Non-epithelial ovarian cancer

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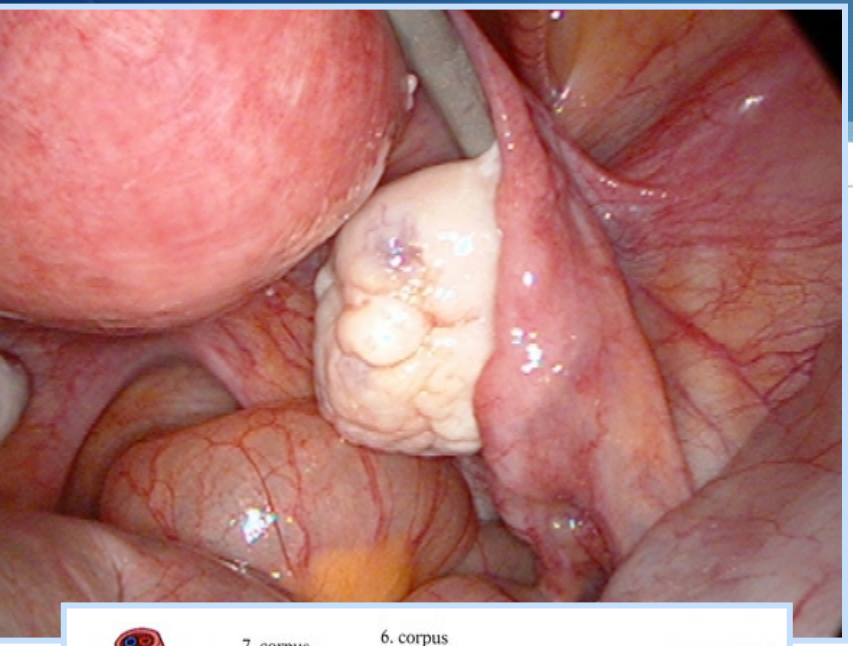
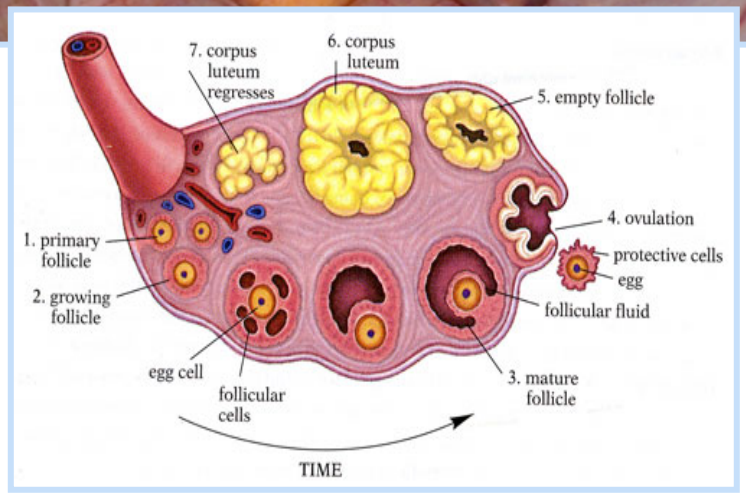
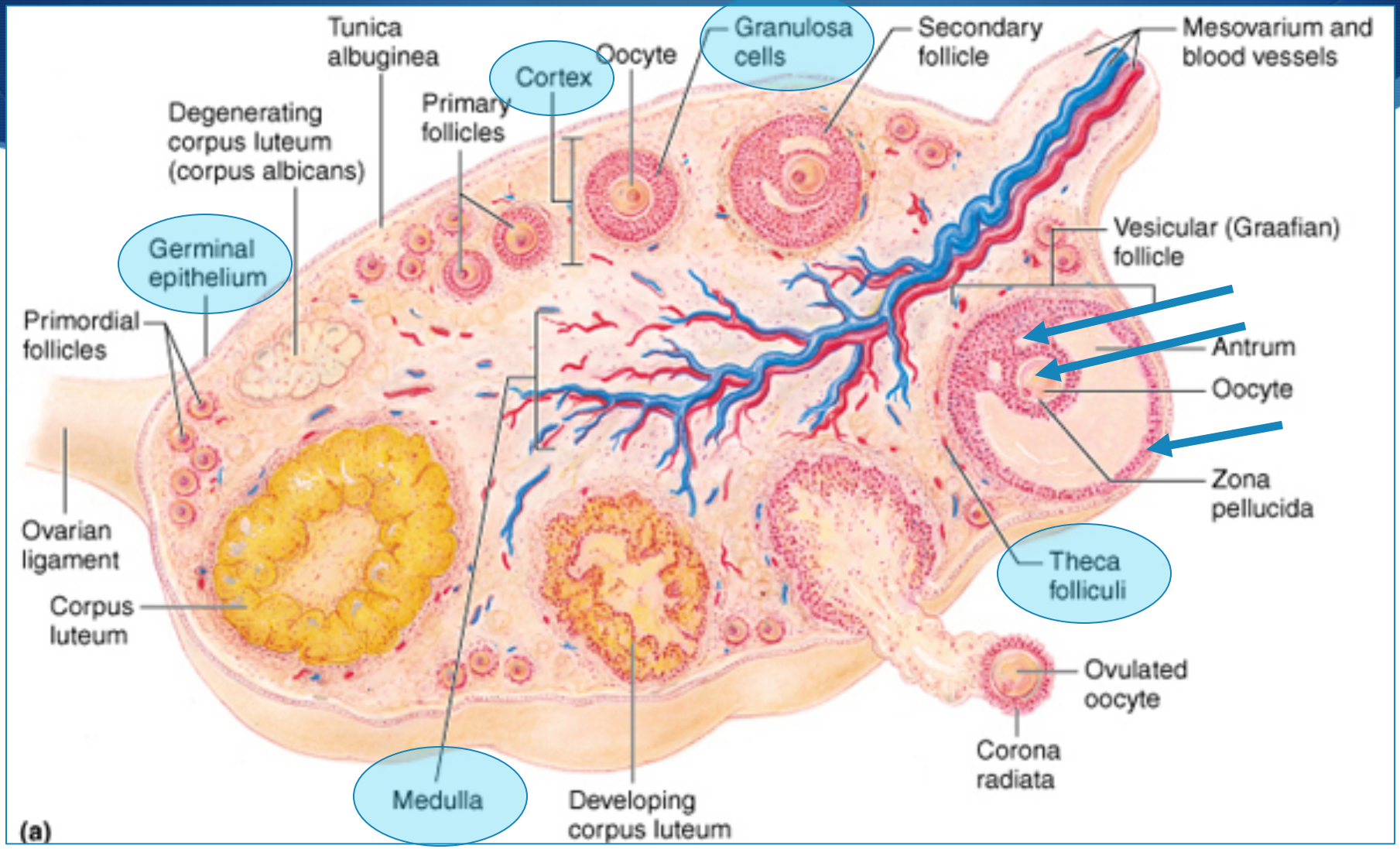
Types of Ovarian Cancer





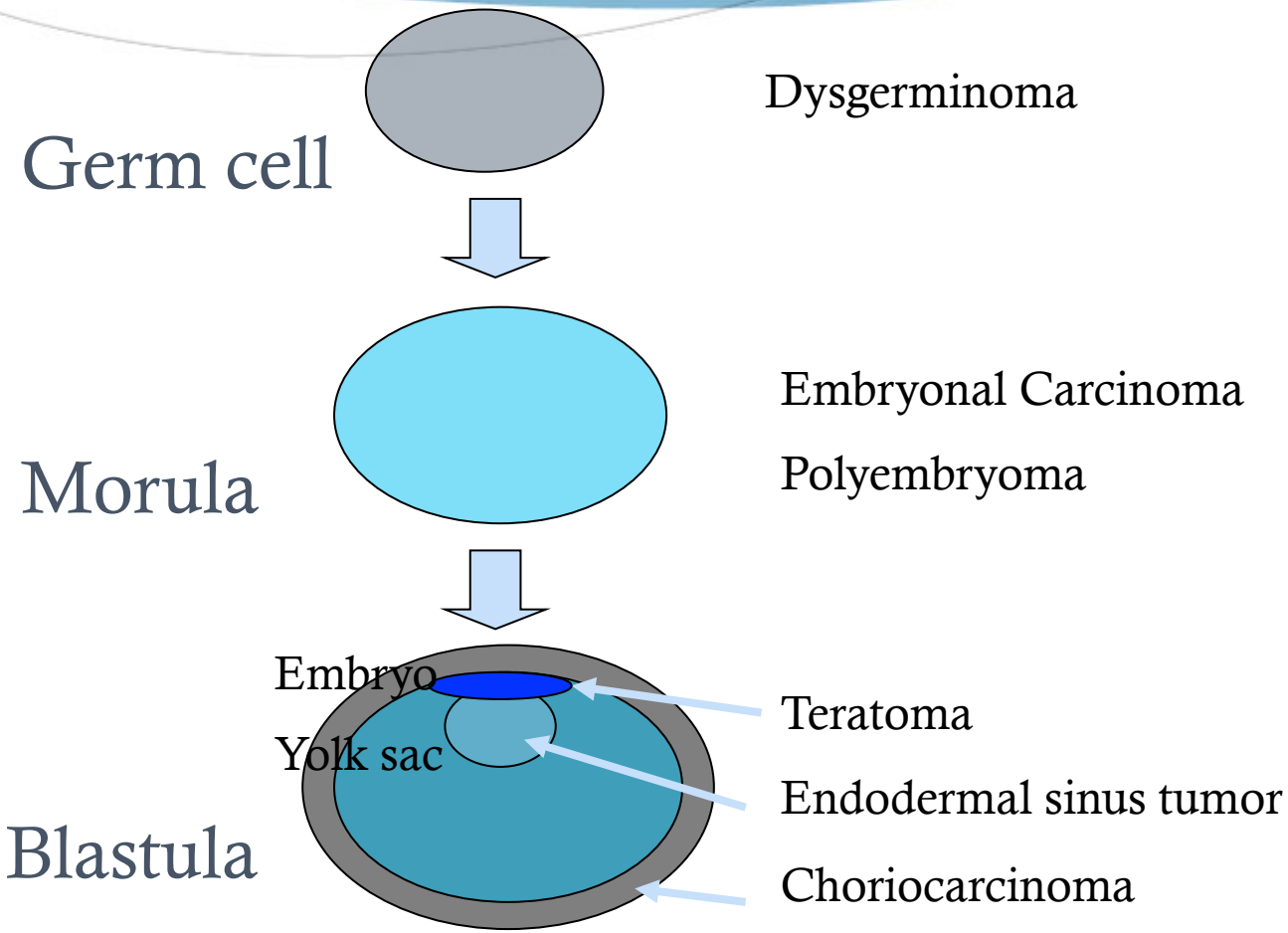
1. Epithelial Ovarian Cancer (90%)
   - Serous/Papillary serous (80%)
   - Mucinous (10%)
   - Endometrioid (10%)
   - Clear Cell
   - Brenner Tumors
   - *Borderline Tumors*
2. Germ Cell Tumors
   - Dysgerminoma
   - Yolk Sac Tumors/Endodermal sinus tumor
   - Embryonal Carcinoma
   - Choriocarcinoma
   - Teratomas
3. Sex-cord Stromal Tumors
   - Granulosa Cell Tumors
   - Fibrosarcoma
   - Sertoli-Leydig Tumors


Tunica albuginea
Cortex
Oocyte
Granulosa cells
Secondary follicle
Mesovarium and blood vessels
Degenerating corpus luteum (corpus albicans)
Primary follicles
Germinal epithelium
Vesicular (Graafian) follicle
Primordial follicles
Antrum
Oocyte
Zona pellucida
Ovarian ligament
Theca folliculi
Corpus luteum
Ovulated oocyte
Corona radiata
Medulla
Developing corpus luteum
(a)

