

# CNS

- Normal
  - -Neurons
  - -Glia
    - Astrocytes
    - Oligodendrocytes
    - Ependymal Cells
    - Microglia
- Pathology (13 Questions)

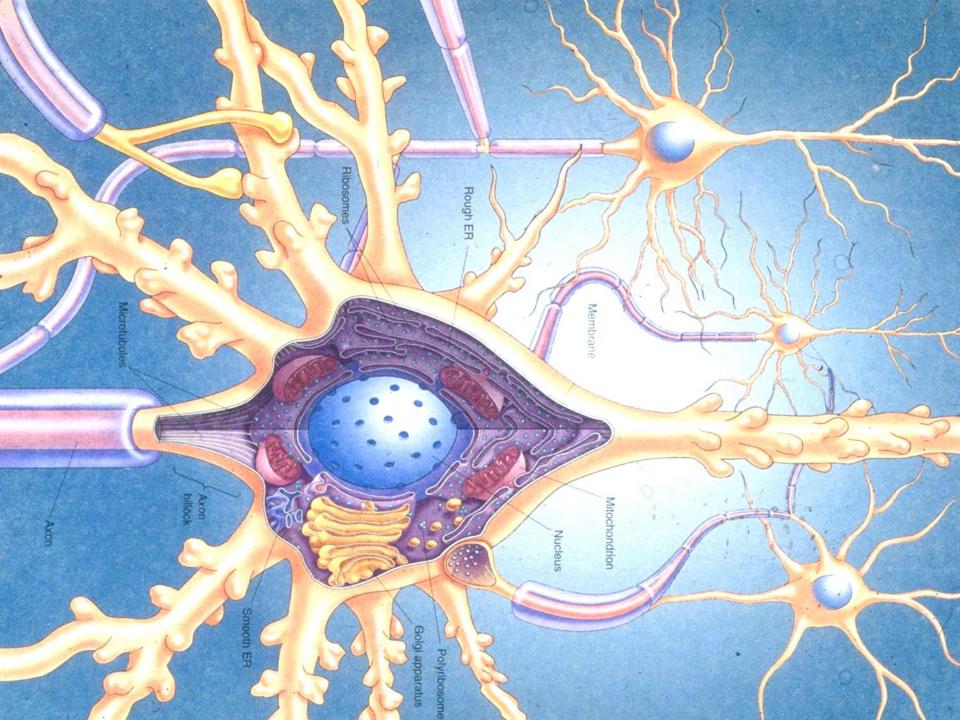
#### **Classical Disease Patterns**

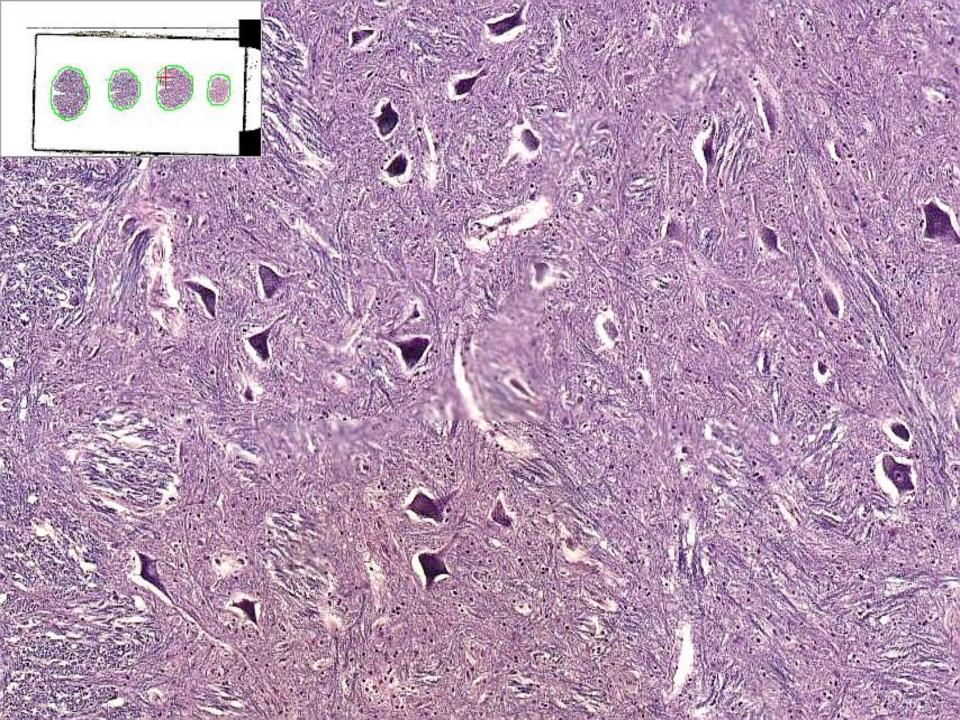
- Degenerative
- Inflammatory
- Neoplastic

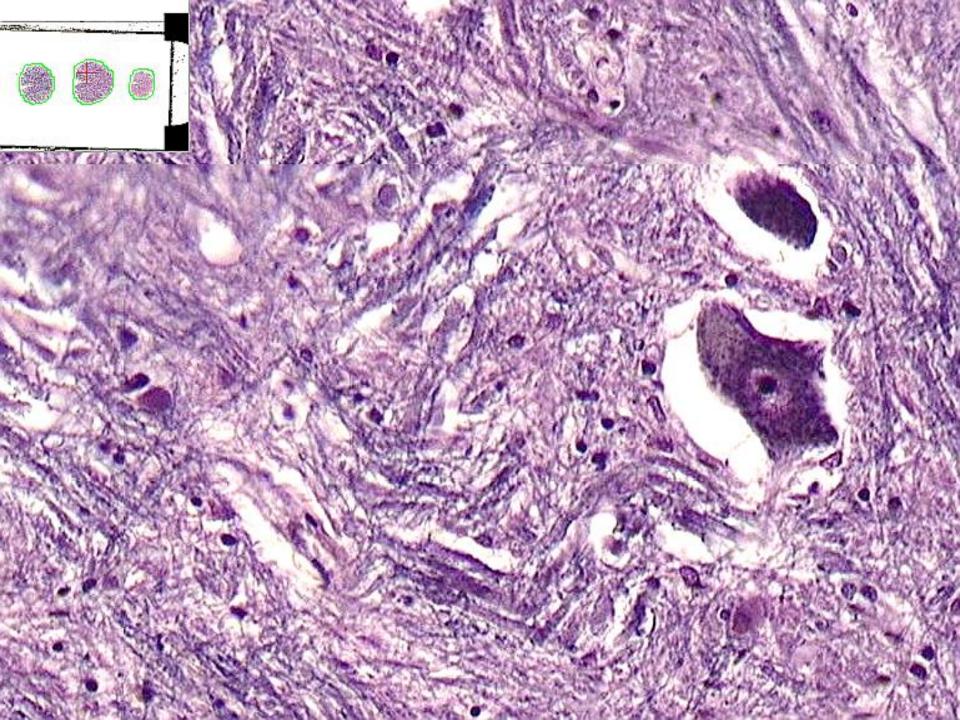
#### Classical CNS Disease Patterns

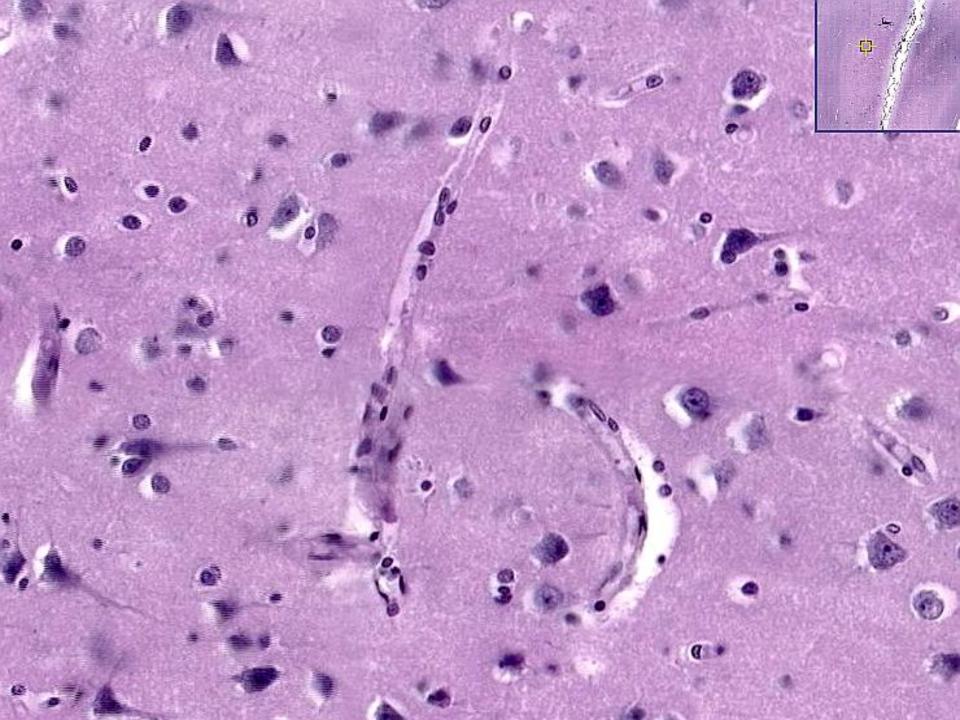
- Degenerative
- Inflammatory
- Neoplastic
- Traumatic

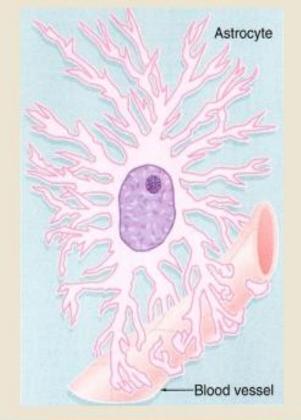
- 1) What are general patterns of CNS cell pathology?
- 2) What are the consequences of ↓↑ CNS pressure?
- 3) What are common patterns of CNS malformations?
- 4) What are common perinatal CNS injuries?
- 5) What are the patterns of CNS trauma?
- 6) What are the patterns of CNS vascular disease?
- 7) What are the patterns of CNS infection?
- 8) What are the patterns of CNS prion disease?
- 9) What are the patterns of CNS demyelinating disease?
- 10) What are the patterns of CNS degenerative disease?
- 11) What are the CNS genetic metabolic diseases?
- 12) What are the CNS acquired metabolic/toxic diseases?
- 13) What are the CNS tumors?

