Oncology
Benign and malignant epithelial tumors. Soft tissue tumors and bone tumors. (Benign and malignant mesenchymal tumors).

Dentistry

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Tumor

- **Neoplasm** – new tissue other than the primary tissue, formed as a result of abnormal, uncoordinated, autonomous and senseless proliferation of cells, independent on primary stimulation

- Based on the biological behaviour
  1. benign
  2. malignant
Tumor growth

• **Extensive and excessive growth**
  – proliferation of the cells – changes in the regulation (shorter cell cycle / longer life span)

• **Uncoordinated growth**
  – tumor doesn’t grow in conformity with surrounding tissues

• **Independent growth**
  – autonomous growth, limited regulation
Pseudotumors

- Inflammatory tumor
- Hyperplasia
- Cysts
  - Congenital cysts (thyroglossal duct cyst)
  - Acquired cysts (cysts of salivary glands)
  - Implantation cysts (epidermoid cyst)
  - Parasitic cysts (Echinococcus gr.)
- Pathologic material deposition (amyloid)
Reasons of the tumor development

• Physical
• Chemical
• Biological

→ cause formation of mutations and induce malignant transformation of the cell
Reasons of the tumor development

• Physical
  – Ultraviolet radiation (UV) (sunlight, UV lamps)
    • Mostly UVB 280 – 320 nm
  – Infrared
  – Ionizing radiation
    • X rays, α, β, γ radiation
      – diagnostic methods, radon, industry

• Chemical
  1. cancerogenic substances (mutagens)
  2. procancerogenic substances – need metabolic activation in the body
Reasons of the tumor development

• Biological
  – Viruses
    • Retrovirus HTLV-I (T-cell leukemia / lymphoma)
    • Human DNA papillomavirus (epidermoid carcinoma)
    • DNA virus hepatitis B (hepatocellular carcinoma)
    • RNA virus hepatitis C (hepatocellular carcinoma)
    • EBV (Epstein-Barr virus) (Burkitt lymphoma)
    • HHV-8 (Kaposi sarcoma)
  – Oncogenes – part of the DNA responsible for the tissue growth – cause cell proliferation
  – Metaplasia – change of one type of differentiated tissue to another type
BENIGN vs. MALIGNANT Tu

- well demarcated
- compression of adjacent tissues, encapsulated
- smaller (usually)
- slower growth
- no metastases
- prognosis based on local complications
- **Expansive** growth

- poorly demarcated
- invades, destroys adjacent tissues, no capsule
- larger
- faster growth
- metastasize
- death by local and metastatic complications
- **Infiltrative** growth
MALIGNANT Tu – microscopic characteristics

- loss of basal polarity
- cells are pleomorphic
- NC ratio increased
- anisonucleosis
- hyperchromatism
- prominent nucleoli
- mitotic figures (atypical)
- multinucleated giant cells
- chromosomal abnormalities

- cellular atypia correlates with aggressiveness of the tumor
Neoplasia

- precancerous lesions
  - morphologically altered tissues with higher risk of malignant transformation

- carcinoma in situ

- invasive tumor

- METASTASES:
  - per continuitatem
  - hematogenous
  - lymphogenous
Classification systems for M.Tu

• **Grading** – histological differentiation of tumor (G1, G2, G3, G4)

• **Staging** – describes the extent of spread of tumor (based on clinical tests), most used system: **TNM classification**
  - Tx,0,1,2,3,(4) → size of primary tumor
  - Nx/0/1/2/3 → lymphatic node involvement
  - Mx/0/1 → metastases
Tumor classification

1. **Tumors from one type of cells**
   - epithelial
     - squamous epithelium
     - glandular epithelium
     - transitional epithelium
   - mesenchymal (non-epithelial, similar group: „soft tissue“)
     - fibrous tissue – cartilage – bone
     - muscle
     - fat tissue
     - vasoformative tissue
     - hemopoietic tissue
   - neuroectodermal
   - placental (trofoblast)
2. Other tumors:

**Mixed tumors** – combination of 2 types of tumors
- adenosquamous Ca, adenoacanthoma, carcinosarcoma

**Teratoma** – tumor arising from 1, 2 or all 3 germ cell layers

**Blastoma** – arising from partially differentiated cells

**Hamartoma** – composed of haphazardly arranged tissues which can normally be found in affected organ

**Choristoma** – composed of ectopic tissue not normally present in affected organ
Neoplasia types

Squamous epithelium

- begin: papilloma
- malignant: carcinoma
Papilloma (43)

