DISEASES OF THE CENTRAL NERVOUS SYSTEM
(C: Brain tumors 1)

Normal cells of CNS

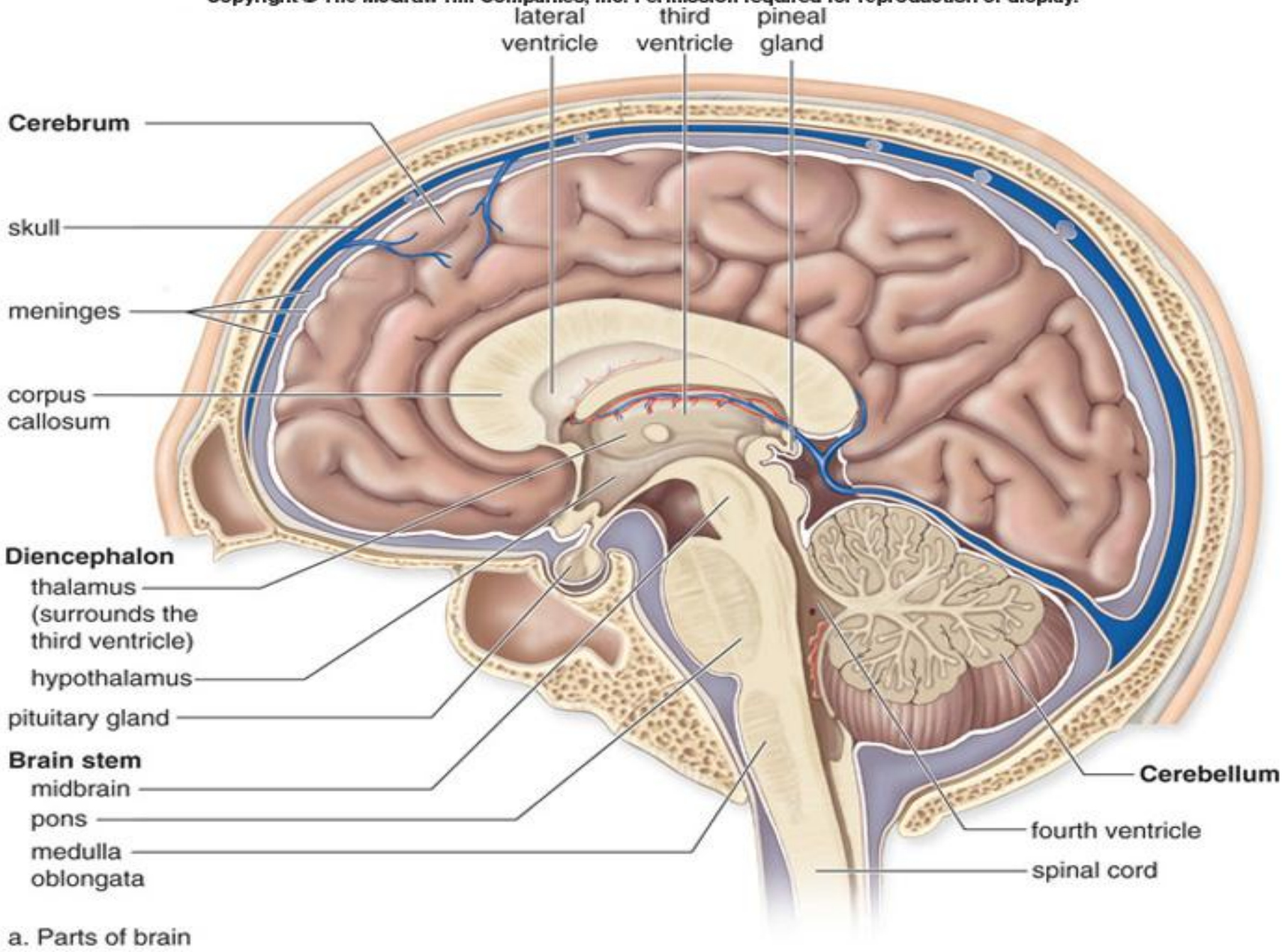
A. **Neuroglial cells**

1. **Astrocytes**: Star-shaped, responsible for nutritional supply and insulation of neurons.
2. **Oligodendrocytes**: Form the myelin sheath.
3. **Ependymal cells**: Lining of the ventricular chambers, aqueduct, central canal of the spinal cord.
4. **Microglia**: Native macrophages of the CNS.

