

# How to Recognize Gynecologic Cancer Cells from Pelvic Washing and Ascetic Specimens

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# Pelvic Washing and Ascetic Specimens

- Obtaining a pelvic washing sample is a common surgical procedure for gynecologic malignancies.
- The findings from those washing specimens have a significant impact for the decision of clinical management.
- They are mainly applied to gynecologic carcinomas, particularly for the carcinomas of ovary, fallopian tube, and/or peritoneum.
- Prior to initiating neoadjuvant chemotherapy, an accurate cytologic or pathologic diagnosis is typically required.

# Perspectives of Cytopathologists

- Difficult to make definitive diagnosis on cytologic specimens
- The most common diagnosis is “Negative” vs “Positive for adenocarcinoma” or “Atypical”
- Within the positive category, most of the time without specifying cancer source.
- Part of the reasons are: these are cytologic specimens, not resection or biopsy specimens; lack of specific markers (previously).

# Perspectives of Gynecologists or Oncologists

- Expect to be more specific for positive specimens: primary site (**gyn vs non-gyn**).
- “Atypical” is the most annoying diagnosis.
- They do not care much for washing diagnosis when the cancers are in the advanced stages or ovarian cancer with exophytic growth.
- But they do care in the following situations:
  - Lower stage (stage 1A vs 1C)
  - Presence of extensive adhesions (Positive vs reactive)
  - Presence of other cancers (breast cancer metastasis vs PSC)
- Significant attention to those patients for neoadjuvant chemotherapy from ascetic samples.

# Neoadjuvant Chemotherapy

- Give chemotherapy prior to “debulking’ surgery.
- Started from two decades ago
- Almost exclusively for
  - Advanced stage ovarian cancer
  - Patients were medically too compromised to tolerate primary surgical cytoreduction.
- Diagnostic imaging criteria are developed to identify patients with advanced stage ovarian cancer who are unlikely to be optimally surgically cytoreduced at the initial surgery.

# Neoadjuvant Chemotherapy:

## Selective criteria and diagnostic accuracy (%)

- The selection criteria:
  - Physical examination consistent with advanced ovarian cancer (70)
  - Diagnostic imaging studies consistent with an advanced stage ovarian cancer that is unlikely to be optimally cytoreduced (85-90)
  - Cytologic or histologic specimens consistent with an ovarian epithelial cancer (>95)



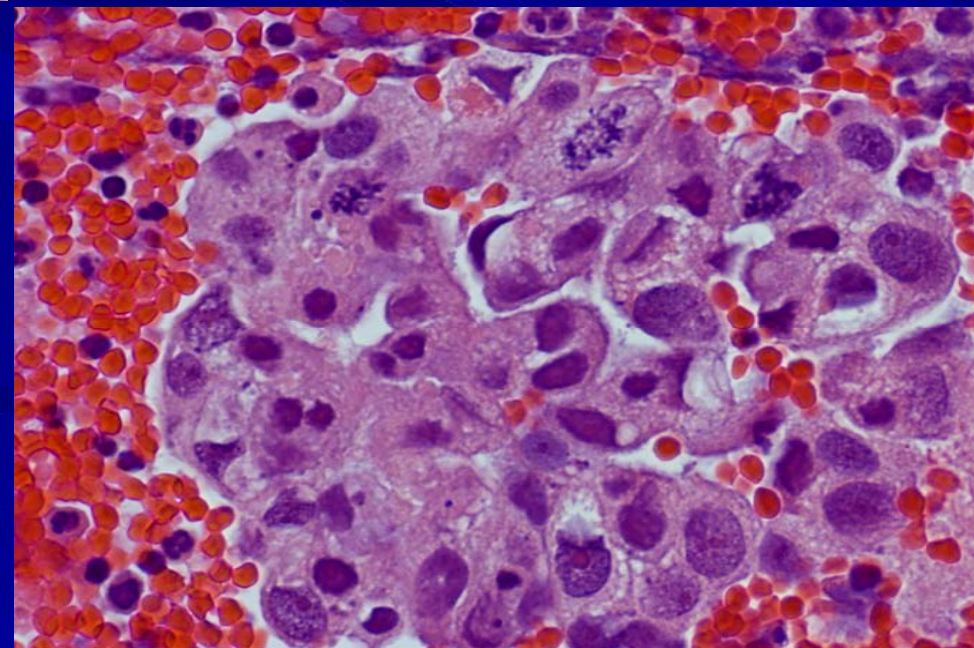
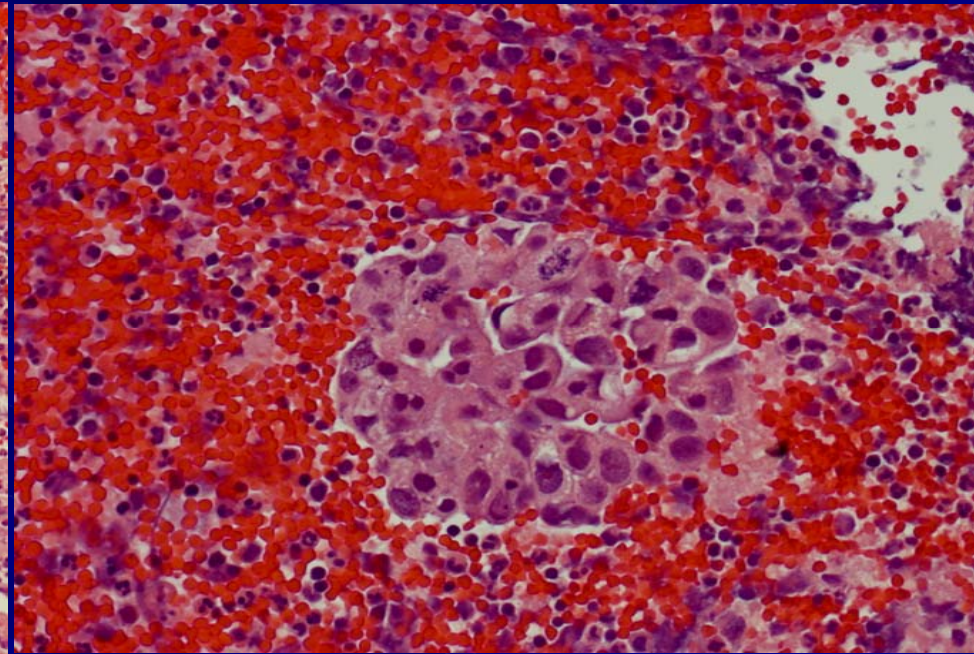
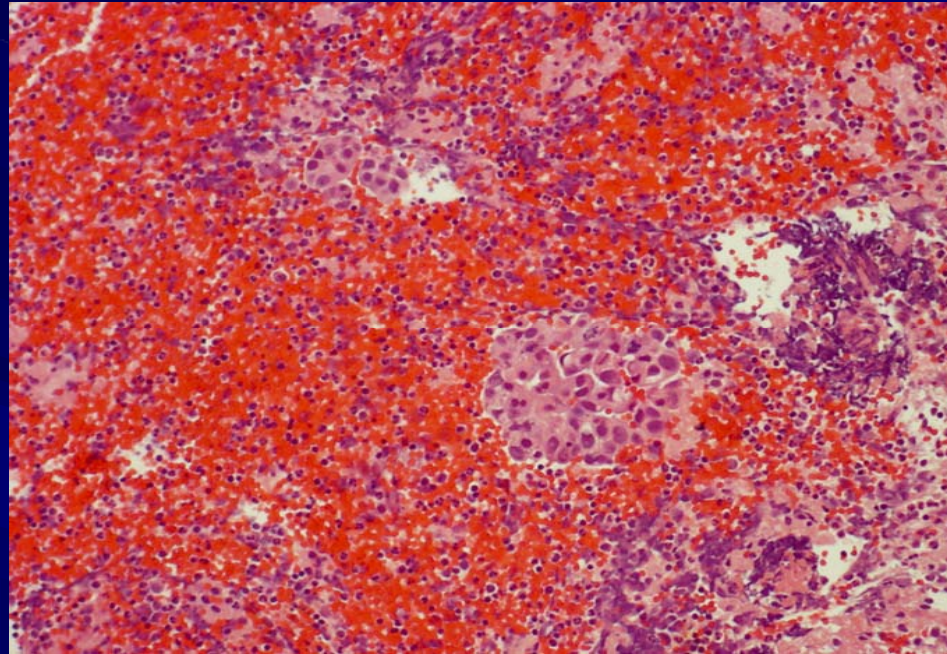
# Pelvic Gynecologic Cancer Related Cytology

- **Ovarian epithelial carcinoma (OEC)**: the most common. Among them, **pelvic serous carcinoma (PSC)** is the most prevalent:
  - Fallopian tube
  - Ovary
  - Peritoneum
- **Metastatic cancers**: GI, breast, mesothelioma, GU, etc
- **Ovarian sex-cord stromal tumors**: less common
- **Endometrial cancer**: less common
  - Mostly endometrial serous carcinoma
- **Cervical cancer**: rare