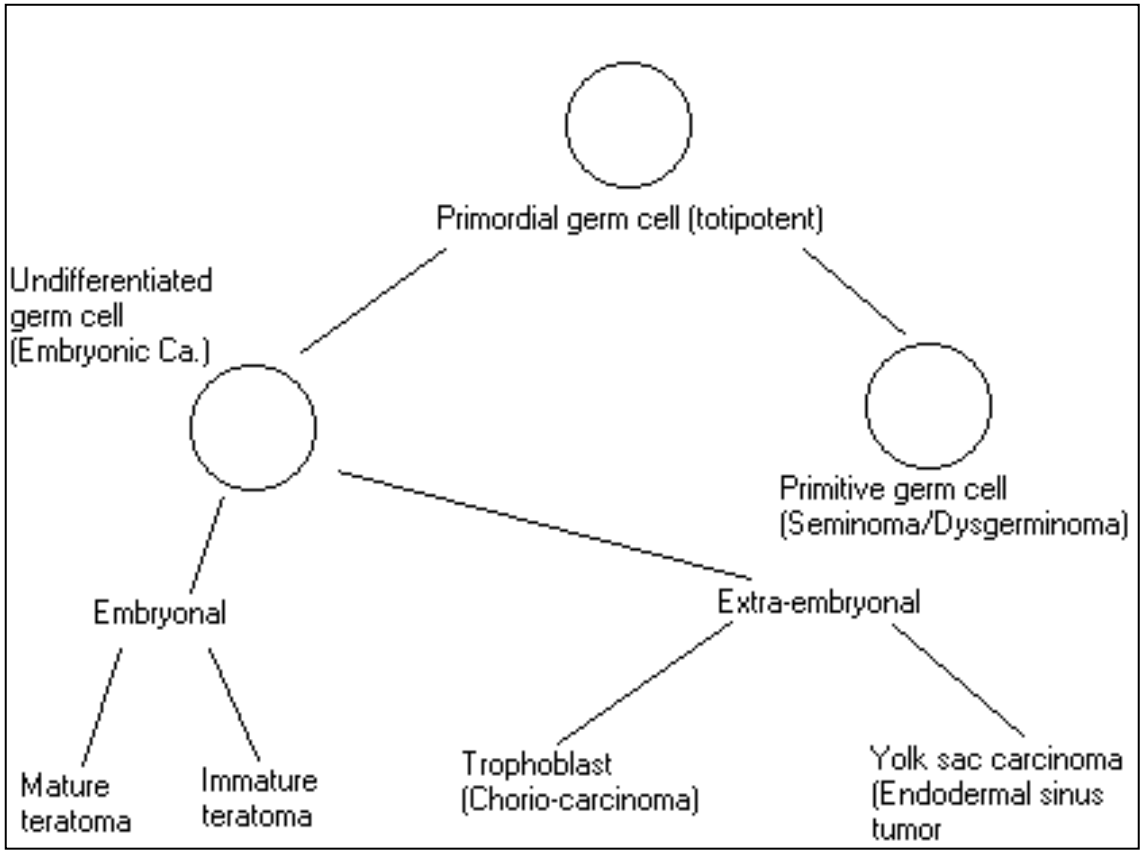
Germ Cell Tumors

- 20% of all ovarian tumors
- 2-3% of ovarian malignancies
- Presentation at young age (early 20's)
- Tumor markers
  - hCG
  - αFP
  - LDH

Evolution of Germ Cell Tumors



Ovarian Germ Cell Tumors



Germ Cell Tumors

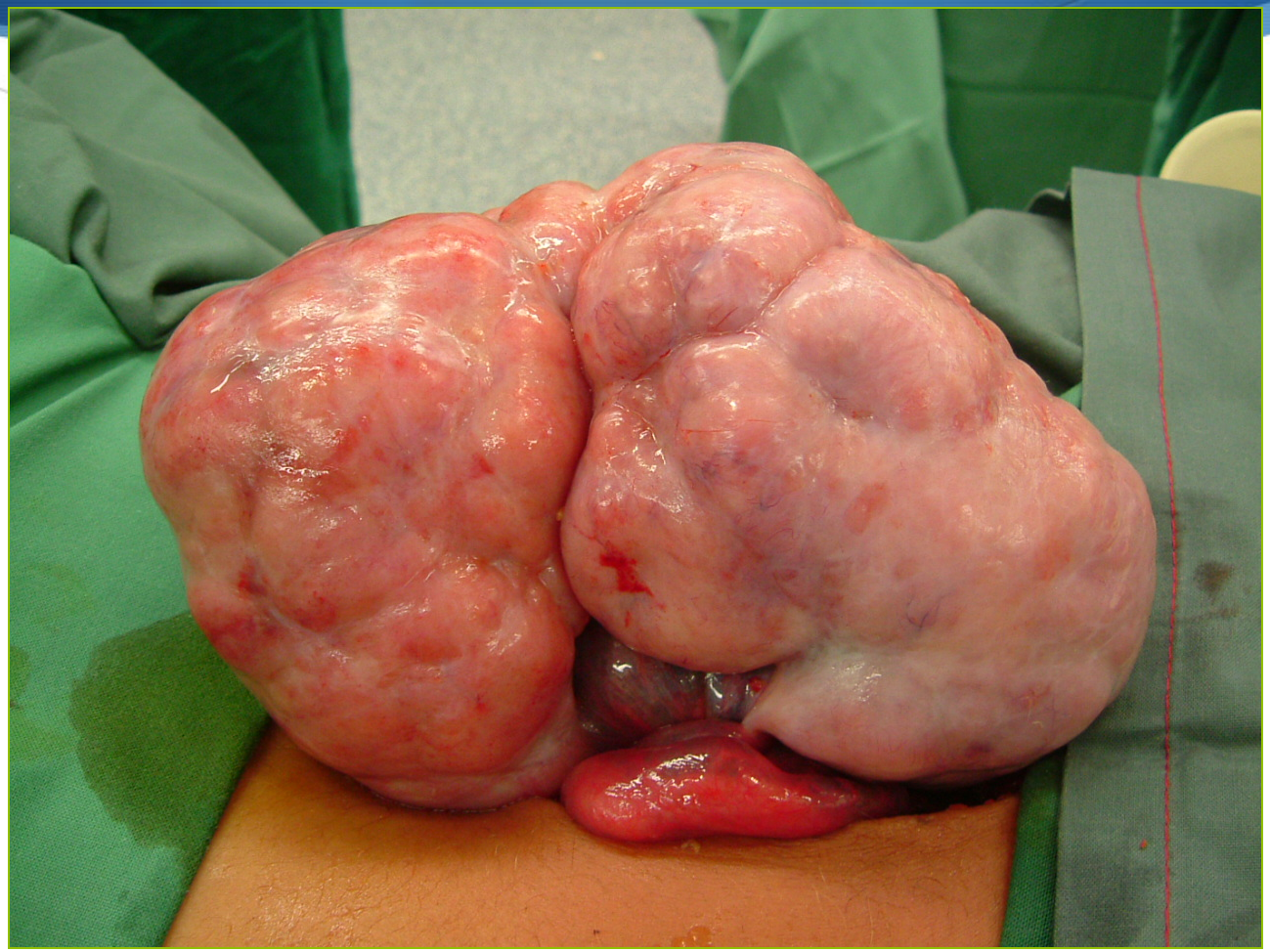
- Dysgerminoma
- Endodermal sinus tumor
- Teratoma
  - Immature
  - Mature
  - Struma ovarii
  - Carcinoid
- Choriocarcinoma
- Embryonal carcinoma
- Polyembryoma
- Mixed GCT
- Combo GCT/Stromal
  - Gonadoblastoma
  - Other

Subtype	Frequency of OGCT	Benign/ Malignant	Uni- or Bi-lateral	Tumour Markers Expressed	Metastasis Route
Dysgerminoma	35-50%	Malignant	10-15% are bilateral	Serum lactic dehydrogenase and serum hCG	Lymphatic system
Endodermal sinus tumor EST	20%	Malignant	Usually unilateral	AFP (commonly), alpha1-antitrypsin (rarely)	Intraperitoneally and hematogenously
Embryonal carcinoma	Rare	Malignant	Usually unilateral	AFP and hCG	Intraperitoneally
Polyembryoma	Rare			AFP and hCG	
Choriocarcinoma	Very rare	Malignant	Usually unilateral	HCG	
Teratoma	Immature account for 20% of malignant GCT	Benign or malignant	12-15% are bilateral	Immature teratomas sometimes secrete AFP serum LDH and CA-125	
Mixed GCT	10-15%	Dependent upon the cell types present		Dependent upon the cell types present	

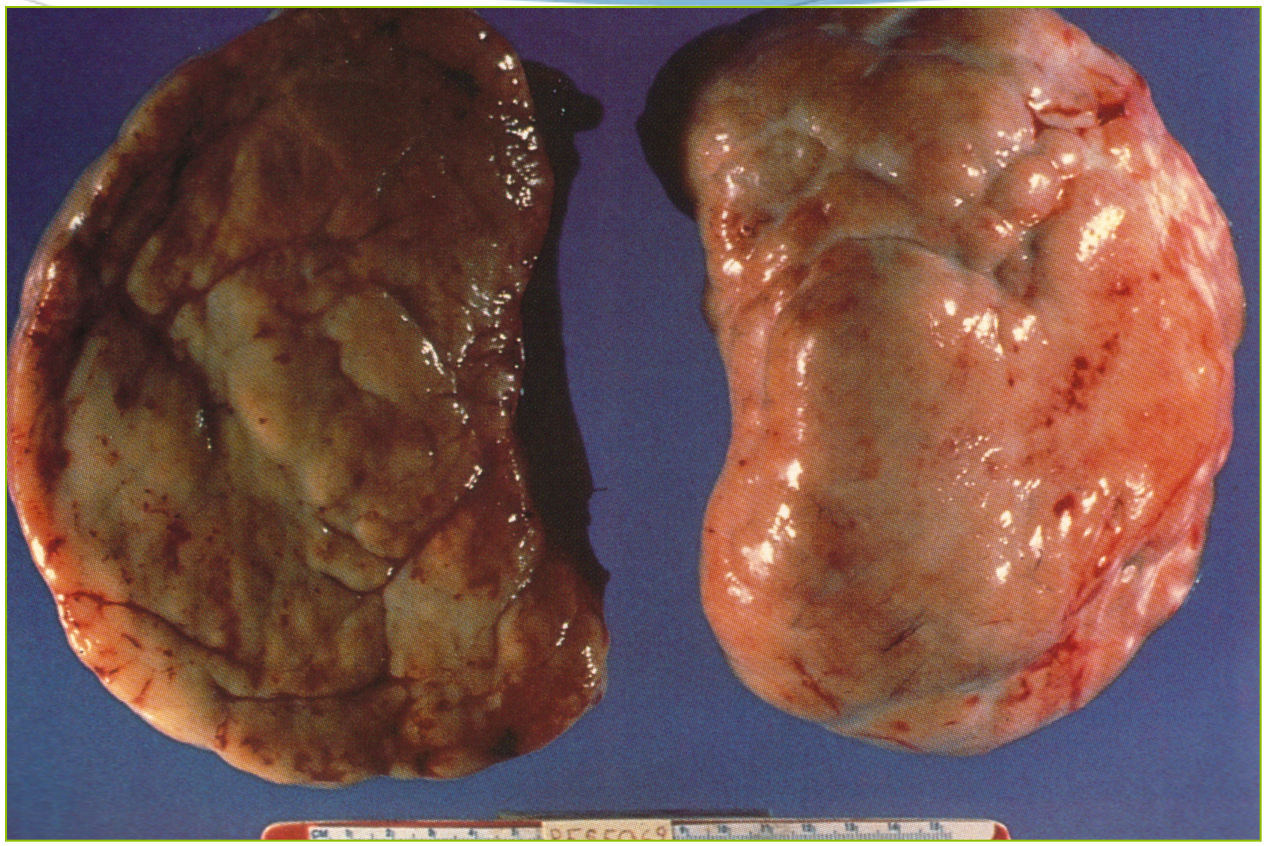
Dysgerminoma

- Lance Armstrong
- Incidence
  - 1-2% of ovarian tumors
  - 3-5% of ovarian malignancies
  - 40% of all GCT
  - Peak incidence age 19
  - 67% stage IA
- 10-15% bilaterality
  - 20% in "normal appearing" opposite ovary

Dysgerminoma

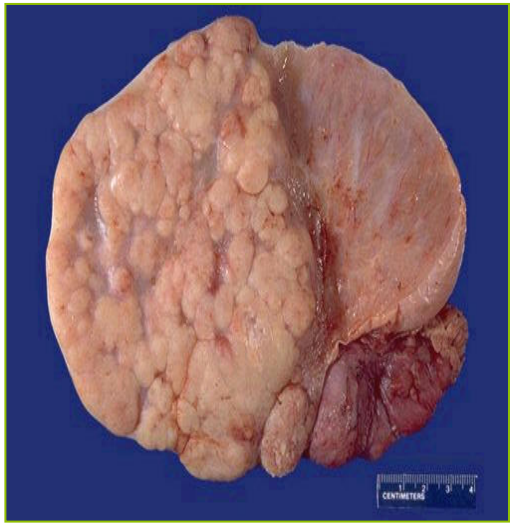


Dysgerminoma



Dysgerminoma

- Presentation
  - Solid, lobulated, and can be large
  - 15% associated with mature cystic teratoma
  - Associated with gonadal dysgenesis and gonadoblastoma
  - High growth fraction, lymphatic spread
- Tumor markers
  - LDH, placental alkaline phosphatase
- Survival
  - Overall =86%
  - Stage I =90%