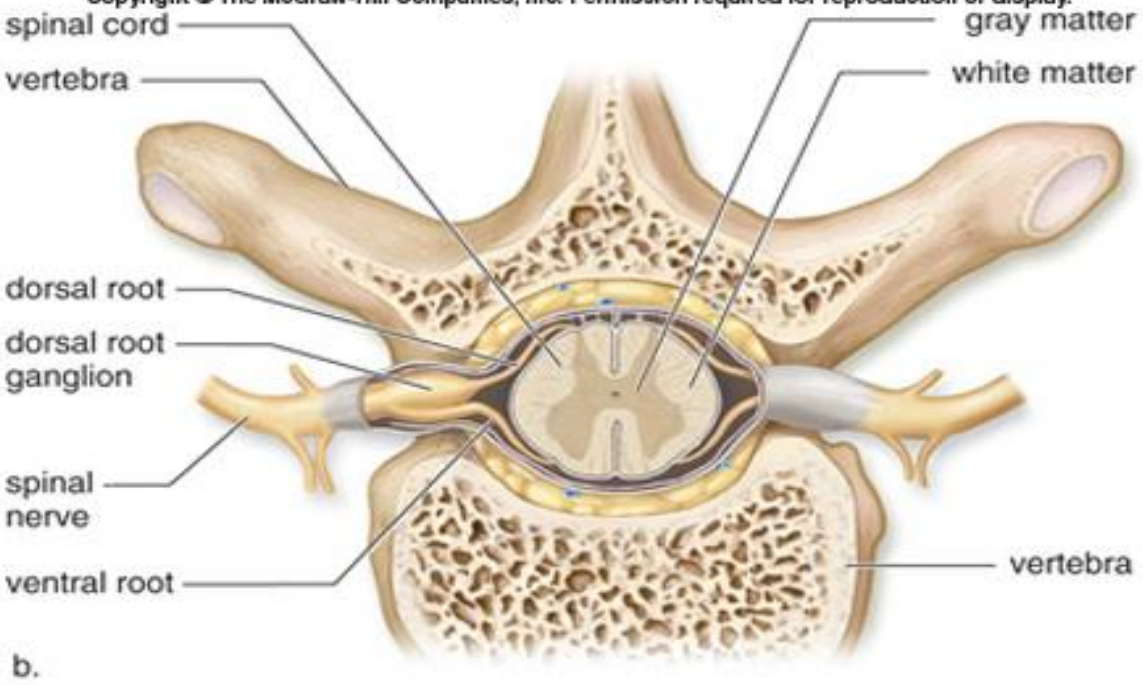
B. **Neuronal cells**

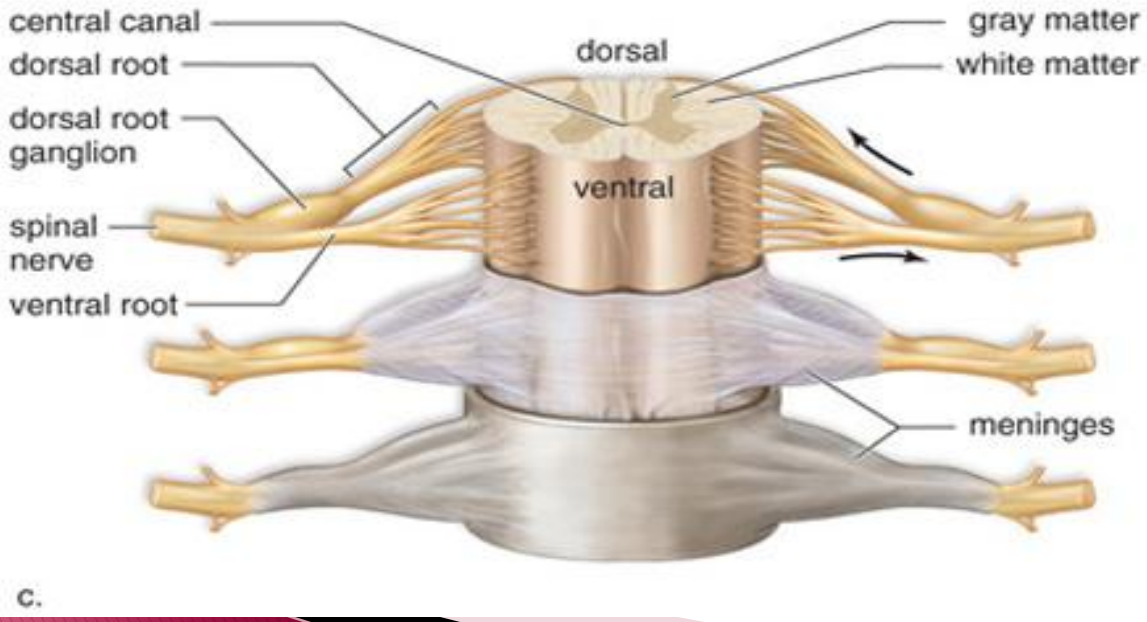
C. **Meningeal cells**

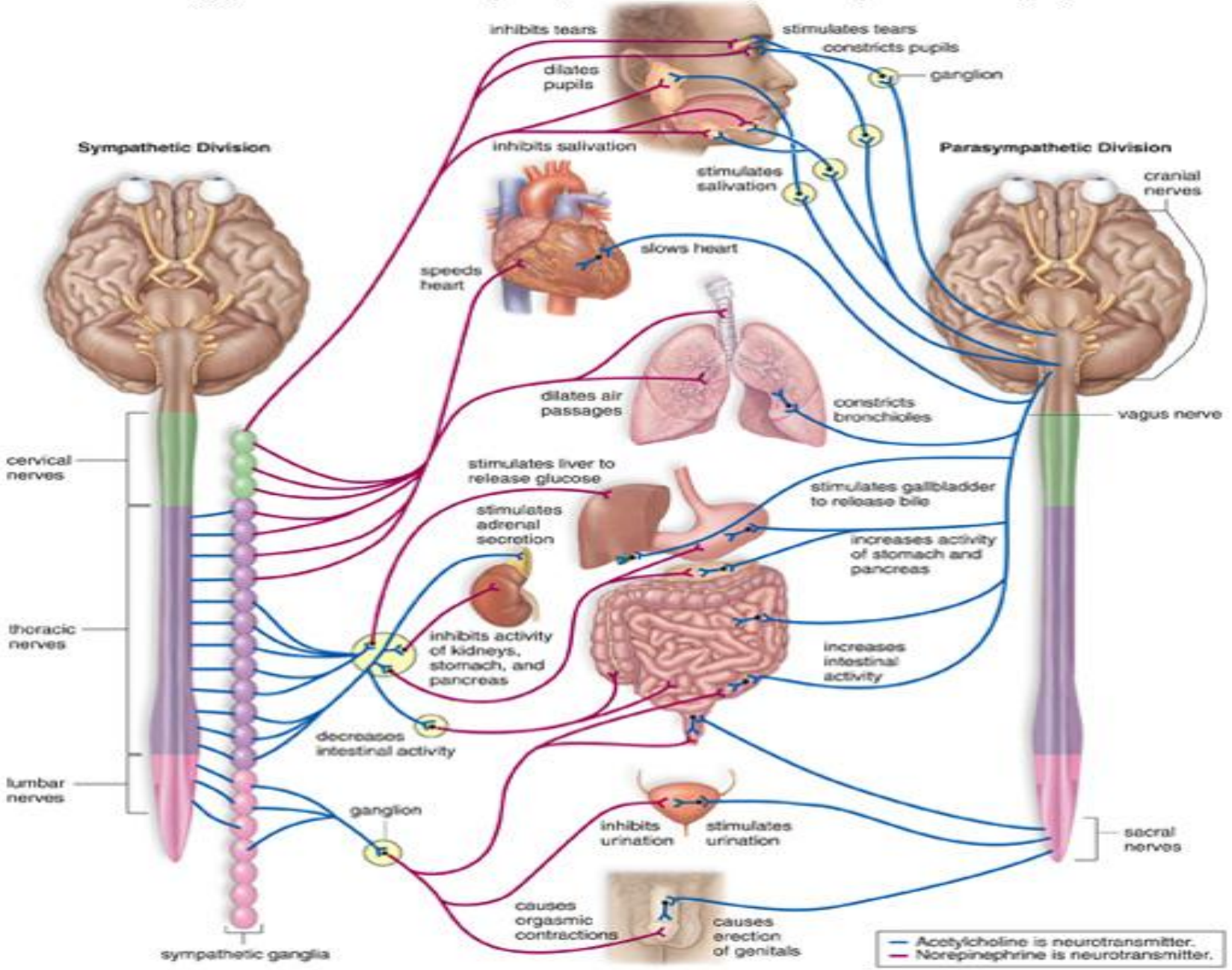
D. **Endothelial cells**



a. Parts of brain







TUMOURS OF THE NERVOUS SYSTEM

WHO classification of tumors of the Central Nervous System

- For the past century, the classification of brain tumors has been based largely on the concepts of histogenesis that tumors can be classified **according to**:
  1. their microscopic similarities with different putative cells of origin and
  2. their presumed levels of differentiation.

- The characterization of such histological similarities has been primarily **dependent on**:
  A. light microscopic features in hematoxylin and eosin–stained sections,
  B. immunohistochemical expression of lineage-associated proteins, and
  C. ultrastructural characterization.

I. ***Historical:***

1. **1979 WHO classification of CNS tumors, Geneva, (1st edition):** The first edition of the classification of nervous system tumors was published in 1979 and took almost a decade to complete depends on ***Histological typing*** of CNS tumors.
2. **1993 WHO classification of CNS tumors, Heidelberg (2nd edition):** The second edition followed in 1993 and was considered a great step forward as it incorporated the advances in classification resulting from the introduction of ***immunohistochemistry*** into diagnostic pathology.

- **2000 WHO classification of CNS tumors, Lyon, (3rd edition), International Agency for Research on Cancer (IARC) Press,** incorporated the ***genetic profiles*** as an additional aid to the definition of brain tumors.
- The third edition formal classification is accompanied by definitions and ICD-O codes.
- In contrast to the previous ***'WHO Blue Books'*** (as the series is commonly termed), **the third edition included** concise sections on the epidemiology, clinical signs and symptoms, imaging, prognosis and predictive factors.

4. **2007 WHO classification (4th edition):** This is the classification used until 2015.

- Listed for each tumor are the WHO official name, the ICD-O code with Arabic numeral, where /0 indicates "benign" tumor, /3 malignant tumor, and /1 borderline tumor, and with Roman numeral the WHO Grade; a parameter connected with the "aggressiveness" of the tumor.
- This version covered many techniques to diagnose the disease, which was also included in the textbook of neurosurgery (Youman 6th edition).

II. *Currently :*

- As of 2016, clinicians are using **revised WHO grade 4th edition** which incorporates recent advance ***in molecular pathology*** into the classification of CNS tumor entities.