**What are the cytologic features for OEC?**



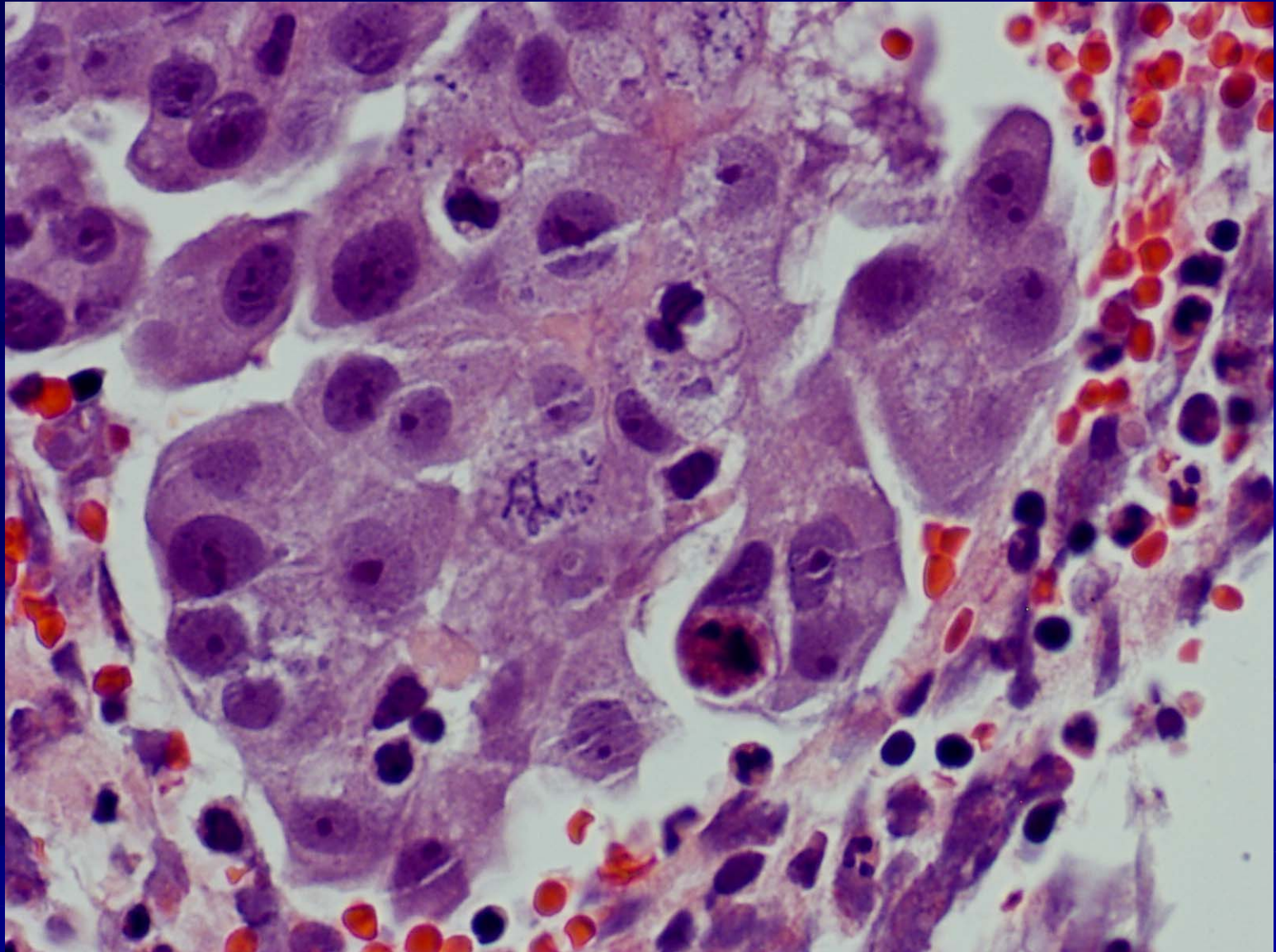
# Cytologic features of OEC



**Malignant cells with abundant cytoplasm not typical of mucinous carcinoma**



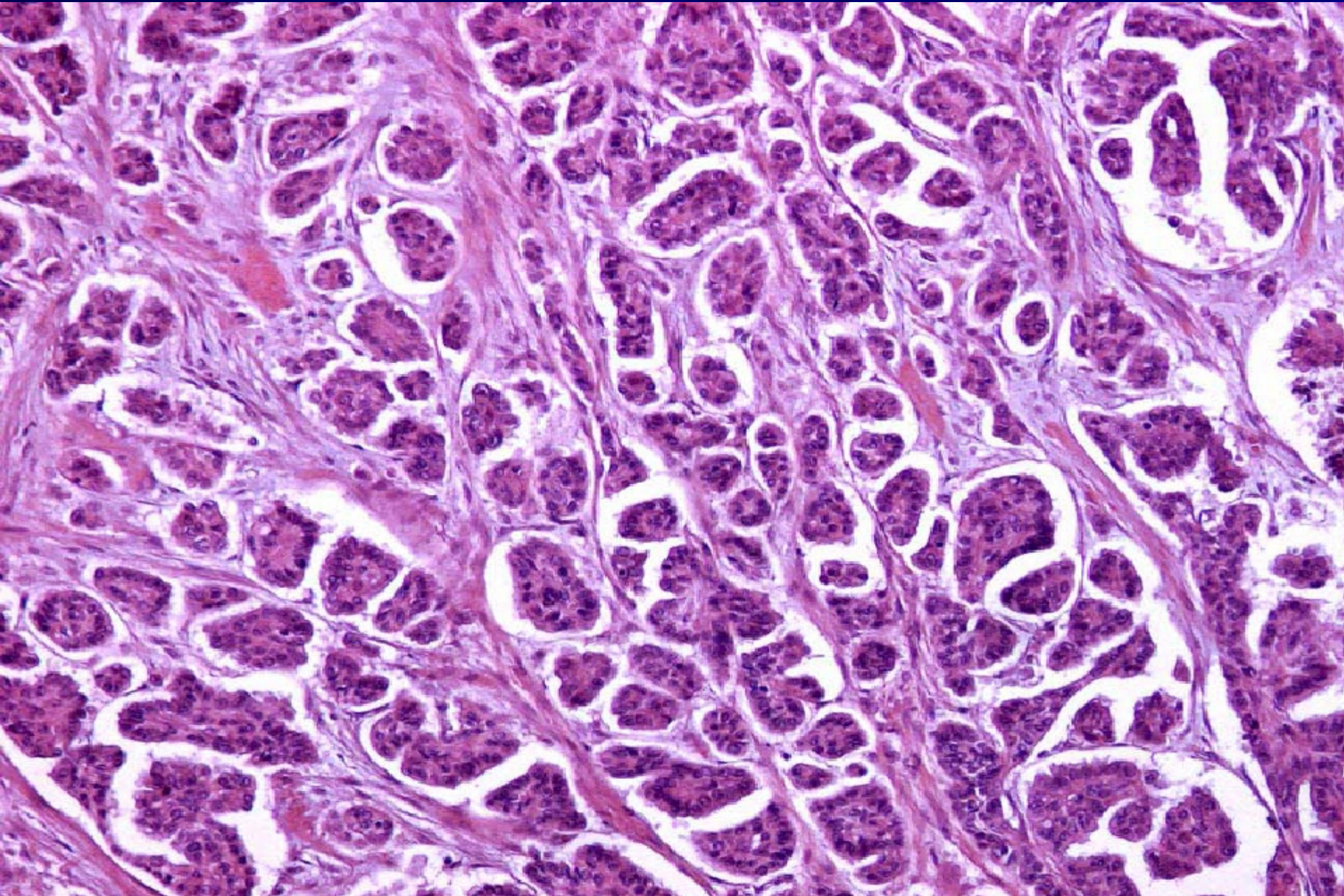
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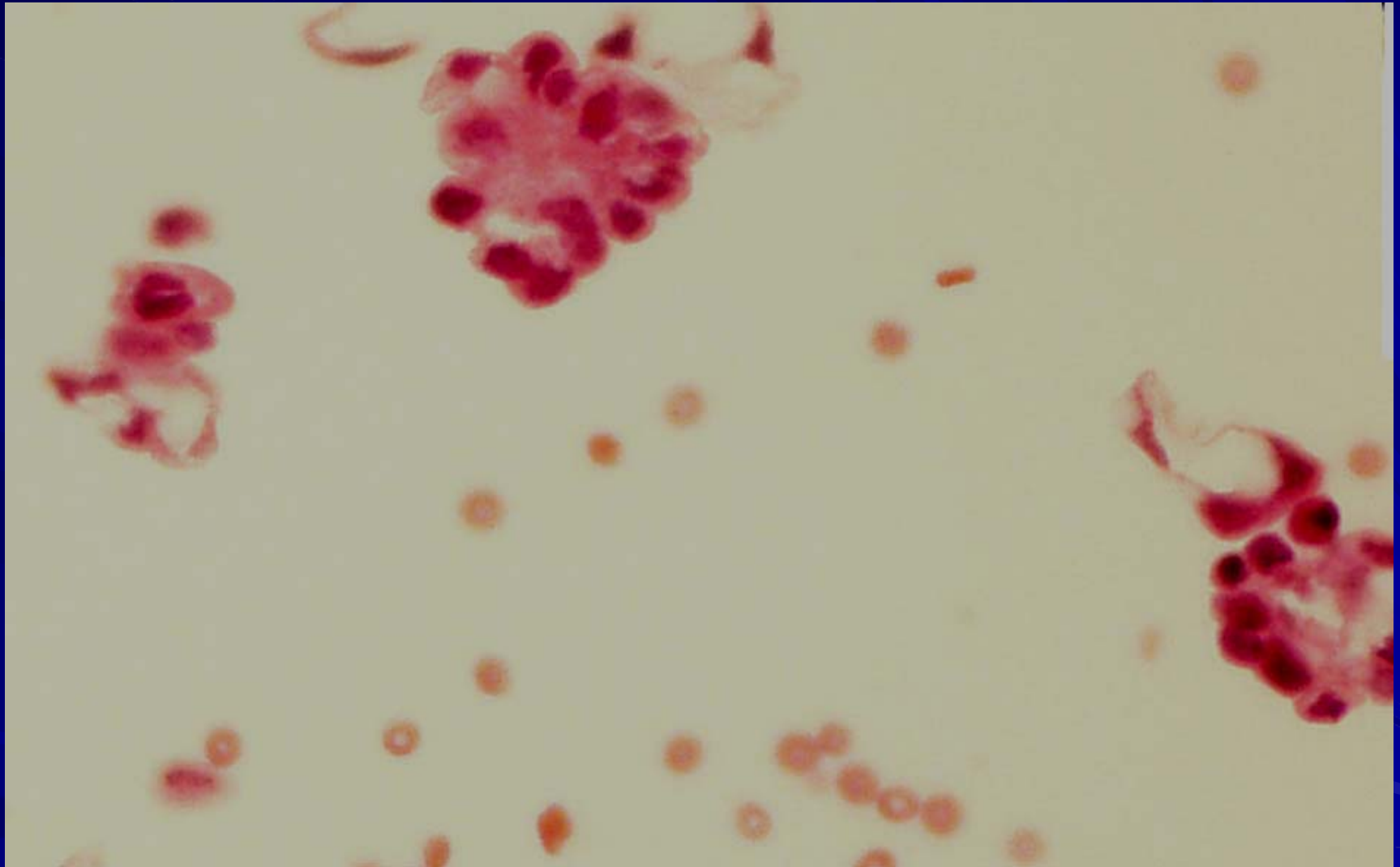


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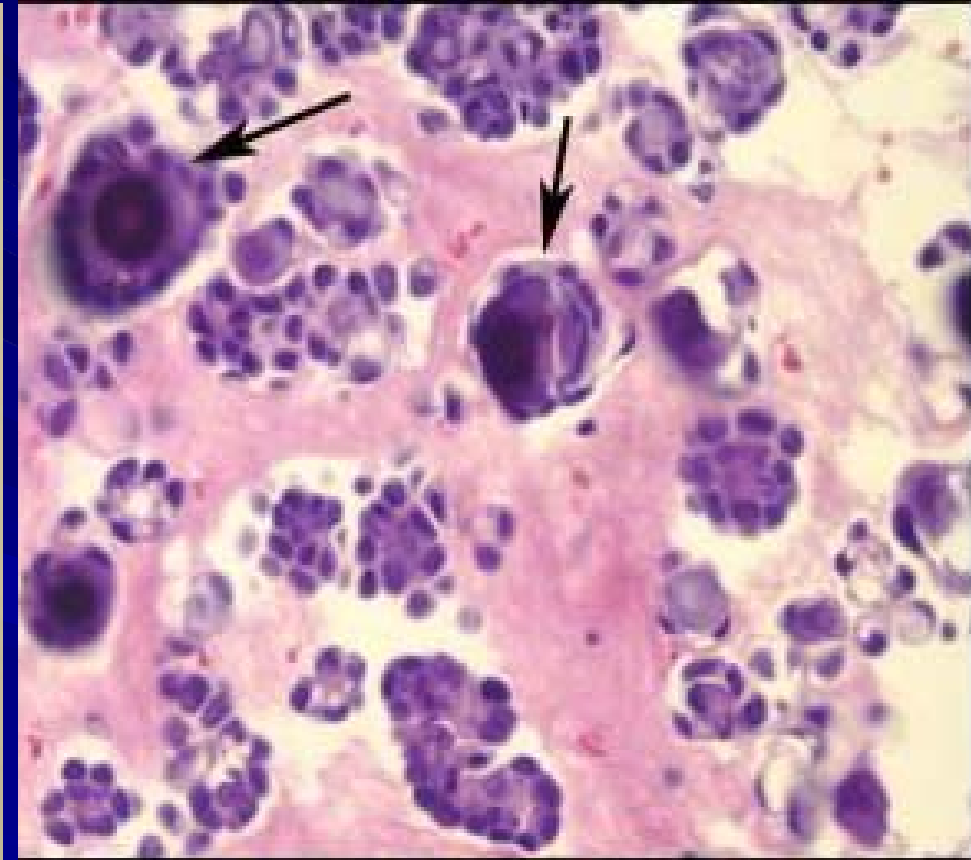


