Melanocytic, Brain and Children's Tumors
Melanocytic Tumors

• Melanocytic Nevi
  – Acquired Melanocytic Nevus
  – Congenital Melanocytic Nevi

• Malignant Melanoma
  – Superficially-spreading melanomas
  – Lentigo maligna melanomas
  – Nodular melanomas

Note: General immunohistochemical findings include expression of S100 antigen and HMB-45 antigen. Melanocytic tumors are derived from neuroectodermal tissue.
Melanocytic Nevi

• Synonyms: pigmented nevus, mole. Definition: Tumor of modified melanocytes (nevus cells).
• The melanocytic nevi are classified according to their location and cytologic features.
Acquired Melanocytic Nevus

This dark brown, slightly raised, sharply demarcated skin lesion measuring several millimeters is composed of aggregates or “nests” of oval melanocytes. Several types are differentiated according to their position.

- **Junctional nevi** occur in children at the junction between dermis and epidermis (A).
- **Compound nevi** occur in young adults. Nests of melanocytes form “droplets” extending deep into the dermis and diminish in size as they mature (vertical maturation).
- **Intradermal nevi** occur in adults. They exhibit nests of melanocytes in the dermis that are not in contact with the epidermis. These nevi regress, producing fibrosis.

Congenital Melanocytic Nevi

These nevi are present at birth. Histologic findings are identical to acquired nevi, although the lesions themselves are usually larger and covered with hair.
Special forms of nevocellular nevi:

- **Spindle and epithelioid cell nevi** occur in children and young adults. These benign tumors consist of epithelioid and spindle melanocytes (usually without melanin) and are histologically similar to malignant melanomas.

- **Blue nevi** can occur at different ages. The solitary lesion is a flat, blue or black tumor of melanin-containing spindle melanocytes interwoven with the fascicular structure of the dermis.

- **Dysplastic nevi** occur in young adults. These are multiple brownish tumors measuring up to 1 cm and consisting of variably polymorphic melanocytes. These lesions have an increased rate of malignant degeneration and can become malignant melanomas.
**Malignant Melanoma**

- Definition: A highly malignant tumor in the skin or mucosa adjacent to the skin.
- Pathogenetic factors include susceptibility genes, beta-catenin mutation, and exposure to ultraviolet radiation.
- Malignant melanomas may exhibit radial or vertical patterns of growth.
- Radial growth melanomas include superficial spreading melanomas and lentigo maligna melanomas.
- Vertical growth melanomas include nodular melanomas.
Superficially-spreading melanomas can occur anywhere but on the volar surfaces of the hands or feet, most often on the back in men and in the calves in women.

- Morphologic findings include a flat, brownish, irregularly colored tumor in which nests of melanocytes extend in and along the epidermis.
Lentigo maligna melanomas occur in skin damaged by ultraviolet radiation (especially in the face), where they develop from lentigo maligna, a precancerous lesion.

- Morphologic findings include a flat, brownish pale, irregularly colored, ill-defined tumor extending as bands of atypical cells in and along the basal layer of the epidermis in the presence of a deficient basement.
Nodular melanomas can occur anywhere.

- Morphologic findings include primarily vertical spread of raised nodular tumor tissue, usually dark brown, consisting of atypical melanocytes, some of which are pigmented.

**Note:** The prognosis for melanoma depends on the depth of the lesion; the deeper the penetration, the worse the prognosis.
Children’s tumors

• There is a predomination of benign tumors of mesenchymal origin (hemangiomas, fibromatosis, lymphangioma)

• There is a predisposition of certain organs and tissues in tumor formation

• Among the of malignant tumors there is a domination of leukemia, neuroblastoma and soft tissue sarcomas
Children’s tumors

• About 80 - 90% of tumors among children under a year have an innate nature (disontogenetic origin). Innate nature of tumors observed in 25% of cases between the ages of 0 and 14 years

• Many tumors of childhood are of disontogenetic origin (two thirds of benign tumors) i.e. associated with tissue malformations
Children’s tumors

- Tumors especially at an early age are often combined with congenital malformations.
  - nephroblastoma combined with Wiedemann syndrome - Beckwith (macroglossia + gigantism + exophthalmos) and aniridia
  - neurofibromatosis type 1 - with congenital malformations of the limbs
  - hereditary neoplastic syndromes hamartomas (von Hippel-Lindau syndrome, Gorlin - Sturge - Weber, Gardner, tuberous sclerosis)
  - autosomal recessive gene dermatoses (Werner syndrome, Rotmund - Thompson, Reed, etc.)
  - chromosomal syndromes (Down's syndrome, etc.)
Children’s tumors

