

The 21st Korea-Taiwan-Japan  
Joint Meeting for Gynecological Pathology  
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# *Special lecture* **Peritoneal lesions**

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# Contents

1. Mesothelial lesions
2. Müllerian lesions
3. Mesenchymal tumors
4. Miscellaneous primary tumors
5. Secondary tumors
6. Other tumor-like lesions

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# Mesothelial lesions

## Neoplasia

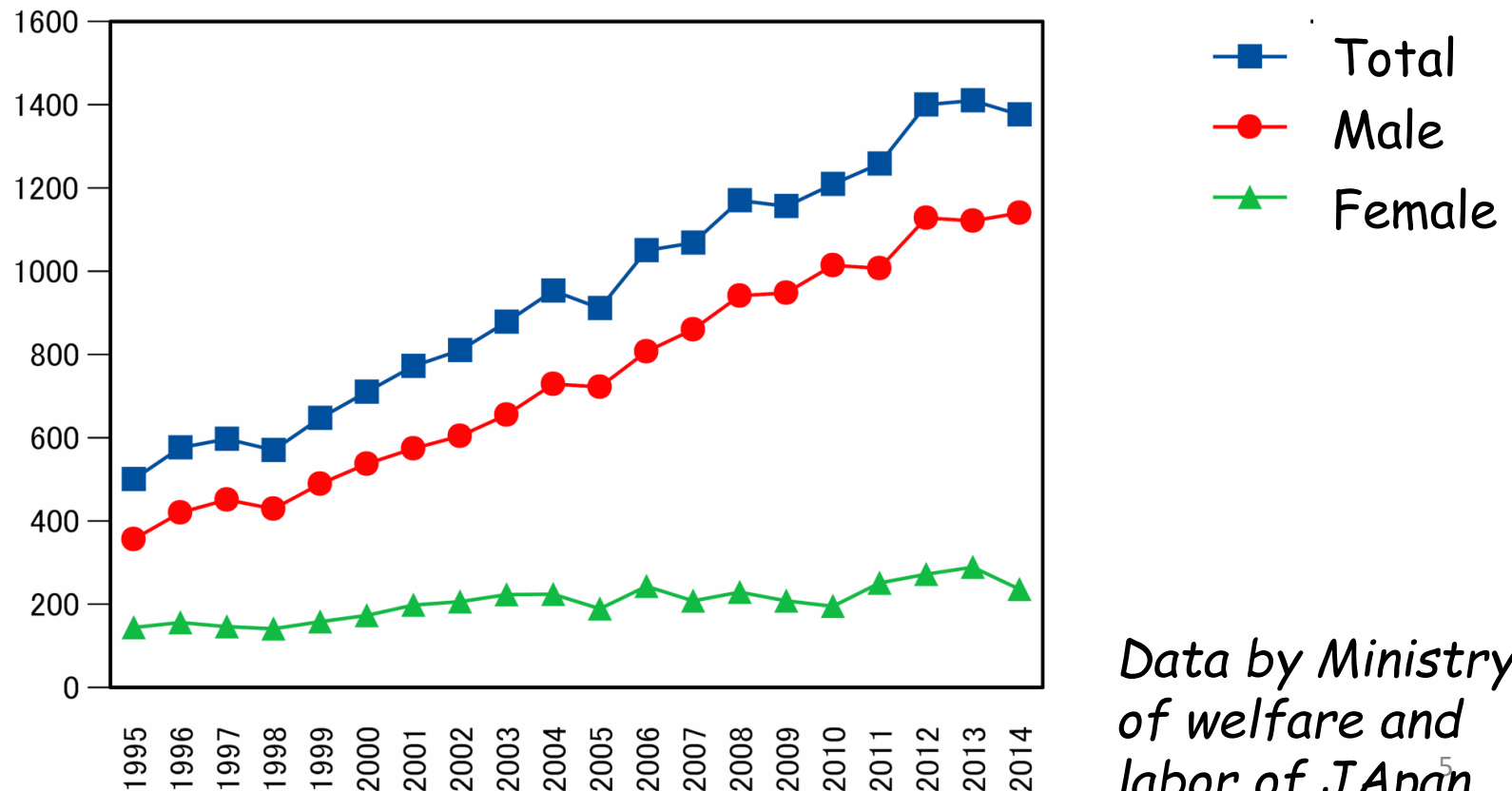
- Malignant mesothelioma
- Well-differentiated papillary mesothelioma
- Adenomatoid tumor

## Non-neoplastic lesions

- Peritoneal inclusion cyst
- Mesothelial hyperplasia

# Malignant mesothelioma

- Rare 7/1000,000 population
- M:F=7:3
- Increase of death of disease x3/20yrs



# Peritoneal mesothelioma

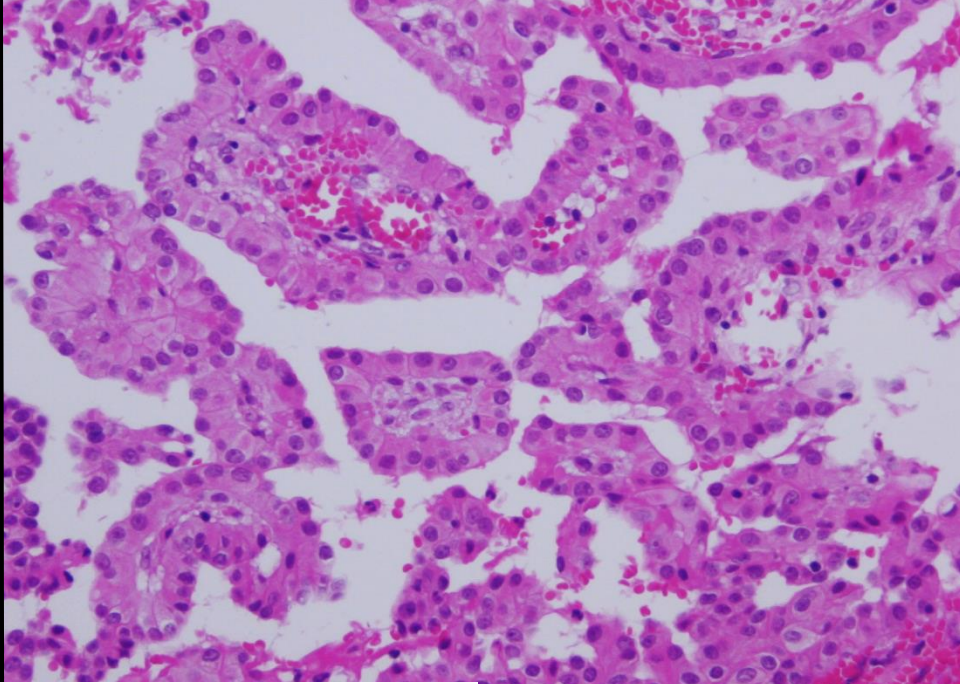
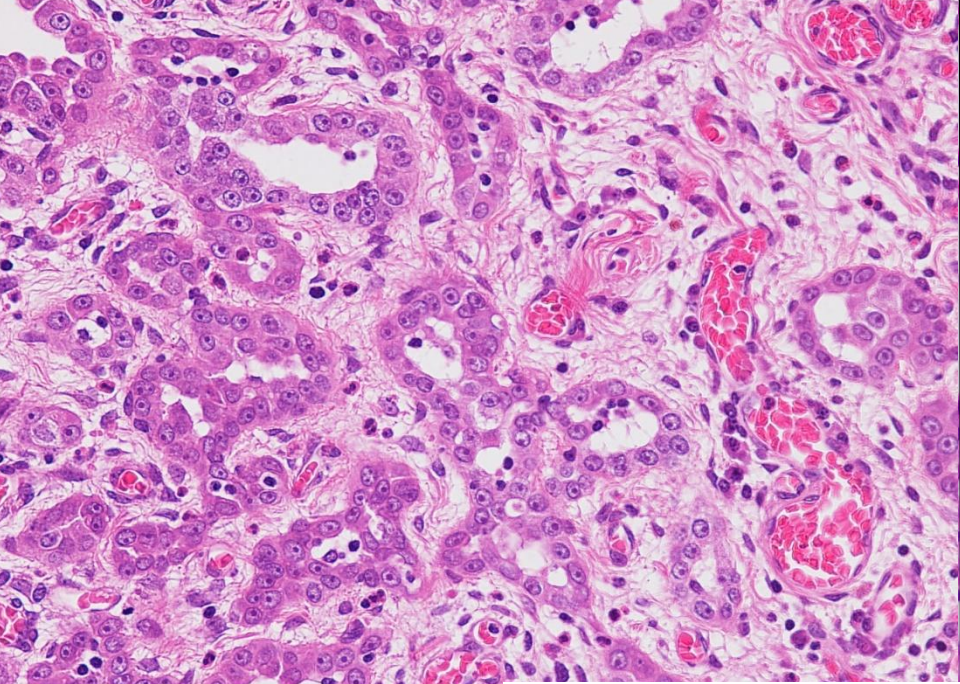
- 10% of all malign mesothelioma
- M:F=7:3 (Japanese mesothelioma registry)  
M:F=1.5:1 (*Hillerdal G. Br J Dis Chest. 1983;77:321-343*)
- Heavy asbestos exposure is a higher risk for development of peritoneal mesothelioma in men  
Asbestos exposure in brief period is a higher risk for pleural mesothelioma  
*Antman KH. Chest. 1993;103:373S-376S*
- Half of the pts with no history of asbestos exposure

# Female peritoneal mesothelioma

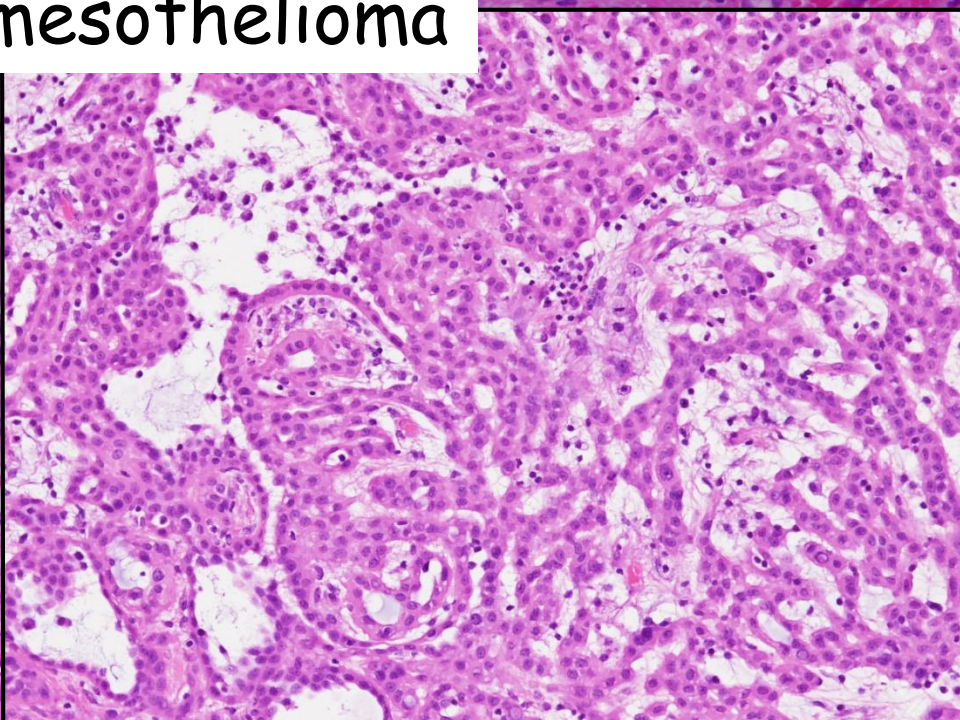
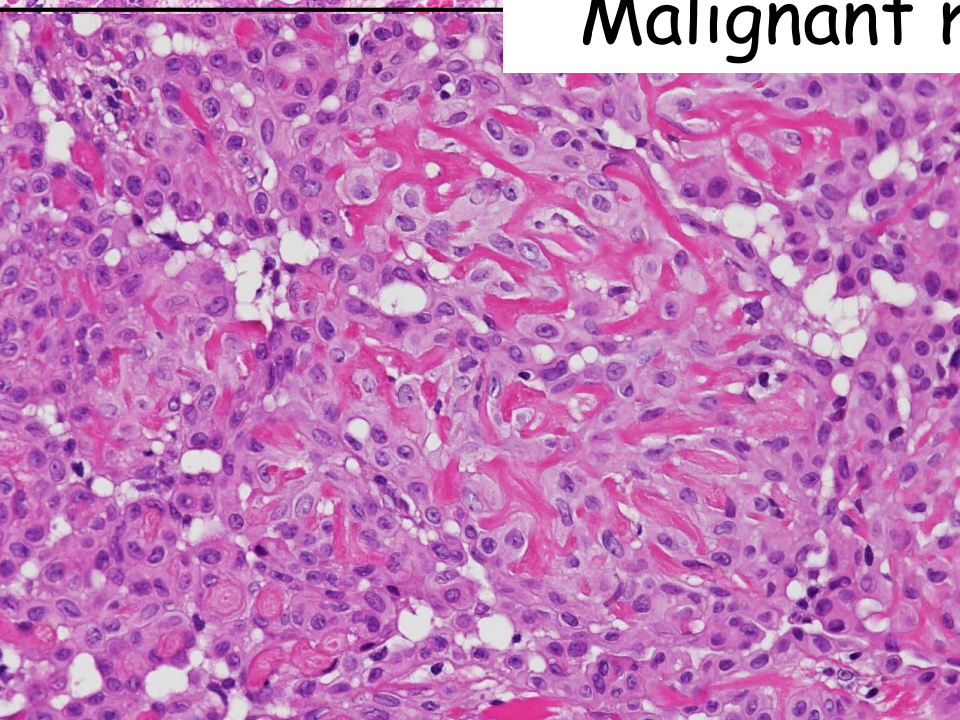
- Age: 17-92 (mean 47.4) yrs (n=75 cases)
- **No** association with asbestos exposure
- Abdominal discomfort, distention, weight loss
- Most cases are **epithelioid type** (tubular > papillary > solid, mixed)
- Tumor cells: polygonal, cuboidal/low columnar, eosinophilic cytoplasm, **mild to moderate** nuclear atypia, mitoses may be infrequent
- Minor foci may **resemble WDPM**