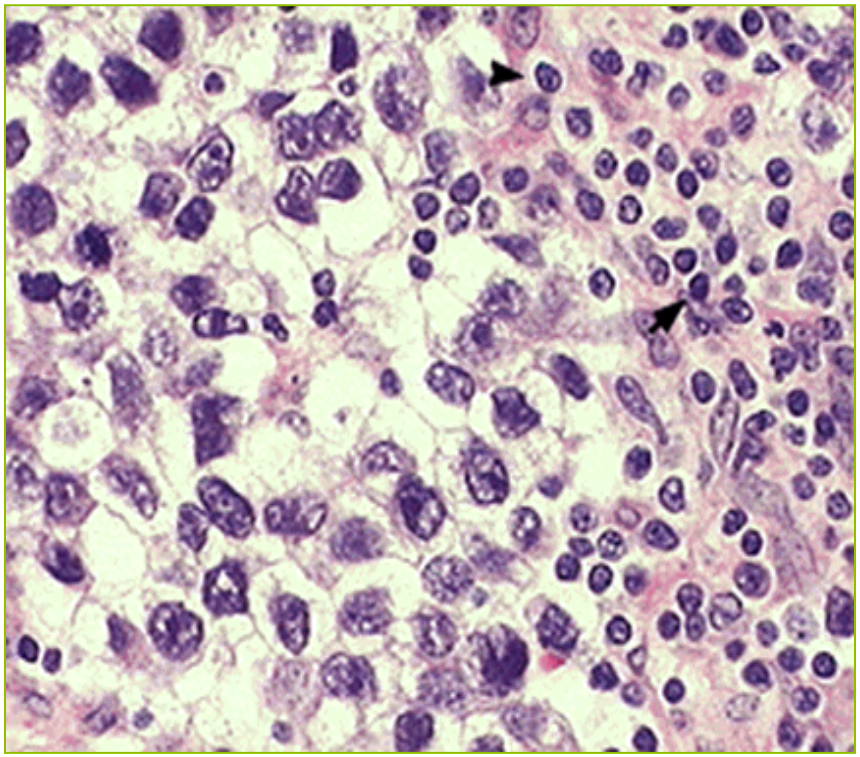


Dysgerminoma

- Fertility-sparing surgery
  - 85% of patients are younger than 35 yo
  - Consider uterine preservation (IVF)
- Radiosensitive
- Chemotherapy
  - Combination, dose-intense regimen

Dysgerminoma

- Large, round, ovoid or polygonal cells
- Nest and cords of primitive appearing germ cells
- Lymphatic space invasion is common



Dysgerminoma

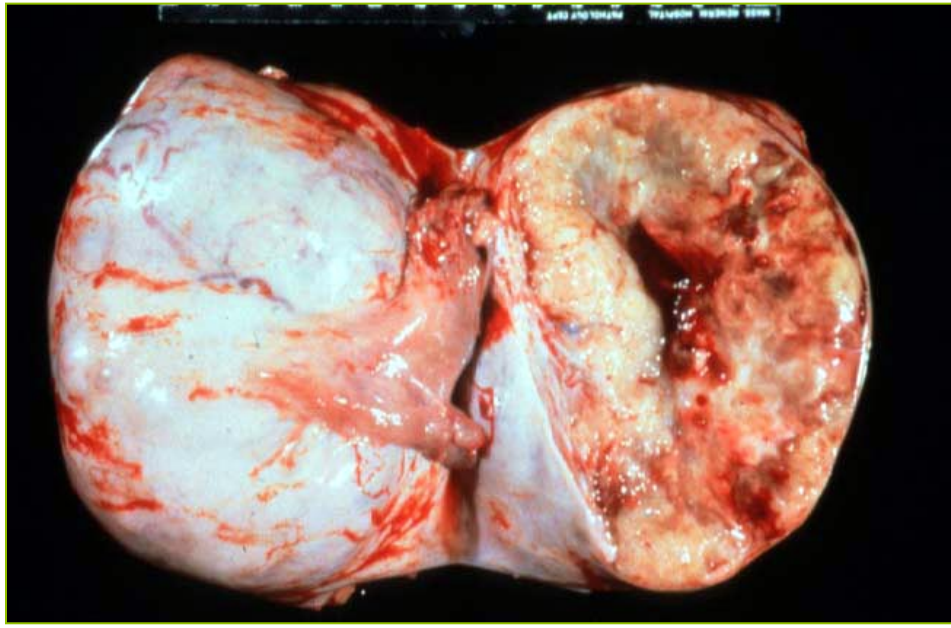
	Incidence	Survival
Stage IA	70%	92% 10-year
Stage IB	10%	>90% 5-year
Stage II, III	15%	>90%
Stage IV	5%	80%

Endodermal Sinus Tumor

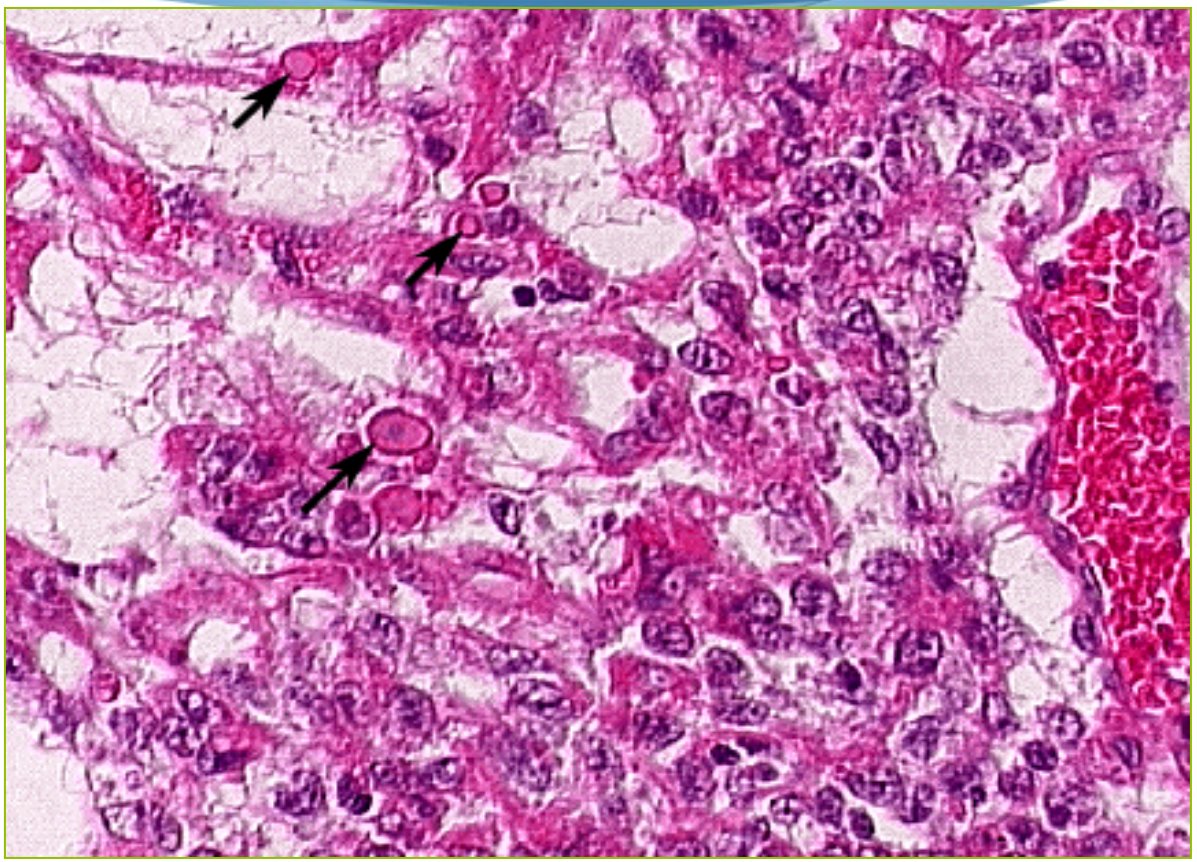
- Presentation
  - 20% of all GCT
  - Median age 19 yo
  - Abdominal pain, large mass
  - 10-30 cm common
  - Very rapid growth, intra-abdominal and hematological spread
- Tumor marker: AFP, α_1 antitrypsin
- Synonyms
  - Yolk sac tumor
- Survival
  - Overall survival =70%
  - Stage I =90%

Endodermal Sinus Tumor

- Solid tumor with hemorrhage and gelatinous necrosis on cut surface
- Microscopy
  - Hyaline globules
  - Reticular Pattern
  - Schiller-Duval bodies
    - Single blood vessel surrounded by neoplastic cells

