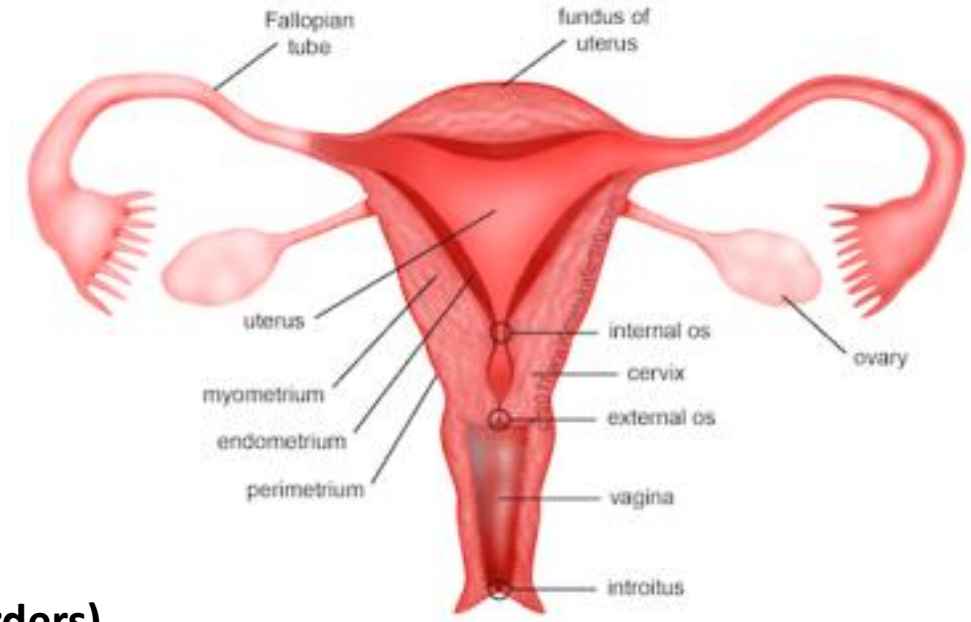
Pathology of the female genital tract

Common illnesses of the female genital tract



- **Before menarche**
  - **Developmental anomalies**
  - **Tumors (ovarial teratoma)**
  - **Amenorrhea**
- **Fertile years**
  - **PCOS, ovarian cysts**
  - **Endometriosis**
  - **Ectopic pregnancy (placental disorders)**
  - **Infections (viral, bacterial, fungal, etc.)**
  - **Tumors (HPV-associated cervical cancer, BRCA-associated ovarian cancer, leiomyoma etc.)**
  - **Infertility**
- **Peri- and postmenopausa:**
  - **Tumors (non HPV-associated)**

Common symptoms

- Menstrual disorders: stronger, painful or **irregular**
- Postmenopausal **bleeding** (endometrium cc!)
- **Dyspareunia**
- Lower abdominal **pain** (younger patients endometriosis!)
- **Ascites** (ovarian cancer)
- Change of **discharge** (infections)
- Effects of **hormone** secreting ovarian tumors (estrogen, testosterone)

Tumors: vulva and vagina

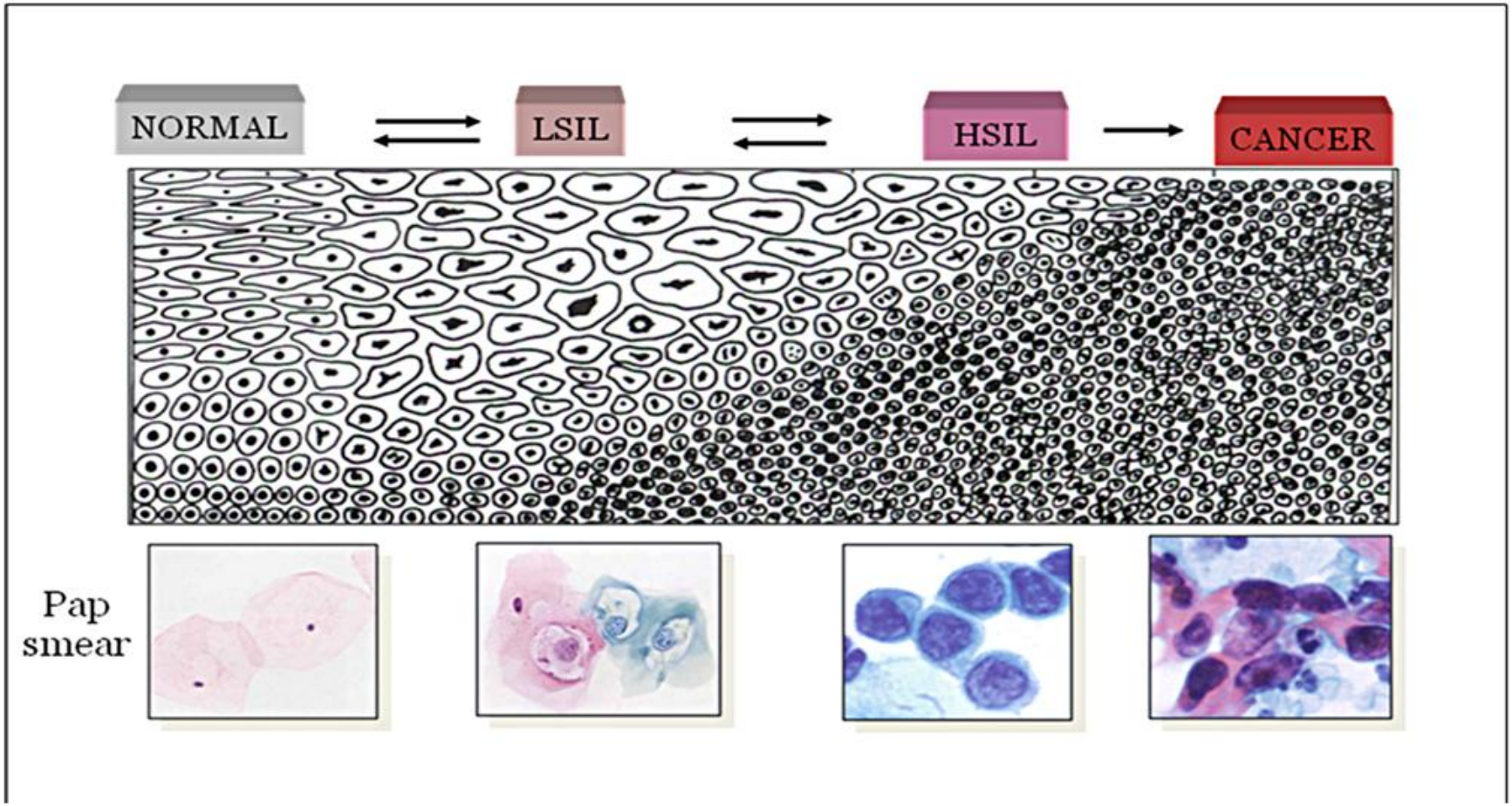
- Precancerous lesions
- Vulva
  - HPV: VIN I-III, LSIL/HSIL
  - **lichen sclerosus** (leukoplakia – white plaques)
- Vagina
  - HPV: VAIN I-III, LSIL/HSIL

- Vulva and vagina carcinoma: **90% squamous cell carcinoma**
  - Vagina: sarcoma botryoides= embryonal rhabdomyosarcoma

Tumors: cervix

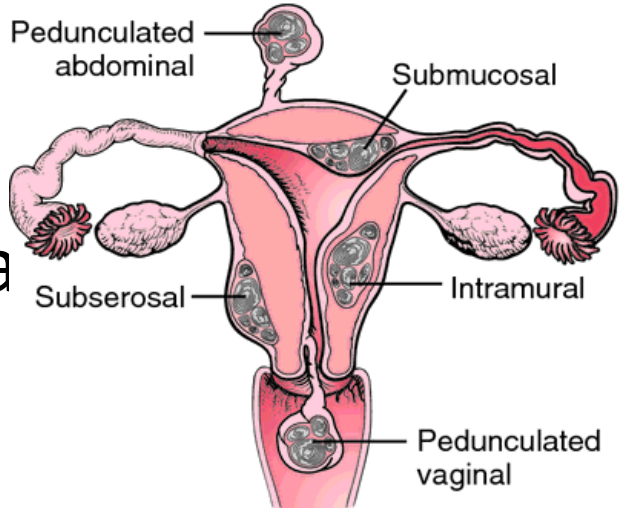
- Precancerous lesion: **LSIL/HSIL** (HPV!)
- Invasive cervical carcinoma: mostly squamous cell carcinoma
- **Prevention:** Vaccine for HPV and regular cervical carcinoma screening

(See lecture&practice from previous semester)



Tumors: Corpus uteri

- **Smooth muscle tumors**: leiomyoma and leiomyosarcoma



- Tumors of the endometrium:
  - **Adenocarcinoma**
  - **Stromal sarcoma: very rare**

Tumors: ovaries

- **Epithelial** tumors:
  - **Serous**
  - **Mucinous** (can contain endocervical, intestinal and endometrial epithelium) >>> *pseudomyxoma peritonei*
  - **Endometrioid** tumors
  - **Brenner tumor**