*Baker PM, et al. Am J Clin Pathol. 2005;123:724-737.*





Malignant mesothelioma





# Female peritoneal mesothelioma

## Immunohistochemistry

|          | Recommended | Others |
|----------|-------------|--------|
| Positive | calretinin  | CK7    |
|          | WT-1        | Pan CK |
|          | D2-40       |        |
|          | CK5/6       |        |
| Negative | MOC-31      | CEA    |
|          | Ber-EP4     | TTF-1  |
|          | PAX8*       |        |
|          | ER*, PgR*   |        |
|          | Caludin 4   |        |

Loss of BAP 1 in only 50% of peritoneal mesothelioma 9

# Asbestos-Related Health Damage Relief System in Japan

- Act took effect on March 27, 2006
- Provides relief benefit (medical care expenses) to sufferers of the designated diseases and to the bereaved of those DOD
- Diseases covered by the benefits: The following diseases caused by asbestos

1) Mesothelioma

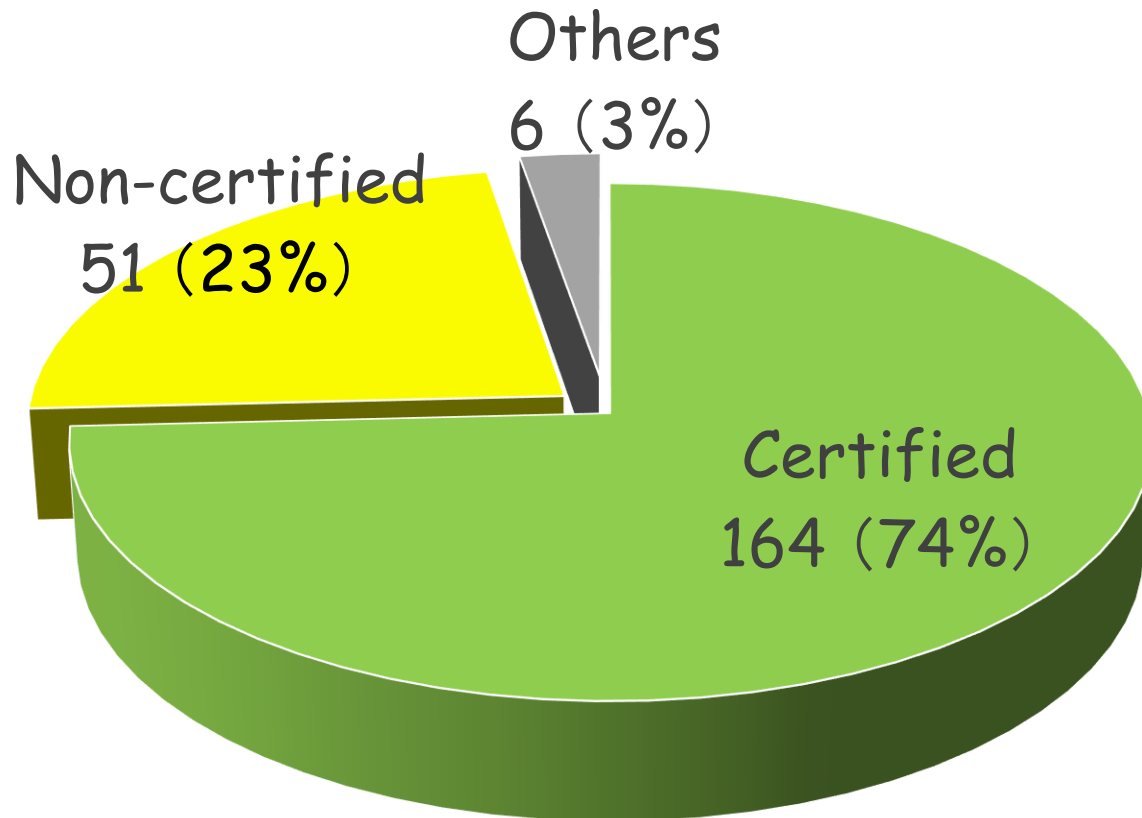
2) Malignant neoplasm of lung and bronchus

3) Asbestosis with heavy respiratory dysfunction

4) Diffuse pleural thickening with heavy respiratory dysfunction

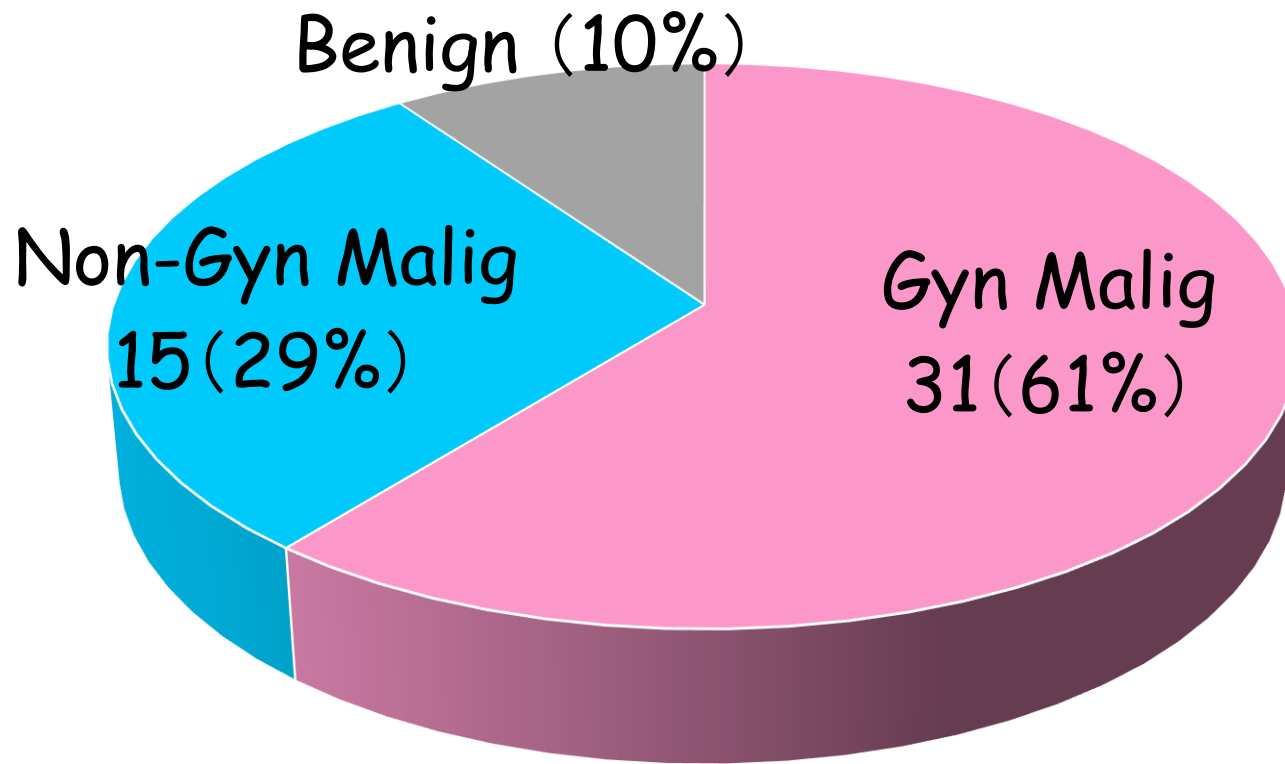
# Results of female pts applied with peritoneal mesothelioma

Submission of pathology slides: 221 Pts  
March 31, 2006 ~ March 31, 2017



# Panel diagnosis in non-certified pts (51)

March 31, 2006 ~ March 31, 2017



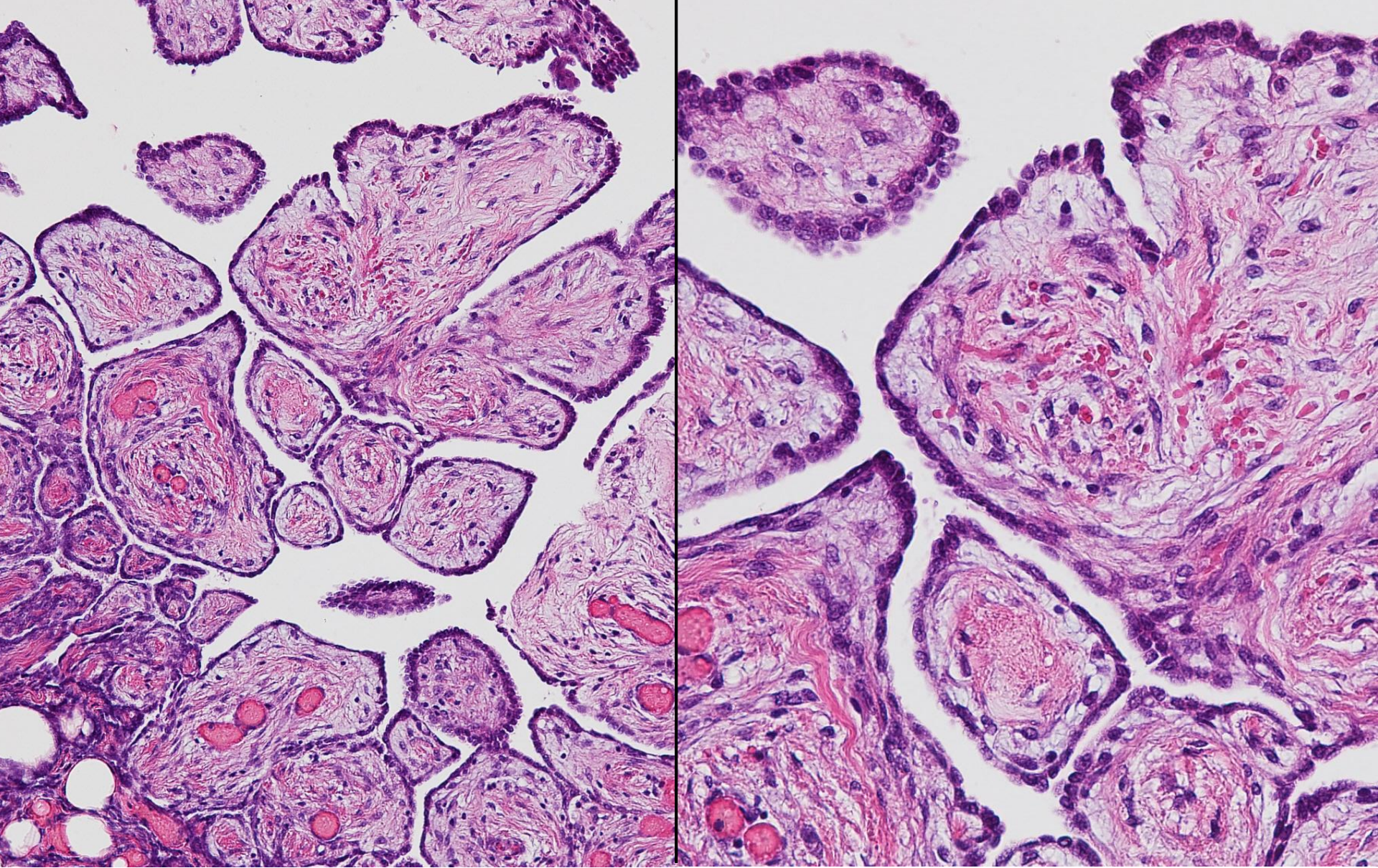
# Well-differentiated papillary mesothelioma