• Common benign tumor
• Exophytic or endophytic (inverse) growth
• Viral infection (HPV – Human Papiloma Virus)

• Composed of stratified squamous epithelium
• Mitoses may be found in irritated papilloma
Papilloma, HE

Exophytically growing tumor composed of fibrous stroma and stratified squamous epithelium.
Stratified squamous epithelium with normal maturation, without atypia

Fibrous stroma with capillaries

Papilloma, HE
Squamous cell carcinoma (45)
(Spinocellular carcinoma, epidermoid carcinoma)

• malignant transformation and proliferation of the *stratum spinosum*

• Male to female ratio 2:1
• chemical and physical irritation (smoking), sun exposure (skin)

• tissues with primary squamous epithelium or the metaplastic epithelium (e. g. in bronchi, oesophagus)

• Micro: solid islets and stripes of atypical cells, penetration into lymphatic and blood vessels, loss of stratification and differentiation to stratum granulosum
• **keratinization** - the deposition of keratin inside cells/formation of keratin pearls, depends on the level of differentiation

• **Screening:** cervical carcinoma, bronchogenic carcinoma
Squamous cell carcinoma, HE

Atypical squamous cells forming islets

Formation of keratin pearls
Squamous cell carcinoma, HE

Transition of normal squamous epithelium into carcinoma
Mitoses

Formed of keratin pearls

Squamous cell carcinoma, HE
Basal cell carcinoma (basalioma) (46)

- **Most common** malignant tumor of skin, tight association with sun exposure

- without metastases (**semimalignant**), locally destructive
- frequent relapses – adequate surgical extirpation with histopathological examination of the borders is necessary

- Pearly papule, grows predominantly endophytically, with the dermis infiltration, and surface exulceration (**ulcus rodens**)

- Micro: proliferation of cells similar to the immature cells of the basal layer of the epidermis (basal layer), variable histological features, growth in islands with peripheral pallisading
Superficial ulceration

Islands of immature basal-like cells growing infiltratively into dermis

Basal cell carcinoma, HE
Basal cell carcinoma, HE

Immature basal-like cells with cellular atypia

Peripheral pallisading

Inflammatory barrier reaction
Neoplasia types

Glandular epithelium

- begin: adenoma
- malignant: adenocarcinoma
Adenomatous polyp (44)

• Benign
• Exophytic nodule, polyp with thin / broad-based stalk, cauliflower-like surface

• Micro:
  1. **Tubular** – closely packed tubules with fibrovascular stroma
  2. **Villous** – thin, tall, finger-like processes lined externally by neoplastic cells
  3. **Tubulovillous**
Exophytically growing polyp composed of fibrous stroma and covered by intestinal epithelium.
Intestinal epithelium

Fibrovascular stroma

Adenomatous polyp, HE
Benign and malignant epithelial tumors

Tumors of glandular epithelium

Adenocarcinoma (47)
(Carcinoma adenomatosum)

• most frequent malignant tumor
• transformation and proliferation of the exocrine and endocrine gland epithelium or columnar epithelium of mucous membranes
• „de novo“ or secondary (malignant transformation of adenoma, abnormal or dysplastic epithelial proliferation)
Benign and malignant epithelial tumors

Tumors of glandular epithelium

Adenocarcinoma

*(Carcinoma adenomatosum)*

1. **classification according to localisation** (in PARENCHYMATOUS ORGANS / ORGANS WITH LUMEN)

   • in *parenchymatous organs*
     - irregular nodular structure, often without capsule
     - **trabecular** – equal proportion of stroma and parenchyma
     - **scirrhous** – stroma predominance
     - **medullary** – parenchyma predominance
     - **gelatinous** – mucus
     - **cystic** – cystic cavities
Predominance of tumor cells to supporting stroma

Medullary adenocarcinoma, HE
Medullary adenocarcinoma, HE

Predominance of tumor cells to supporting stroma
Scirrhotic adenocarcinoma, HE

Abundant stroma among tumor cells with marked cellular atypia
Scirrhotic adenocarcinoma, HE

Abundant stroma among tumor cells with marked cellular atypia
Benign and malignant epithelial tumors