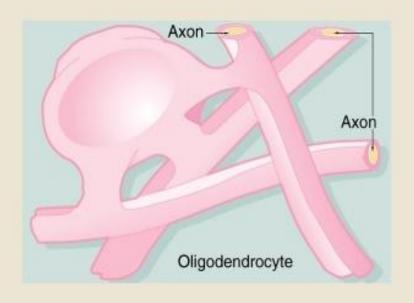


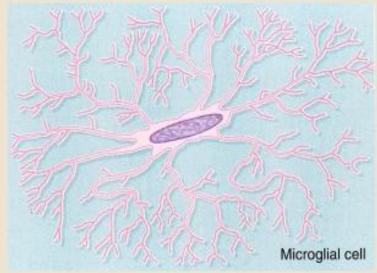


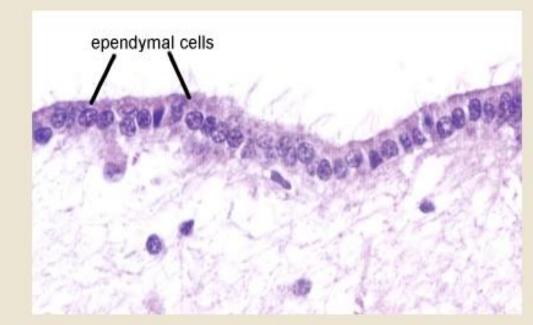


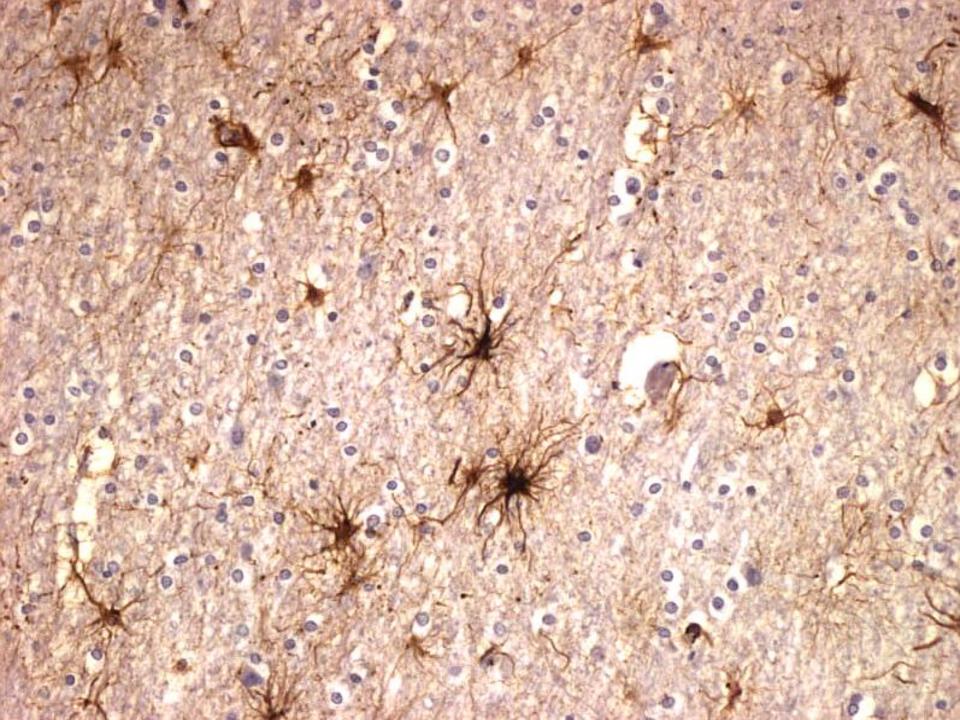


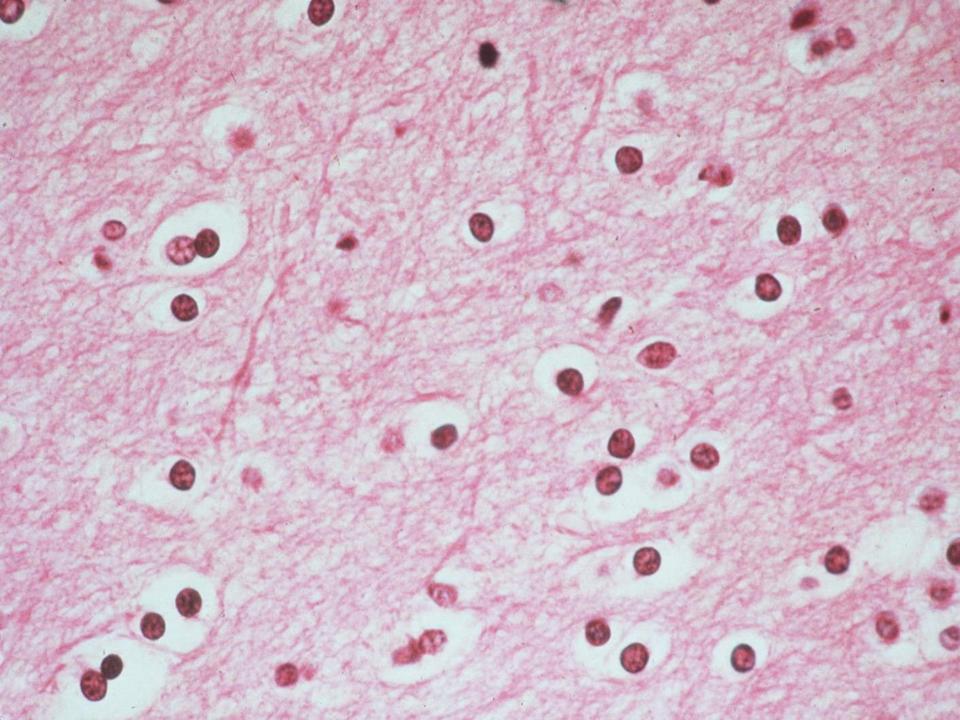


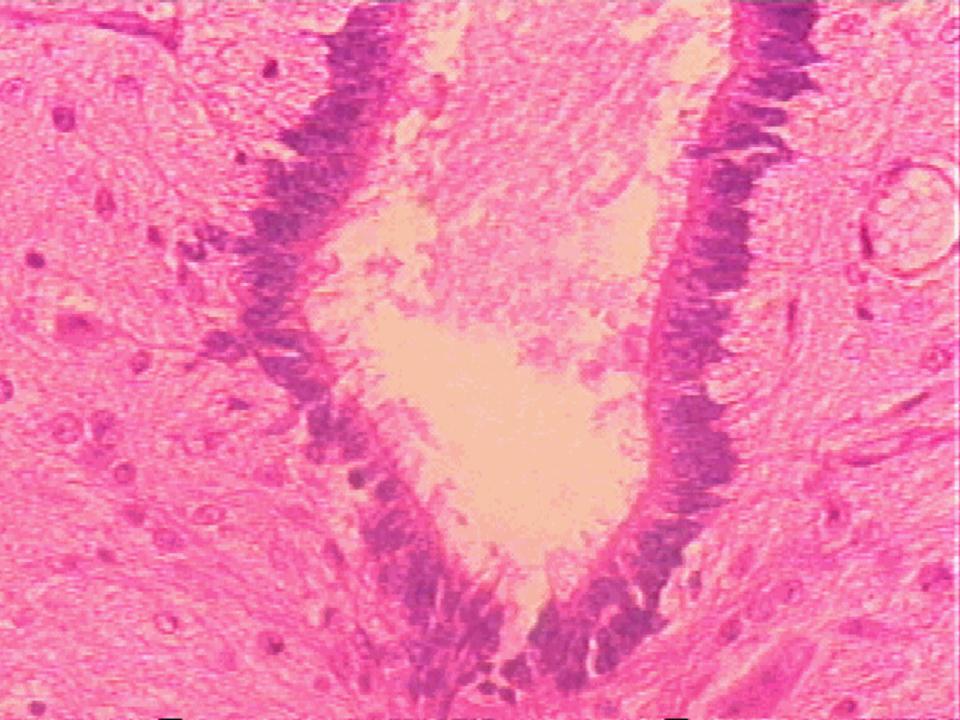


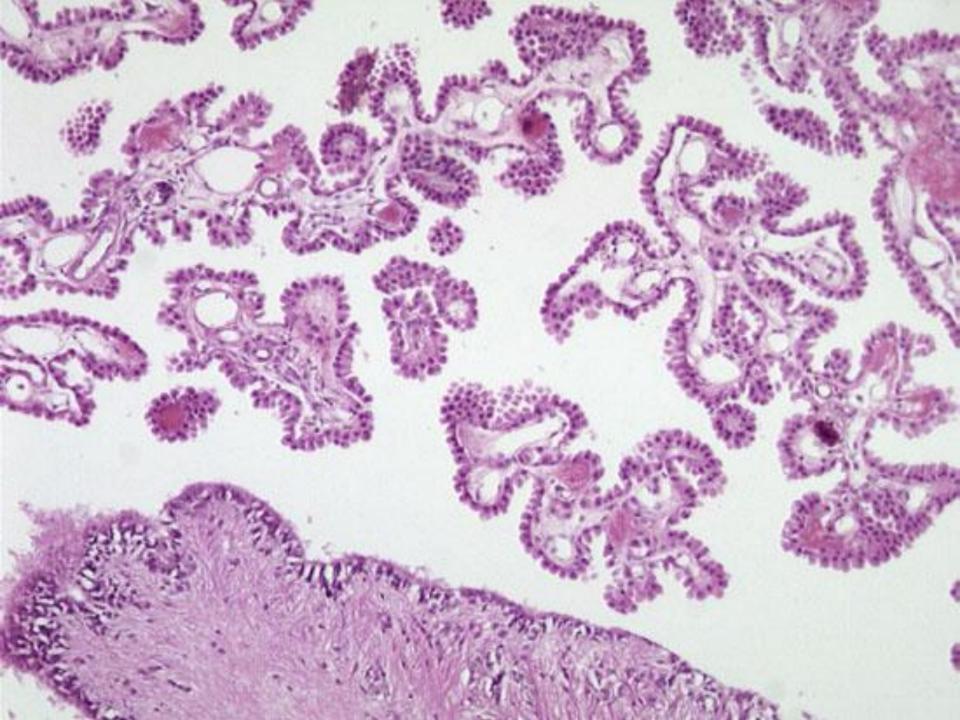


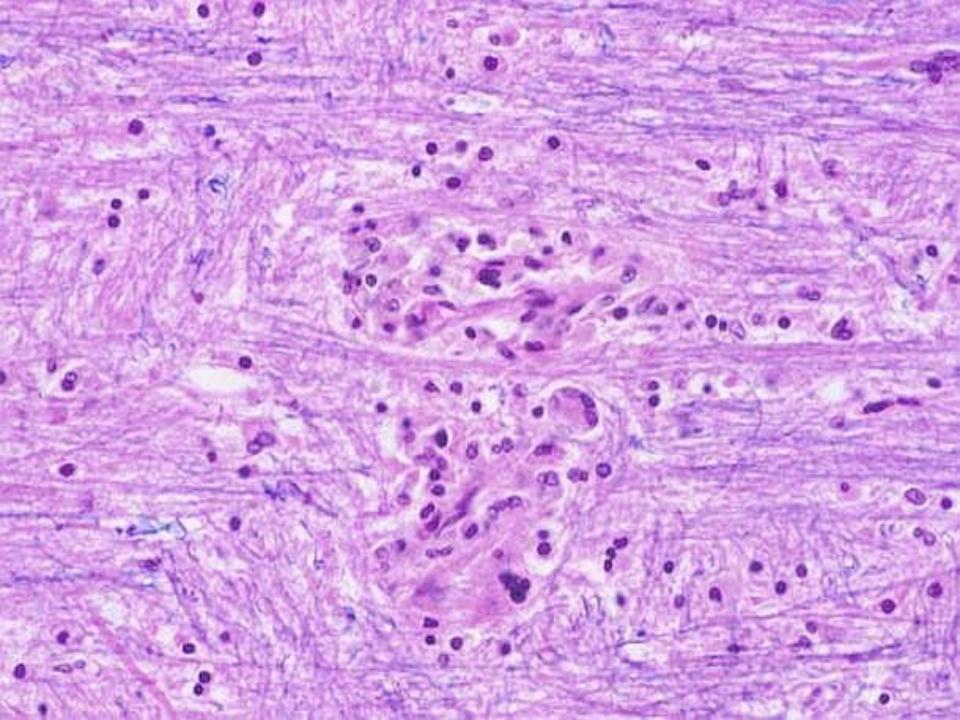












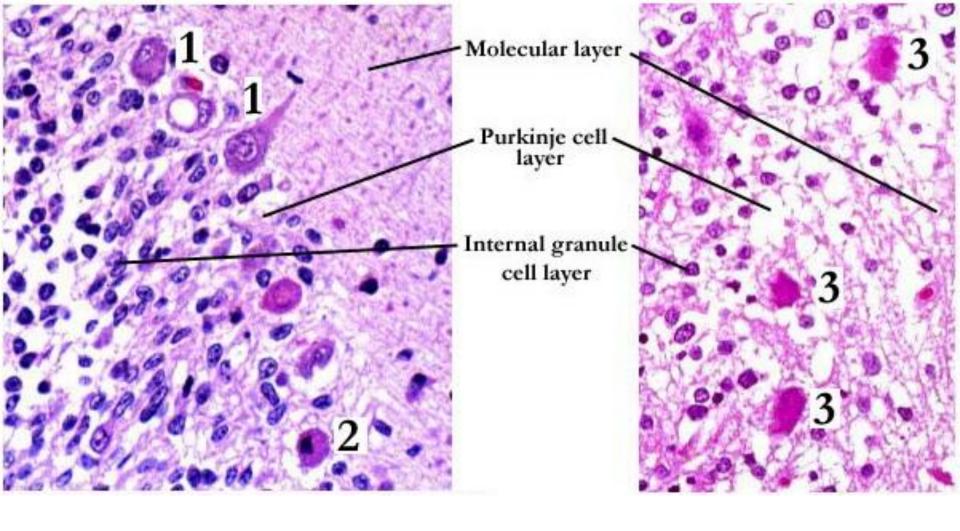
#### **CELLULAR REACTIONS**

#### Neurons

- Acute (RED neuron, karyolysis)
- Subacute, chronic, cell loss, gliosis
- Axonal
- Inclusions (lipid, prot., carb., viruses)

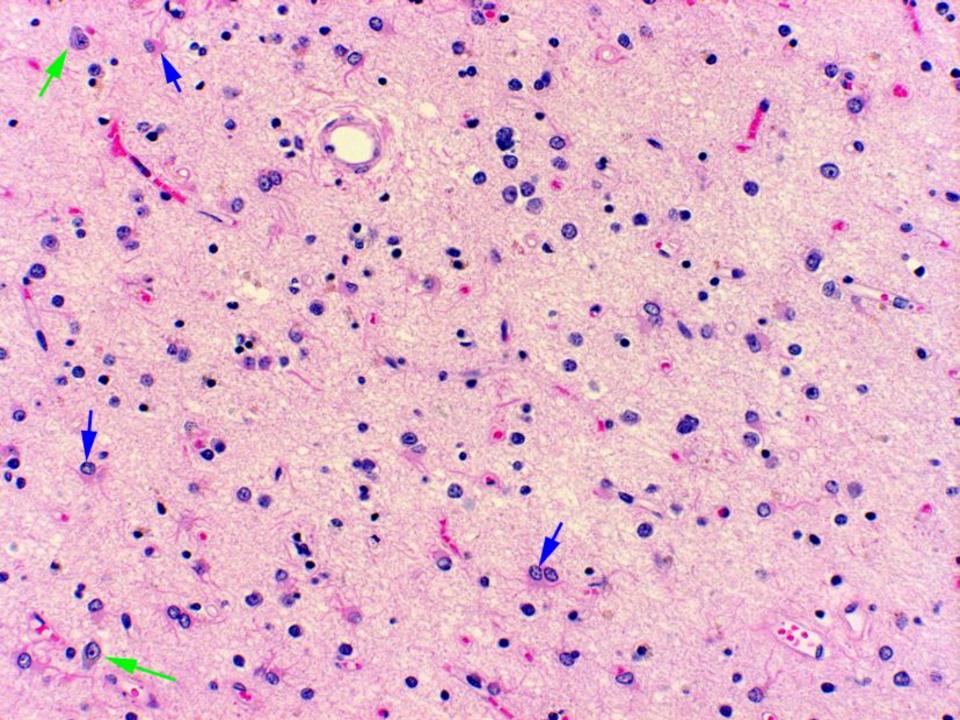
# · Glia, "gliosis"

- Swelling
- Fibers
- Inclusions



#### **ACUTE NEURONAL INJURY**

### "RED" NEURONS



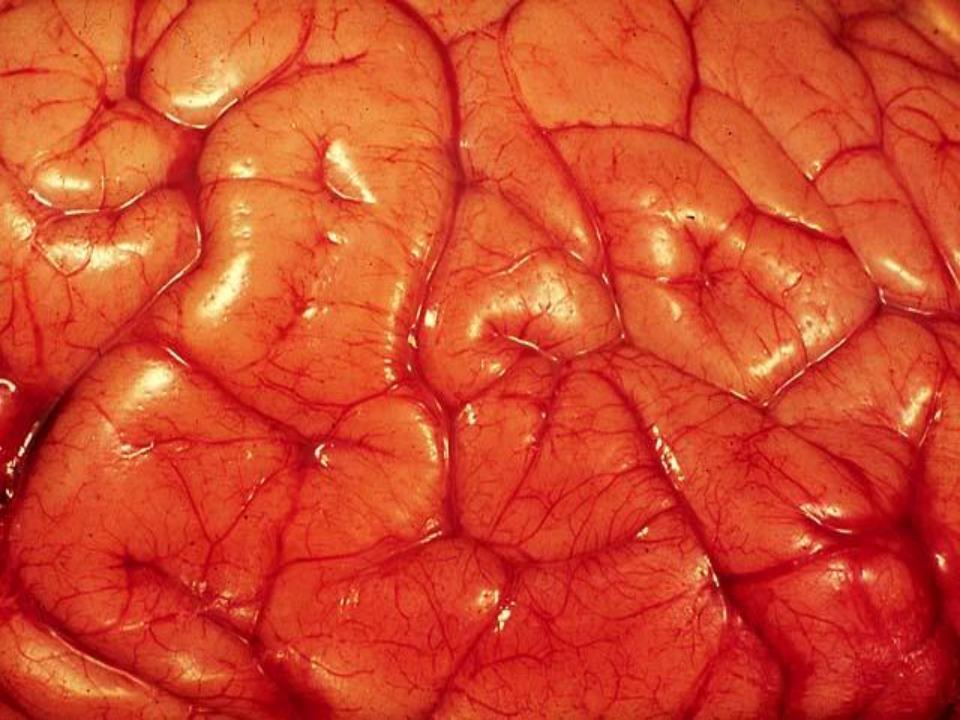
## CEREBRAL EDEMA

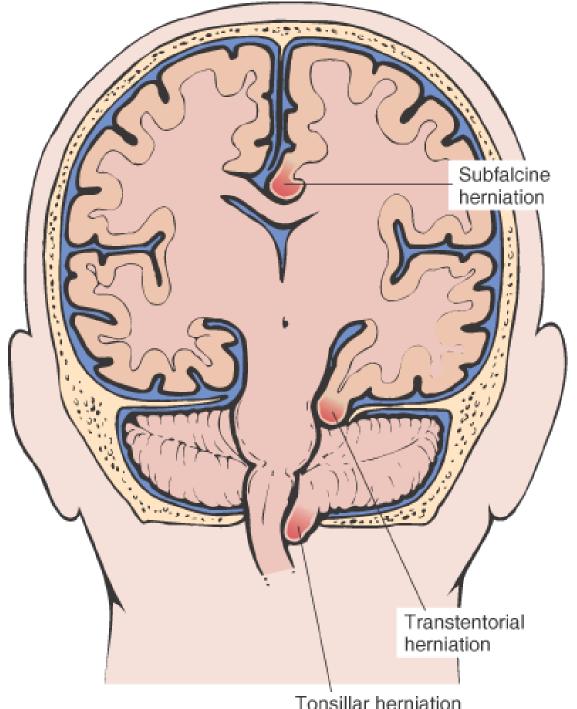
(normal weight 1200-1300 grams)

- Vasogenic (disrupted BBB)
  - -Intravascular → INTER-cellular
- Cytotoxic
  - → INTRA-cellular