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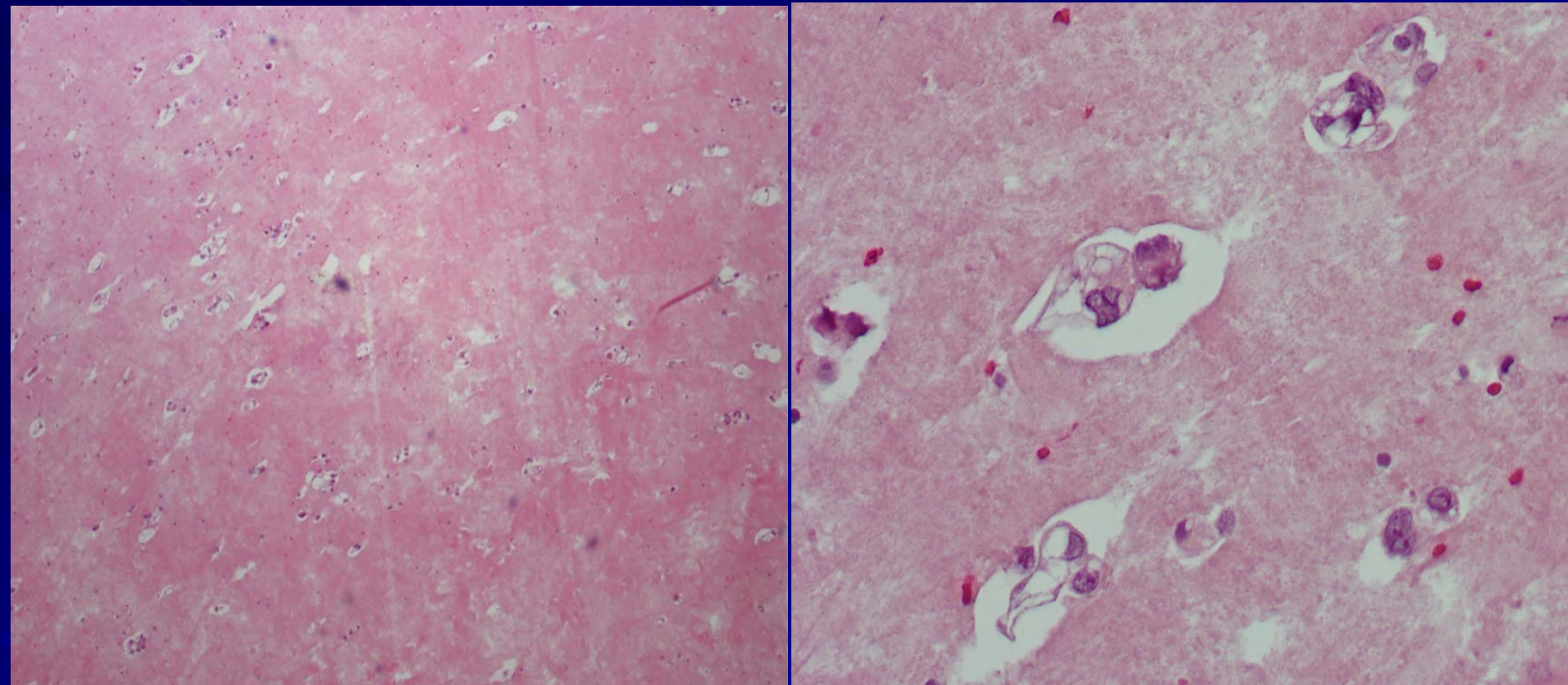
Micropapillary structures or minimal architectural features suggesting papillary formation, particularly when presence of psammoma bodies

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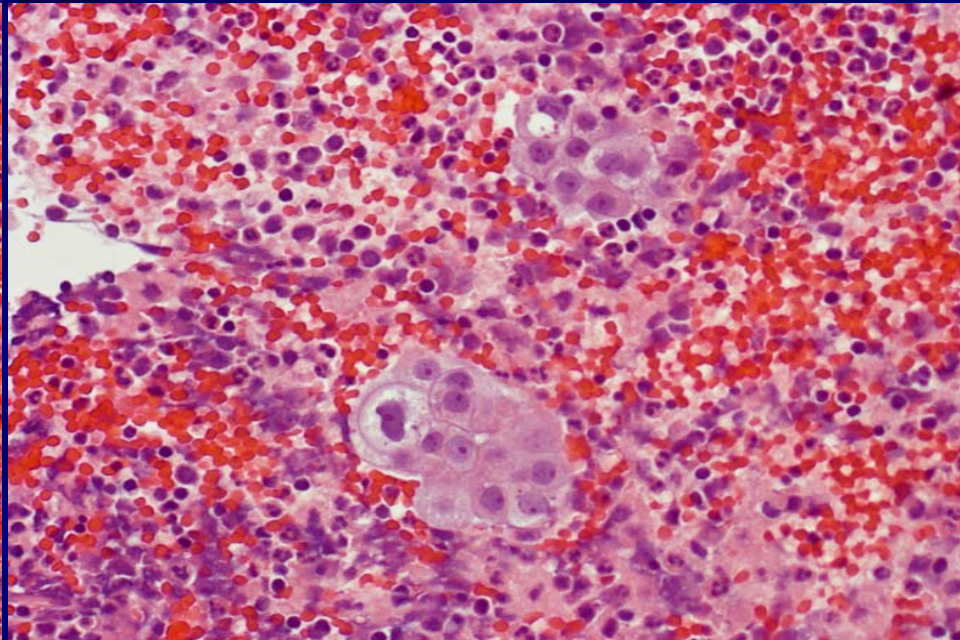
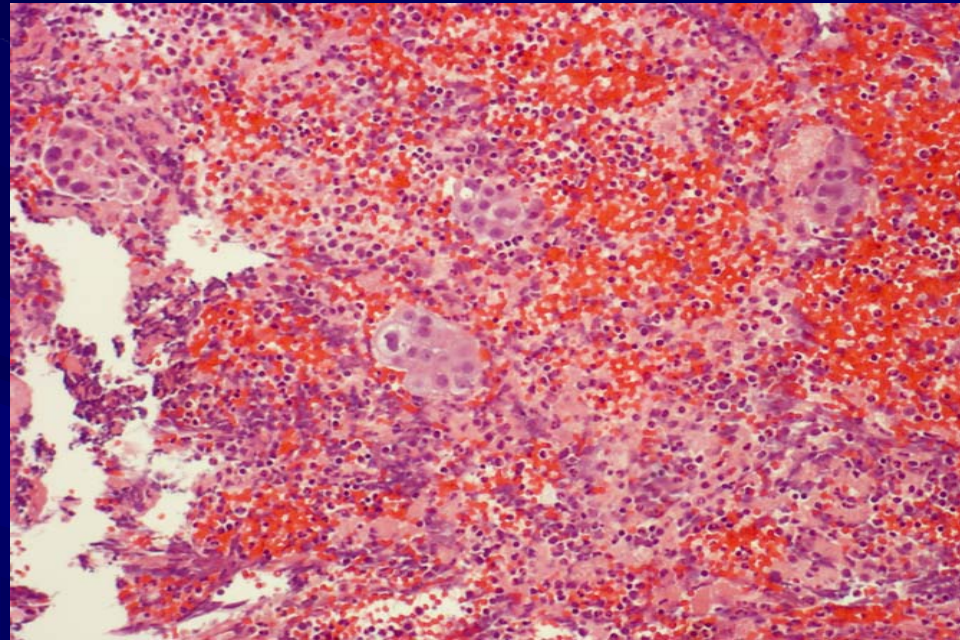
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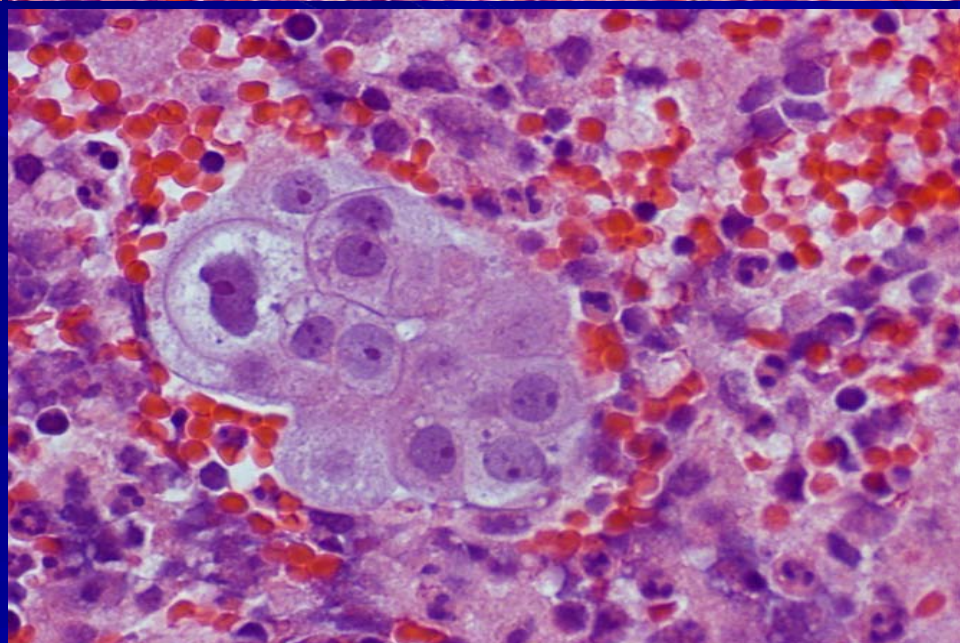
Malignant cells with vacuoles or a hint of clear cell differentiation suggests clear cell carcinoma or a serous or an endometrioid carcinoma with clear cell features



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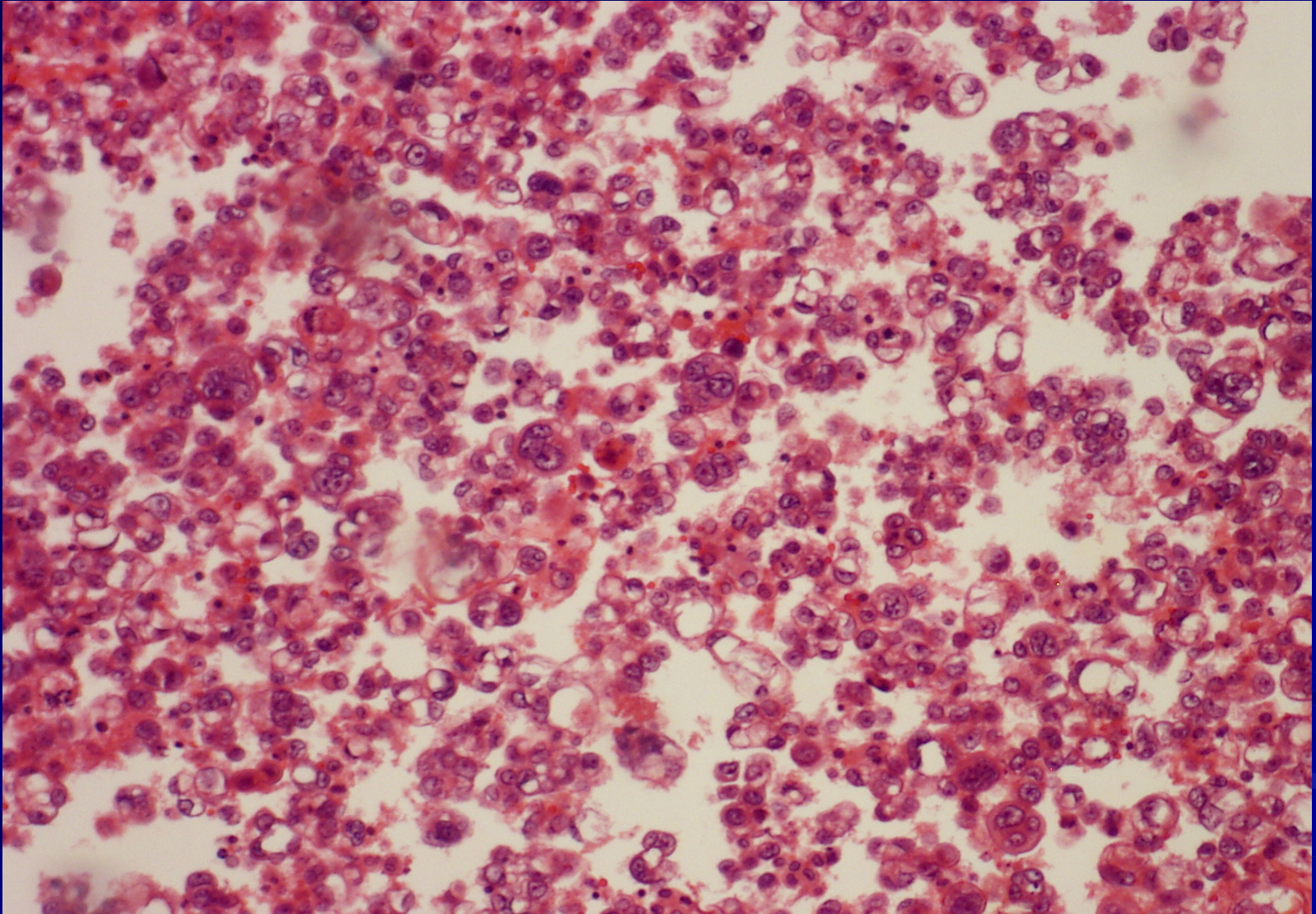