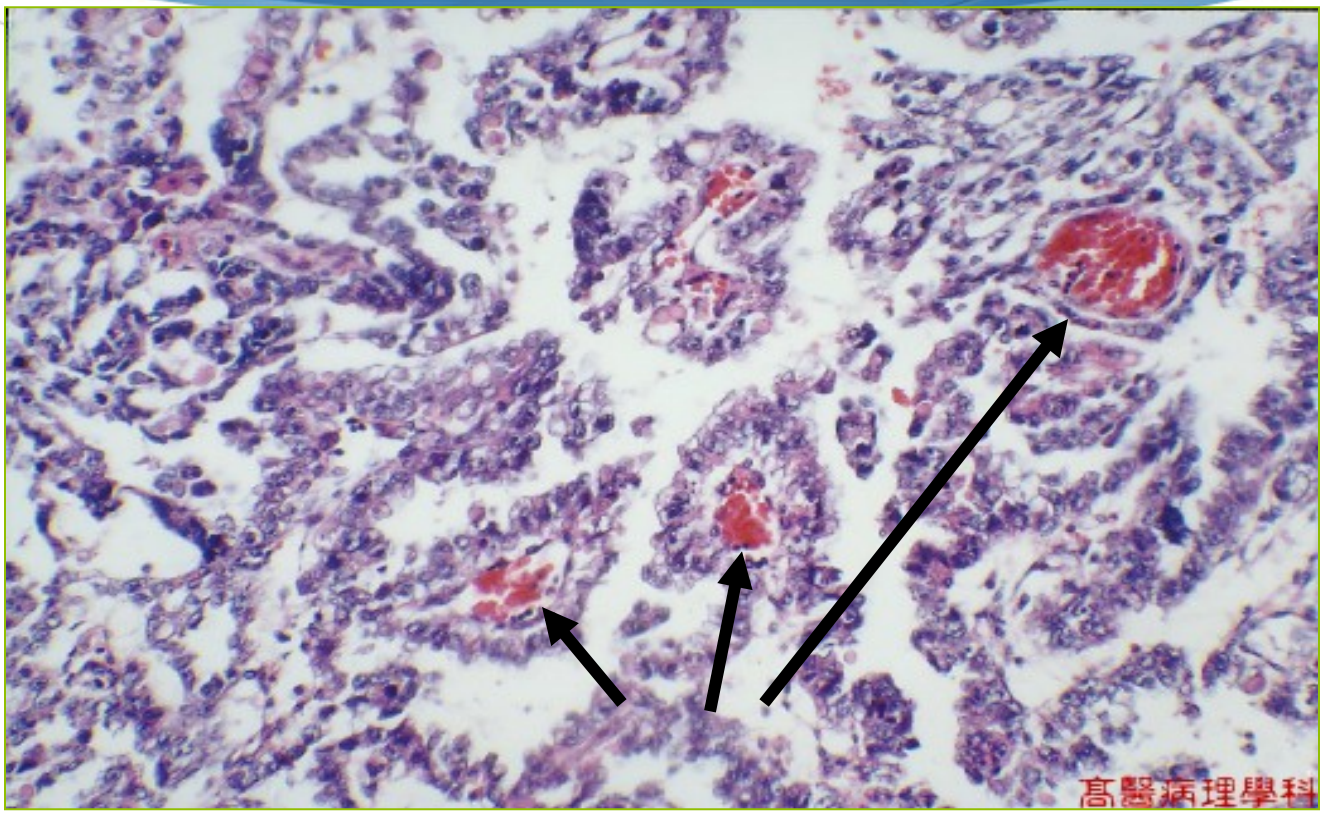


Endodermal Sinus Tumor



Hyaline globules → α_1 anti-trypsin

Endodermal Sinus Tumor



Schiller-Duval bodies

Teratomas

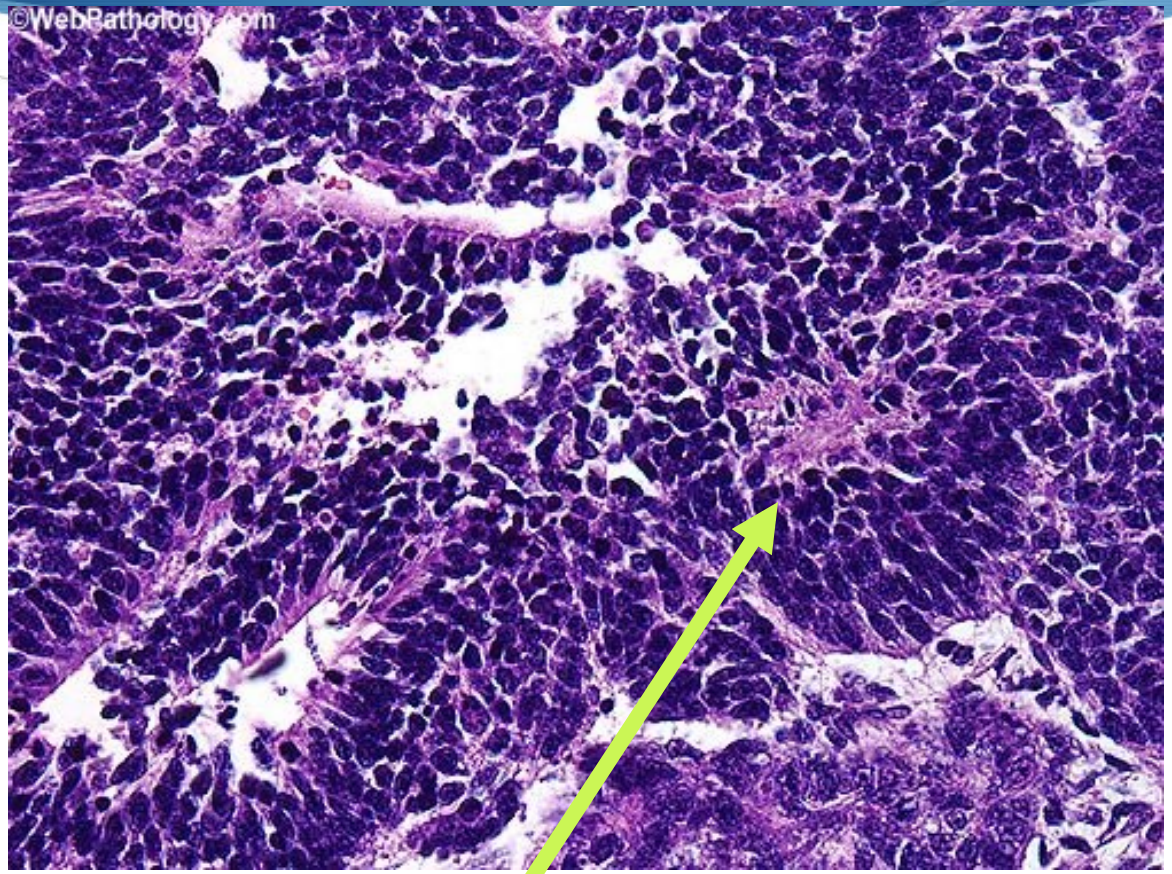
- Immature
- Mature
- Specialized
  - Struma ovarii
  - Carcinoid

Immature Teratoma

- Presentation
  - 20% of all GCT
  - 75% in first 2 decades of life
  - 12-15% bilateral
  - 60-70% are Stage I
- *Rarely* produce tumor markers: αFP and CA-125
- Grade is determined by % immature neural tissue
- Stage IA grade 1 → no adjuvant therapy
- Survival
  - Overall =63%
  - Stage I =75%

Immature Teratoma

Immature Teratoma



Primitive neural elements

Immature Teratoma

Grade	Scully	Norris
0	Well differentiated	All mature; rare mitoses
1	Well differentiated; rare embryonal tissue	Some immature and neuroepithelium
2	Moderate embryonal; atypia and mitoses	Immature neuroepithelium ≤ 3 lpf
3	Large embryonal; atypia and mitoses	Immature neuroepithelium in ≥ 4 lpf

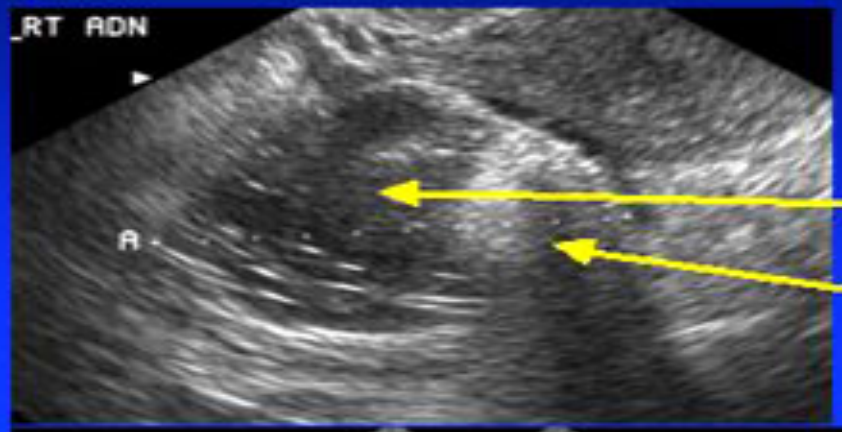
Significance of Grading

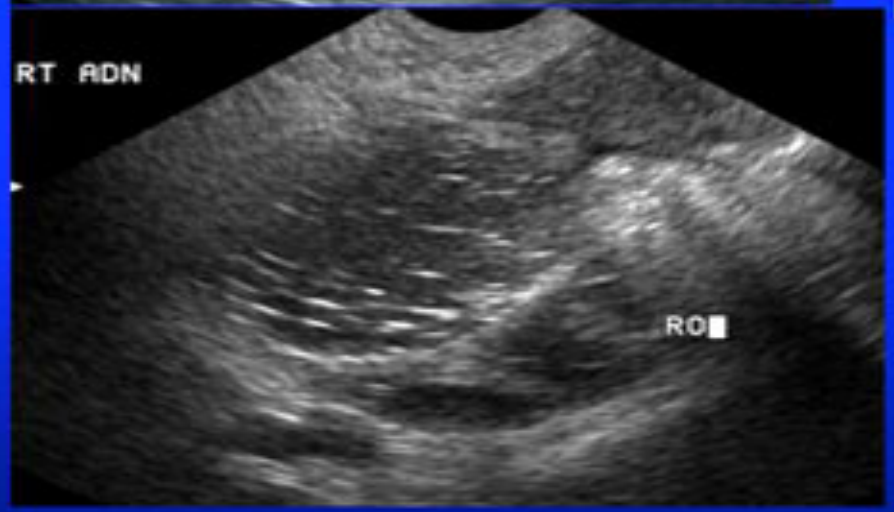
Grade	Number	Tumor Deaths
1	22	4 (18%)
2	24	9 (37%)
3	10	7 (70%)

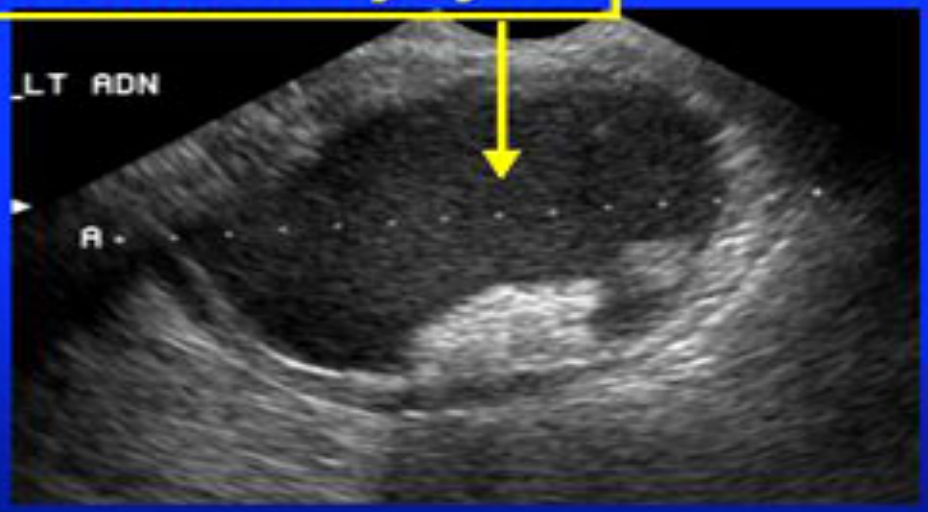
Mature Teratoma

- 5-25% of all ovarian tumors
  - 10-20% bilateral
- Most common ovarian tumor of young women
- Sonography
  - Complex, cystic and solid
  - Fat/fluid or hair/fluid level, calcifications
  - High MI score
- 1-2% with malignant degeneration
  - Rokitansky's protuberance
  - Squamous cell cancers possible