- Children more often than adults have a genetic causality and a genetic predisposition to tumor growth.
  - In the presence of paired organs tumor occurs in both
  - Occurrence of more then one malignant tumor at the same child
  - Multiple tumor foci in the same organ
  - Tumor growth in uncharacteristic for its places (germ cell in region of head and neck, rhabdomyosarcomas of vagina and bladder, retroperitoneal neuroblastoma, etc.)
  - Combination of malignant tumors with congenital malformations, hereditary metabolic disease, primary benign tumors
  - Occurrence of unusual and rare tumors.
Morphological features of childhood tumors

1. High level of proliferation of tumor cells and rapid growth typical not only for cancer but also some benign tumors
2. Noted the ability of some malignant tumors to differentiate, aging, and even spontaneous regression (neuroblastoma, retinoblastoma and germinocellular tumors)
3. Expressed variability of histological structure not only in the group of tumors of the same origin, but also within the same tumor (nephroblastoma, yolk sac tumor)
4. The high frequency of nodal metastases in sarcomas and carcinomas with hematogenous metastasis.
5. A benign tumor can have an infiltrative growth (angioma, fibromatosis), and some malignant tumors initially grow expansively (Wilms' tumor, neuroblastoma)
Structure of benign tumors at children

1st place - vascular tumors
2nd place - epithelial tumors
3rd place - bone tumors
4th place - teratomas
5th place - fibrous and adipose tissue tumors
Structure of malignant tumors at children

1st place - tumors of hematopoietic and lymphoid tissues
2nd place - tumors of the central nervous system
3rd place - neuroblastoma
4th place - soft tissue sarcoma
5th place - kidney tumors
• Hamartia (Greek: "error") - abnormal development, irregular relation in embryogenesis of tissues encountered for this body is the basis for occurrence of hamartomas.

• Choristoma (Greek "separable, separate") - a site normally formed tissue located in an unusual place for it.
  – Chorista is ectopic differentiated tissue that has become displaced into the tissue of another germ layer.

• Gemartoblastoma - disontogenetic malignant tumor developing on the basis of gemartoma

• Progonoma - version of tissue differentiation violation in the embryonic period, characterized by formation of tissue structures inherent to the evolutionary precursor to these species.
  – Vestige refers to persisting rudimentary parts of organs that normally regress during intrauterine development.
Dysontogenetic Tumors

General definition: Tumor arising from hetero-topic embryonic tissue that became displaced from its original location during embryonic development and was therefore unable to develop further.

Several types of tumors are differentiated according to the stage of development at which the heterotopic embryonic tissue remains frozen.

- Teratoma
- Embryonal Tumors (Blastomas)
- Embryonal Tumors Arising from Vestigial Tissue
Teratoma

- Occurrence: These tumors account for 30% of all tumors in the newborn and occur primarily in the gonads (especially in young boys) and less often in the mid-line of the mediastinum (especially in young adults), in the retro-peritoneum, and within the cranium. Sacrococcygeal teratomas (occurring especially in girls) are usually present before birth.

- General definition: The tumor consists of pluripotential cells exhibiting a disorderly mixture of differentiated tissue from all three germ layers.

- Histogenesis: The tumors are derived from unfertilized germ cells.

- Teratomas are classified as mature or immature, depending on the degree of differentiation of the tissue that forms the tumor.
Mature Teratoma

- Definition: Benign cystic tumor exhibited mature tissue from all three germ layers.
- Ovarian dermoid cysts represent a special form of teratoma. These benign, sharply demarcated, cystic tumors contain hair and sebum. Differentiated tissues such as sebaceous glands, hair follicles, squamous epithelium, teeth, cartilage, bone, and nerve tissue may be found within the walls of these cysts. Thyroid tissue is also present on occasion.
Nasopharyngeal teratoma.
Sacroccocygeal teratoma
Immature Teratoma

• Occurrence: These tumors are found primarily in the gonads where they occur most often in young boys. Rarely, they occur in the midline of the mediastinum, in the retroperitoneum, and within the cranium.

