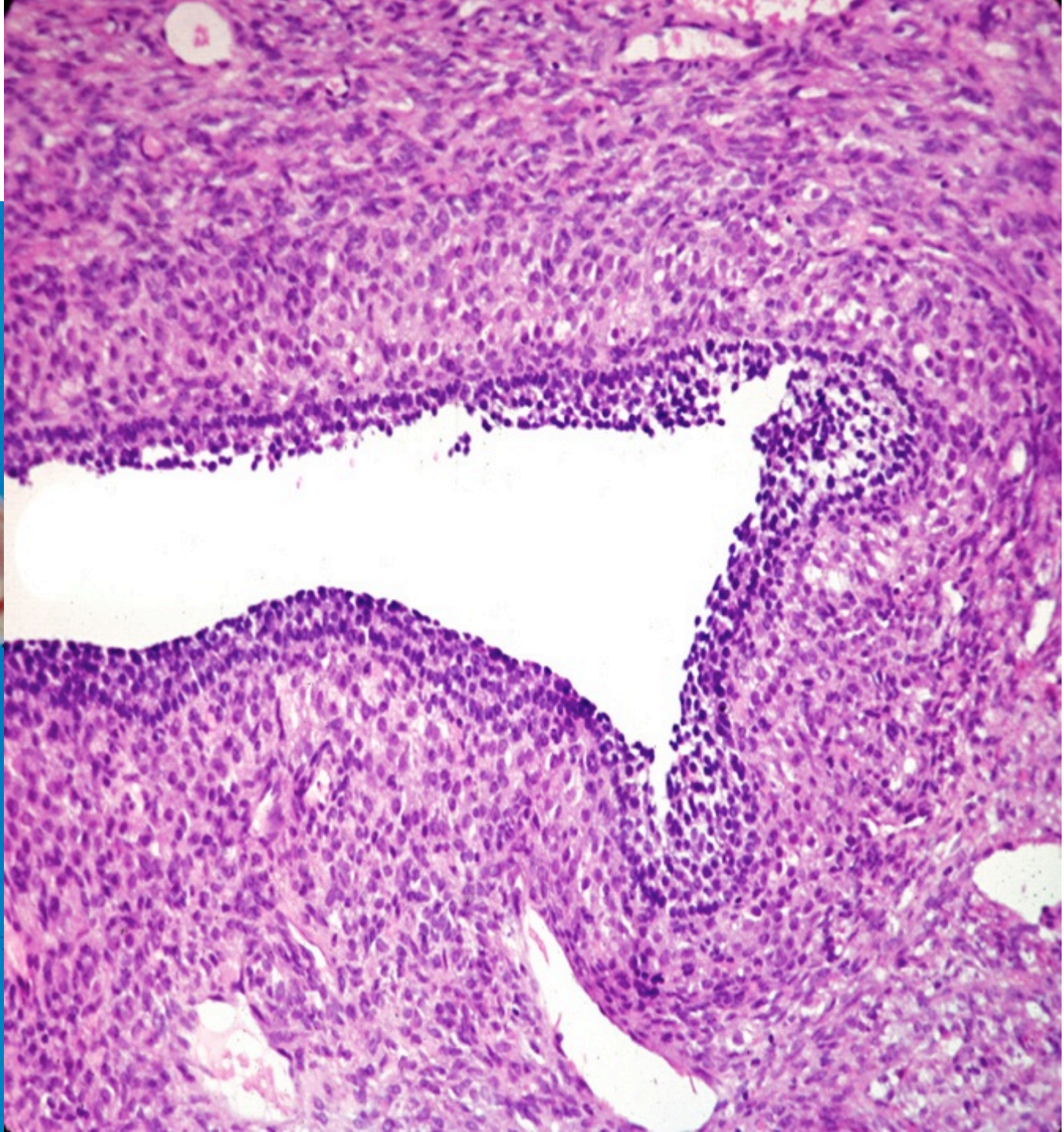
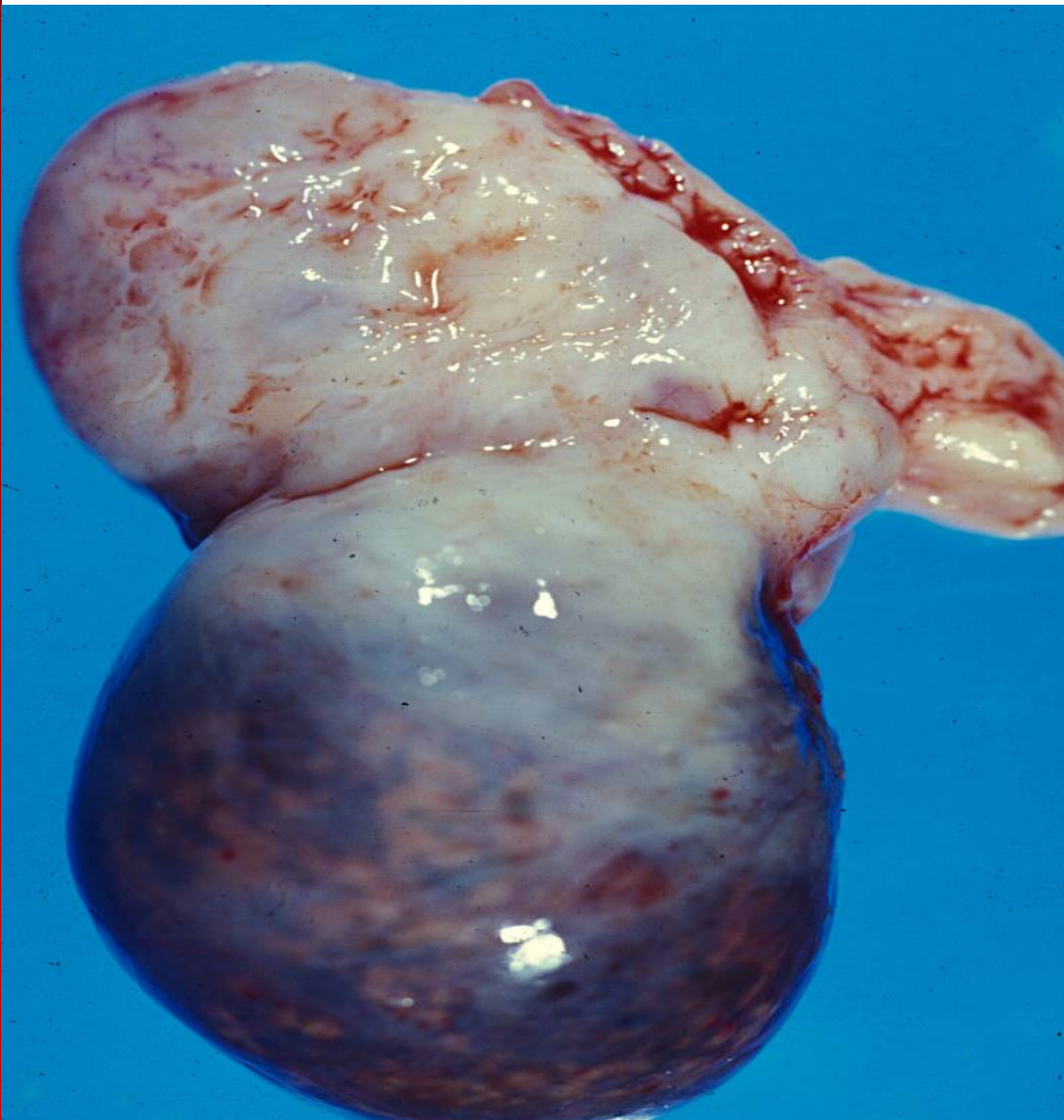
## Follicular Cysts in Adolescents

- Majority are incidental finding
- Up to 8 cm in diameter
- Resolve in 4-6 weeks
- May rupture or torsion and cause pain/peritoneal signs





# FOLLICULAR CYST





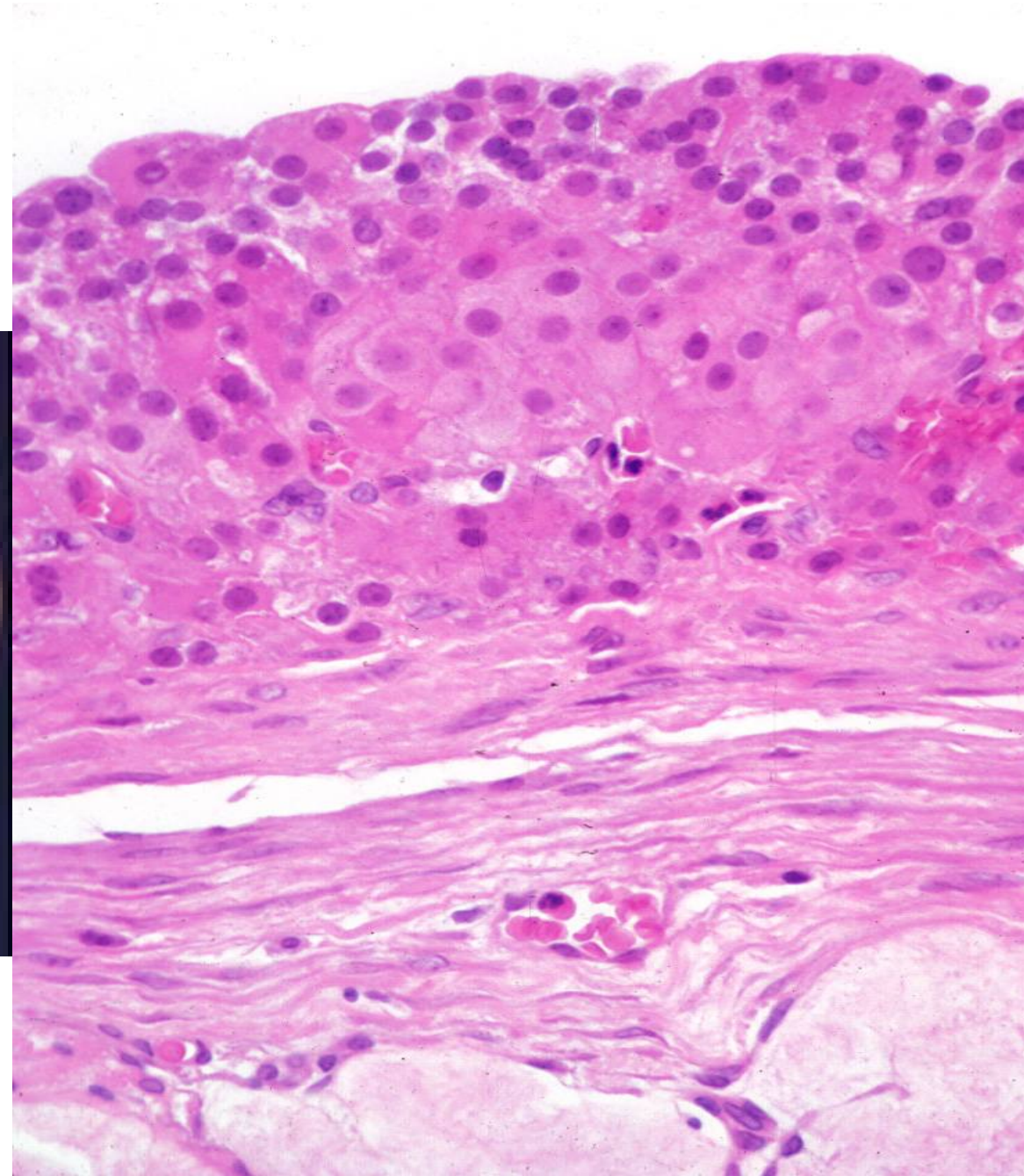
# FUNCTIONAL OVARIAN CYSTS

## Corpus Luteum Cysts

- Less common than follicular
- Corpus luteum = “cyst” when  $> 3$  cm
- Halban's syndrome: persistent CL cyst, delayed menses, mass, acute pain (mimicking ectopic pregnancy)

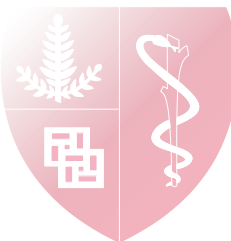
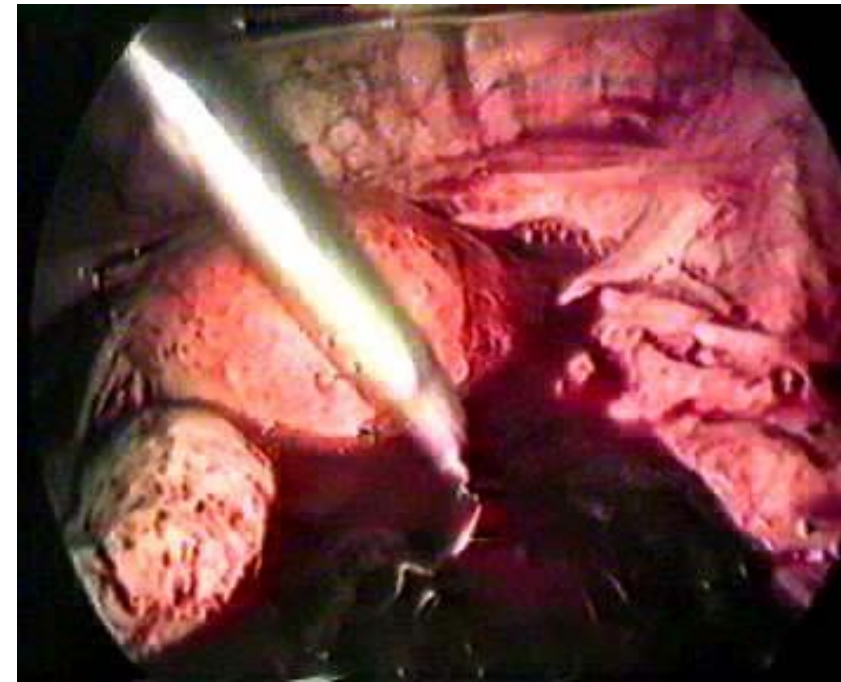
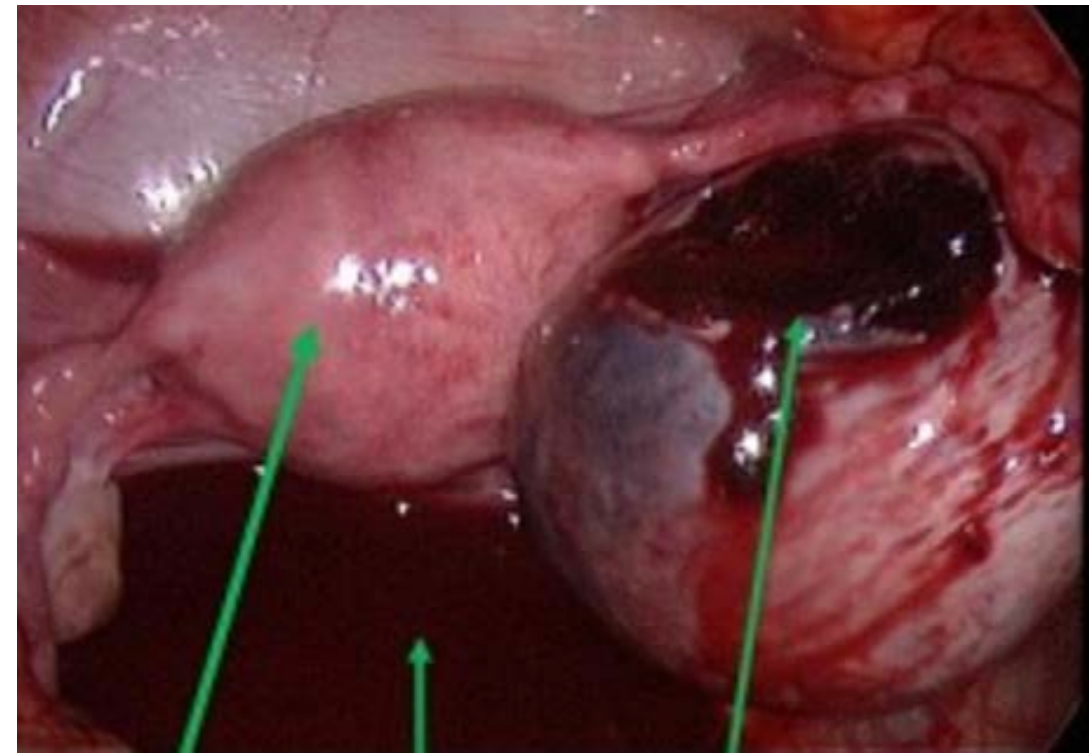


# CORPUS LUTEUM CYST

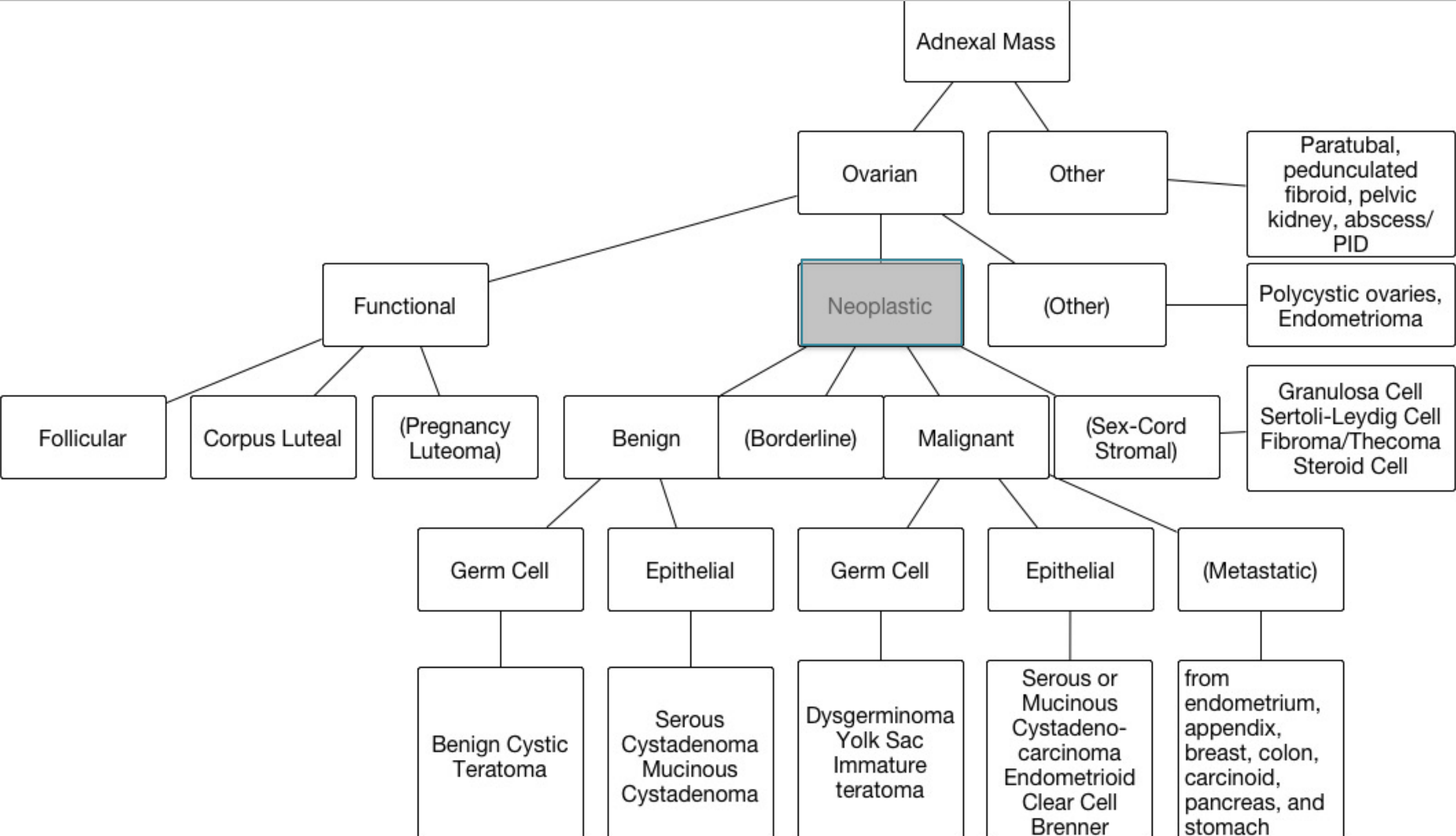


# FUNCTIONAL OVARIAN CYSTS: Corpus Luteum

- Ruptured Corpus Luteum with hemoperitoneum
  - Menstrual history (d 20-26)
  - May have delayed menses
  - Associated with bleeding disorders/anticoagulation
  - Right-sided 66%