The International Classification of Diseases for Oncology (ICD-O Coding)

- ICD-O Coding
- The *International Classification of Diseases for Oncology (ICD-O)* has been used for more than 30 years, principally in tumor or cancer registries, for coding the site (topography) and the histology (morphology) of the neoplasm, usually obtained from a pathology report. and serves as an indispensable interface between pathologists and cancer registries.
- By agreement with the *College of American Pathologists CAP)*, the morphology section of ICD-O is incorporated into the *Systematized Nomenclature of Medicine (SNOMED)* classification.
- It assures that histopathological data, population-based incidence, and mortality data become available for epidemiological and oncological studies.
- The histology (morphology) code is increasingly complemented by genetic characterization of human neoplasms

- In 1976 the WHO publishes the **first edition** of the International Classification of Diseases for Oncology (ICD-O).
- The ICD-O-2, **Second Edition** was published in 1990, followed by the ICD-O-3, **Third Edition** in 2000.
- The topography section of the third edition remained the same as in the second edition, which was based on the neoplasm section of the ***International Statistical Classification of Diseases and Related Health Problems, 10th Revision*** **(ICD-10)**, however, the morphology section was revised.
- The **third edition** of ICD-O (ICD-O-3) contains the codes proposed in the previous edition of the WHO Blue Books.

- **International Classification of Diseases for Oncology, Third Edition (ICD-O-3) introduce a Behavior Code for Neoplasms**
- /0 Benign
- /1 Uncertain whether benign or malignant
  - Borderline malignancy
  - Low malignant potential
  - Uncertain malignant potential
- /2 Carcinoma *in situ*
  - Intraepithelial
  - Non-infiltrating
  - Non-invasive
- /3 Malignant, primary site
- /6 Malignant, metastatic site
  - Malignant, secondary site
- /9 Malignant, uncertain whether primary or metastatic site

The 2007 WHO classification of the tumors of the CNS

The following is a simplified version of the 2007 WHO classification of the tumors of the CNS

1. **Tumors of neuroepithelial tissue**
   - 1.1. **Astrocytic tumors** (Astrocytomas, a type of brain tumor)
     - 1.1.1 Pilocytic astrocytoma (ICD-O 9421/1, WHO grade I)
       - 1.1.1a *Pilomyxoid astrocytoma* (ICD-O 9425/3, WHO grade II)
     - 1.1.2 Subependymal giant cell astrocytoma (ICD-O 9384/1, WHO grade I)
     - 1.1.3 Pleomorphic xanthoastrocytoma (ICD-O 9424/3, WHO grade II)
     - 1.1.4 Diffuse astrocytoma (ICD-O 9400/3, WHO grade II)
     - 1.1.5 Anaplastic astrocytoma (ICD-O 9401/3, WHO grade III)
     - 1.1.6.Glioblastoma (ICD-O 9440/3, WHO grade IV)
       - 1.1.6a *Giant cell glioblastoma* (ICD-O 9441/3, WHO grade IV)
       - 1.1.6b *Gliosarcoma* (ICD-O 9442/3, WHO grade IV)
     - 1.1.7 Gliomatosis cerebri (ICD-O 9381/3, WHO grade III)

1.2. **Oligodendroglial tumors**

1.2.1 Oligodendroglioma (ICD-O 9450/3, WHO grade II)

1.2.2 Anaplastic oligodendroglioma (ICD-O 9451/3, WHO grade III)

1.3. **Oligoastrocytic tumors**

1.3.1 Oligoastrocytoma (ICD-O 9382/3, WHO grade II)

1.3.2 Anaplastic oligoastrocytoma (ICD-O 9382/3, WHO grade III)

1.4. **Ependymal tumors**

1.4.1 Subependymoma (ICD-O 9383/1, WHO grade I)

1.4.2 Myxopapillary ependymoma (ICD-O 9394/1, WHO grade I)

1.4.3 Ependymoma (ICD-O 9391/3, WHO grade II)

1.4.4 Anaplastic ependymoma (ICD-O 9392/3, WHO grade III)

1.5. **Choroid plexus tumors**

1.5.1 Choroid plexus papilloma (ICD-O 9390/0, WHO grade I)

1.5.2 Atypical choroid plexus papilloma (ICD-O 9390/1, WHO grade II)

1.5.3 Choroid plexus carcinoma (ICD-O 9390/3, WHO grade III)

1.6. **Other neuroepithelial tumors**

1.6.1 Astroblastoma (ICD-O 9430/3, WHO grade I)

1.6.2 Chordoid glioma of the third ventricle (ICD-O 9444/1, WHO grade II)

1.6.3 Angiocentric glioma (ICD-O 9431/1, WHO grade I)

1.7. **Neuronal and mixed neuronal-glial tumors**

1.7.1 Dysplastic gangliocytoma of cerebellum (Lhermitte-Duclos) (ICD-O 9493/0)

1.7.2 Desmoplastic infantile astrocytoma/ganglioglioma (ICD-O 9412/1, WHO grade I)

1.7.3 Dysembryoplastic neuroepithelial tumor (ICD-O 9413/0, WHO grade I)

1.7.4 Gangliocytoma (ICD-O 9492/0, WHO grade I)

1.7.5 Ganglioglioma (ICD-O 9505/1, WHO grade I)

1.7.6 Anaplastic ganglioglioma (ICD-O 9505/3, WHO grade III)

1.7.7 Central neurocytoma (ICD-O 9506/1, WHO grade II)

1.7.8 Extraventricular neurocytoma (ICD-O 9506/1, WHO grade II)

1.7.9 Cerebellar liponeurocytoma (ICD-O 9506/1, WHO grade II)

1.7.10 Papillary glioneuronal tumor (ICD-O 9509/1, WHO grade I)

1.7.11 Rosette-forming glioneuronal tumor of the fourth ventricle (ICD-O 9509/1, WHO grade I)

1.7.12 Paraganglioma (ICD-O 8680/1, WHO grade I)

1.8. **Tumors of the pineal region**

1.8.1 Pineocytoma (ICD-O 9361/1, WHO grade I)

1.8.2 Pineal parenchymal tumor of intermediate differentiation (ICD-O 9362/3, WHO grade II, III)

1.8.3 Pineoblastoma (ICD-O 9362/3, WHO grade IV)

1.8.4 Papillary tumors of the pineal region (ICD-O 9395/3, WHO grade II, III)

1.9. **Embryonal tumors**

1.9.1 Medulloblastoma (ICD-O 9470/3, WHO grade IV)

1.9.1b *Medulloblastoma with extensive nodularity* (ICD-O 9471/3, WHO grade IV)

1.9.1c *Anaplastic medulloblastoma* (ICD-O 9474/3, WHO grade IV)

1.9.2. CNS Primitive neuroectodermal tumour (ICD-O 9473/3, WHO grade IV)

1.9.2a *CNS Neuroblastoma* (ICD-O 9500/3, WHO grade IV)

1.9.3 Atypical teratoid/rhabdoid tumor (ICD-O 9508/3, WHO grade IV)

2. Tumors of cranial and paraspinal nerves

2.1 Schwannoma (ICD-O 9560/0, WHO grade I)

2.2 Neurofibroma (ICD-O 9540/0, WHO grade I)

2.3 Perineurioma (ICD-O 9571/0, 9571/3, WHO grade I, II, III)

2.4 Malignant peripheral nerve sheath tumor (MPNST) (ICD-O 9540/3, WHO grade II, III, IV)

3. Tumors of the meninges

3.1 Tumors of meningothelial cells

3.1.1 Meningioma (ICD-O 9530/0, WHO grade I)

3.1.1l *Atypical meningioma* (ICD-O 9539/1, WHO grade II)

