TUMORS OF THE CENTRAL NERVOUS SYSTEM

1. 1-2% of all malignant neoplasms
2. The most common solid cancer of childhood (2nd to leukemias for all malignancies)
3. 85% of central nervous system tumors occur within the brain and the remainder in the spinal cord.
4. Primary CNS tumors are classified according to cell of origin: astrocytes, oligodendrocytes, ependymal cells, neurons, meningothelial cells, choroid plexus etc.

Tumors arising in the parenchyma
a) Diffuse gliomas
   ▪ Astrocytoma
   ▪ Oligodendroglioma
b) Other astrocytic tumors
   ▪ Pilocytic astrocytoma
   ▪ Subependymal giant cell astrocytoma
   ▪ Pleomorphic xanthoastrocytoma
c) Ependymal tumors
d) Neuronal and mixed neuronal-glial tumors
   ▪ Central neurocytoma
   ▪ Ganglioglioma
   ▪ Dysembryoplastic neuroepithelial tumor (DNET)
e) Embryonal tumors
   ▪ Medulloblastoma
   ▪ Primitive neuroectodermal tumor (PNET)
   ▪ Atypical teratoid/rhabdoid tumor (AT/RT)

2) Tumors arising from the coverings
a) Meningioma
b) Hemangiopericytoma
c) Chondroma
d) Leiomyoma
e) Osteoma
f) Hemangioma
g) Lipoma

3) Tumors of Pituitary Gland
a) Pituitary adenoma
b) Craniopharyngioma

4) Tumors of Pineal Gland
a) Germinoma
b) Pineocytoma

5) Tumors of Cranial and Peripheral Nerves
a) Schwannoma
b) **Neurofibroma**  
c) **Malignant Peripheral Nerve Sheath Tumor (MPNST)**

5. Adults - 70% supratentorial  
6. Children - 70% infratentorial  
7. There is no premalignant or in situ stages  
8. The distinction between a "benign" and "malignant" tumor is less evident than in other sites (e.g. glial tumors with benign histology will infiltrate the brain and are fatal, when located in an area where surgical resection is not possible)  
9. Surgical resection is restricted because of the functional anatomic considerations, (e.g. removal of a lesion in the motor area will leave the patient paralyzed for the rest of their life).  
10. No/very rare spread outside CNS

11. **Gliomas**

a. **Diffuse (infiltrating) Astrocytoma**  
   Grading :
   - Diffuse astrocytoma – well-differentiated (WHO grade II), anaplastic astrocytoma (WHO grade III), glioblastoma (WHO grade IV)  
   - They arise in cerebral hemispheres and may involve more than one lobe; if 3 or more lobes involved = gliomatosis cerebri  
   - High grade (anaplastic and glioblastoma) show contrast enhancement on brain MRI; glioblastoma may cross corpus callosum = “butterfly lesion”  
   - Presentation: seizures, focal neurologic deficits, signs of increased intracranial pressure; in GBM symptoms develop rapidly over the span of days or weeks  
   **Gross:**  
   - Poorly defined grey infiltrative tumors  
   - Infiltrate beyond grossly evident margin  
   **Microscopic:**  
   - Hypercellularity and pleomorphism; mitotic figures define an anaplastic (grade III) and grade IV lesions; endothelial microvascular proliferation and/or necrosis are present in glioblastoma (grade IV)  
   **Positive immunostains:**  
   - GFAP  
   - IDH1 (isocitrate dehydrogenase) mutations are common in low grade

b. **Oligodendroglioma**  
   - Tumor of oligodendrocytes  
   - Most frequent in the frontal lobe  
   - Presentation: seizures, focal neurologic deficits, headache  
   **Morphology:**  
   - Sheets of uniform cells with round nuclei, small nucleoli, and clear perinuclear halos (“fried eggs”)  
   - Delicate network of anastomosing capillaries ("chicken-wire" vasculature)  
   - Calcifications
- Deletions of chromosomes 1p and 19q can be demonstrated by FISH and predict better response to therapy

b. Non-infiltrating
   - Ependymomas
     Malignant tumor of ependymal cells
     Intraventricular, most common location in childhood is the 4th ventricle, in adults – spinal cord
     Presentation: increased intracranial pressure (HA, nausea, vomiting, dizziness)
     Morphology:
     Monomorphic cells with perivascular pseudorosettes (tumor cells arranged around vessels with intervening anuclear fibrillary zone of ependymal processes)
   - Pilocytic astrocytoma
     Benign tumor of children and young adults, most commonly located in cerebellum
     Common imaging finding: cystic tumor with mural nodule
     Morphology:
     Piloid cells with long, hair-like, processes
     Biphasic pattern (compact areas alternating with myxoid/microcystic areas).
     Rosenthal fibers and eosinophilic granular bodies (EGBs) are common
     GFAP positive
     Activating BRAF (V600E) mutation is common
   - Mixed neuronal-glial tumors (Ganglioglioma)
     Common scenario: young person with a history of seizures and cystic, calcified lesion in the temporal lobe
     Morphology:
     Mixture of dysplastic neurons and infiltrating glial component (usually low-grade astrocytoma), perivascular lymphocytic cuffs, eosinophilic granular bodies (EGBs)