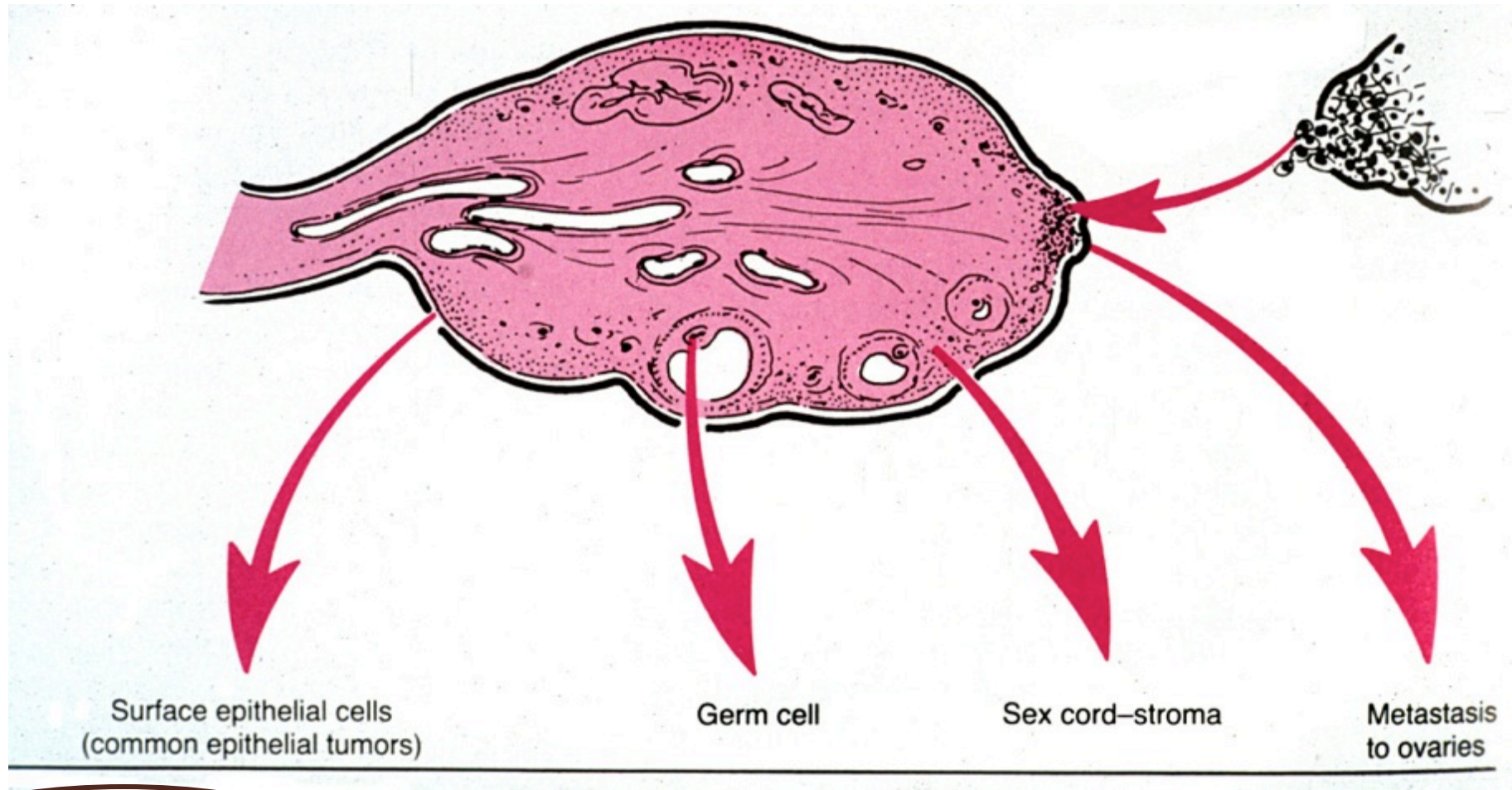




# Ovary: Neoplasms

- **Surface epithelial neoplasms**
- **Sex cord gonadal stromal tumors**
- **Germ cell tumors**
- **Metastases**



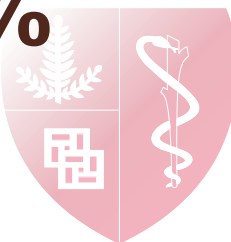


**65-70%**

**5-10%**

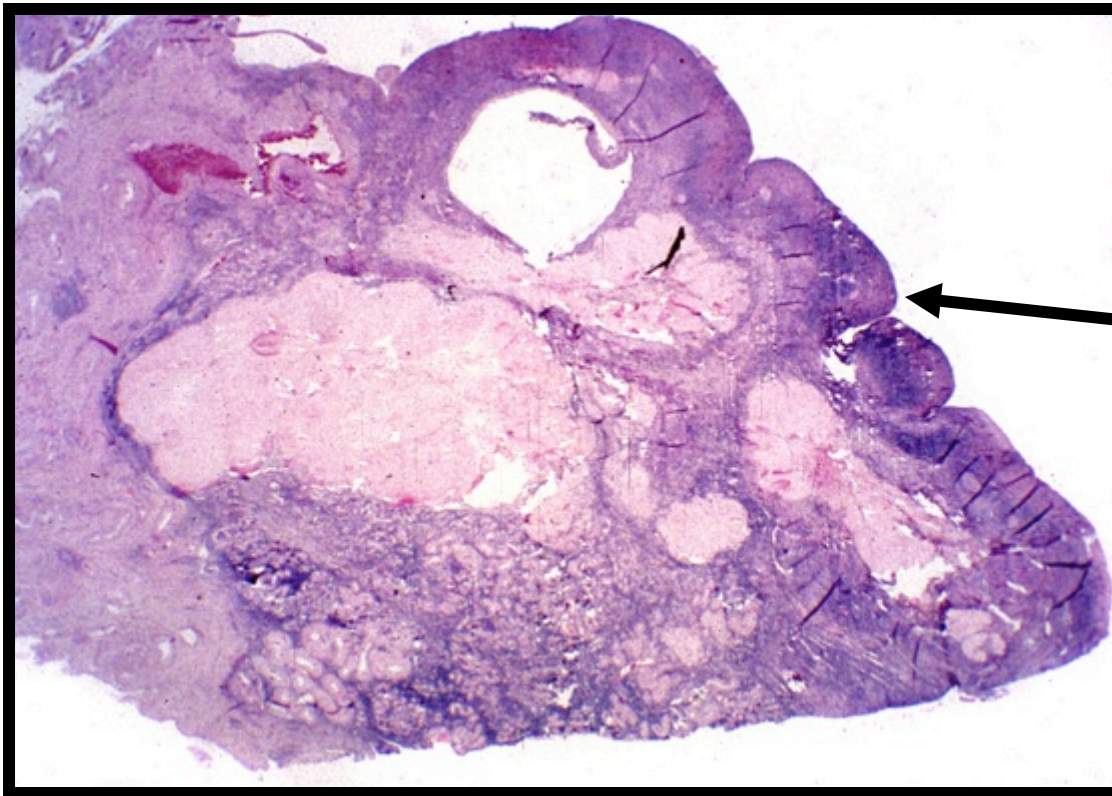
**15-20%**

**5%**



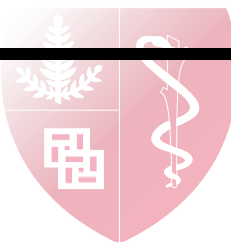


# Ovarian Epithelial Neoplasms

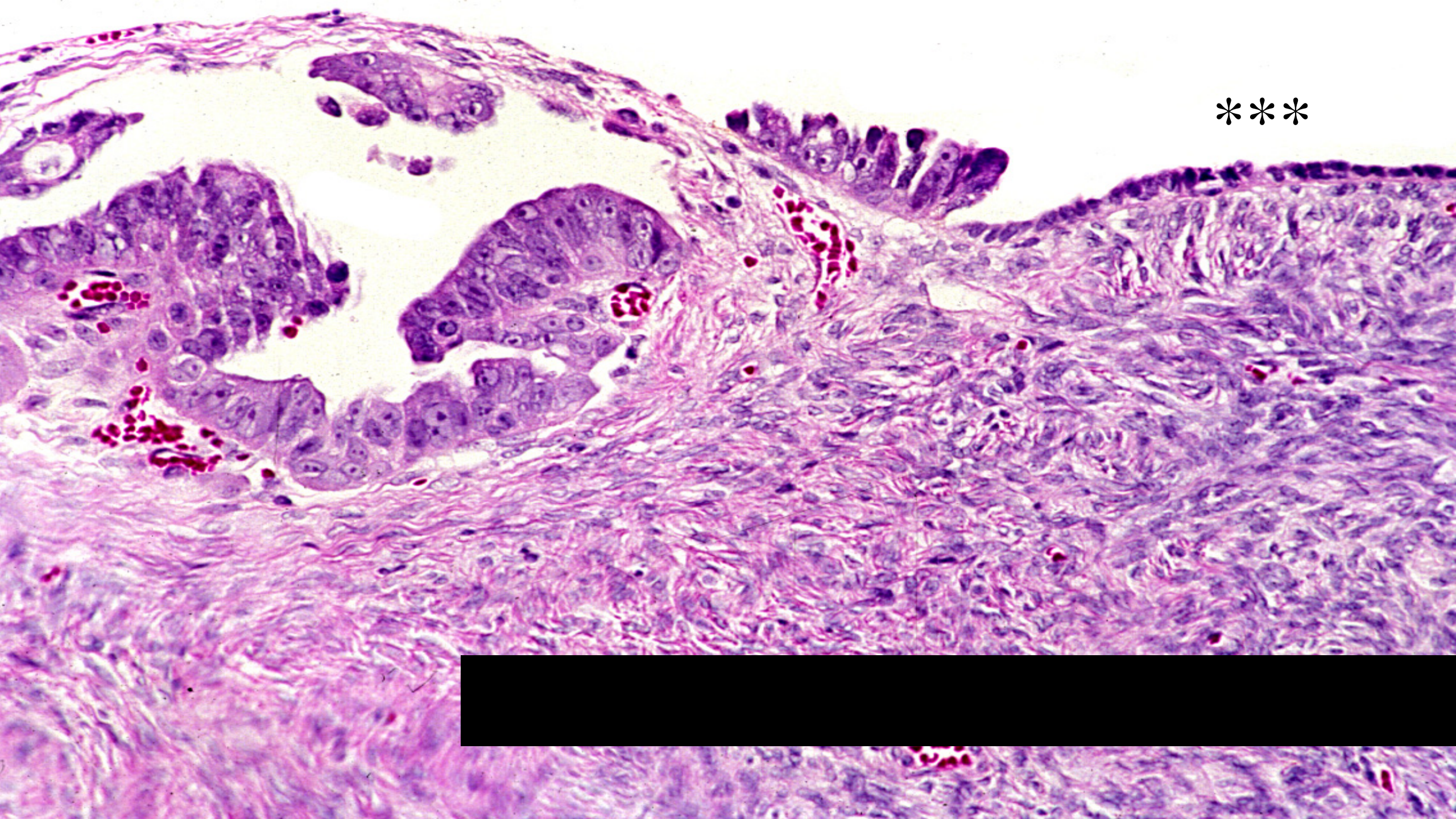


- **Serous (tubal-like)\***
- **Endometrioid**
- **Clear cell**
- **Mucinous**
- **Brenner**

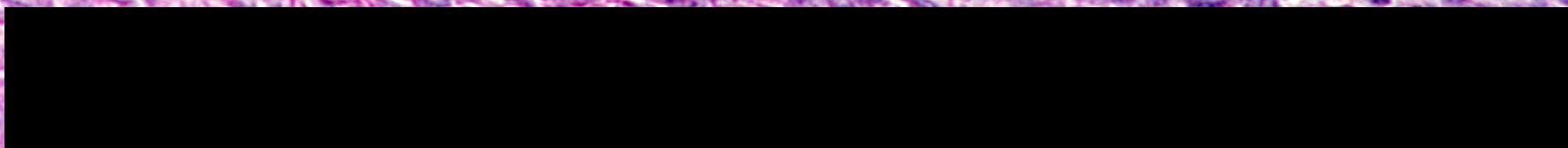
\* Prototype for ovarian epithelial tumors







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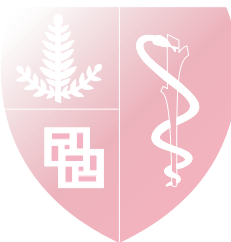




# Ovarian Epithelial Tumor

## Classification: Clinical Behavior

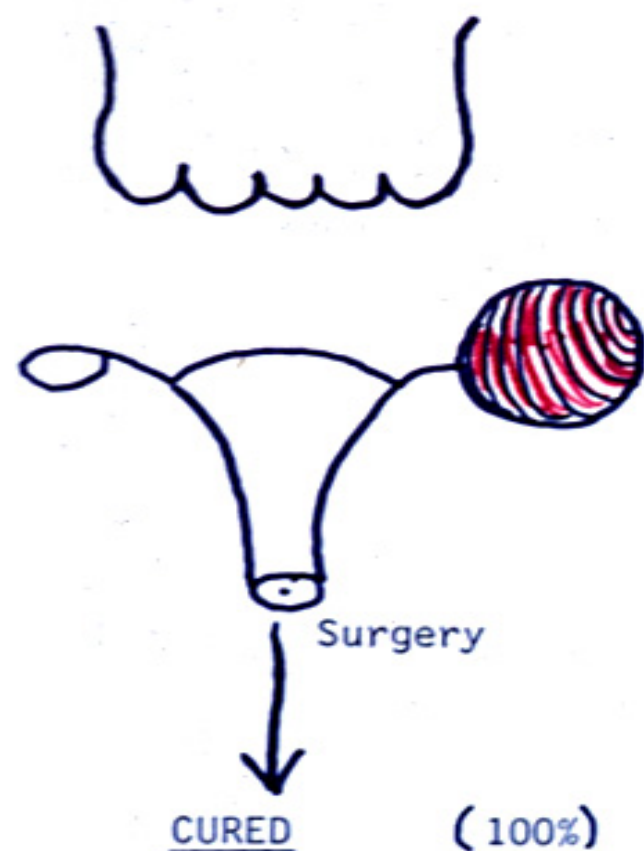
- **Benign**
- **Borderline (low malignant potential)**
- **Malignant**



