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: secondary follicle
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!
Gland/stroma ratio increased
cystic glands

Thickened endometrium
Carcinoma of the endometrium

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Type I</th>
<th>Type II</th>
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<tbody>
<tr>
<td>Age</td>
<td>55-65 yr</td>
<td>&gt;70 yr</td>
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<tr>
<td>Etiology</td>
<td>Unopposed estrogen stimulation</td>
<td>Not associated with estrogen stimulation</td>
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<tr>
<td>Morphology</td>
<td>Endometrioid adenocarcinoma</td>
<td>Serous carcinoma</td>
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<td></td>
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<td>Clear cell carcinoma</td>
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<tr>
<td>Precursor</td>
<td>Endometrium hyperplasia</td>
<td>Atrophic endometrium</td>
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<td>Polyp</td>
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<td>Tubal metaplasia</td>
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<tr>
<td>Prognosis</td>
<td>Good</td>
<td>Poor</td>
</tr>
</tbody>
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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
Myometrial invasion

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