Tumors of glandular epithelium

Adenocarcinoma
*(Carcinoma adenomatosum)*

- on the surface of *organ with lumen*
  - Exophytic or endophytic growth
  - **Endophytic** has forms as described before
  - **Exophytic** can be according to the appearance: papillary, polypous, villous, disciform (central necrosis)
Adenocarcinoma, HE

Endophytic infiltrative growth
Adenocarcinoma, HE

Adenocarcinoma structures infiltrating muscle layer of intestine
Benign and malignant epithelial tumors

Tumors of glandular epithelium

Adenocarcinoma
(*Carcinoma adenomatosum*)

2. classification: according to **the source**:
   - Adenocarcinoma of **trabecular glands** (liver, cortex of adrenal gland, hypophysis) is solid with trabecular form
   - Adenocarcinoma of **tubular, acinar and alveolar glands** and of **collumnar epithelium**
   - Both types resemble original tissue based on the degree of differentiation

3. classification: according to **mucus production**:
   - **Carcinomas of signet-ring cells** – mucus in cytoplasm
   - **Mucinous carcinomas** – mucus extracellularly, in stroma
MESENCHYMYMAL TUMORS (SOFT TISSUE TUMORS)
Mesenchymal tissue  
(mesodermal origin)

- fibrous connective tissue
- adipose tissue
- muscle tissue (smooth, skeletal)
- vessels (blood, lymphatic)
- synovium
- hemopoietic tissue
- chorda dorsalis
- bone, cartilage

Soft tissue

- fibrous connective tissue
- adipose tissue
- muscle tissue (smooth, skeletal)
- vessels
- synovium

(mesodermal origin)

+ peripheral and autonomic nerves

(neuroectodermal origin)
Soft tissue tumors

• less frequent than epithelial tumors
• M <1% of all malignant tumors, but:
  – often highly malignant
  – dg challenge – heterogeneous group
  – deep location → late dg → 10% mts at dg. (lungs, liver, bones, brain)
• etiology unknown (trauma, virus, genes...)
• de novo (primitive mesenchymal cells)
• grading, staging
Location

**BENIGN**
- superficial (dermis, subcutis)
- small

- even if located superficially, size >5cm is suspicious of malignancy and should be biopsied!

**MALIGNANT**
- deep-seated
- large

![Pie chart showing distribution of different locations for benign and malignant tumors.](chart.png)
Soft tissue and bone tumors

Classification by the dignity (WHO)

• **benign**
  – lipoma, ...

• **intermediate, locally aggressive** (locally destructive growth, recurrence, do not metastasise)
  – desmoid fibromatosis

• **intermediate, rarely metastasising** (locally destructive growth, recurrence, metastasis in cca. 2%)
  – dermatofibrosarcoma protuberans

• **malignant**
WHO classification of tumours of soft tissue (2013)

Mesenchymal tissue

- fibrous connective tissue
- adipose tissue
- muscle tissue (smooth, skeletal)
- vessels (blood, lymphatic)
- synovium
- hemopoetic tissue
- chorda dorsalis
- bone, cartilage

FIBROBLASTIC TUMORS

- **Benign:** FIBROMA
- **Intermediate, locally aggressive:** DESMOID-TYPE FIBROMATOSIS
- **Intermediate, rarely mts:** DFSP
- **Malignant:** FIBROSARCOMA
Fibroma (20)

- structurally similar to fibrous connective tissue (fibroblasts + collagen bundles)

- types:
  - f.durum (firm) – predominantly collagen fibers
  - f.molle (soft) – predominantly tumor cells

- well demarcated pink nodule with smooth surface
- skin, soft tissue
Fibroma, HE

Exophytically growing tumor covered by epidermis
Fibroma durum, HE

Tumor composed predominantly of collagen fibers, with only few fibroblasts
Fibroma molle, HE

Tumor composed predominantly of fibroblasts, with smaller amount of fibrous stroma.
Fibroblasts are regular, without mitoses or cellular atypia.
FIBROBLASTIC TUMORS

FIBROSARCOMA (28)

- **Infantile type**: favorable prognosis, mts rarely
- **Adult type**: more frequent in males

- in various locations, most frequently on extremities, **gluteal region** (sometime in scars)
  - **Macro**: fish meat
  - **Micro**: spindle-shaped cells arranged in herringbone pattern, atypia
Longitudinal fibroblasts are arranged in "herringbone" pattern, cellular atypia is present.
Fibrosarcoma, HE

Atypical fibroblasts
Fibrosarcoma, HE

Atypical fibroblasts
WHO classification of tumours of soft tissue (2013)