  - **Benign, borderline and malignant forms!**

Tumors: ovaries

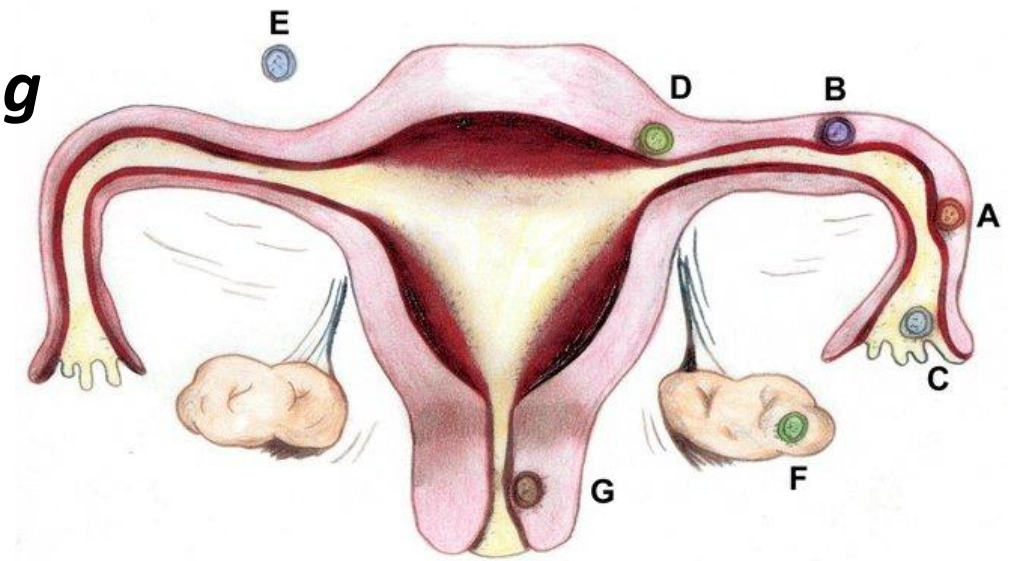
- **Germ cell tumors**
  - Teratomas (benign mature, malignant immature, special: struma ovarii)
  - Dysgerminoma
  - Choriocarcinoma
  - Yolk sac tumor
- **Sex cord- stromal tumors** – derived from the sex cord of the embryonic gonad
  - Granulosa - theca cell tumors
  - Fibrothecomas
  - Sertoli – Leydig cell tumors
- **Metastasis**
  - Mostly bilateral
  - Krukenberg tumor : signet cell carcinoma of the stomach

Practice slides

- Ectopic pregnancy
- Endometriosis
- Endometrium hyperplasia
- Endometrium carcinoma
- Follicular cyst
- Ovarial tumors

Ectopic pregnancy

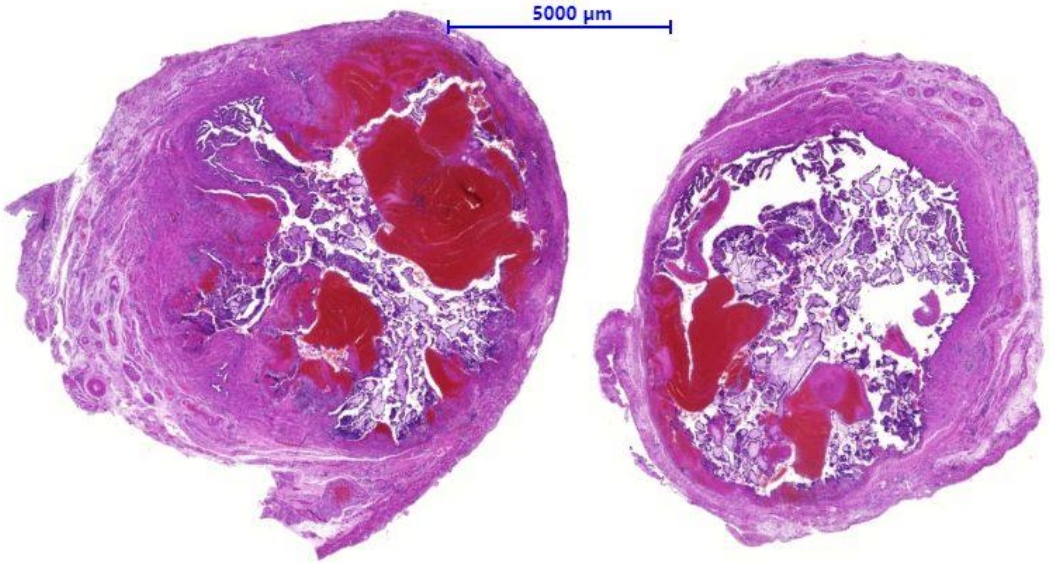
- Inplantation of the fetus in the **fallopian tube**, **cervix, ovaries, abdominal cavity**
- Must exclude when examining young female patients with abdominal pain!
- Tubal pregnancy complications:
  Intratubal hematoma
  intraperitoneal bleeding
  acute abdomen



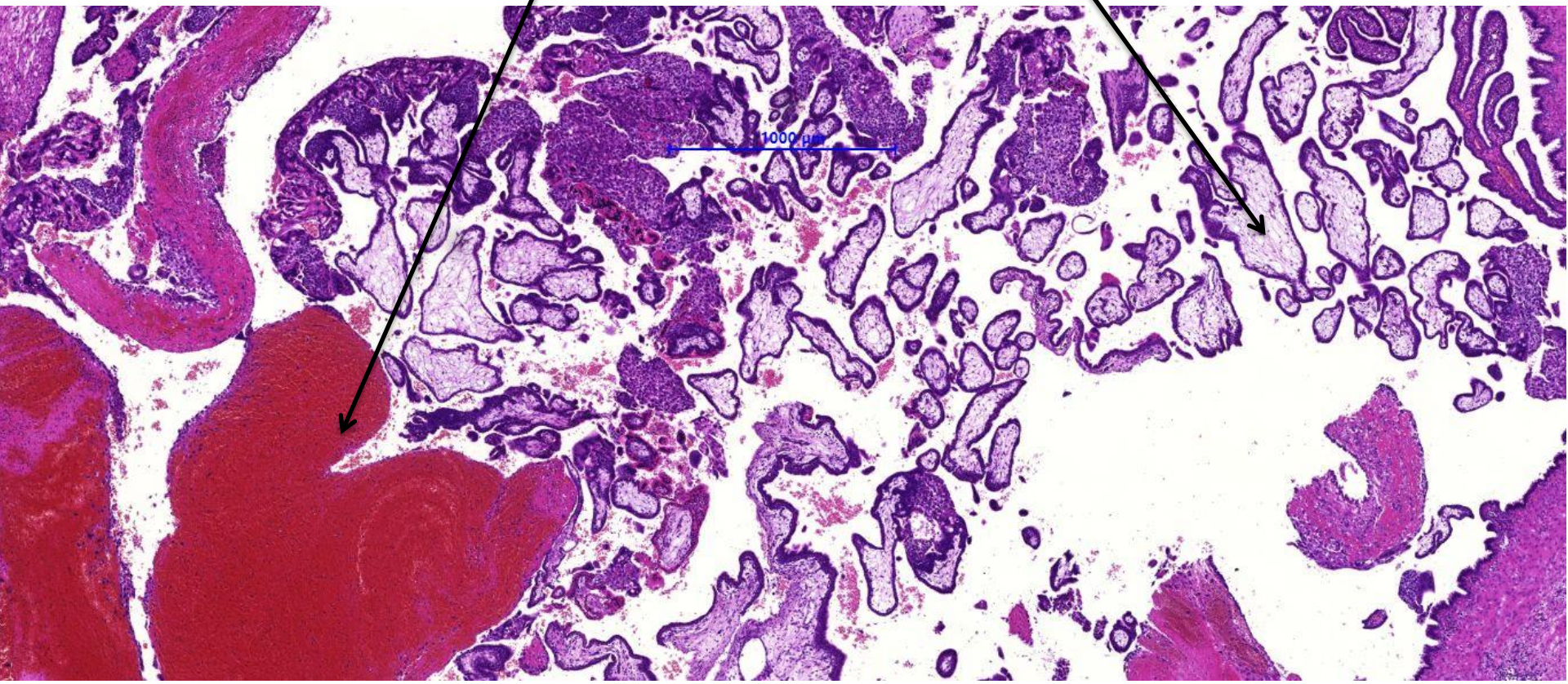
Ectopic pregnancy: ultrasound and macroscopy

Extrauterine gravidity - microscopy

- Placental tissue: chorionic villi, decidua, cytotrophoblast, syncytiotrophoblast
- Hemorrhage
- Curettage: decidua, Arias-Stella reaction



Hemorrhage, chorionic villi



Structure of chorionic villi: outer layer of syncytiotrophoblast and an inner cytotrophoblast layer (+blood vessels, macrophages)