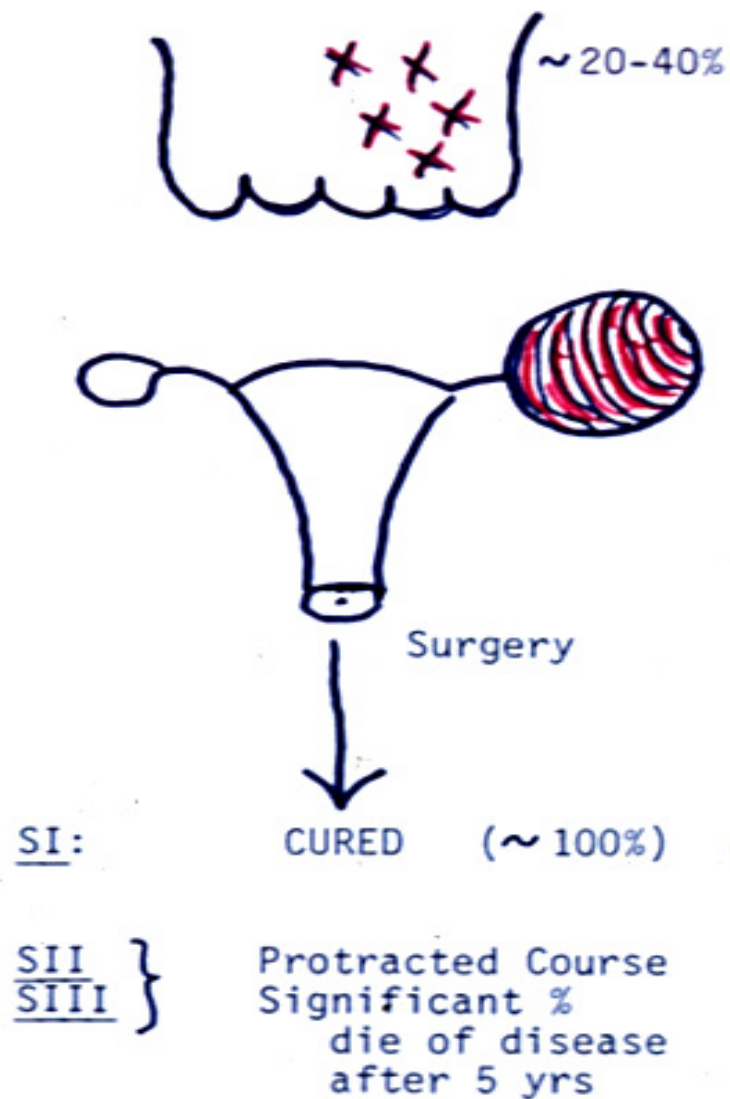
SEROUS NEOPLASMS

Surgery Alone

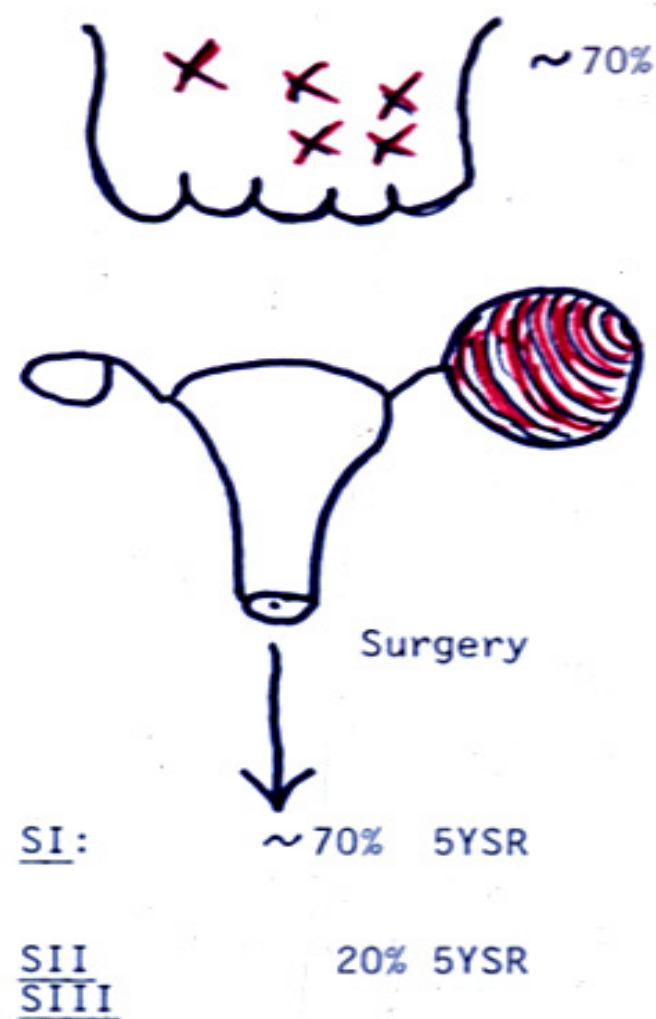
Group A



Group B

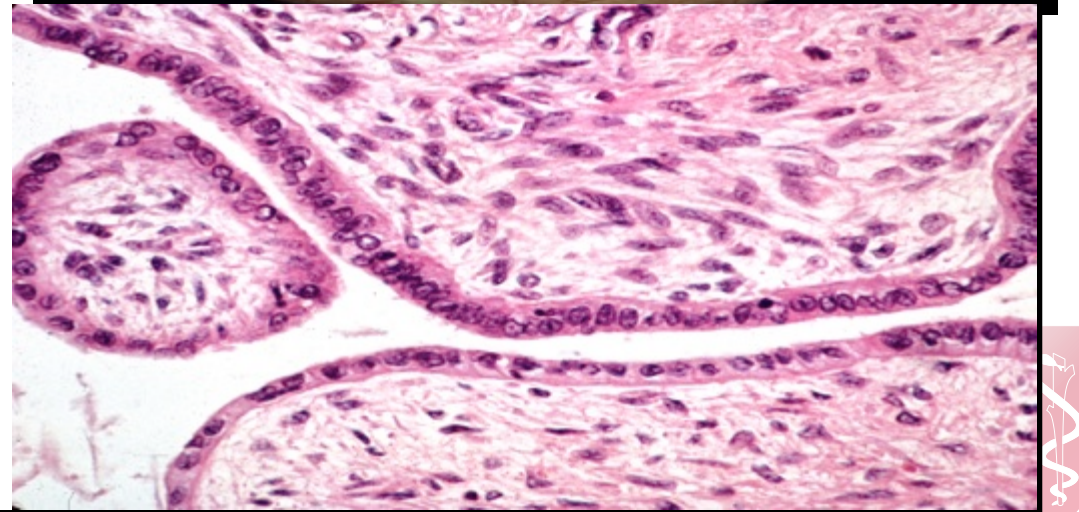
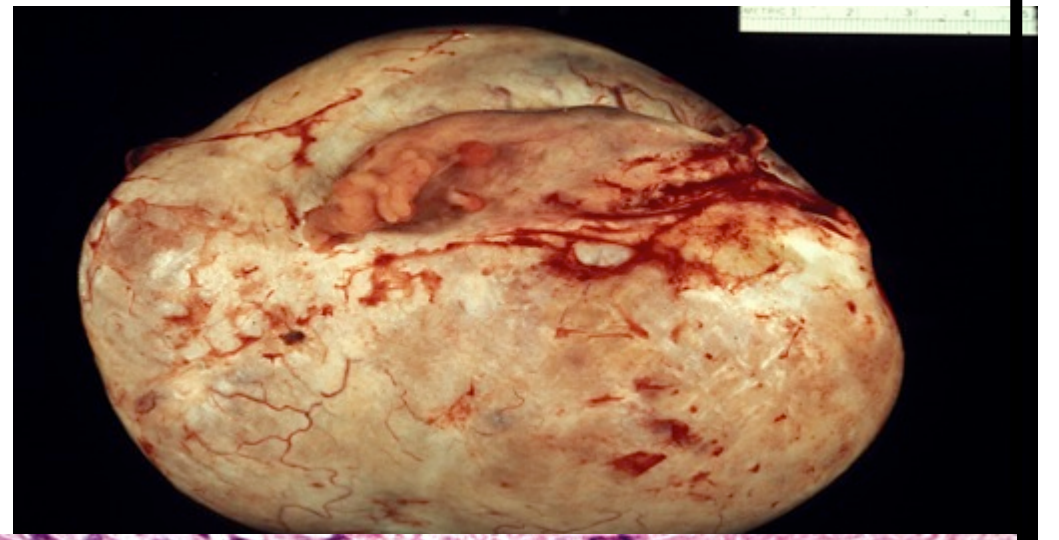


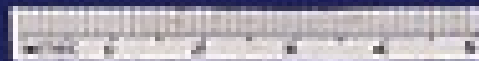
Group C



# Benign Neoplasm

- **Unilateral**
- **Simple, unilocular cyst**
- **Simple architecture**
- **Benign cytology**
- **Excision is curative**

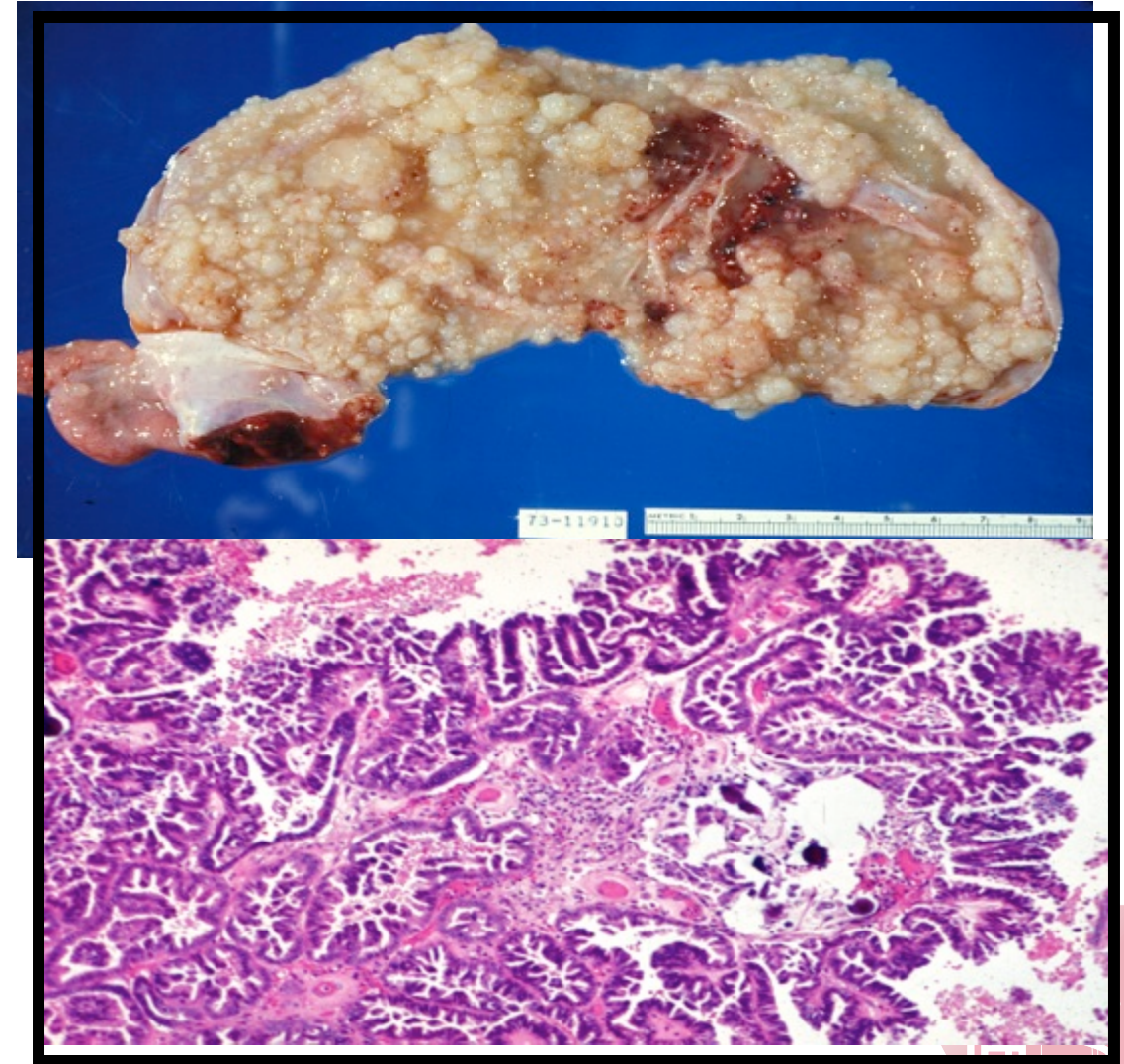




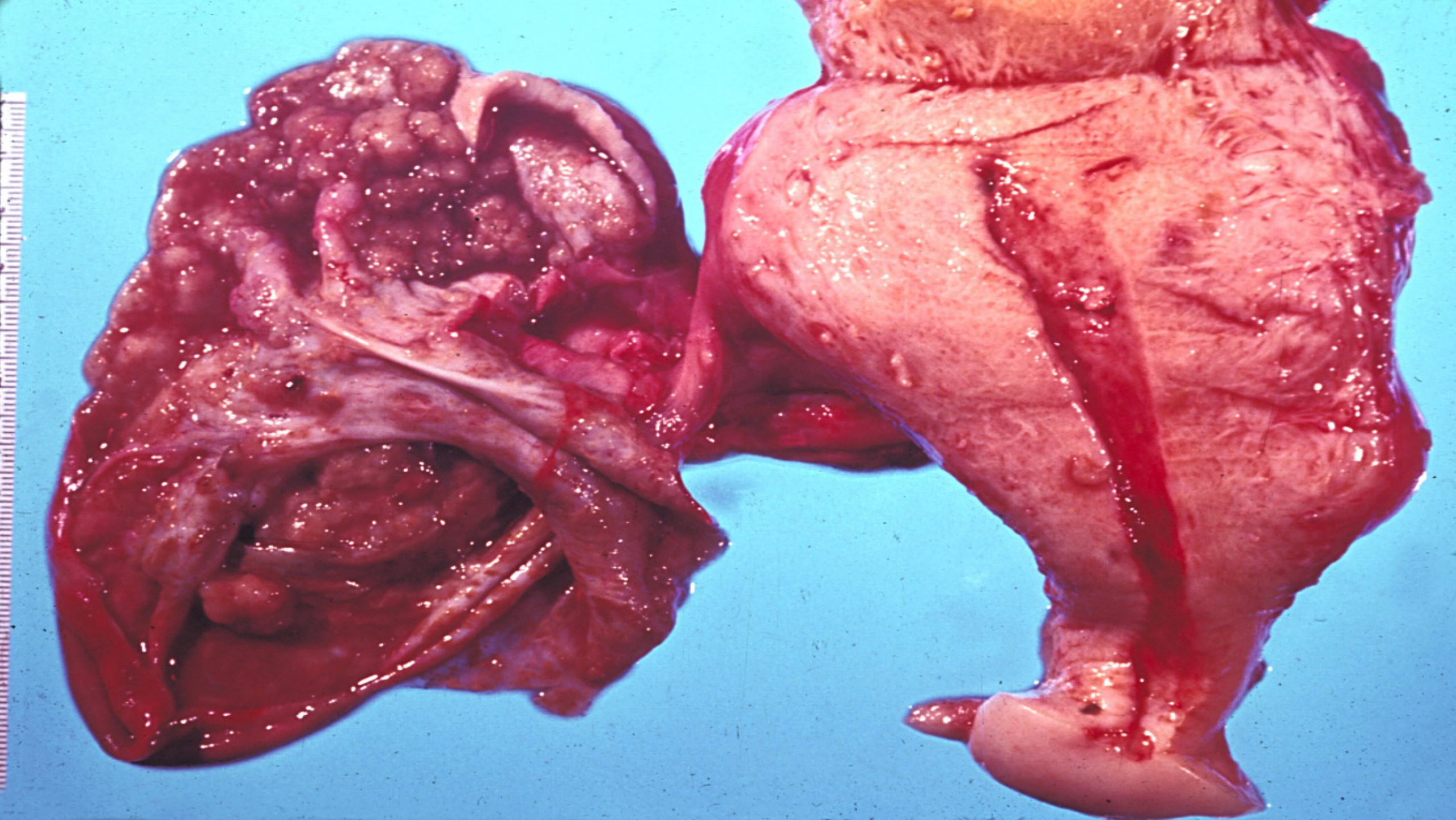


# Borderline Tumor

- **Bilateral**
- **Multilocular cyst**
- **Papillary excrescences**
- **Simple excision not curative**
- **Indolent, even if high stage**



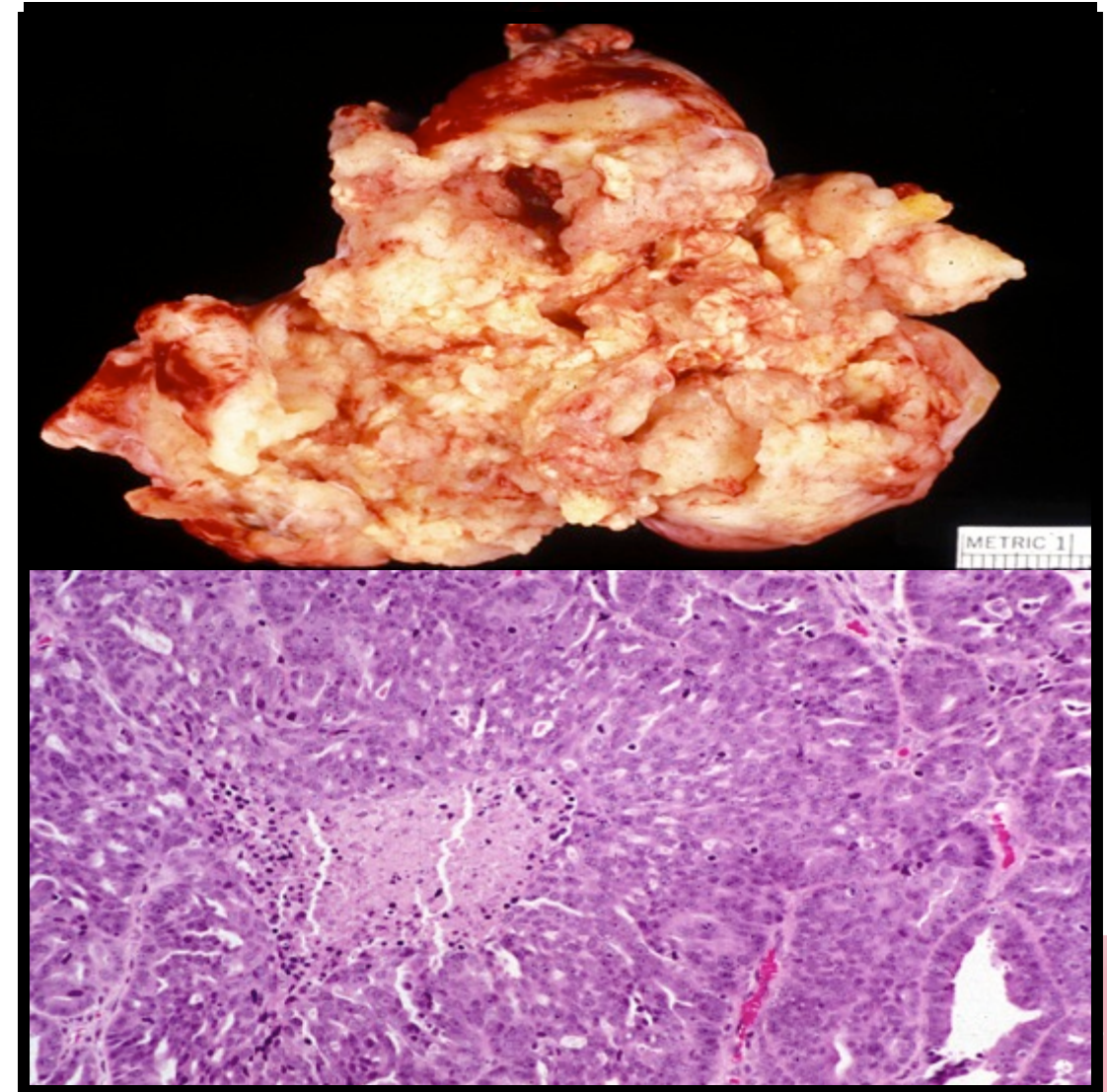




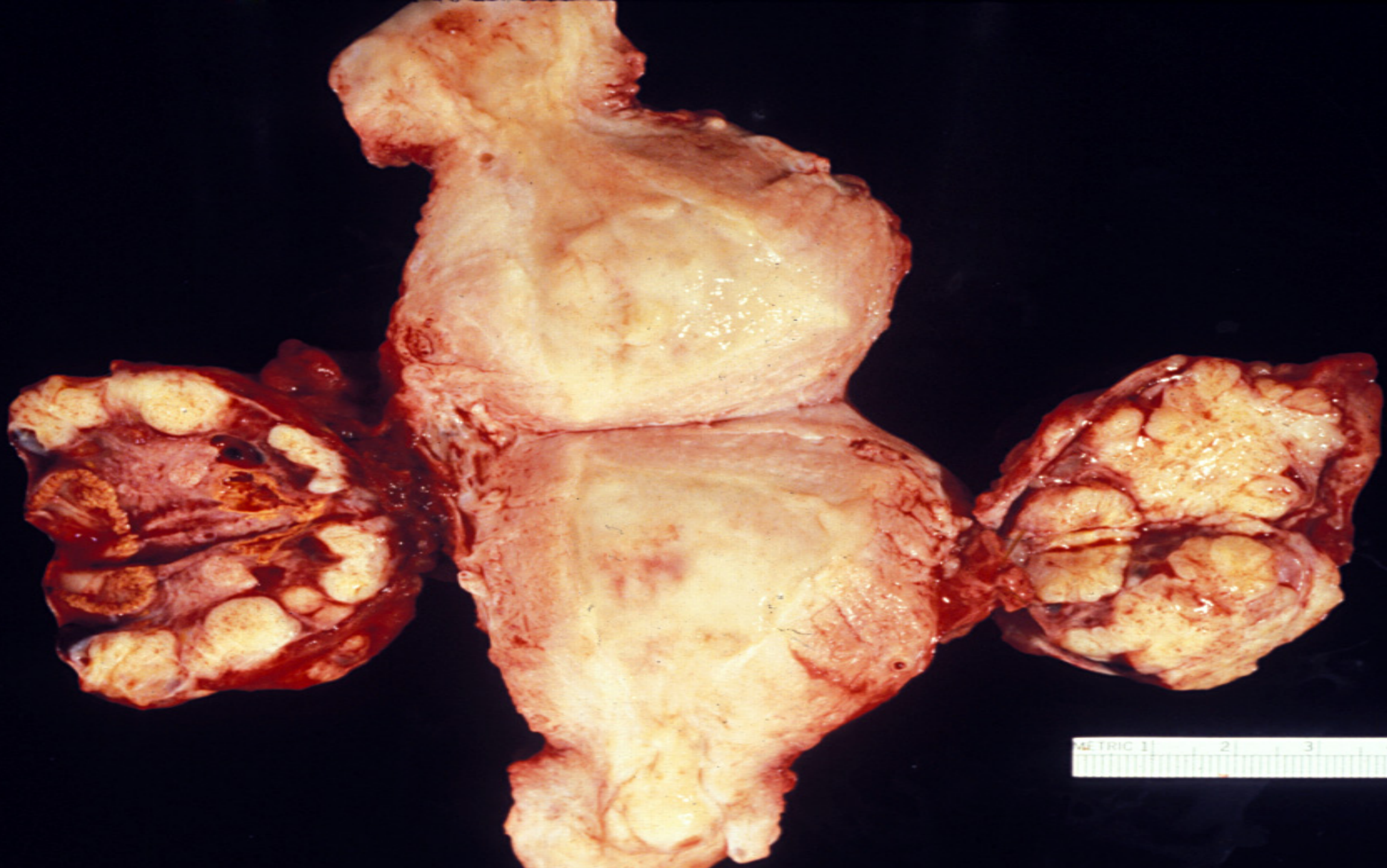


# Malignant Neoplasm

- **Bilateral**
- **Solid, multilocular cyst**
- **Stromal invasion**
- **Malignant cytology**
- **High mortality**  
esp if high stage