• Definition: This solid or small cystic tumor consists of minimally differentiated epithelial or mesenchymal tissues in the form of ciliated epithelium, hyaline cartilage, and bone.
Malignant Teratoma

• A teratoma with malignant transformation (TMT) is a very rare form of teratoma that may contain elements of somatic (non germ cell) malignant tumors such as carcinoma or sarcoma.
Embryonal Tumors (Blastomas)

• General definition: These are highly malignant tumors of undifferentiated cells of an organ primordium that are no longer pluripotential.

• Pathogenesis: The tumor arises during embryonic development and usually manifests itself in early childhood.
Neuroblastoma

*Occurrence*: The tumor usually occurs in the adrenal medulla, less often in the sympathetic chain.

*Definition*: This lesion is a malignant tumor of the sympathetic nervous system that forms catecholamine.

*Metastasis* occurs early via hematogenous dissemination and follows the vena cava pattern.
Neuroblastoma

*Morphologic findings* include a grayish-red, pulpy tumor of small cells with little cytoplasm that occasionally form pseudorosettes of Homer Wright. Secondary maturation of the tumor cells to ganglion cells may occur, successively resulting in ganglioneuroblastoma, ganglioneuroma. Spontaneous remissions are possible.
Nephroblastoma (Wilm’s tumor)

• The most common malignant neoplasm of the urinary tract at children.
• Tumor could be localized not only in kidney, but in the sacroccocygeal region, mediastinum, testis
• Often combined with a variety of congenital malformation.
• Typical symptoms are:
  – an abnormally large abdomen
  – abdominal pain
  – fever
  – nausea and vomiting
  – blood in the urine (in about 20% of cases)
  – high blood pressure in some cases
Nephroblastoma (Wilm’s tumor)

• Macro: dense painless formation, gray, often having a smooth or rough surface.

• Wilms' tumor is a tumor containing metanephrhic blastema, stromal and epithelial derivatives.

• Characteristic is the presence of abortive tubules and glomeruli surrounded by a spindled cell stroma. The stroma may include striated muscle, cartilage, bone, fat tissue, fibrous tissue. The tumor is compressing the normal kidney parenchyma.

• Pathologically, a triphasic nephroblastoma comprises three elements:
  – blastema
  – mesenchyme
  – epithelium
Nephroblastoma (Wilm’s tumor)

Wilms' tumors may be separated into 2 prognostic groups based on pathologic characteristics:

• Favorable - Contains well developed components mentioned above
• Anaplastic - Contains diffuse anaplasia (poorly developed cells)
Embryonal Tumors Arising from Vestigial Tissue

Craniopharyngioma

• Definition: This semimalignant, locally invasive tumor arises from vestiges of the embryonic structures involved in the development of the anterior pituitary (pituitary diverticulum or pouch of Rathke).

• Morphology: The tumor consists primarily of squamous epithelium with communicating reticular epithelial strands. It exhibits the palisade-like epithelial arrangement seen in basal cell carcinomas and the open reticular pattern of epithelium.
Soft tissue tumors at children

• Vessel tumors
  – Lymphangioma
  – Hemangioma

• Rhabdomyosarcoma
Axillary lymphangioma
Lymphangioma
Cavernous hemangioma
Rhabdomyosarcoma

- Rhabdomyosarcomata is the most common malignant tumor of soft tissue at children (~ 50%).
- For children aged 2-6 years, often localized in the neck and head (nasopharynx).
- At teenagers - in the genital area and retroperitoneal.
- Often in those organs where normally no mature skeletal muscle (in the wall of bladder, nasopharynx, vagina).
- At adults is extremely rare.
Morphological classifications of rhabdomyosarcoma

The first group (favorable prognosis)
- botrioid
- embryonal
- spindle cell

The second group (bad prognosis)
- alveolar
- pleomorphic
Rhabdomyosarcoma

The main microscopic diagnostic feature is the presence of *rabdomioblasts*.

*Rabdomioblasts* look like a relatively large cells with displaced to the periphery of the nucleus and wide rim intensely eosinophilic cytoplasm. They can acquire a variety of shapes - round, oval, elongated, ribbon-like, rocket-like.

The modern approach involves obligatory immunohistochemical verification of the histogenesis of the tumor.
Embryonal rhabdomyosarcoma
Alveolar rhabdomyosarcoma
Pleomorphic rhabdomyosarcoma