Nonepithelial Tumors
General Definitions

• **Mesenchymal Tumors**

These tumors consist of tissues that originate in the middle germ layer or mesoderm, primarily from the pluripotential supporting tissue of the embryo (mesenchyma). This definition applies to tumors of connective tissue, supporting tissue, and muscle.

Exceptions:

- Tumors of the kidney, adrenal cortex, and mesothelia can develop an epithelial tissue pattern.
- Cells of the hemopoietic and lymphopoietic systems are derived from mesoderm. However, they do not form a distinct group of tumors.
- Schwann cell and melanocytic tumors, which are derived from ectodermal tissue, form mesenchymal patterns of growth.
General Definitions

• Soft Tissue Tumors
This is a collective term for nonepithelial tumors that arise exclusively from cells of non-skeletal tissue including peripheral nerve tissue.

Exceptions:
The following tumors are not considered soft tissue tumors:
– Tumors of the macrophage system and tumors of the hemopoietic and lymphopoietic systems;
– Tumors of supporting tissue such as bone and glia;
– Melanocytic tumors.
Benign Nonepithelial Tumors

- General morphology: These tumors exhibit striking similarity to their physiologic tissue of origin. For this reason, the names of these neoplasms include the tissue of origin with the suffix “-oma” (for example, a tumor of fatty tissue is a lipoma).
- Clinical presentation: These tumors grow slowly and can become very large.

Malignant Nonepithelial Tumors

- General morphology: Because of fleshy appearance of their cut surface, these tumors are known as sarcomas (from Greek sarx, flesh).
- Clinical presentation: These tumors grow rapidly with extensive tissue destruction and produce primarily hematogenous metastases.

Rule of thumb: In grading sarcomas, malignancy increases with decreasing similarity to the tissue of origin, and in direct proportion to the mitosis count (10 or more mitoses in the visual field at 40-power magnification), and the extent of tumor necroses.
Fibrous Tumors

**Fibroma**

- Occurrence: Ubiquitous and common.
- Definition and morphology: Benign, nodular, fibrous tumor. Depending on their collagen content, fibromas are referred to as hard or soft.

**Fibrosarcoma**

- Occurrence: Rare, found primarily in the lower extremities.
- Definition: Malignant, metastasizing fibrous tumor.
- Histologic findings include spindle-shaped and polymorphic tumor cells in a “herring bone” pattern.
- Immunohistochemical findings include tumor cells with a cytoskeleton containing vimentin. The prognosis is generally unfavorable and depends on the tumor stage and extent of its spread.
Muscle Tumors

Leiomyomas

- Occurrence: These common tumors usually occur in groups in the uterus, intestinal tract, and vascular walls.
- Definition: A benign spherical tumor composed of mature smooth muscle cells.
- Histologic findings include a swirling pattern of interwoven tumor cells with cigar-shaped nuclei. Each tumor cell (smooth muscle cell) has a “sock” of basement membrane wrapped around it. Regressive changes such as hyalinization, calcification, and/or ossification may be present. However, no necrosis will occur.

Leiomyosarcoma

- Occurrence: This rare tumor occurs in the retroperitoneum and, rarely, in the uterus.
- Definition: A malignant nodular tumor composed of immature smooth muscle cells.
- Histologic findings generally resemble a hypercellular leiomyoma often with only slight cellular polymorphism but with mitoses. Necroses are usually present as well.
- Immunohistochemical findings include tumor cells with a cytoskeleton containing actin. The prognosis depends on the tumor stage.
Muscle Tumors

Rhabdomyoma

• Occurrence: This very rare tumor occurs primarily in the heart.
• Definition: Benign tumor of mature striated muscle cells.
• Histologic findings include “spider cells” (polygonal spider-like tumor cells with vacuolar cytoplasm (containing glycogen), some of which exhibit striations.