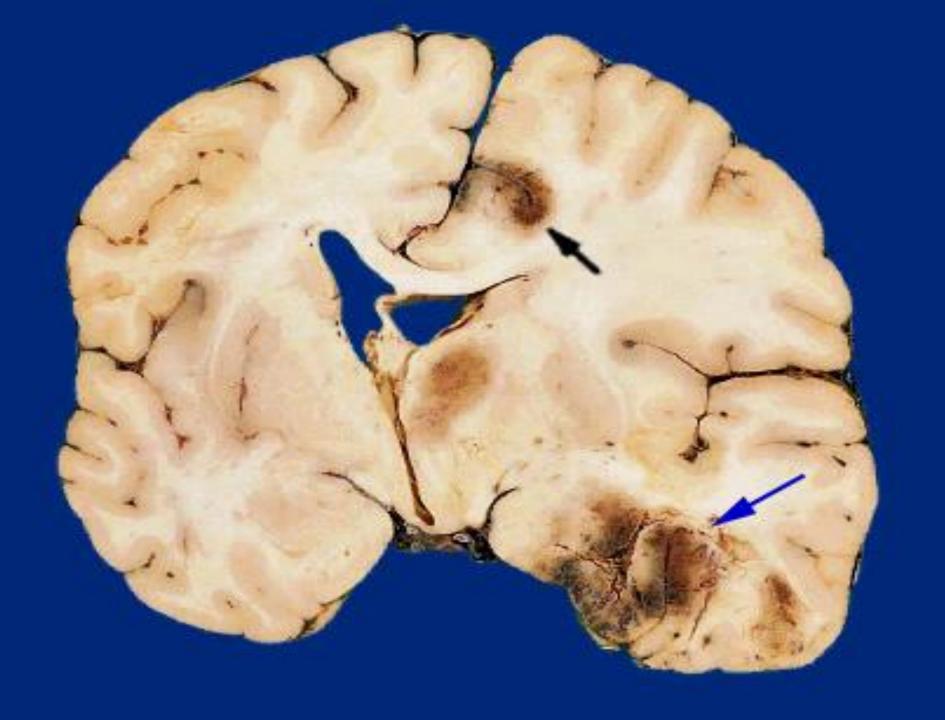
### CEREBRAL EDEMA

- Subfalcine (SUPRA-tentorial)
- Cingulate (TENTORIAL)
- Cerebellar tonsilar (SUB-tentorial, or INFRA-tentorial)

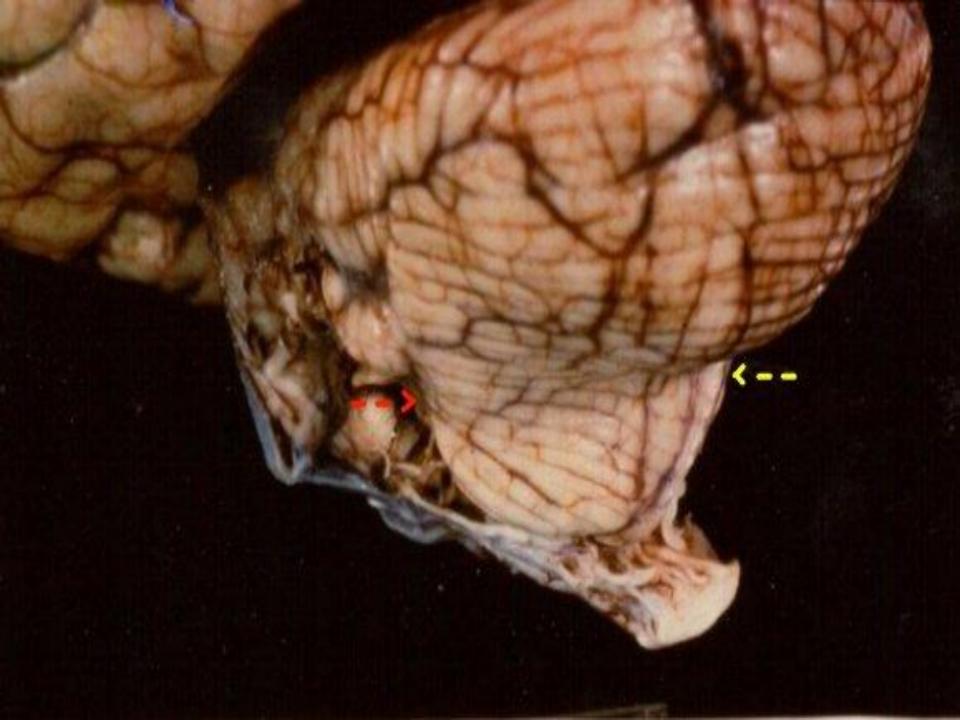




Tonsillar herniation



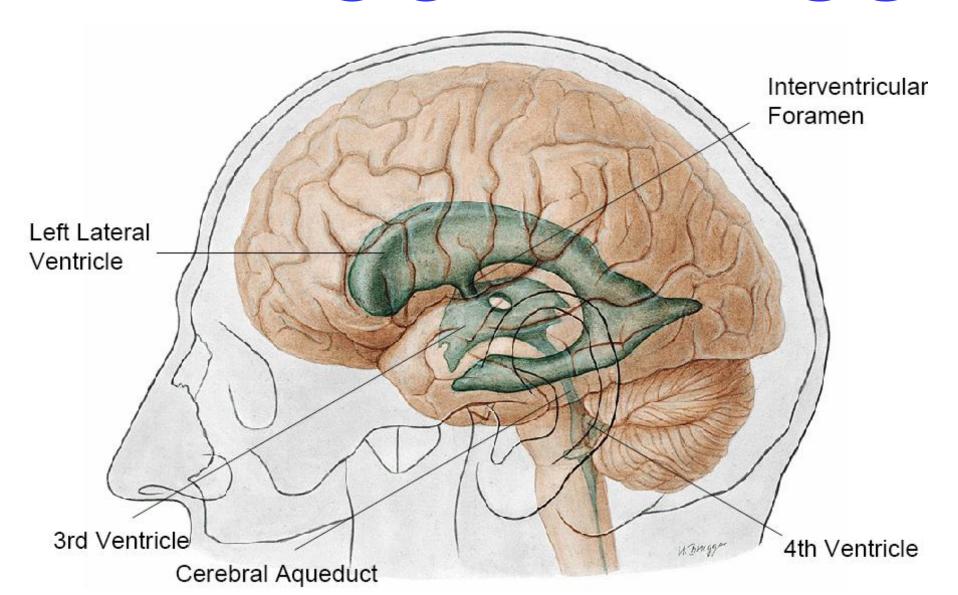




## CEREBRAL EDEMA

- DDX:
  - **–EVERYTHING**
- SYMPTOMS
  - -HEADACHE
  - -HALLUCINATIONS
  - -COMA
  - -DEATH

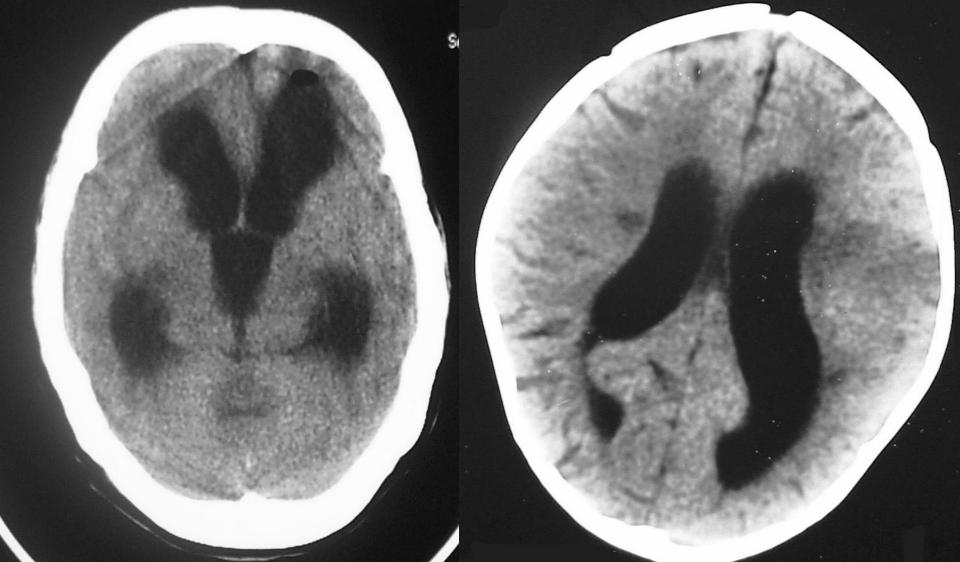
# HYDROCEPHALUS

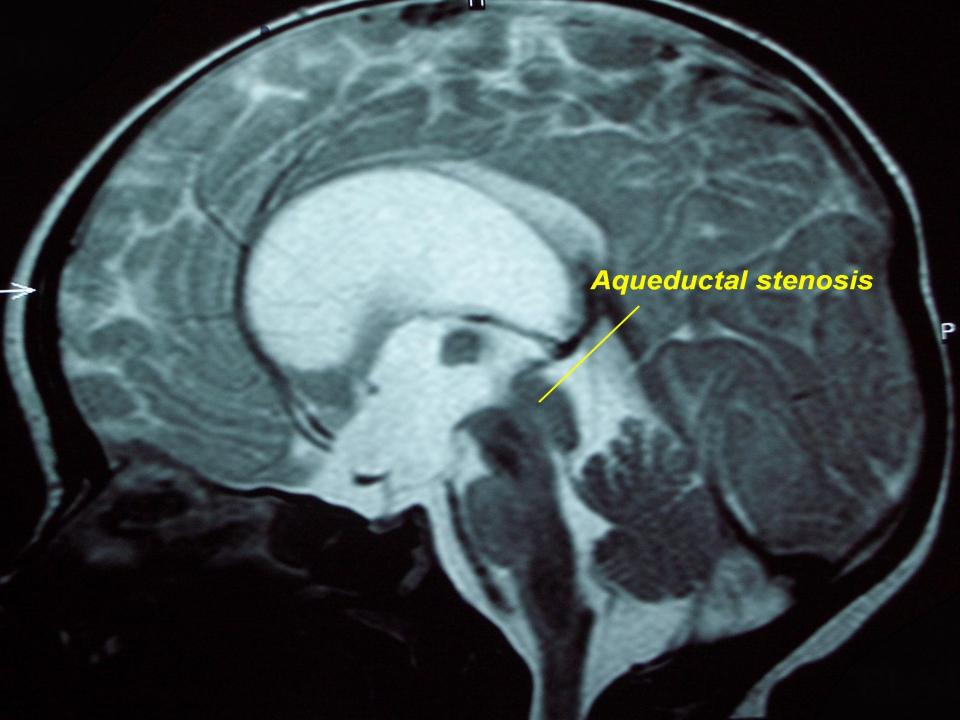


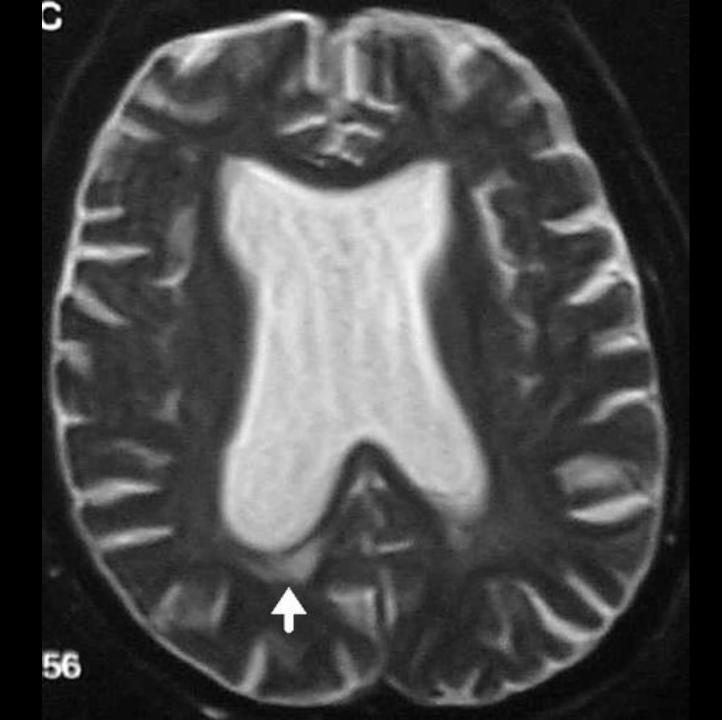
# HYDROCEPHALUS

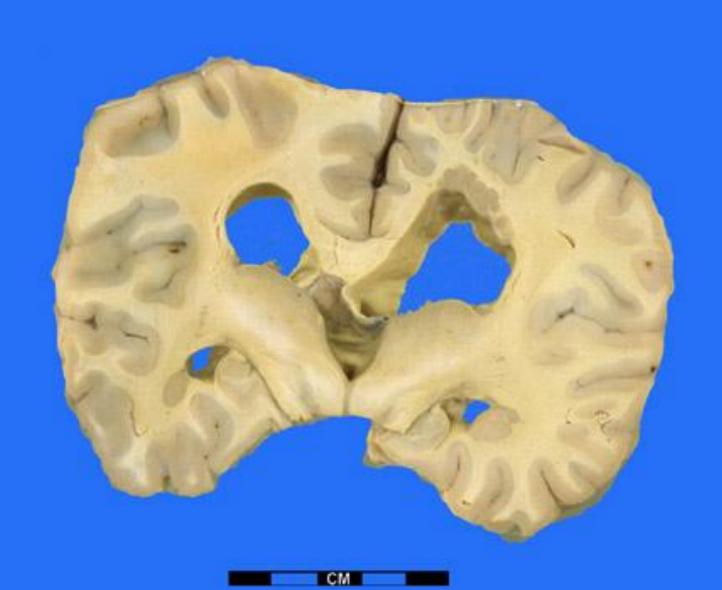
- Impaired RESORPTION
- Increased PRODUCTION
- OBSTRUCTION
- COMMUNICATING (entire)
- NON-COMMUNICATING (part)
- HIGH Pressure
- NORMAL Pressure











#### **CNS MALFORMATIONS**

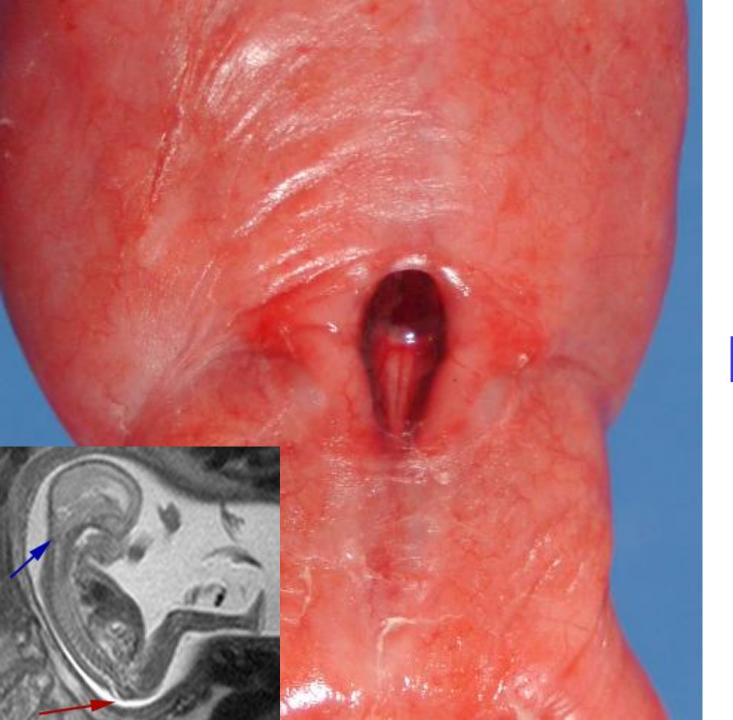
#### Neural Tube

Anencephaly, Encephalocele, Spina Bifida

#### Forebrain

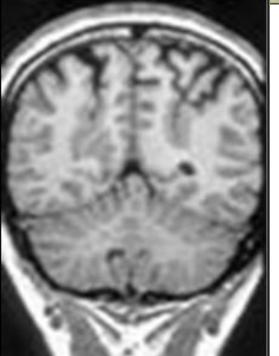
- Polymicrogyria, Holoprosencephaly, Agenesis of Corpus Callosum
- Posterior Fossa (Infratentorial)
  - Arnold Chiari (infratentorial herniation), Dandy-Walker (cerebellar cyst)
- Syringomyelia/Hydromyelia





