1 OVERVIEW AND CLASSIFICATION

In the decade since the publication of the previous Fascicle on tumors of the central nervous system (CNS), many new entities have been described and the prognostic significance of certain tumor subtypes has been established. Grading criteria have been refined and molecular features have been correlated with tumor type and grade. While important to affected patients, the newly described lesions are usually rarities, unlikely to be seen by a single pathologist, whereas the refined grading criteria of common lesions, such as meningiomas, are both practical and globally relevant. An updated international consensus, or at least general agreement, on CNS tumor classification was published in 2007 by the World Health Organization (WHO) (1) and is outlined in Table 1-1.

In light of these developments, the present volume has been revised extensively. The classifications of both existing entities and newly described lesions have been brought into close alignment with the WHO system. Among the new lesions/variants are chordoid glioma of the third ventricle, cerebellar liponeurocytoma, large cell/anaplastic medulloblastoma, and papillary glioneuronal tumor. Entities described in the new millennium, such as papillary tumor of the pineal region, have also been included. The new WHO classification/grading system for meningiomas is described in detail.

The present book retains the outline of its predecessor and differs only slightly from the organization of the WHO book (1). For example, hemangiopericytoma and melanocytic tumors are discussed here in separate chapters, Tumors of Mesenchymal Tissue and Melanocytic Neoplasms, respectively, whereas the WHO publication combines them in a single chapter on meningeal tumors. These, and other minor variations, are only cosmetic distinctions that do not detract from the similarity of our classification scheme and that of the WHO.

Not withstanding widespread pessimism, CNS tumors are often surgically curable, thanks to advances in both neuroimaging and surgical techniques. Such cures are usually found among patients with relatively well-circumscribed tumors, but sometimes achieved even in those with diffuse, infiltrating lesions. It is essential to recognize the better-delimited tumors since they often lend themselves to resection, or at least debulking, that can permit a period of observation until the need for additional therapy, if any, becomes apparent. The significance of tumor architecture as it pertains to diagnosis and treatment is thus emphasized in the descriptions of individual entities throughout the book. Our first Appendix subdivides CNS tumors on the basis of demarcation; the large section on astrocytic neoplasms in chapter 3 is organized around this feature.

As three-dimensional, multiplanar forms of macroscopic examination, neuroradiologic techniques are important to pathologists for establishing the degree of circumscription, chronicity, vascularity, mineralization, and metabolic activity of various tumors. We discuss these techniques in regard to both neoplastic and non-neoplastic lesions. Chapter 2 reviews normal radiologic anatomy.

Despite the sophistication of neuroimaging, reactive lesions, such as demyelinating diseases, occasionally are biopsied in expectation of a neoplasm, with the very real potential for pathologic misdiagnosis and overtreatment. The admonition that pathologists remain alert to the possibility of a non-neoplastic lesion is repeated throughout this book. It is stressed in chapter 19 on reactive and inflammatory masses, and in two appendices that present the histologic features of non-neoplastic and low-grade lesions. A third appendix is an algorithm that ensures that non-neoplastic and low-grade entities are given full consideration in the differential diagnosis of a suspected CNS neoplasm.

Grading criteria, always artificial and arbitrary, are discussed at length throughout the text. For example, the prognostic implications

of mitotic counts and MIB-1 indices are recurring themes. The latter is an increasingly appreciated prognostic factor, with results often calculated to tenths of a percent, although there is surprisingly little information regarding interinstitutional reproducibility.

Techniques of the burgeoning field of molecular diagnostics are increasingly employed in tumor classification and grading. Examples relevant to CNS tumors include the status of chromosomes 1p and 19q in infiltrating gliomas; gain of chromosome 7, amplification and mutation of *EGFR*, and loss of heterozygosity on chromosomes 10, 17p, and 9p in diffuse astrocytomas; amplification or overexpression of *c-myc* in medulloblastomas; chromosomal imbalances in grades II and III meningiomas; mutations of *INI1* in atypical teratoid/rhabdoid tumor; and an ever growing list of gene expression profiles in multiple tumor types. We illustrate approaches of practical value, while assuming that morphologic findings will endure as a context in which to evaluate molecular findings.

Table 1-1

WORLD HEALTH ORGANIZATION CLASSIFICATION OF TUMORS OF THE NERVOUS SYSTEM[a]