Rhabdomyosarcoma

• Occurrence: This rare tumor occurs in the head and neck region and genitals in infants and in the extremities in adults.
• Definition: A group of highly malignant tumors of embryonic striated muscle tissue.
• Histologic findings include stellate and spindle- shaped polymorphic tumor cells with striations in cytoplasmic tails (“tadpole cells”). Regressive change include necroses.
• Immunohistochemical findings include tumor cells with a cytoskeleton containing desmin and myosin. The prognosis is very poor.
Tumors of Fatty Tissue

**Lipoma**
- **Occurrence:** This tumor is found in subcutaneous and submucosal tissue. Rarely, it may also occur at intramuscular sites, and these tumors tend to recur. It is the most common benign mesenchymal tumor.
- **Definition:** Benign solid tumor of mature tumor cells (adipocytes) that store fat in a single vacuole.
- **Histologic findings:** Perfectly mimic fatty tissue but with the connective tissue organizing it into the lobular structure typical of fatty tissue.

**Liposarcoma**
- **Occurrence:** This tumor is found in the thigh, back, and retroperitoneum.
- **Definition:** Malignant soft yellowish tumor of fat cell precursors (preadipocytes).
- **Histologic findings:** Fat is stored in multiple vacuoles in the cytoplasm and nucleus of the tumor cell, creating a typical scalloped nucleus. Regressive changes include necroses and myxoid degeneration of the stroma.
Tumors of Fatty Tissue

Lipoma

Liposarcoma
Cartilage Tumors

Chondroma

- Occurrence: The tumor occurs within the bones of the hands and feet.
- An osteochondroma is a neoplasm arising as cartilage-capped bony outgrowth on a skeletal bone.
- Definition and morphology: A benign tumor of mature chondrocytes that perfectly mimics hyaline cartilage.

Chondrosarcoma

- Occurrence: The tumor arises in the pelvis or in long cortical bones such as the humerus, tibia, and femur.
- Definition and morphology: This is a slow-growing malignant tumor arising from chondrocyte precursors, some of which develop into bizarre giant cells, and exhibiting some of the characteristics of hyaline cartilage. Regressive changes include necrosis, bleeding, and osteolysis.
Chondrosarcoma
Bone Tumors

**Osteoma**

- **Occurrence:** The tumor arises primarily in bones that develop from the desmocranium.

- **Definition and morphology:** This benign tumor arising from osteocytes perfectly mimics cancellous lamellar bone with a fibrous fatty medulla. It exhibits slowly expansive growth.

**Osteosarcoma**

- **Occurrence:** This tumor is found primarily in long bones in adolescents. It is the most common malignant tumor of the skeletal system.

- **Definition:** A highly malignant sarcoma of plur- ipotential osteocyte precursors.

- **Histologic findings:** include sarcomatous stromal tissue with polymorphic cells with an uncalcified tumor osteoid and disorganized tumorous cancellous tissue.

- **One of the following types of osteosarcoma will occur:**
  - Proliferation of osteoblasts successively leads to bone remodeling and an osteoplastic osteosarcoma.
  - Proliferation of osteoclasts successively leads to dis-solution of bone and an osteolytic osteosarcoma.
Osteosarcoma
Tumors from nervous tissue
Features of Brain Tumors

- Disontogenetic nature
- Absolute clinical malignancy
- Infiltrative growth pattern even in morphologically benign tumors
- Metastasizing by CSF pathways, very rare outside of cranial cavity
- Formation of typical histological structures
Specific to neural tumors rhythmic structure

True rosette

False perivascular rosette

Homer Wright rosette

Palisades
Ependymoma. True rosette
Ependymoma. Perivascular rosette.
Homer-Wright rosette in medulloblastoma
Palisades in schwannoma
Glioblastoma. Foci of necrosis with formation of pseudopalisades
Degree determination of tumor malignancy in central nervous system

Histological degree determination of malignancy (Grade) is based on identification and combination of the following major pathological signs:

1. nuclear atypism
2. mitosis
3. Vascular (endothelial) proliferation
4. necrosis
NEUROEPITHELIAL TUMORS

• Astrocytal tumors
• Oligodendroglial
• Ependymal
• Tumors of choroid plexus
• Neuronal
• Pineal
• Embryonic
ASTROCYTAL TUMORS

• Astrocytomas - the most common CNS tumors in infants

• The main histological types:
  • Pilocytic (children) G1
  • Fibrillar astrocytoma (adults) G2
  • Protoplasmic astrocytoma G2