Endometriosis

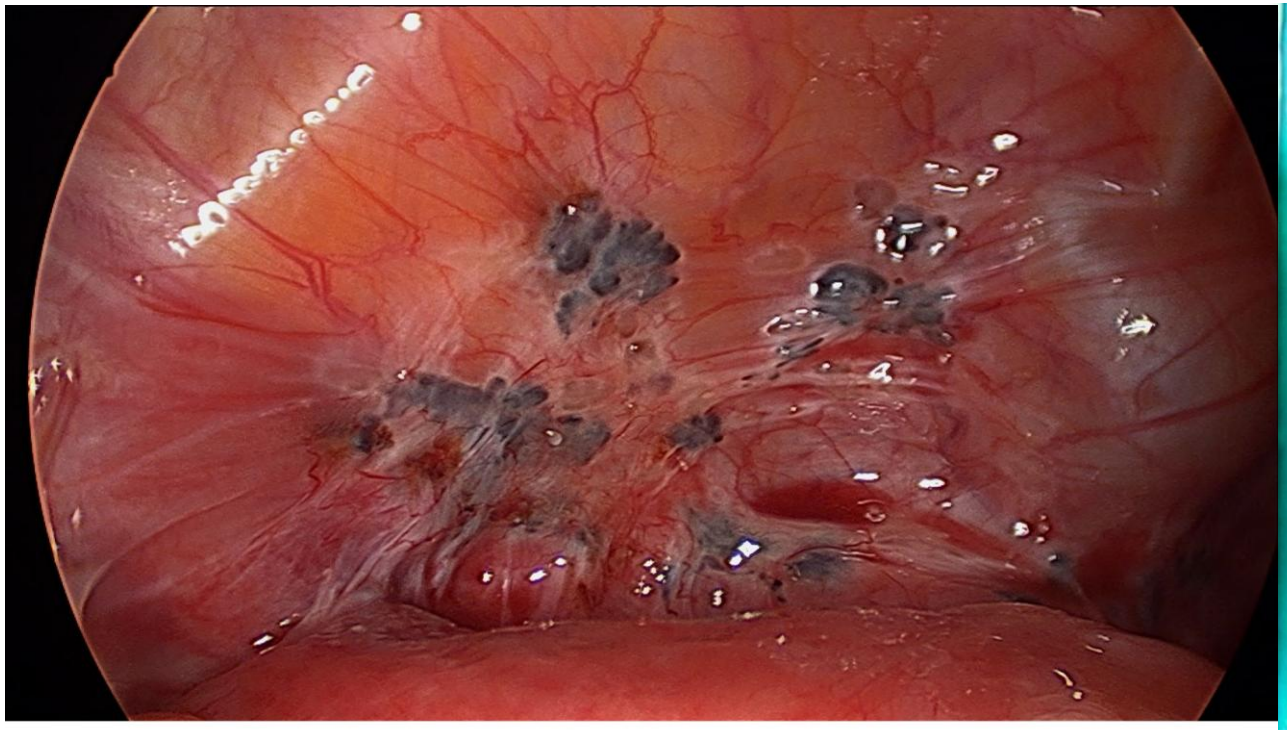
- Common illness of young women
- Presence of functioning endometrial tissue in an atypical localization
- Difficult to treat
- Common cause of infertility
- **Development**:

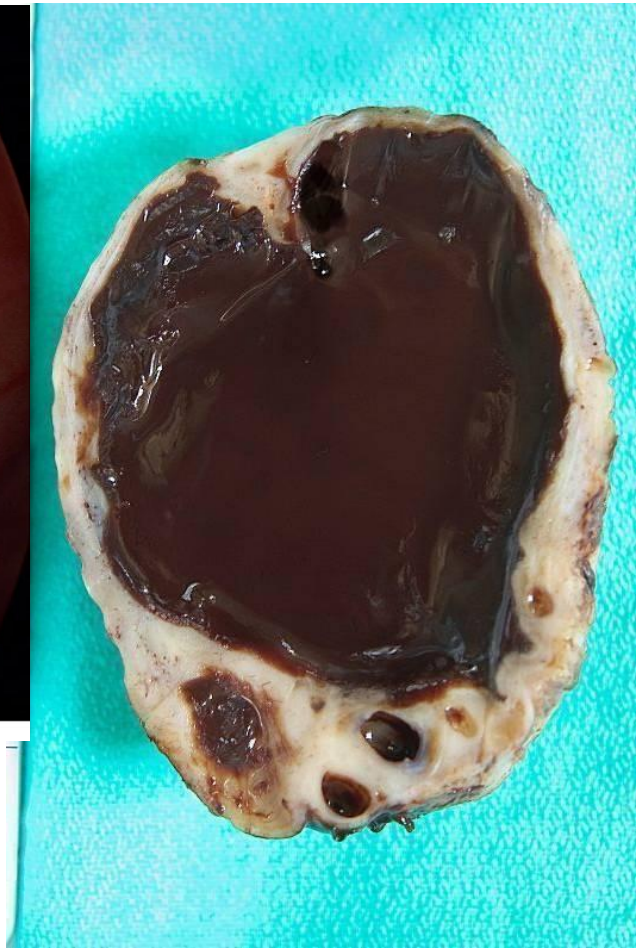
  - Retrograde menstruation through the fallopian tubes, with subsequent implantation of endometrial tissue in the peritoneum (regurgitation theory)
  - Hematogenous spread of endometrial tissue during menstruation (vascular invasion theory)
  - endometrium arises directly from coelomic epithelium (metaplastic theory)

Endometriosis

- **Symptoms**: lower abdominal pain, that increases with menstrual cycle pain
- **Localization:**
  - Uterus (deeper layers): adenomyosis
  - **Fallopian tube**: infertility
  - **Ovaries**: **chocolate cyst** (colour due to hemosiderin from previous bleedings)
  - **Peritoneum**: **adhesion**, pain
  - **Cesarian section scar**
  - **Inguinal canal**
  - **DIE** (deep infiltrating endometriosis): rectum (**hematochezia**), bladder (**macrohaematuria**), vaginal wall, sacroiliac ligaments
  - Extra pelvical organs (rare)

Endometriosis as seen during laparoscopy and macroscopically (chocolate cyst)