TUMOURS OF NEUROEPITHELIAL TISSUE	
Astrocytic Tumours	
Pilocytic astrocytoma	9421/1
Pilomyxoid astrocytoma	*9425/3*[b]
Subependymal giant cell astrocytoma	9384/1
Pleomorphic xanthoastrocytoma	9424/3
Diffuse astrocytoma	9400/3
Fibrillary astrocytoma	9420/3
Protoplasmic astrocytoma	9410/3
Gemistocytic astrocytoma	9411/3
Anaplastic astrocytoma	9401/3
Glioblastoma	9440/3
Giant cell glioblastoma	9441/3
Gliosarcoma	9442/3
Gliomatosis cerebri	9381/3
Oligodendroglial Tumours	
Oligodendroglioma	9450/3
Anaplastic oligodendroglioma	9451/3
Oligoastrocytic Tumours	
Oligoastrocytoma	9382/3
Anaplastic oligoastrocytoma	9382/3
Ependymal Tumours	
Subependymoma	9383/1
Myxopapillary ependymoma	9394/1
Ependymoma	9391/3
Cellular	9391/3
Papillary	9393/3
Clear cell	9391/3
Tanycytic	9391/3
Anaplastic ependymoma	9392/3
Choroid Plexus Tumours	
Choroid plexus papilloma	9390/0
Atypical choroid plexus papilloma	*9390/1*
Choroid plexus carcinoma	9390/3
Other Neuroepithial Tumours	
Astroblastoma	9430/3
Chordoid glioma of the 3rd ventricle	9444/1
Angiocentric glioma	*9431/1*
Neuronal and Mixed Neuronal-Glial Tumours	
Dysplastic gangliocytoma of cerebellum (Lhermitte-Duclos)	9493/0
Desmoplastic infantile astrocytoma/ganglioglioma	9412/1
Dysembryoplastic neuroepithelial tumour	9413/0
Gangliocytoma	9492/0
Ganglioglioma	9505/1
Anaplastic ganglioglioma	9505/3
Central neurocytoma	9506/1
Extraventricular neurocytoma	*9506/1*
Cerebellar liponeurocytoma	*9506/1*
Papillary glioneuronal tumour	*9509/1*
Rosette-forming glioneuronal tumour of the 4th ventricle	*9509/1*
Paraganglioma of the filum terminale	8680/1
Tumours of the Pineal Region	
Pineal parenchymal tumours	
Pineocytoma	9361/1
Pineal parenchymal tumour of intermediate differentiation	9362/3
Pineoblastoma	9362/3
Papillary tumour of the pineal region	*9395/3*

[a]Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, eds. WHO Classification of Tumours of the Central Nervous System. Lyon: IARC Press; 2007.

[b]The italicized numbers are provisional codes proposed for the 4th edition of ICD-O. While they are expected to be incorporated into the next ICD-O edition, they currently remain subject to change.

Table 1-1 (Continued)

Embryonal Tumours	
Medulloblastoma	9470/3
Desmoplastic/nodular medulloblastoma	*9471/3*
Medulloblastoma with extensive nodularity	*9471/3*
Anaplastic medulloblastoma	*9474/3*
Large cell medulloblastoma	9474/3
CNS primitive neuroectodermal tumour (PNET)	9473/3
Medulloepithelioma	9501/3
Neuroblastoma	9500/3
Ganglioneuroblastoma	9490/3
Ependymoblastoma	9392/3
Atypical teratoid/rhabdoid tumor	9508/3
TUMOURS OF CRANIAL AND PARASPINAL NERVES	
Schwannoma (Neurinoma)	9560/0
Cellular	9560/0
Plexiform	9560/0
Melanotic	9560/0
Neurofibroma	9540/0
Plexiform	9550/0
Perineurioma	9571/0
Intraneural perineurioma	9571/0
Soft tissue perineurioma	9571/0
Malignant Peripheral Nerve Sheath Tumour (MPNST)	9540/3
Epithelioid	9540/3
MPNST with divergent meschymal and/or epithelial differentiation	9540/3
Melanotic	9540/3
TUMOURS OF THE MENINGES	
Tumours of Meningothelial Cells	
Meningioma	9530/0
Meningothelial	9531/0
Fibrous (fibroblastic)	9532/0
Transitional (mixed)	9537/0
Psammomatous	9533/0
Angiomatous	9534/0
Microcystic	9530/0
Secretory	9530/0
Lymphoplasmacyte-rich	9530/0
Metaplastic	9530/0
Clear Cell	9538/1
Chordoid	9538/1
Atypical	9539/1
Papillary	9538/3
Rhabdoid	9538/3
Anaplastic	9530/3
Mesenchymal Tumours	
Lipoma	8850/0
Angiolipoma	8861/0
Hibernoma	8880/0
Liposarcoma (intracranial)	8850/3
Solitary fibrous tumour	8815/0
Fibrosarcoma	8810/3
Malignant fibrous histiocytoma	8830/3
Leiomyoma	8890/0
Leiomyosarcoma	8890/3
Rhabdomyoma	8900/0
Rhabdomyosarcoma	8900/3
Chondroma	9220/3
Chondrosarcoma	9220/3
Osteoma	9180/0
Osteosarcoma	9180/3
Osteochondroma	9210/0
Haemangioma	9120/0
Epithelioid haemangioendothelioma	9133/1
Haemangiopericytoma	9150/1
Angiosarcoma	9120/3
Kaposi sarcoma	9140/3
Primary Melanocytic Lesions	
Diffuse melanocytosis	8728/0
Melanocytoma	8728/1
Malignant melanoma	8720/3
Meningeal melanomatosis	8728/3
Other Neoplasms Related to the Meninges	
Haemangioblastoma	9161/1
LYMPHOMAS AND HAEMOPOIETIC NEOPLASMS	
Malignant lymphomas	9590/3
Plasmacytoma	9731/3
Granulocytic sarcoma	9930/3
GERM CELL TUMOURS	
Germinoma	9064/3
Embryonal carcinoma	9070/3
Yolk sac tumour	9071/3
Choriocarcinoma	9100/3
Teratoma	9080/1
Mature	9080/0
Immature	9080/3
Teratoma with malignant transformation	9084/3
Mixed germ cell tumours	9085/3
TUMOURS OF THE SELLAR REGION	
Craniopharyngioma	9350/1
Adamantinomatous	9351/1
Papillary	9352/1
Granular cell tumour	9582/0
Pituicytoma	*9432/1*
Spindle cell oncocytoma	*8291/0*
METASTATIC TUMOURS	

REFERENCES

1. Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, eds. WHO Classification of Tumours of the Central Nervous System. Lyon: IARC Press; 2007. (In press)