Bilateral ovarian dermoids with typical features

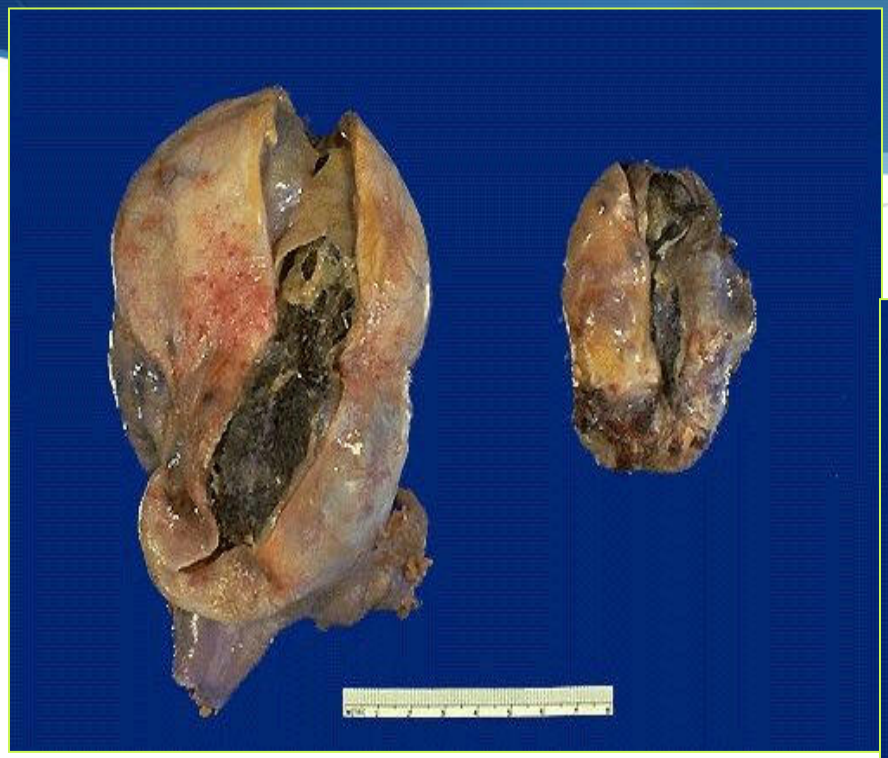


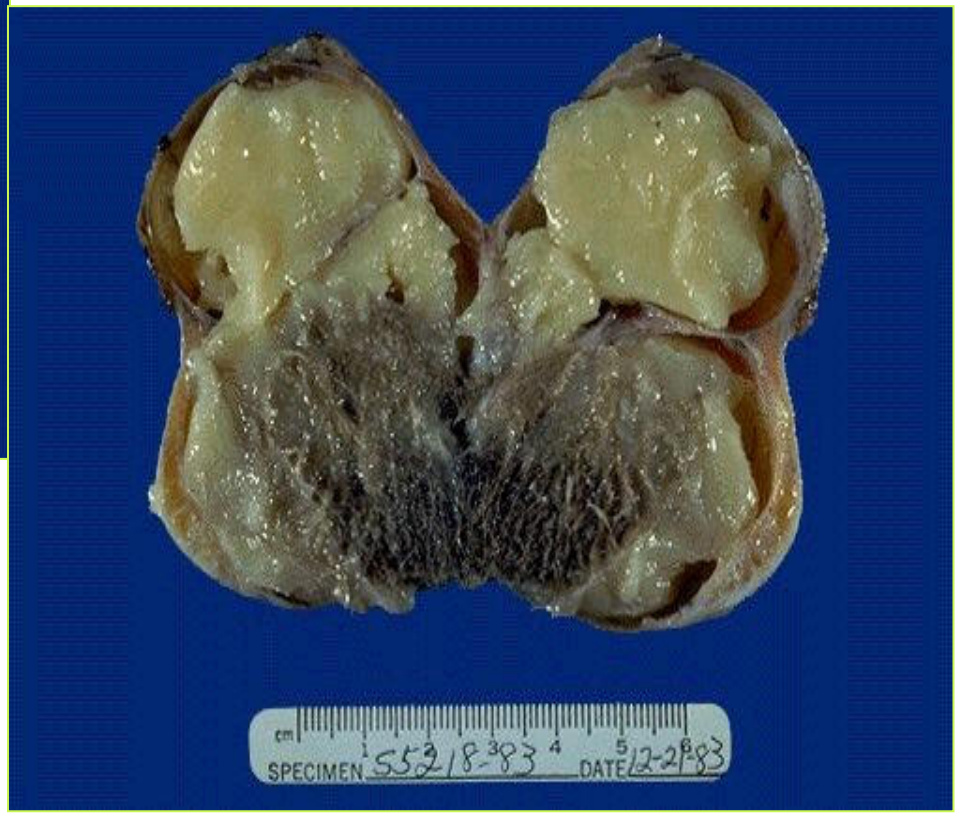




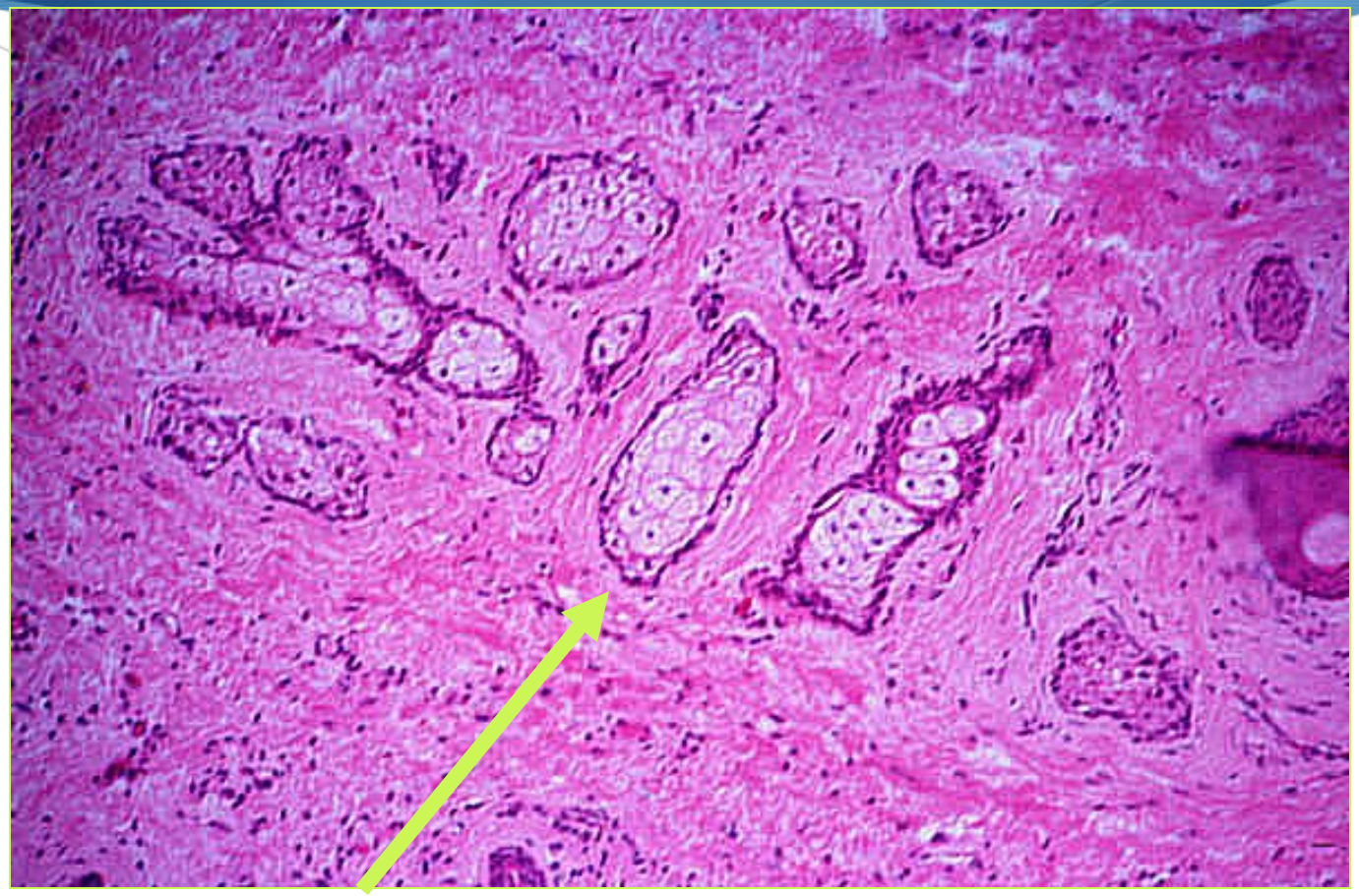
- Cystic with linear strands
- Solid echogenic mass
- Predominantly cystic

Mature Teratoma



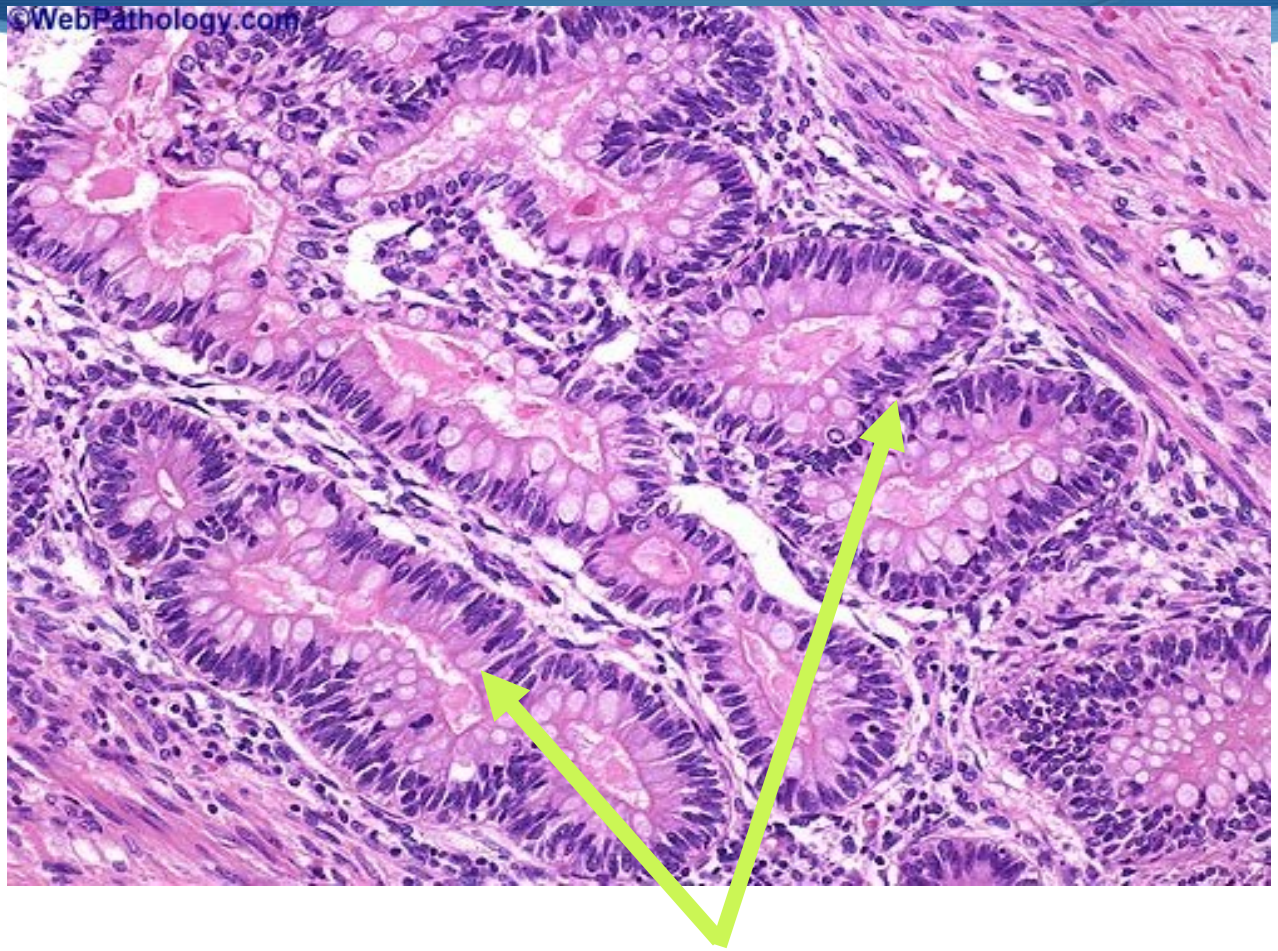


Mature Teratoma



Sebaceous glands

Mature Teratoma



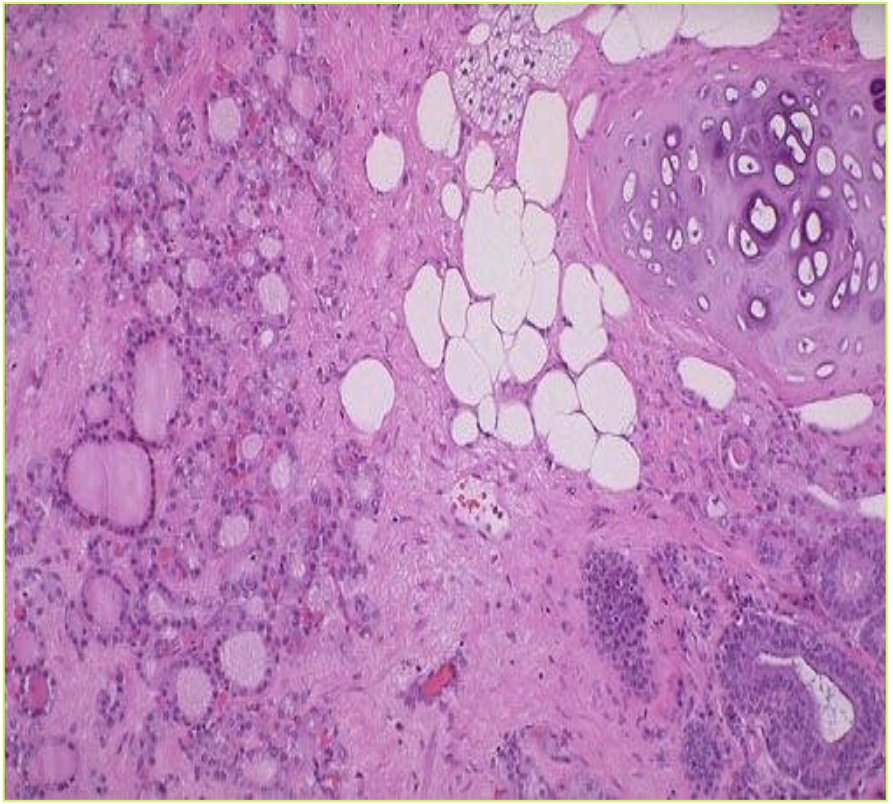
Intestinal gland formation

Specialized Teratomas

- Struma ovarii
  - 2-3% of all teratomas
  - 25-35% have symptoms of hyperthyroidism
  - Usually benign, but may undergo malignant transformation
- Carcinoid tumors
  - Associated with GI or respiratory epithelium
  - Primary ovarian tumors are rare (N=50)
  - Often older postmenopausal women
  - 1/3 have carcinoid syndrome from serotonin
  - Symptoms resolve with excision
  - 5-hydroxyindoleacetic acid in urine

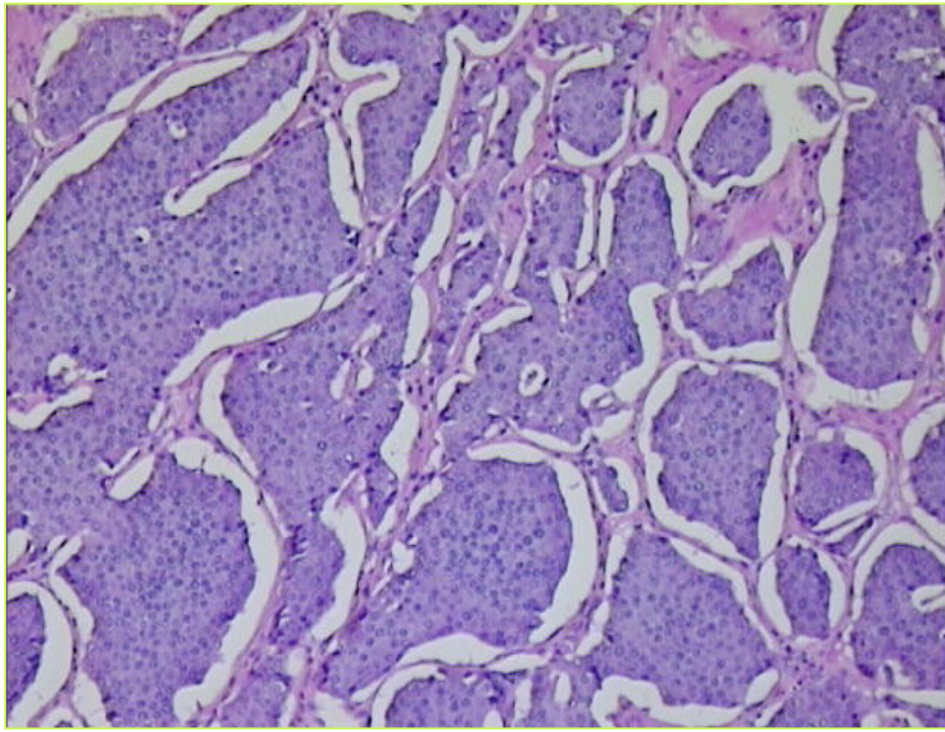
Struma Ovarii

- Follicles contain vividly eosinophilic, acellular colloid
- Variation in follicular size is typical
- Can have rich vascularity



Ovarian Carcinoid

- Insular pattern
- Round uniform cells
- Fibroconnective tissue background
- 80% with neurosecretory granules

