• Epidemiology
  - Primary 1x: Mets 10x
  - 2/3 brain vs 1/3 spinal cord
  - Most CNS tumors remained confined to the cranial cavity and spinal canal as they rarely metastasize but they are still malignant in that they grow and recur
  - Distinction b/t benign vs malignant is not that clear based on histology but it doesn’t matter b/c the problem with brain tumors is not metastasis but mass effect which benign cancers can also cause
  - Tumors are usually of glial cell origin
  - Genetic Syndromes: NF, TS, vHL, Li-Fraumeni, Cowden, Turcot
  - NB you can also CNS cysts (epidermoid, dermoid, colloid cyst of 3rd ventricle), lipoma, chordoma (remnant of embryonic notochord), craniopharyngioma (refer)

• S/S (all dependent on where the tumor is located)
  - HA/N/V: chronic daily HA/N/V that occur in the morning often waking up the pt, worsens w/ increased ICP eg. when head in dependent position and when straining, etc, headache typically does not lateralize to side of tumor
  - Focal Deficits: CN deficits, nystagmus, motor/sensory changes, personality change
  - CVA: tumor “steals” blood away from normal CNS tissue or compresses normal vessels causing ischemic changes
  - DVT-PE: more common in brain cancers than in many other cancers such that 30% of these pts have DVT-PE, therefore search for them, some advocate IVC filter placement
  - Seizures: occurs when tumors are involving especially the surface of the brain, currently there is no role for seizure prophylaxis, AEDs are only indicated if pt has had a seizure, it is important to use non-enzyme inducing AEDs so as to not stimulate cytochrome P450 metabolism of chemo, 10% of new onset seizures in adults are 2/2 tumor

• Peritumoral Edema: vasogenic edema surrounding tumor 2/2 absence of tight jxns in tumor blood vessels and tumor production of factors which increase permeability inducing mass effect, if acute sx then decrease ICP w/ mannitol/hyperventilation/VF shunt vs chronic management w/ strong steroids specifically dexamethasone, given chronic use of strong steroids pts often develop chronic steroid complications: (1) PCP therefore give prophylactic treatment
  - NB you can also CNS cysts (epidermoid, dermoid, colloid cyst of 3rd ventricle), lipoma, chordoma (remnant of embryonic notochord), craniopharyngioma (refer)
  - CNS metastasis can present as:
    - Leptomeningeal Carcinomatosis: cancer that metastasizes to meninges (lymphoma, SCLC, breast, melanoma, GI) via the bloodstream, S/S: focal deficits from CN palsies and radiculopathy, obstructive hydrocephalus, meningismus, Dx: CSF cytology (55% + after single LP), leukocytosis, elevate protein, low glucose, MRI but high false negative, Tx: w/ intra-thecal chemo via LP or Ommaya Reservoir (MTX, Ara-C, topotecan) after you ensure no CSF blocks on flow study and if there is (50% of cases) then focal irradiation to restore flow, very poor prognosis in the order of weeks to months

• Mets
  - “LLLots of Bad Stuff Kills Glia Too”: Lung, Lung, Lung, Breast, Skin, Kidney, GI, Thyroid (also you can have local extension of adjacent tumor as in cranial metastasis and choroid)
  - Mets sometimes herald the dx of new cancer (lung) while others occur late in course of dz long after diagnosis of cancer has been made (breast)
  - Brain mets occur in 25% of cancer pts!!!
  - Tx: dexamethasone to decrease edema and if the lesion is solitary and systemic dx is well controlled then NS or if <3 lesions and <3cm then stereotactic XRT or just whole brain XRT
  - CNS metastasis can present as:
    - Brain Mets: multiple (single uniquely in breast/colon/RCC) well circumscribed lesions at grey-white jxn in cerebral hemispheres around vessels w/ exquisite vasogenic edema, hemorrhage is common w/ melanoma and RCC
    - Epidural Cord Compression: cancer that metastasizes to bone (breast, lung, prostate) followed by extension of the metastatic deposit from the vertebral body into epidural space, S/S: focal radicular pain, Tx: steroids, emergent radiation, surgical resection
    - Leptomeningeal Carcinomatosis: cancer that metastasizes to meninges (lymphoma, SCLC, breast, melanoma, GI) via the bloodstream, S/S: focal deficits from CN palsies and radiculopathy, obstructive hydrocephalus, meningismus, Dx: CSF cytology (55% + after single LP), leukocytosis, elevate protein, low glucose, MRI but high false negative, Tx: w/ intra-thecal chemo via LP or Ommaya Reservoir (MTX, Ara-C, topotecan) after you ensure no CSF blocks on flow study and if there is (50% of cases) then focal irradiation to restore flow, very poor prognosis in the order of weeks to months
  - Paraneoplastic Neurologic Syndromes: rare non-metastatic but rather immune mediated complications of non-CNS cancer, usually the C/PNS are immune privileged sites b/c of the BBB, thus Ag in the C/PNS never see the immune system, but when there is aberrant expression of neuronal Ag by tumor outside of C/PNS an immune response can be elicited, these antibodies which are trying to kill tumor are able to cross BBB for unknown reasons and attack CNS, 2/3 of cases neurologic Sx arise BEFORE diagnosis of cancer by months to years, Dx: check serum/CSF antibodies, Tx: remove tumor, steroids, IVIG, plasma exchange
- **Astrocytomas**
  - **Schwannoma**
  - **Meningioma**