3.1.1o *Anaplastic meningioma* (ICD-O 9530/3, WHO grade III)

3.2 Mesenchymal tumors

3.2.1 Lipoma (ICD-O 8850/0)

3.2.2 Angiolipoma (ICD-O 8861/0)

3.2.3 Hibernoma (ICD-O 8880/0)

3.2.4 Liposarcoma (ICD-O 8850/3)

3.2.5 Solitary fibrous tumor (ICD-O 8815/0)

3.2.6 Fibrosarcoma (ICD-O 8810/3)

3.2.7 Malignant fibrous histiocytoma (ICD-O 8830/3)

3.2.8 Leiomyoma (ICD-O 8890/0)

3.2.9 Leiomyosarcoma (ICD-O 8890/3)

3.2.10 Rhabdomyoma (ICD-O 8900/0)

3.2.11 Rhabdomyosarcoma (ICD-O 8900/3)
3.2.12 Chondroma (ICD-O 9220/0)
3.2.13 Chondrosarcoma (ICD-O 9220/3)
3.2.14 Osteoma (ICD-O 9180/0)
3.2.15 Osteosarcoma (ICD-O 9180/3)
3.2.16 Osteochondroma (ICD-O 9210/0)
3.2.17 Hemangioma (ICD-O 9120/0)
3.2.18 Epithelioid hemangioendothelioma (ICD-O 9133/1)
3.2.19 Hemangiopericytoma (ICD-O 9150/1, WHO grade II)
3.2.20 Anaplastic hemangiopericytoma (ICD-O 9150/3, WHO grade III)
3.2.21 Angiosarcoma (ICD-O 9120/3)
3.2.22 Kaposi Sarcoma (ICD-O 9140/3)
3.2.23 Ewing Sarcoma - PNET (ICD-O 9364/3)

3.3 **Primary melanocytic lesions**

3.3.1 Diffuse melanocytosis (ICD-O 8728/0)

3.3.2 Melanocytoma (ICD-O 8728/1)

3.3.3 Malignant melanoma (ICD-O 8720/3)

3.3.4 Meningeal melanomatosis (ICD-O 8728/3)

3.4 **Other neoplasms related to the meninges**

3.4.1 Hemangioblastoma (ICD-O 9161/1, WHO grade I)

4. Tumors of the hematopoietic system

4.1 Malignant Lymphomas (ICD-O 9590/3)

4.2 Plasmocytoma (ICD-O 9731/3)

4.3 Granulocytic sarcoma (ICD-O 9930/3)

5. Germ cell tumors

5.1 Germinoma (ICD-O 9064/3)

5.2 Embryonal carcinoma (ICD-O 9070/3)

5.3 Yolk sac tumor (ICD-O 9071/3)

5.4 Choriocarcinoma (ICD-O 9100/3)

5.5 Teratoma (ICD-O 9080/1)

5.6 Mixed germ cell tumors (ICD-O 9085/3)

6. Tumors of the sellar region

6.1 Craniopharyngioma (ICD-O 9350/1, WHO grade I)

6.2 Granular cell tumor (ICD-O 9582/0, WHO grade I)

6.3 Pituicytoma (ICD-O 9432/1, WHO grade I)

6.4 Spindle cell oncocytoma of the adenohypophysis (ICD-O 8991/0, WHO grade I)

7. Metastatic Tumors

Tumors that originate outside CNS and spread secondarily to CNS via hematogenous route or by direct invasion from adjacent tissues. Most common primary tumor sites are:

7.1 Lung

7.2 Breast

7.3 Melanoma

7.4 Renal

7.5 Colorectal

WHO classification and grading of tumors of the central nervous system 2016

WHO classification of tumours of the central nervous system

Diffuse astrocytic and oligodendroglial tumours	
Diffuse astrocytoma, IDH-mutant	9400/3
Gemistocytic astrocytoma, IDH-mutant	9411/3
Diffuse astrocytoma, IDH-wildtype	*9400/3*
Diffuse astrocytoma, NOS	9400/3
Anaplastic astrocytoma, IDH-mutant	9401/3
Anaplastic astrocytoma, IDH-wildtype	*9401/3*
Anaplastic astrocytoma, NOS	9401/3
Glioblastoma, IDH-wildtype	9440/3
Giant cell glioblastoma	9441/3
Gliosarcoma	9442/3
Epithelioid glioblastoma	*9440/3*
Glioblastoma, IDH-mutant	9445/3*
Glioblastoma, NOS	9440/3
Diffuse midline glioma, H3 K27M–mutant	9385/3*
Oligodendroglioma, IDH-mutant and 1p/19q-codeleted	9450/3
Oligodendroglioma, NOS	9450/3
Anaplastic oligodendroglioma, IDH-mutant and 1p/19q-codeleted	9451/3
Anaplastic oligodendroglioma, NOS	*9451/3*
Oligoastrocytoma, NOS	*9382/3*
Anaplastic oligoastrocytoma, NOS	*9382/3*
Other astrocytic tumours	
Pilocytic astrocytoma	9421/1
Pilomyxoid astrocytoma	9425/3
Subependymal giant cell astrocytoma	9384/1
Pleomorphic xanthoastrocytoma	9424/3
Anaplastic pleomorphic xanthoastrocytoma	9424/3
Ependymal tumours	
Subependymoma	9383/1
Myxopapillary ependymoma	9394/1
Ependymoma	9391/3
Papillary ependymoma	9393/3
Clear cell ependymoma	9391/3
Tanycytic ependymoma	9391/3
Ependymoma, *RELA* fusion–positive	9396/3*
Anaplastic ependymoma	9392/3
Other gliomas	
Chordoid glioma of the third ventricle	9444/1
Angiocentric glioma	9431/1
Astroblastoma	9430/3
Choroid plexus tumours	
Choroid plexus papilloma	9390/0
Atypical choroid plexus papilloma	9390/1
Choroid plexus carcinoma	9390/3

Neuronal and mixed neuronal-glial tumours	
Dysembryoplastic neuroepithelial tumour	9413/0
Gangliocytoma	9492/0
Ganglioglioma	9505/1
Anaplastic ganglioglioma	9505/3
Dysplastic cerebellar gangliocytoma (Lhermitte–Duclos disease)	9493/0
Desmoplastic infantile astrocytoma and ganglioglioma	9412/1
Papillary glioneuronal tumour	9509/1
Rosette-forming glioneuronal tumour	9509/1
Diffuse leptomeningeal glioneuronal tumour	
Central neurocytoma	9506/1
Extraventricular neurocytoma	9506/1
Cerebellar liponeurocytoma	9506/1
Paraganglioma	8693/1
Tumours of the pineal region	
Pineocytoma	9361/1
Pineal parenchymal tumour of intermediate differentiation	9362/3
Pineoblastoma	9362/3
Papillary tumour of the pineal region	9395/3
Embryonal tumours	
Medulloblastomas, genetically defined	
Medulloblastoma, WNT-activated	9475/3*
Medulloblastoma, SHH-activated and *TP53*-mutant	9476/3*
Medulloblastoma, SHH-activated and *TP53*-wildtype	9471/3
Medulloblastoma, non-WNT/non-SHH	9477/3*
Medulloblastoma, group 3	
Medulloblastoma, group 4	
Medulloblastomas, histologically defined	
Medulloblastoma, classic	9470/3
Medulloblastoma, desmoplastic/nodular	9471/3
Medulloblastoma with extensive nodularity	9471/3
Medulloblastoma, large cell / anaplastic	9474/3
Medulloblastoma, NOS	9470/3
Embryonal tumour with multilayered rosettes, C19MC-altered	9478/3*
Embryonal tumour with multilayered rosettes, NOS	*9478/3*
Medulloepithelioma	9501/3
CNS neuroblastoma	9500/3
CNS ganglioneuroblastoma	9490/3
CNS embryonal tumour, NOS	9473/3
Atypical teratoid/rhabdoid tumour	9508/3
CNS embryonal tumour with rhabdoid features	*9508/3*
Tumours of the cranial and paraspinal nerves	
Schwannoma	9560/0
Cellular schwannoma	9560/0
Plexiform schwannoma	9560/0