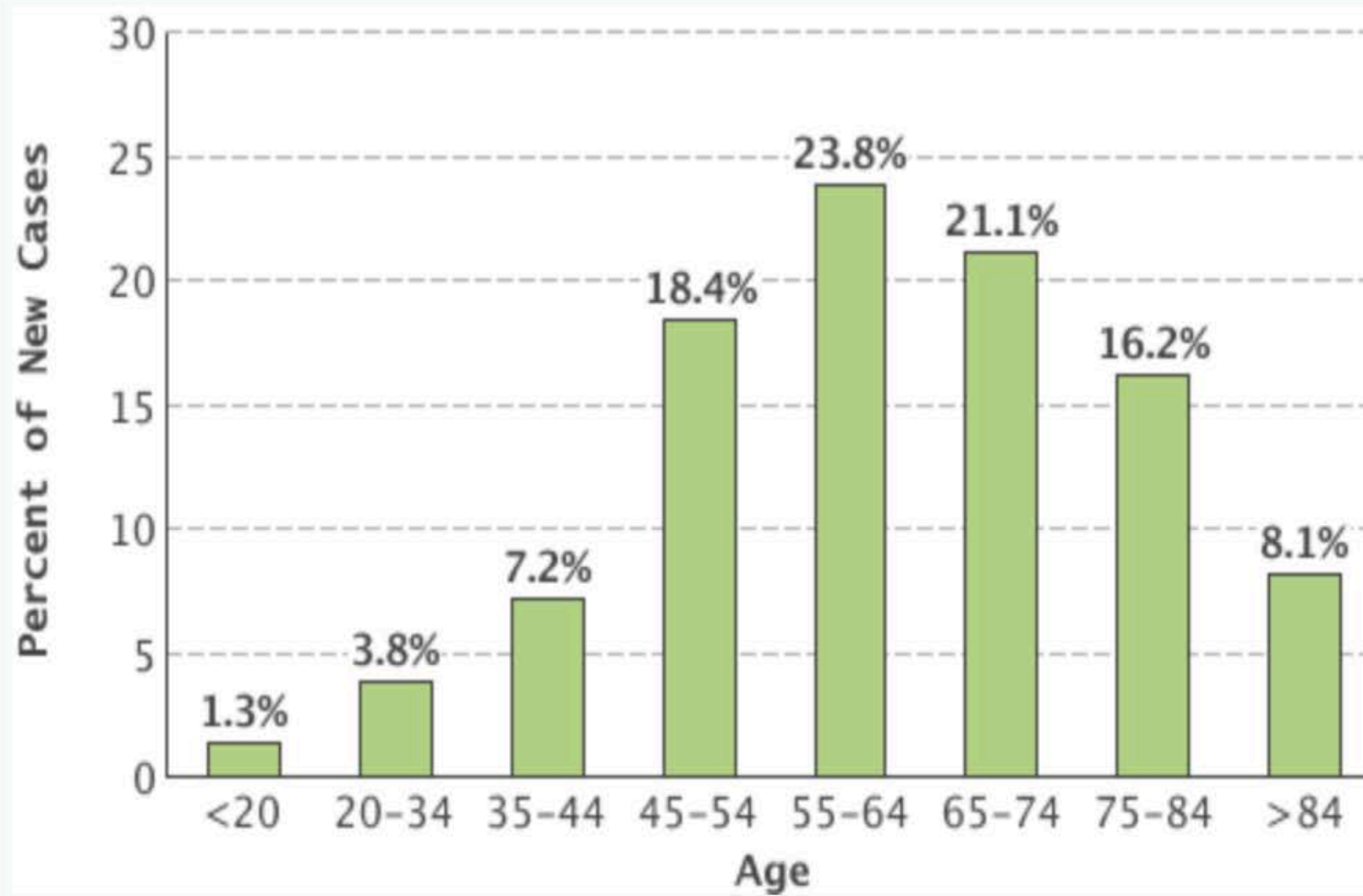


# Ovarian Carcinoma

- Ovarian Cancer is relatively Rare—
  - 1.3% of all cancer cases in US
  - 17<sup>th</sup> most common type of cancer
  - Lifetime risk of developing ovarian cancer 1.3%
- Leading cause of death due to gyn malignancies
- Ranks fifth in cancer deaths among women
- Ranks 2<sup>nd</sup> in cancer deaths in developed countries



## Percent of New Cases by Age Group: Ovary Cancer



Ovary cancer is most frequently diagnosed among women aged 55-64.

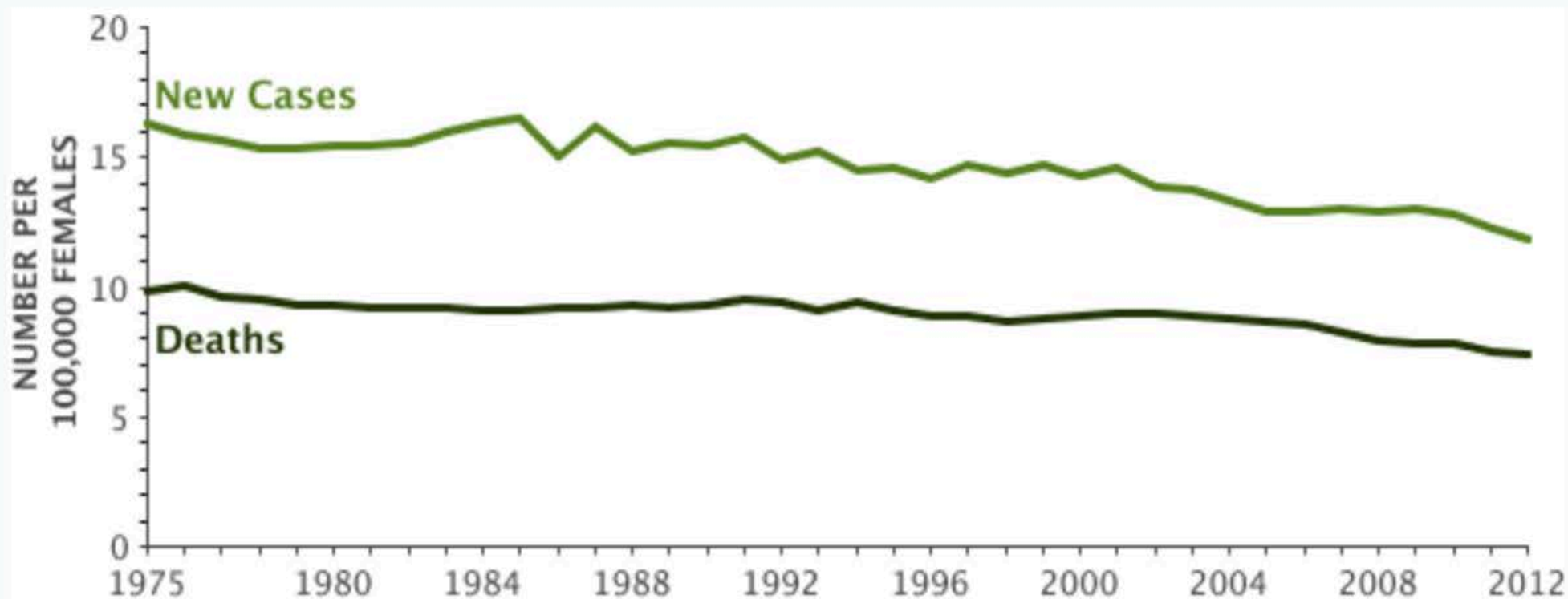
**Median Age  
At Diagnosis**

**63**



## New Cases, Deaths and 5-Year Relative Survival

[View Data Table](#)



Year	1975	1980	1985	1990	1995	1999	2003	2007
5-Year Relative Survival	33.7%	38.1%	38.7%	40.4%	42.1%	42.9%	44.3%	44.1%

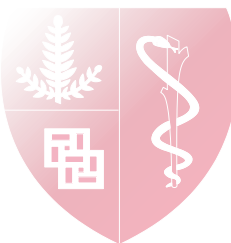
# Ovarian Carcinoma Risk Factors

- Older age
- Nulliparity
- Infertility
- Early menarche and late menopause
- Most epithelial ovarian cancers are sporadic, but 5-10% are hereditary (BRCA1 and BRCA2 genes)
  - BRCA1—35-70% lifetime risk of ovarian cancer
  - BRCA2—10-30% lifetime risk of ovarian cancer
- Family/personal history of breast cancer
- Family/personal history of colon/endometrial cancer (Lynch syndrome/HNPCC)
- Endometriosis/ Endometriomas



# Ovarian Carcinoma: Early Detection

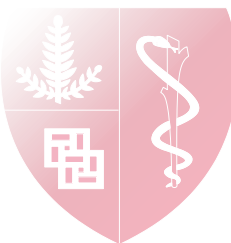
- Once felt to be “silent killer”
- Early ovarian cancer often asymptomatic
- Persistent symptoms may suggest dx:
  - Abdominal swelling (due to mass or ascites)
  - Pelvic pressure/abdominal pain
  - Early satiety
  - Urinary symptoms





# Ovarian Carcinoma: Screening

- Screening = ASYMPTOMATIC women
- Transvaginal ultrasound and CA-125 have not been found to lower deaths from ovarian cancer. Thus **ovarian cancer screening is not currently recommended**
- Research into other markers or combination or markers is ongoing



# Distinguishing Malignant Mass from Benign

- CA125 >200 in postmenopausal woman with pelvic mass has 96% PPV for Ca
- Premenopausal women, low specificity
- Size > 8 cm suggests neoplasm
- Ultrasound characteristics suggesting malignancy:
  - Solid and cystic components
  - Bilaterality
  - Dense septae with vascular flow



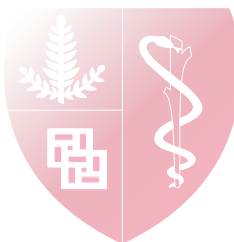
# Ovarian Cancer Patterns of Spread

- Exfoliation of cells that implant on peritoneal surfaces: pelvis, paracolic gutters, intestinal mesenteries, right hemidiaphragm
- Lymphatic dissemination to pelvic and para-aortic lymph nodes
- Hematogenous spread uncommon



# New Insights into the Pathophysiology of Ovarian Cancer

- Proposed 2 distinct types of Ovarian Epithelial Carcinoma with distinct molecular profiles
  - Type 1—endometrioid, clear-cell, and low-grade serous
    - Mostly arise from endometriosis or from borderline serous tumors
  - Type 2—high-grade serous with majority arising from fimbriated end of Fallopian tube
    - Usually present at advanced states
    - Rapid peritoneal seeding from fimbria



# New Insights into the Pathophysiology of Ovarian Cancer

- Implications for prevention
  - Oral Contraceptives
  - Tubal ligation has shown lower risk of endometrioid and clear-cell carcinoma
  - Salpingectomy as prevention
    - BRCA—RR surgeries
    - At time of hysterectomy
    - Rather than tubal ligation (Postpartum or interval sterilization)
  - Genetic counseling and testing for all patients with high-grade serous cancer

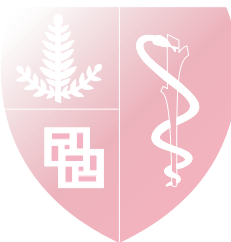




# Ovarian Carcinoma

## Primary Prevention

- Use of Combined oral contraceptive DECREASED RISK
  - OC use for as little as 3-6 mos associated with decreased risk;
  - The risk is lower the longer the pill is continued
  - 50% decreased at 5 yrs
  - Effect lasts after stopping the pill



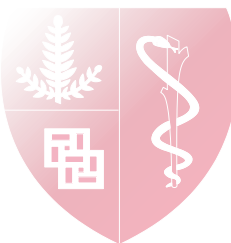
# Risk Reduction with Family History

- Genetic counseling/testing for affected relative
- Full pedigree analysis including maternal & paternal Family History –autosomal dominant inheritance
- Well established role for prophylactic Bilateral salpingo-oophorectomy in BRCA carriers

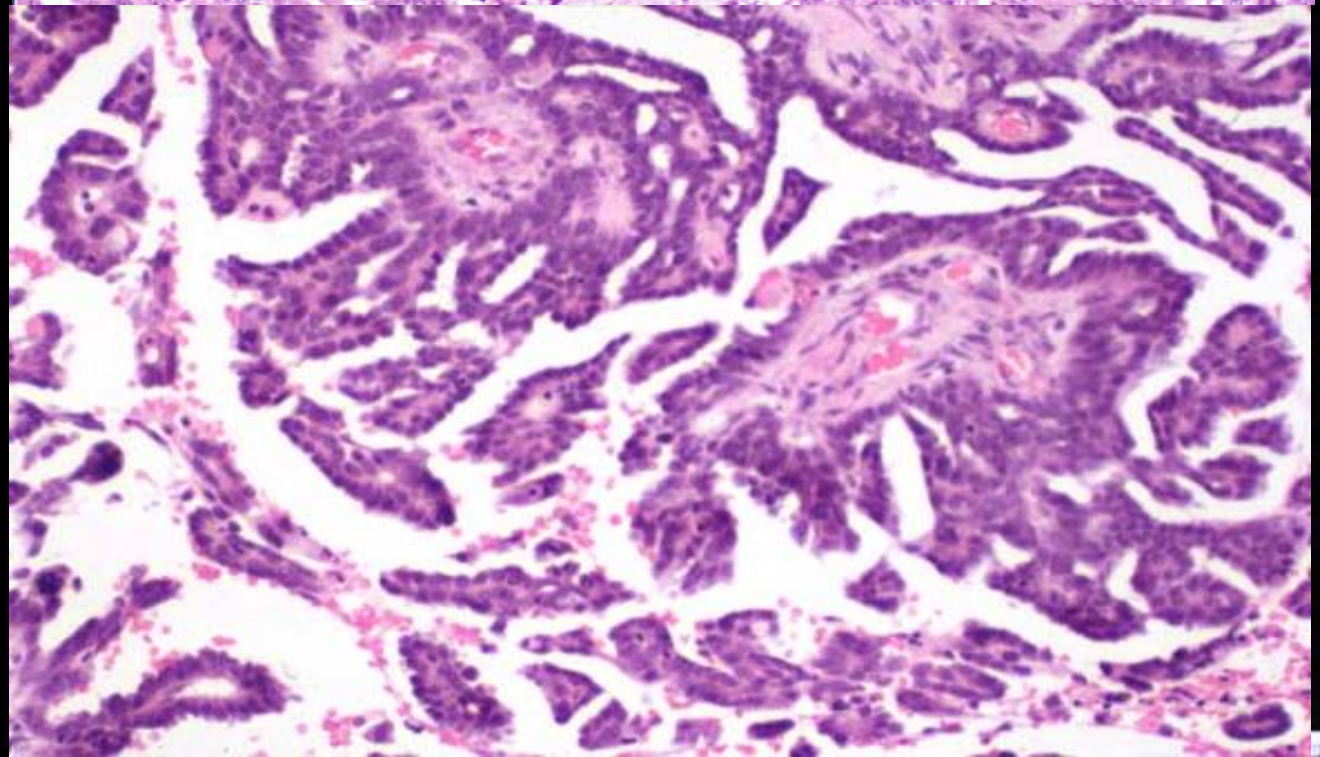
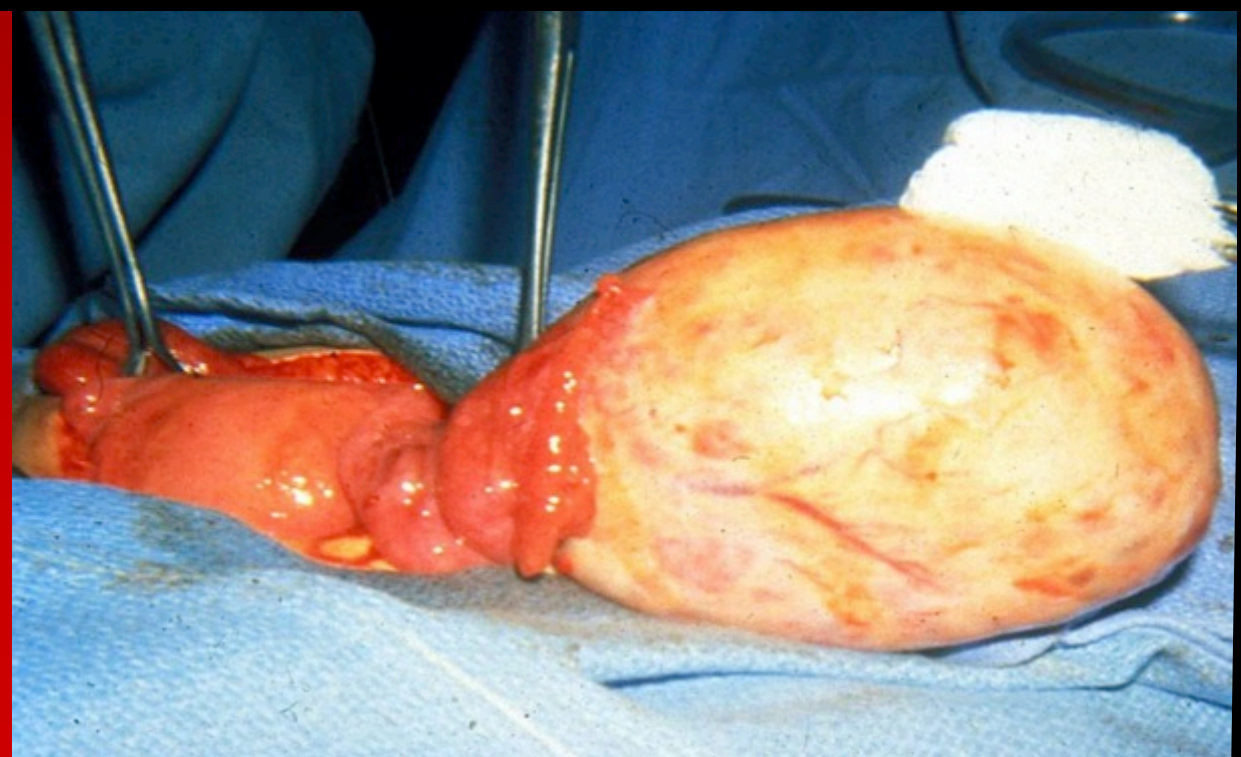
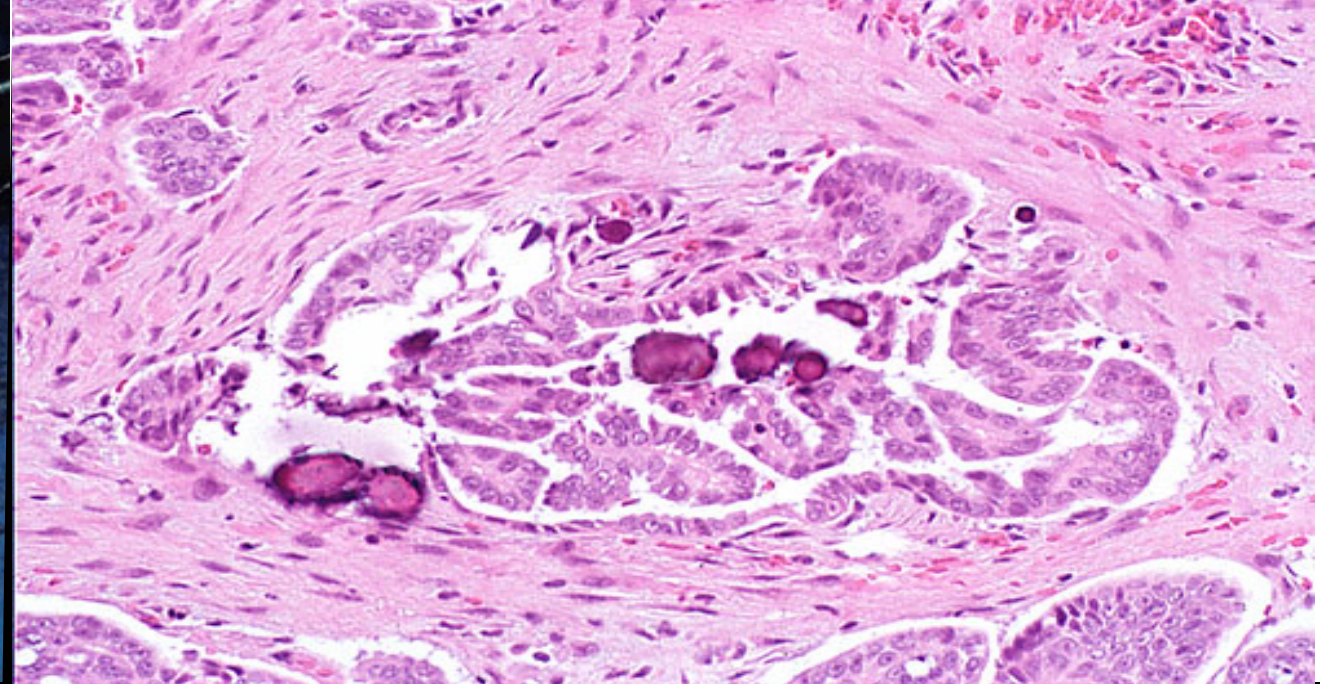
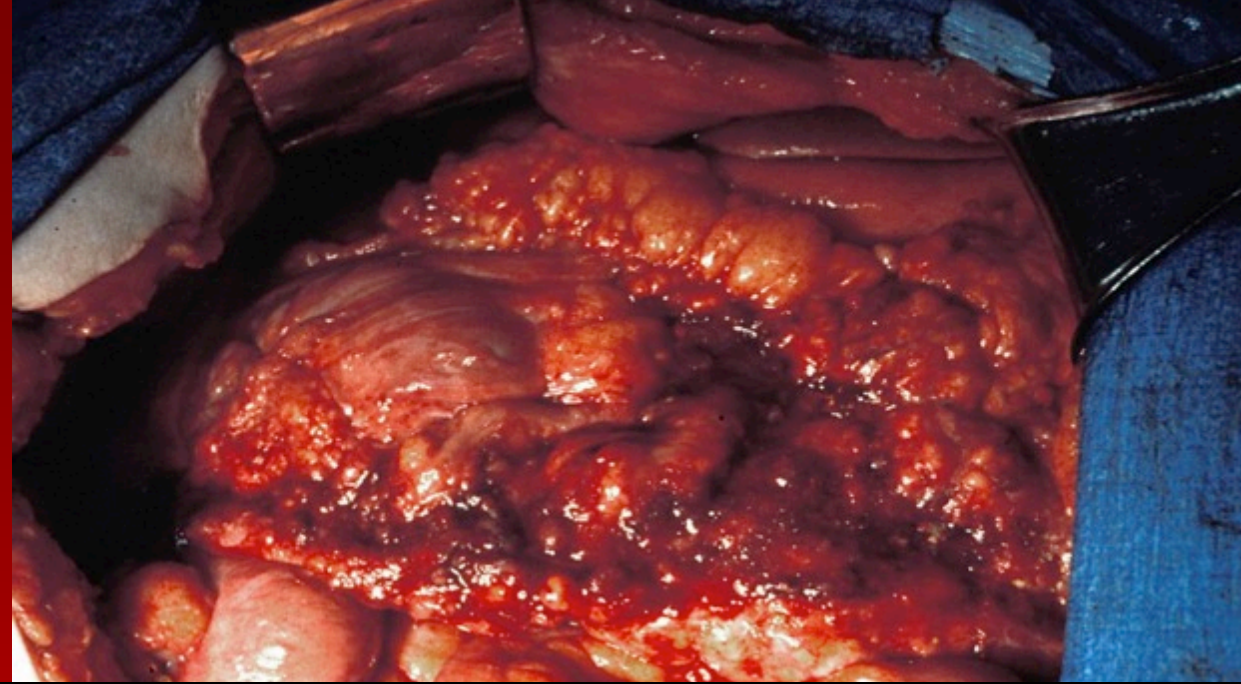