# SPINA BIFIDA

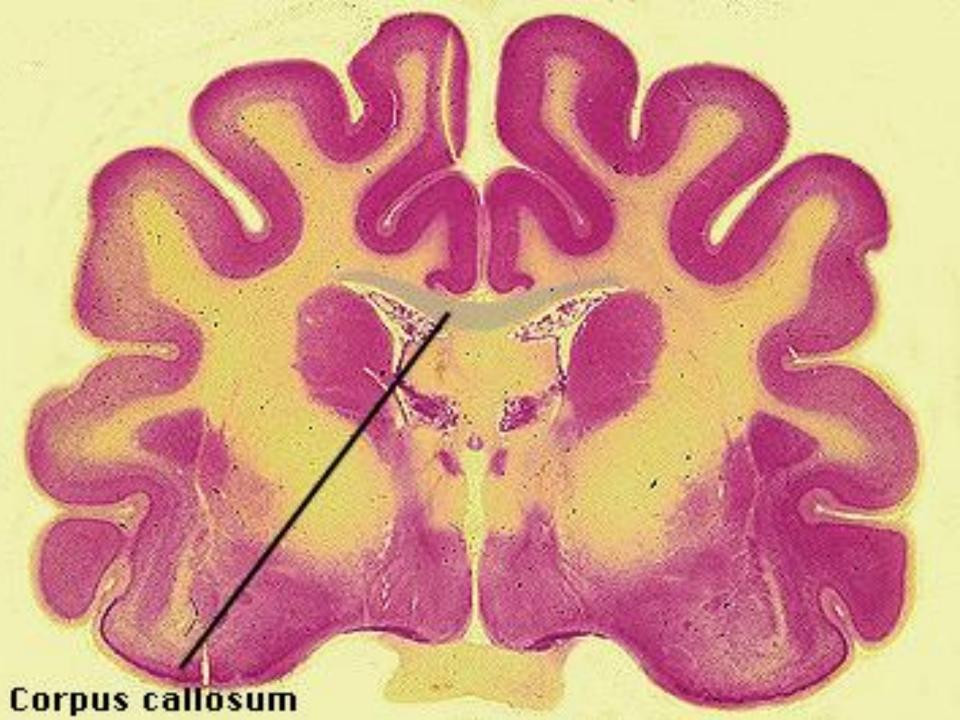


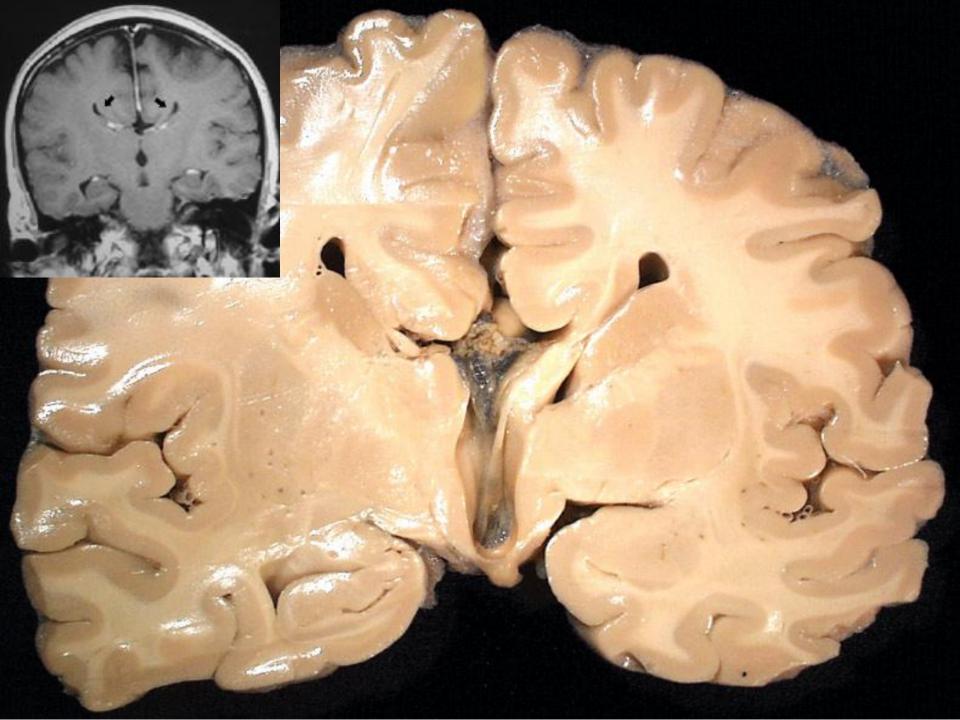


### **POLYMICROGYRIA**



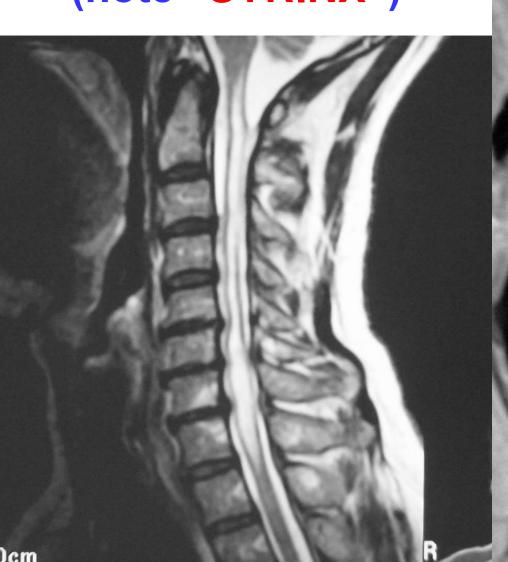
### HOLOPROSENCEPHALY

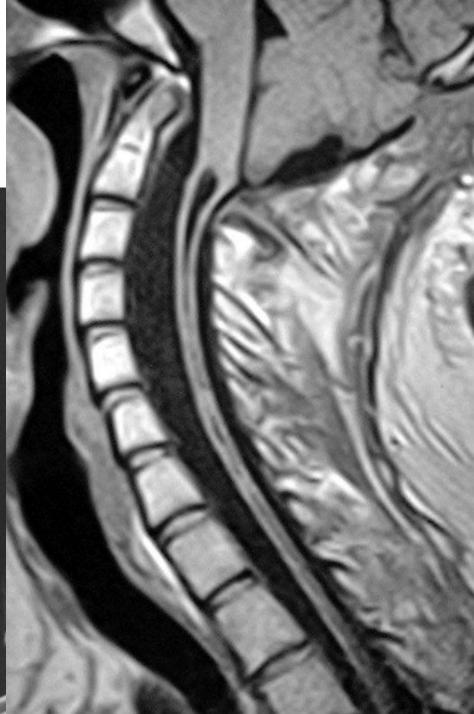




#### **SYRINGOMYELIA**

(note "SYRINX")

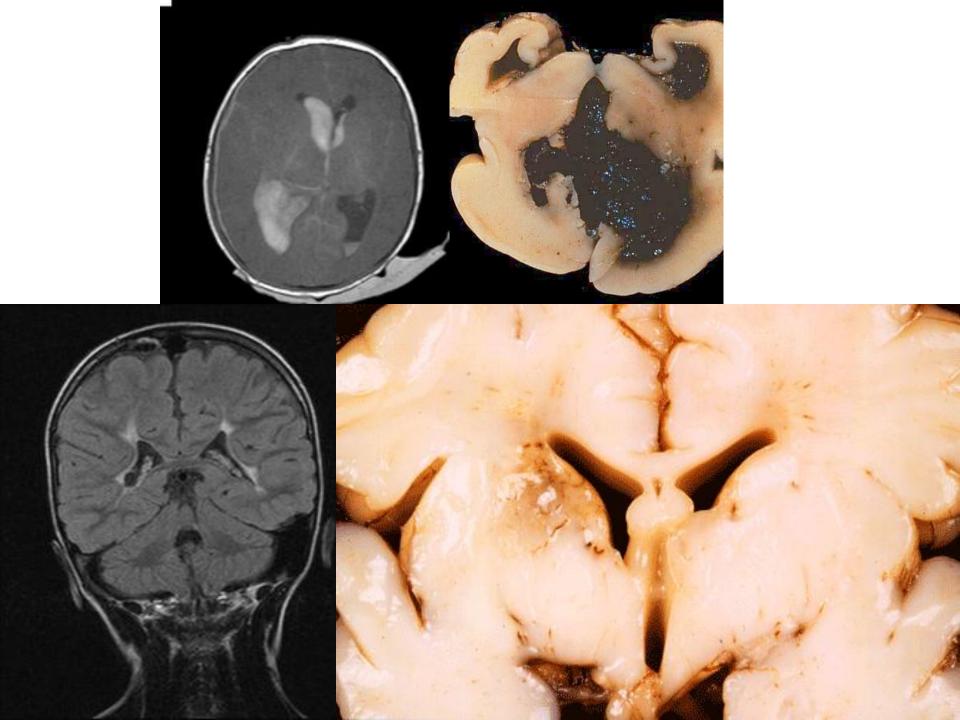




## PERINATAL Brain Injuries

- Intraparenchymal Hemorrhage
- Intraventricular hemorrhage (premies)
- Periventricular "leukomalacia" (i.e., infarcts)

 Cerebral "Palsy" refers to nonprogressive diffuse cerebral pathology apparent at childbirth



## **CNS TRAUMA**

- Skull Fractures
- Parenchymal Injuries
- Traumatic Vascular Injury
- Sequelae
- Spinal Cord Trauma

## **BRAIN TRAUMA**

- Contusion (bruise)
- Laceration (tear)
- Coup/Contre-Coup
- Concussion





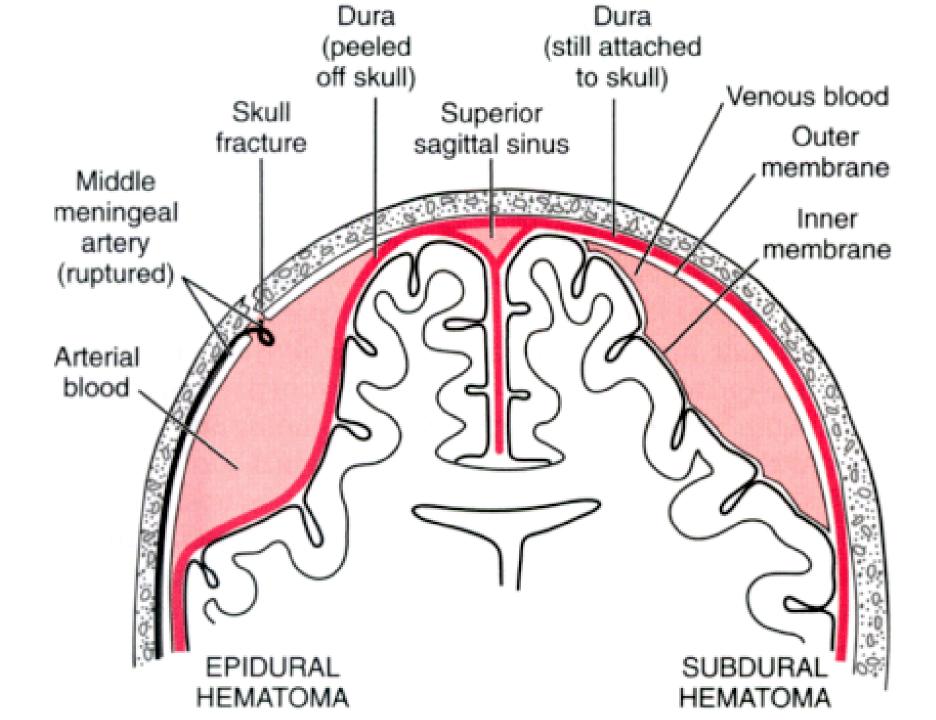
#### "HAIRLINE"

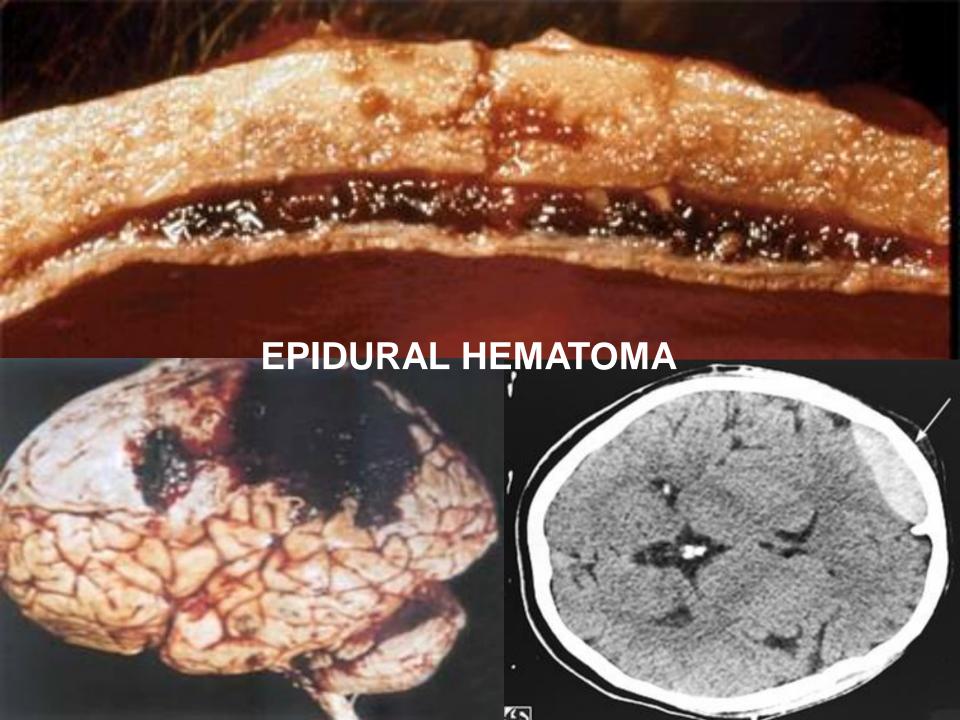
"DEPRESSED", aka

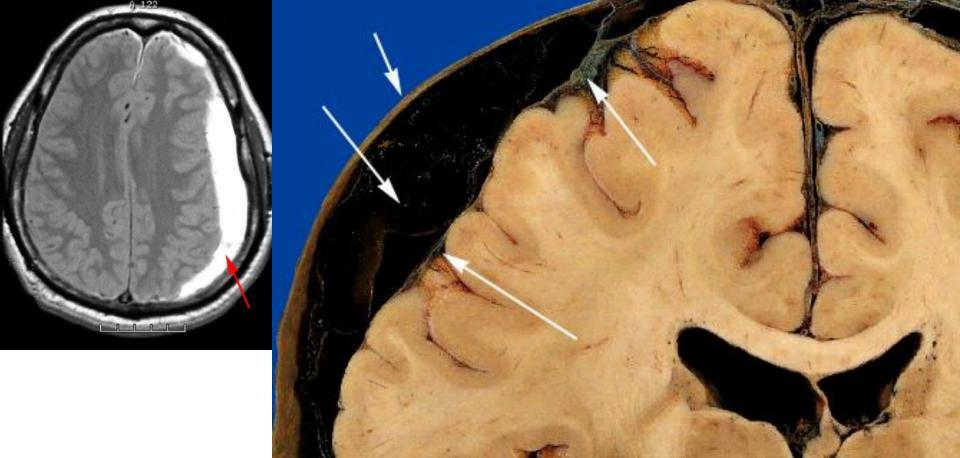
"DISPLACED"