- Gross: Papillary, well circumscribed tumor, 0.1-2cm, 50% multiple
- Micro: papillary, wide fibrous stroma, bland nuclei, rare mitosis, inv<0.5cm
- dDx: malignant mesothelioma
- 23 -75 years (median, 47 y; mean, 48.6 y)
- No hx of asbestos exposure
- Incidental finding
- Favorable prognosis

*Daya D, et al. Cancer. 1990;65:292-296.*

*Malpica A, et al. Am J Surg Pathol. 2012;36:117-127.*





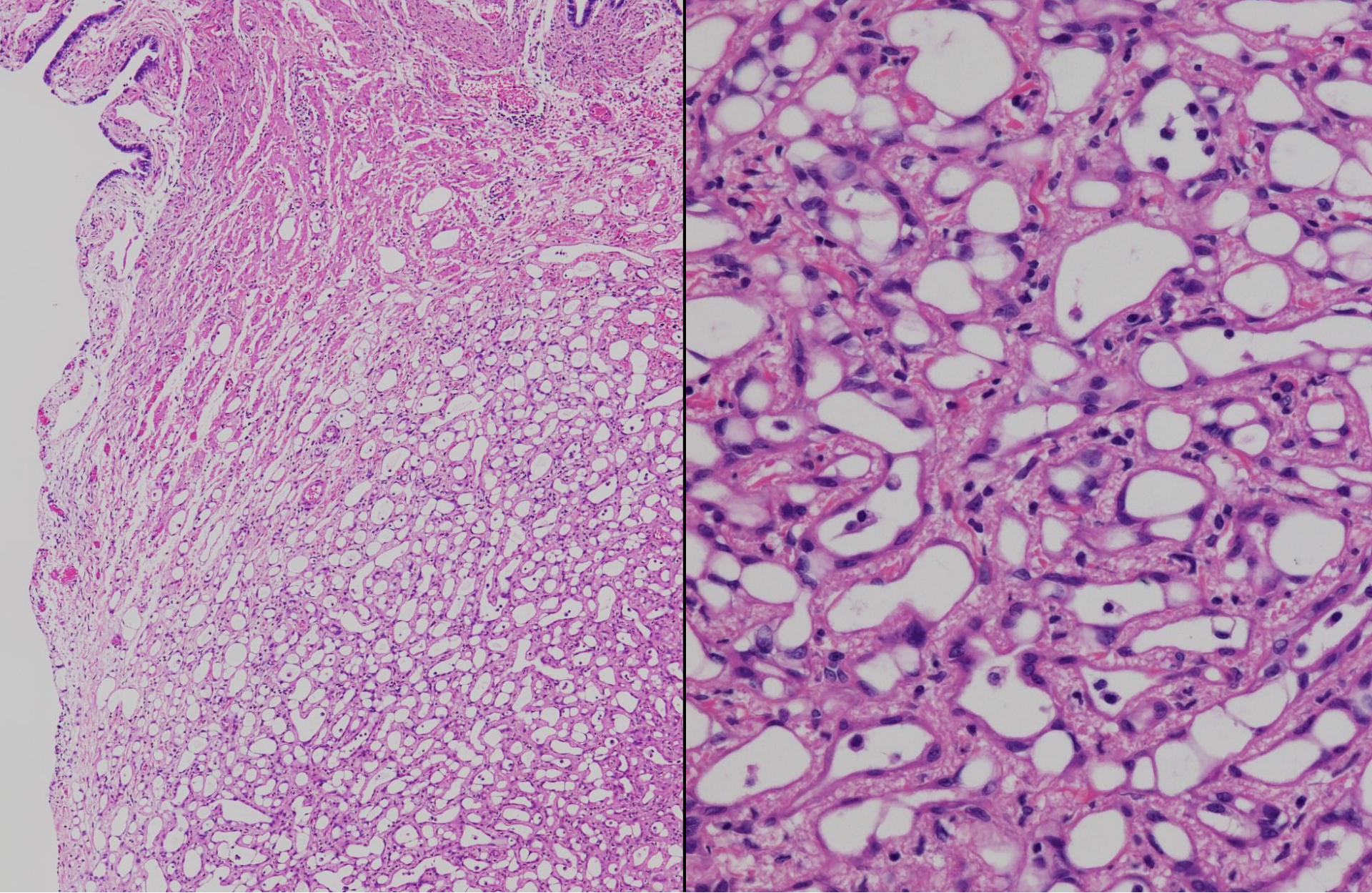
Well-differentiated papillary mesothelioma



# Adenomatoid tumor

- Adults
- Incidental finding
- Benign
- Gross: Small, firm nodules
- Micro: cells with cytoplasmic **vacuoles/eosinophilic** abundant cytoplasm, bland round to oval nuclei, rare mitosis; anastomosing gland-like spaces>solid nests
- Immunohx: cytokeratin+, vimentin+, WT1+, calretinin, CK5/6, thrombomodulin+
- **dDx: metastatic carcinoma**





Adenomatoid tumor



# Infarcted adenomatoid tumor

- Solitary solid mass 1.1-3.5cm
- **Necrosis** in the center of the tumor
- Proliferation of **fibroblasts, myofibroblasts**
- Tumor cells often arranged in a **solid nest** ( 4 males and one female-paratubal mass)

Skinnider BF, et al. Am J Surg Pathol 2004; 28: 77-83

# Peritoneal inclusion cyst

- Cyst-forming mesothelial proliferation
- Rare
- Women of reproductive age
- Unilocular>>>multilocular
- Multilocular cyst
  - up Ø20cm, ass w previous surgery, endometriosis, inflammatory process
- Most of them **reactive** rather than neoplastic

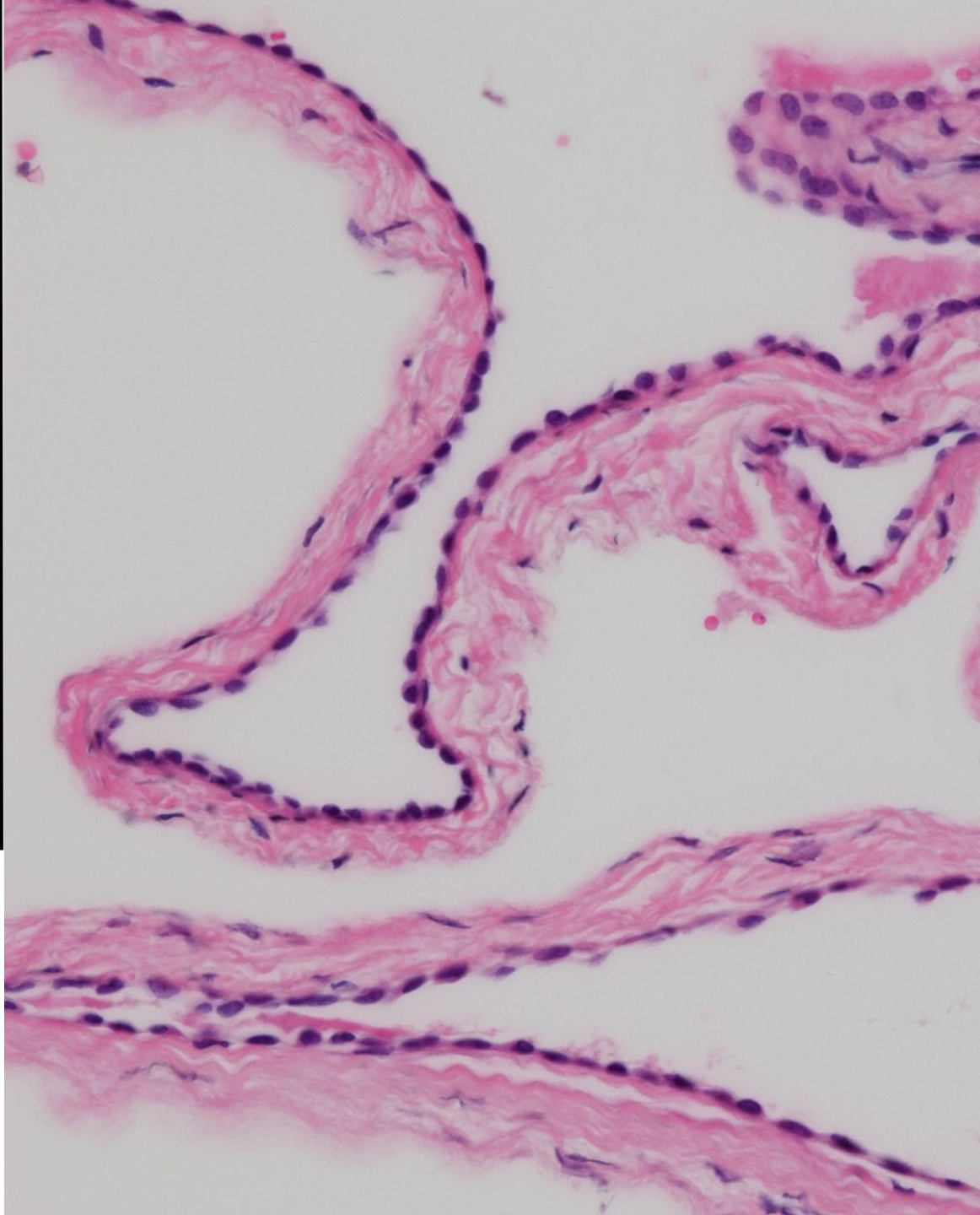


# Peritoneal inclusion cyst

- AKA
  - Multilocular peritoneal inclusion cyst
  - Mesothelial inclusion cyst
  - Benign cystic mesothelioma\*
  - Multicystic mesothelioma\*
- \* Not recommended (WHO2014)