Melanotic schwannoma	9560/1
Neurofibroma	9540/0
Atypical neurofibroma	9540/0
Plexiform neurofibroma	9550/0
Perineurioma	9571/0
Hybrid nerve sheath tumours	
Malignant peripheral nerve sheath tumour	9540/3
Epithelioid MPNST	9540/3
MPNST with perineurial differentiation	9540/3
Meningiomas	
Meningioma	9530/0
Meningothelial meningioma	9531/0
Fibrous meningioma	9532/0
Transitional meningioma	9537/0
Psammomatous meningioma	9533/0
Angiomatous meningioma	9534/0
Microcystic meningioma	9530/0
Secretory meningioma	9530/0
Lymphoplasmacyte-rich meningioma	9530/0
Metaplastic meningioma	9530/0
Chordoid meningioma	9538/1
Clear cell meningioma	9538/1
Atypical meningioma	9539/1
Papillary meningioma	9538/3
Rhabdoid meningioma	9538/3
Anaplastic (malignant) meningioma	9530/3
Mesenchymal, non-meningothelial tumours	
Solitary fibrous tumour / haemangiopericytoma**	
Grade 1	8815/0
Grade 2	8815/1
Grade 3	8815/3
Haemangioblastoma	9161/1
Haemangioma	9120/0
Epithelioid haemangioendothelioma	9133/3
Angiosarcoma	9120/3
Kaposi sarcoma	9140/3
Ewing sarcoma / PNET	9364/3
Lipoma	8850/0
Angiolipoma	8861/0
Hibernoma	8880/0
Liposarcoma	8850/3
Desmoid-type fibromatosis	8821/1
Myofibroblastoma	8825/0
Inflammatory myofibroblastic tumour	8825/1
Benign fibrous histiocytoma	8830/0
Fibrosarcoma	8810/3
Undifferentiated pleomorphic sarcoma / malignant fibrous histiocytoma	8802/3
Leiomyoma	8890/0
Leiomyosarcoma	8890/3
Rhabdomyoma	8900/0
Rhabdomyosarcoma	8900/3
Chondroma	9220/0
Chondrosarcoma	9220/3
Osteoma	9180/0
Osteochondroma	9210/0
Osteosarcoma	9180/3
Melanocytic tumours	
Meningeal melanocytosis	8728/0
Meningeal melanocytoma	8728/1
Meningeal melanoma	8720/3
Meningeal melanomatosis	8728/3
Lymphomas	
Diffuse large B-cell lymphoma of the CNS	9680/3
Immunodeficiency-associated CNS lymphomas	
AIDS-related diffuse large B-cell lymphoma	
EBV-positive diffuse large B-cell lymphoma, NOS	
Lymphomatoid granulomatosis	9766/1
Intravascular large B-cell lymphoma	9712/3
Low-grade B-cell lymphomas of the CNS	
T-cell and NK/T-cell lymphomas of the CNS	
Anaplastic large cell lymphoma, ALK-positive	9714/3
Anaplastic large cell lymphoma, ALK-negative	9702/3
MALT lymphoma of the dura	9699/3
Histiocytic tumours	
Langerhans cell histiocytosis	9751/3
Erdheim–Chester disease	9750/1
Rosai–Dorfman disease	
Juvenile xanthogranuloma	
Histiocytic sarcoma	9755/3
Germ cell tumours	
Germinoma	9064/3
Embryonal carcinoma	9070/3
Yolk sac tumour	9071/3
Choriocarcinoma	9100/3
Teratoma	9080/1
Mature teratoma	9080/0
Immature teratoma	9080/3
Teratoma with malignant transformation	9084/3
Mixed germ cell tumour	9085/3
Tumours of the sellar region	
Craniopharyngioma	9350/1
Adamantinomatous craniopharyngioma	9351/1
Papillary craniopharyngioma	9352/1
Granular cell tumour of the sellar region	9582/0
Pituicytoma	9432/1
Spindle cell oncocytoma	8290/0
Metastatic tumours	

The morphology codes are from the International Classification of Diseases for Oncology (ICD-O) [742A]. Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour; /2 for carcinoma in situ and grade III intraepithelial neoplasia; and /3 for malignant tumours. The classification is modified from the previous WHO classification, taking into account changes in our understanding of these lesions.
*These new codes were approved by the IARC/WHO Committee for ICD-O. *Italics*: Provisional tumour entities. **Grading according to the 2013 *WHO Classification of Tumours of Soft Tissue and Bone*.

A synopsis of the 2016 WHO grades of tumors of the CNS is given in the following table:

WHO grades of select CNS tumours	
Diffuse astrocytic and oligodendroglial tumours	
Diffuse astrocytoma, IDH-mutant	II
Anaplastic astrocytoma, IDH-mutant	III
Glioblastoma, IDH-wildtype	IV
Glioblastoma, IDH-mutant	IV
Diffuse midline glioma, H3 K27M–mutant	IV
Oligodendroglioma, IDH-mutant and 1p/19q-codeleted	II
Anaplastic oligodendroglioma, IDH-mutant and 1p/19q-codeleted	III
Other astrocytic tumours	
Pilocytic astrocytoma	I
Subependymal giant cell astrocytoma	I
Pleomorphic xanthoastrocytoma	II
Anaplastic pleomorphic xanthoastrocytoma	III
Ependymal tumours	
Subependymoma	I
Myxopapillary ependymoma	I
Ependymoma	II
Ependymoma, *RELA* fusion–positive	II or III
Anaplastic ependymoma	III
Other gliomas	
Angiocentric glioma	I
Chordoid glioma of third ventricle	II
Choroid plexus tumours	
Choroid plexus papilloma	I
Atypical choroid plexus papilloma	II
Choroid plexus carcinoma	III
Neuronal and mixed neuronal-glial tumours	
Dysembryoplastic neuroepithelial tumour	I
Gangliocytoma	I
Ganglioglioma	I
Anaplastic ganglioglioma	III
Dysplastic gangliocytoma of cerebellum (Lhermitte–Duclos)	I
Desmoplastic infantile astrocytoma and ganglioglioma	I
Papillary glioneuronal tumour	I
Rosette-forming glioneuronal tumour	I
Central neurocytoma	II
Extraventricular neurocytoma	II
Cerebellar liponeurocytoma	II
Tumours of the pineal region	
Pineocytoma	I
Pineal parenchymal tumour of intermediate differentiation	II or III
Pineoblastoma	IV
Papillary tumour of the pineal region	II or III
Embryonal tumours	
Medulloblastoma (all subtypes)	IV
Embryonal tumour with multilayered rosettes, C19MC-altered	IV
Medulloepithelioma	IV
CNS embryonal tumour, NOS	IV
Atypical teratoid/rhabdoid tumour	IV
CNS embryonal tumour with rhabdoid features	IV
Tumours of the cranial and paraspinal nerves	
Schwannoma	I
Neurofibroma	I
Perineurioma	I
Malignant peripheral nerve sheath tumour (MPNST)	II, III or IV
Meningiomas	
Meningioma	I
Atypical meningioma	II
Anaplastic (malignant) meningioma	III
Mesenchymal, non-meningothelial tumours	
Solitary fibrous tumour / haemangiopericytoma	I, II or III
Haemangioblastoma	I
Tumours of the sellar region	
Craniopharyngioma	I
Granular cell tumour	I
Pituicytoma	I
Spindle cell oncocytoma	I