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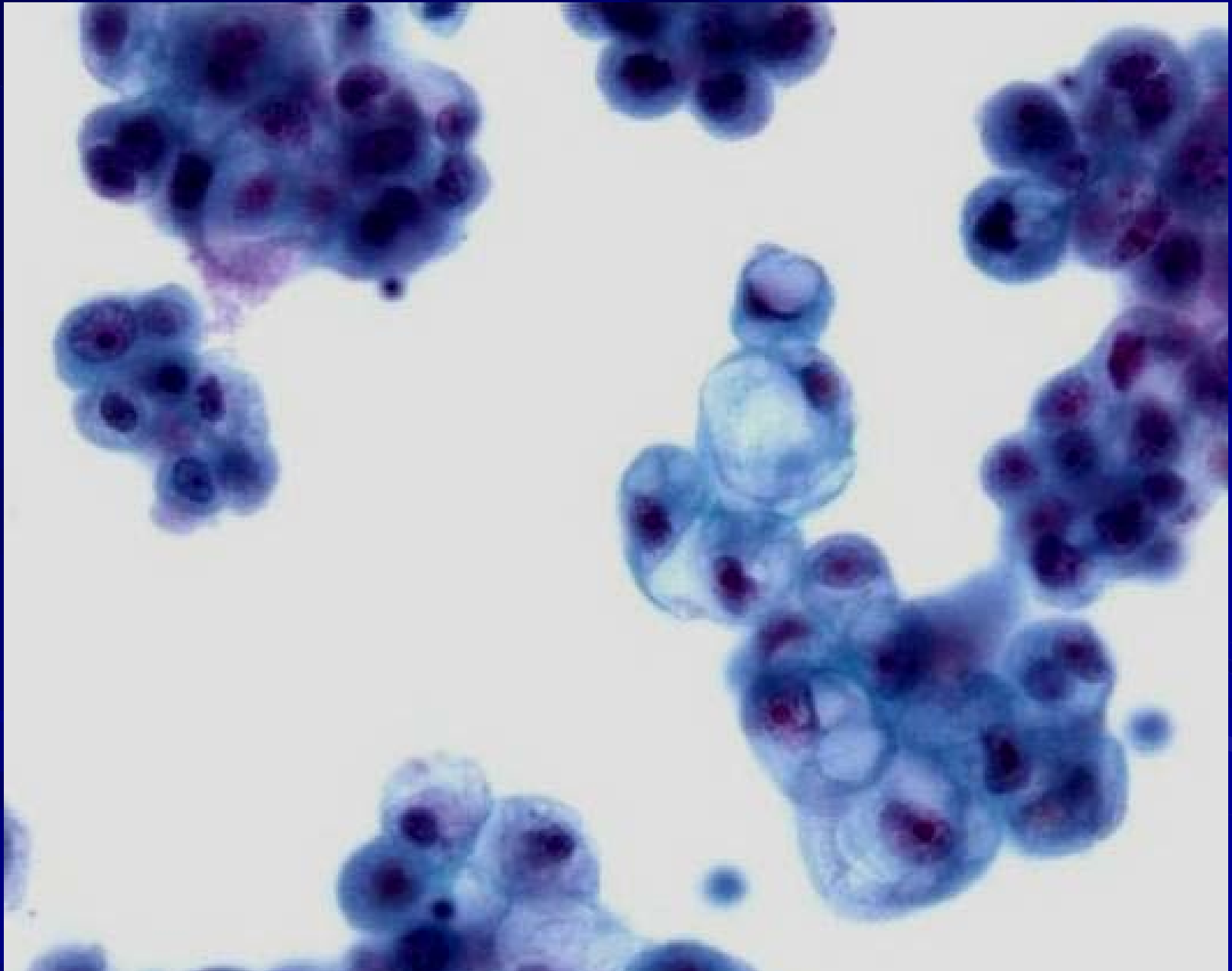


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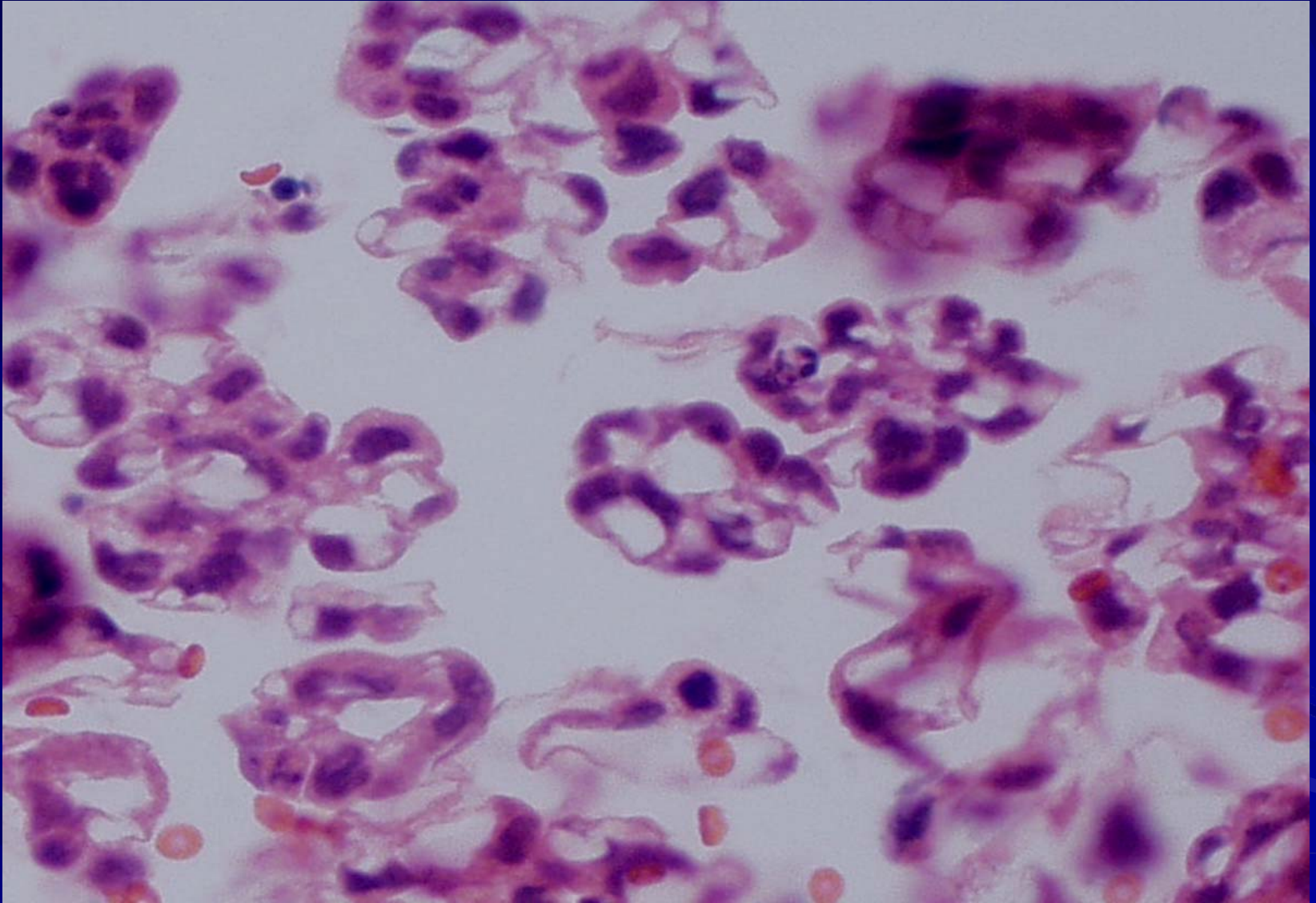
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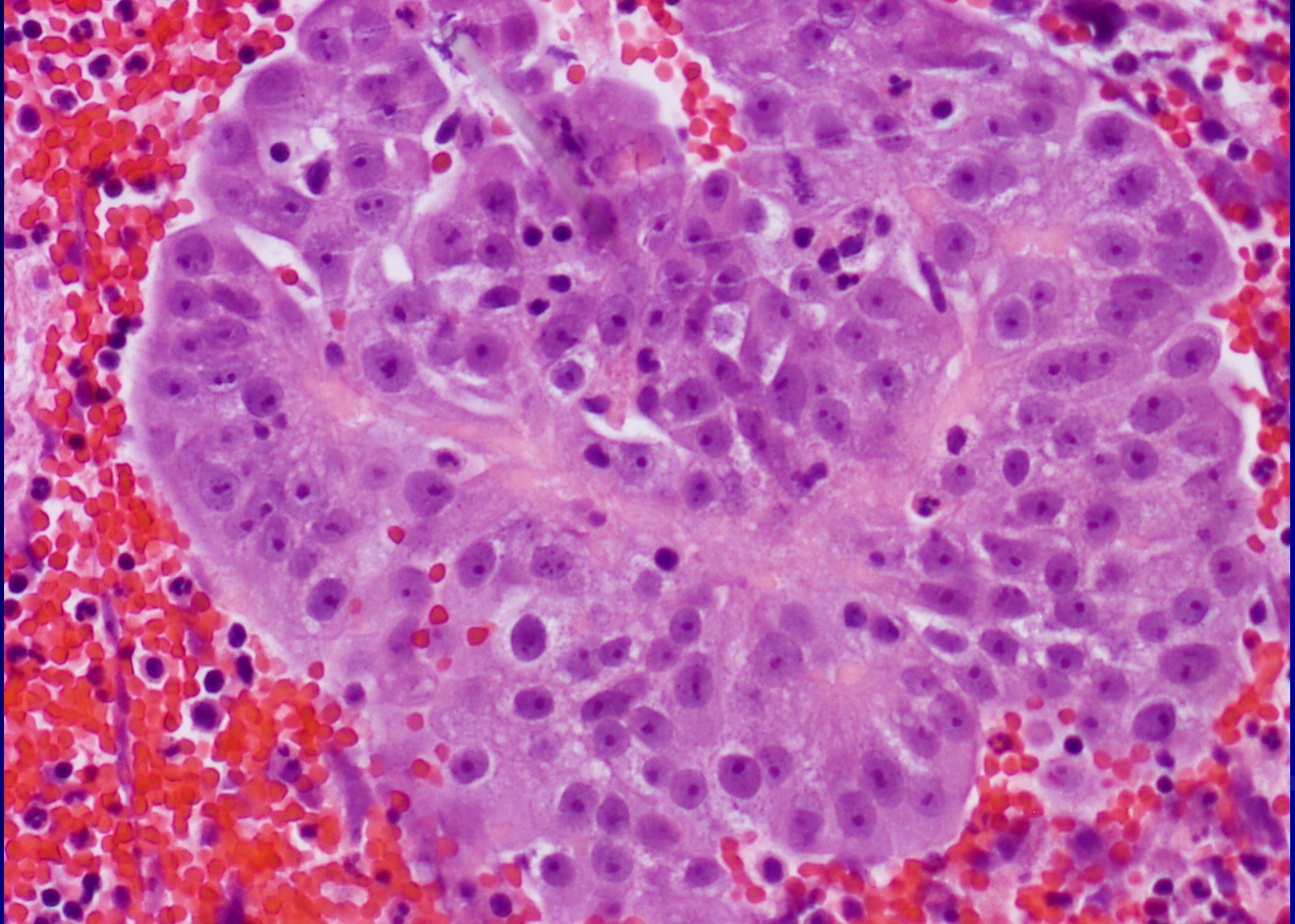
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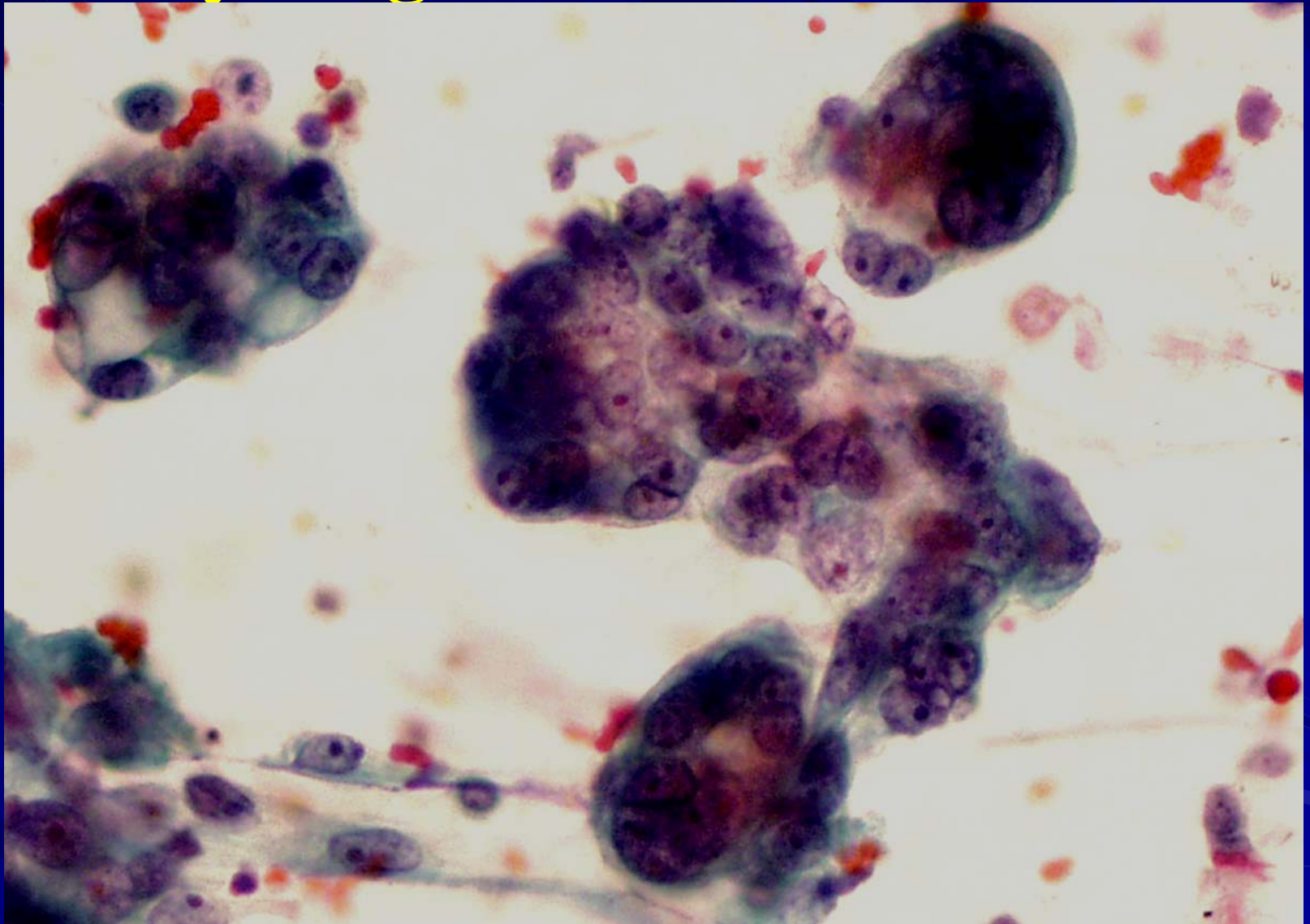


