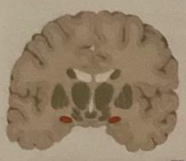
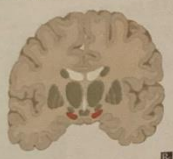
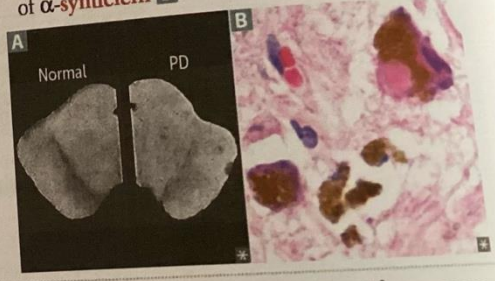
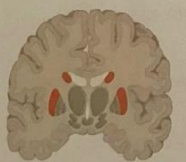
Dementia	Decline in cognitive ability (eg, memory, executive function) with intact consciousness. Reversible causes of dementia include depression (pseudodementia), hypothyroidism, vitamin B_{12} deficiency, neurosyphilis, normal pressure hydrocephalus.	
Neurodegenerative		
Alzheimer disease  R	Most common cause of dementia in older adults. Advanced age is the strongest risk factor. Down syndrome patients have ↑ risk of developing early-onset Alzheimer disease, as amyloid precursor protein (APP) is located on chromosome 21. ↓ ACh in brain. Associated with the following altered proteins: ▪ ApoE-2: ↓ risk of sporadic form ▪ ApoE-4: ↑ risk of sporadic form ▪ APP, presenilin-1, presenilin-2: familial forms (10%) with earlier onset ApoE-2 is "protwoctive," ApoE-4 is "four" Alzheimer disease.	Widespread cortical atrophy, especially hippocampus. Narrowing of gyri and widening of sulci. Senile plaques A in gray matter: extracellular β-amyloid core; may cause amyloid angiopathy → intraparenchymal hemorrhage; Aβ (amyloid-β) is derived from cleavage of APP. Neurofibrillary tangles B: intracellular, hyperphosphorylated tau protein = insoluble cytoskeletal elements; number of tangles correlates with degree of dementia. Hirano bodies: intracellular eosinophilic proteinaceous rods in hippocampus.
Frontotemporal dementia	Formerly called Pick disease. Early changes in personality and behavior (behavioral variant), or aphasia (primary progressive aphasia). May have associated movement disorders.	Frontal and/or temporal lobe atrophy. Inclusions of hyperphosphorylated tau (round Pick bodies C) or ubiquitinated TDP-43.
Lewy body dementia	Visual hallucinations ("haLewycinations"), dementia with fluctuating cognition/ alertness, REM sleep behavior disorder, and parkinsonism.	Intracellular Lewy bodies primarily in cortex. Called Lewy body dementia if cognitive and motor symptom onset < 1 year apart, otherwise considered dementia 2° to Parkinson disease.

Neurodegenerative movement disorders		
Parkinson disease  R	Loss of dopaminergic neurons in substantia nigra pars compacta (depigmentation in A). Symptoms typically manifest after age 60 ("body TRAP"): ▪ Tremor (pill-rolling tremor at rest) ▪ Rigidity (cogwheel or leadpipe) ▪ Akinesia/bradykinesia → shuffling gait, small handwriting (micrographia) ▪ Postural instability (tendency to fall) Dementia is usually a late finding.	Affected neurons contain Lewy bodies: intracellular eosinophilic inclusions composed of α-synuclein B. Think "Parkinsynuclein." 
Huntington disease  R	Loss of GABAergic neurons in striatum. Autosomal dominant trinucleotide $(CAG)_n$ repeat expansion in huntingtin (*HTT*) gene on chromosome 4 (4 letters) → toxic gain of function. Symptoms typically manifest between age 30 and 50: chorea, athetosis, aggression, depression, dementia (sometimes initially mistaken for substance use).	Atrophy of caudate and putamen with ex vacuo ventriculomegaly. ↑ dopamine, ↓ GABA, ↓ ACh in brain. Neuronal death via NMDA receptor binding and glutamate excitotoxicity. Anticipation results from expansion of CAG repeats. Caudate loses ACh and GABA.