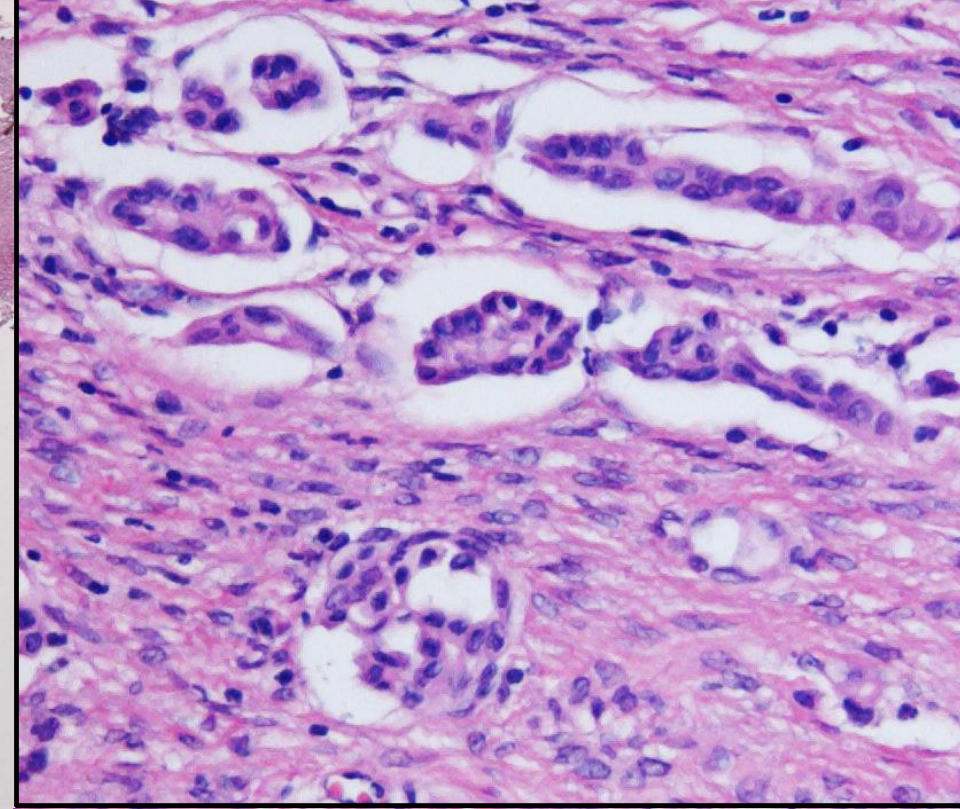
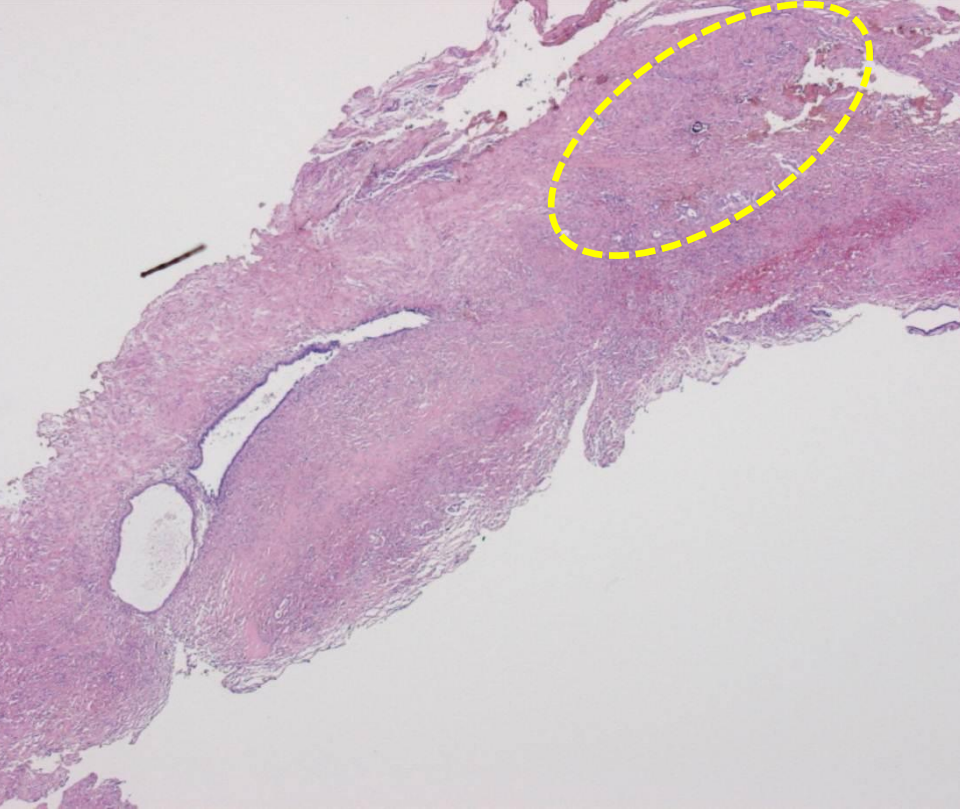
Peritoneal  
inclusion cyst



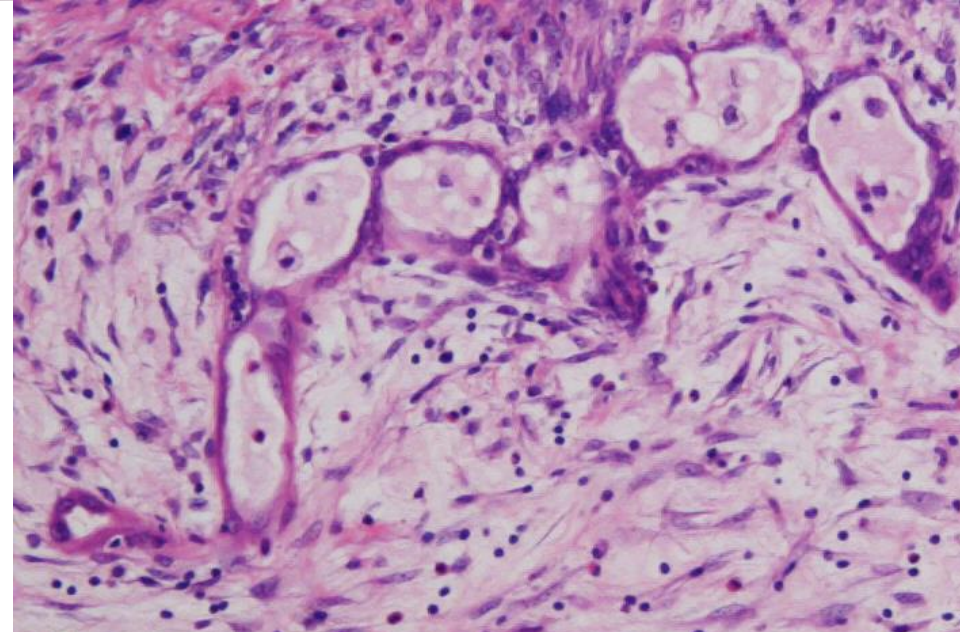
# Mesothelial hyperplasia

- Salpingitis, peritonitis, pelvic endometriosis, etc
- Grossly unidentifiable
- Stratification, papillary, enlarged mesothelial cells
- **Mesothelial entrapment** in the peritoneal stroma/ovarian stroma
- dDx : invasive carcinoma (adenocarcinoma), malignant mesothelioma





Entrapped hyperplastic  
mesothelial cells  
in the endometriotic  
cyst



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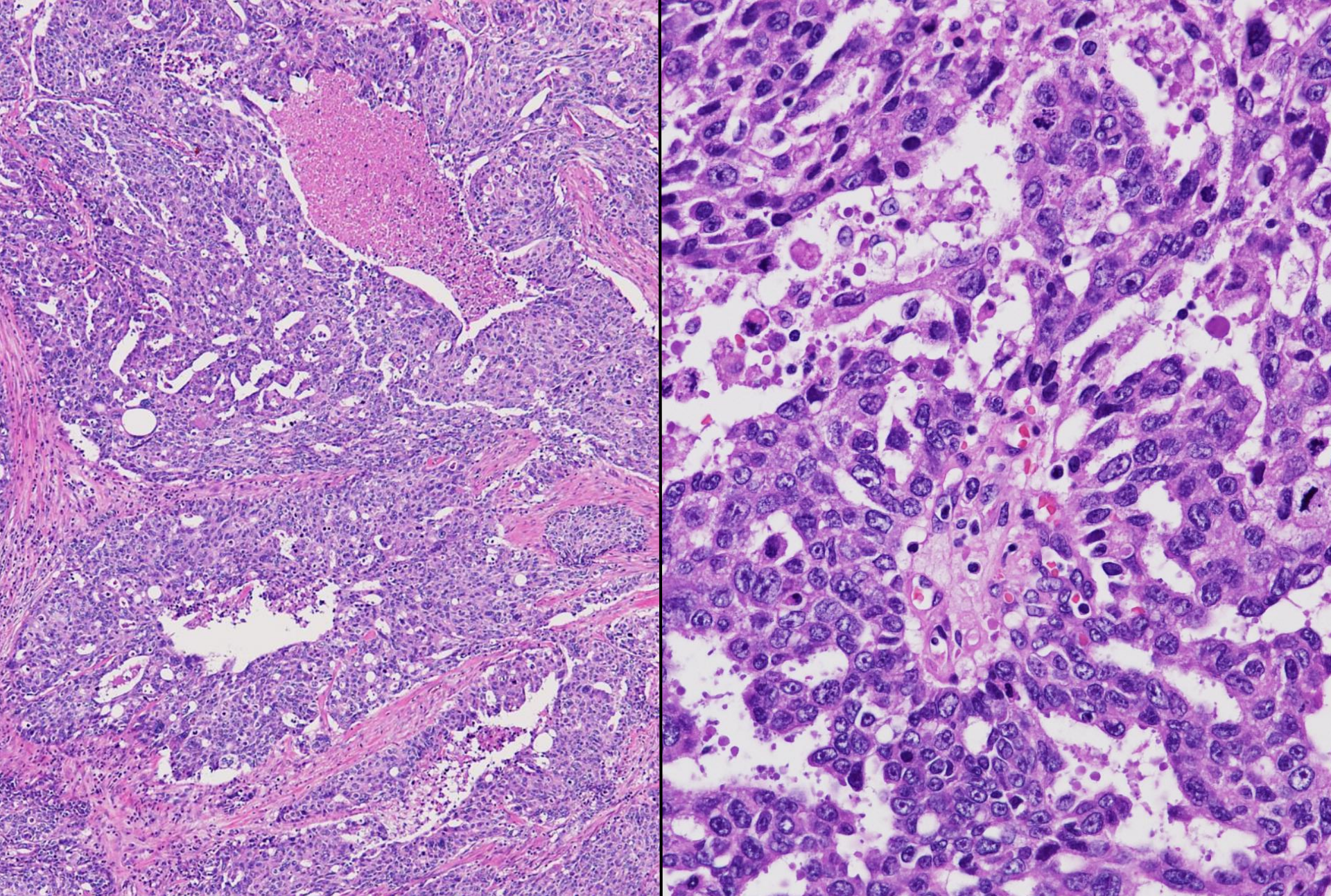
1. Mesothelial lesions
- 2. Müllerian lesions**
3. Mesenchymal tumors
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# Müllerian-type neoplasia

- Serous carcinoma: high-grade>>>low-grade
- Serous borderline tumor
- Müllerian adenosarcoma
- Endometrioid stromal sarcoma
- Carcinosarcoma
- Endometrioid carcinoma
- Clear cell carcinoma
- Mucinous carcinoma





High-grade serous carcinoma



# Classical criteria for peritoneal serous carcinoma

## Carcinoma in the peritoneum

- Both **ovaries** are either normal in size or enlarged by a benign process
- The bulk of the tumor in the extrovarian sites is greater than on the ovarian surface
- Microscopically ovaries reveal
  - 1) No tumor
  - 2) Tumor confined to the surface epithelium
  - 3) Tumor is  $<5 \times 5$  mm in the ovarian substance

