1] Primary
- CNS Lymphoma
- Benign → Meningioma
  - Meningioma
  - Atypical Meningioma
  - Anaplastic Meningioma
- Malignant → Glioma

Glioma
- Astrocytoma
  - Pilocytic [Benign]
  - Diffuse
    - IDH mutant (Grem.A)
    - IDH wild
    - NOS
  - Anaplastic
    - IDH mutant
    - IDH wild
    - NOS
  - Glioblastoma
    - IDH mutant
    - IDH wild
- Oligodendroglioma
  - Oligodendrog.
    - IDH mut.
    - NOS
  - Anaplastic Oligod.glio.
    - IDH mut.
    - NOS
- Ependymoma
  - Subependymoma
  - Myxopapillary epend.
  - Ependymoma
  - Rela fusion positive epend.
  - Supratentorial epend.
  - Anaplastic epend.
- Miscellaneous Gliomas
  - Subependymal Giant Cell Astrocytoma (SEGA)
  - Pleomorphic Xanthoastrocytoma
  - Anaplastic pleomorphic Xanthoastrocytoma

Neuronal Tumors
- Gangliglioma
- Gangliocytoma
- Neurocytoma
- Dysembryoblastic Neuroepithelial tumor

Poorly Differentiated tumors or Embryonal tumors
- a) Medulloblastoma
- b) Atypical Teratoid / Rhabdoid Tumor

World Brain Tumour Day is on 8th June

*] WHO Grading of Brain Tumors :-

Grade 1 ⇒ AMEN⊖	A :- Atypia
Grade 2	M :- Mitotic activity
Grade 3	E :- Endoth. proliferⁿ
Grade 4 ⇒ AMEN⊕	N :- Necrosis

2] Secondary (Metastasis)
- Lungs
- Skin
- Breast
- Kidney
- GIT
- Choriocarcinoma

*) Prostate Never gives 2° to Brain

IDH - ISOCITRATE DEHYDROGENASE

Most common tumors of brain-**Metastasis** secondary to lungs>breast

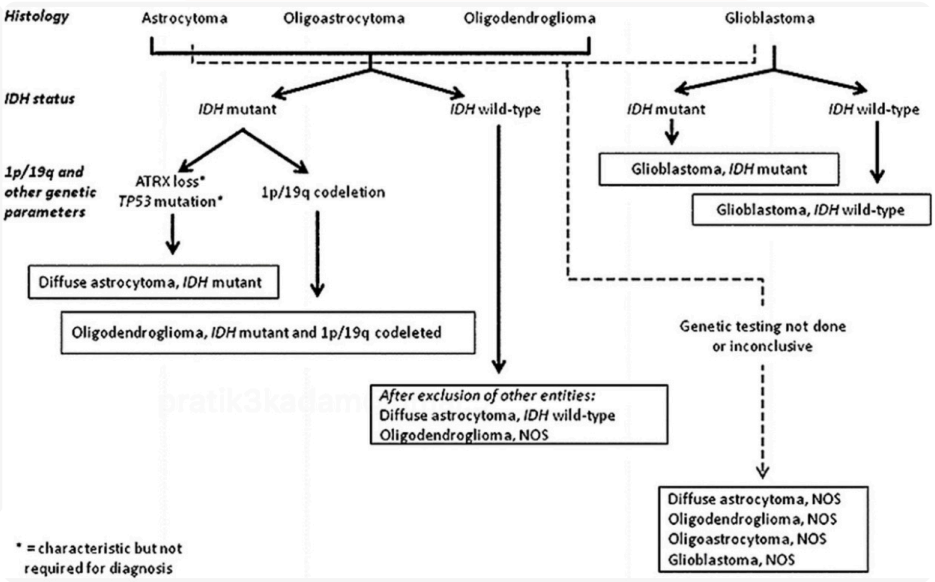
Most common primary CNS tumor-**glioma**>meningioma

Most common primary CNS tumor in children is a **pilocytic astrocytoma**

Most common primary CNS tumor in adults is **astrocytoma**

Most common primary **malignant** tumor of the brain in children is **medulloblastoma**

Most common primary **malignant** tumor of the brain in adults is **glioblastoma multiforme**



*] Predominantly Pediatric tumours :-

- Brain tumors are the second most common cause of pediatric cancer after leukemia, accounting for approx. 20% of all cases of pediatric cancer.