# Cytologic features of OEC



The presence of prominent nucleoli, commonly seen in high-grade serous and clear cell carcinomas

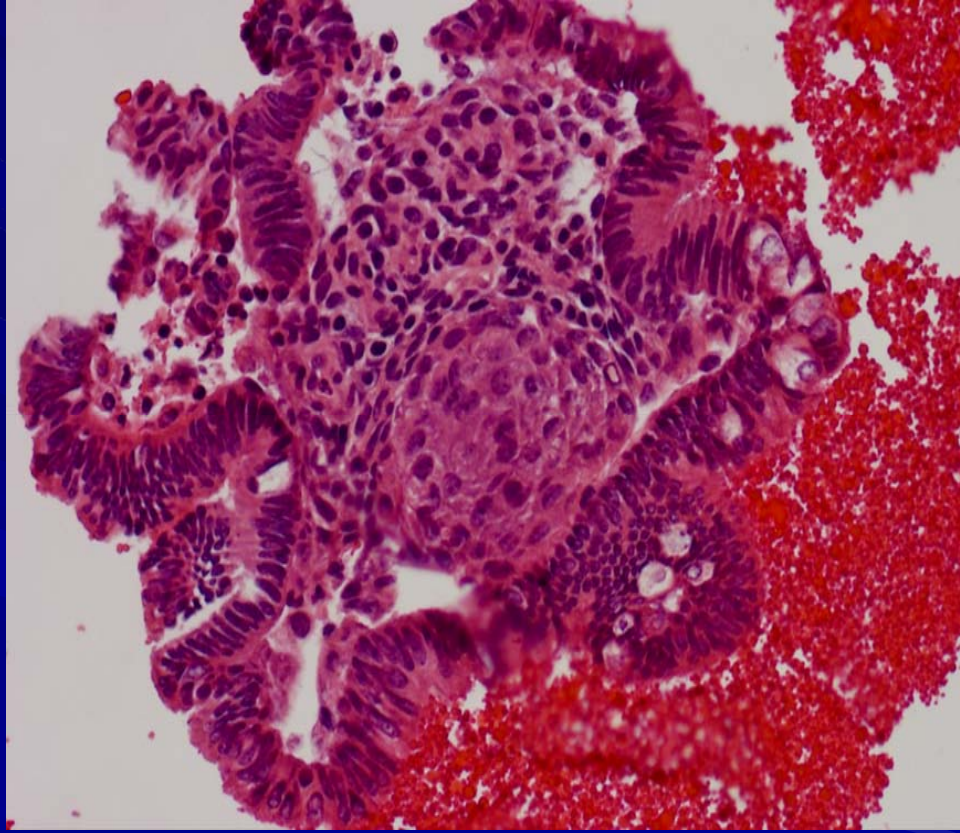
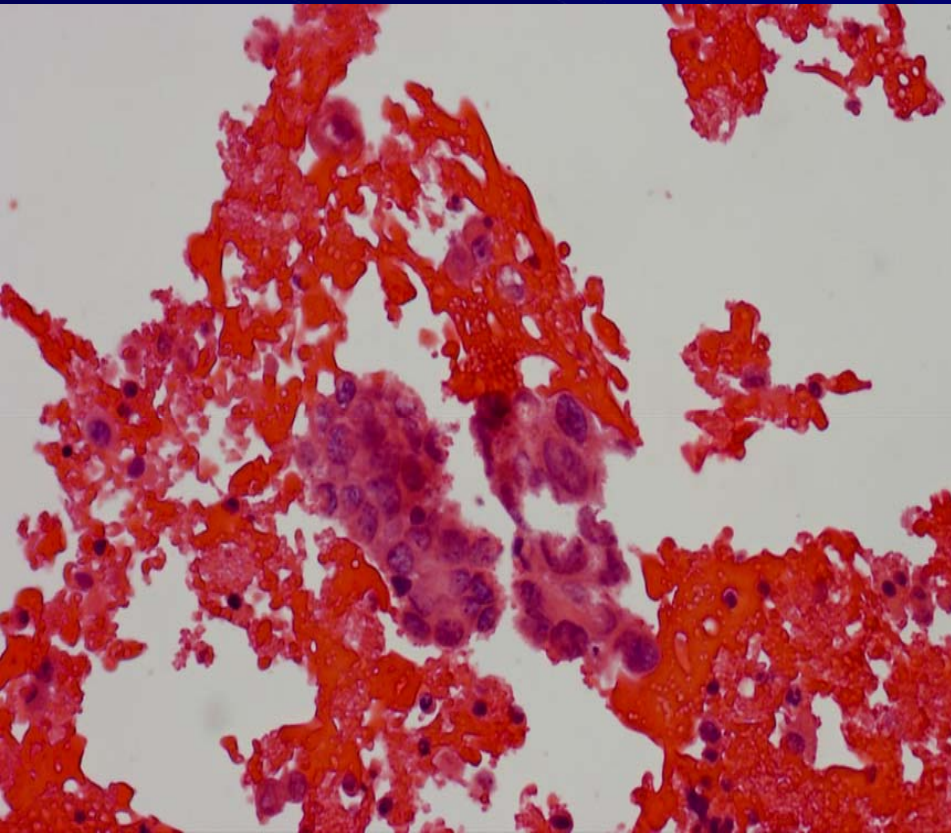
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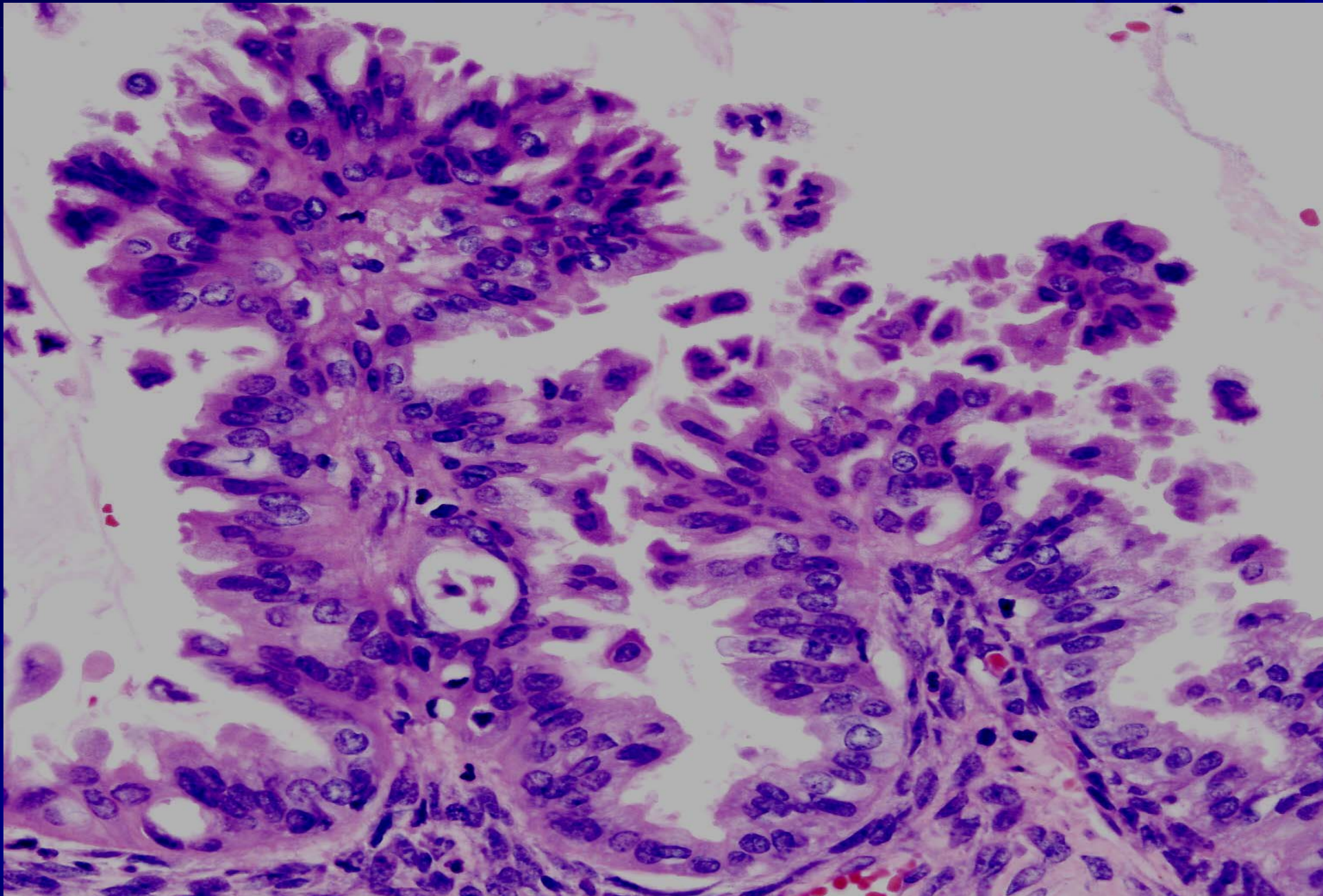
# Cytologic features of OEC