Mesenchymal tissue

- fibrous connective tissue
- adipose tissue
- muscle tissue (smooth, skeletal)
- vessels (blood, lymphatic)
- synovium
- hemopoietic tissue
- chorda dorsalis
- bone, cartilage

ADIPOCYTIC TUMORS

- **Benign:** LIPOMA, HIBERNOMA

- **Intermediate, locally aggressive:**
  - ATYPICAL LIPOMATOUS TUMOR
    (= well differentiated LS)

- **Malignant:** LIPOSARCOMA
  (dedifferentiated, pleomorphic, myxoid)
ADIPOCYTIC TUMORS

LIPOMA (22)

- most common mesench. Tu
- adults
- gross and microscopic appearance like mature adipose tissue (adipocytes)
- frequently subcutaneous (superficial), in deep tissues - retroperitoneum, mediastinum, omentum
Lipoma, HE

Mature adipose tissue without atypia
Mature adipose tissue without atypia
ADIPOCYTIC TUMORS

LIPOSARCOMA (308)

- 6th decade
- deep soft tissue - lower extremities, retroperitoneum, mediastinum

- Macro: fish-meat appearance (yellow or gray-yellow color)

- Micro: lipoblasts

- well differentiated - rarely mts
- dedifferentiated - high risk for recurrence and mts
Liposarcoma, HE

- Atypical mitosis
- Atypical lipoblasts with fat droplets, with cellular and nuclear atypia
Liposarcoma, HE

Atypical lipoblasts with fat droplets, with cellular and nuclear atypia
WHO classification of tumours of soft tissue (2013)

Mesenchymal tissue

- fibrous connective tissue
- adipose tissue
- muscle tissue (smooth, skeletal)
- vessels (blood, lymphatic)
- synovium
- hemopoetic tissue
- chorda dorsalis
- bone, cartilage

SMOOTH-MUSCLE TUMORS

- Benign: LEIOMYOMA
- Malignant: LEIOMYOSARCOMA

SKELETAL-MUSCLE TUMORS

- Benign: RHABDOMYOMA
- Malignant: RHABDOMYOSARCOMA
  (embryonal, alveolar, pleomorphic, spindle cell/sclerosing)
LEIOMYOMA (27)

- dermis, uterus, GIT

- **Macro:** well demarcated, elastic round white-yellowish tissue, nodular on cross-section

- **Micro:** resembles smooth muscle tissue
Leiomyoma of uterus

Well demarcated white-grey nodule
Leiomyoma of uterus, HE

Tumor with pseudocapsule

Myometrium
Fascicles of uniform smooth muscle cells

Leiomyoma of uterus, HE
Leiomyoma of uterus, HE

Fascicles of uniform smooth muscle cells
WHO classification of tumours of soft tissue (2013)

Mesenchymal tissue

- fibrous connective tissue
- adipose tissue
- muscle tissue (smooth, skeletal)
- vessels (blood, lymphatic)
- synovium
- hemopoetic tissue
- chorda dorsalis
- bone, cartilage

VASCULAR TUMORS
- Benign: HEMANGIOMA, LYMPHANGIOMA
- Intermediate, locally aggressive: KAPOSI SARCOMA
- Malignant: ANGIOSARCOMA

PERICYTIC (PERIVASCULAR) TUMORS
- Benign: GLOMUS TUMOR
- Malignant: MALIGNANT GLOMUS TUMOR
VASCULAR TUMORS

CAPILLARY HEMANGIOMA OF SKIN (25)

- inborn (some variants) – spontaneous regression
- acquired

- **Macro:** red spot / slightly protruding nodule on the skin surface (large hemangioma – naevus flammeus)
- **Micro:** thin capillaries in dermis lined by endothelium, frequently not sharply demarcated
Capillary hemangioma, HE

Thin capillaries with endothelium in fibrous stroma
CAVERNOUS HEMANGIOMA IN LIVER

- **grossly** - dark red area in liver, bleeds if cross-sectioned

- **microscopically** – wide thin-walled vascular channels lined by endothelium, separated by fibrous septae
Hepatocytes

Wide space filled by blood, lined by endothelium

Cavernous hemangioma, HE
Cavernous hemangioma, HE

Wide space filled by blood, lined by endothelium
WHO classification of tumors of bone (2013)