	Pilocytic astrocytoma	Medulloblastoma	Ependymoma	Craniopharyngioma	Pinealoma
Precursor	• Astrocytes	• Primitive, neuroectodermal tissue	• Ependymal cells	• Rathke pouch	• Pineal gland
Typical location	• Posterior cranial fossa (infratentorial)	• Cerebellar vermis (infratentorial)	• 4th ventricle (infratentorial)	• Suprasellar region (supratentorial)	• Dorsal midbrain (infratentorial)
Typical histology	• **Rosenthal fibers**: eosinophilic fibers with corkscrew-like configuration • GFAP positive	• Small round blue cells • Homer-Wright rosette	• **Perivascular pseudorosettes**: tumor cells that are arranged in a papillary structure around a central blood vessel	• Nests of stratified squamous epithelium with internal areas of lamellar keratin deposits • Cholesterol crystals	• Large vacuolated cells with round nuclei (fried egg cells) • Lymphoid stroma

In children, most primary brain tumors arise infratentorially, craniopharyngiomas being an important exception!

Recent update: For the first time, the WHO classification of CNS tumors uses molecular parameters in addition to histology to define many tumor entities, thus formulating a concept for how CNS tumor diagnoses should be structured in the molecular era. The WHO 2016 Classification has incorporated integrated phenotypic and genotypic approach for the sub-classification of various CNS tumors. For example, **diffuse gliomas are subclassified** based on ***IDH* mutation status, *ATRX* mutation status, and 1p/19q codeletion status.** And, for the diagnosis of **oligodendroglioma**, it is **essential to have both *IDH* mutation and 1p/19q codeletion.**

	Glioblastoma multiforme	Meningioma	Hemangioblastoma	Schwannoma	Oligodendroglioma	Pituitary adenoma
Precursor	• Astrocytes	• Arachnoid cap cells	• Uncertain origin	• Schwann cells	• Oligodendrocytes	• Pituitary adenotrophic cells (typically lactotrophs)
Typical locations	• Cerebral hemispheres (supratentorial) • May cross the midline (butterfly glioma)	• Extra-parenchymal tumor that can occur in supratentorial or infratentorial regions	• Cerebellum (infratentorial)	• **Cerebellopontine angle** (infratentorial)	• Frontal lobes (supratentorial)	• Sella turcica (supratentorial)
Typical histology	• Pleomorphic anaplastic cells that form pseudopalisades due to central necrosis or hemorrhage • Microvascular proliferation • GFAP positive	• Spindle cells arranged in whorls • Psammoma bodies	• Densely packed thin-walled capillaries	• Spindle cells in palisades **Antoni A tissue**) alternating with myxoid areas (**Antoni B tissue**) • S-100 positive	• Large vacuolated cells with round nuclei (fried egg cells) • Chicken-wire pattern of capillary anastomoses	• Monomorphic, acidophilic or basophilic, polygonal cells arranged in sheets or cords

⇒ Predom. ADULT Brain Tumours

*) 1° Tumours :-

1] Risk factors :- i) Radiation
ii) Smoking
iii) Familial syndromes → Li-Fraumeni syn :- P53 mutation → 2° Glioblastoma
→ Medulloblastoma
→ Turcot syn :- APC mutation or Mismatch Repair gene mutation → Colon cancer
→ Medulloblastoma
→ Gorlin syn :- PTCH mutation → Basal cell Carcinoma of skin
→ Medulloblastoma
→ Cowden syn :- PTEN mutation ∴ aka PTEN Hamartoma syn. → Cerebellar Gangliocytoma aka :- Lhermitte Duclos syndrome + Facial Trichilemomas
→ Von-Hippel Lindau syn. :- 3p mutation → Hemangioblastoma
→ Tuberous sclerosis → TSC 1 & 2 gene → CNS Hamartomas & SEGA
→ Neurofibromatosis → NF_1 :- Optic Nerve Glioma
→ NF_2 :- 'MISME' → Schwannoma, Meningioma & Ependymoma

2] Clinical features :- i) Headache
ii) Vomiting
iii) Seizures
iv) ↑ICT [Bradycardia, HTN & Apnea]

3] General principles :- i) Adults :- Mostly supratentorial in location
ii) Children :- Mostly Infratentorial in location