#### **HEMATOMAS/HEMORRHAGE**

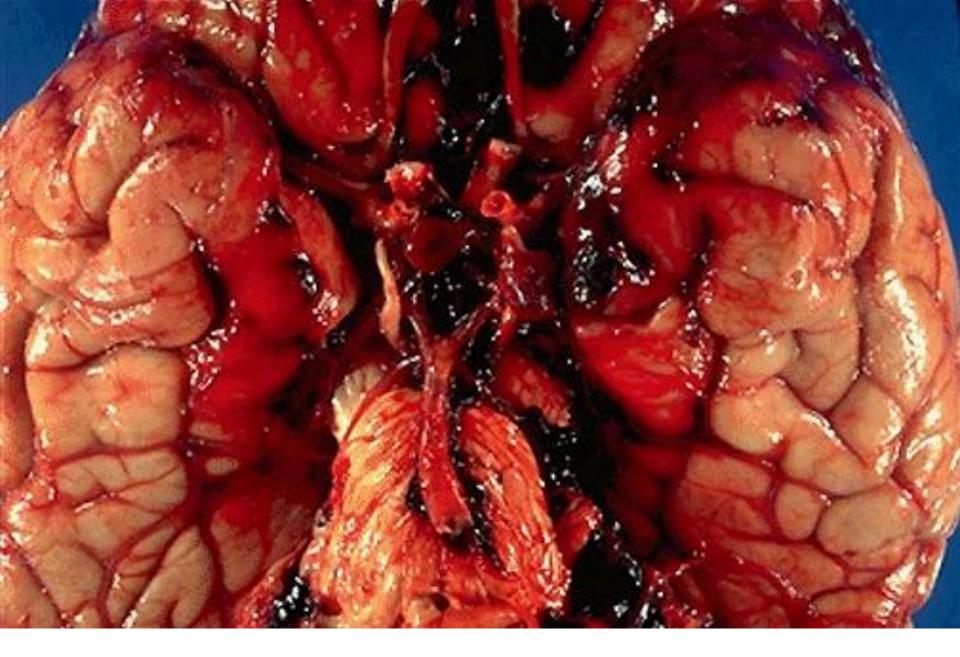
- EPIDURAL (fx)
- SUBDURAL (trauma NO fx)
- SUBARACHNOID (arterial, no trauma)
- INTRAPARENCHYMAL (any)
- INTRAVENTRICULAR (no trauma, rare in adults, common in premies)



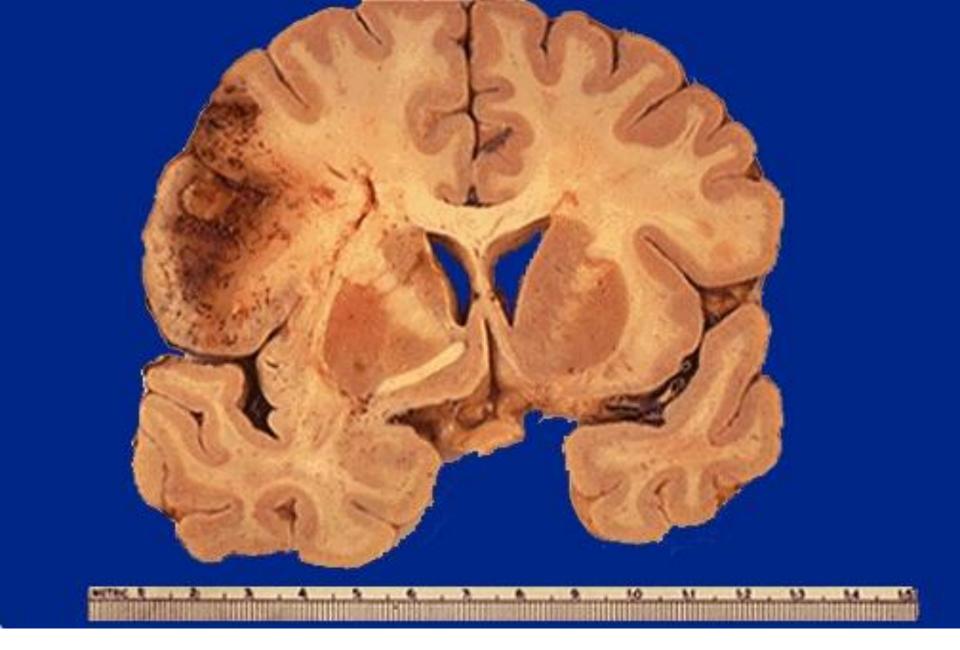




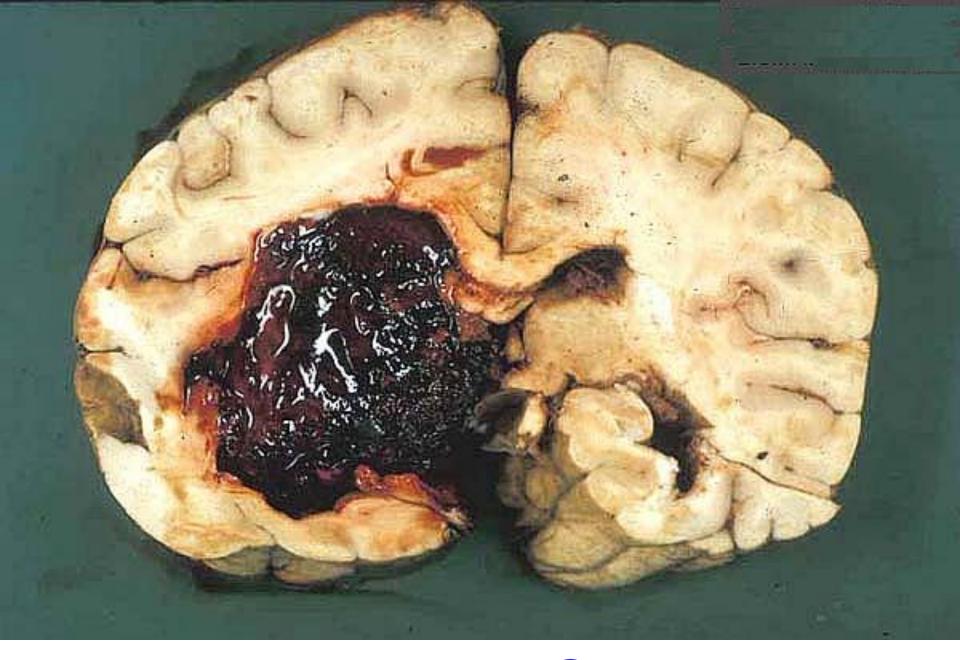
## SUBDURAL HEMATOMA



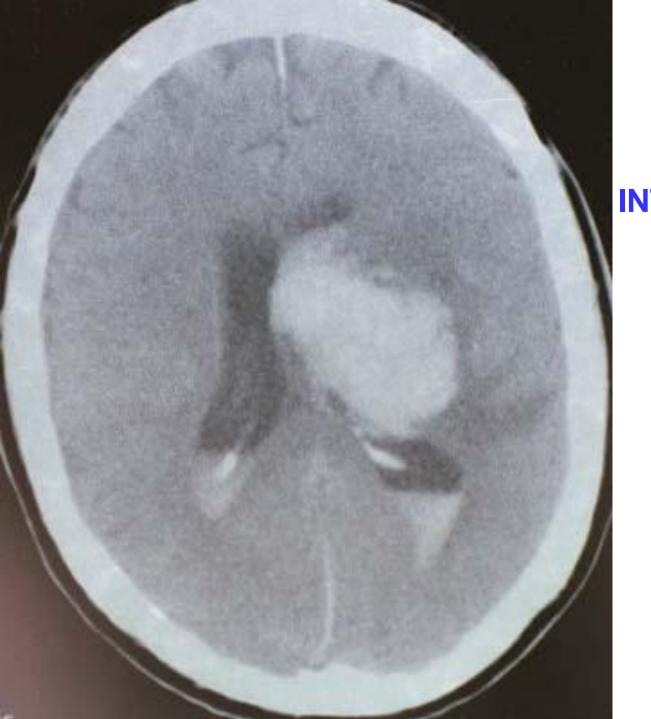
## **SUBARACHNOID**



#### INTRAPARENCHYMAL



#### INTRAPARENCHYMAL



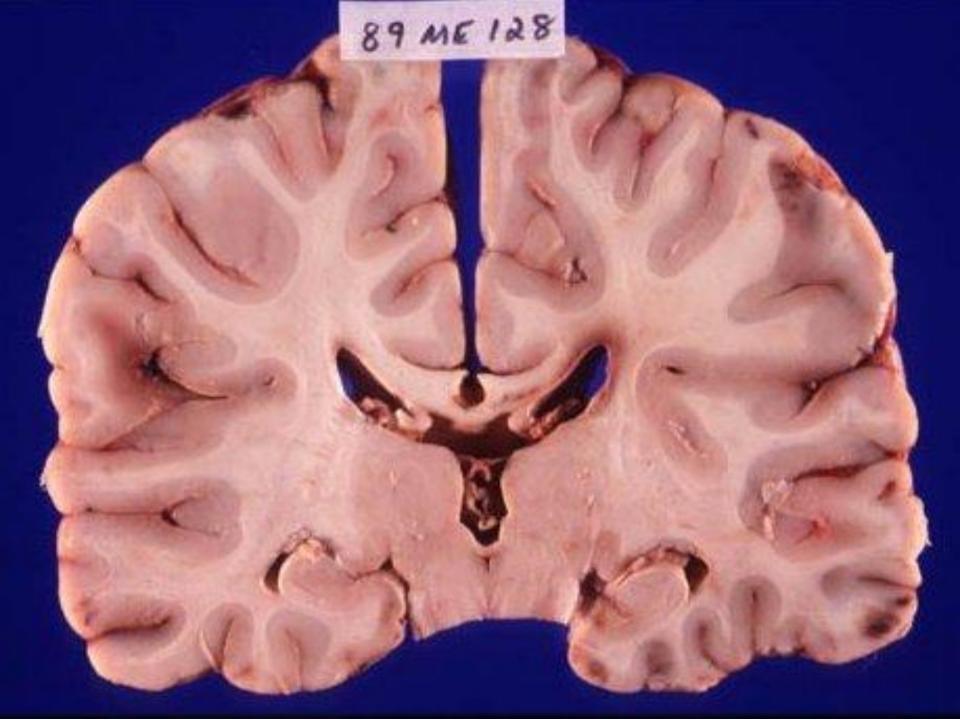
#### INTRAVENTRICULAR

#### **CNS TRAUMA SEQUELAE**

Hydrocephalus (WHY?)

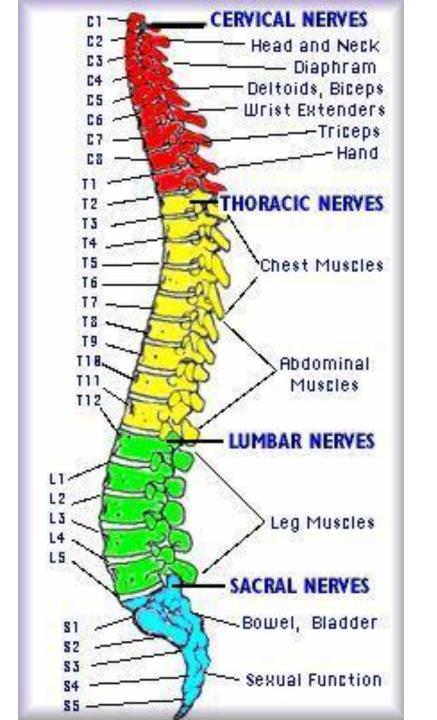
Dementia (Punch Drunk Syndrome)

Diffuse Axonal Injury (white matter)



#### SPINAL CORD TRAUMA

- Parallels BRAIN patterns of injury on a cellular basis
- Usually secondary to spinal column displacement
- Level of injury mirrors motor loss: Death→ Quadriplegia → Paraplegia



# Cerebrovascular Diseases (CVA, "Stroke")

- Ischemic (↓ blood and 02)
  - Global
  - Focal (regional):
  - ACUTE: edema → neuronal microvacuolization → pyknosis → karyorrhexis → neutrophils
  - CHRONIC: macrophages → gliosis

Hemorrhagic (rupture of artery/aneurysm)

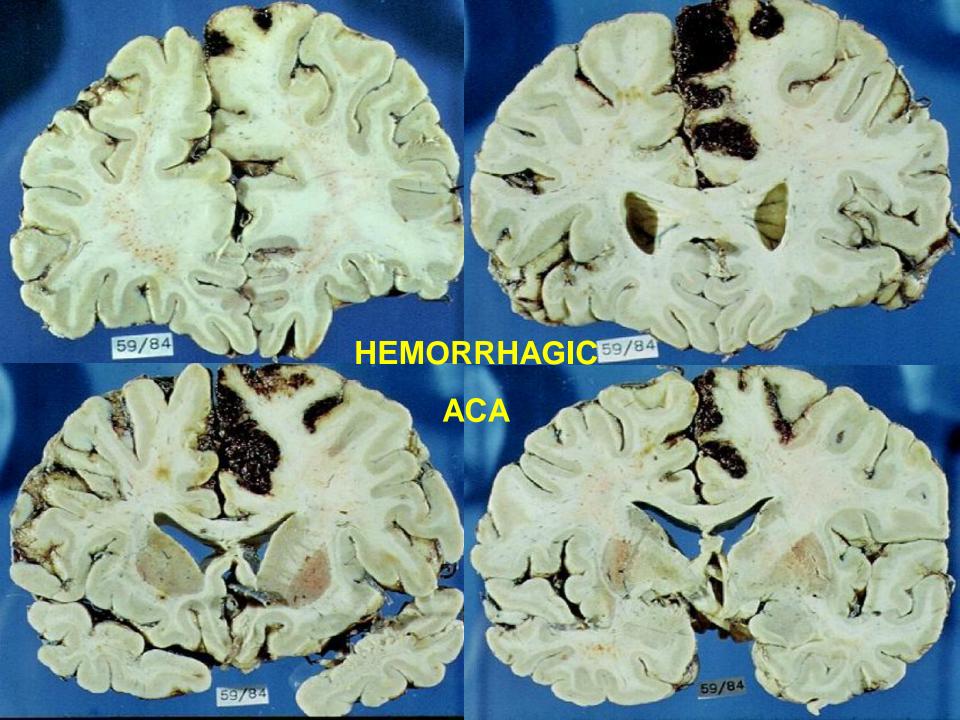
Anterior Cerebral A.