# Ovarian Cancer Surgical Staging

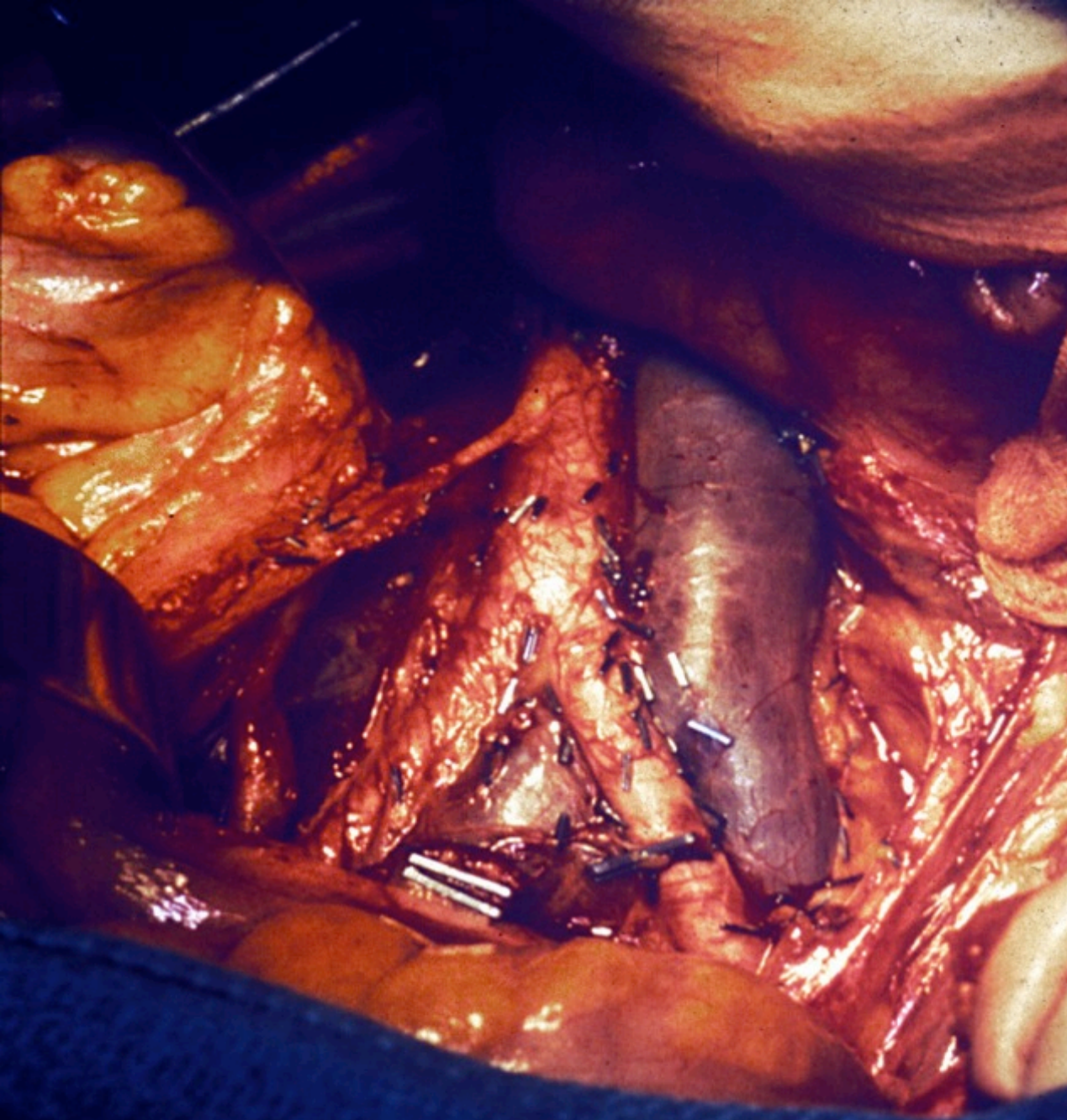
- Preoperative exclusion of metastases
- Surgical staging:
  - Cytology of ascitic fluid or pelvic washings
  - Intact removal of tumor with frozen section
  - Systematic exploration of the abdomen with biopsy of any suspicious lesions/areas or random biopsies of peritoneum
  - Cytology/sampling of diaphragm
  - Infracolic omentectomy
  - Exploration and sampling of para-aortic lymphadenectomy/node sampling





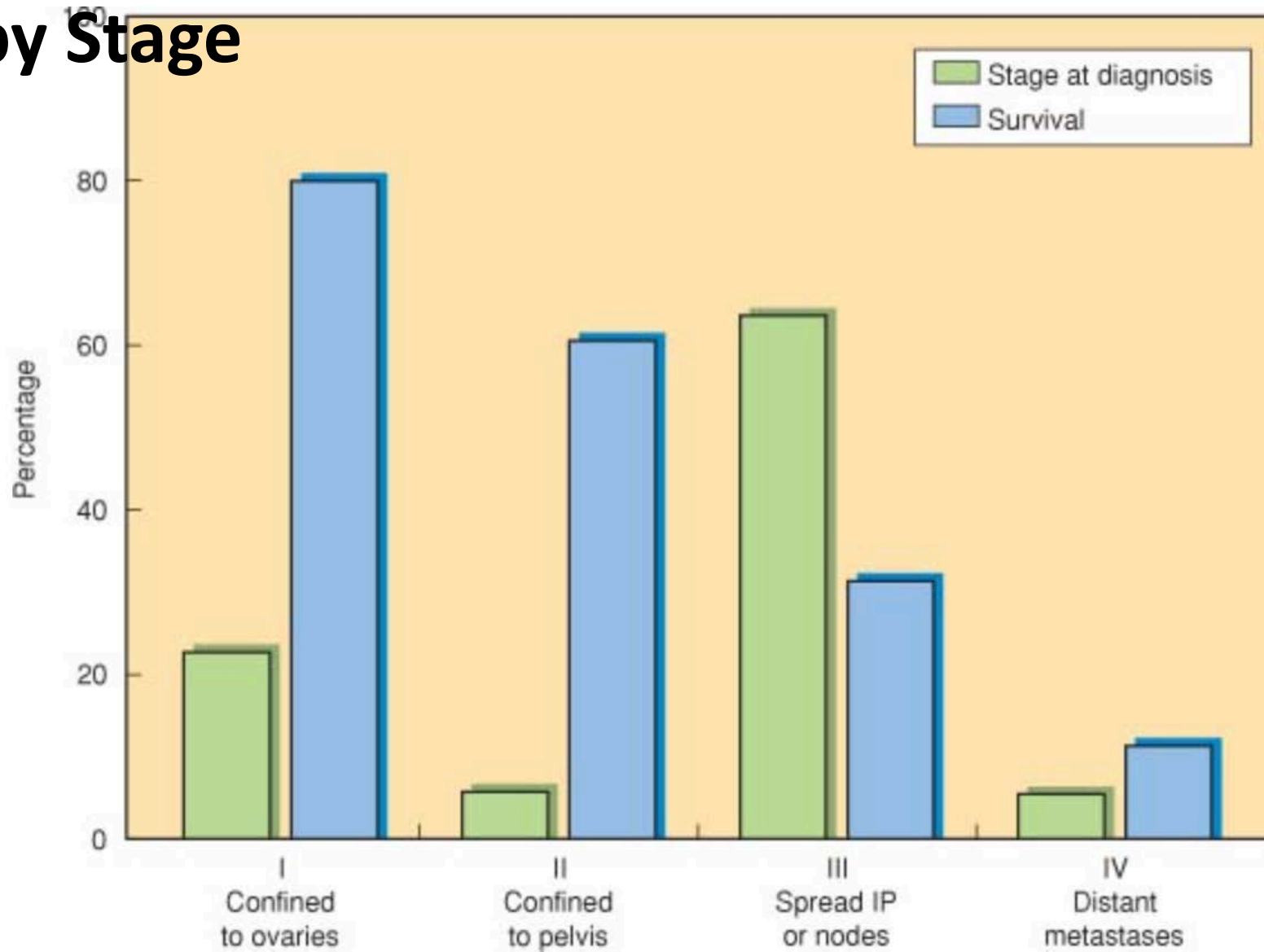








# 5-Yr Survival of Women with Epithelial Ovarian Cancer by Stage



From Berek & Hacker's Gynecology Oncology, 6<sup>th</sup> Ed 2015



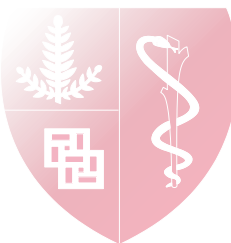
# Ovarian Cancer Treatment

- Early-Stage Low-risk (Stage 1A, grade 1)  
Surgery with no adjuvant chemotherapy
- Early-Stage High-risk (poorly differentiated, + ascites, capsular involvement)
  - Adjuvant chemotherapy, whole-abd radiation, or pelvic radiation plus chemo
- Advanced-Stage cancer—platinum and taxane-based combination chemotherapy



# Other Types of Ovarian Epithelial Neoplasms

- Endometrioid
- Clear cell
- Mucinous
- Brenner



# Endometrioid

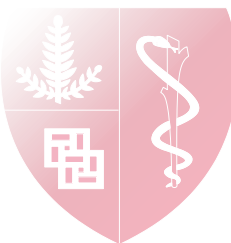
- Second most common histologic type of ovarian carcinoma
- Bilateral 40%
- Looks like endometrial adenocarcinoma arising in uterine corpus



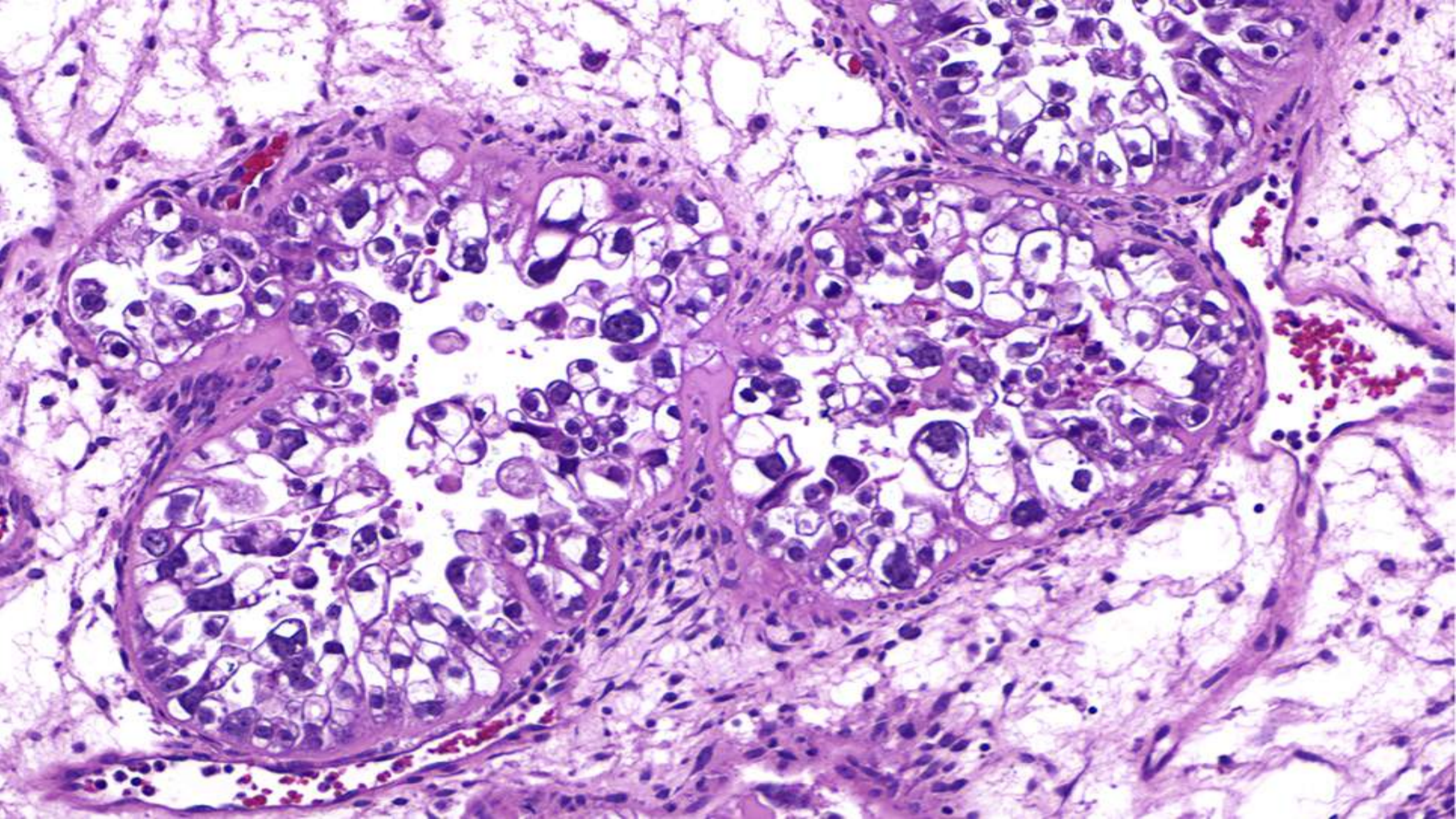


# Clear Cell Carcinoma

- Third most common histologic type of ovarian carcinoma
- Poor response to standard chemotherapy
- Associated with thromboembolic events
- Associated with endometriosis
- More common in Asian countries