*) Astrocytoma :-

a) Non-Infiltrating

1] Juvenile Pilocytic Astrocytoma :- Grade 1

i) M/C Benign tumor of Brain in Children

ii) M/C site :- Cerebellum (Post. Fossa)

iii) Grossly :- large cystic mass ± Mural Nodule

DD ⇒ Hemangioblastoma → ⊖ Hypoxia → HIF1α → ↑VEGF → Angiogenesis

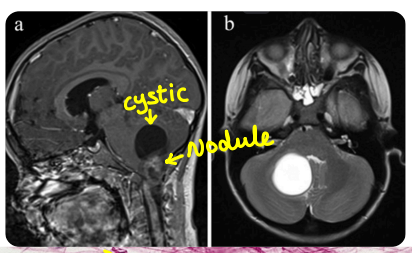
when O_2 becomes ⊖ → activates VHL gene (Tumor suppressor) → Degrades HIF1α

∴ when VHL mutated → Foamy cells separated by lots of vessels ≈ Large cystic mass ± Mural Nodule & is ⊕ for Inhibin α

iv) M/E :- *) Bipolar / Piloid cells → Hair like processes & are GFAP ⊕

*) Rosenthal fibres in cytoplasm of Astrocytes made up of HS proteins ∴ Pink

v) Tumors are Biphasic ± both loose microcystic & fibrillary areas



vi) M/C mutation :- BRAF gene ⊗ [P53 mutations are rare & ass.c Aggressive astrocytoma]

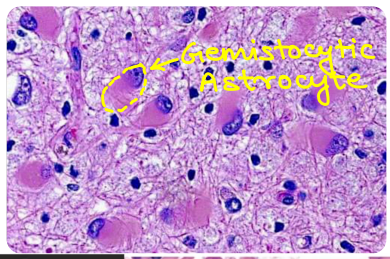
vii) Gen. has Good progno but if it originates near floor of Third Ventricle &/extends into Hypothalamic region via Optic tract then has poor prognosis

If in Optic Nerve → Optic glioma → due to NF_1 mutation

viii) Surgical resection is curative in 80 to 100% cases

b) Infiltrating :- These are now combined c Infiltrating oligodendrogliomas coz of same IDH mutations

- Low Grade :- P53 mutation / PDGF-α overactivity
- High Grade :- Rb & p16 / CDK2Na overactivity

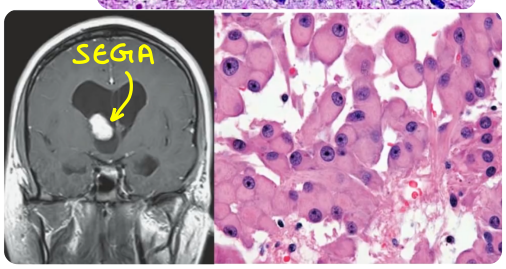


2] Diffuse / Fibrillary :- Grade II

i) IDH mutant variant is Gemistocytic astrocytoma :- Poor prognosis, low grade tumour in which GFAP combines in cytoplasm to give it a ground glass opacity & pushes the nucleus to periphery

DD ⇒ SEGA :- same M/E findings but cells are larger in size, it is ass c Tuberous sclerosis & the tumour protrudes into the ventricle

⇒ M/C site :- foramen of Monro



3] Anaplastic :- Grade III

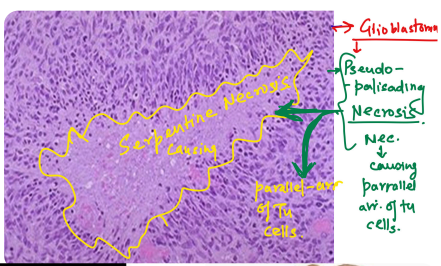
4] Glioblastoma :- Grade IV

Telomerase reverse transcriptase

- IDH wild :- M/C type, Elderly, Bad progno, aka 1°Glioblastoma (denovo), M/C Muta^n :- TERT > P53
- IDH mutant :- Young age, low grade, Good progno, aka 2°Glioblastoma, M/C muta^n :- P53 > TERT
- NOS :- Not otherwise specified → 1% cases

i) Grows rapidly from one end to another ⟵ ○ ⟶

- M/E :- ∴ High vascularity
  - Rapid Angiogenesis (endo. cell prolif.^{n}) → Glomeruloid body
  - Viable Tumour cells → Pseudopallisading
  - Necrosis → serpentine necrosis inducing
- Gross :- Crosses the midline & M/C site ⇒ Frontal lobe & aka Butterfly Glioma or Blood Butterfly tumour



ii) Worst Prognosis

iii) Rx :- TEMOZOLOMIDE

iv) Li-fraumeni syn. is ass c 2° Glioblastoma

v) Brainstem glioma mutation in children ⇒ H3.3K27M mutation

*) Receptor on the Neuronal membrane that induces development of Glioma ⇒ CD133, it is also used as a marker for leukemia & Glioblastoma stem cells, also used for identifying Immature leukemic stem cells in AML & pro-Bleukemia