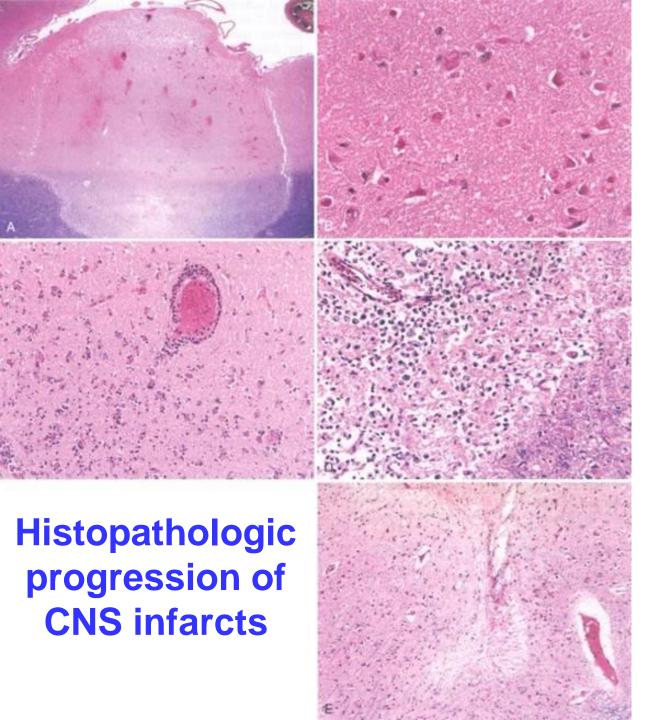
Middle Cerebral A.

Posterior Cerebral A.



# THROMBOTIC MCA



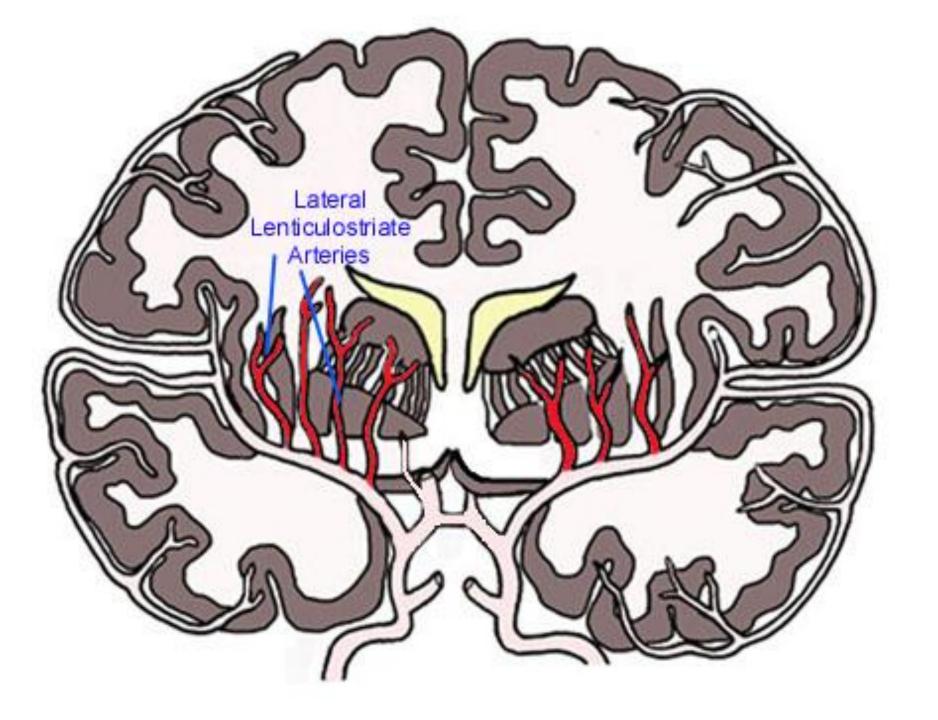


- A) EDEMA
- **B) "RED" NEURONS**
- C) POLYs
- D) MONO's (MACs)
- E) GLIOSIS

## HYPERTENSIVE CVA

- Intracerebral
- Basal Ganglia Region

(lenticulostriate arteries of internal capsule, putamen)

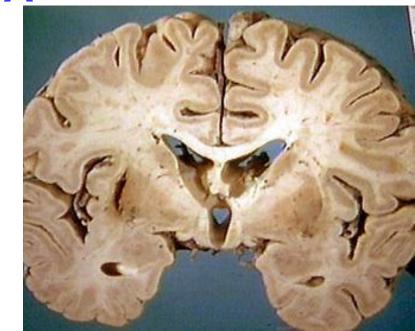


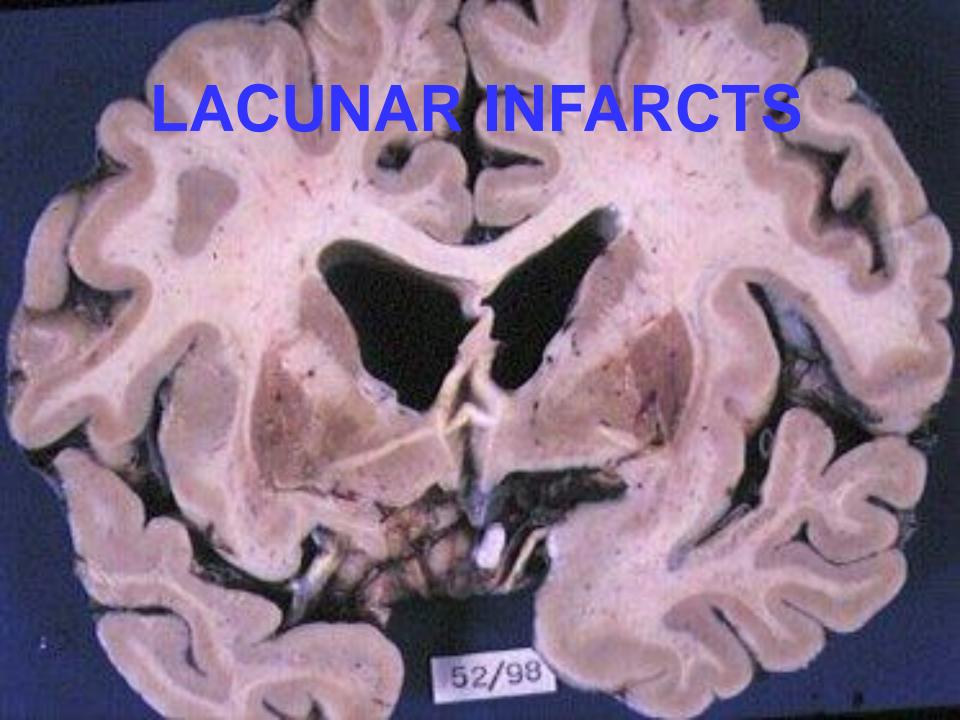




HYPERTENSIVE CVA





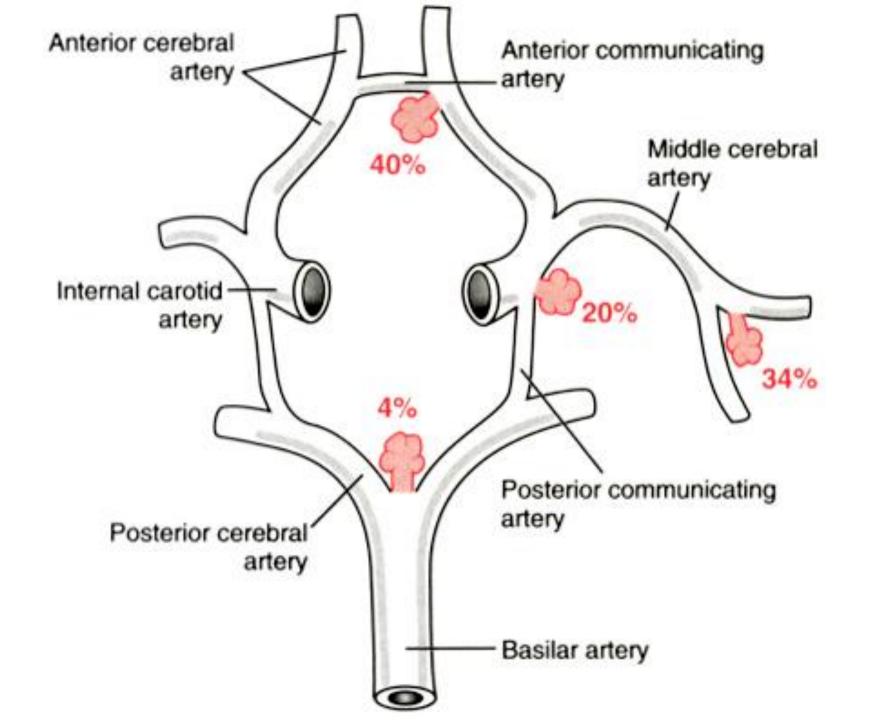




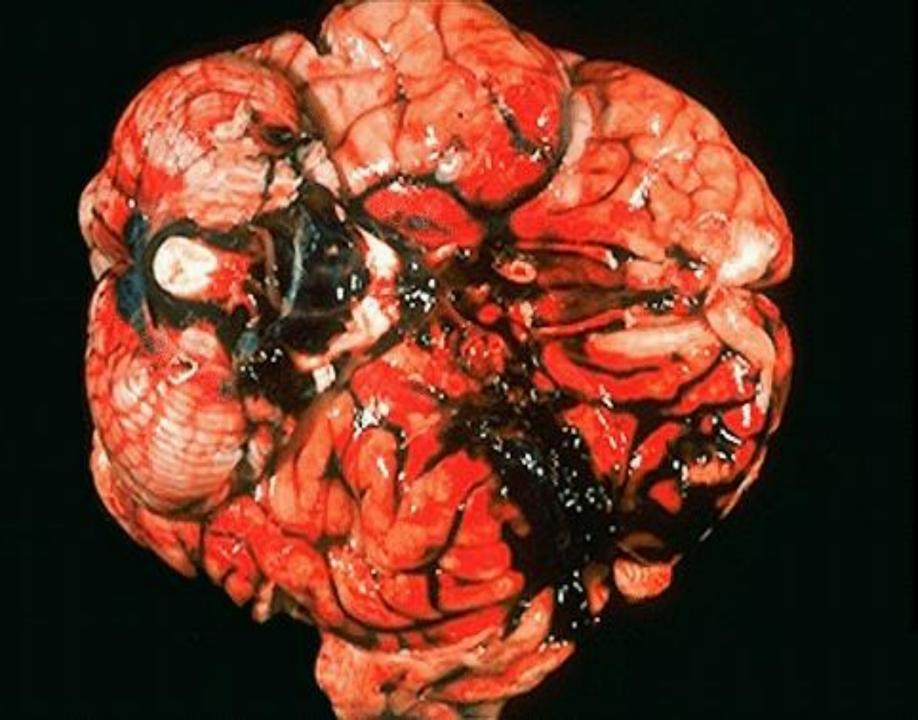
# SUBARACHNOID HEMORRHAGE

 Rupture of large intracerebral arteries which are the primary branches of the anatomical circle (of Willis)

- Congenital ("berry" aneurysms)
- Atherosclerotic (atherosclerotic aneurysms, or direct wall rupture)







#### HYPERTENSIVE ENCEPHALOPATHY

#### ACUTE

- Headaches
- Confusion
- Anxiety
- Convulsions

#### CHRONIC

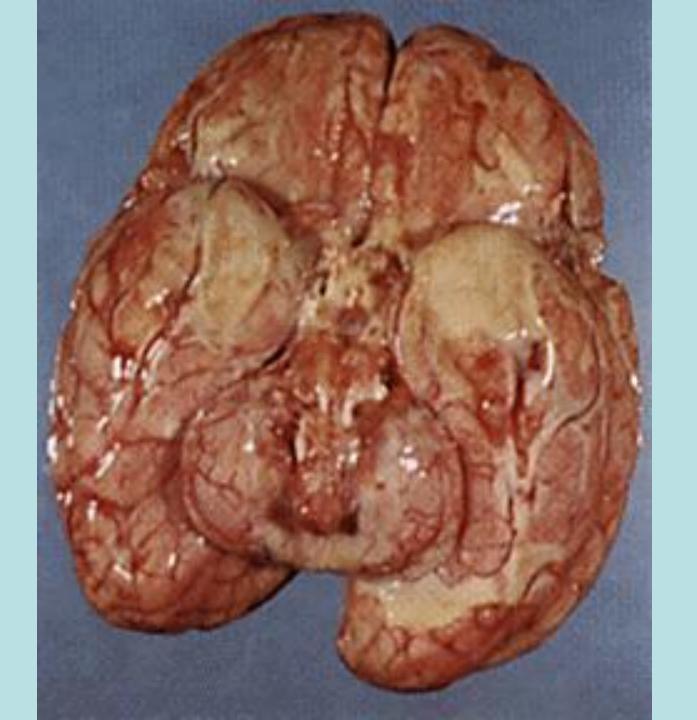
- Dementia (MID, Multi-Infarct-Dementia)
- Gait Disturbances
- Basal Ganglia symptoms

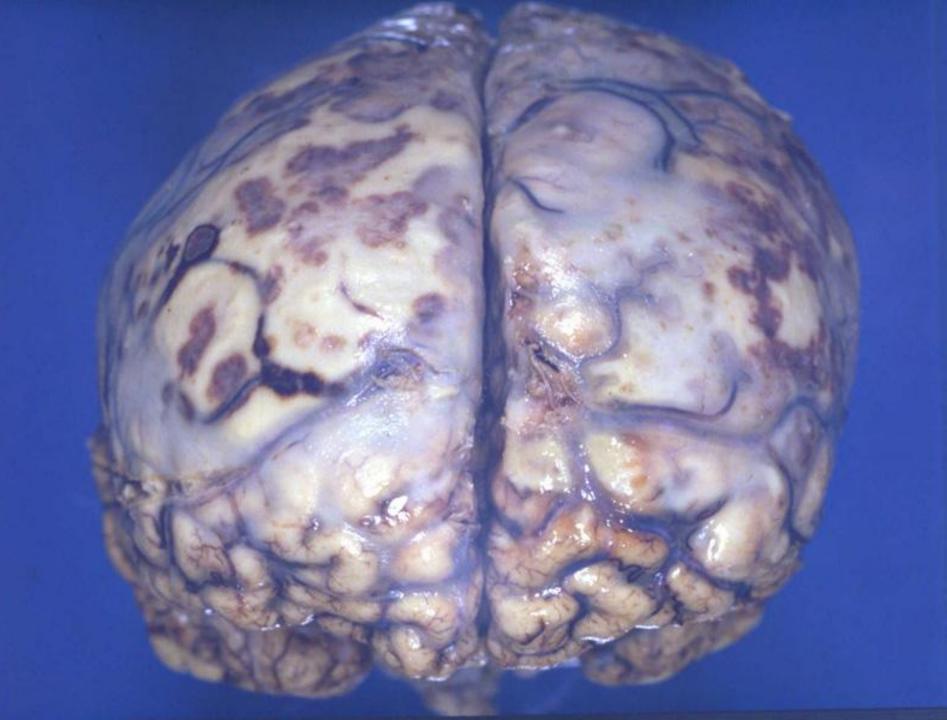
### **CNS INFECTIONS**

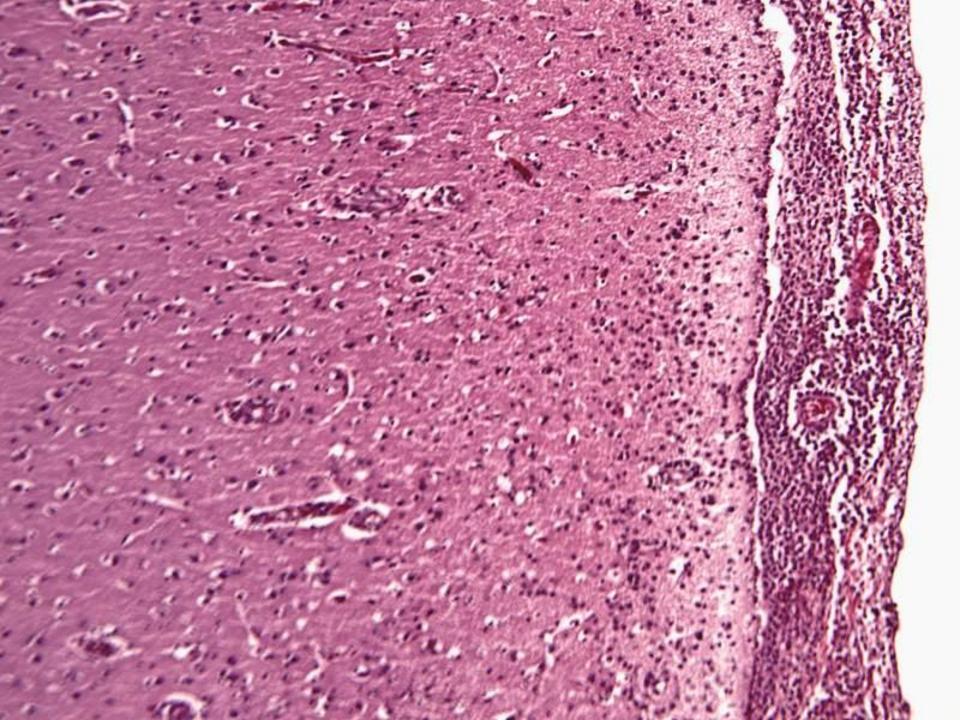
- ACUTE MENINGITIS
- ACUTE FOCAL SUPPURATIVE
- CHRONIC BACTERIAL
- VIRAL
- FUNGAL
- OTHER