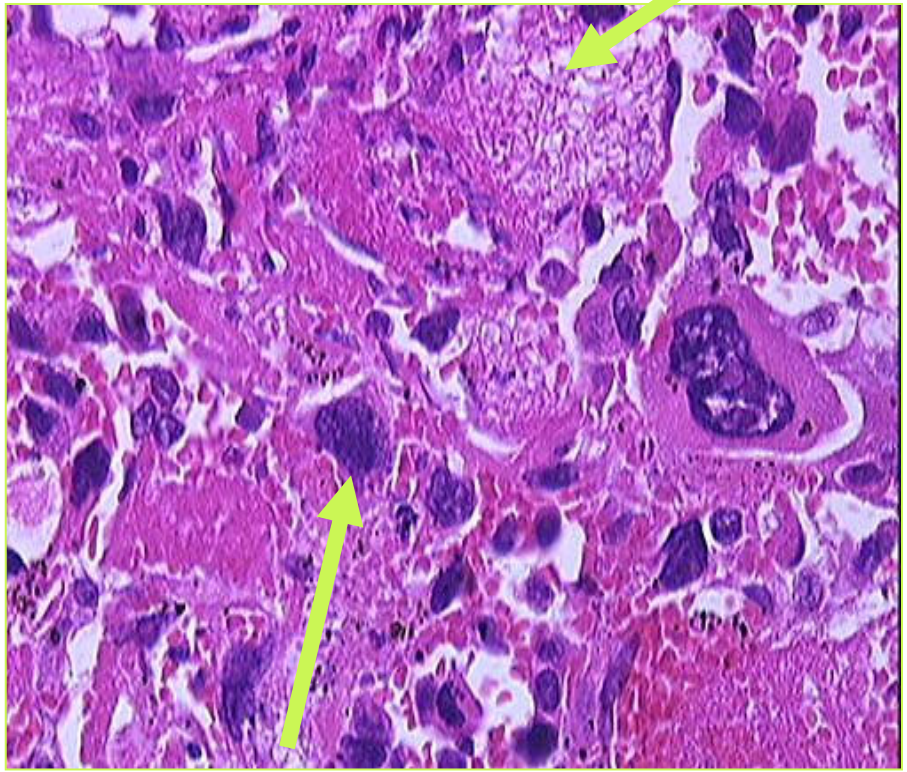


Choriocarcinoma

- Presentation
  - Uncommon, aggressive tumor
  - Often part of mixed GCT
  - Consider met from gestational chorioCA
  - Mean age 20 yo, children common
  - Half of premenarchal → precocious puberty
- Tumor marker
  - hCG

Choriocarcinoma

- Cytotrophoblast
  - Smaller cells
  - Smaller nuclei
- Syncitiotrophoblast
  - Larger cells
  - Eosinophilic cytoplasm
  - Bizarre nuclei
- Hemorrhage

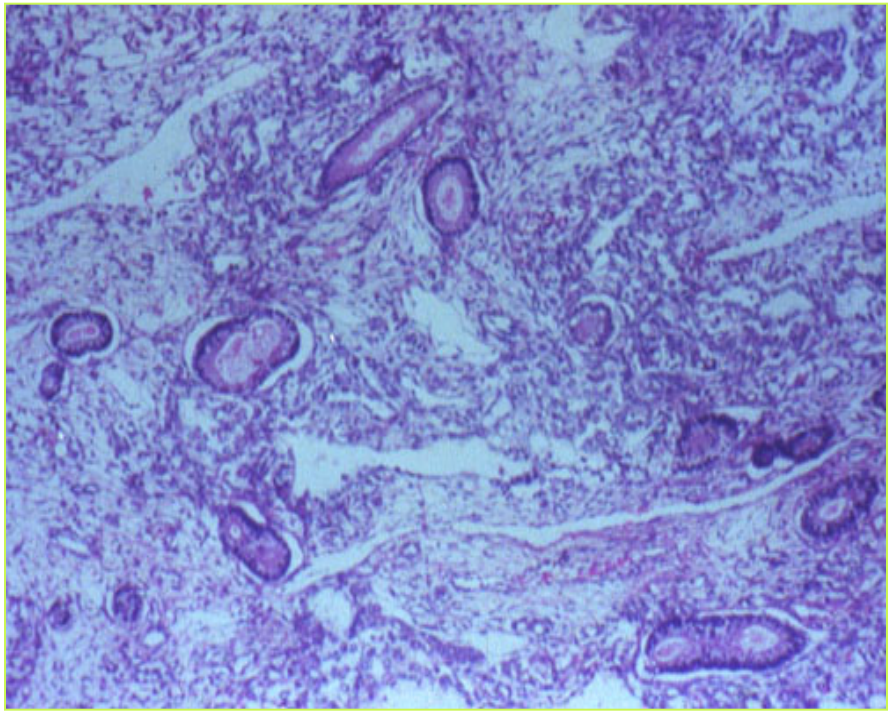


Embryonal Carcinoma

- Presentation
  - Mean age < 30 yo
  - Only 4% of GCT and often part of mixed tumor
  - 60% Stage IA
  - Poorly differentiated germ cell tumor
  - Aggressive, intra-abdominal spread and mets common
- Tumor markers: hCG, αFP
- Survival
  - Overall =40%
  - Stage I =75%

Embryonal Carcinoma

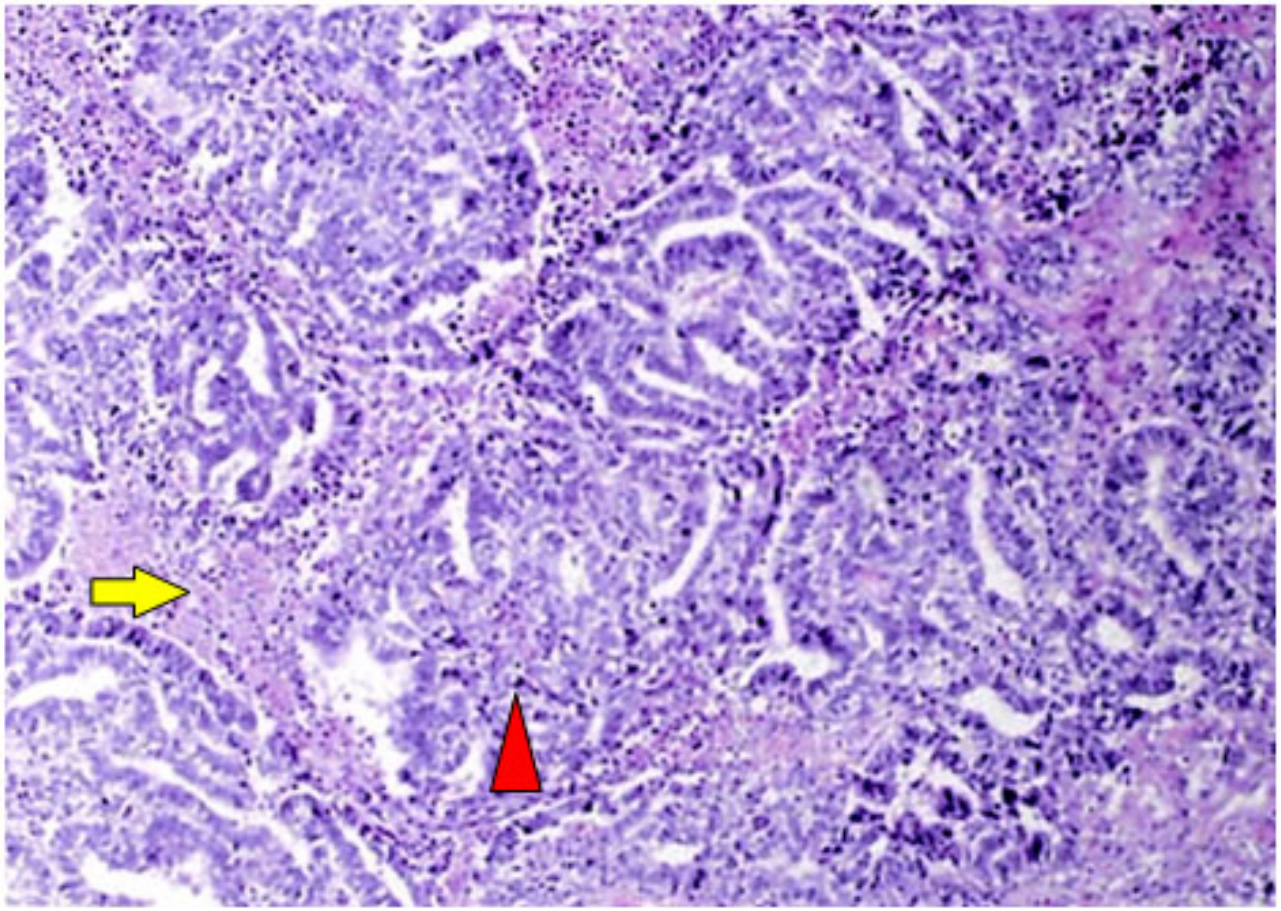
- Large, primitive cells
- Papillary or gland-like formation, occasional
- Sheets and ribbons



Polyembryona

- Best classified as a mixed tumor
  - Never found in pure form
  - Fewer than 50 cases
  - All under age 40
- Resembles embryonal carcinoma
  - Embryo days 13-15
- Treated like other mixed GCT
- Tumor markers: hCG, αFP

Mixed GCT
Embryonal and Choriocarcinoma

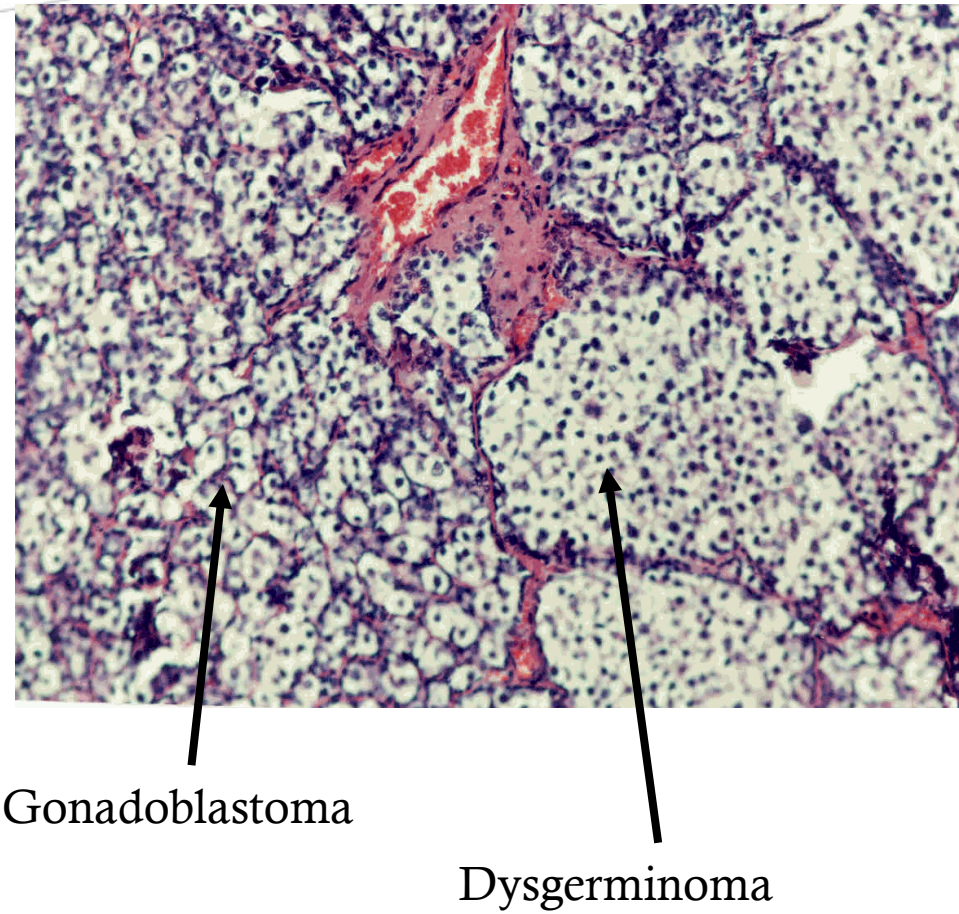


Gonadoblastoma

- Combined Germ Cell / Sex Cord Stromal Tumor
- Presentation
  - Age 1-38
  - Small tumors
  - Phenotypic ♀ with virilization
    - 90% have Y chromosome
    - 22% from streak gonads
  - Bilaterality 30-50%
- Check chromosomes for dysgenic gonads
  - BSO if Y present
  - If testicular feminization syndrome, await puberty before BSO

Gonadoblastoma

- Large germ cells, clear cytoplasm
- Nests of primordial germ cells surrounded by specialized stromal cells
- Associated sex cord stromal cells



Tumor Markers
Germ Cell Tumors

Histology	AFP	hCG	LDH	PLAP	CA-125
Dysgerminoma	-	+	+	+	+
Endodermal sinus tumor	+	-	+	-	+
Immature teratoma	+	-	-	-	+
Embryonal CA	+	+	-	+	-
ChorioCA	-	+	-	+	-