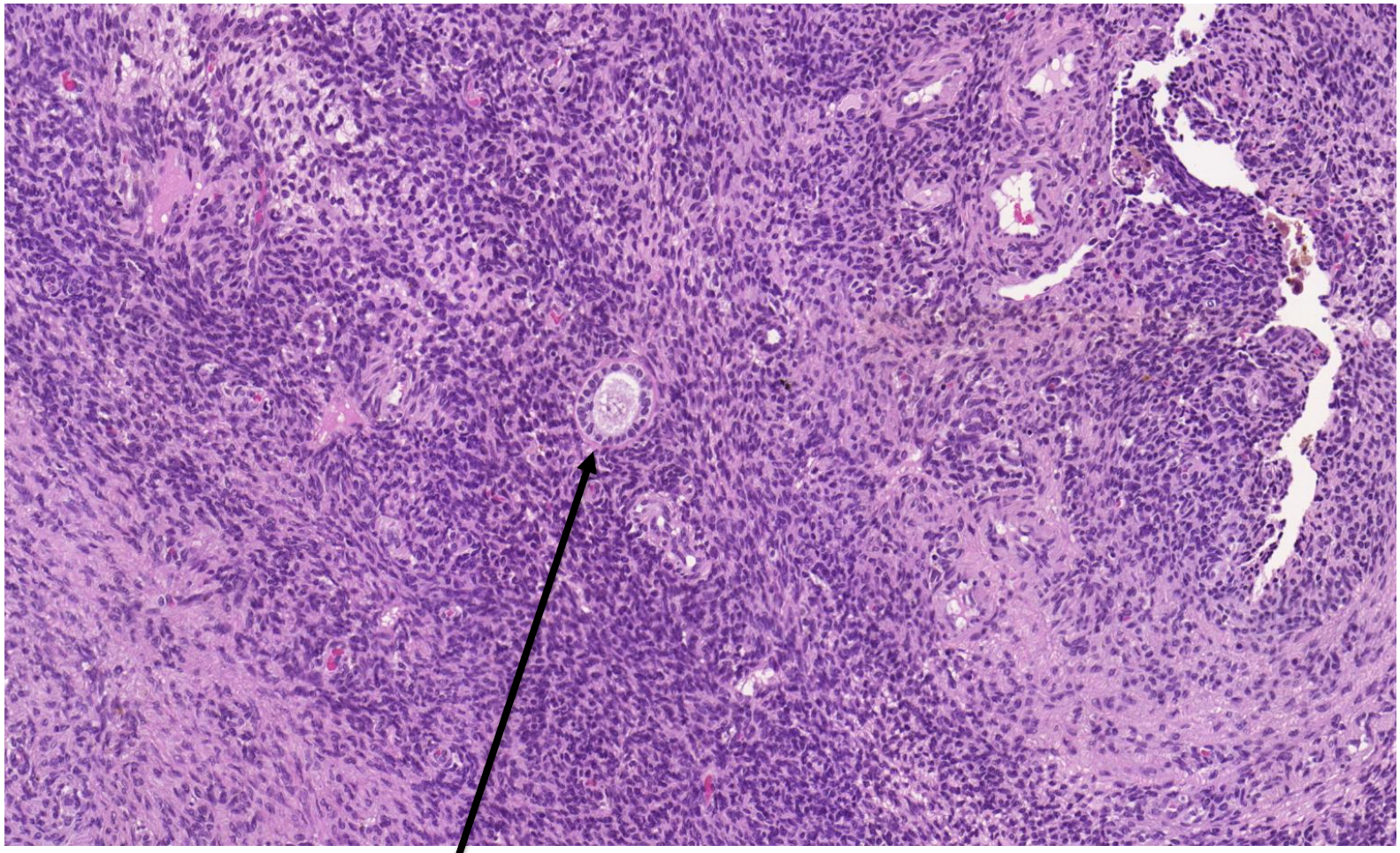




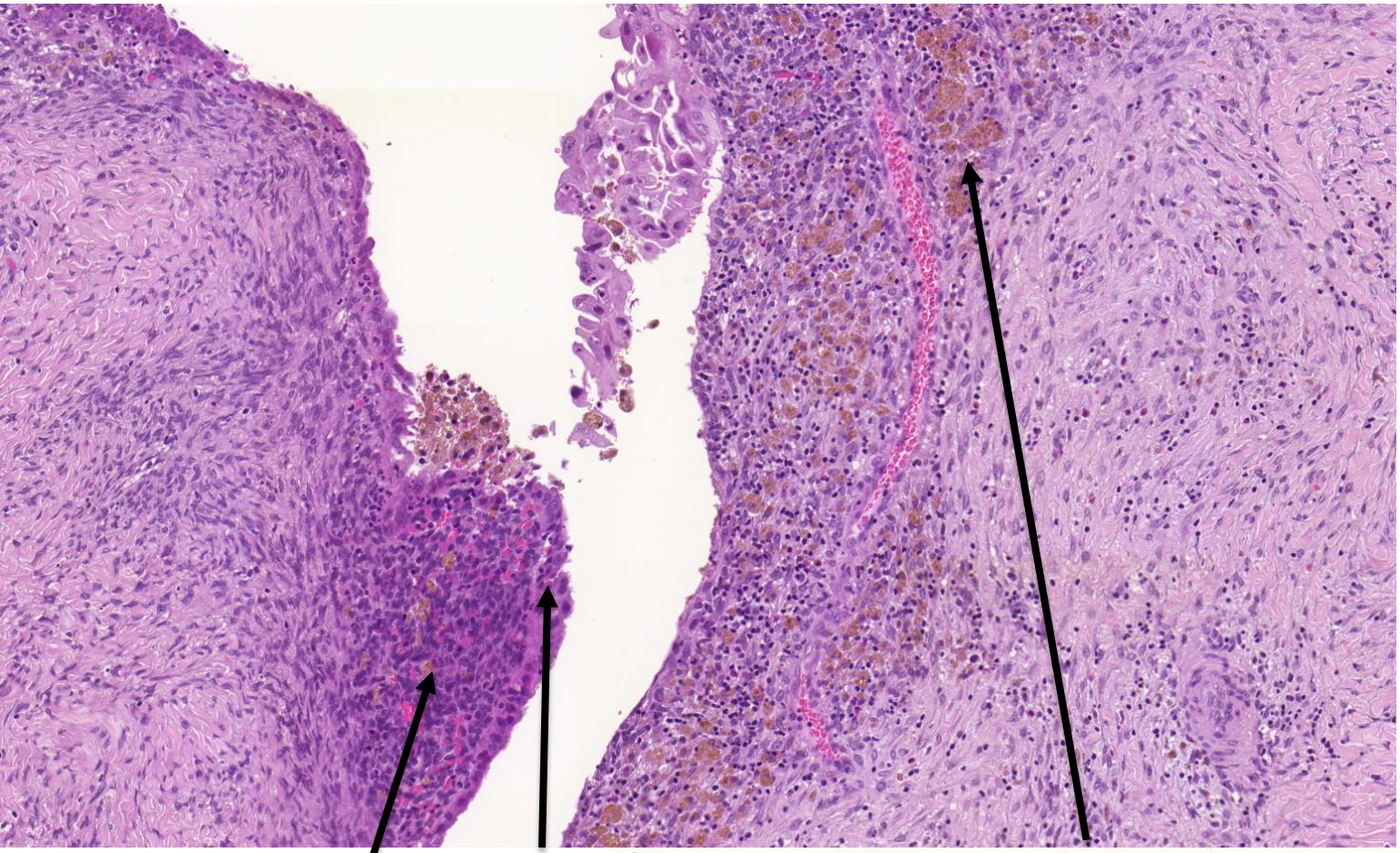
Endometriosis - microscopy

- Endometrial epithelium
- Endometrial stroma
- Haemosiderin (macrophages)

Where are we?

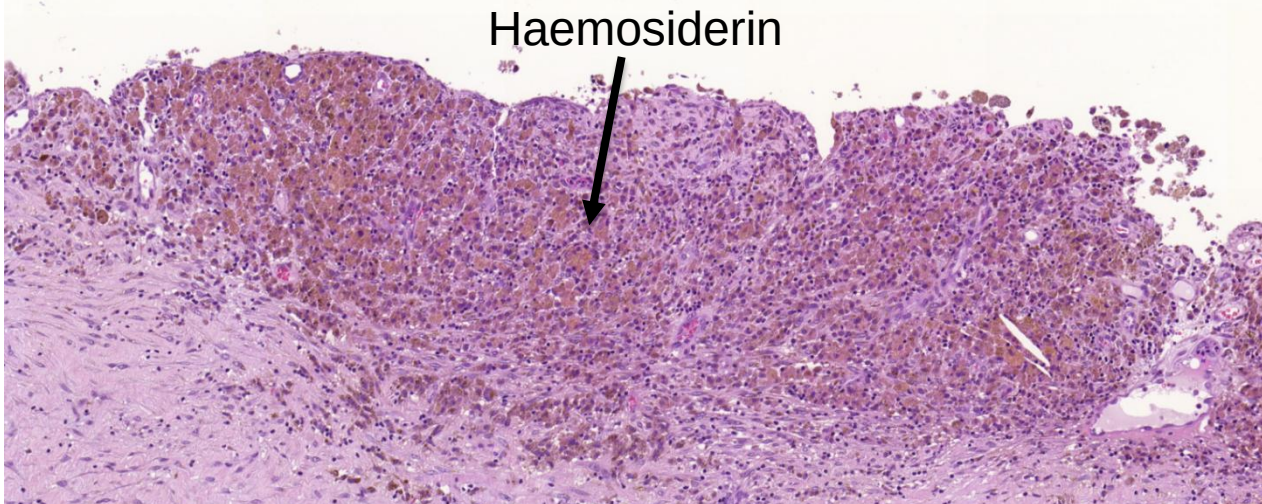


Ovarium: secundary follicule



Endometrium stroma and epithelium

Haemosiderin



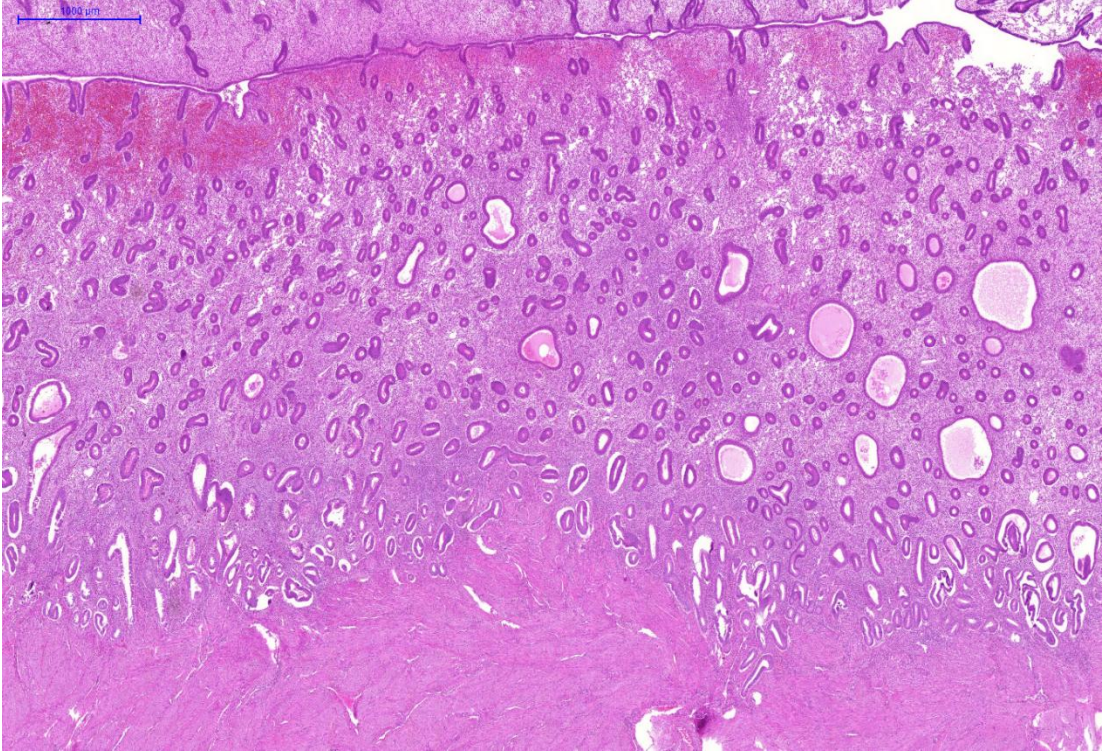
Endometrium hyperplasia

- **Simplex** hyperplasia (without atypia)
- **Complex** hyperplasia (without atypia)
- Hyperplasia with **atypia = EIN**: endometrial intraepithelial neoplasma

- Cause: **Prolonged estrogen stimulation** *(anovulation, PCOS, estrogen secreting ovarian tumor, hormone containing medication, obesity)*
- Symptoms: irregular bleeding
- Endometrium carcinoma risk increases with the severity of the atypia