### INFECTIONS

- Meningitis (generally\* bacterial)
  - E. coli, Strep B (neonates)
  - H. influenzae (children)
  - Neisseria meningitidis (adults)
  - Strep. pneumoniae, Listeria (elderly)
  - PMNs in CSF, INCREASED protein, REDUCED glucose
- Encephalitis (generally viral)
  - Arboviruses, HSV, CMV, V/Z, polio, rabies, HIV
  - Lymphs and macrophages in perivascular "Virchow-Robbins" spaces
- Meningoencephalitis



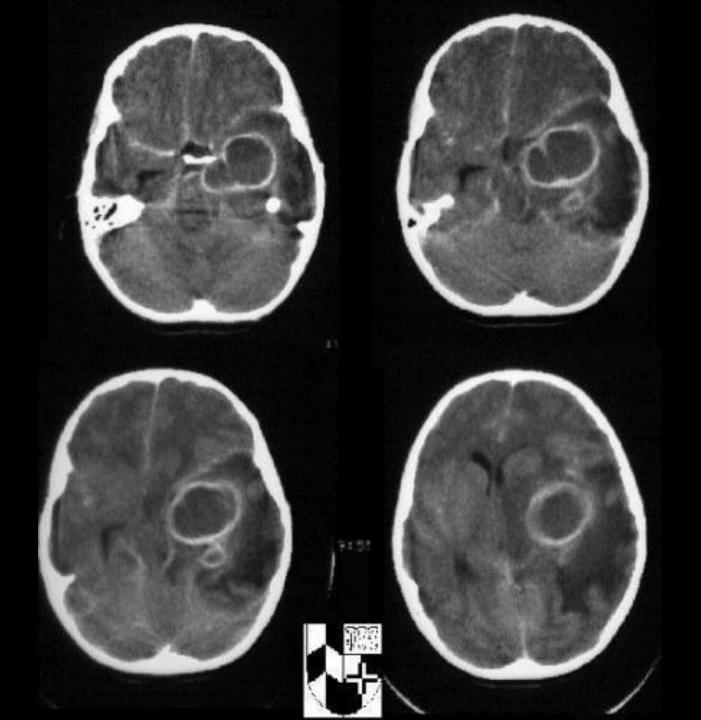


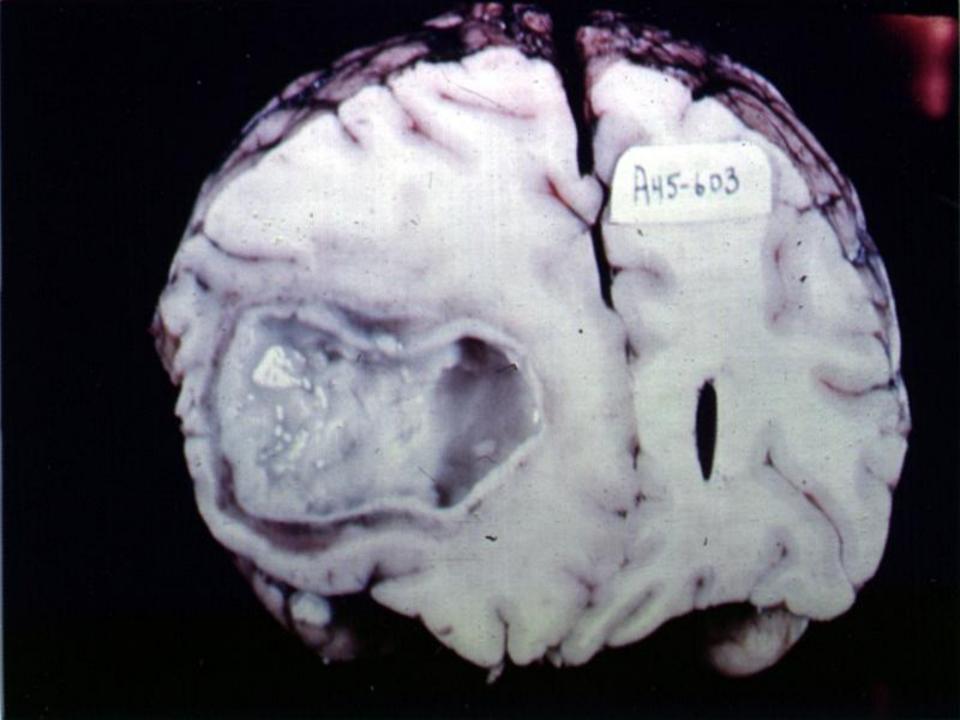


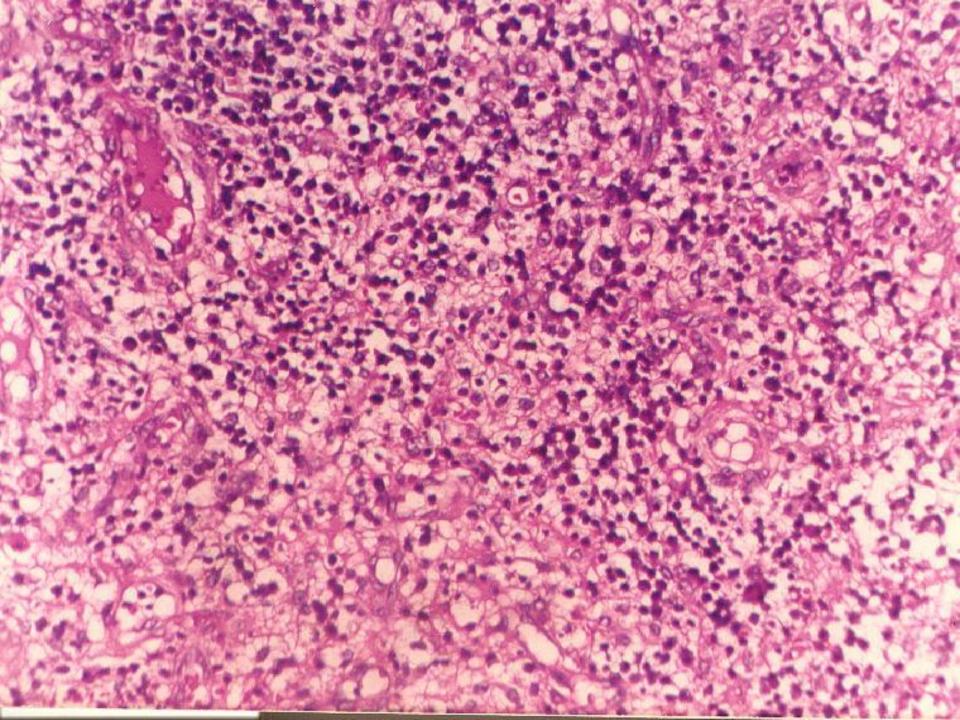
### ACUTE FOCAL SUPPURATIVE CNS INFECTIONS

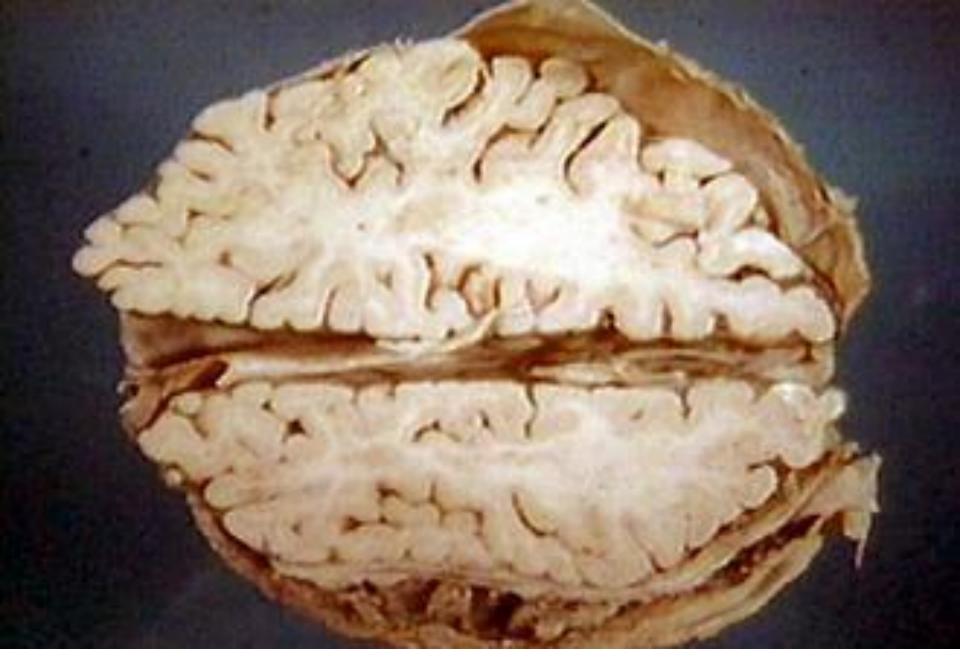
#### CEREBRAL ABSCESSES

- Local (mastoiditis, sinusitis)
- Hematogenous (tooth extraction, sepsis)
- Staph, Strep
- Often fibrous capsule, liquid center
- SUBDURAL EMPYEMA (IN SINUSITIS)
- EXTRADURAL ABSCESS (IN OSTEOMYELITIS)









**SUBDURAL EMPYEMA** 

# CHRONIC BACTERIAL Meningo-encephalits

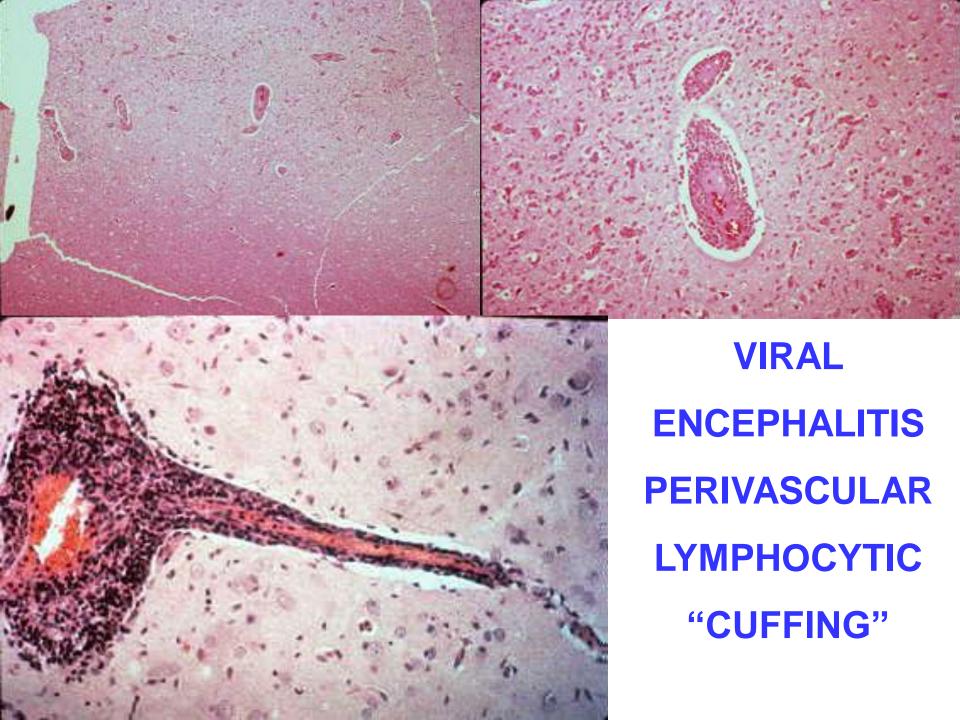
- TB, brain and meninges
- SYPHILIS, gummas in brain
- LYME DISEASE (Neuro-Borreliosis)