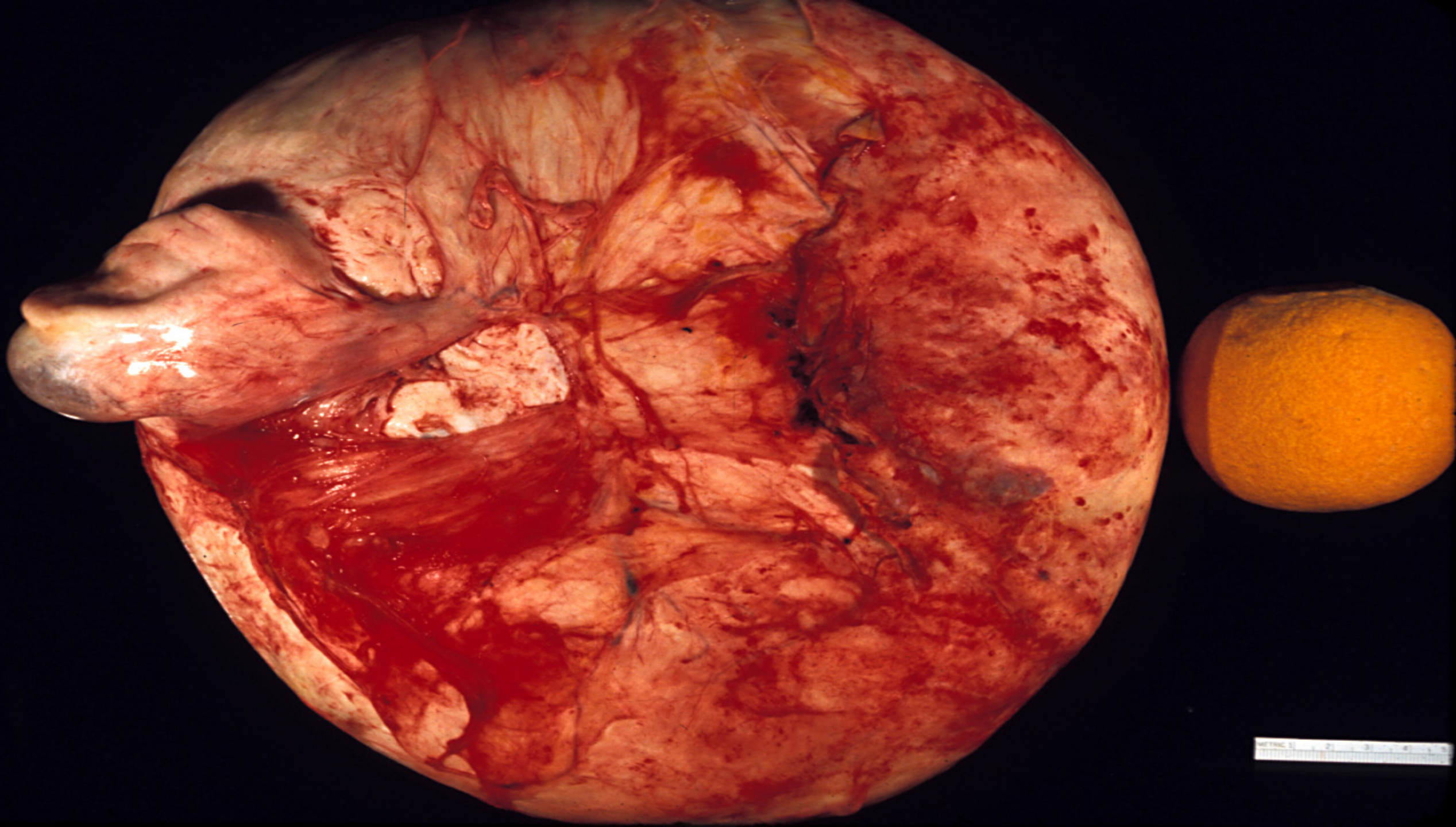


# Mucinous

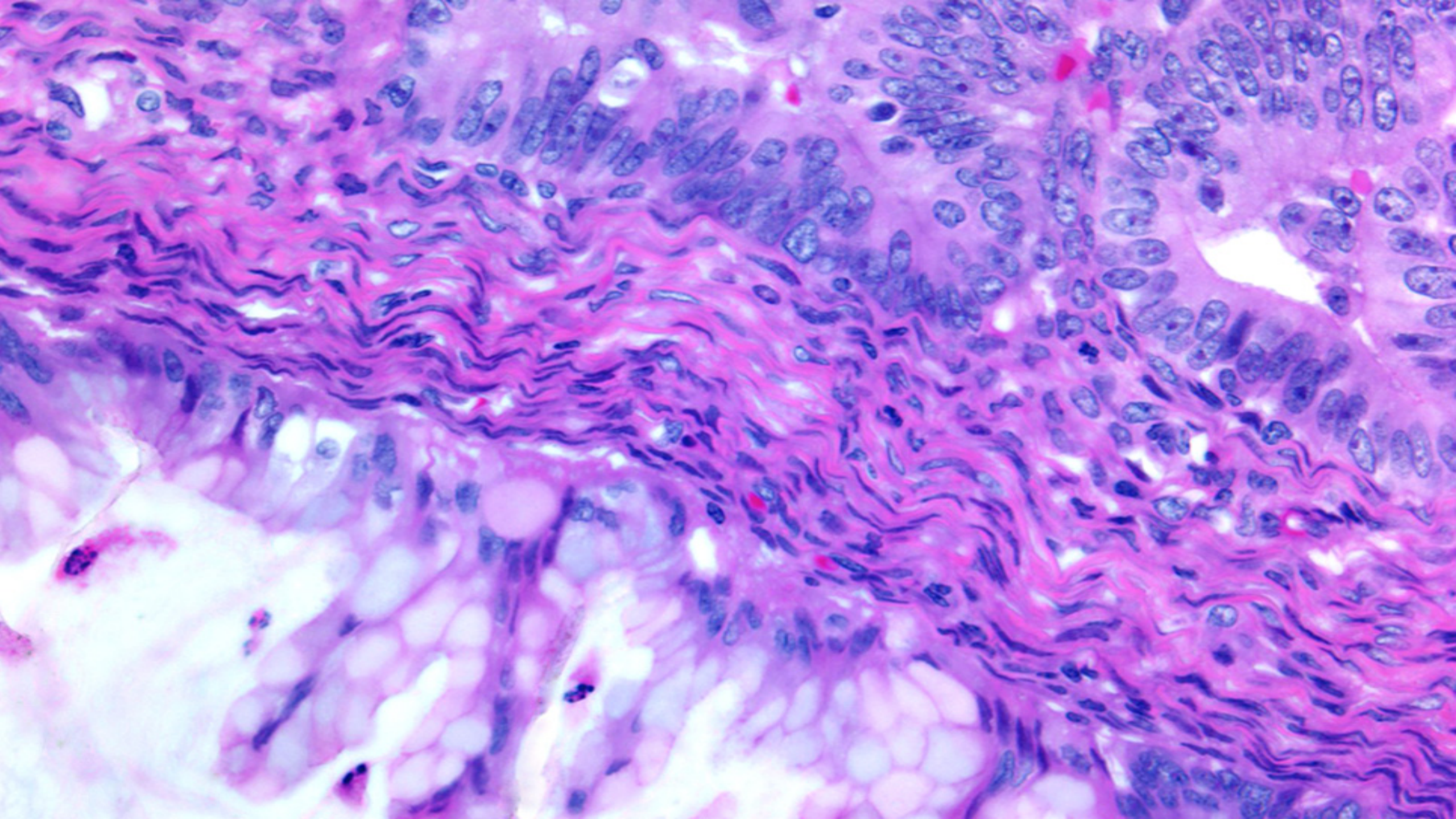
- 90% benign
- May be quite large
- Unilateral
- Pseudomyxoma peritonei is associated with appendiceal mucinous tumors with secondary involvement of ovary



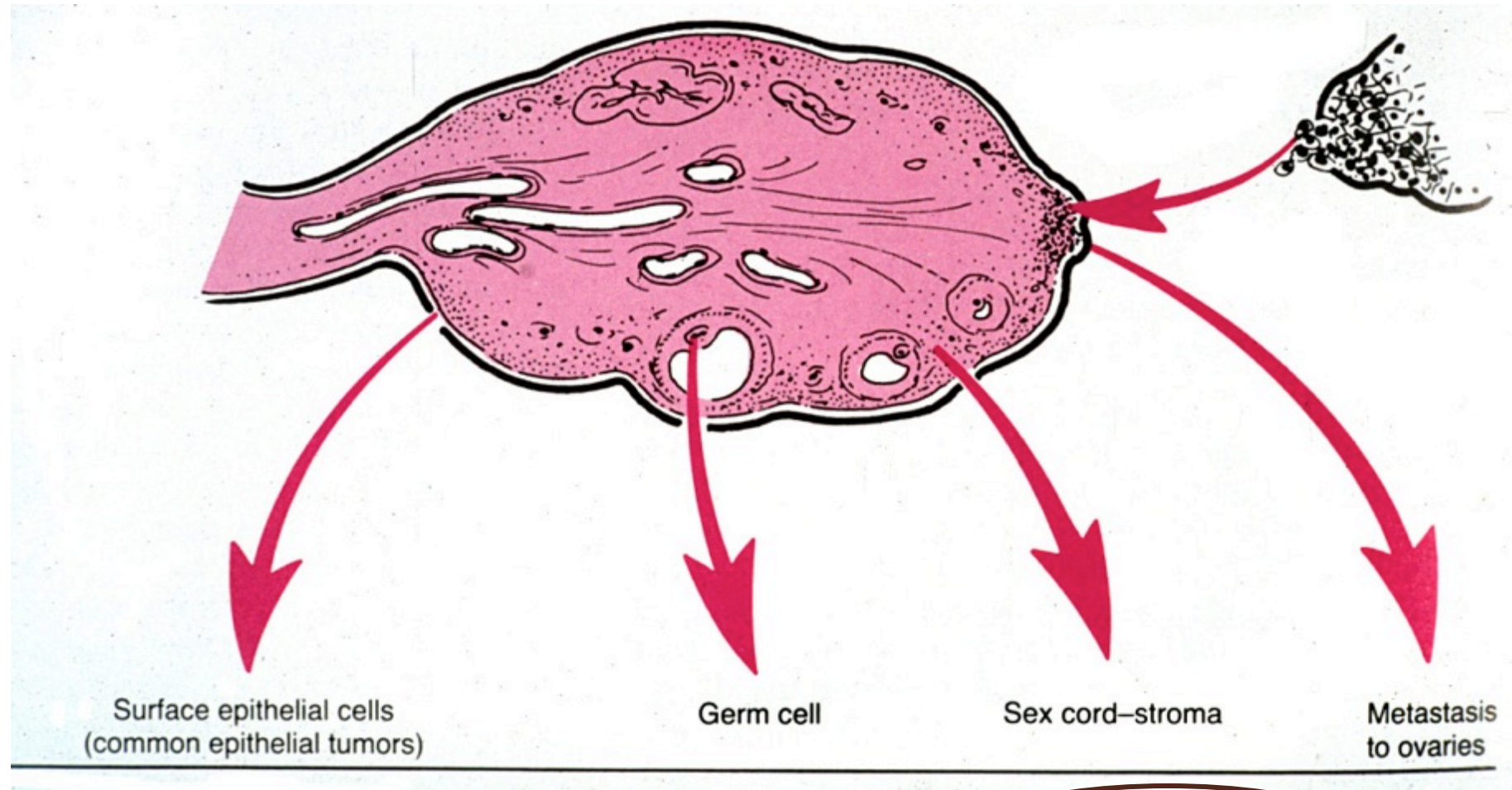










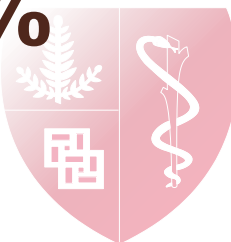


**65-70%**

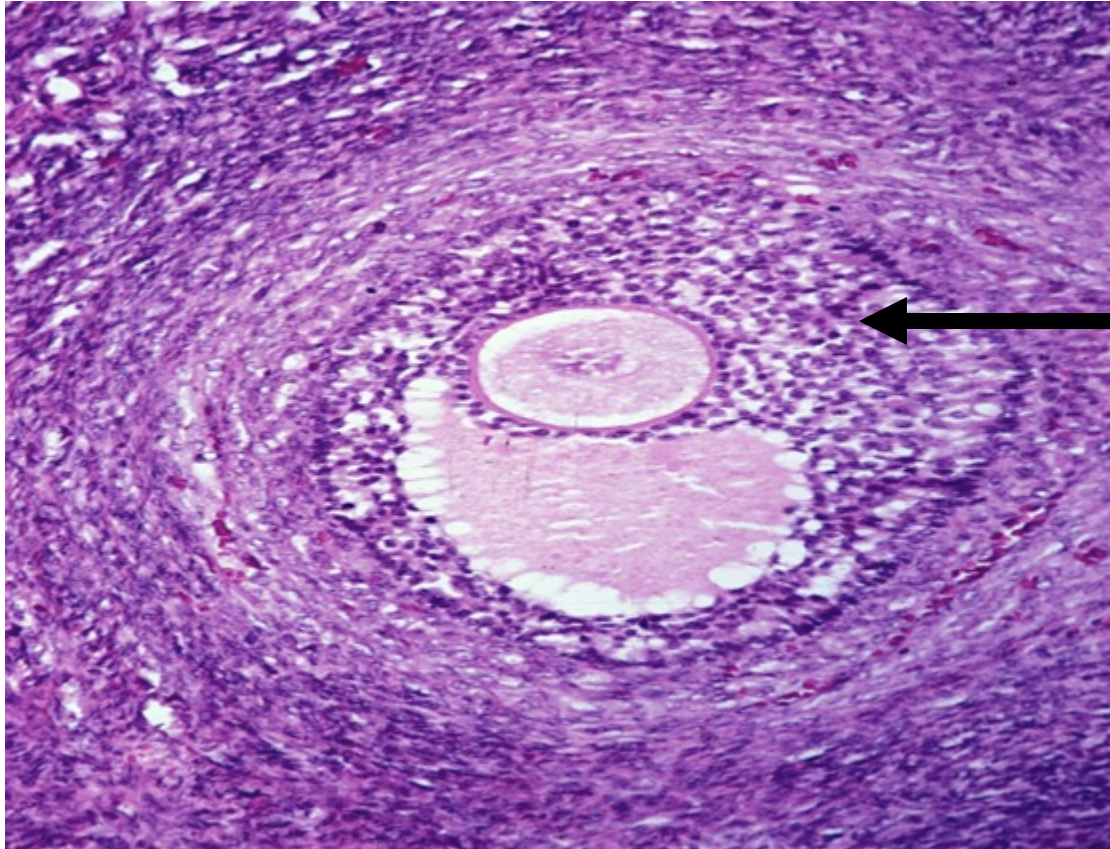
**5-10%**

**15-20%**

**5%**



# Sex-Cord Stromal Tumors

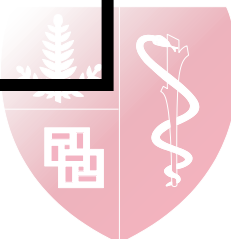


**Granulosa cell**

**Sertoli-Leydig cell**

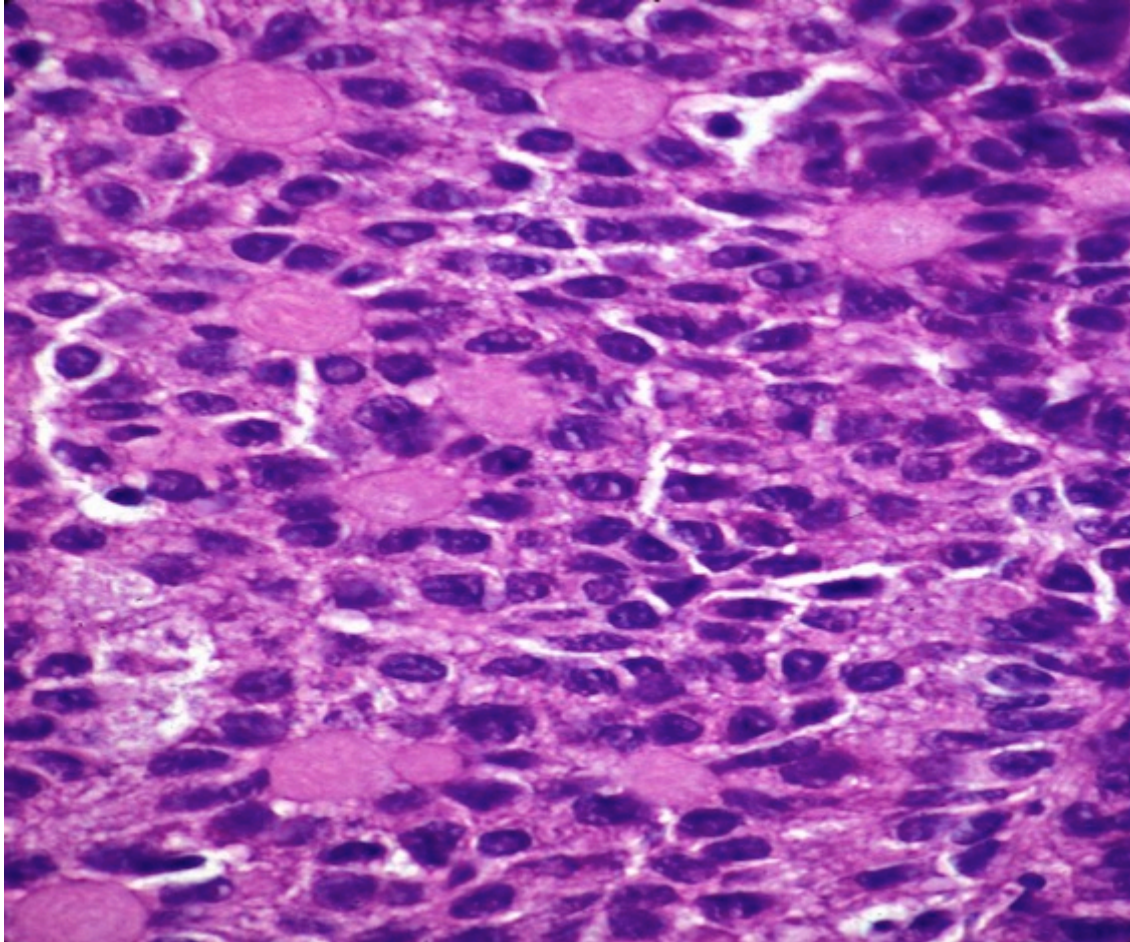
**Fibroma/thecoma**

**Steroid cell**

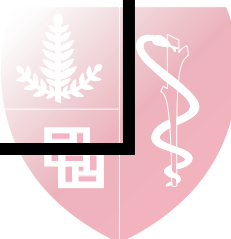




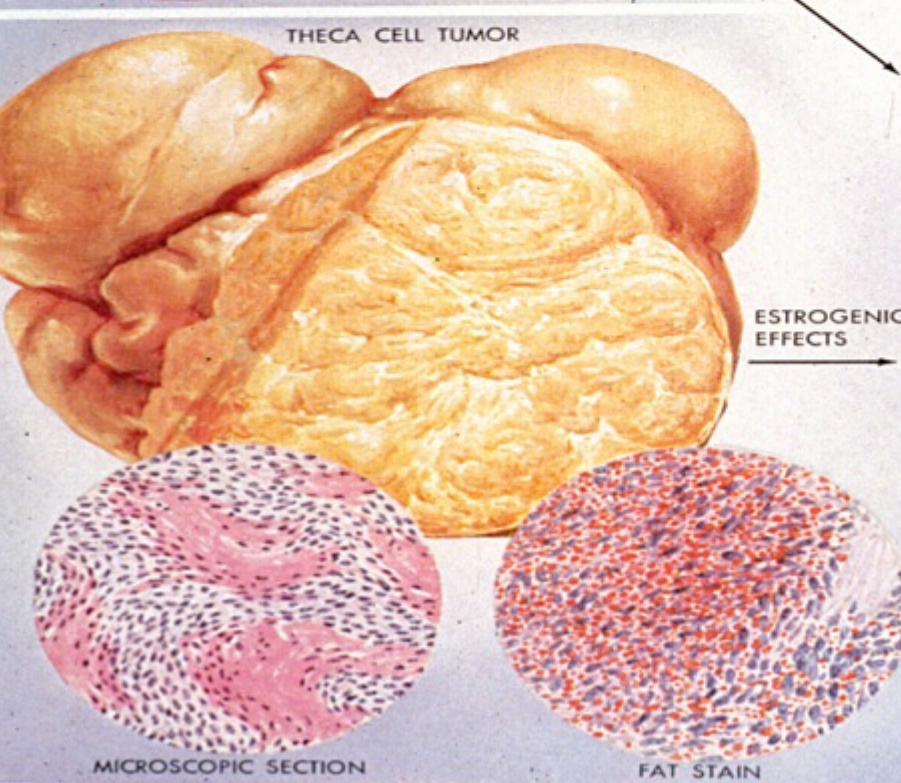
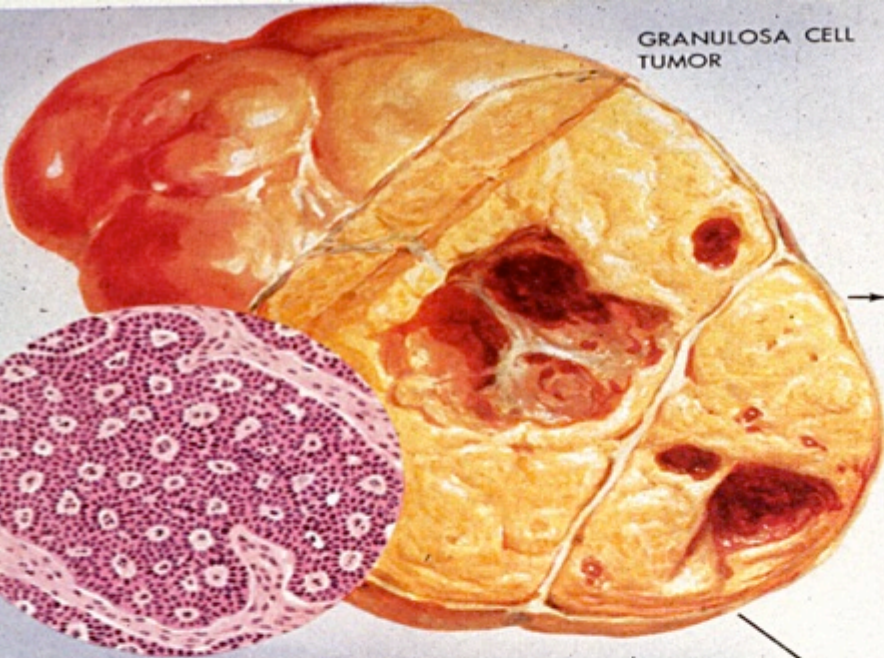
# Granulosa Cell Tumors