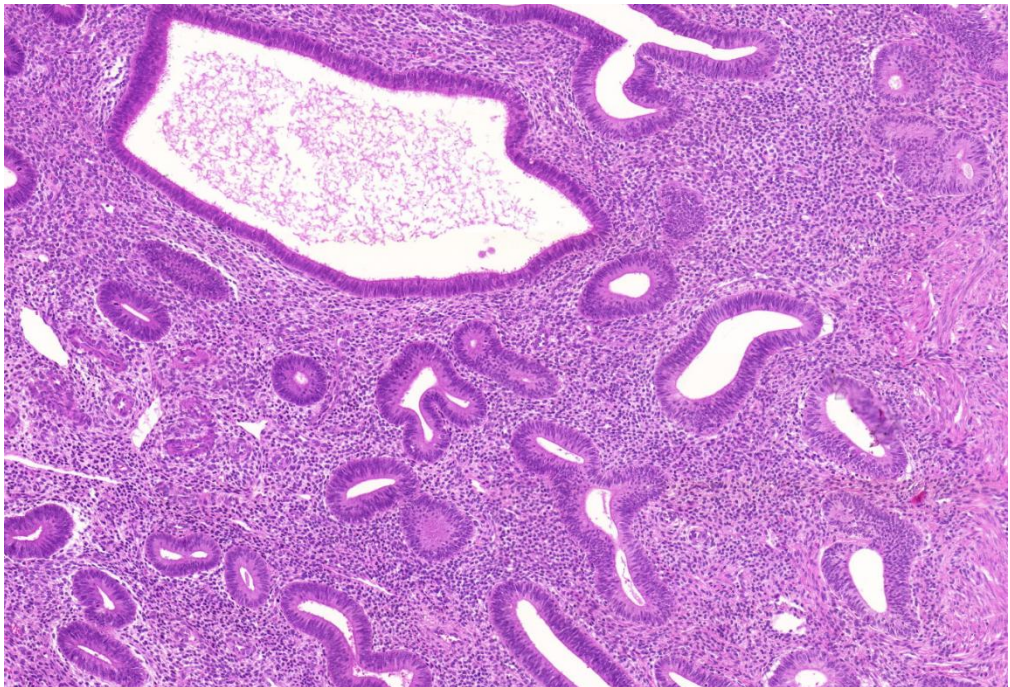
Simplex hyperplasia of the endometrium

- Macroscopy: **Endometrium is thickened or polyp formation**
- Microscopy: **Gland/stroma ratio increased, simplex (=round/oval) often cystic glands** (not confluent)
  - Without cellular atypia!



Thickened endometrium

Gland/stroma ratio increased
cystic glands

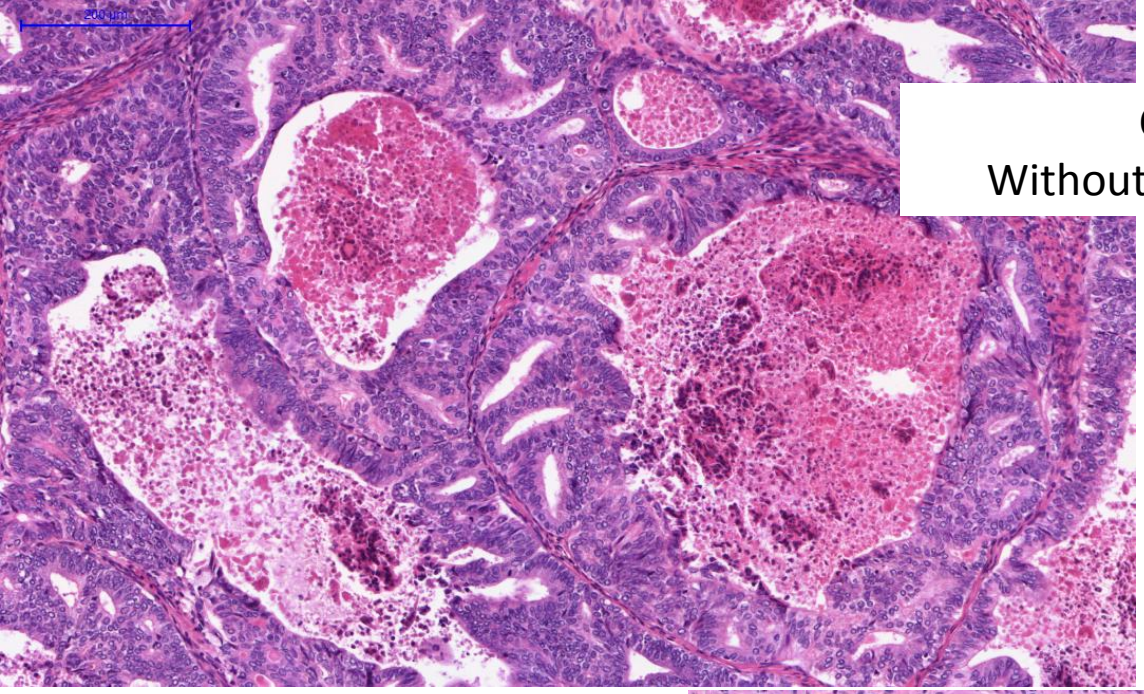


Carcinoma of the endometrium

Characteristics	Type I	Type II
Age	55-65 yr	>70 yr
Etiology	Unopposed estrogen stimulation	Not associated with estrogen stimulation
Morphology	Endometrioid adenocarcinoma	• Serous carcinoma • Clear cell carcinoma
Precursor	Endometrium hyperplasia	• Atrophic endometrium • Polyp • Tubal metaplasia
Prognosis	Good	Poor

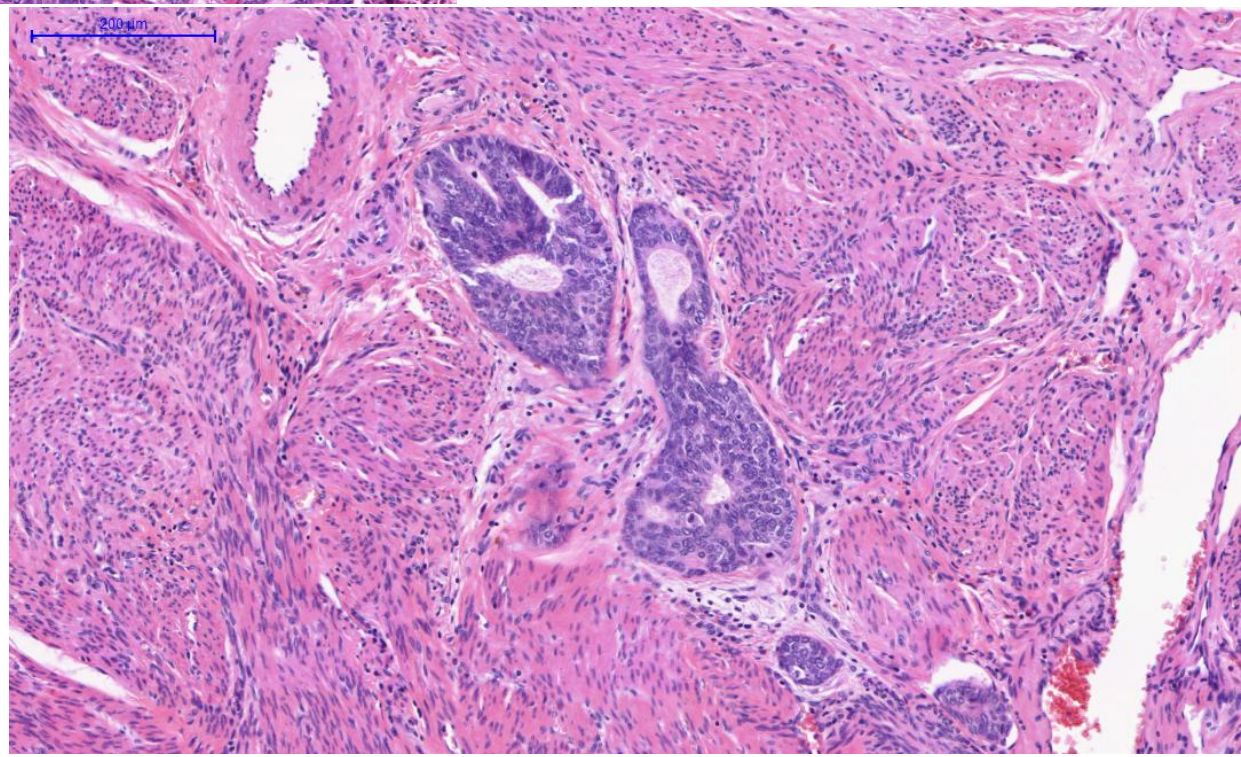
Carcinoma of the endometrium (Endometrioid adenocarcinoma)

- Macroscopy
  - Endometrium is thickened
  - Polypoid structure
  - Myometrial invasion (can not be seen macroscopically – Ultrasound sensitivity is low)
- Microscopy
  - Confluent glands (solid areas are often seen), without stroma
  - Necrosis
  - Cellular atypia



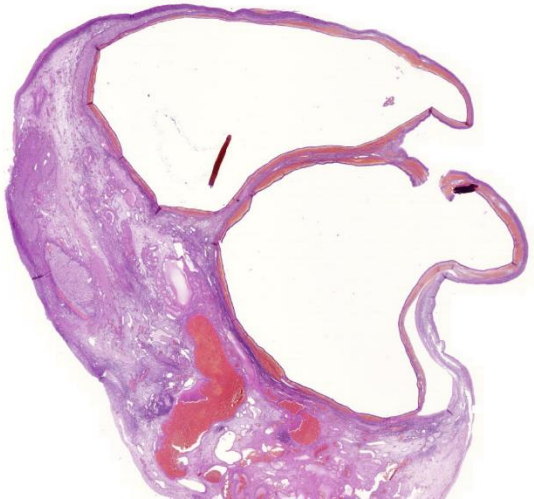
Cribriform glands, necrosis
Without stroma (compare to hyperplasia!)