WHO grades of select CNS tumours

Diffuse astrocytic and oligodendroglial tumours	
Diffuse astrocytoma, IDH-mutant	II
Anaplastic astrocytoma, IDH-mutant	III
Glioblastoma, IDH-wildtype	IV
Glioblastoma, IDH-mutant	IV
Diffuse midline glioma, H3 K27M–mutant	IV
Oligodendroglioma, IDH-mutant and 1p/19q-codeleted	II
Anaplastic oligodendroglioma, IDH-mutant and 1p/19q-codeleted	III
Other astrocytic tumours	
Pilocytic astrocytoma	I
Subependymal giant cell astrocytoma	I
Pleomorphic xanthoastrocytoma	II
Anaplastic pleomorphic xanthoastrocytoma	III
Ependymal tumours	
Subependymoma	I
Myxopapillary ependymoma	I
Ependymoma	II
Ependymoma, *RELA* fusion–positive	II or III
Anaplastic ependymoma	III
Other gliomas	
Angiocentric glioma	I
Chordoid glioma of third ventricle	II
Choroid plexus tumours	
Choroid plexus papilloma	I
Atypical choroid plexus papilloma	II
Choroid plexus carcinoma	III
Neuronal and mixed neuronal-glial tumours	
Dysembryoplastic neuroepithelial tumour	I
Gangliocytoma	I
Ganglioglioma	I
Anaplastic ganglioglioma	III
Dysplastic gangliocytoma of cerebellum (Lhermitte–Duclos)	I
Desmoplastic infantile astrocytoma and ganglioglioma	I
Papillary glioneuronal tumour	I
Rosette-forming glioneuronal tumour	I
Central neurocytoma	II
Extraventricular neurocytoma	II
Cerebellar liponeurocytoma	II
Tumours of the pineal region	
Pineocytoma	I
Pineal parenchymal tumour of intermediate differentiation	II or III
Pineoblastoma	IV
Papillary tumour of the pineal region	II or III
Embryonal tumours	
Medulloblastoma (all subtypes)	IV
Embryonal tumour with multilayered rosettes, C19MC-altered	IV
Medulloepithelioma	IV
CNS embryonal tumour, NOS	IV
Atypical teratoid/rhabdoid tumour	IV
CNS embryonal tumour with rhabdoid features	IV
Tumours of the cranial and paraspinal nerves	
Schwannoma	I
Neurofibroma	I
Perineurioma	I
Malignant peripheral nerve sheath tumour (MPNST)	II, III or IV
Meningiomas	
Meningioma	I
Atypical meningioma	II
Anaplastic (malignant) meningioma	III
Mesenchymal, non-meningothelial tumours	
Solitary fibrous tumour / haemangiopericytoma	I, II or III
Haemangioblastoma	I
Tumours of the sellar region	
Craniopharyngioma	I
Granular cell tumour	I
Pituicytoma	I
Spindle cell oncocytoma	I

WHO classification of tumors of the central nervous system 2016

- **Diffuse astrocytic and oligodendroglial tumors**
- Diffuse astrocytoma, IDH-mutant 9400/3
  Gemistocytic astrocytoma, IDH-mutant 9411/3
- Diffuse astrocytoma, IDH-wildtype 9400/3
- Diffuse astrocytoma, NOS 9400/3

- Anaplastic astrocytoma, IDH-mutant 9401/3
- Anaplastic astrocytoma, IDH-wildtype 9401/3
- Anaplastic astrocytoma, NOS 9401/3

- Glioblastoma, IDH-wildtype 9440/3
  - Giant cell glioblastoma 9441/3
  - Gliosarcoma 9442/3
  - Epithelioid glioblastoma 9440/3
- Glioblastoma, IDH-mutant 9445/3*
- Glioblastoma, NOS 9440/3

- Diffuse midline glioma, H3 K27M-mutant 9385/3*

- Oligodendroglioma, IDH-mutant and 1p/19q-codeleted 9450/3
- Oligodendroglioma, NOS 9450/3
- Anaplastic oligodendroglioma, IDH-mutant and 1p/19q-codeleted 9451/3
- Anaplastic oligodendroglioma, NOS 9451/3

- Oligoastrocytoma, NOS 9382/3
- Anaplastic oligoastrocytoma, NOS 9382/3

- **Other astrocytic tumors**
- Pilocytic astrocytoma 9421/1
  Pilomyxoid astrocytoma 9425/3
- Subependymal giant cell astrocytoma 9384/1
- Pleomorphic xanthoastrocytoma 9424/3
- Anaplastic pleomorphic xanthoastrocytoma 9424/3

- **Ependymal tumors**
- Subependymoma 9383/1
- Myxopapillary ependymoma 9394/1
- Ependymoma 9391/3
  - Papillary ependymoma 9393/3
  - Clear cell ependymoma 9391/3
  - Tanycytic ependymoma 9391/3
- Ependymoma, RELA fusion-positive 9396/3*
- Anaplastic ependymoma 9392/3

- **Other gliomas**
- Chordoid glioma of the third ventricle 9444/1
- Angiocentric glioma 9431/1
- Astroblastoma 9430/3

- **Choroid plexus tumors**
- Choroid plexus papilloma 9390/0
- Atypical choroid plexus papilloma 9390/1
- Choroid plexus carcinoma 9390/3

- **Neuronal and mixed neuronal-glial tumors**
  Dysembryoplastic neuroepithelial tumor 9413/0
- Gangliocytoma 9492/0
- Ganglioglioma 9505/1
- Anaplastic ganglioglioma 9505/3
- Dysplastic cerebellar gangliocytoma (Lhermitte-Duclos disease) 9493/0
- Desmoplastic infantile astrocytoma and ganglioglioma 9412/1
- Papillary glioneuronal tumor 9509/1
- Rosette-forming glioneuronal tumor 9509/1
- Diffuse leptomeningeal glioneuronal tumor
- Central neurocytoma 9506/1
- Extraventricular neurocytoma 9506/1
- Cerebellar liponeurocytoma 9506/1
- Paraganglioma 8693/1

- **Tumors of the pineal region**
- Pineocytoma 9361/1
- Pineal parenchymal tumor of intermediate 1p/19q-codeleted 9450/3 differentiation 9362/3
- Pineoblastoma 9362/3
- Papillary tumor of the pineal region 9395/3

- **Embryonal tumors**
  - Medulloblastomas, genetically defined
  - Medulloblastoma, WNT-activated 9475/3*
  - Medulloblastoma, SHH-activated and TP53-mutant 9476/3*
  - Medulloblastoma, SHH-activated and TP53-wildtype 9471/3
  - Medulloblastoma, non-WNT/non-SHH 9477/3*
    - Medulloblastoma, group 3
    - Medulloblastoma, group 4
- Medulloblastomas, histologically defined
  - Medulloblastoma, classic 9470/3
  - Medulloblastoma, desmoplastic/nodular 9471/3
  - Medulloblastoma with extensive nodularity 9471/3
  - Medulloblastoma, large cell / anaplastic 9474/3
- Medulloblastoma, NOS 9470/3

- Embryonal tumor with multilayered rosettes, C19MC-altered 9478/3*
- Embryonal tumor with multilayered rosettes, NOS 9478/3
- Medulloepithelioma 9501/3
- CNS neuroblastoma 9500/3
- CNS ganglioneuroblastoma 9490/3
- CNS embryonal tumor, NOS 9473/3
- Atypical teratoid/rhabdoid tumor 9508/3
- CNS embryonal tumor with rhabdoid features 9508/3

