Histological grade (Core)

Reason/Evidentiary Support

In as many pathology reports of CNS neoplasms as possible, the diagnosis should include a grade based on the WHO 2016 classification (see Table 2 below).[1,2] This scheme differs from the approaches in many other organ systems in that in most circumstances, the diagnosis dictates a given WHO grade rather than a range of grades within a diagnostic category. The scale of WHO grades from I to IV reflects the natural histories of various tumour types, rather than their shifting prognoses with changes in therapeutic practice over time.[3] Roughly speaking, a WHO grade I tumour is considered benign and potentially curable by surgery, although in unfavourable locations, such tumours may still create significant morbidity. WHO grade II tumours typically are slowly growing malignancies that often recur and are associated with significant mortality, albeit with survival times of many years in most cases. WHO grade III tumours are rapidly growing malignancies with typical survivals of only a few years if treated with surgery alone. Nearly all such tumours are designated as "anaplastic". WHO grade IV neoplasms are highly aggressive malignancies with rapid mortality (typically in less than 2 years after diagnosis) in the absence of adjuvant therapies (e.g., glioblastomas and embryonal neoplasms). Progression from lower-grade malignancy to higher-grade forms occurs in some CNS neoplasms, most commonly the diffuse gliomas (Table 3) and to a lesser extent in the meningiomas (Table 4). There are exceptions to the automatic assignment of a single WHO grade based on diagnosis, mostly in entities for which definite parameters for histological grading have not been established yet. Other bone and soft tissue neoplasms occurring within the neural axis are classified and graded using the same criteria as in other parts of the body. Lastly, it should be noted that in some cases, assigning a WHO grade is not possible or could cause more confusion than clarification for clinical colleagues (e.g., when the exact tumour subtype remains unclear). In such cases, it is preferable to omit the WHO grade from the final diagnosis.

Table 2 WHO Grades Based on Histologically Defined Diagnostic Category (based on histological appearance only, i.e., not full 2016 CNS WHO diagnoses)[#]

Tumour Group	Tumour Type	Grade I	Grade II	Grade III	Grade IV
Astrocytic tumours	Diffuse astrocytoma		**X**		
	Anaplastic astrocytoma			**X**	
	Glioblastoma (and variants)				**X**
	Pilocytic astrocytoma	**X**			
	Pilomyxoid astrocytoma (grade not assigned)				
	Subependymal giant cell astrocytoma	**X**			
	Pleomorphic xanthoastrocytoma		**X**		
	Anaplastic pleomorphic xanthoastrocytoma			**X**	
Oligodendrogliomas	Oligodendroglioma		**X**		
	Anaplastic oligodendroglioma			**X**	
Oligoastrocytomas	Oligoastrocytoma		**X**		
	Anaplastic oligoastrocytoma			**X**	

Ependymal tumours	Ependymoma		**X**		
	Anaplastic ependymoma			**X**	
	Subependymoma	**X**			
	Myxopapillary ependymoma	**X**			
Choroid plexus tumours	Choroid plexus papilloma	**X**			
	Atypical choroid plexus papilloma		**X**		
	Choroid plexus carcinoma			**X**	
Other neuroepithelial tumours	Chordoid glioma of the third ventricle		**X**		
	Angiocentric glioma	**X**			
Neuronal-glial tumours	Gangliocytoma	**X**			
	Desmoplastic infantile ganglioglioma/ astrocytoma (DIG/DIA)	**X**			
Tumour Group	**Tumour Type**	**Grade I**	**Grade II**	**Grade III**	**Grade IV**
	Dysembryoplastic neuroepithelial tumour	**X**			
	Ganglioglioma	**X**			
	Anaplastic ganglioglioma			**X**	
	Central neurocytoma		**X**		
	Extraventricular neurocytoma		**X**		
	Cerebellar liponeurocytoma		**X**		
	Papillary glioneuronal tumour	**X**			
	Rosette-forming glioneuronal tumour of the fourth ventricle	**X**			
	Paraganglioma of the spinal cord	**X**			
Pineal parenchymal tumours	Pineocytoma	**X**			
	Pineal parenchymal tumour of intermediate differentiation		**X**	**X**	
	Pineoblastoma				**X**
	Papillary tumour of the pineal region		**X**	**X**	
Embryonal tumours	Medulloblastoma				**X**
	CNS embryonal tumour, NOS				**X**
	Medulloepithelioma				**X**
	CNS Neuroblastoma				**X**
	CNS Ganglioneuroblastoma				**X**
	Ependymoblastoma				**X**
	Atypical teratoid/rhabdoid tumour				**X**
Cranial and peripheral nerve tumours	Schwannoma (and variants)	**X**			

	Neurofibroma (and variants)	**X**			
	Perineurioma	**X**			
	Malignant peripheral nerve sheath tumours (MPNST)		**X**	**X**	**X**
Meningeal tumours	Meningioma (and variants)	**X**			
	Atypical meningioma		**X**		
	Clear cell meningioma		**X**		
	Chordoid meningioma		**X**		
	Anaplastic meningioma			**X**	
	Papillary meningioma			**X**	
	Rhabdoid meningioma			**X**	
Mesenchymal tumours[4,5]	(Named as soft tissue counterpart)	**X**	**X**	**X**	**X**
	Solitary fibrous tumour / Haemangiopericytoma	**X**	**X**	**X**	
Tumours of uncertain histogenesis	Haemangioblastoma	**X**			

Tumour histology and grade are strong predictors of clinical behaviour for different CNS tumours, including diffusely infiltrating astrocytomas and meningiomas. Tables 3 and 4 list the grading criteria for these common CNS tumour types.

Table 3 WHO Grading System for Diffuse, Infiltrating Astrocytomas[#]

WHO Grade	**WHO Designation**	**Histologic Criteria**
II	Diffuse astrocytoma	Nuclear atypia
III	Anaplastic astrocytoma	Nuclear atypia and mitotic figures
IV	Glioblastoma	Nuclear atypia, mitotic figures, and microvascular proliferation and/or necrosis

Table 4 WHO Grading of Meningiomas[#]

WHO grade I	**Benign meningioma** (and variants) None of the criteria below for WHO grades II or III
WHO grade II	**Atypical meningioma** Mitotic figures ≥4/10 high-power fields (HPF) ***or*** At least 3 of 5 parameters: Sheeting architecture (loss of whorling and/or fascicles) Small cell formation Macronucleoli Hypercellularity Spontaneous necrosis

	or Brain invasion ***or*** **Clear cell meningioma** ***or*** **Chordoid meningioma**
WHO grade III	**Anaplastic (malignant) meningioma** Mitotic figures ≥ 20/10 HPF ***or*** Frank anaplasia (sarcoma, carcinoma, or melanoma-like histology) ***or*** **Papillary meningioma** ***or*** **Rhabdoid meningioma**

[#]Modified from the original versions in Brat DJ, Parisi JE, DeMasters BK et al. Protocol for the Examination of Specimens From Patients with Tumors of the Central Nervous System. 2014. Available at www.cap.org/cancerprotocols.

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1 Louis DN, Ohgaki H, Wiestler OD and Cavenee WK (eds) (2016). *WHO Classification of Tumours of the Central Nervous System, Revised. Fourth Edition*, IARC, Lyon.

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4 Perry A and Brat DJ (2010). *Practical Surgical Pathology: A Diagnostic Approach*. Elsevier, Philadelphia.

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