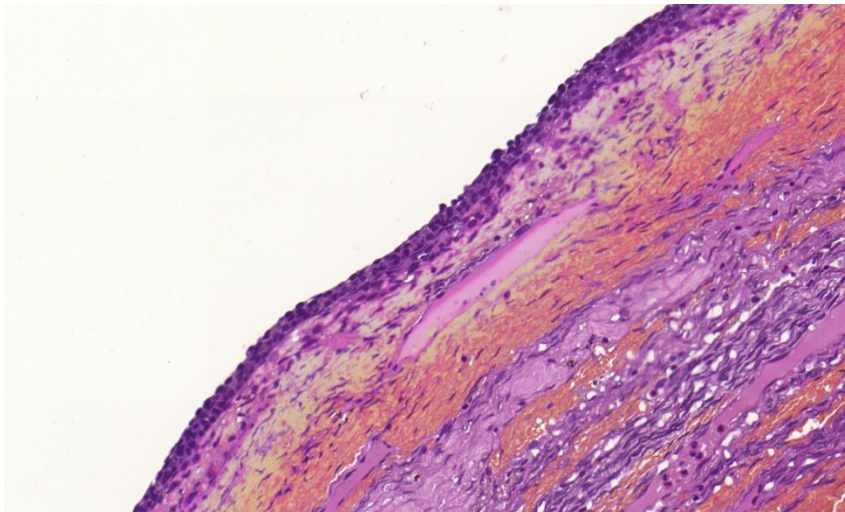
Myometrial invasion



Cystic follicle

- Originate in unruptured graafian follicles
- Contain serous fluid
- Granulosa or luteal cell lining
- Symptoms: lower abdomen pressure, can rupture and cause acute abdomen

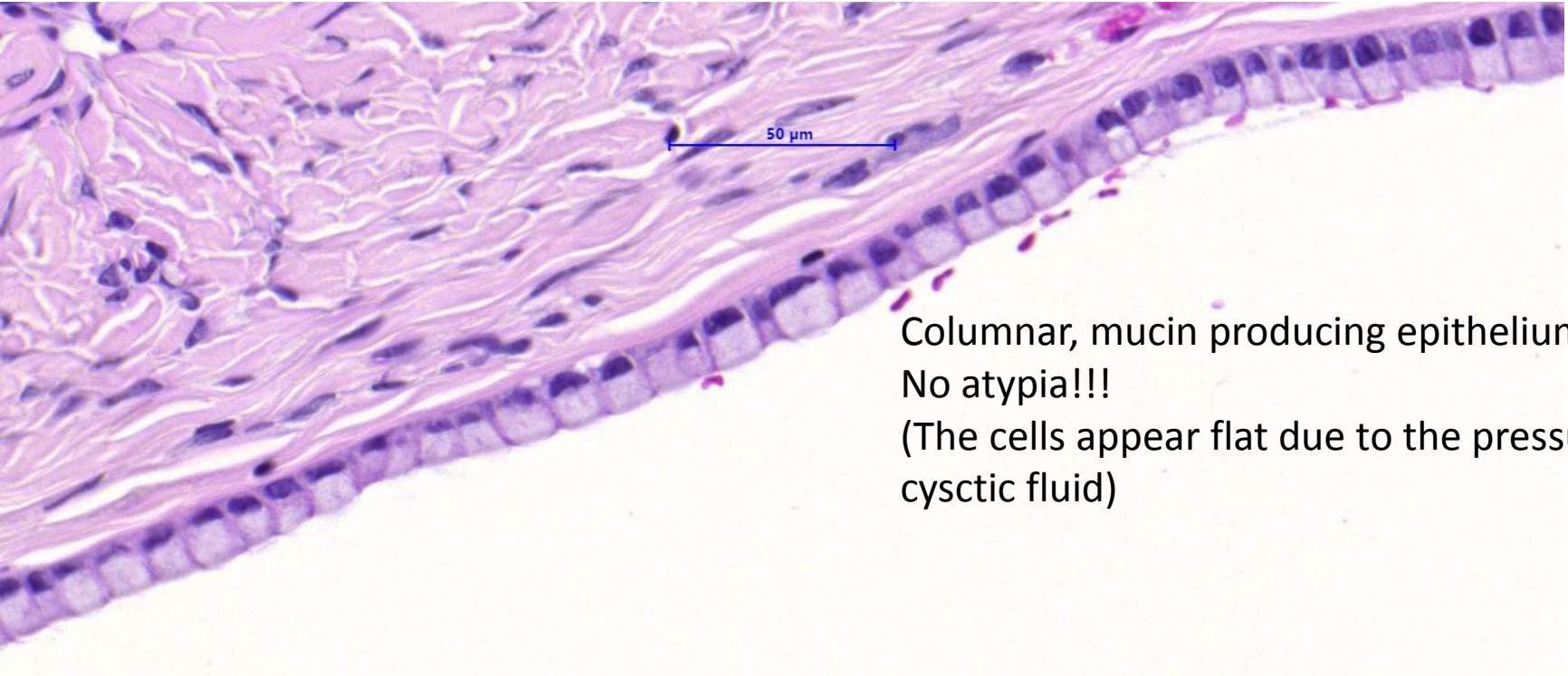




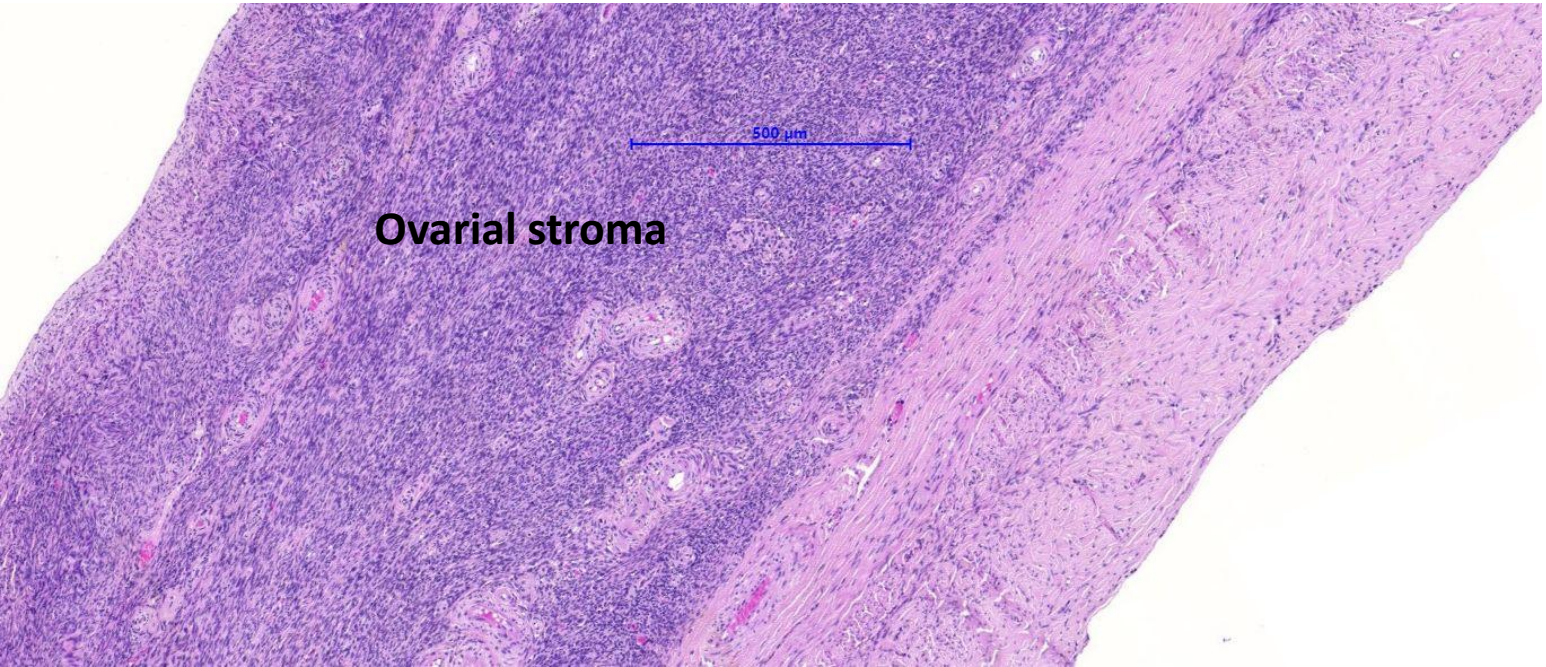
Cystadenoma mucinosum

- Benign ovarial tumor
- Can be large, **multilocular** structure (solid areas are suspicious for malignancy)
- Microscopy
  - **Benign**: Cystic wall is thin, lined with a single layer of columnar epithelium, without atypia
  - **Malignant**: complex papillary proliferation, cellular atypia, invasion (peritoneal spread: pseudomyxoma peritonei)
  - **Borderline**: **structural and cellular atypia, without invasion!**