- **Tumors of the cranial and paraspinal nerves**
- Schwannoma 9560/0
  Cellular schwannoma 9560/0
  Plexiform schwannoma 9560/0
- Melanotic schwannoma 9560/1
- Neurofibroma 9540/0
  Atypical neurofibroma 9540/0
  Plexiform neurofibroma 9550/0
- Perineurioma 9571/0
- Hybrid nerve sheath tumors
- Malignant peripheral nerve sheath tumor 9540/3
  Epithelioid MPNST 9540/3
  MPNST with perineurial differentiation 9540/3

- **Meningiomas 9530/0**
- Meningioma
- Meningothelial meningioma 9531/0
- Fibrous meningioma 9532/0
- Transitional meningioma 9537/0
- Psammomatous meningioma 9533/0
- Angiomatous meningioma 9534/0
- Microcystic meningioma 9530/0
- Secretory meningioma 9530/0
- Lymphoplasmacyte-rich meningioma 9530/0
- Metaplastic meningioma 9530/0
- Chordoid meningioma 9538/1
- Clear cell meningioma 9538/1
- Atypical meningioma 9539/1
- Papillary meningioma 9538/3
- Rhabdoid meningioma 9538/3
- Anaplastic (malignant) meningioma 9530/3

- **Mesenchymal, non-meningothelial tumors 8815/0**
- Solitary fibrous tumor/hemangiopericytoma**
  Grade 1 8815/0
  Grade 2 8815/1
  Grade 3 8815/3
- Hemangioblastoma 9161/1
- Hemangioma 9120/0
- Epithelioid haemangioendothelioma 9133/3
- Angiosarcoma 9120/3
- Kaposi sarcoma 9140/3
- Ewing sarcoma / PNET 9364/3
- Lipoma 8850/0
- Angiolipoma 8861/0
- Hibernoma 8880/0
- Liposarcoma 8850/3
- Desmoid-type fibromatosis 8821/1

- Myofibroblastoma 8825/0
- Inflammatory myofibroblastic tumor 8825/1
- Benign fibrous histiocytoma 8830/0
- Fibrosarcoma 8810/3
- Undifferentiated pleomorphic sarcoma / malignant fibrous histiocytoma 8802/3
- Leiomyoma 8890/0
- Leiomyosarcoma 8890/3
- Rhabdomyoma 8900/0
- Rhabdomyosarcoma 8900/3
- Chondroma 9220/0
- Chondrosarcoma 9220/3
- Osteoma 9180/0
- Osteochondroma 9210/0
- Osteosarcoma 9180/3

- **Melanocytic tumors**
- Meningeal melanocytosis 8728/0
- Meningeal melanocytoma 8728/1
- Meningeal melanoma 8720/3
- Meningeal melanomatosis 8728/3

- **Lymphomas**
- Diffuse large B-cell lymphoma of the CNS 9680/3
- Immunodeficiency-associated CNS lymphomas
  AIDS-related diffuse large B-cell lymphoma
  EBV-positive diffuse large B-cell lymphoma, NOS

- Lymphomatoid granulomatosis 9766/1
- Intravascular large B-cell lymphoma 9712/3
- Low-grade B-cell lymphomas of the CNS T-cell and NK/T-cell lymphomas of the CNS Anaplastic
- large cell lymphoma, ALK-positive 9714/3
- Anaplastic large cell lymphoma, ALK-negative 9702/3
- MALT lymphoma of the dura 9699/3

- **Histiocytic tumors**
- Langerhans cell histiocytosis 9751/3
- Erdheim-Chester disease 9750/1
- Rosai-Dorfman disease 9755/3
- Juvenile xanthogranuloma
- Histiocytic sarcoma

- **Germ cell tumors**
- Germinoma 9064/3
- Embryonal carcinoma 9070/3
- Yolk sac tumor 9071/3
- Choriocarcinoma 9100/3
- Teratoma 9080/1
  Mature teratoma 9080/0
  Immature teratoma 9080/3
- Teratoma with malignant transformation 9084/3
- Mixed germ cell tumor 9085/3

- **Tumors of the sellar region**
- Craniopharyngioma 9350/1
  Adamantinomatous craniopharyngioma 9351/1
  Papillary craniopharyngioma 9352/1
- Granular cell tumor of the sellar region 9582/0
- Pituicytoma 9432/1
- Spindle cell oncocytoma 8290/0

- **Metastatic tumors**

- **The present review summarizes the major changes between the 2007 and 2016 CNS WHO classifications.**
- The 2016 update contains numerous differences from the 2007 WHO classification of brain tumors.
- Tumor diagnoses should consist of a histopathological name followed by the genetic features following a comma as adjectives, as in: *Diffuse astrocytoma, IDH-mutant* and *Medulloblastoma, WNT-activated*.
- The WHO classifications use spellings that are hybrid between American and British English.

- For entities with more than one genetic determinant, the multiple necessary molecular features are included in the name: *Oligodendroglioma, IDH-mutant* and *1p/19q-codeleted*.
- For a tumor lacking genetic mutation, the term *wild type* can be used: *Glioblastoma, IDH-wild type*.
- However, in most situations, a formal *wild type* diagnosis is not available, and a tumor lacking a diagnostic mutation is given an NOS designation.

- For tumor entities in which a specific genetic alteration is present or absent, the terms “positive” can be used if the molecular characteristic is present: *Ependymoma, RELA fusion-positive*.
- For sites lacking any access to molecular diagnostic testing, a diagnostic designation of NOS is permissible for some tumor types.
- An NOS designation implies that there is *insufficient information to assign a more specific code*.

- NOS in most instances refers to tumors that have not been fully tested for the relevant genetic parameter(s), but in rare instances may also include tumors that have been tested but do not show the diagnostic genetic alterations.
- NOS does not define a specific entity; rather it designates lesions that cannot be classified into any of the narrow defined groups.
- NOS designation thus represents those cases about which we do not know enough pathological, genetic and clinical data and which should, therefore, be subject to future study before additional refinements in classification can be made.

- With regard to formatting, italics are used for specific gene symbols (e.g., *ATRX*) but not for gene families (e.g., IDH, H3).
- To avoid numerous sequential hyphens, *wild type* has been used without a hyphen and en-dashes have been used in certain designations (e.g., RELA fusion-positive).
- Finally, as in the past, WHO grades are written in Roman numerals (e.g., I, II, III and IV; not 1, 2, 3 and 4).
- These have been added into the classification in those places where such diagnoses are possible.