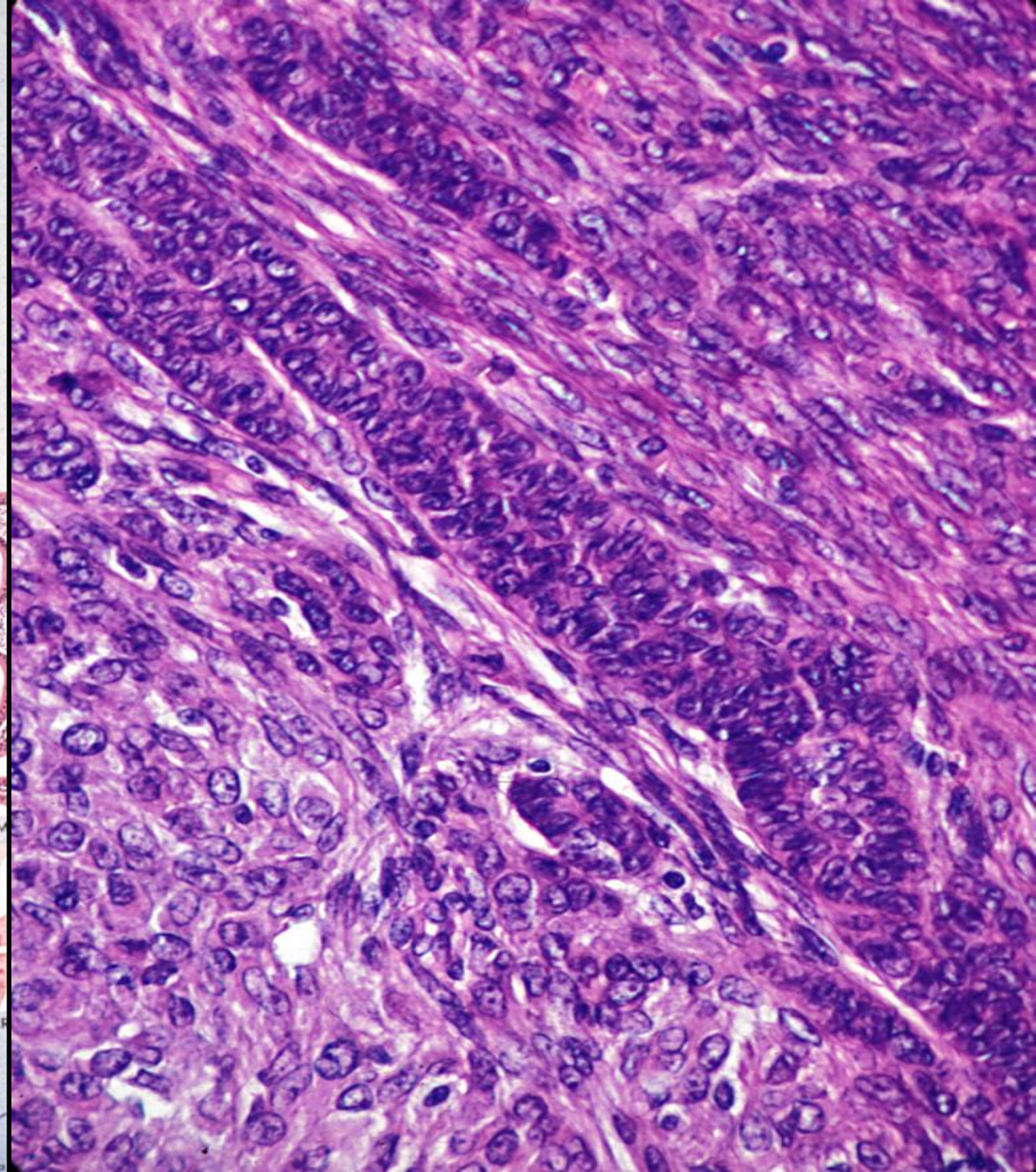
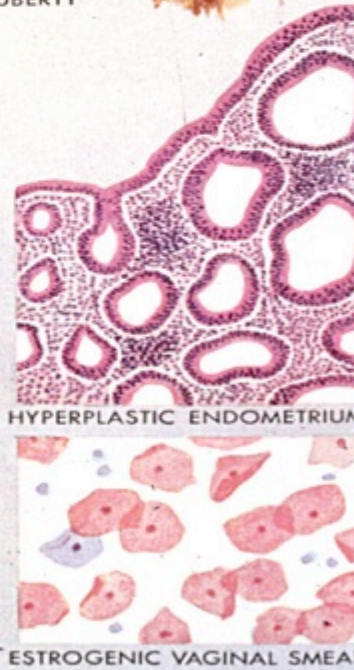
- **Solid, cystic, often hemorrhagic**
- **Call-Exner bodies**
- **Hyperestrogenic**
- **Benign or low grade malignant**
- **Adult/ juvenile**





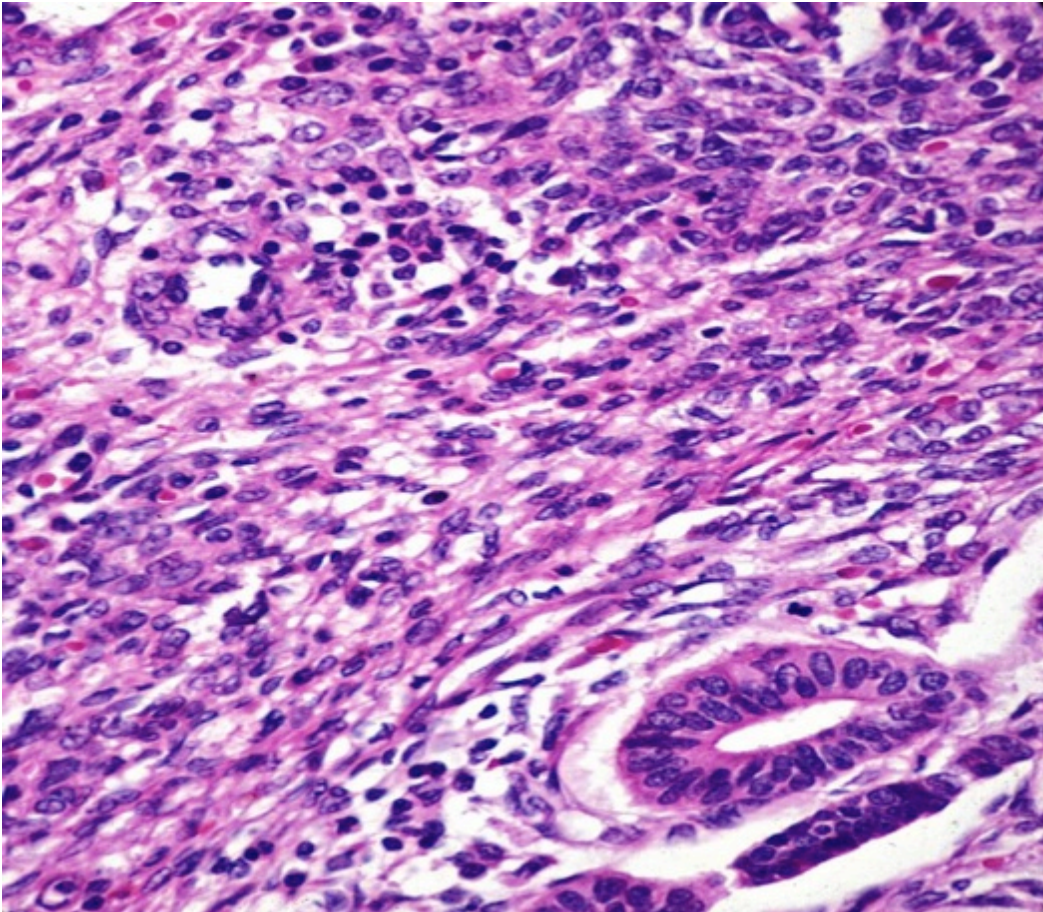


ESTROGENIC EFFECTS

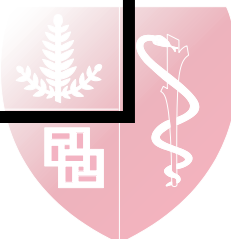




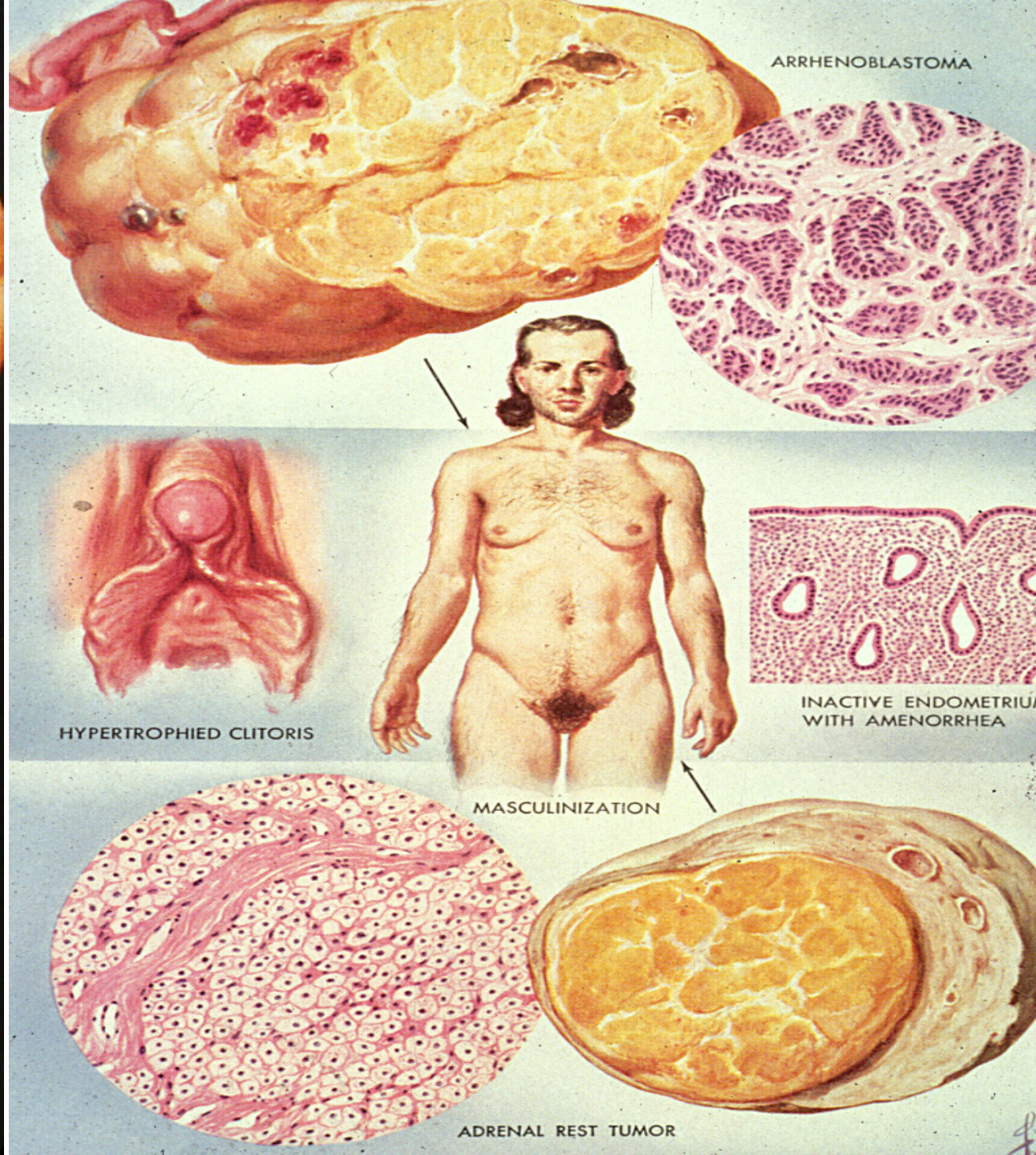
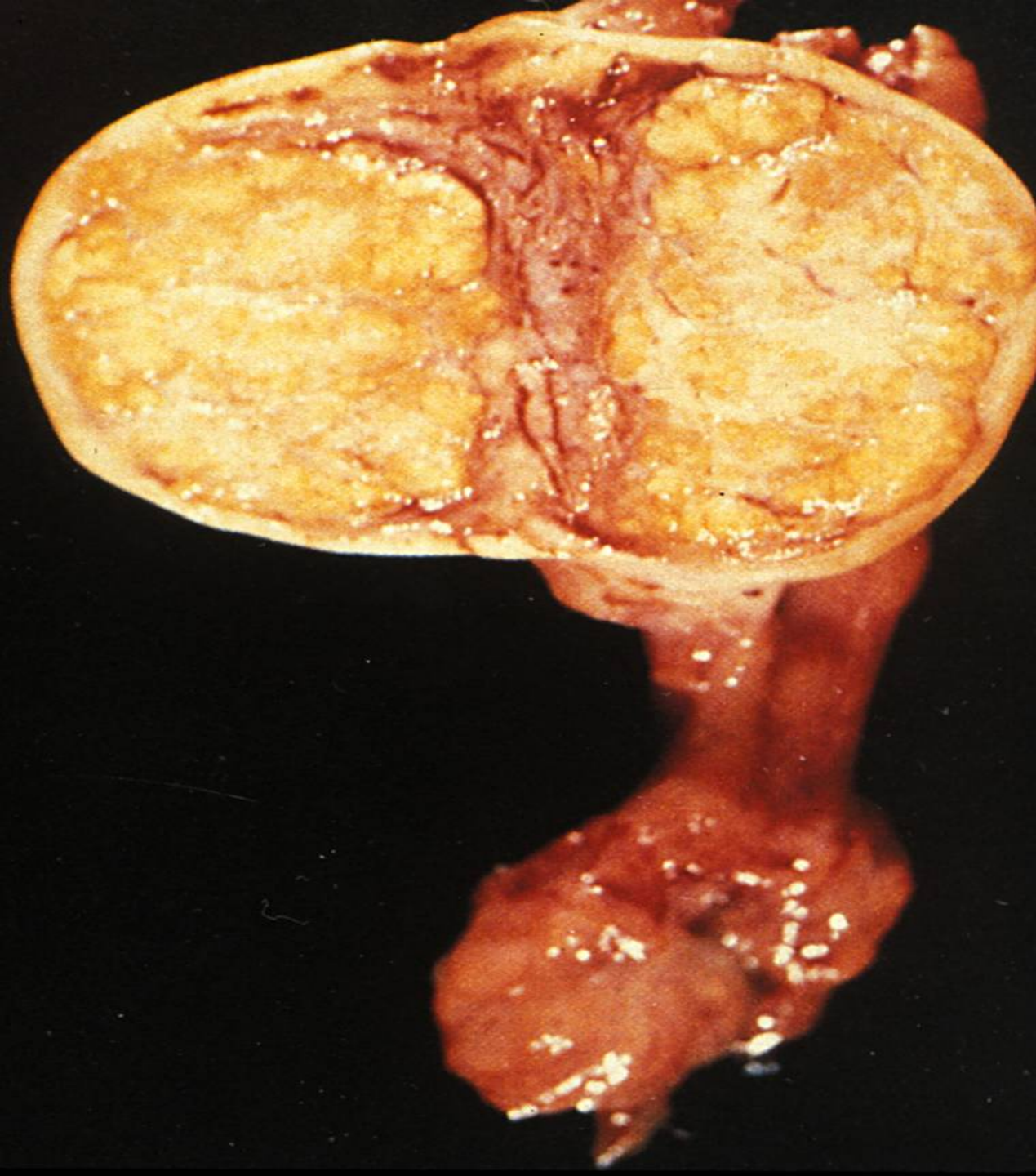
# Sertoli-Leydig Cell Tumors



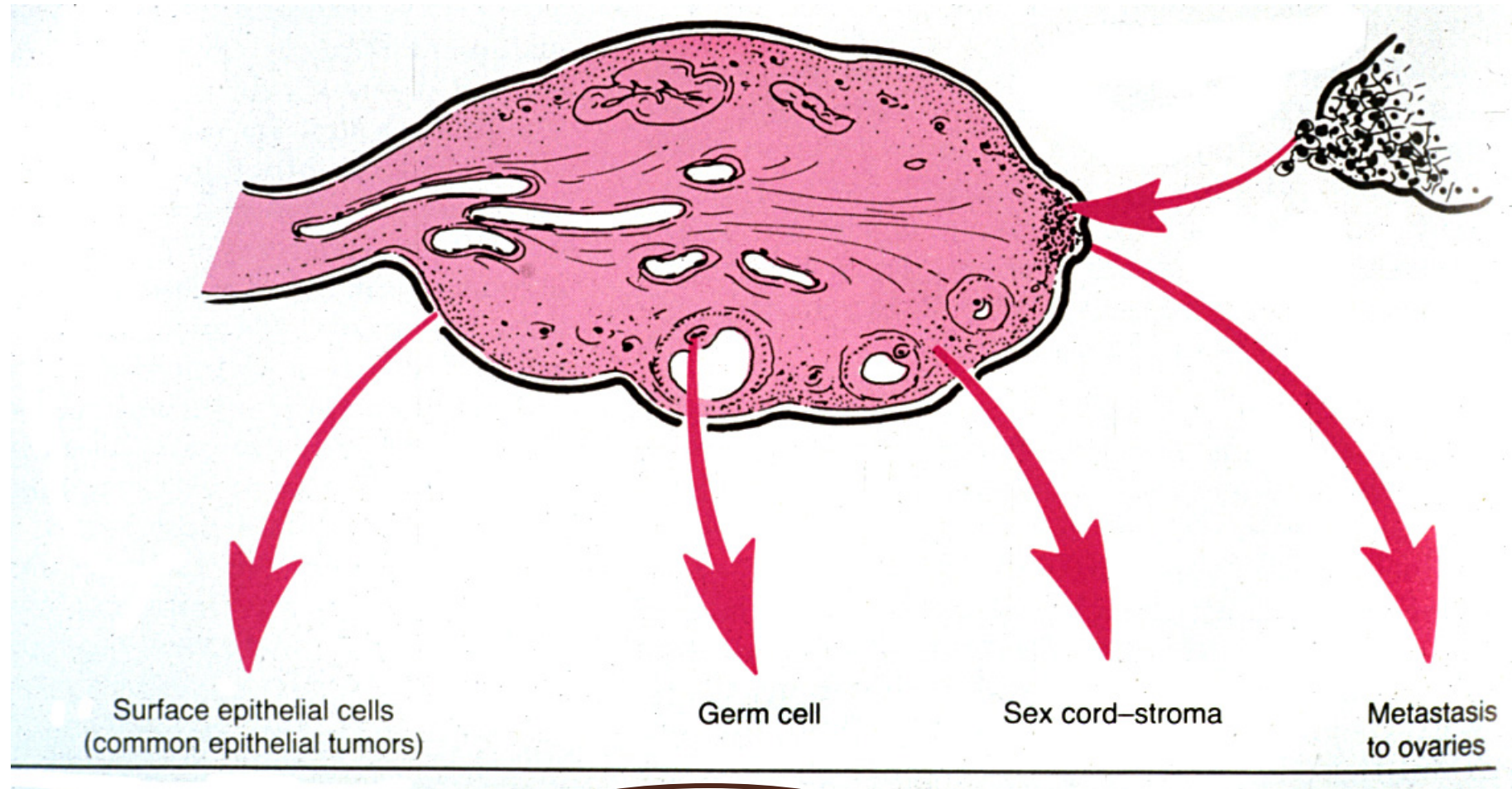
- **Solid, often yellow**
- **Sertoli tubules, Leydig cells**
- **Virilizing**
- **Malignant**
- **Adolescent/young adult**