• Anaplastic astrocytoma G3

• Glioblastoma multiforme - undifferentiated glioma, astrocytoma with remnants of G4
Astrocytoma with multiple cysts
Cerebellum pilocytic astrocytoma in the form of a large cyst
Astrocytoma. Diffuse infiltrative type of growth
Pilocytic (juvenile) astrocytoma
Protoplasmic astrocytoma
Glioblastoma with foci of necrosis and hemorrhage, intracranial metastases in the opposite hemisphere of brain.
Glioblastoma. Foci of necrosis with the formation pseudopalisade, expressed cellular atypia, proliferation of vascular endothelium
Oligodendroglialma

- 5-15% of gliomas
- Localization in frontal and lateral parts of cerebral hemispheres
- Are more common among middle-aged
- Could be mixed with astrocytomas variants histological structure
- Grow slowly
- Rarely metastasize
- Variants: oligodendroglialma (G2), anaplastic oligodendroglialma (G3)
- Morphology: Ill-defined tumor of small, densely packed tumor cells (exhibiting a dark nucleus in bright cytoplasm) that creates a honeycomb pattern. Signs of regression include bleeding, cysts, and calcification.
Oligodendroglioma
Oligodendroglioma of brain with arcade blood vessels and calcification
Anaplastic oligodendrogliaoma
Ependymoma

• More common in infants
• Localization: children in 4-th ventricle, adults usually in spinal cord
• Arise from the ependymal lining the ventricles and liquor conducting system
• Micro: tumor cells form a true rosette, Homer Wright rosette, and perivascular pseudorossette
Ependymoma of 4-th cerebrum ventricle
Ependymoma. Perivascular rosette.
Ependymoma. True rosette
Choroid plexus tumors

- Rare (0.5% Op. CNS), usually in children in the lateral ventricles in adults IV ventricle.
- Grow slowly, gradually break outflow of liquor, causing hydrocephalus.
- Horioioidpapilloma and choroidcarcinoma
- The terminology does not match the histogenesis!
- The name given to the tumor in relation to characteristic of histological features - a tumor composed of papillary structures (papillae).
Embryonal tumors

- Medullary epithelioma
- Neuroblastoma (*sympathicoblastoma?*)
  - Ganglioneuroblastoma
- Ependymoblastoma
- Primitive neuroectodermal tumors (PNET)
  - PNET of cerebellum - Medulloblastoma
Medulloblastoma

- The most common PNET
- Second frequency at children CNS tumor
- Localization – cerebellum
- Grade 4
- Characteristically ingrowth IV ventricle and as a consequence development of hydrocephalus
- Micro: tumor is formed by small undifferentiated cells with hyperchromatic nuclei, cells form a Homer-Wright rosettes
Homer-Wright rosettes in medulloblastoma
Meningioma

- The tumor arises from cells of brain arachnoid membrane
- Usually occurs in adults
- Macro: looks like a node associated with the meninges
- Variety: meningothelial, psammomatous, fibroblastic, microcystic, angiomatous
- Typical histological structures: tumor cells form vortexlike structures, could be foci of dystrophic calcification in the form of psammom
Meningothelial meningioma

Psammoma bodies
Peripheral nervous system tumors

• Schwannoma (neurilemmoma/ neurinoma)
• Neurofibroma and neurofibromatosis
Schwannoma

- A benign tumor arising from Schwann cells form nerve membranes
- Usually occurs in middle age
- Two variants of structure - Antoni A (cells form a true palisades), Antoni B (no palisades)
Neurilemmoma of acoustic nerve
Schwannoma, Antoni type A  
Schwannoma, Antoni type B
Neurofibroma

• Occurrence: A solitary lesion may be present, or the tumor may occur as multiple lesions in type 1 neurofibromatosis (Recklinghausen disease)

• Definition and morphology: Benign encapsulated Schwann-cell tumor arising from craniospinal and peripheral nerves. The cut surface of the tumor is whitish-yellow.

• Histologic findings include spindle-shaped tumor cells in a loose, undulating, fibrous mesh.
Neurofibromatosis (type 1)

- Mutation of neurofibromin gene (NF1) - chromosome 17.
- Clinically: multiple neurofibromas, 6 and more skin spots such as "coffee au lait", pigmented retina hamartomas, sided schwannomas of auditory nerve, optic nerve and other peripheral nerves and the combination with congenital malformations (megacolon), Wilms' tumor, multiple lipomas, etc.
Vater-Pacini corpuscles