Germ Cell Tumors Treatment

- Surgery
  - Importance of staging in early disease
  - Fertility-sparing surgery often required
  - Can preserve uterus for future IVF, even if BSO
  - Debulking improves outcome

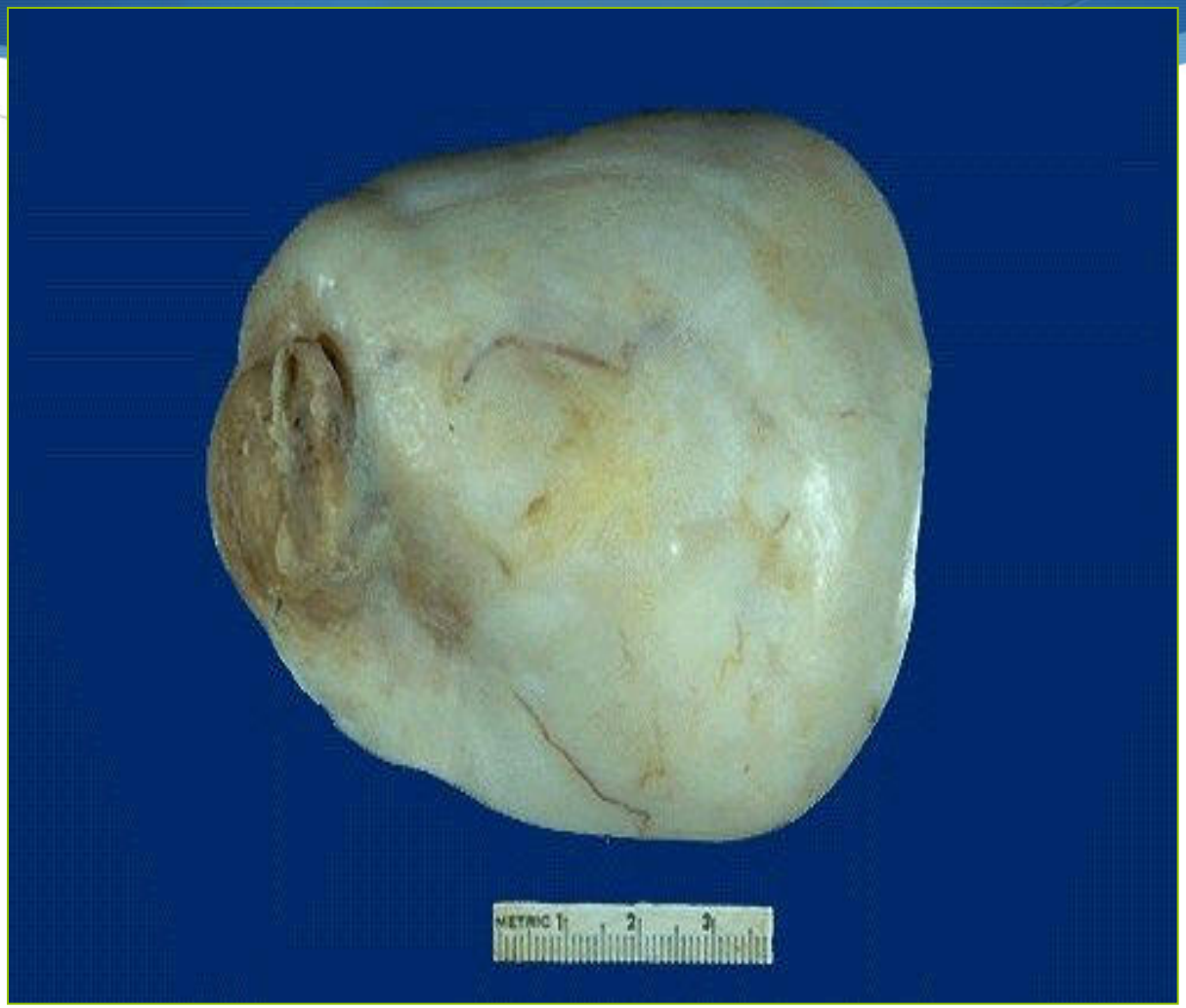
Chemotherapy Germ Cell Tumors

- BEP
  - Bleomycin 20 U/m^2 weekly x 9
  - Etoposide 100 mg/m^2 days 1-5 q 3 weeks x 3
  - Cisplatin 20 mg/m^2 days 1-5 q 3 weeks x 3
- VAC
  - Vincristine 105 mg/m^2 weekly x 12
  - Act D 0.5 mg days 1-5 q 4 weeks
  - Cytoxan 5-7 mg/kg days 1-5 q 4 weeks
- VBP
  - Vinblastine 12 mg/m^2 q 3 weeks x 4
  - Bleomycin 20 U/m^2 weeks x 7, 8 on week 10
  - Cisplatin 20 mg/m^2 days 1-5 q 3 weeks x 3

Sex-cord Stromal Tumors

- Fibroma
- Granulosa cell tumors
  - Inhibin, CA-125
- Sertoli-Leydig tumors
  - CA-125, αFP, sTest
- Steroid cell tumors
  - sTest (50-75% virilized)
- Gynandroblastoma
  - ♀ and ♂ components

Fibroma



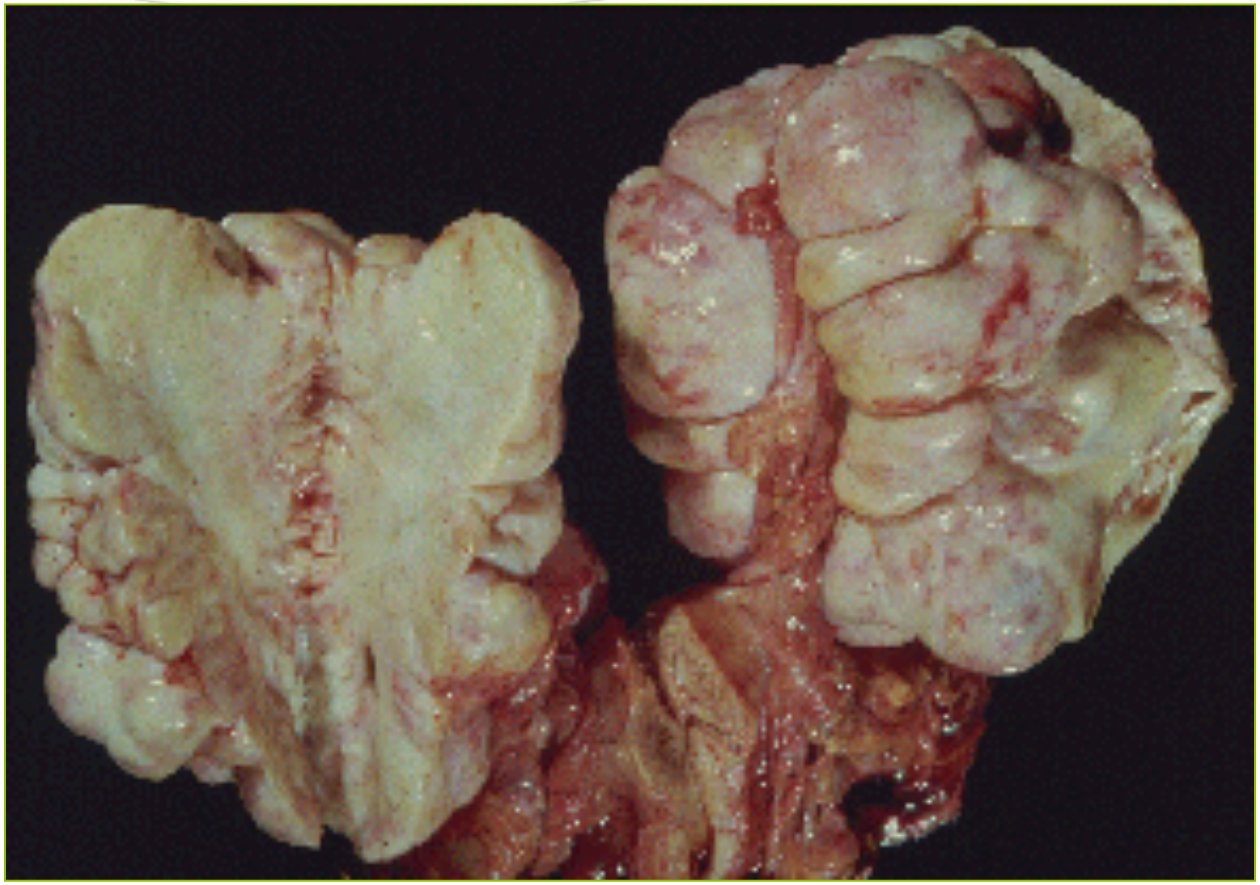
Granulosa Cell Tumor

- Presentation
  - Adult (95%) and juvenile types
  - Solid and/or cystic- variable
  - Estrogen, occasional androgen
  - 80% palpable on examination
  - Hemoperitoneum in 15%
  - 80-90% Stage I
  - Low grade, late relapse
- Estrogen excess and the endometrium
  - 25% proliferative
  - 55% hyperplastic
  - 13% adenocarcinoma

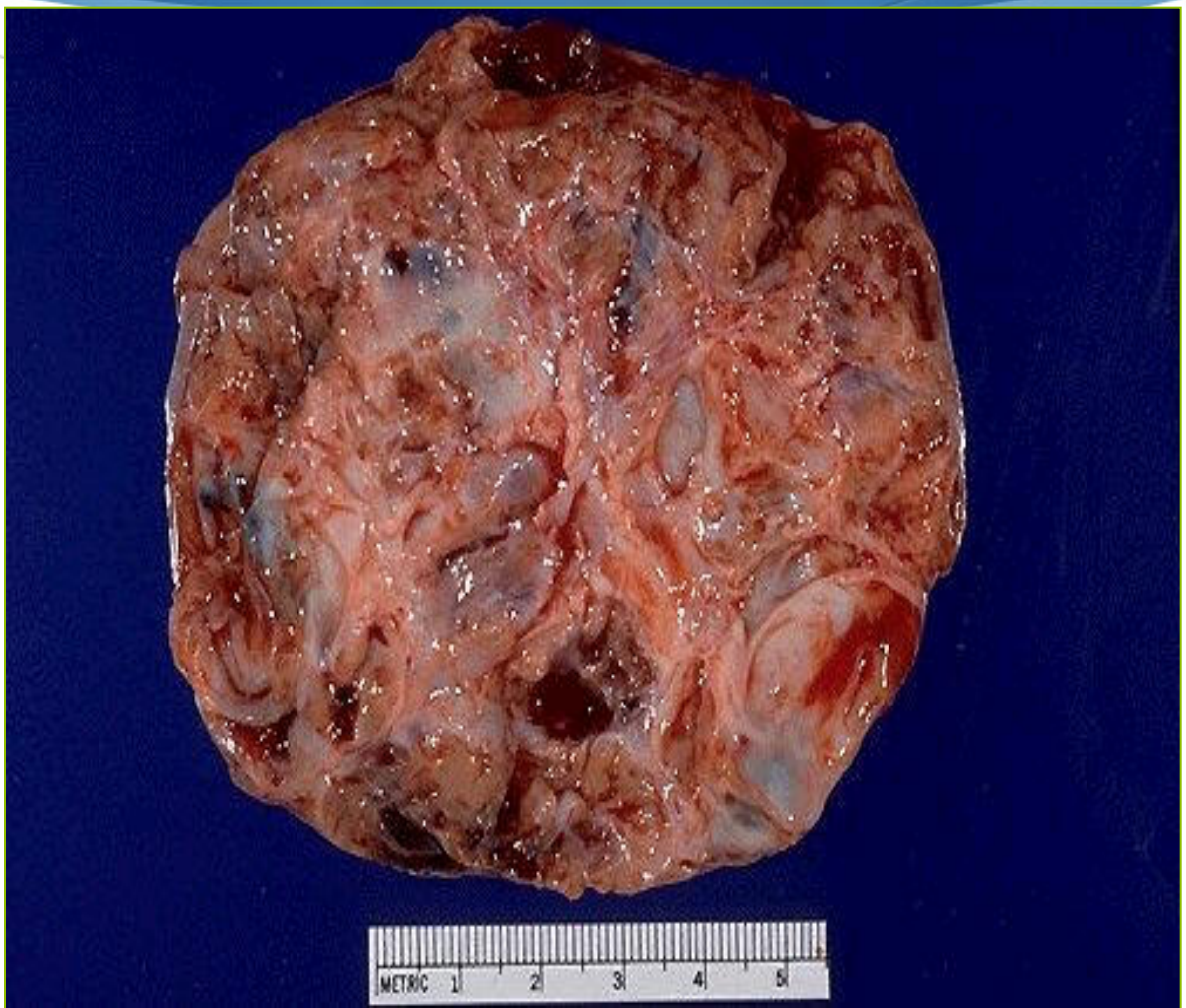
Granulosa Cell Tumor Treatment

- Juvenile
  - High cure rate
- Adult
  - Resection
  - Chemotherapy
    - BEP
    - Carboplatin and Taxol
    - GnRH analogs