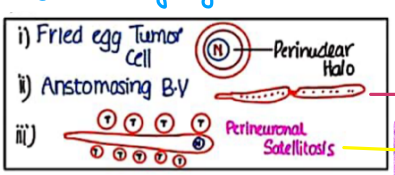
vii) It is the M/C 1° malignant tumour in Adults

*) Oligodendroglioma :-

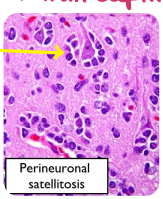
i) Common in age group of 40-50 yrs & M/C site :- White matter of Cerebral Hemispheres

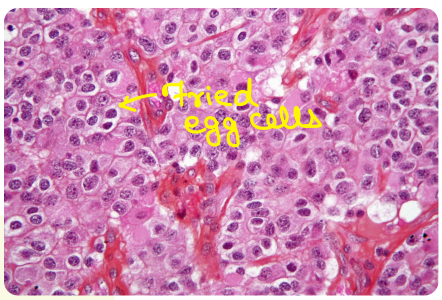
ii) Gross :- Gelatinous gray mass in white matter c Hemorrhage & Calcification

iii) M/E :-



→ Thin capillaries aka Chicken Wire Capillaries





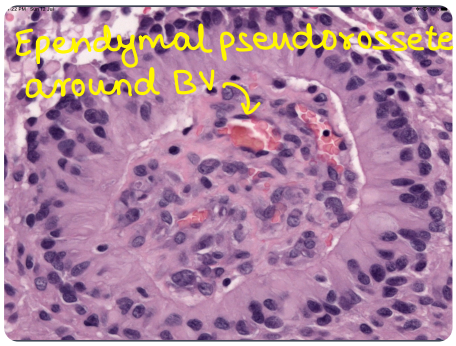
Fried eggs in pathology :-

- **Oligodendroglioma** on histopathology
- **Hairy cell leukemia** on bone marrow biopsy
- **Seminoma/Dysgerminoma** on light microscopy
- **Mycoplasma pneumonia** fried egg colonies on **Eaton agar**

iv) Mutations seen are :-

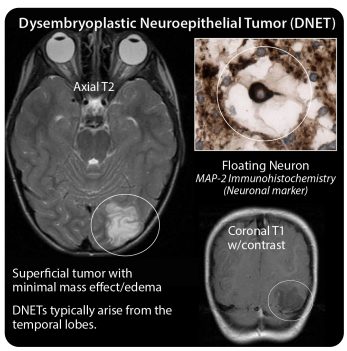
Mutations	Chemo-radiation
IDH 1, IDH 2 → M/C	sensitive
1p 19q codeletion → Loss of Heterozygosity (LOH)	sensitive
9p loss,10q loss, CDKN2A	resistant

*) Ependymoma :- Origin is from the Ventricular lining ie. from Ependymal Cells
- →Children :- Origin is from Floor of 4th Ventricle → Hydrocephalus & CSF metastasis
- →Adult :- Origin is from SC (Filum terminale) & is ass c Neurofibromatosis-2



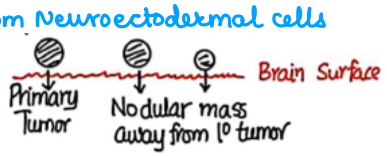
i) M/E :- Perivascular Pseudorossettes are seen
ii) GFAP (Glial Fibrillary Acidic Protein) positive
iii) Poor prognosis c Rela fusion protein +ve ependymoma
iv) Myxopapillary ependymoma :- Grade 1
→ slow growing, arising from filum terminale
→ Contain papillary elements in Myxoid (Acidic & Neutral mucopolysaccharides) background, admixed c Ependymoma like cells

*) Neuronal tumors :-
i) M/C → Ganglioglioma
ii) Dysembryoplastic neuroepithelial tumour shows floating Neurons in a pool of mucopolysaccharide rich fluid surrounding Neoplastic glia c out anaplastic features



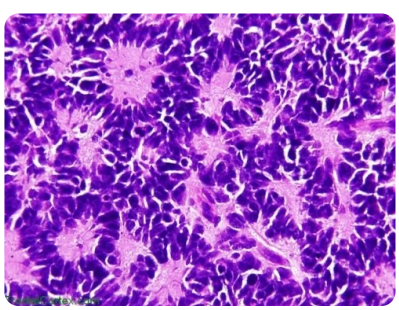
*) Undifferentiated tumour
- → coz Both Glial & Neuronal Component present