Ultrasound image and macroscopy



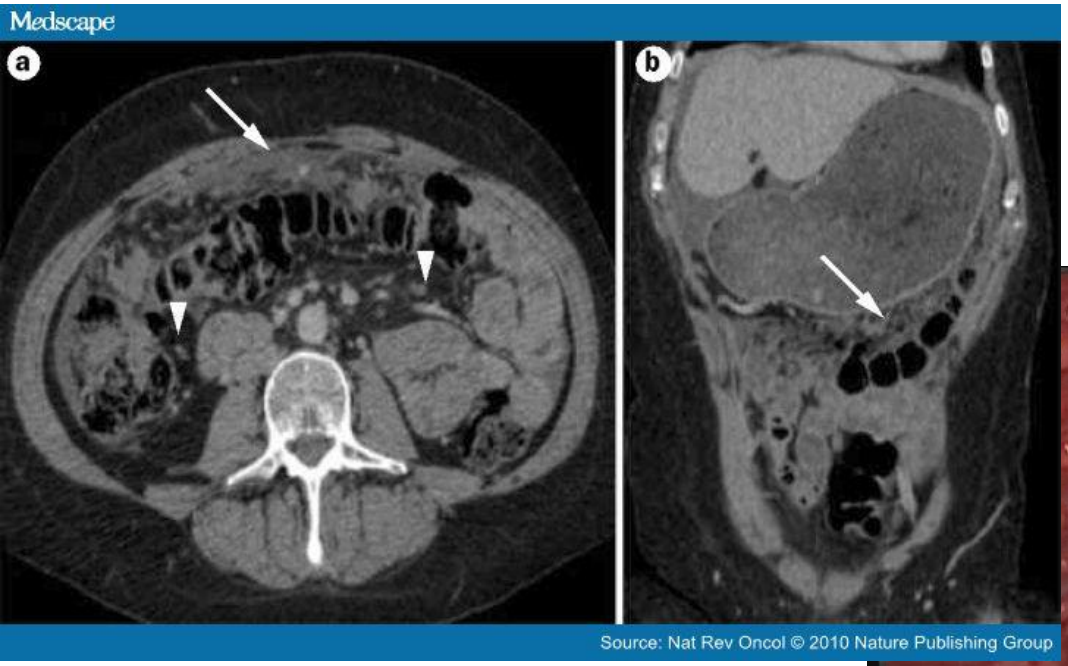
Columnar, mucin producing epithelium
No atypia!!!
(The cells appear flat due to the pressure of cysctic fluid)

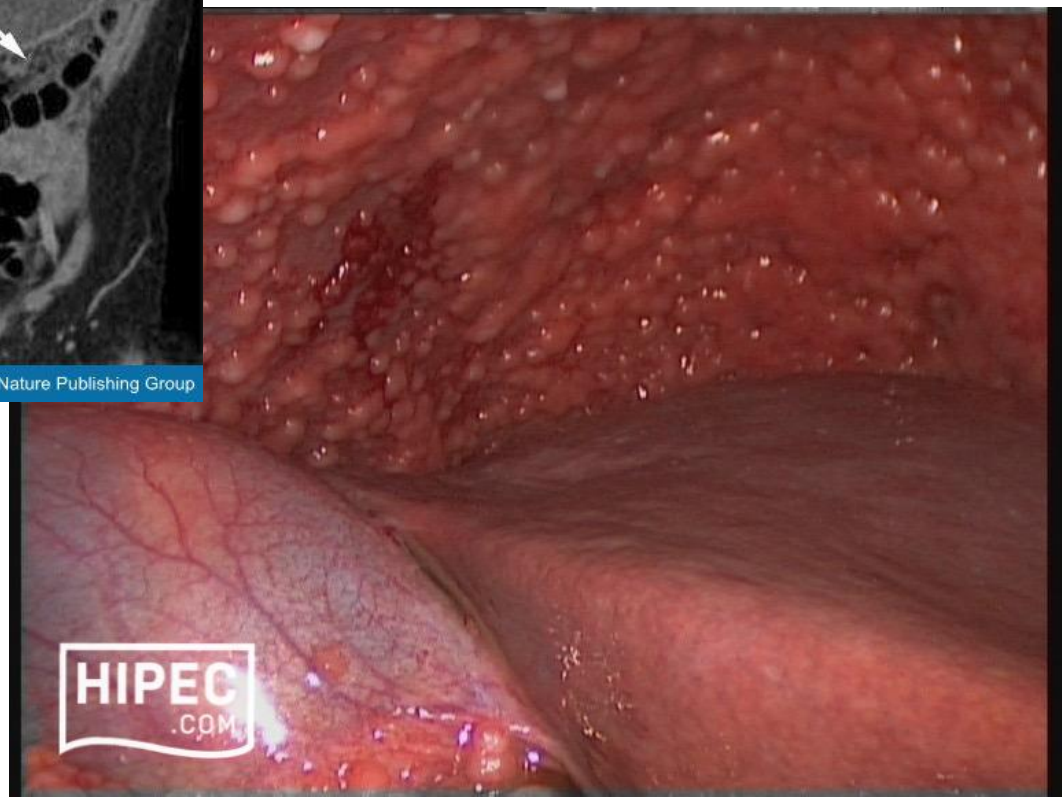


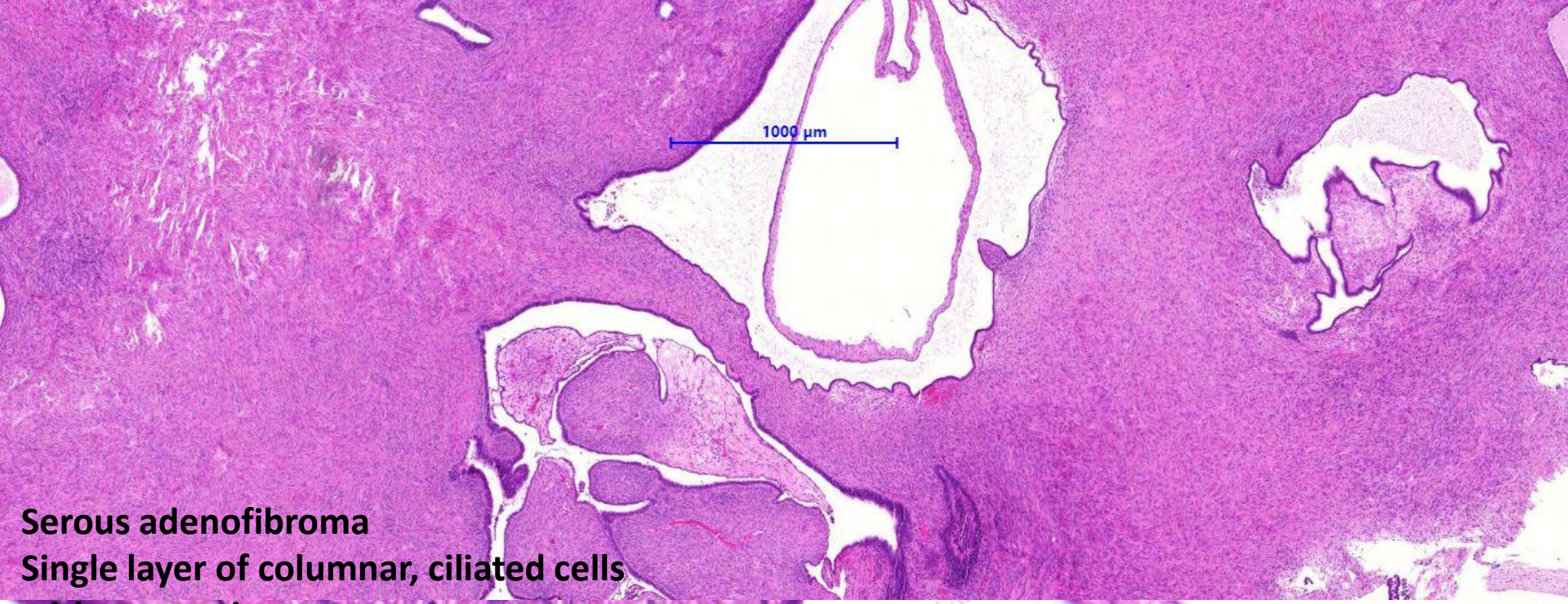
Serous carcinoma

- Cystic (=cystadenocarcinoma) and/or solid
- Usually smaller than mucinous carcinoma
- Often bilateral
- Peritoneal tumor spread: peritoneal **carcinosis + ascites**
- **Microscopy**
  - complex papillary proliferation, solid growth, cellular atypia (usually high grade), psammoma bodies, stromal and vascular invasion
  - **Borderline (low malignant potential)**: structural complexity and cytologic atypia (low grade), but without invasion → peritoneal spread is possible (=peritoneal implantation), because the ovaries are intraperitoneal organs!