**Squamous metaplasia is indicative of endometrioid carcinoma**

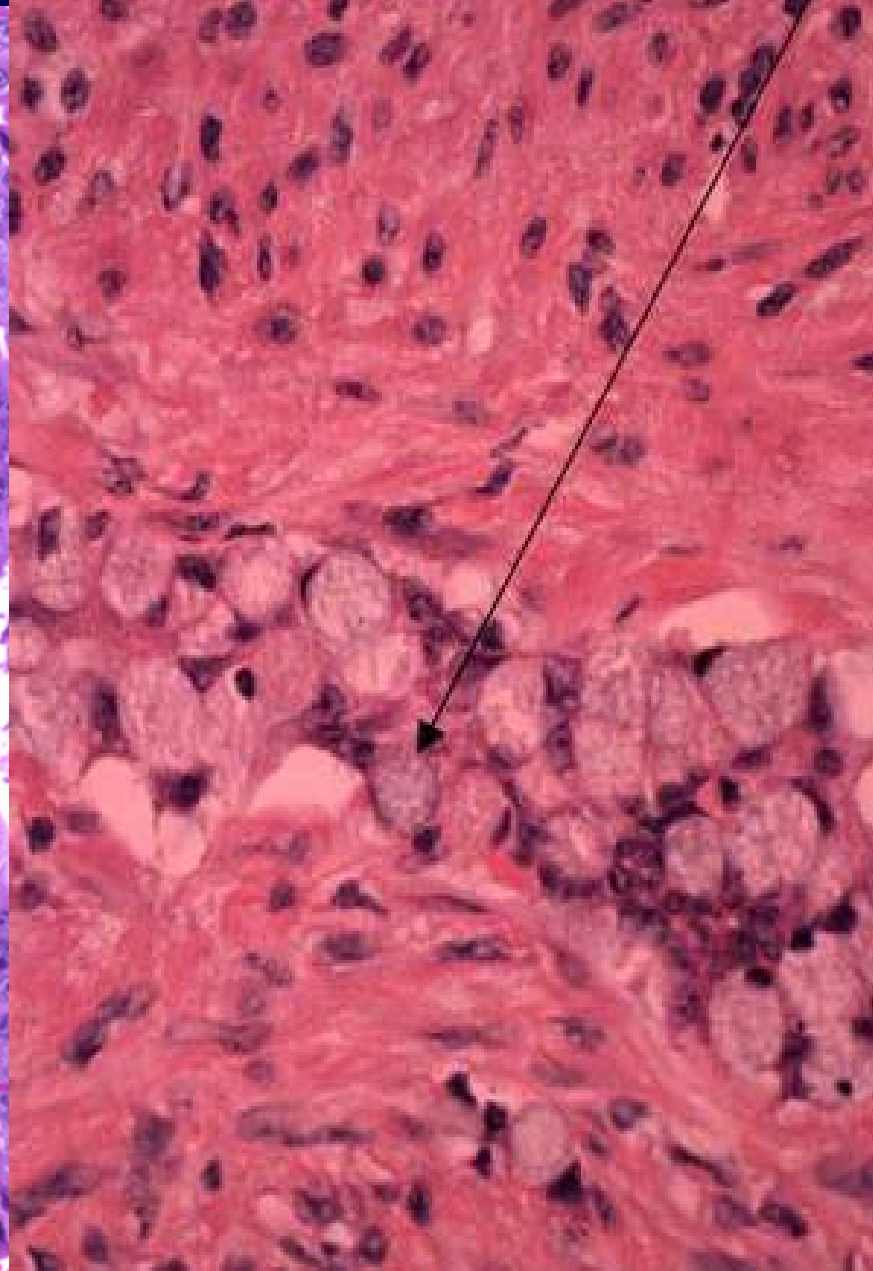
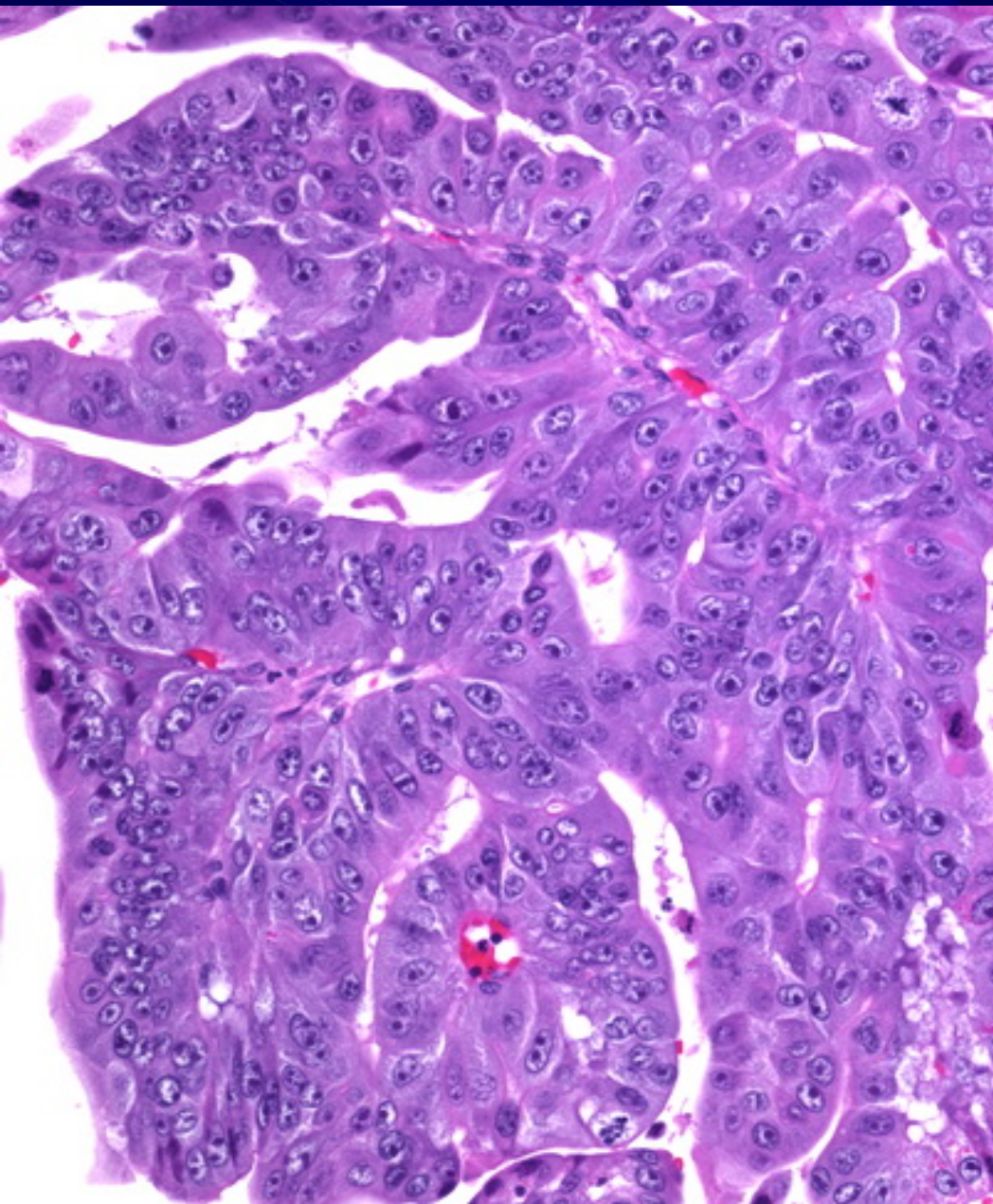


# Cytologic features of OEC





# Cytologic features of OEC



# Biomarkers useful to aid the diagnosis and differential diagnosis

- PAX8
- ER/PR
- p53
- WT1, CA125, BerEP4
- Inhibin, Calretinin
- Breast 2 (GCDFP15)
- CDX2
- CK7, CK20

# PAX8

- PAX genes encode a family of nine well-characterized paired-box transcription factors (PAX1–PAX9), play roles in embryogenesis
- A reasonably good “Mullerian” marker identifying epithelial cells of Mullerian origin.
- Nuclear location
- Can't tell the difference between benign vs borderline or malignant.
- Also positive in kidney and thyroid tissues

# ER and PR

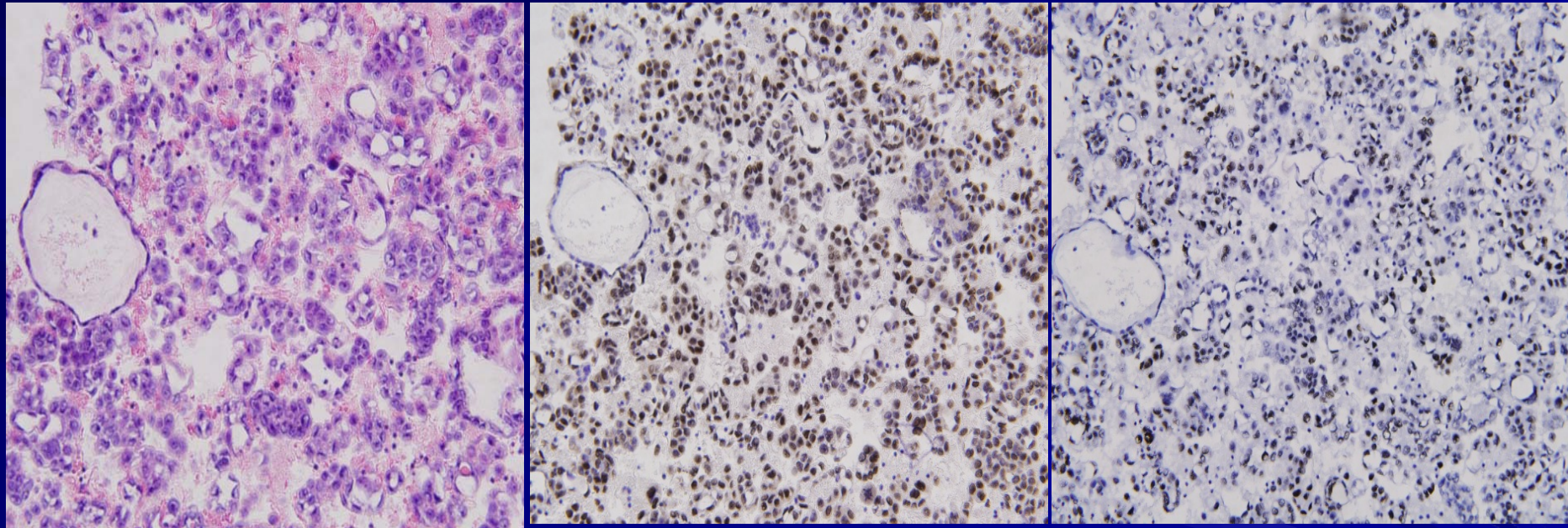
- High-grade serous carcinoma (HGSC):
  - ER is almost always positive: about 90% cases are positive ranging from 20 to 70% tumor cells.
  - PR is almost always negative
- Low-grade serous carcinoma
  - Both ER and PR show various degree of positivity.



# p53

- All or none phenomenon in high-grade serous carcinoma
  - Positive is defined by 75% or more cells stained or majority cancer cells stained in cytology
  - No cancer cell stained
- Various stainings in other cancers mainly depending on the degree of differentiation.