12. Embryonal neoplasms
   - Medulloblastoma
     Malignant tumor presenting mainly in childhood
     Derived from undifferentiated neuroectodermal cells
     Cerbellar vermis (fourth ventricle)
     Spreads along CSF pathways
     Discrete, contrast enhancing mass on MRI
     Morphology:
     Highly cellular with sheets of anaplastic cells ("small blue cells")
     May contain Homer-Wright rosettes (tumor cells surrounding central fibrillary zone)
     "Roof of the 4th ventricle. Child. Blue, blue, blue"
     WHO 2016: molecular classification of medulloblastomas
13. Meningioma
- Most common primary brain tumor
- Benign slow-growing tumor derived from meningothelial cells of the arachnoid layer
- Presentation: neurological signs due to compression of adjacent structures, depend on tumor location; headache and seizures are common but non-specific
- Extra-axial (outside of brain parenchyma), discrete dura-based masses, compresses adjacent brain but does not infiltrate
- Dural “tail” on imaging
- Multiple suggest NF2
- Morphology
  Meningotheliomatous (syncytial) meningioma – cells grow in syncytial lobules (no discernible cell borders), whorls and psammoma bodies (concentric laminated calcifications)
  Fibrous (fibroblastic) meningioma – fascicles of spindle cells with abundant intercellular collagen
  “Psammomas and whorls in middle-aged girls”

14. Craniopharyngioma
- Benign tumor of children and young adults
- May recur with incomplete surgical resection
- Suprasellar partially calcified frequently cystic mass
- Presentation: visual deficits (compression of optic chiasm – bitemporal hemianopsia), endocrine deficiencies
- Calcifications seen on CT
- Originates from epithelial remnants of Rathke’s pouch (anterior surface of pituitary stalk)
- 2 variants: adamantinomatous (children and adults) and papillary (adults)
- Morphology
  Stratified squamous epithelium with peripheral "picket fence" palisading of nuclei, nodules of wet keratin, and loosely knit epithelium called stellate reticulum.

15. Schwannoma
- Benign tumor of Schwann cell origin
- Involves cranial and peripheral nerves
- Common intracranial location: cerebellopontine angle (“acoustic neuroma”, involves VIII cranial nerve) – presents with hearing loss and tinnitus
- Bilateral acoustic schwannomas – NF2
- S100 immunohistochemistry positive

16. Primary CNS lymphoma
- Most are diffuse large B-cell lymphomas (DLBCL)
- Older adults (60-80s)
- Immunodeficient patients are at increased risk – EBV-related
- Present with cognitive dysfunction, psychomotor slowing and focal neurological deficits
- Single or multiple lesions, most are supratentorial
- Histologic findings: perivascular (angiocentric) growth of large atypical lymphoid cells
- Worse prognosis than systemic DLBCL

17. Metastatic tumors
- Most common from lung, breast, kidney, GI tract, melanoma
- Sarcomas rare
- Sharply demarcated both grossly and at the microscopic level; located at grey-white junction; can be multiple
- Hemorrhagic metastases: lung, melanoma, renal cell carcinoma, choriocarcinoma
- Cytokeratin immunohistochemistry positive

Familial Tumor Syndrome Summary

<table>
<thead>
<tr>
<th>Disease</th>
<th>Chromosome</th>
<th>Gene (protein)</th>
<th>Nervous System Tumor(s)</th>
<th>Key findings</th>
</tr>
</thead>
</table>
| Neurofibromatosis 1| 17q11.2    | NF1 (neurofibromin)| - Plexiform Neurofibroma
- Malignant peripheral nerve sheath tumor
- Optic glioma
- Acoustic Schwannoma | Lisch Nodules
Café–au-lait spots |
| Neurofibromatosis 2| 22q12      | NF2 (merlin)       | - Bilateral acoustic schwannomas
- Meningiomas          |                                                        |
| Tuberous sclerosis | 9q 16p     | TSC1 (9q) hamartin | - Cortical tubers
- Subependymal hamartomas
- (subependymal giant cell astrocytoma) | Adenoma Sebaceous
Seizures
Mental retardation |
| Von Hippel-Lindau  | 3p         | VHL                | Hemangioblastoma                                                                      | Renal cell carcinoma                     |