# Origin of "ovarian or peritoneal" high-grade serous carcinoma

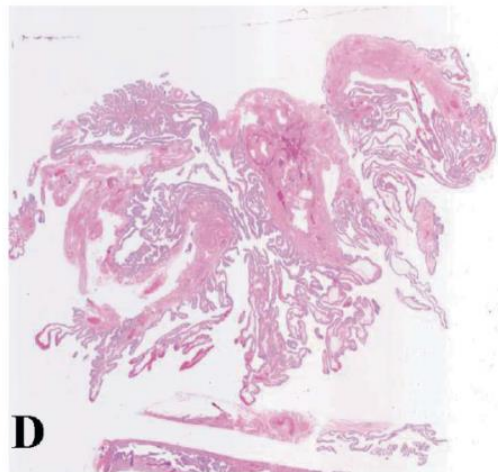
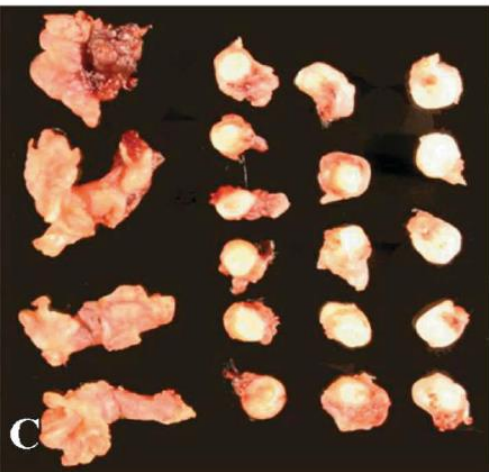
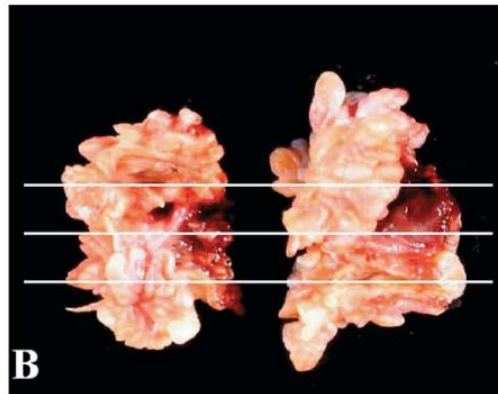
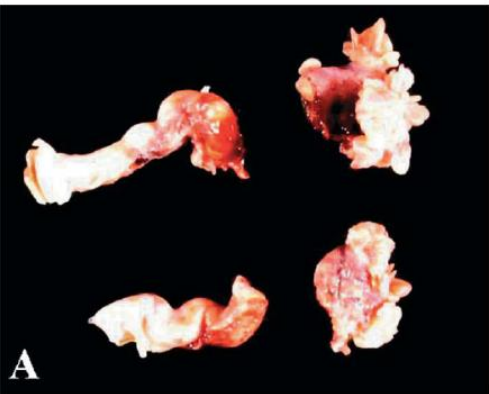
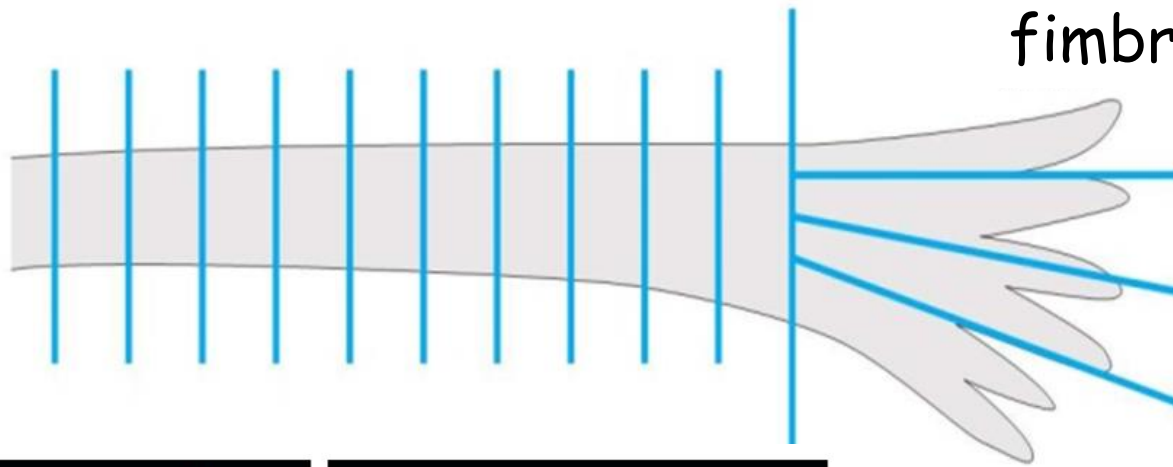
## Tubal origin

Paradigm shift

- Studies using RRSO in women with *BRCA1/2* mutation
- Examination of fallopian tubes by SEE-FIM protocol, perspective studies

## Traditional model

- No precursor lesion
- Arise from surface epithelial inclusion cyst
- Decision of primary site based on tumor volume



Protocol for **S**ectioning and  
**E**xtensively **E**xamining the  
**FIM**briated end (**SEE-FIM**)

*Medeiros F, et al. Am J Surg  
Pathol 30;230-236, 2006*



# Serous intraepithelial carcinoma (STIC)

- Intraepithelial proliferation of atypical cells identical to HGSC in the tube
- 50-60% of extrauterine HGSC
- *RRSO tubes of women with BRCA1/2 mutation*
- >90% in fimbria
- Possible to spread to peritoneum and ovary
- Imhx: aberrant expression of p53

# Criteria for peritoneal high-grade serous carcinoma 2014- (WHO 2014)

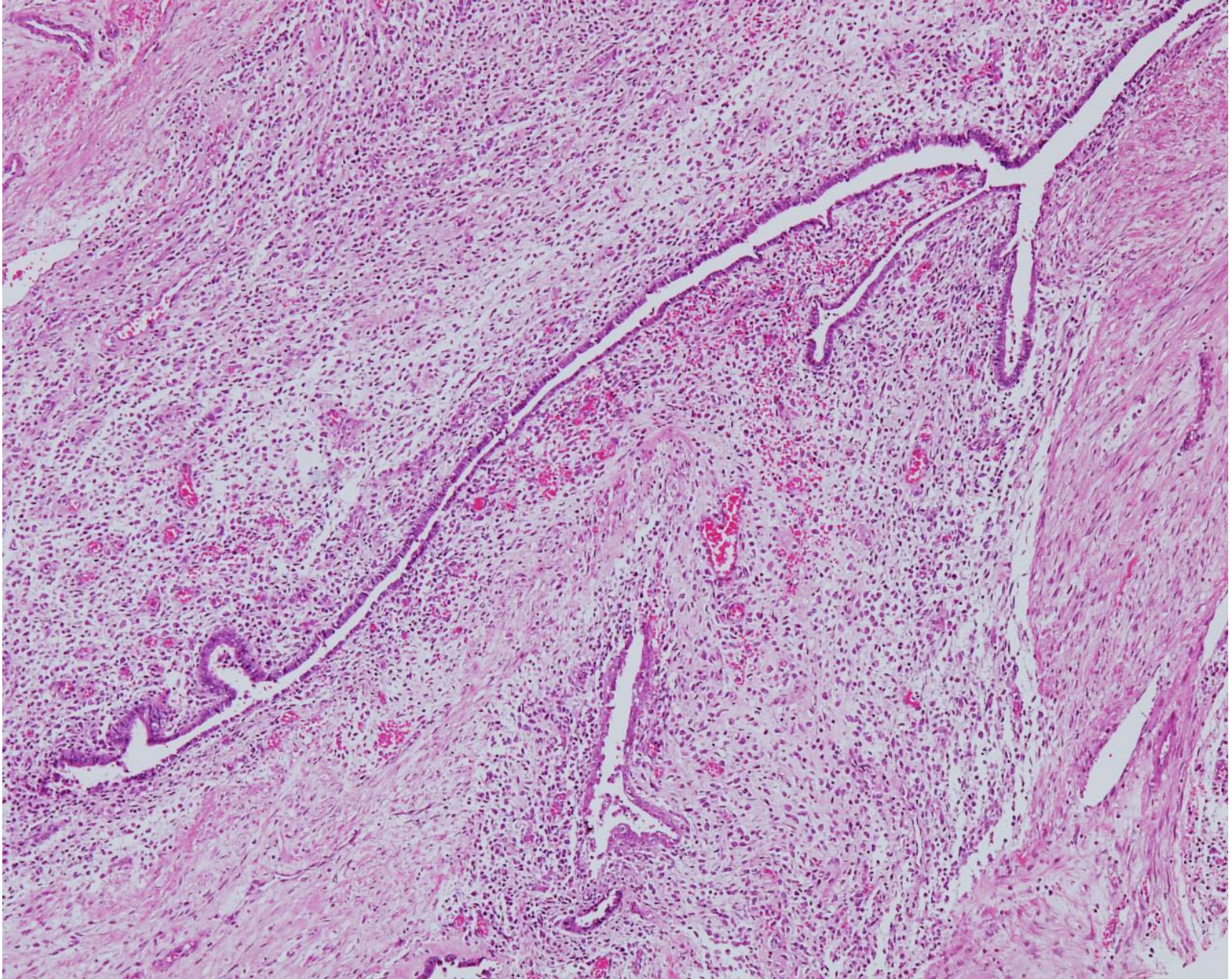
- Carcinoma in the peritoneum
- Both ovaries and fallopian tubes are **grossly and microscopically** normal or enlarged only by a normal process

# Malignant tumors associated with endometriosis

|               | Extraova (%) | Ova (%)  | Total(%)  |
|---------------|--------------|----------|-----------|
| Adenosarcoma  | 3 (33.3)     | 0        | 3 (8.3)   |
| Clear cell Ca | 4 (44.4)     | 9 (33.3) | 13 (36.1) |
| Endom Ca      | 1            | 8 (29.7) | 9 (23.1)  |
| Serous Ca     | 1            | 5 (18.5) | 6 (16.7)  |
| Mucinous Ca   | 0            | 1        | 1         |
| Serous BT     | 0            | 3 (11.1) | 3 (8.3)   |
| Mucinous BT   | 0            | 1        | 1         |
| Total         | 9 (100)      | 27 (100) | 36 (100)  |

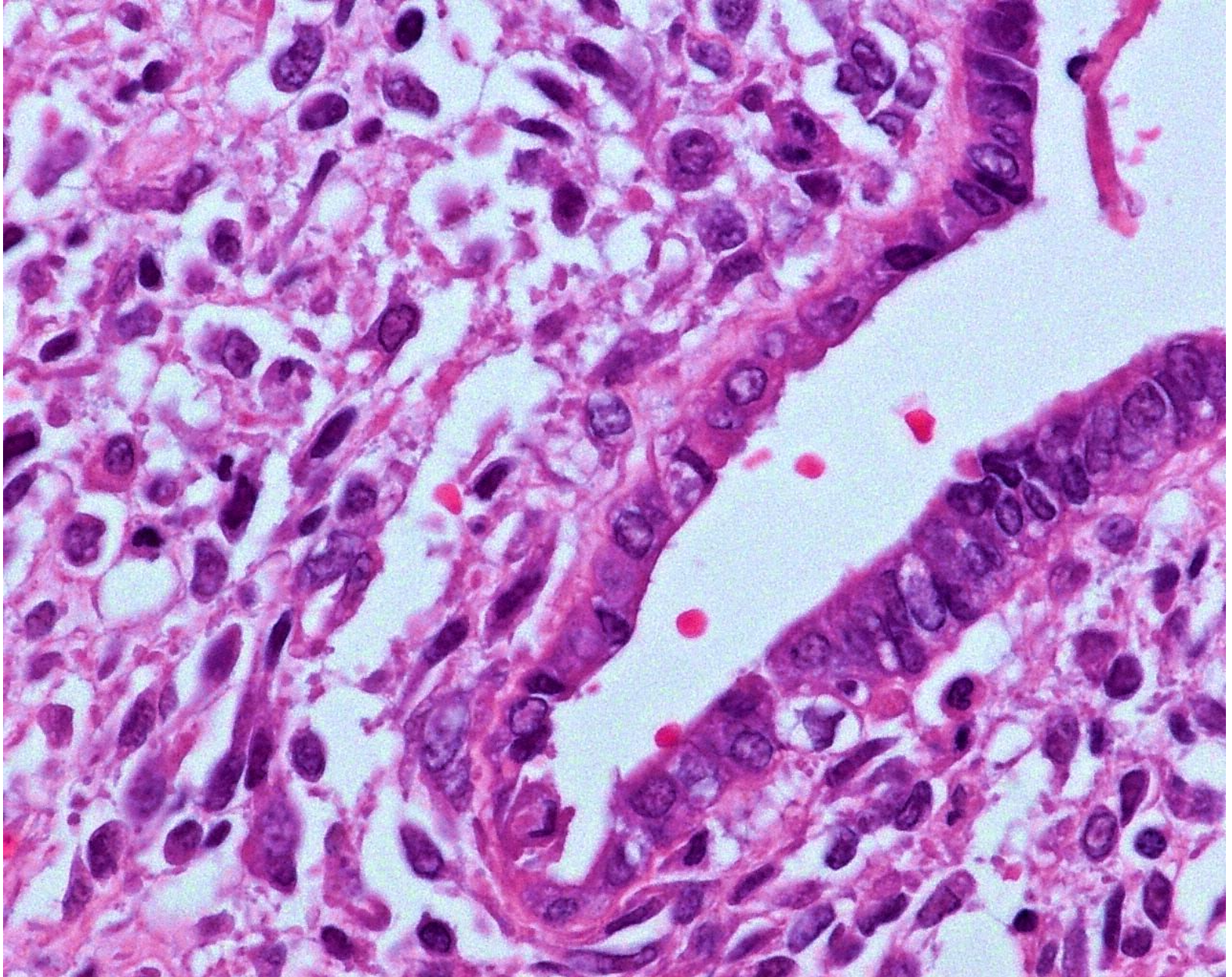
*Stern RC et al. Int J Gynecol Pathol, 2001, 20:133-9*





Adenosarcoma (arising in pelvic endometriosis)