# High-grade serous carcinoma

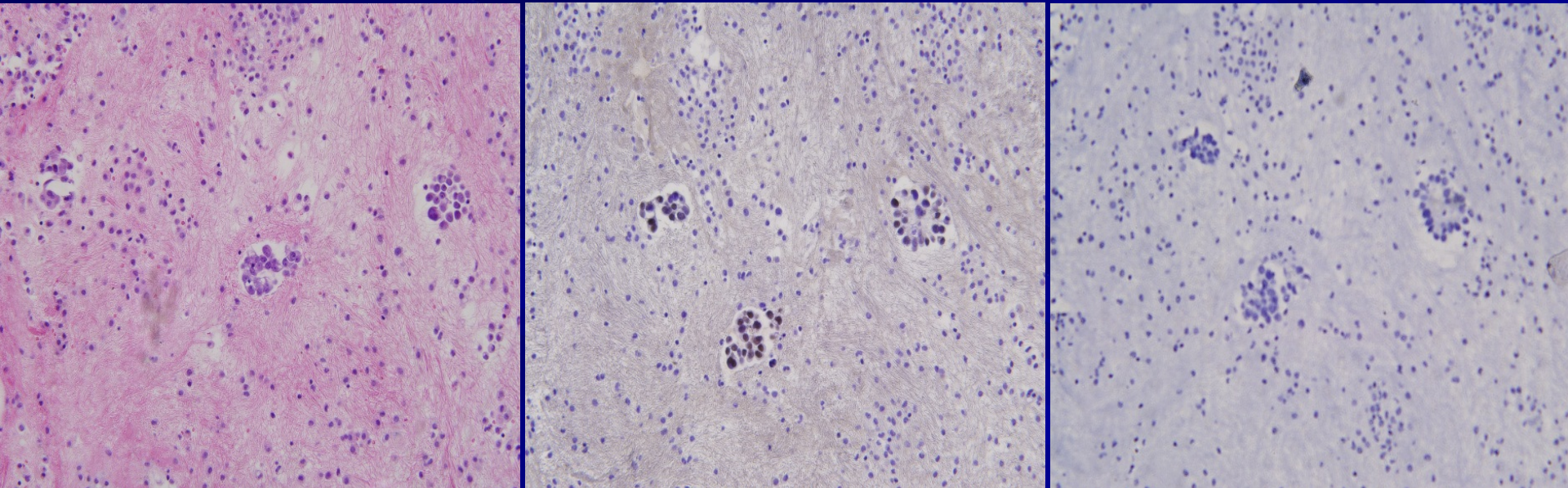


**PAX8**

**p53**



# Borderline tumor or low-grade serous carcinoma



**PAX8**

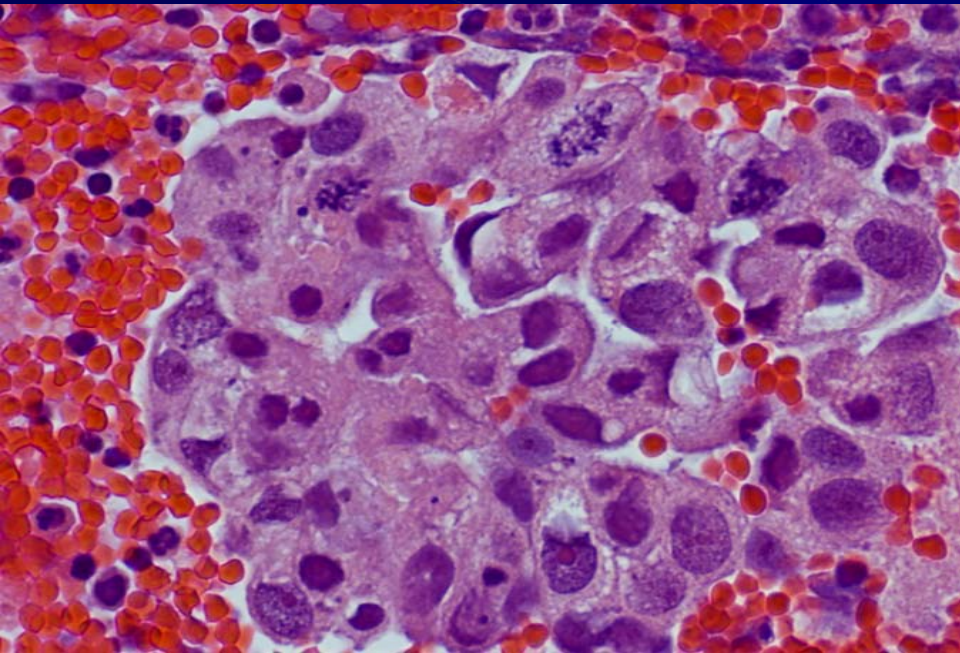
**p53**



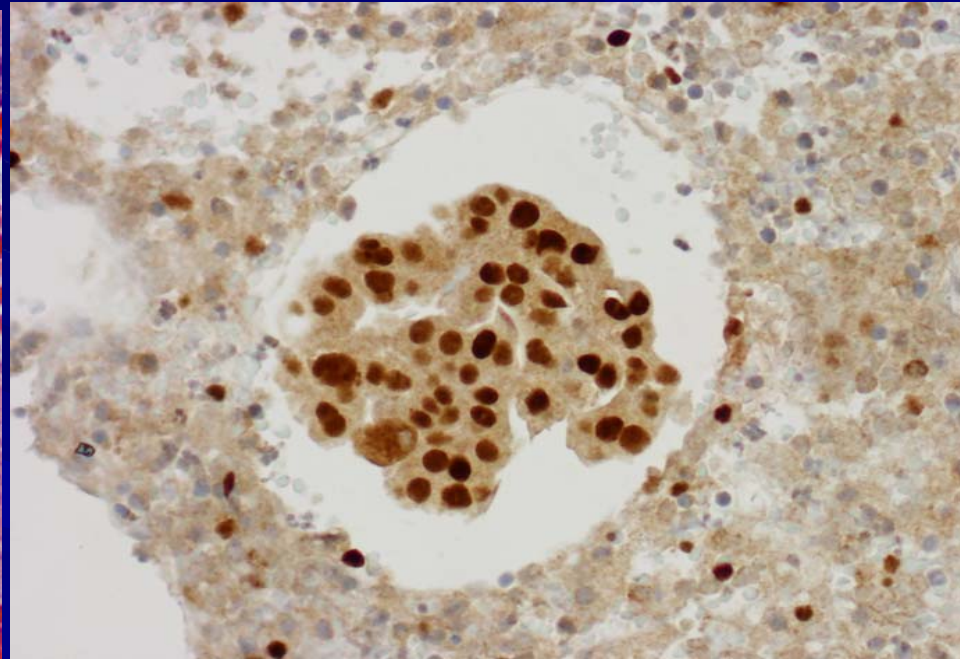
# Common differential diagnoses from pelvic cytology specimens

- Breast cancer metastasis vs OEC
- Mesothelioma vs OEC
- GI vs GYN primary
- Reactive mesothelial cells vs positive cytology
- Endometrioid vs serous carcinoma

# Breast metastasis vs OEC: PAX 8



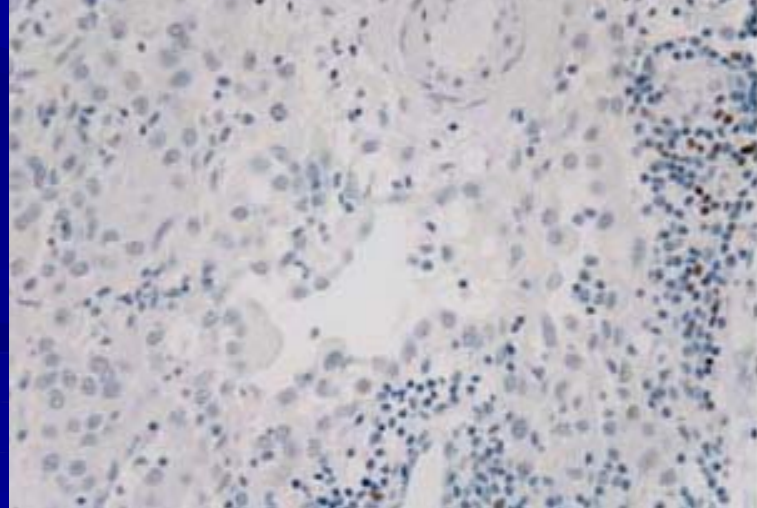
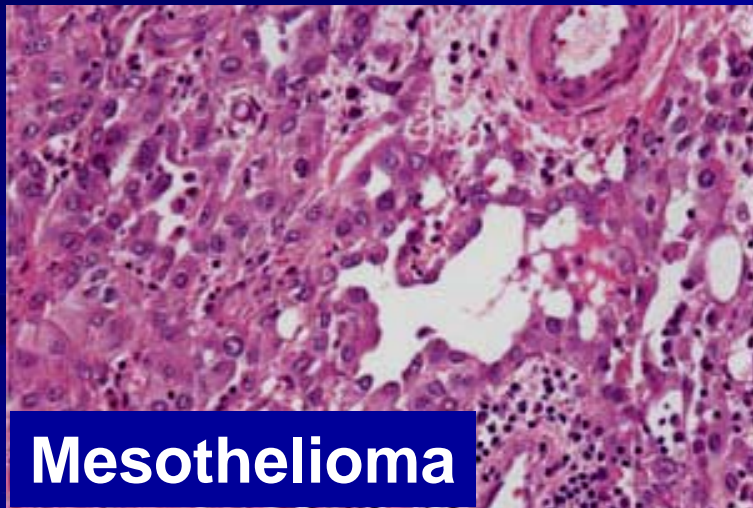
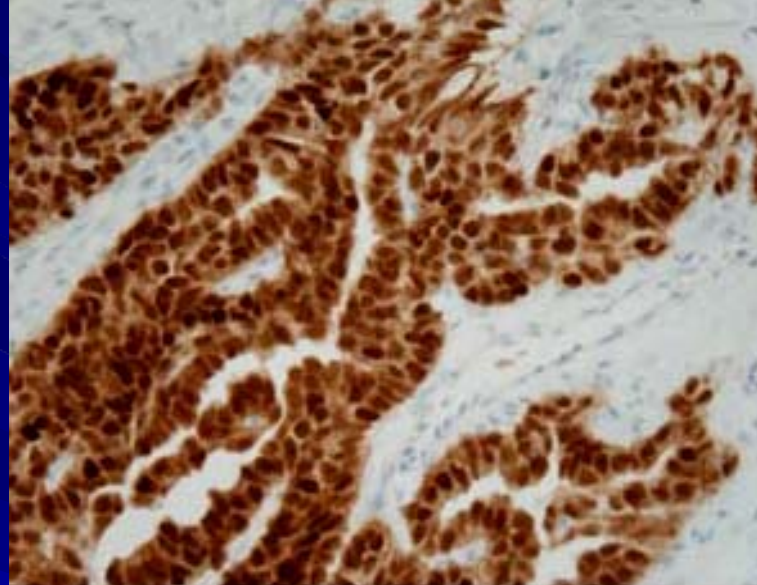
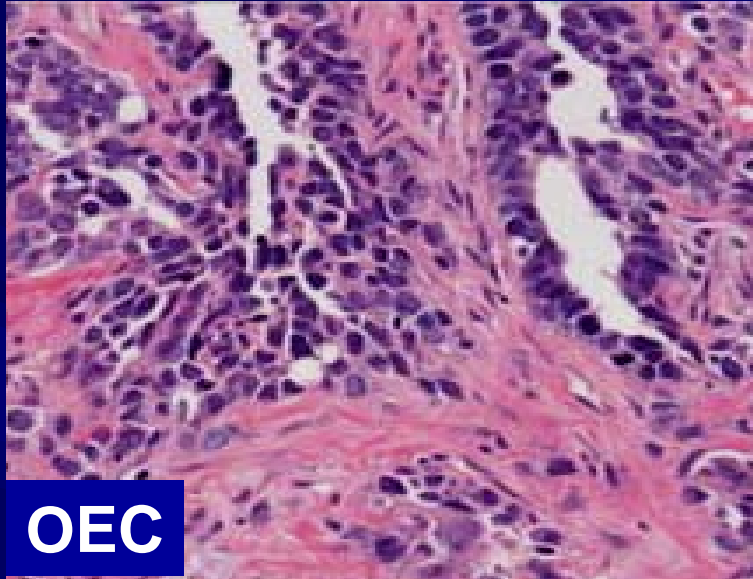
**OEC**