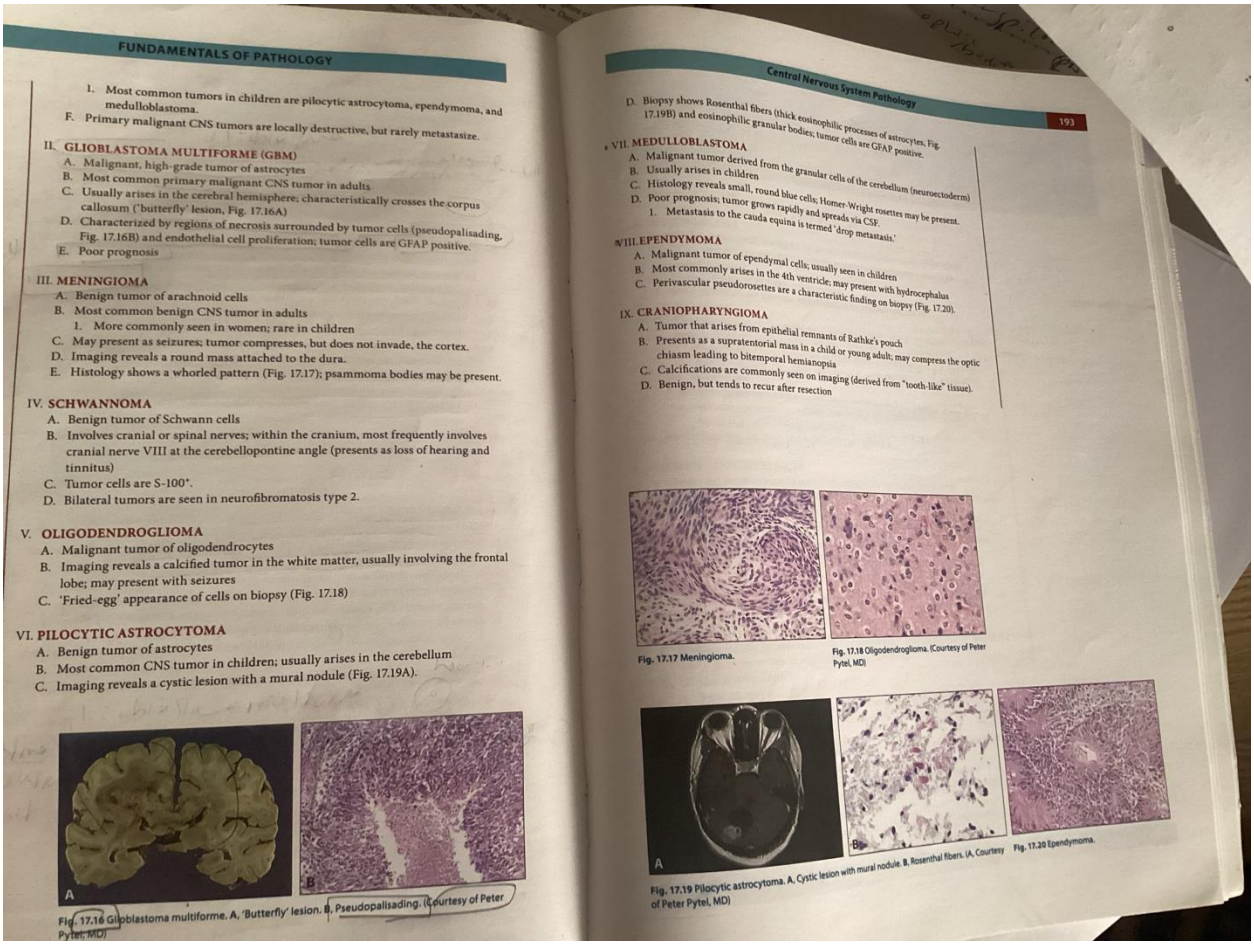
Adult primary brain tumors

TUMOR	DESCRIPTION	HISTOLOGY
Glioblastoma	Grade IV astrocytoma. Common, highly malignant 1° brain tumor with ~ 1-year median survival. Found in cerebral hemispheres. Can cross corpus callosum ("butterfly glioma" A). Associated with *EGFR* amplification.	Astrocyte origin, GFAP ⊕. "Pseudopalisading" pleomorphic tumor cells B border central areas of necrosis, hemorrhage, and/or microvascular proliferation.
Oligodendroglioma	Relatively rare, slow growing. Most often in frontal lobes C. Often calcified.	Oligodendrocyte origin. "Fried egg" cells—round nuclei with clear cytoplasm D. "Chicken-wire" capillary pattern.
Meningioma	Common, typically benign. Females > males. Occurs along surface of brain or spinal cord. Extra-axial (external to brain parenchyma) and may have a dural attachment ("tail" E). Often asymptomatic; may present with seizures or focal neurologic signs. Resection and/or radiosurgery.	Arachnoid cell origin. Spindle cells concentrically arranged in a whorled pattern; psammoma bodies (laminated calcifications, arrow in F).