  - **Part of NF in the cerebellum**
  - **NB nerves, 2° CN 8/5/7/12/10/11**
  - **Benign tumor of peripheral nerve sheaths**
  - **High rate of recurrence**
  - **Unique Tx incl**
  - **May compress surrounding tissue and vessels**
  - **Alth and become symptomatic during pregnancy**
  - **Often express progesterone receptors and hence they grow in size**
  - **Increased r/o breast cancer**
  - **Seizures**
  - **Many found incidentally**
  - **Removable**
  - **Sometimes compress underlying tissue nevertheless easily removable**

  - **Experimental Studies**
  - **NovoCure device** (pt wears a device on head for most of the day which creates an alternating electric field that disrupts cancer cell replication)

<table>
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<th>Adult (Supratentorial/Lateralized)</th>
<th>Child (Infratentorial/Midline)</th>
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**Astrocytomas:**
- **Pilocytic Astrocytoma (I)** 20yo, Diffuse Astrocytoma (II) 30yo, Anaplastic Astrocytoma (III) 40yo, Glioblastoma Multiforme - GBM (IV) 50yo
  - **Insidiously infiltrate brain tissue without distinct boundaries therefore often large upon Dx** (it is important to know that disease exists beyond the enhancing component seen on imaging)
  - **Lesions are heterogeneous therefore don’t do a stereotactic biopsy b/c you might get a false negative**
  - **Spread along white matter tracts and often cross corona collicum into opposite hemispheres**
  - **Pathology:** Pseudopalisading Necrosis, Rosenthal Fibers, Glomeruloid Bodies
  - **Imaging:** ring enhancing lesions (DDx: mets, abscess, lymphoma, toxo)
  - **These tumors become progressively more malignant as time they acquire more mutations**
  - **Given the infiltrative nature of these tumors it was originally believed that surgical resection was futile but with the advent of intra-operative MRI >80% of tumor can be removed and so now surgery is advocated**
  - **After surgery you should always repeat MRI w/in 96hrs exactly b/c beyond this time will not permit distinction b/t residual g tumor and the development of normal post-op changes**
  - **There is controversy on the timing of irradiation (at dx or at time of progression)**
  - **RFs:** most cases are idiopathic but there is some evidence for the following: ionizing radiation, NF, tuberous sclerosis (NB cthersy on the timing of irradiation)

**Meningioma (I-III)**
- **Occurs in slightly younger adults (~40yo) and almost always women**
  - **Pathology:** Psamomma Bodies, Whorl Formations
  - **Extracerebral well defined mass that are attached to dura and sometimes compress underlying tissue nevertheless easily removable**
  - **Many found incidentally**
  - **Seizures are common Sx**
  - **Increased r/o breast cancer**
  - **Often express progesterone receptors and hence they grow in size and become symptomatic during pregnancy**
  - **Although benign they can cause significant morbidity if they grow and compress surrounding tissue and vessels**
  - **Unique Tx include anti-progesterones**
  - **NB high rate of recurrence**