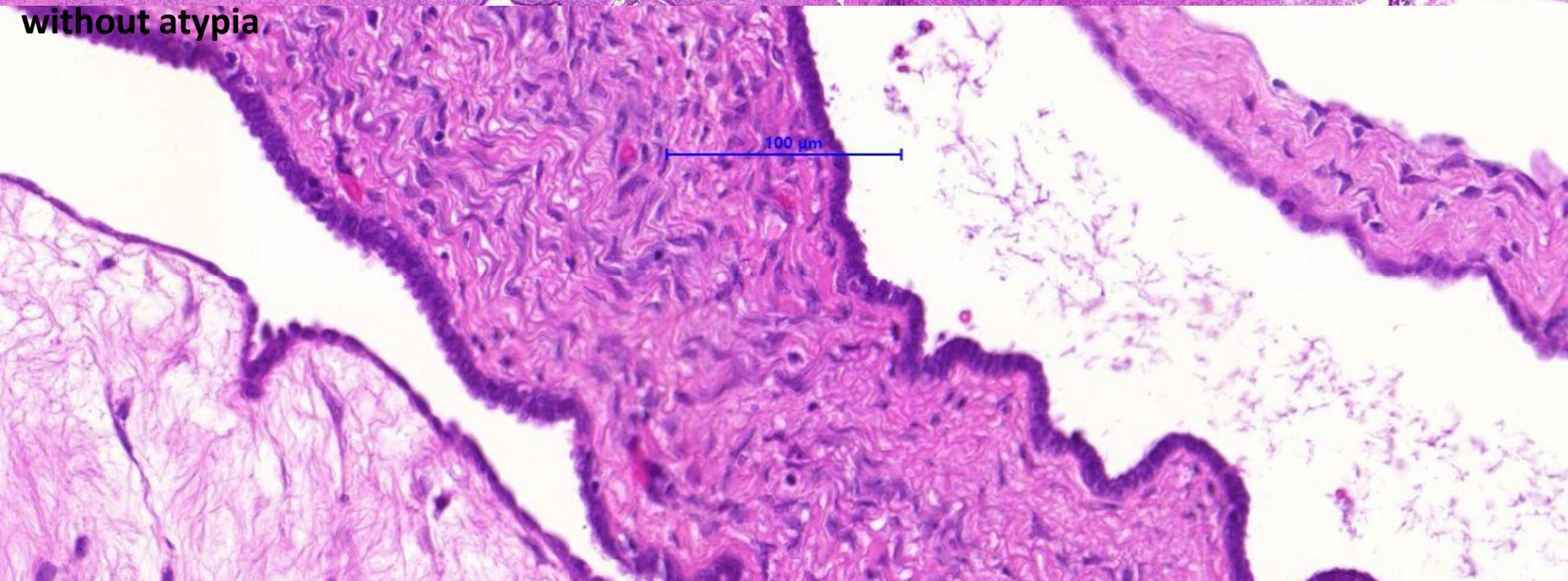
Peritoneal tumor spread: CT-scan and during laparoscopy

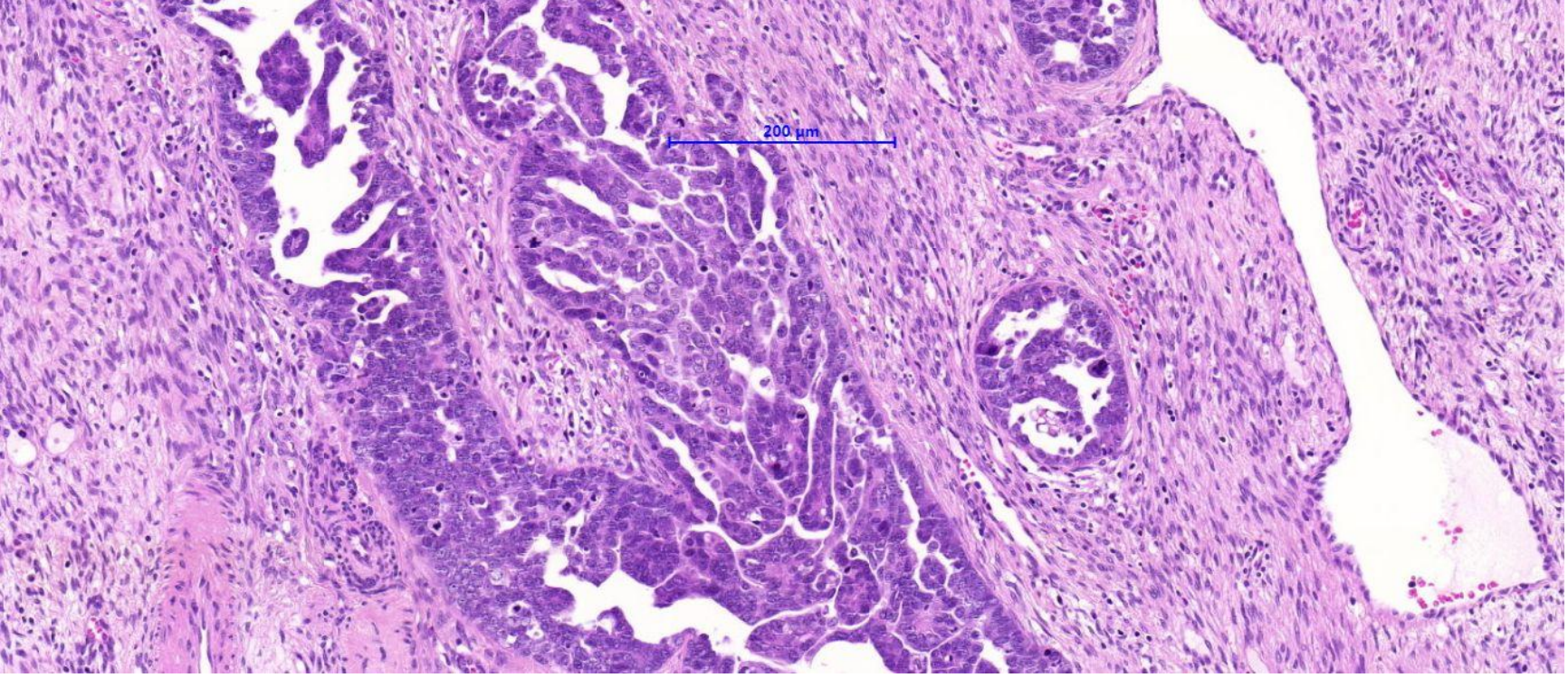




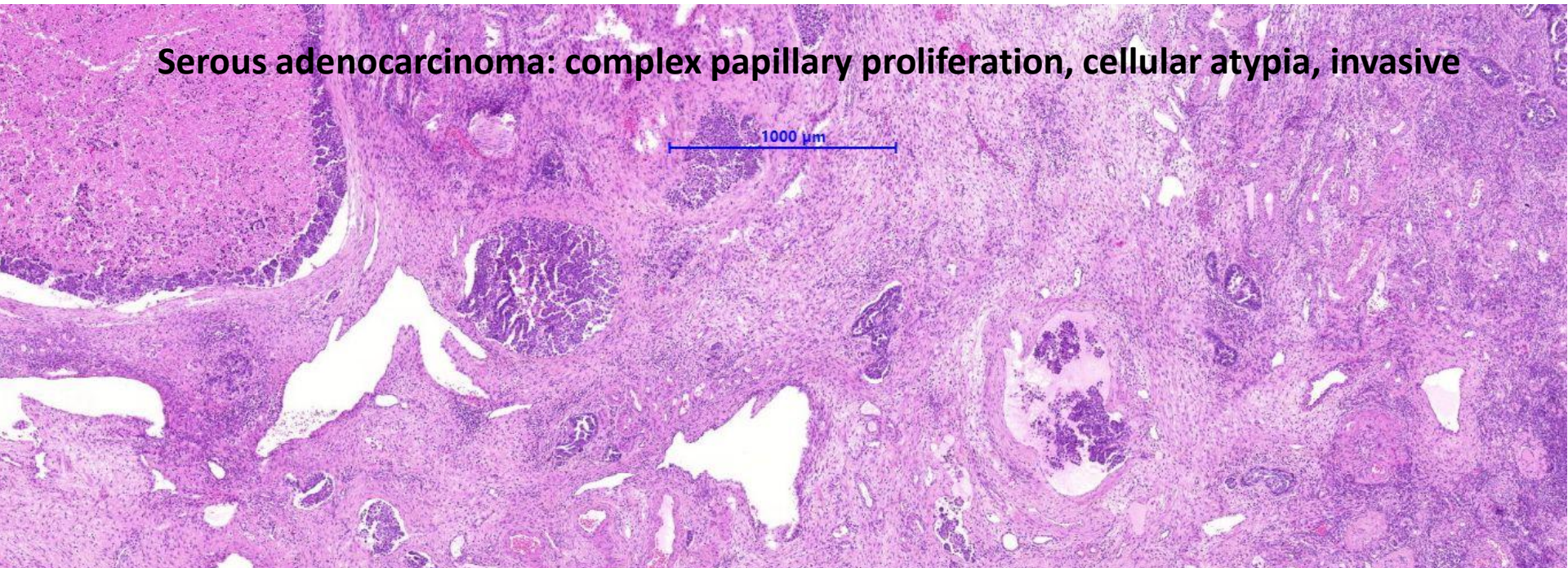


Serous adenofibroma
Single layer of columnar, ciliated cells without atypia





Serous adenocarcinoma: complex papillary proliferation, cellular atypia, invasive



Psammoma bodies