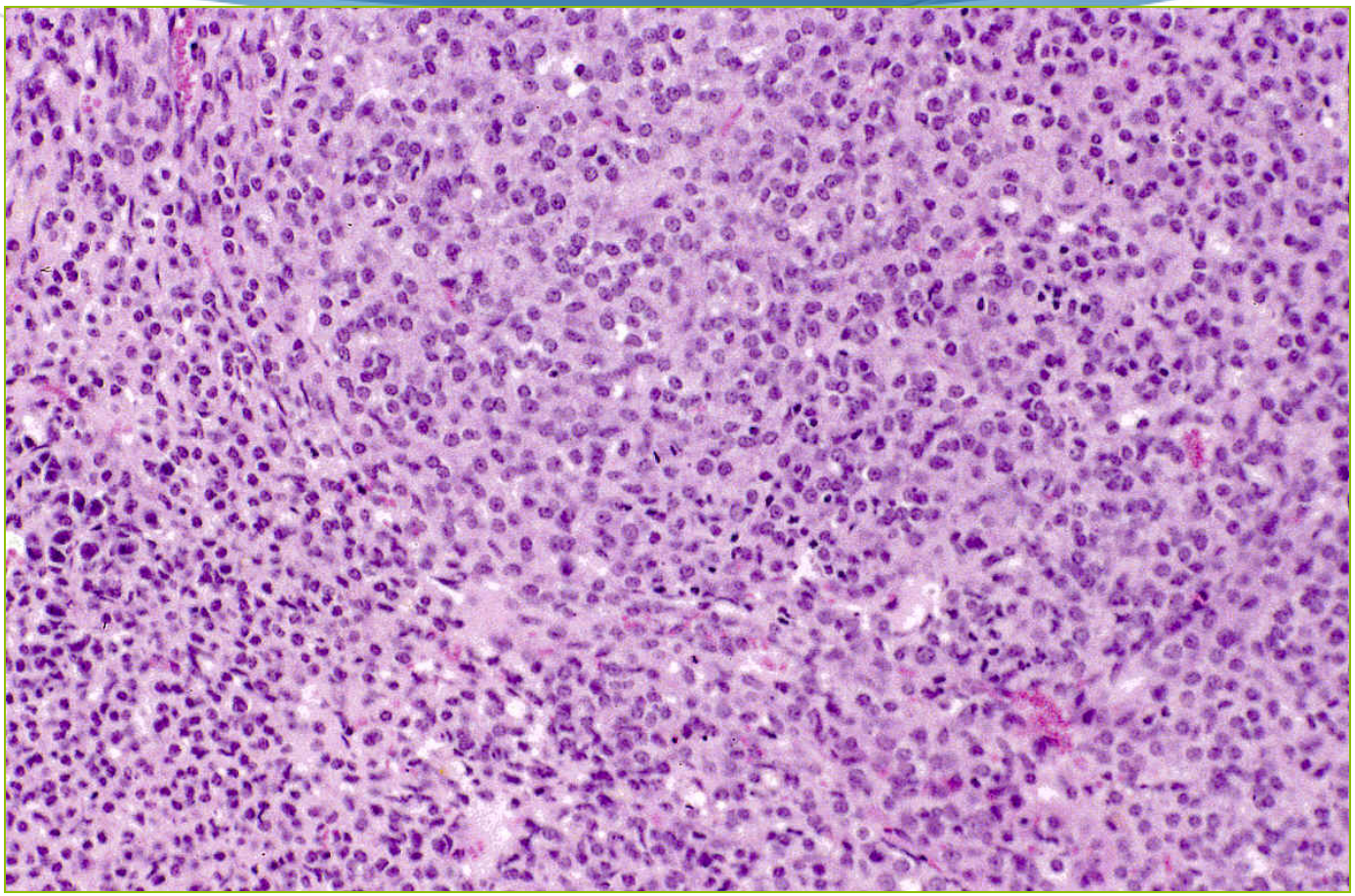
Granulosa Cell Tumor



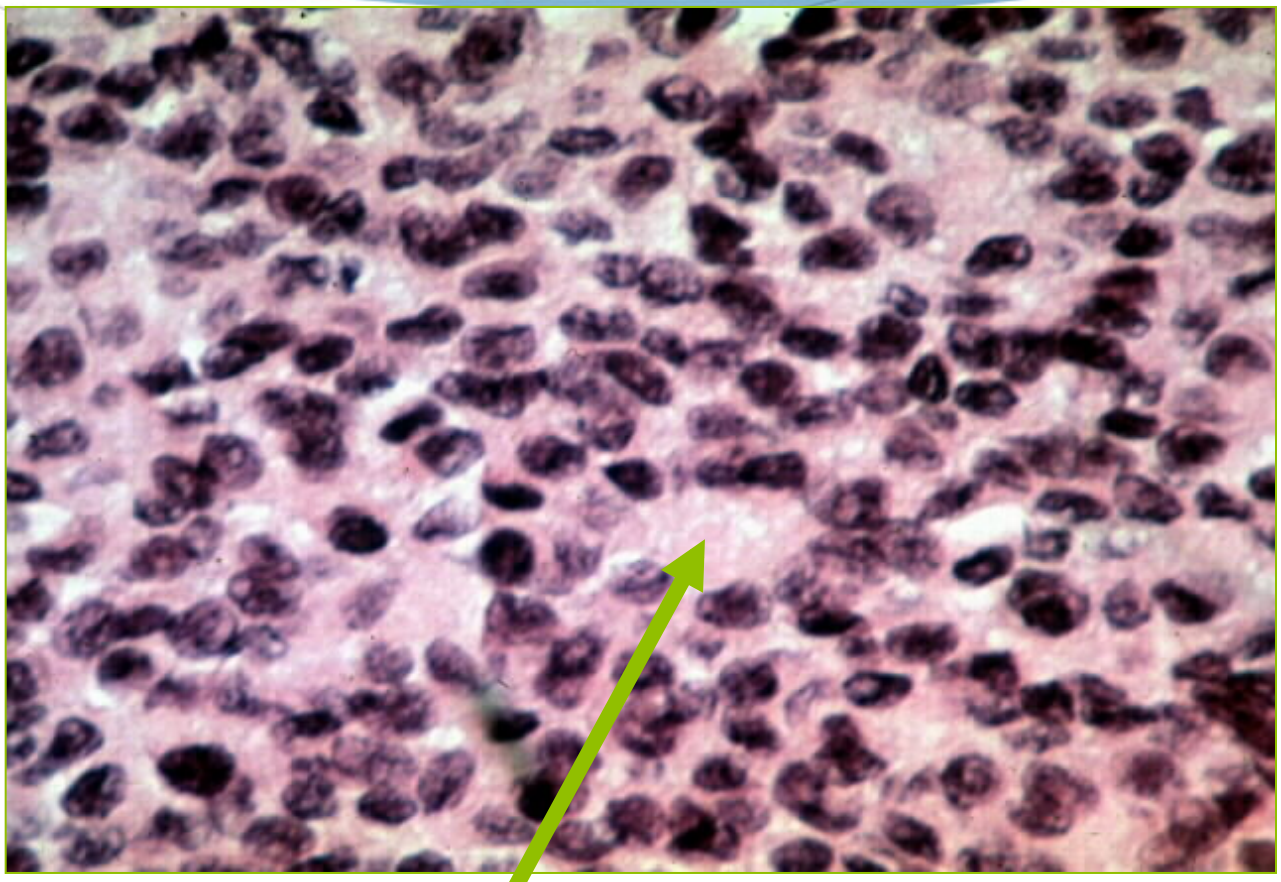
Granulosa Cell Tumor



Granulosa Cell Tumor



Granulosa Cell Tumor



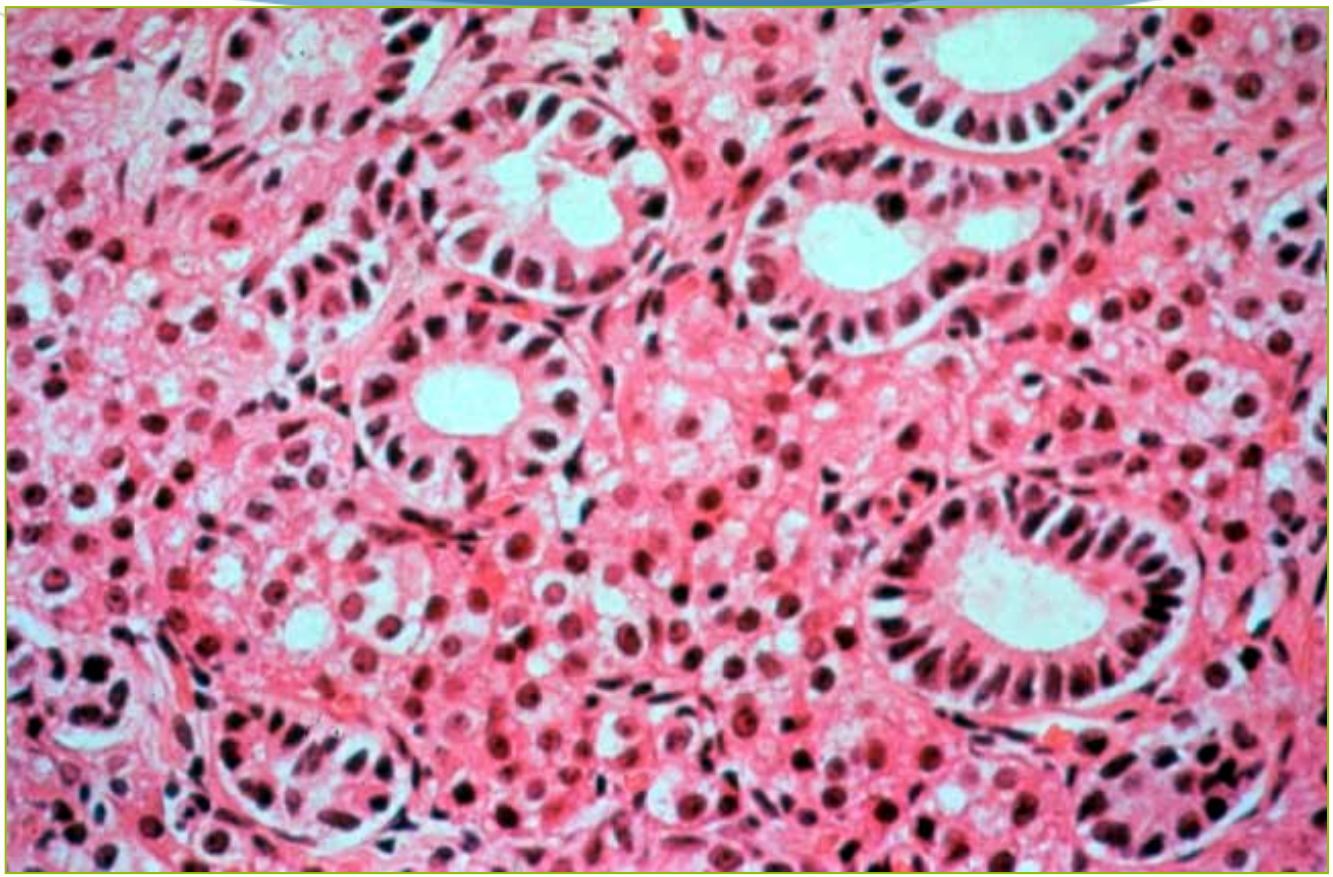
Call-Exner bodies

Sertoli-Leydig Tumors

- Benign
  - Sertoli cell tumors→ no hormones
  - Leydig tumors→ testosterone
- Potentially Malignant
  - Sertoli-Leydig tumors
  - Arrhenoblastoma, androblastoma
  - Grade 3
    - 44% five-year survival

Grade	% Cancer
1	0
2	10
3	60

Sertoli-Leydig Tumor



Well-differentiated tubules

Treatment Summary

Germ Cell and Stromal Tumors of the Ovary

Dysgerminoma	USO staging if possible	BEP x 3 cycles if stage II-IV
Endodermal sinus tumor	Debulk but preserve fertility	BEP x 3-4 cycles
Embryonal carcinoma	As above	BEP x 3-4 cycles
Malignant teratoma	As above	BEP or VAC x 3-4 cycles
Granulosa cell tumor	USO if young o/w TAH/BSO	BEP x 3-4 cycles GnRH agonists for advanced ds.
Sertoli-leydig cell	As above	BEP or VAC x 3-4 cycles

Summary

1. Common in young women
2. Tumor markers
3. Treatment
   - Fertility-sparing surgery
   - Chemosensitive→ BEP for 3-6 cycles
   - Radiosensitive
4. No adjuvant chemo for:
   - Stage I pure dysgerminoma
   - Stage IA grade 1 immature teratoma