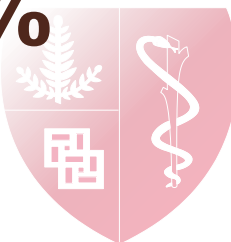


**65-70%**

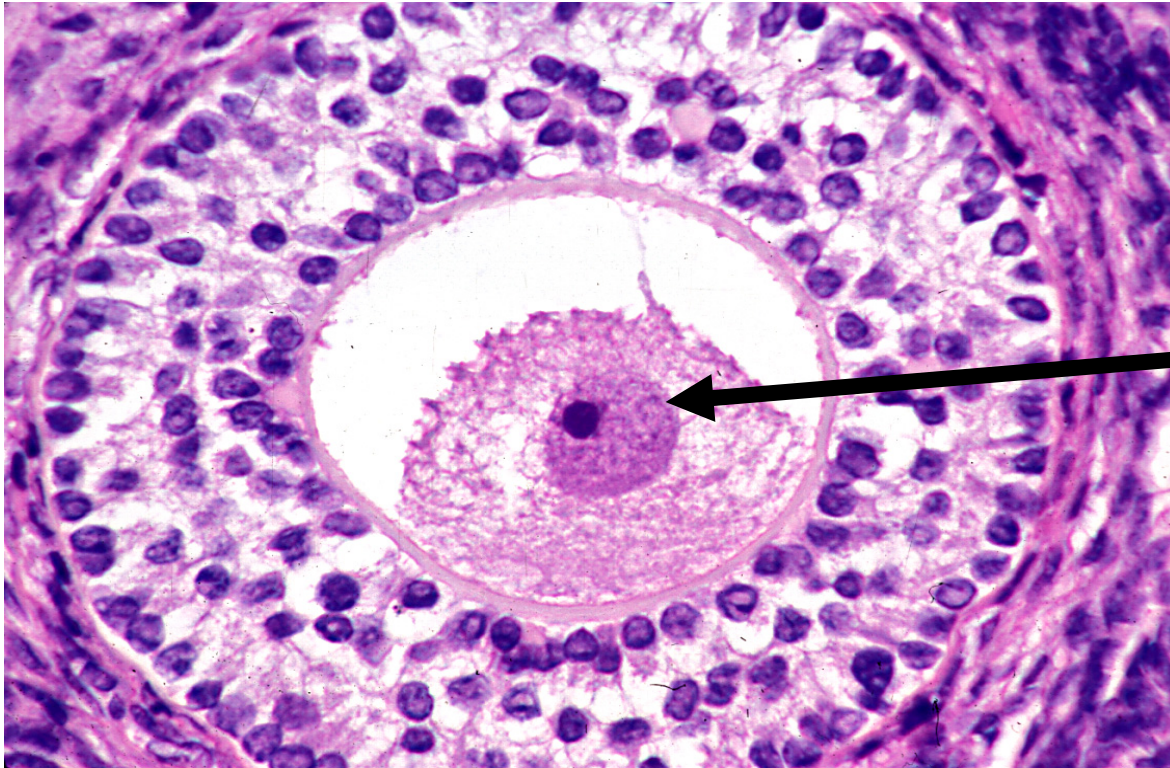
**5-10%**

**15-20%**

**5%**



# Germ Cell Neoplasms



## **BENIGN:**

**Dermoid cyst  
(mature teratoma)**

## **MALIGNANT:**

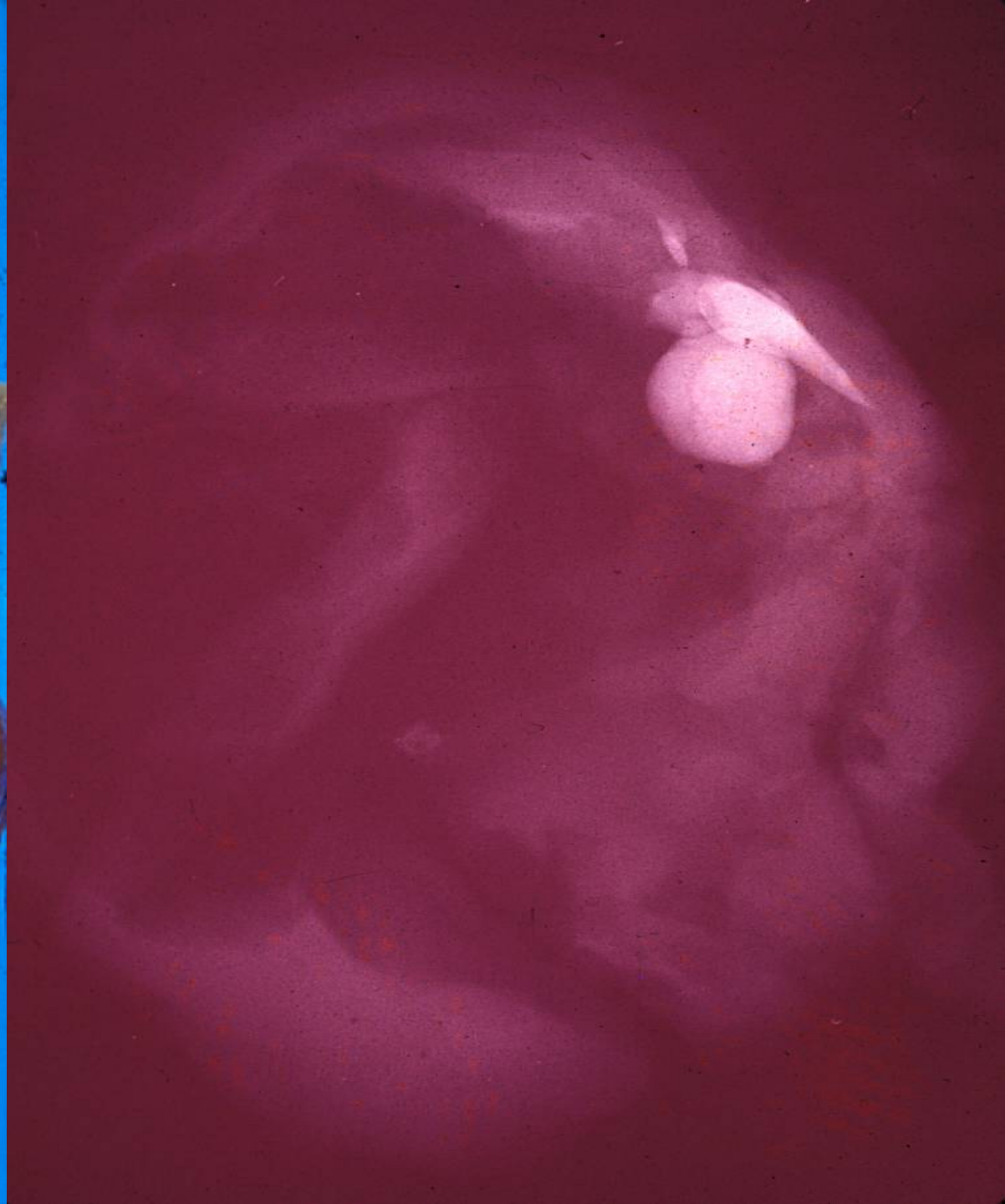
**Dysgerminoma  
Yolk sac tumor  
Immature teratoma**



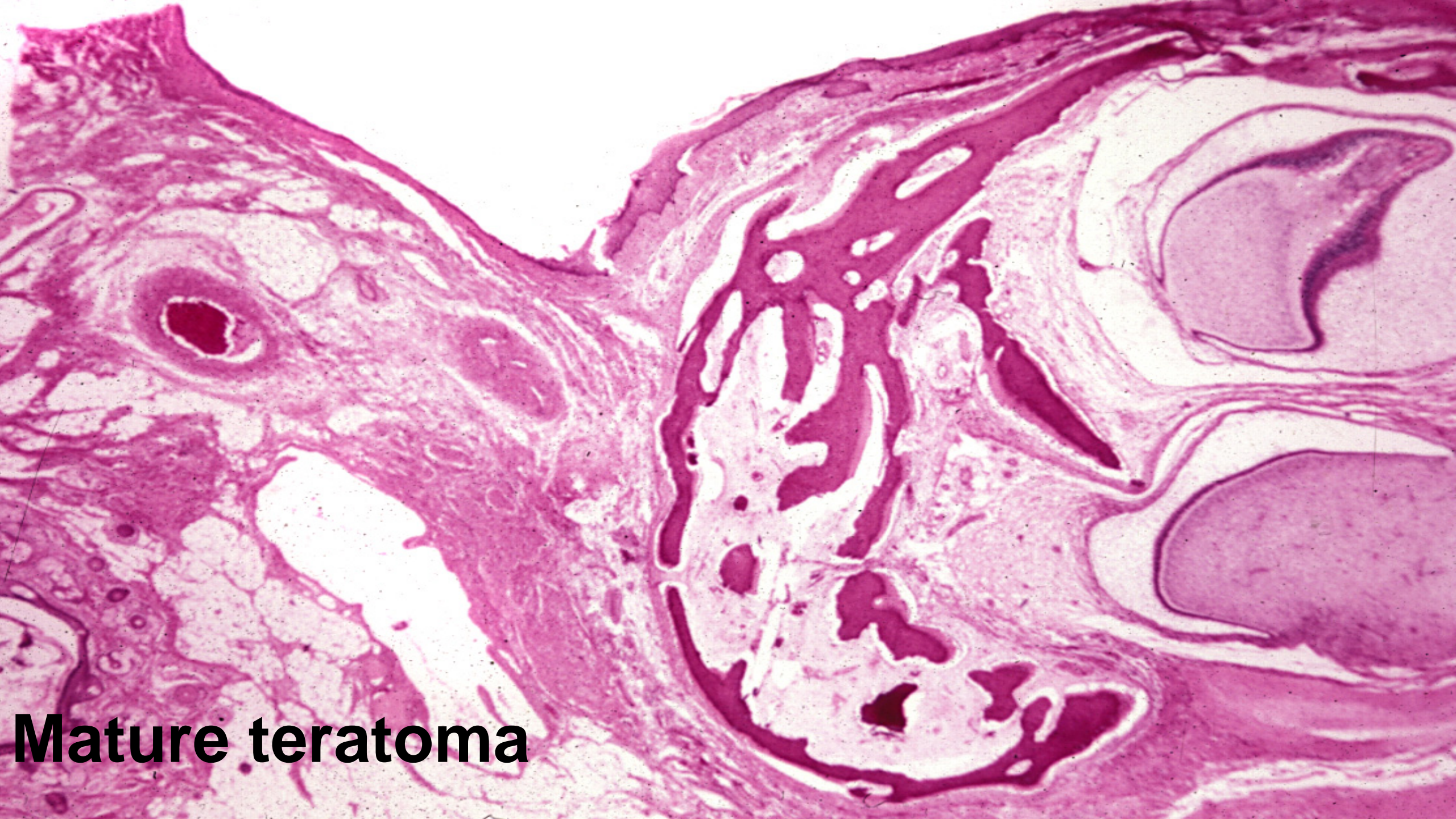




**Mature teratoma**





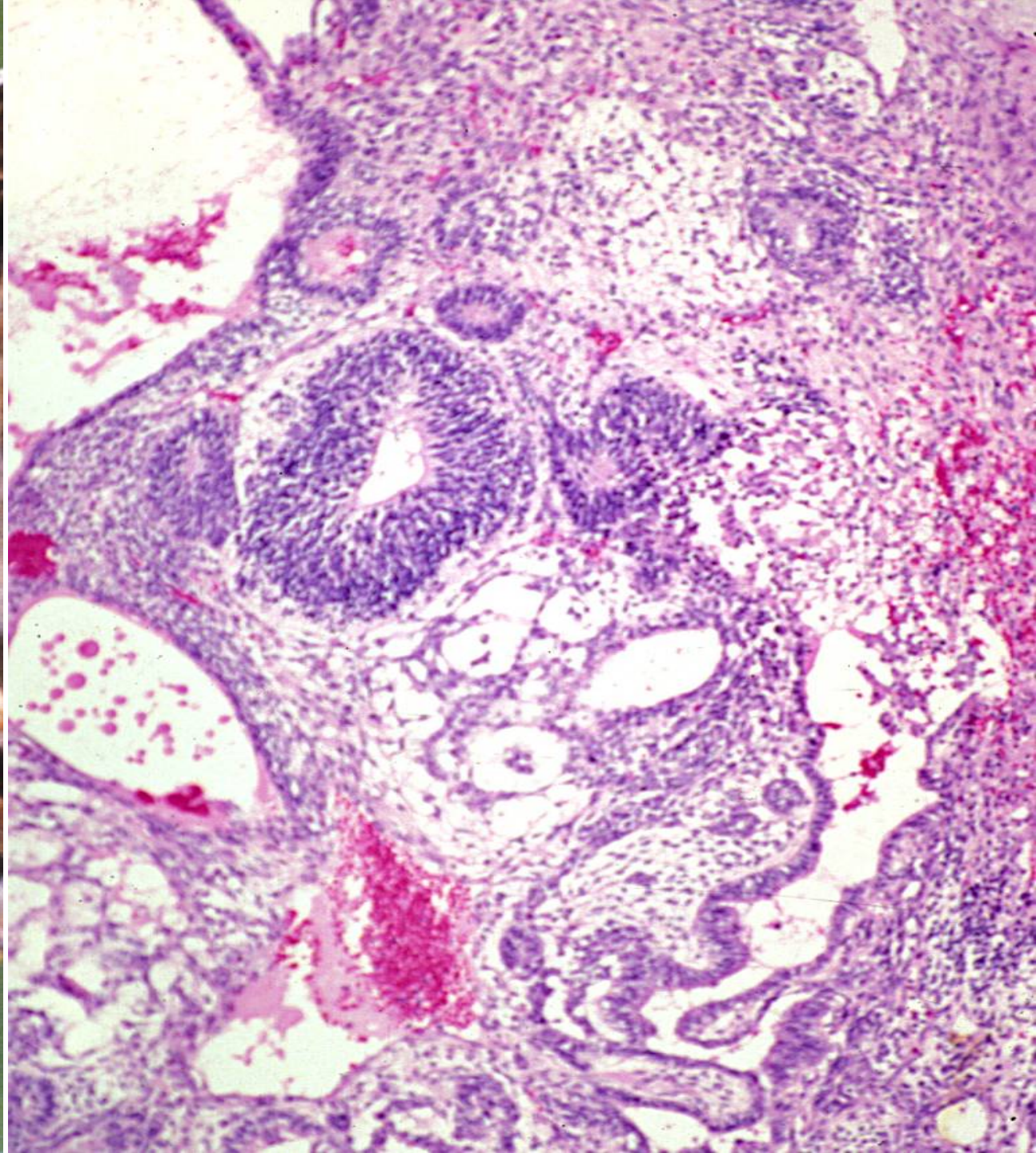


**Mature teratoma**





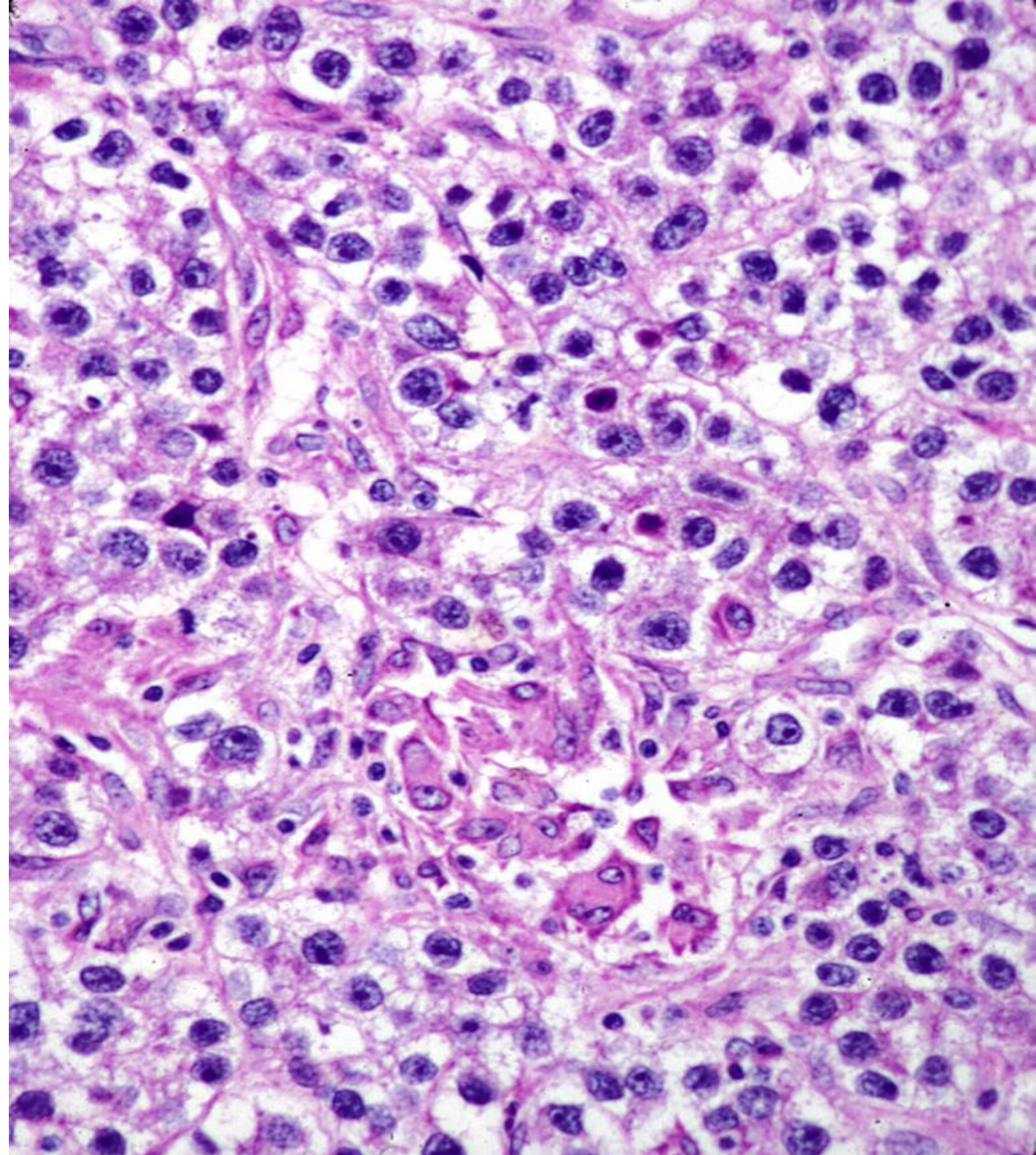
**Immature teratoma**







**Dysgerminoma**

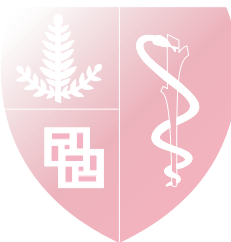




# OTHER

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- Inflammation
  - PID
- Endometriosis
  - Endometriomas



# ENDOCRINE FUNCTION

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- RARE:
- Hyperestrogenism with Granulosa Cell Tumor (Endometrial stimulation)
  - Precocious puberty
  - AUB in reproductive age
  - Postmenopausal women
- Virilization with Sertoli-Leydig Cell Tumor
  - Hirsutism, deepening of voice, clitoromegaly





# ENDOCRINE FUNCTION: Common

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- Chronic anovulation—Polycystic Ovary Syndrome (PCOS)
  - Prevalence 5-10% of adult women
  - Rule out other causes of androgen excess: CAH, ov tumor
    - Anovulation/oligo-ovulation (irregular menses)
    - Polycystic ovaries on US
    - Clinical or biochemical signs of hyperandrogenism
  - Increased risk endometrial hyperplasia and CA
  - Associated with obesity (65 +%)
  - Associated with insulin resistance/DM