1) Medulloblastoma :-
i) M/C 1° malignant tumour of Brain in children
ii) M/C site :- Cerebellum & arises from Neuroectodermal cells
iii) Metastasis occurs through CSF :- rapid growth can occlude CSF flow → Hydrocephalus

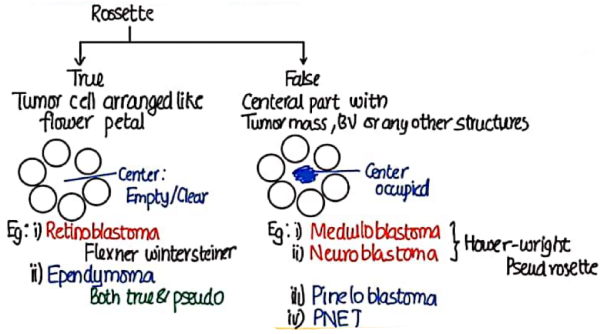


} DROP METASTASES

iv) M/E → *) Homer Wright Rosettes
*) Atypical cells ⊕
*) ↑ Mitotic activity → Ki-67 ⊕

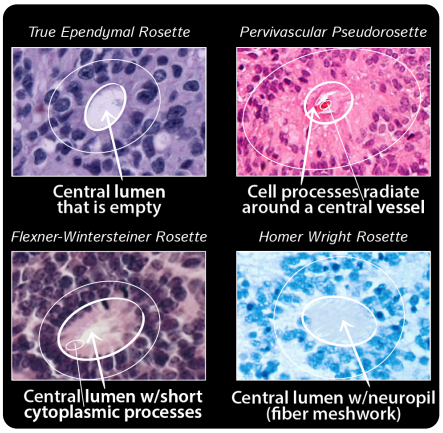


v) Tumours are midline in children & lateral in Adults
vi) Tumors c ↑ Neurotropin receptor TrK-C or ↑ Intranuclear β-catenin have good progno
vii) CHANG staging is used
viii) Highly Radiosensitive & Rx c Excision & Radiation
ix) WHO classification :-
a) WNT type → *) Mutation in WNT signalling pathway
*) ass. c → Monosomy-6 & β-catenin
*) Best prognosis
b) SHH type → *) Mutation in SHH pathway (Sonic Hedgehog signalling) → Medulloblastoma, Basal Cell Ca of Skin
*) N-MYC amplification present

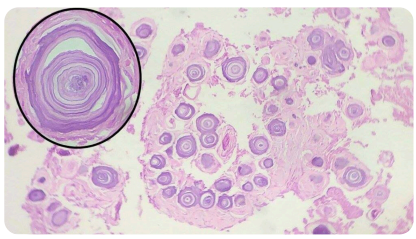


c) Group 3 → *) MYC amplification present + Isochromosome 17q (i17q)
*) Worst prognosis
d) Group 4 → *) only i17q present

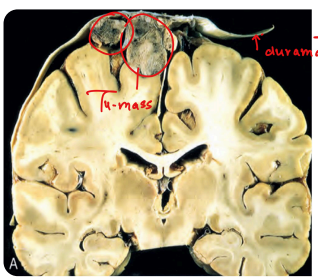
*) Presence of i17q or MYC amplification is ass c Poor Prognosis
*) M/C genetic alteration is i17q (loss of material from 17p)



*) Meningioma :-
i) Arise from Arachnoid Cap cells (Meningothelial Cells) & are attached to dura
ii) Loss of Heterozygosity of the long arm of chr. 22 → Deletion of NF_2 gene (encoding Merlin) → U/L to B/L acoustic neuroma
In meningioma c/out NF-2 ⊗, M/C mutation is in TRAF-7 (TNF-receptor ass. receptor 7)
iii) Gritty on cutting due to Calcified Psammoma bodies & En-Mass spread
iv) Common site :- Parasagittal aspect of the Brain Convexity c slight female predom.
& expresses Progesterone receptors & grow rapidly during pregnancy
vi) Meningeal carcinomas are M/C ass. c lung & Breast Ca

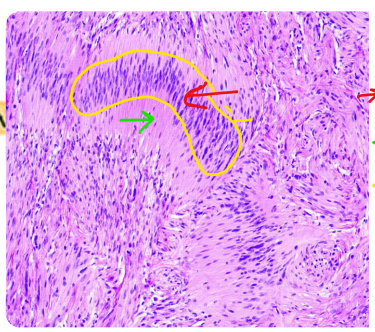


⇒ Variants :- a) Low grade → Fibroblastic
Syncytial
Secretory
Transitional
b) High grade → Anaplastic :- Worst progno
Atypical