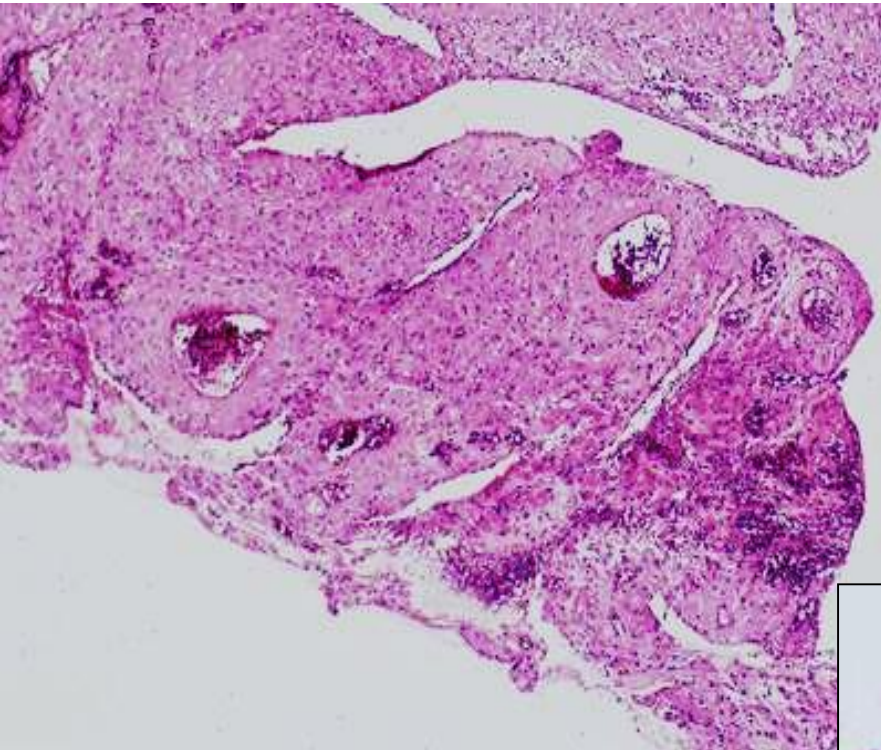


Adenosarcoma (arising in pelvic endometriosis)

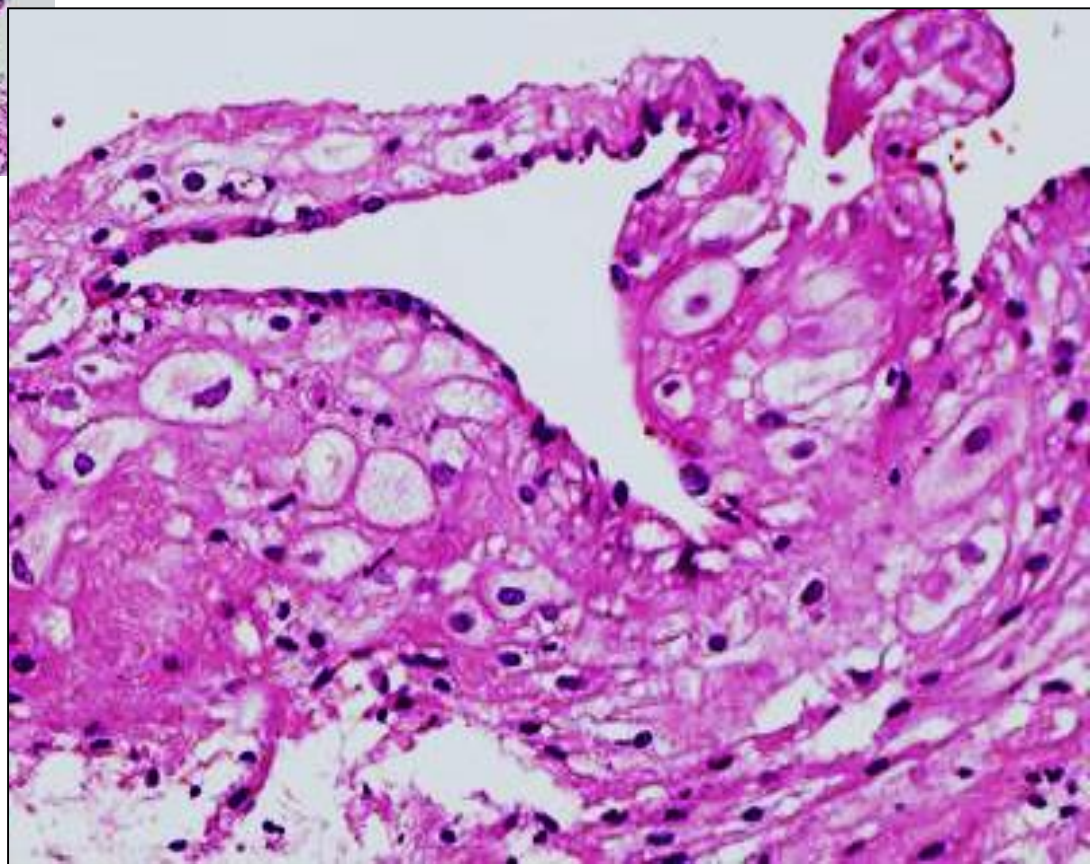
# Non-neoplastic Müllerian lesions

- Endometriosis and its related lesions  
Endosalpingiosis, endocervicosis, Müllerianosis
- Ectopic decidua
- Endometriosis with pregnancy effect
- May mimic neoplastic process, both clinically and pathologically





Endometriosis with  
decidual change:  
-white flat elevated  
lesion in the Douglas'  
Pouch at c-section (preg  
38w)



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3. **Mesenchymal tumors**
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# Mesenchymal tumors

- Extra-gastrointestinal stromal tumor
- Solitary fibrous tumor
- Desmoid tumor (abdominal fibromatosis)
- Inflammatory myofibroblastic tumor
- Calcifying fibrous tumor
- Leiomyomatosis peritonealis disseminate
- Liposarcoma
- Others

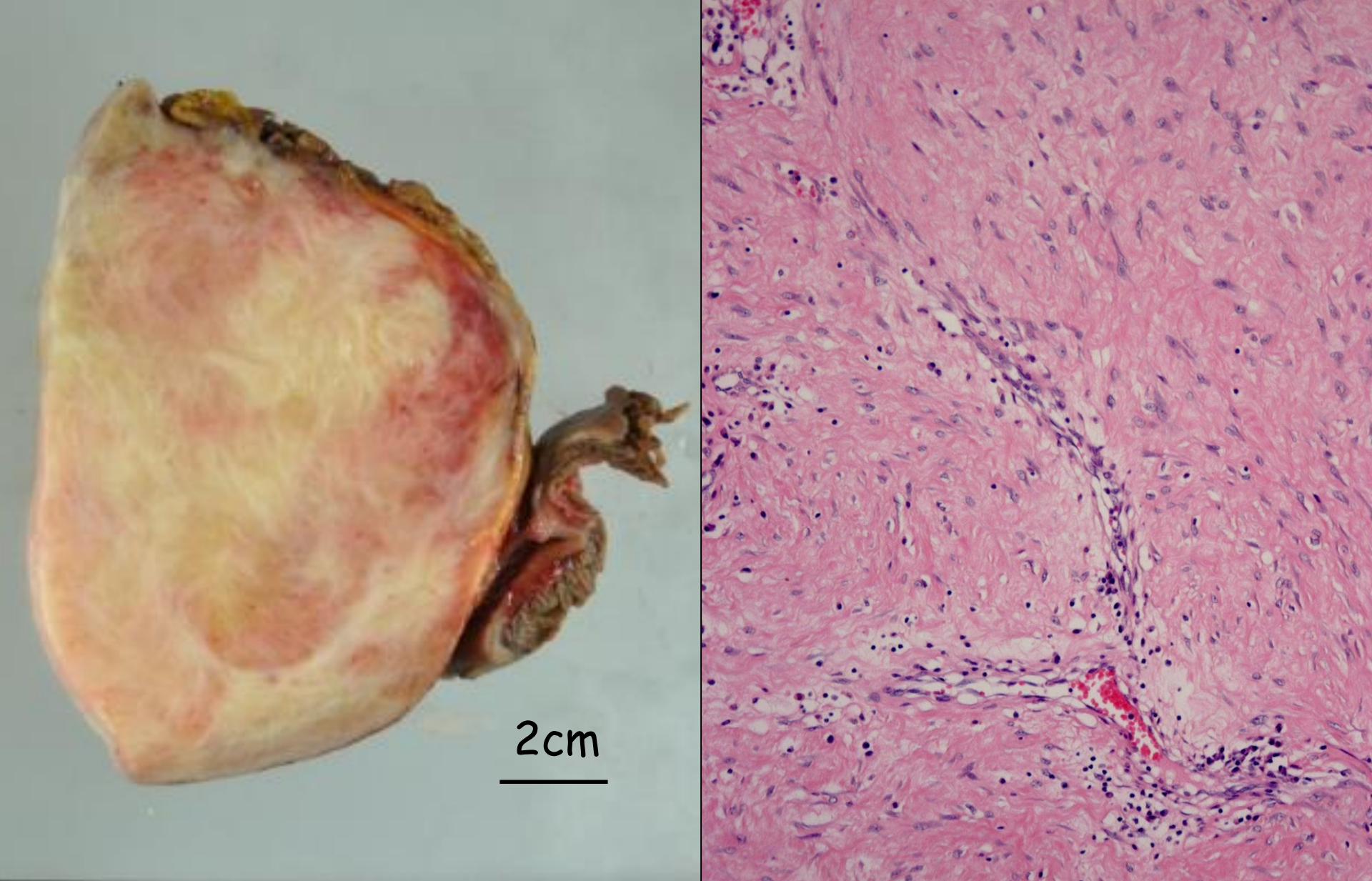
# Solitary Fibrous Tumor

- Localized fibrous tumor with hemangiopericytoma-like vascular pattern
- Originate from submesothelial fibroblast(CD34+)
- Rare in the peritoneal cavity (usually in pleura)
- Most with favorable prognosis; histology does not predict malignant behavior
- Doege-Potter syndrome  
hypoglycemia (insulin-like GF 2)



# Desmoid tumor (abdominal fibromatosis)

- Invasive proliferation of fibroblastic spindle cells in the abdominal wall/cavity
- Adult; F>M
- Sporadic cases; familial adenomatous polyposis (10% of FAP), trisomy (#8,#20); 5q deletion
- Local rec; no distant metastasis



Desmoid tumor (abdominal fibromatosis)

# Inflammatory myofibroblastic tumor

- Proliferation of myofibroblastic spindle cells with lymphoplasmacytic infiltrate
- Children, young adults
- Presentation: mass, fever, growth failure, weight loss, anemia, thrombocytosis, polyclonal hypergammaglobulinemia
- Imhx: SMA+, desmin+
- ALK gene rearrangement 60%
- Local rec; metastasis- histology cannot predict prognosis

Gynecologic Oncology Reports 12 (2015) :9-12



# Calcifying fibrous tumor

- Fibrous tumor with calcification, well circumscribed, abundant collagen, lymphoplasmacytic infiltration
- Serosa of stomach, small intestine
- Incidental finding
- Young adults, adults

