Breast
Breast pathology

- inflammations
- fibrocystic changes
  - nonproliferative
  - proliferative
- tumors
  - epithelial
  - fibroepithelial
Inflammatory diseases

• puerperal mastitis
• mammary duct ectasia
Puerperal mastitis

- occurs within 2-3 weeks of the start of lactation
- result of infection via the mammary duct system
- can be sporadic (at home) or epidemic (in the hospital)
- most common organism: Staphylococcus aureus
- requires prompt antibiotic treatment
Mammary duct ectasia

- unknown etiology
- diffuse dilatation of the ducts, ductal rupture
- periductal inflammation

- clinical features:
  - spontaneous intermittent nipple discharge
  - can be pain, nipple inversion or retraction
  - may simulate carcinoma
Fibrocytic changes

- causes unknown - consequence of periodical hormonal stimulation (estrogen predominance over progesterone)
- condition affecting at least 50% of women of childbearing age
- **Clinical features:**
  - asymptomatic
  - palpable lesion
  - breast pain and/or tenderness
  - can be associated with irregular menses, dysmenorrhea, ovarian cysts
Fibrocystic changes – relation to breast cancer

- **nonproliferative change** – no increased risk of breast cancer
- **usual proliferative change** – approximately 2-fold risk
- **atypical proliferative change**
  - atypical lobular hyperplasia – 5-fold risk
  - atypical ductal hyperplasia – 3 - 5-fold risk
Nonproliferative fibrocystic changes

- cysts and fibrosis
- most common type
- usually bilateral
- no increased risk of breast cancer
Intraductal proliferative changes

- group of cytologically and architecturally diverse proliferations
- majority originate in the terminal duct-lobular unit
- three categories:
  - usual ductal hyperplasia
  - atypical ductal hyperplasia
  - ductal carcinoma in situ
Fibrocystic changes
Lobular proliferative changes

- majority originate in the terminal duct-lobular unit

- three categories:
  - lobular hyperplasia
  - atypical lobular hyperplasia
  - lobular carcinoma in situ
Tumors of the breast
Tumors of the breast

- benign
- malignant

- epithelial
- fibroepithelial
- epithelial-myoeipithelial
- mesenchymal
- tumors of the nipple
- malignant lymphoma
Benign epithelial tumors

**Papilloma**
- intracystic or intraductal
- peripheral or central
- solitary or multiple

**Adenoma**
- tubular
- lactating
- apocrine
Breast cancer
Breast cancer

- most common carcinoma in women
- accounting for 23% of all cancers globally
- incidence increases rapidly with age
Breast cancer - etiology

- multifactorial:
  - diet (high-calorie diet rich in animal fat and proteins)
  - lack of physical exercise
  - reproductive factors
    - infertility or few children, lack of breast-feeding
    - early menarche, late age of menopause
  - hormones
  - hereditary factors (BRCA1, BRCA2)
Breast cancer – clinical features

• the most common clinical sign - palpable mass
• less commonly:
  • - skin retraction
  • - nipple inversion
  • - nipple discharge
  • - change in the shape or size of the breast
• rarely:
  • - enlargement of the axillary lymph nodes (in the absence of any abnormality in the breast)
Breast cancer prevention

**Primary**
- attempts to reduce the risk of the actual development of breast cancer
- bilateral mastectomy – >95% successful
- chemoprevention (tamoxifen) – 50% successful
- limit lifetime estrogen exposure (hormonal therapy etc.)
- healthy diet (low fat diet)
- - weight control
- - cruciferous vegetables

**Secondary**
- early detection and cure
- breast self examination
- - monthly
- - mammography
- - women over 40 years
- - annual
- reduces the death rate from breast cancer by approximately 1/3
- physical examination by a physician (annual)
Breast cancer: precursor lesions
Lobular neoplasia

- includes atypical lobular hyperplasia and lobular carcinoma in situ
- distinction based on the extent of involvement of individual lobular units (LCIS - more than half of the acini of a lobular unit are distended by neoplastic cells)