**PAX8**



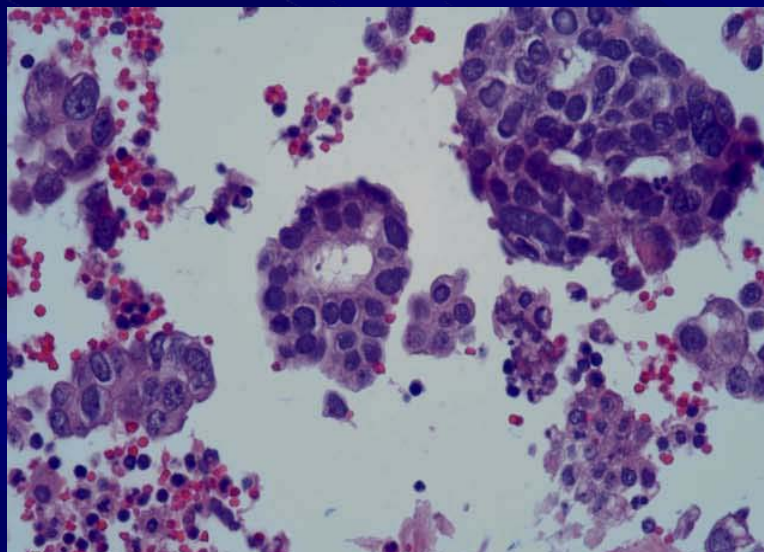
# Mesothelioma vs OEC: PAX8 and Calretinin



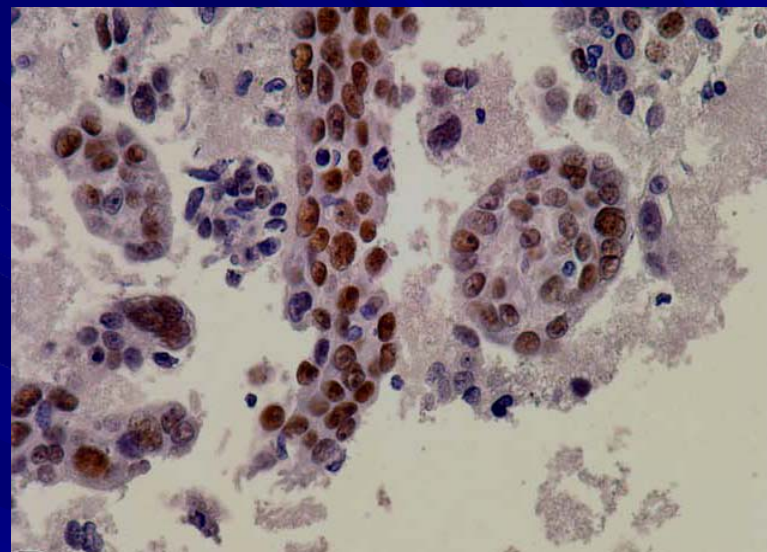


# Colon metastasis vs OEC: PAX8, WT1, ER, CD2, CK7, CK20

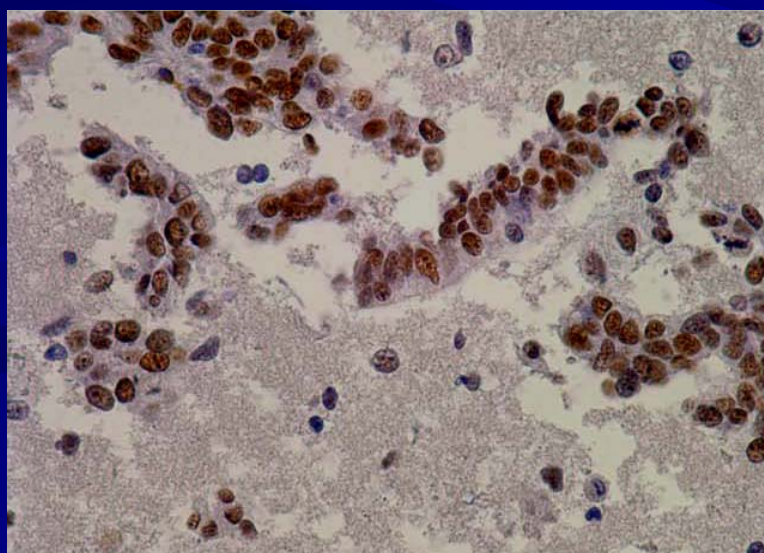
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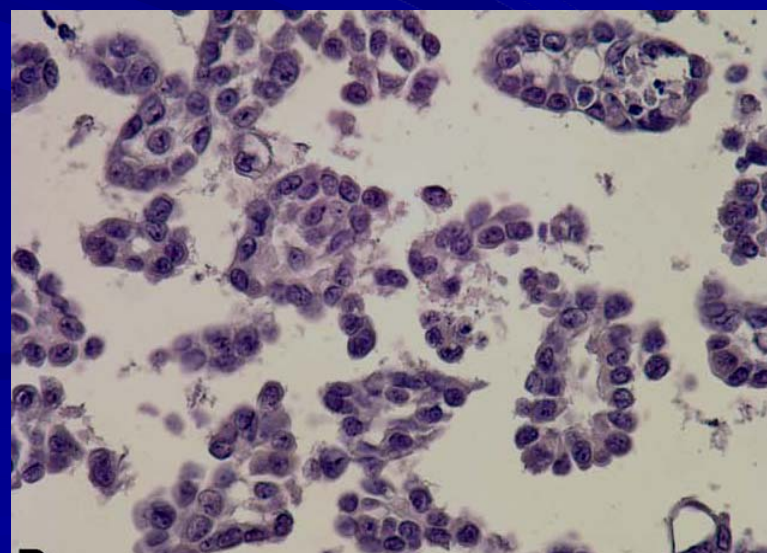
PAX8



WT1

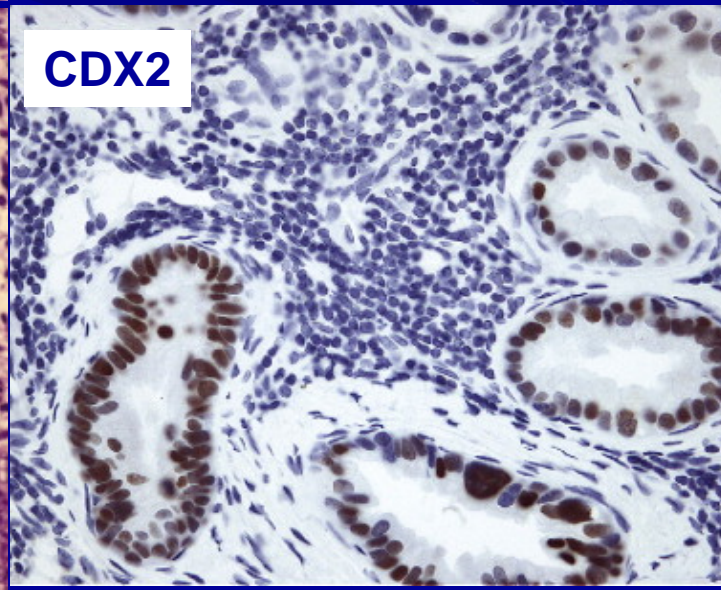
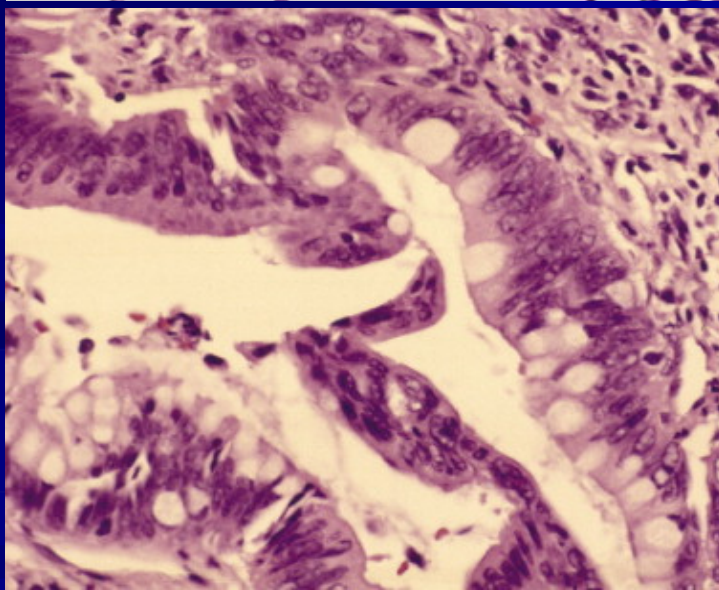
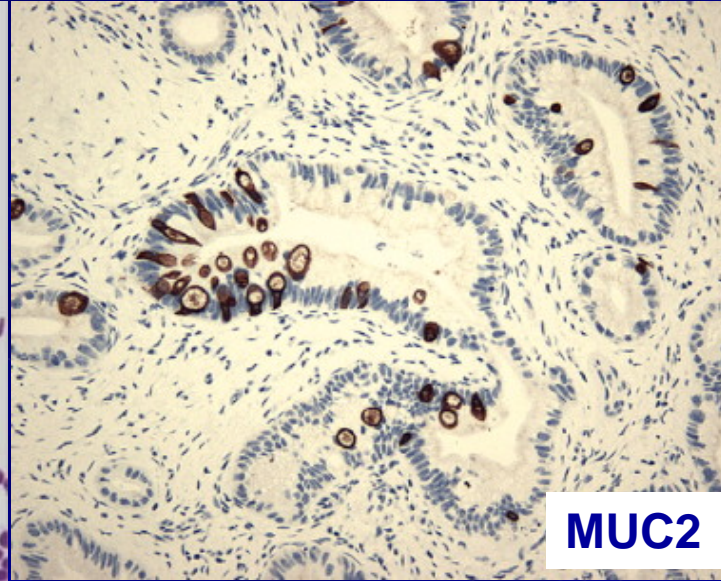
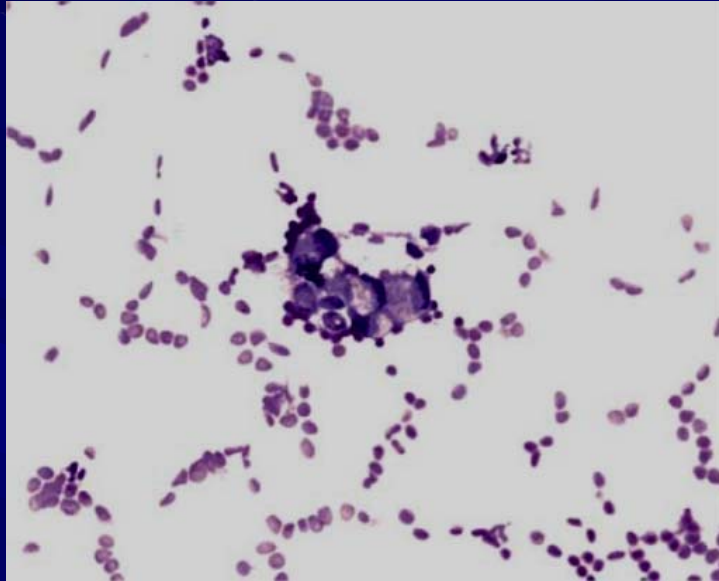


CDX2





# Pancreatic metastasis vs ovarian mucinous carcinoma: PAX8, CDX2



# Reactive mesothelia vs Sex-cord stromal tumors

	<b>Reactive mesothelia</b>	<b>Granulosa cell or Sertoli-Leydig cell tumors</b>
<b>Inhibin</b>	<b>Negative</b>	<b>Positive</b>
<b>Calretinin</b>	<b>Positive</b>	<b>Negative</b>

# Endometrioid vs serous carcinoma

	<b>Endometrioid Carcinoma, G3</b>	<b>HGSC</b>
<b>p53</b>	Focal (typically < 25%)	Diffuse or null
<b>ER</b>	Negative or weak focal (less than 10%)	Apparent, ranging from 10 to 90%
<b>PR</b>	Focal or negative	Negative
<b>WT1</b>	Negative	Positive





*Thank You!*

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