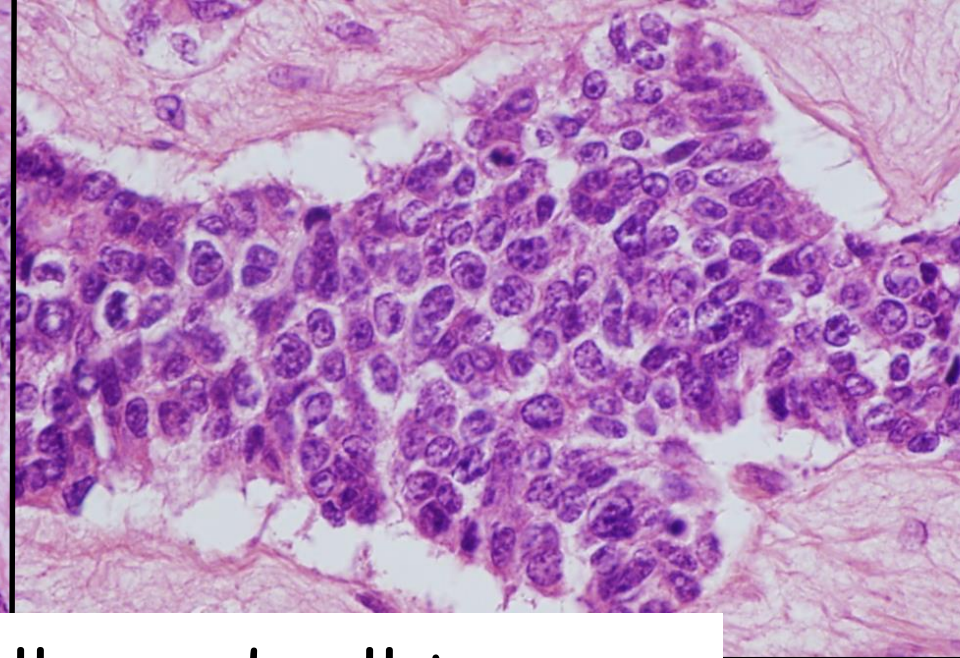
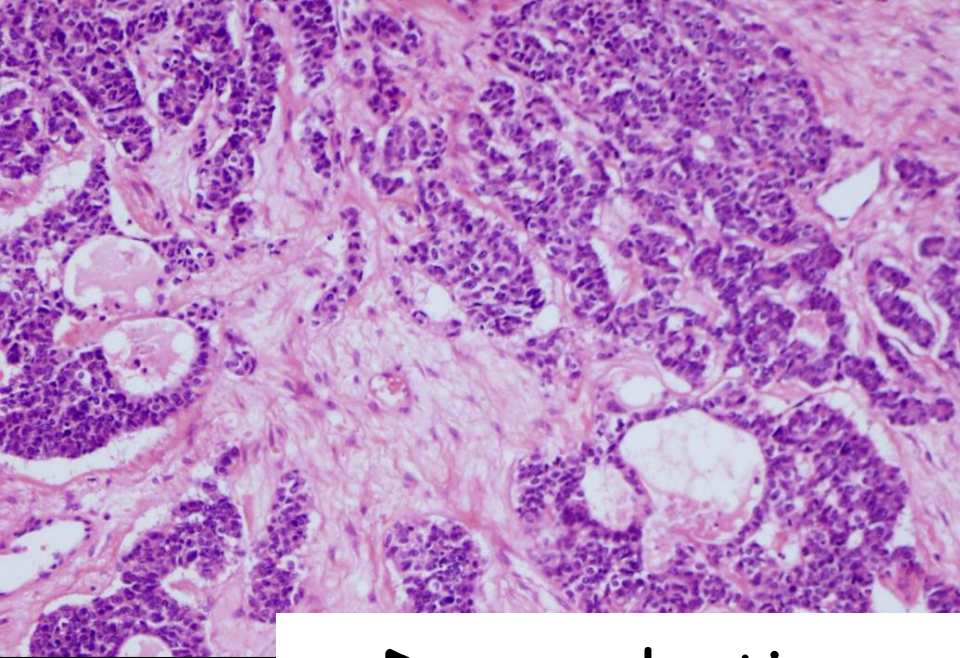
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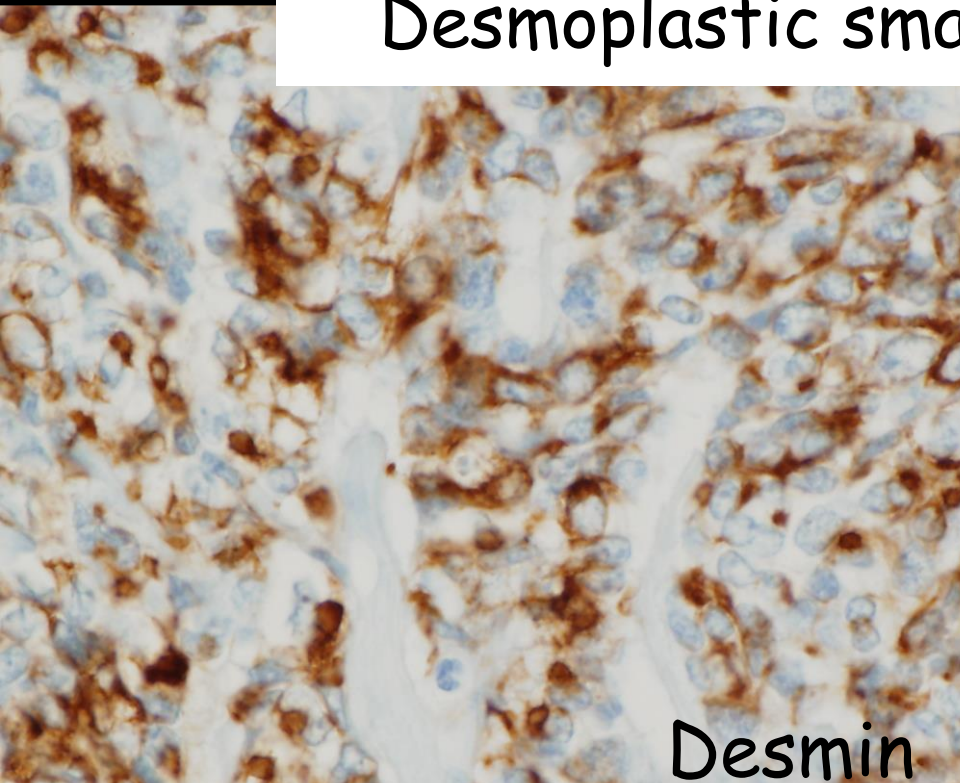
# Desmoplastic small round cell tumor

- Malignant tumor of unknown origin
- Rare
- Adolescents, young adults (15-30yrs)
- Male >>Female (4:1)
- Abdominal and/or pelvic peritoneum
- $t(11;22)(p13;q12) \Rightarrow$  EWS-WT1 fusion protein
- Poor prognosis (OS 50%)

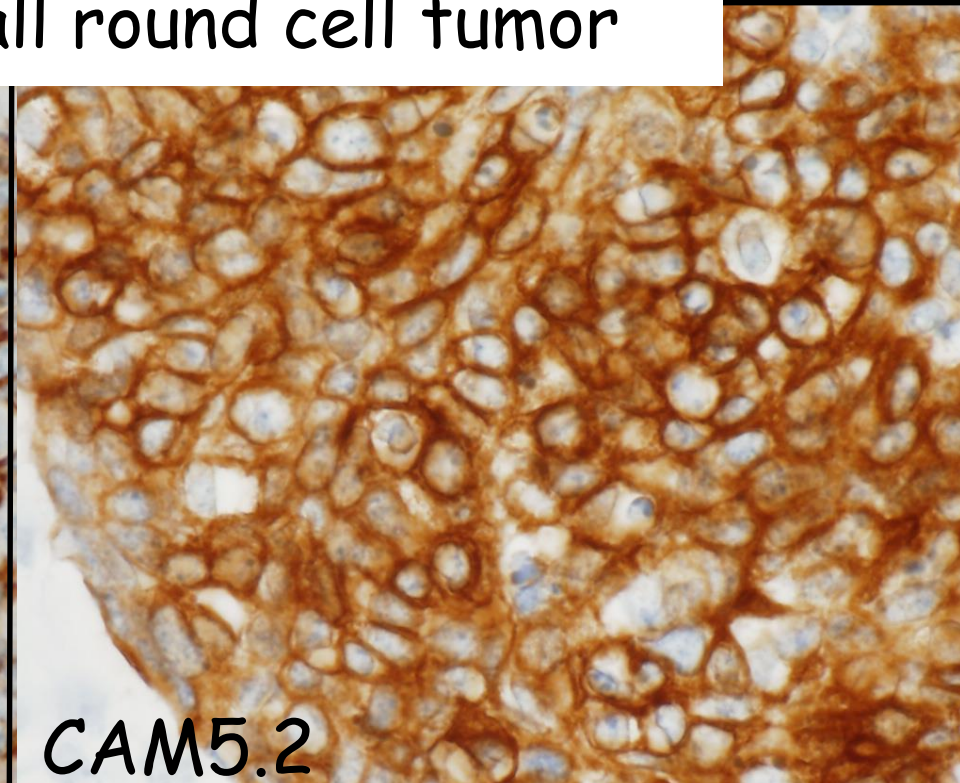




Desmoplastic small round cell tumor



Desmin



CAM5.2

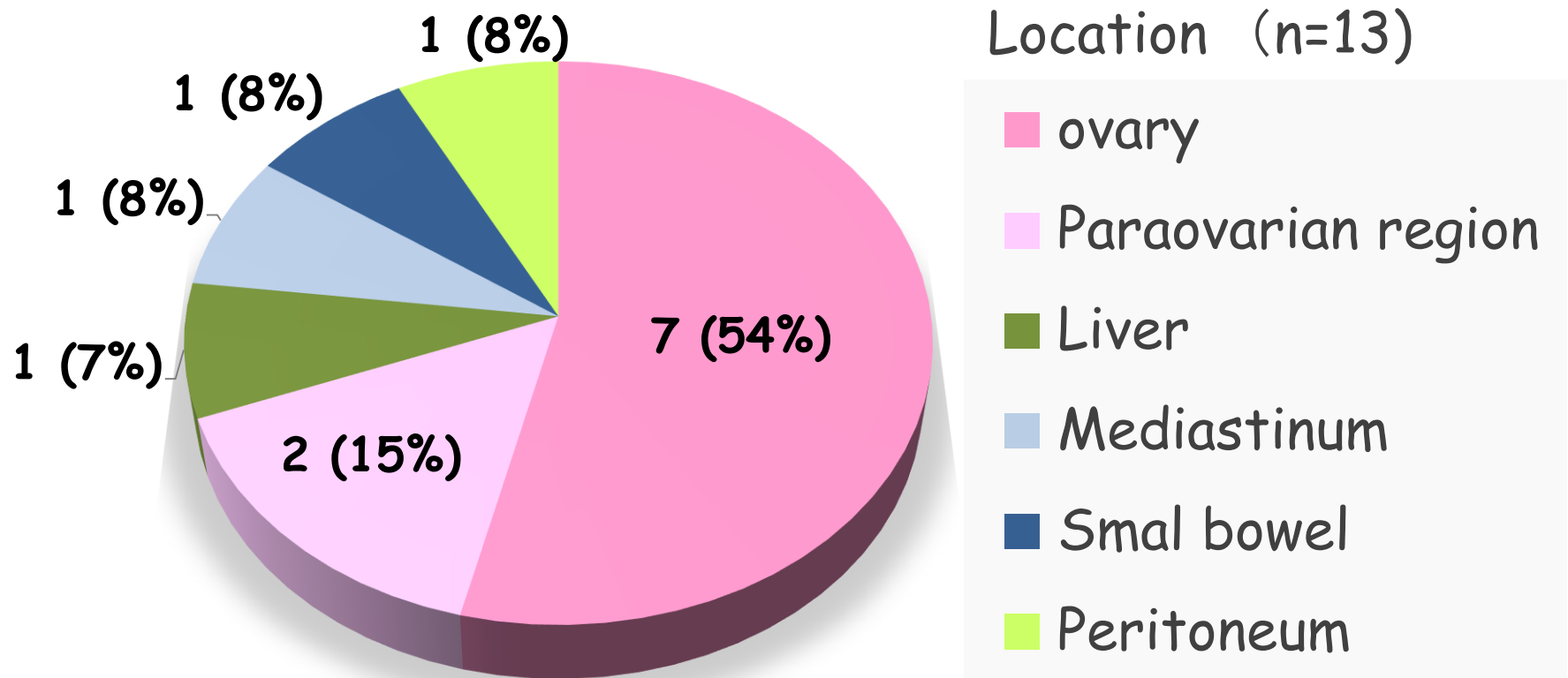
# Peritoneal ependymoma

- Prognosis
- Imhx: some difference from CNS ependymoma
  - ER 100% (10% in CNS epen)
  - PgR 80% (20% in CNS epen)
  - CK7 80% (10% in CNS epen)
  - GFAP 100% (100% in CNS)
  - Am J Surg Pathol 2008;32:710-718
- Pathogenesis: controversial
  - Metaplasia,? teratoma? Aberrant tissue?
- dDX
  - serous carcinoma, malignant mesothelioma, gliomatosis peritonei