- In the last edition, the Arabic numeral after the character "/" indicates the "behavior" of the neoplasia, with the following meaning:
- /0 benign neoplasia
- /1 uncertain neoplasia (benign or malignant)
- /2 neoplasia *in situ*
- /3 primary infiltrative malignant neoplasia
- /6 secondary malignant neoplasia
- /9 malignant neoplasia, uncertain if primitive or secondary

WHO grades of selected CNS tumors

- **Diffuse astrocytic and oligodendroglial tumors**
- Diffuse astrocytoma, IDH-mutant II
- Anaplastic astrocytoma, IDH-mutant III
- Glioblastoma, IDH-wildtype IV
- Glioblastoma, IDH-mutant IV
- Diffuse midline glioma, H3 K27M-mutant IV
- Oligodendroglioma, IDH-mutant and 1p/19q-codeleted II
- Anaplastic oligodendroglioma, IDH-mutant and 1p/19q-codeleted III

- **Other astrocytic tumors**
- Pilocytic astrocytoma I
- Subependymal giant cell astrocytoma I
- Pleomorphic xanthoastrocytoma II
- Anaplastic pleomorphic xanthoastrocytoma III
-
- **Ependymal tumors**
- Subependymoma I
- Myxopapillary ependymoma I
- Ependymoma II
- Ependymoma, RELA fusion-positive II or III
- Anaplastic ependymoma III

- **Other gliomas**
- Angiocentric glioma I
- Chordoid glioma of third ventricle II
- Choroid plexus tumors
- Choroid plexus papilloma I
- Atypical choroid plexus papilloma II
- Choroid plexus carcinoma III

- **Neuronal and mixed neuronal-glial tumors**
- Dysembryoplastic neuroepithelial tumor I
- Gangliocytoma I
- Ganglioglioma I
- Anaplastic ganglioglioma III
- Dysplastic gangliocytoma of cerebellum (Lhermitte-Duclos) I
- Desmoplastic infantile astrocytoma and ganglioglioma I
- Papillary glioneuronal tumor I
- Rosette-forming glioneuronal tumor I
- Central neurocytoma II
- Extraventricular neurocytoma II
- Cerebellar liponeurocytoma II

- **Tumors of the pineal region I**
- Pineocytoma II or III
- Pineal parenchymal tumor of intermediate differentiation
- Pineoblastoma IV
- Papillary tumor of the pineal region II or III

- **Embryonal tumors**
- Medulloblastoma (all subtypes) IV
- Embryonal tumor with multilayered rosettes, C19MC-altered IV
- Medulloepithelioma IV
- CNS embryonal tumor, NOS IV
- Atypical teratoid/rhabdoid tumor IV
- CNS embryonal tumour with rhabdoid features IV

- **Tumors of the cranial and paraspinal nerves**
- Schwannoma I
- Neurofibroma I
- Perineurioma I
- Malignant peripheral nerve sheath tumor (MPNST) I, III or IV
- Meningiomas
- Meningioma I
- Atypical meningioma II
- Anaplastic (malignant) meningioma III

- **Mesenchymal, non-meningothelial tumors**
- Solitary fibrous tumor / hemangiopericytoma I, II or III
- Hemangioblastoma I

- **Tumors of the sellar region**
- Craniopharyngioma I
- Granular cell tumour I
- Pituicytoma I
- Spindle cell oncocytoma I

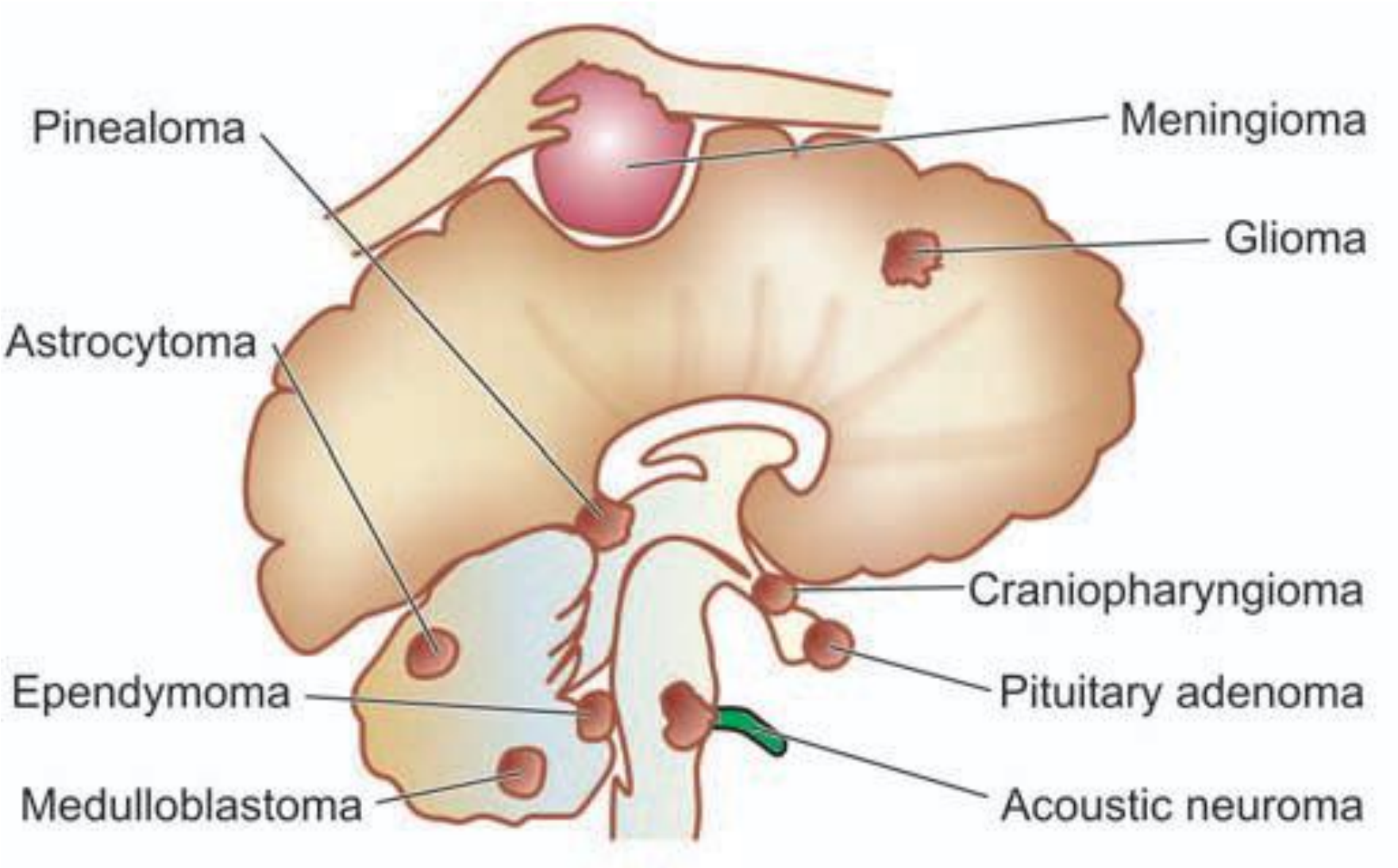
SUMMARY OF TUMOURS OF THE CENTRAL NERVOUS SYSTEM

I. **Tumors of neuroglia (gliomas):**
   1. Astrocytoma.
   2. Oligodendroglioma.
   3. Ependymoma.
      - Ependymoma
      - Myxopapillary pendymoma
      - Subependymoma

II. **Choroid plexus tumors.**
    1. Choroid plexus papilloma.
    2. Choroid plexus carcinoma.
III. **Tumors of neurons:**
    1. Neuroblastoma.
    2. Ganglioneuroblastoma.
    3. Ganglioneuroma.
IV. **Tumors of neurons and neuroglia:**
    1. Ganglioglioma.

V. **Tumors of primitive undifferentiated cells:**
    1. Medulloblastoma.
VI. **Tumors of pineal cells:**
    1. Pineoblastoma.
    2. Pineocytoma.
VII. **Tumors of the meninges:**
    1. Meningioma.
    2. Meningeal hemangiopericytoma.
    3. Meningeal sarcoma.

VIII. **Tumors of nerve sheath cells:**
   I. Schwannoma (neurilemmoma).
   II. Neurofibroma.
IX. **Lymphomas:**
   1. Primary .
   2. Secondary.
X. **Malformative tumors:**
   1. Craniopharyngioma.
   2. Epidermoid cyst
   3. Dermoid cyst.
   4. Colloid cyst.
XI. **Metastatic tumors.**



The anatomic distribution of common intracranial tumours

THANK YOU