**Schwannoma (I)**
- **Benign tumor of peripheral nerve sheaths: 1° head/neck/arms nerves, 2° CN 8/5/7/12/10/11 (in order of incidence)**
  - **NB “acoustic neuroma” refers to schwannoma of CN-8 which arise in the cerebellopontine angle, usually unilateral but if bilateral then part of NF-II**
  - **S/S depend on which nerve is involved**

**Medulloblastoma (IV)**
- **Very malignancy but fortunately very response to irradiation**
  - **Usually arises at the vermis of the cerebellum followed by “drop metastasis” into 4th ventricles and down spinal cord**
  - **Can cause obstructive hydrocephalus**
  - **Staging is very important for this form of CNS cancer compared to others as they can metastasize to bone/LNs/soft-tissue**

**Glioblastoma Multiforme (IV)**
- **Grade IV**
  - **Diffuse infiltration of brain tissue without distinct boundaries)**
  - **Heterogenous therefore don’t do a stereotactic biopsy b/c you might get a false negative**
  - **Spread along white matter tracts and often cross corona collicum into opposite hemispheres**
  - **Pathology:** Psamomma Bodies, Whorl Formations
  - **Imaging:** ring enhancing lesions (DDx: mets, abscess, lymphoma, toxo)
  - **These tumors become progressively more malignant as time they acquire more mutations**
  - **Given the infiltrative nature of these tumors it was originally believed that surgical resection was futile but with the advent of intra-operative MRI >80% of tumor can be removed and so now surgery is advocated**
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  - **There is controversy on the timing of irradiation (at dx or at time of progression)**
  - **RFs:** most cases are idiopathic but there is some evidence for the following: ionizing radiation, NF, tuberous sclerosis (NB cthersy on the timing of irradiation)

**Neurofibroma (I)**
- **Benign tumor of peripheral nerve sheaths w/ concurrent proliferation of fibroblasts creating a firm mass: 1° small nerves in skin, unlike schwannomas does not involve cranial nerves**
  - **If multiple then part of NF-I**
  - **5% degenerate into Malignant Peripheral Nerve Sheath Tumors (MPNSTs)**
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<thead>
<tr>
<th><strong>Oligodendroglioma (II-III)</strong></th>
<th><strong>Ependymoma (I)</strong></th>
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<td>- Occurs in slightly younger adults (~40yo)</td>
<td>- Arise anywhere on the neuroaxis but most commonly in posterior fossa where the 4th ventricle exists</td>
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<td>- Malignant but they have a more indolent progression then astrocytomas above as pts can survive for up 10-15yrs</td>
<td>- Causes obstructive hydrocephalus</td>
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<td>- White matter cortex w/ leptomeningeal involvement causing seizures</td>
<td>- b/c of its location they are able to disseminate throughout the CNS</td>
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<td>- Like astrocytomas there are benign kinds and very malignant kinds which are able to even metastasize systemically</td>
<td>- surgery/irradiation can be curative</td>
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<td>- Often have calcification on imaging but otherwise look very similar to astrocytomas above</td>
<td>- currently there is no role for chemotherapy</td>
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<td>- Respond better to chemo than astrocytomas especially if they have Loss of Heterozygosity in 1p and 19q indicating that there will be a really good response to chemo, 10yr vs 2yr survival</td>
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<td>- Pts often have several years of subtle neurologic Sx</td>
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<th><strong>Germ Cell Tumor (I-IV)</strong> (refer, similar to those arise in gonads, arise from developmental nests of primitive germs cells in midline structure as in 3rd ventricle and pineal gland, mediastinum, etc)</th>
<th><strong>Hemangioma (III)</strong> (refer, part of vHL syndrome)</th>
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<th><strong>Primary CNS Lymphoma (IV)</strong> (refer, arises from lymphoid tissue in body and somehow selectively migrates into CNS w/ no systemic tumor burden, ~100% DLBCL, ~60yo if immunocompetent vs younger if immunocompromised as in HIV, transplant, etc, can be single or multiple masses in cerebral hemispheres)</th>
<th><strong>Neuroblastoma (III)</strong> (refer)</th>
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<th><strong>Pituitary Adenoma (I)</strong> (refer)</th>
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