- in 85% of patients multicentric
- in 30-67% bilateral

**Histopathology:**
- lobular architecture is maintained
- acini expanded by a monomorphic proliferation of dyscohesive cells with uniform round nuclei and scant cytoplasm
Ductal carcinoma in situ

- a neoplastic proliferation of epithelial cells confined to the mammary ductal-lobular system
- 20-25% of all newly diagnosed breast cancers in countries with screening programme

**Clinical features:**
- palpable mass
- nipple discharge
- Paget disease of the nipple
- 80-85% of cases detected mammographically in the absence of clinical symptoms
- DCIS is precursor (albeit not obligate) to invasive breast cancer
Ductal carcinoma in situ

- **Histopathology:**
- architecture: solid, cribriform, comedo, papillary, micropapillary
- grading based on nuclear features
- - DCIS of low / intermediate / high grade
- common microcalcifications
Invasive ductal carcinoma

- the largest group of invasive breast cancer (50-80%)
- in up to 80% of cases, associated DCIS can be found

**Histopathology**
- very heterogeneous
- architecture: solid, glandular, trabecular...
- tumor cells: regular ... highly atypical

**Grading!**
- based on assessment of:
  - tubule and gland formation
  - nuclear pleomorphism
  - mitotoc count
Invasive lobular carcinoma

• 5-15% of all invasive carcinomas
• usually associated with lobular carcinoma in situ

• **Macroscopy:**
  • frequently poorly circumscribed irregular tumor
  • difficult to define macroscopically because of the diffuse growth pattern

• **Histopathology:**
  • noncohesive cells individually dispersed or arranged in a single-file linear pattern
  • small cells, infrequent mitoses
Breast cancer - prognosis

- Prognostic factors:
  - histological type
  - grade
  - stage
  - lymph node status
  - vascular invasion
- 35-55% 10-year survival
Her2 – human epidermal growth factor receptor 2

• proto-oncogene (promotes cell proliferation and opposes apoptosis)
• amplification or over-expression of the ERBB2 gene occurs in approximately 20-30% of breast cancers
• associated with worse prognosis and increased disease recurrence
• most commonly used medication: Herceptin (trastuzumab)
Inflammatory carcinoma

- rare but very aggressive form of breast cancer
- distinct clinical and/or pathological features
- prominent geographic pattern (more common in north Africa)
- **Clinical features:**
  - rapid breast enlargement and changes in overlying skin (redness, oedema, „orange-peel“ skin)
  - usually no palpable mass
  - common diffuse firmness of the breast
- **Histopathology:**
  - numerous dermal lymphatic tumor emboli
  - underlying invasive carcinoma is often of ductal type (grade 3)
Paget disease of the nipple

- presence of malignant glandular epithelial cells within the squamous epithelium of the nipple
- usually associated with underlying carcinoma
  - invasive ductal carcinoma (50-60%)
  - ductal carcinoma in situ (25-40%)

**Clinical features:**
- eczematous or erythematous changes of the nipple
- may be nipple discharge, ulceration or inversion

**Histopathology:**
- presence of Paget cells within the epidermis
cytokeratin CAM5.2
Fibroepithelial tumors

- biphasic tumors consisting of a proliferation of both epithelial and stromal components

- fibroadenoma
- phyllodes tumor
  - benign
  - borderline
  - malignant
Fibroadenoma

- common benign tumor
- most frequently in women < 30 years
- Clinical features:
  - painless, slow-growing, mobile, well-defined nodule
  - usually up to 3 cm in diameter
  - may be multiple
- Macroscopy:
  - ovoid, well-circumscribed
  - cut surface is grey or white
- Histopathology:
  - admixture of stromal and epithelial proliferation
Phyllodes tumor

- group of tumors histologically resembling fibroadenoma
- stromal hypercellularity (more cellular than FA)
- mitoses
- cytologic atypia
- nature of tumor borders

Clinical features:
- average size 4-5 cm (may be > 10 cm)
- Macroscopy:
  - well-circumscribed
  - characteristic whorled pattern resembling leaf buds (usually larger lesions)