Mesenchymal tissue

- fibrous connective tissue
- adipose tissue
- muscle tissue (smooth, skeletal)
- vessels (blood, lymphatic)
- synovium
- hemopoietic tissue
- chorda dorsalis
- bone, cartilage

OSTEOGENIC TUMORS
- Benign: OSTEOID OSTEOMA
- Malignant: OSTEOSARCOMA

CHONDROGENIC TUMORS
- Benign: CHONDROMA
- Malignant: CHONDROSARCOMA
OSTEOGENIC TUMORS

OSTEOMA

- not considered a true neoplasm
  - hyperplastic post-traumatic or post-inflammatory process (orbit, paranasal sinuses and jaw)
  - **Macro**: bone outgrowth
  - **Micro**: mature compact or spongy bone
OSTEOGENIC TUMORS

OSTEOID OSTEOMA (110)

• young (5-25y), males
• long bones (extremities)

• nocturnal, intense pain, exacerbation after alcohol consumption, relieved by aspirin

• Micro: osteoid, osteoblasts, osteoclasts in vascularized connective tissue
Osteoid osteoma, HE

Islands of osteoid with osteoblasts and osteoclasts

Vascularised irregular fibrous trabeculae

Islands of osteoid with osteoblasts and osteoclasts
OSTEOSARCOMA (52)

- highly malignant tumor, early mts (lungs!!!), high mortality rate
- young (10-25 y), males
- mostly long bones around knee, less proximal humerus

**Macro:** metaphyseal gray tumor, consistency varies according to osteoid content, may include cartilage, frequently bleeding and necrosis

**Micro:** osteoid + pleomorphic, anaplastic cells, marked atypia, numerous mitoses
Osteosarcoma, HE

- Areas of osteoid
- Pleomorphic cells
Osteosarcoma, HE

Mitotic figures
WHO classification of tumours of soft tissue (2013)

Mesenchymal tissue
- fibrous connective tissue
- adipose tissue
- muscle tissue (smooth, skeletal)
- vessels (blood, lymphatic)
- synovium
- hemopoietic tissue
- chorda dorsalis
- bone, cartilage

MYELOID NEOPLASMS
- „solid“ - lymphoma
- „diffuse“ – leukemia
- acute / chronic
- lymph.nodes and bone marrow, also liver, spleen, thymus ...

LYMPHOID NEOPLASM
- changes in PB count, oragnomegaly, B-symptoms...
- th: CHT, RT, bone marrow transplant, targeted therapy
Neoplasia types

Mesenchymal - hemopoietic tissue

- „solid“ - lymphoma
- „diffuse“ – leukemia
- acute / chronic
- Lineage → myeloid, lymphoid, histiocytic
- Lymphatic tissue and bone marrow, liver, spleen, thymus, ...
- lymfadenomegaly, hepatomegaly, splenomegaly, changes in peripheral blood count, B symptoms

LYMPHOCYTIC LINE

- Hodgkin´s lymphoma (36)
- non-Hodgkin´s lymphoma (T- / B- cell) (34)
Hodgkin disease / lymphoma (36)

Tumor cells  - Hodgkin cells, Reed-Sternberg cells (B cell origin)

- antitumor immune reaction – T-lymphocytes

4 histological types:  
1. lymphocyte prevalence
2. nodular sclerosis
3. combined cellularity
4. lymphocyte decline
Hodgkin lymphoma, HE

Mixed inflammatory infiltrate in the background

Hodgkin cell

RS cell
Hodgkin lymphoma

- Hodgkin cell
- RS cell
- CD45 (T-lymphocytes)
- CD30 (RS and Hodgkin cell)
- CD15 (RS and Hodgkin cell)
B-cell chronic lymphatic leukemia (34)

CLL = small lymphocytes proliferation

- max. >50 y., prolonged course
- **clinical symptoms**: fatigue, generalized lymphatic nodules enlargement, hepatosplenomegaly, anaemia, thrombocytopenia
Hypercellular bone marrow infiltrated by monomorphic B-lymphocytes
Portal tracts infiltrated by B-lymphocytes with propagation into liver parenchyma.
Questions

1. What are the main routes of tumor spread?
2. Which carcinoma is typical for seldom metastatic spread? In which organs can a primary carcinoma of this type be found?
3. Is presence of keratinisation in squamous cell carcinoma a favorable prognostic sign?
4. Which organs are primary lymphatic tissues?
5. Which symptoms are collectively referred to as B constitutional symptoms?