# Extra-CNS Ependymoma

## Literature review



Verdun TP, et al. Pathol Res Pract 2015; 211: 268-70

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# Secondary tumors

- Primary tumor: gyn, GI >>> pancreas, breast (lobular carcinoma)
- 

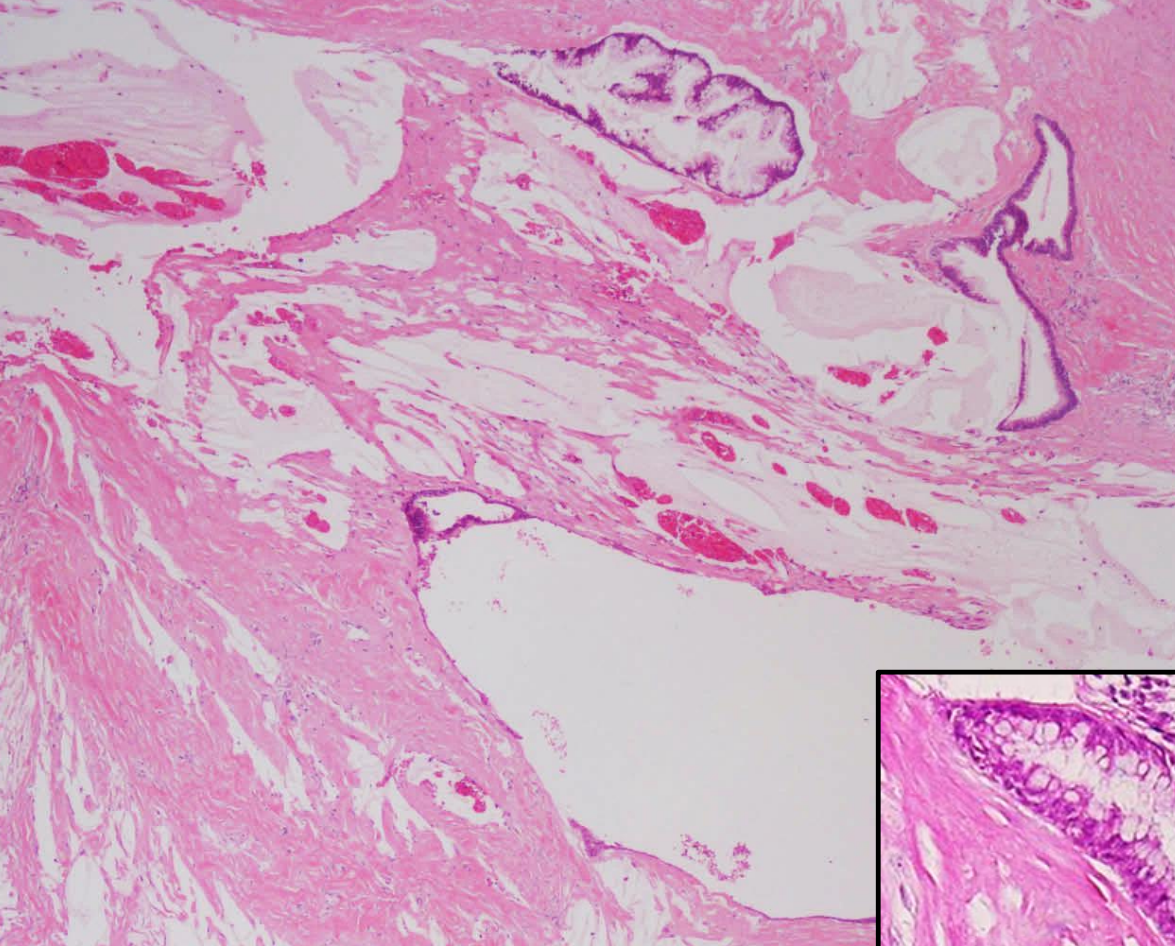
- Peritoneal implant of ovarian serous borderline tumor
- Gliomatosis peritonei

# Peritoneal implant of ovarian serous borderline tumor

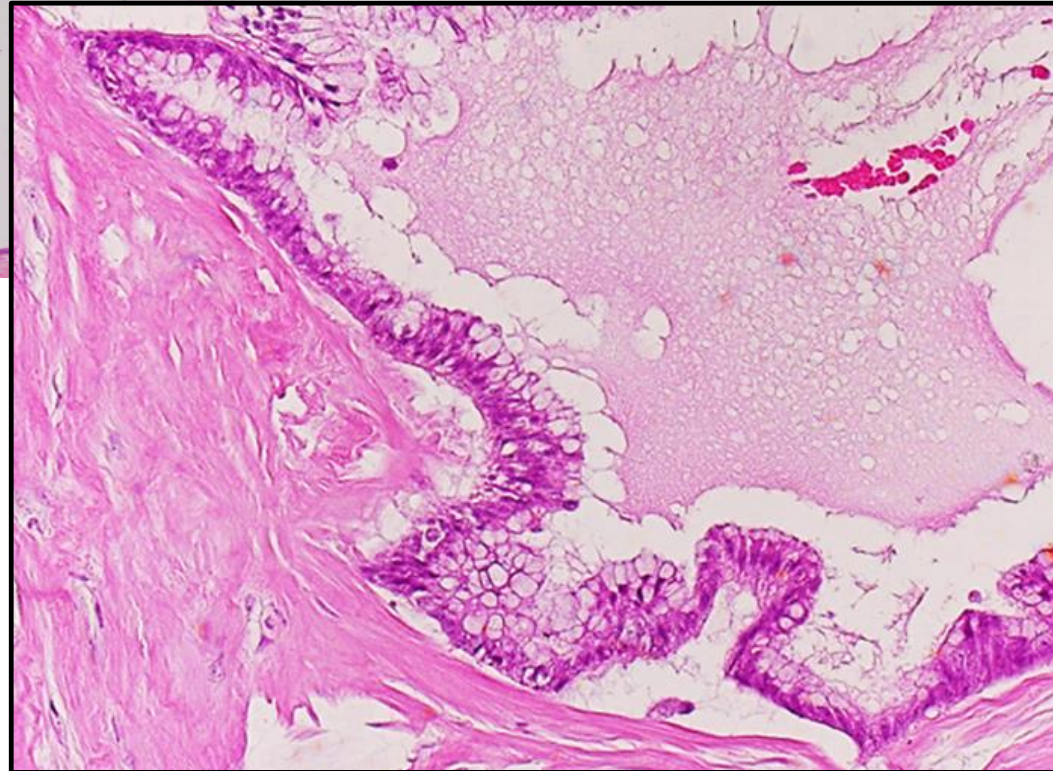
- Pts with ovarian serous borderline with peritoneal lesion
- WHO 2014
  - **implant**: formally called non-invasive implant  
favorable prognosis
  - **low-grade serous carcinoma (LGSC)**: formally called non-invasive implant  
Poor prognosis
- ....invasive implant behave like LGSC they should be designated as such. All other implants that are non-invasive can be designated "implants" (WHO2014)

# Pseudomyxoma peritonei

- **Clinical term** :grossly evident peritoneal involvement by mucoid material due to peritoneal spread of mucinous neoplasm
- Origin: **low-grade appendiceal mucinous neoplasia** >>>mucinous component of ovarian mature cystic teratoma
- Histology: dissecting mucin with fibrosis



Dissecting mucin with  
fibrosis with low-grade  
mucinous tumor cells





# Peritoneal lesions with mucin: Pathology report

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RE Scully et al. *AFIP* 3<sup>rd</sup> series,  
fascicle 23

Ronnett et al. *AJSP*  
1995; 19: 1390-1408

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Mucinous ascites

w LG mucinous tumor cells

w HG mucinous tumor cells

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Organizing mucinous fluid

w LG mucinous tumor cells

w HG mucinous tumor cells

DPAM

PMCA

---

Dissecting mucin with fibrosis

w LG mucinous tumor cells

w HG mucinous tumor cells

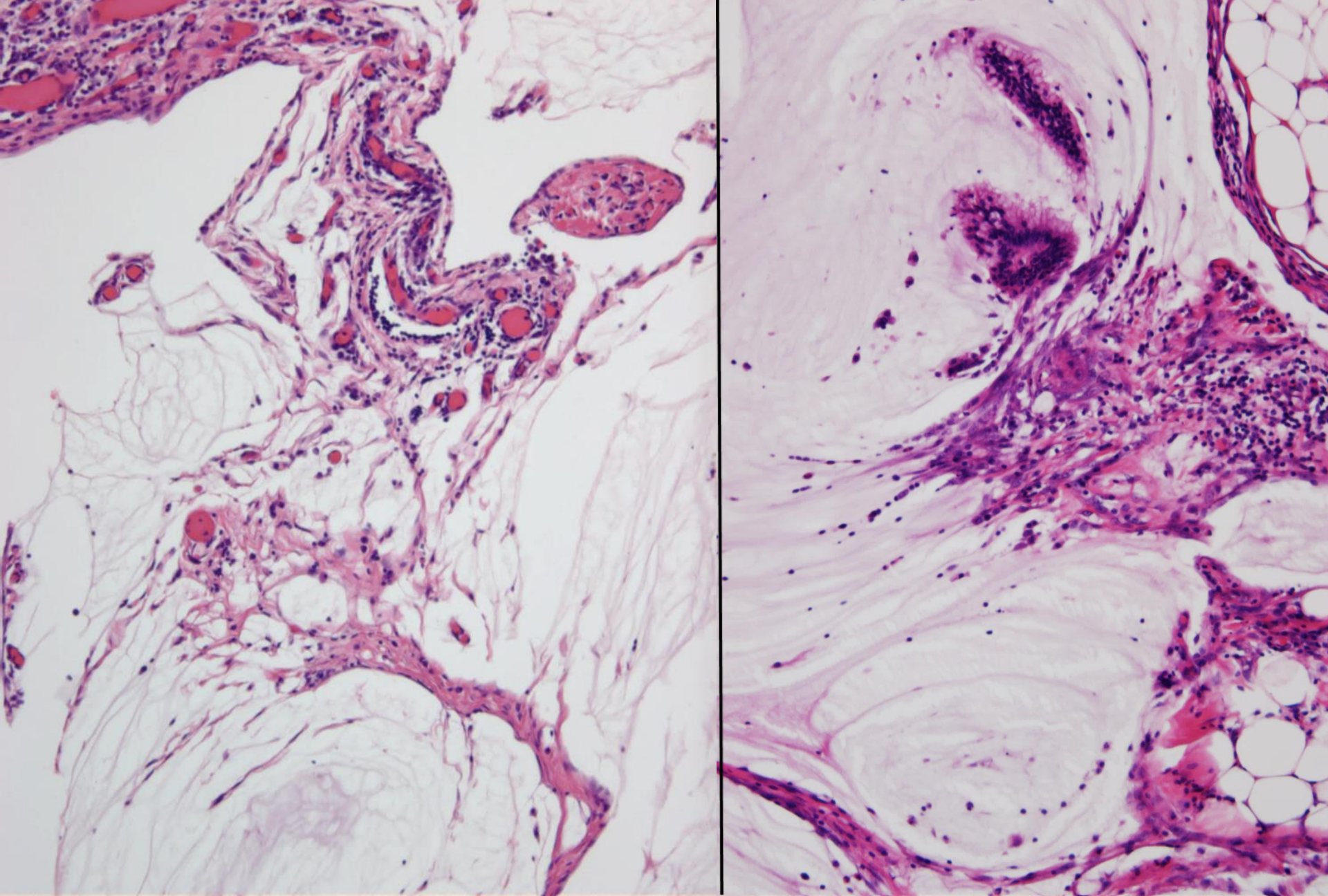
DPAM

PMCA

---

DPAM :Disseminated peritoneal adenomucinosis

PMCA: Peritoneal mucinous carcinomatosis



Organizing mucinous fluid (with low-grade tumor cells)

# Gliomatosis peritonei

- Benign mature glial implants on the peritoneal surface
- Rare complication of ova immature/mature teratoma
- Good prognosis (Grade 0)

# Gliomatosis peritonei

## Histogenesis

- Peritoneal seeding of ovarian teratoma via capsular rupture  
vs.
- Originate from peritoneal pluripotent cells stimulated by GF in ovarian tumor  
(different genetic identity between peritoneal and ova tumor)

Am J Pathol 2001; 159: 51-55

Hum Pathol 2004; 35: 685-688

## with endometrisoia

Int J Dev Biol 2012, 56:969-974

Korean J Pathol 2013, 47:587-591



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# Sclerosing peritonitis a/w ovarian luteinized thecoma

- Reactive submesothelial mesenchymal proliferation; ascites; encases the small bowel to cause bowel obstruction
- Premenopausal pts (mean 28yrs)
- Bil ova lesions ; No endocrine manifestation
- No rec or spread of the ovarian lesion
- Pts may die of sclerosing peritonitis
- Ovarian lesion may be non-neoplastic nature: entrapped follicles and normal structures within the lesions → "thecomatosis" ?

Am J Surg Pathol 2008,32:1273-90

# Peritoneal keratin granuloma

- Response to deposition of keratin derived from lesions in the female reproductive tract
  - ovarian teratoma
  - endometrial carcinoma with sq diff
  - cervical Sq CC (bulky)
- may be confused with metastatic carcinoma