Childhood primary brain tumors

TUMOR	DESCRIPTION	HISTOLOGY
Pilocytic astrocytoma	Low-grade astrocytoma. Most common 1° brain tumor in childhood. Usually well circumscribed. In children, most often found in posterior fossa A (eg, cerebellum). May be supratentorial. Benign; good prognosis.	Astrocyte origin, GFAP ⊕. Bipolar neoplastic cells with hairlike projections. Associated with microcysts and Rosenthal fibers (eosinophilic, corkscrew fibers B). Cystic + solid (gross).
Medulloblastoma	Most common malignant brain tumor in childhood. Commonly involves cerebellum C. Can compress 4th ventricle, causing noncommunicating hydrocephalus → headaches, papilledema. Can involve the cerebellar vermis → truncal ataxia. Can send "drop metastases" to spinal cord.	Form of primitive neuroectodermal tumor (PNET). Homer-Wright rosettes (small blue cells surrounding central area of neuropil D). Synaptophysin ⊕.
Ependymoma	Most commonly found in 4th ventricle E. Can cause hydrocephalus. Poor prognosis.	Ependymal cell origin. Characteristic perivascular pseudorosettes F. Rod-shaped blepharoplasts (basal ciliary bodies) found near the nucleus.
Craniopharyngioma	Most com...	

Pathoma CNs tumors



FUNDAMENTALS OF PATHOLOGY

1. Most common tumors in children are pilocytic astrocytoma, ependymoma, and medulloblastoma.

F. Primary malignant CNS tumors are locally destructive, but rarely metastasize.

II. **GLIOBLASTOMA MULTIFORME (GBM)**
- A. Malignant, high-grade tumor of astrocytes
- B. Most common primary malignant CNS tumor in adults
- C. Usually arises in the cerebral hemisphere; characteristically crosses the corpus callosum ('butterfly' lesion, Fig. 17.16A)
- D. Characterized by regions of necrosis surrounded by tumor cells (pseudopalisading, Fig. 17.16B) and endothelial cell proliferation; tumor cells are GFAP positive.
- E. Poor prognosis

III. **MENINGIOMA**
- A. Benign tumor of arachnoid cells
- B. Most common benign CNS tumor in adults
  1. More commonly seen in women; rare in children
- C. May present as seizures; tumor compresses, but does not invade, the cortex.
- D. Imaging reveals a round mass attached to the dura.
- E. Histology shows a whorled pattern (Fig. 17.17); psammoma bodies may be present.

IV. **SCHWANNOMA**
- A. Benign tumor of Schwann cells
- B. Involves cranial or spinal nerves; within the cranium, most frequently involves cranial nerve VIII at the cerebellopontine angle (presents as loss of hearing and tinnitus)
- C. Tumor cells are S-100+.
- D. Bilateral tumors are seen in neurofibromatosis type 2.

V. **OLIGODENDROGLIOMA**
- A. Malignant tumor of oligodendrocytes
- B. Imaging reveals a calcified tumor in the white matter, usually involving the frontal lobe; may present with seizures
- C. 'Fried-egg' appearance of cells on biopsy (Fig. 17.18)

VI. **PILOCYTIC ASTROCYTOMA**
- A. Benign tumor of astrocytes
- B. Most common CNS tumor in children; usually arises in the cerebellum
- C. Imaging reveals a cystic lesion with a mural nodule (Fig. 17.19A).

Fig. 17.16 Glioblastoma multiforme. A, 'Butterfly' lesion. B, Pseudopalisading. (Courtesy of Peter Pytel, MD)

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D. Biopsy shows Rosenthal fibers (thick eosinophilic processes of astrocytes; Fig. 17.19B) and eosinophilic granular bodies; tumor cells are GFAP positive.

VII. **MEDULLOBLASTOMA**
- A. Malignant tumor derived from the granular cells of the cerebellum (neuroectoderm)
- B. Usually arises in children
- C. Histology reveals small, round blue cells; Homer-Wright rosettes may be present.
- D. Poor prognosis; tumor grows rapidly and spreads via CSF.
  1. Metastasis to the cauda equina is termed 'drop metastasis.'

VIII. **EPENDYMOMA**
- A. Malignant tumor of ependymal cells; usually seen in children
- B. Most commonly arises in the 4th ventricle; may present with hydrocephalus
- C. Perivascular pseudorosettes are a characteristic finding on biopsy (Fig. 17.20).

IX. **CRANIOPHARYNGIOMA**
- A. Tumor that arises from epithelial remnants of Rathke's pouch
- B. Presents as a supratentorial mass in a child or young adult; may compress the optic chiasm leading to bitemporal hemianopsia
- C. Calcifications are commonly seen on imaging (derived from "tooth-like" tissue).
- D. Benign, but tends to recur after resection

Fig. 17.17 Meningioma.

Fig. 17.18 Oligodendroglioma. (Courtesy of Peter Pytel, MD)

Fig. 17.19 Pilocytic astrocytoma. A, Cystic lesion with mural nodule. B, Rosenthal fibers. (A, Courtesy of Peter Pytel, MD)

Fig. 17.20 Ependymoma.