*) Schwannoma
- aka Accoustic neuroma (=arising from 8th cranial nerve)
↓
MC Site : Inferior vestibular branch
- a/w NF-2 gene mutation
- M/E : * Antoni-A
* Antoni-B

Palisading of cell : Cellular Area → Antoni A
Verocay Bodies
Hypo cellular Area : Antoni-B



Schwannoma
→ Antoni-A (Hypercellular)
→ Antoni-B – Hypocellular
→ Verocay Bodies.
(seen in Antoni "A" - areas)

*) Primary CNS Lymphoma → M/C CNS Neoplasm c ↓ Immunity
- Adults : MC Site : Frontal lobe
- These are DLBL (B cell Lymphoma)
- a/w ↓ immunity Eg : AIDS
- a/w Latent EBV infection
- Surgical treatment is not curative
↳ only for tissue diagnosis

- M/E :

1° CNS Lymphoma	2° CNS Lymphoma
* Reticulin stain :	* Reticulin stain :
→ Reticulin Fibers	
Individual tumor cell is seperated individually HOOPING SIGN ⊕	Cluster of tumor cell present Hooping Sign ⊖

*) Extranodal Germ Cell Tumours :- i) eg. Pineal & Suprasellar region tumours & occur in Midline in Young adults
ii) M/C site :- Mediastinum Overall) but M/C site in Brain :- Pineal Gland

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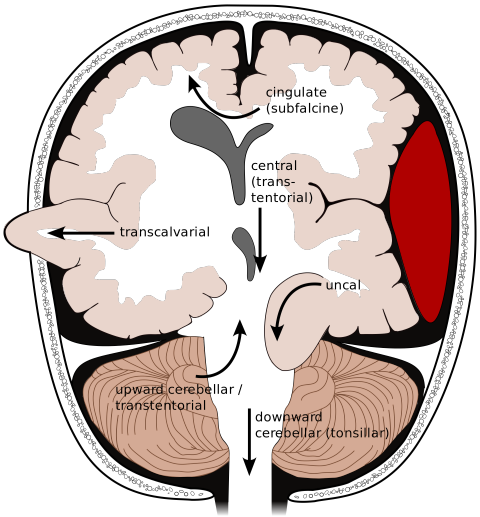
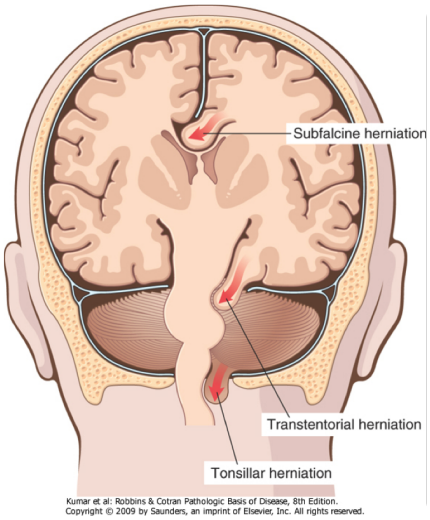
Brain Herniations





2) Subfalcine / Cingulate Herniations :- Compresses Ant. Cerebral art. branches

3) Tonsillar Herniation :- Displacement of Cerebellar Tonsil into the Foramen Magnum

1) **Transtentorial (uncinate, mesial temporal) herniation** occurs when the medial aspect of the temporal lobe is compressed against the free margin of the tentorium.

- With increasing displacement of the temporal lobe, the third cranial nerve is compromised, resulting in pupillary dilation and impairment of ocular movements on the side of the lesion.
- The posterior cerebral artery may also be compressed, resulting in ischemic injury to the territory supplied by that vessel, including the primary visual cortex.
- **When the extent of herniation is large enough, the contralateral cerebral peduncle may be compressed, resulting in hemiparesis ipsilateral to the side of the herniation; the compression in the peduncle in this setting is known as the Kernohan notch.** / Kernohan-Woltman Sign
- Progression of transtentorial herniation is often accompanied by **secondary hemorrhagic lesions in the midbrain and pons, termed Duret hemorrhages**.
- These linear or flameshaped lesions usually occur in the midline and paramedian regions and are believed to be due to the distortion or tearing of penetrating veins and arteries supplying the upper brainstem.