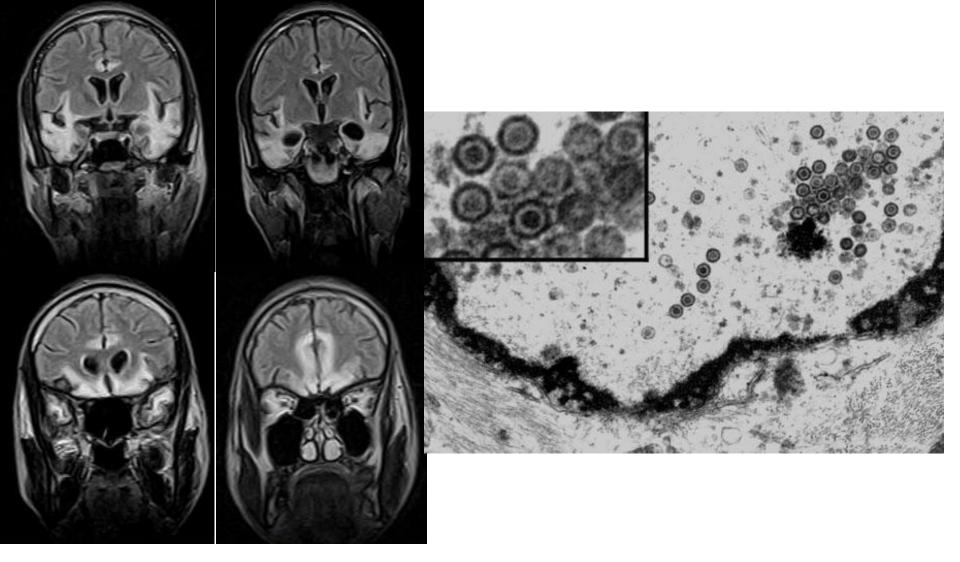


### TUBERCULOMA

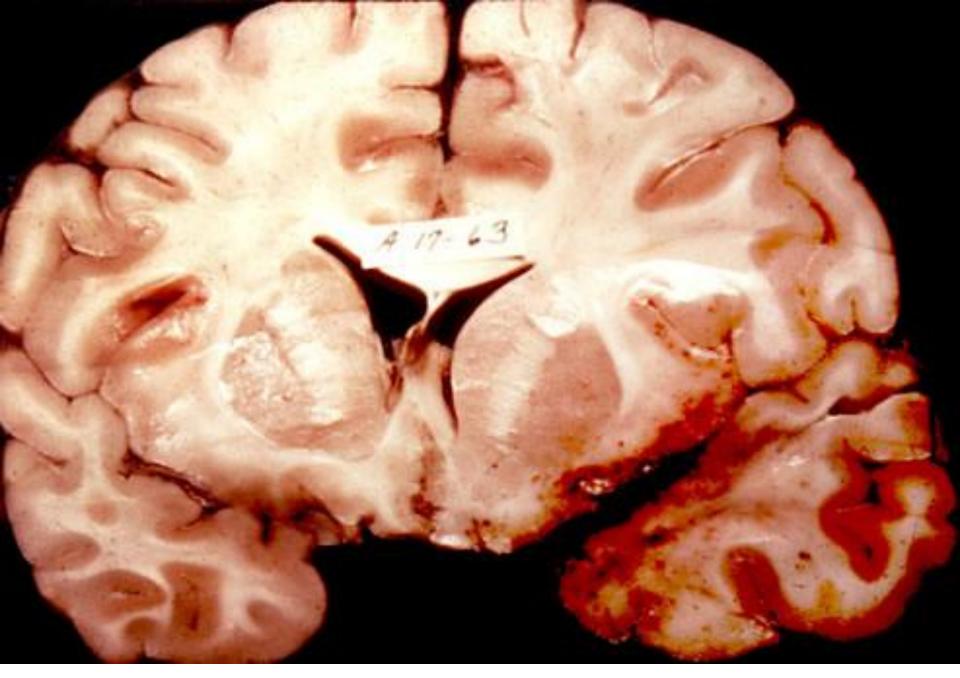
# VIRAL Meningo-encephalitis

- ARBO VIRUSES (West Nile, Equines, Venez., many more)
- HSV1
- HSV2
- V/Z
- CMV
- POLIO
- RABIES
- HIV
- Progressive Multifocal Leukoencephalopathy (JC)
- Subacute Sclerosing Panencephalitis (Measles)

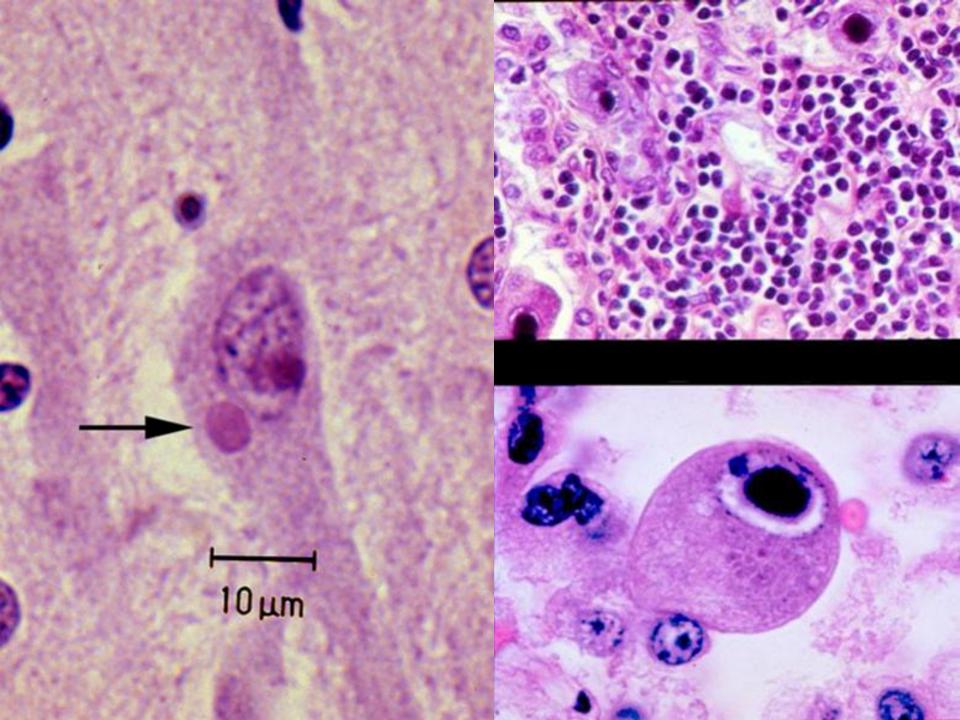


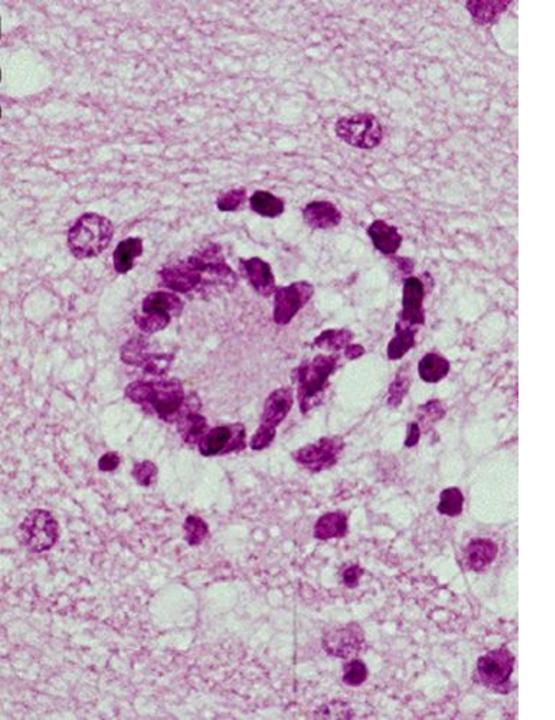


Bitemporal encephalitis is HSV until proven otherwise!



**HSV = TEMPORAL lobe(s)** 





**PERIVASCULAR GIANT CELLS** in WHITE **MATTER** in HIV

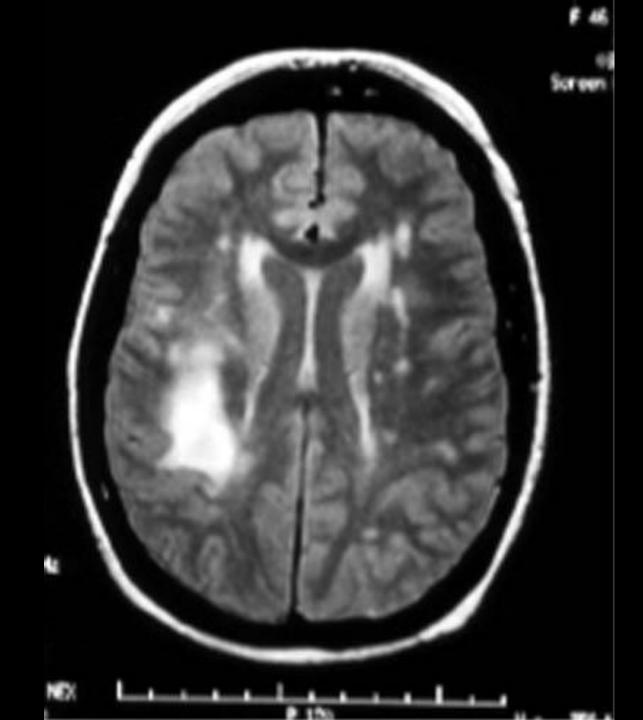
**ENCEPHALITIS** 

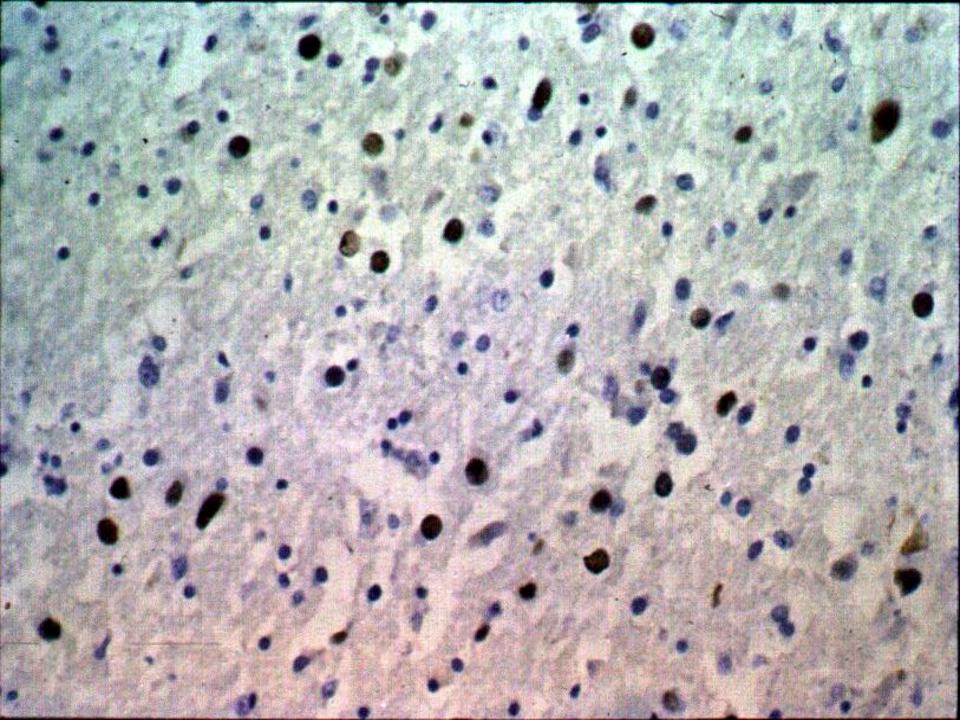
### PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML)

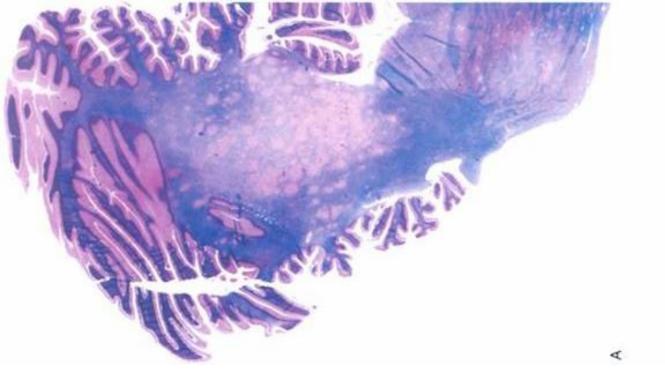
JC Polyoma virus is the cause

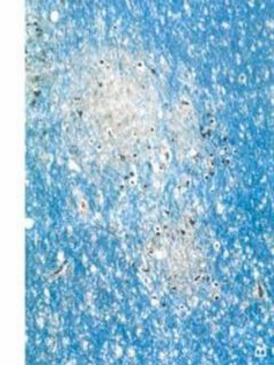
Primarilly affects oligodendocytes

Ergo, demyelination is the main feature









# 

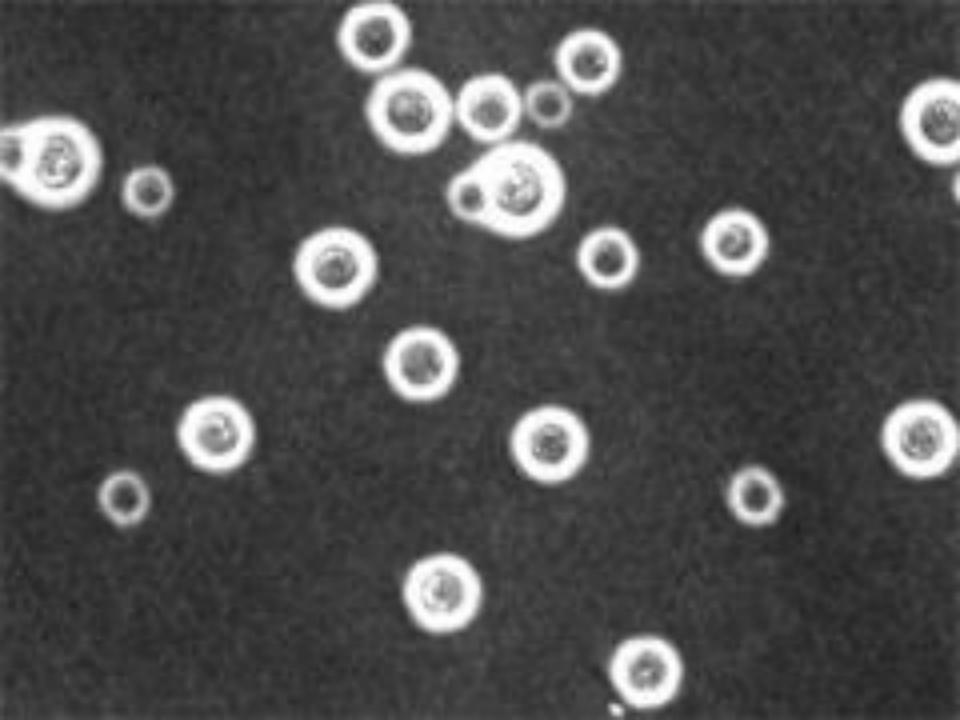
## SUBACUTE SCLEROSING PANENCEPHALITIS (SSPE)

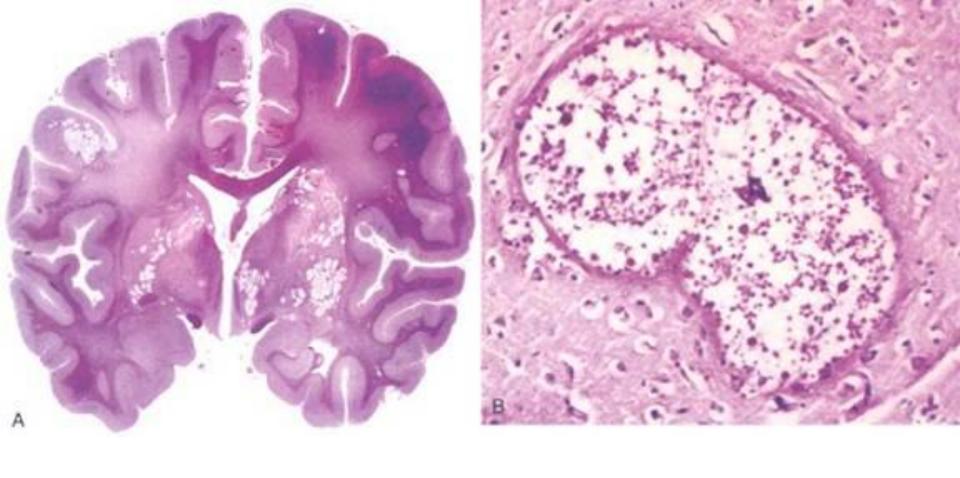
- VERY rare since measles eradicated
- Thought to be caused by measles virus

# FUNGAL MENINGO-ENCEPHALITIS • CRYPTOCOCCUS

- CANDIDA
- ASPERGILLIS
- MUCOR

(Mostly in immunocompromised hosts)

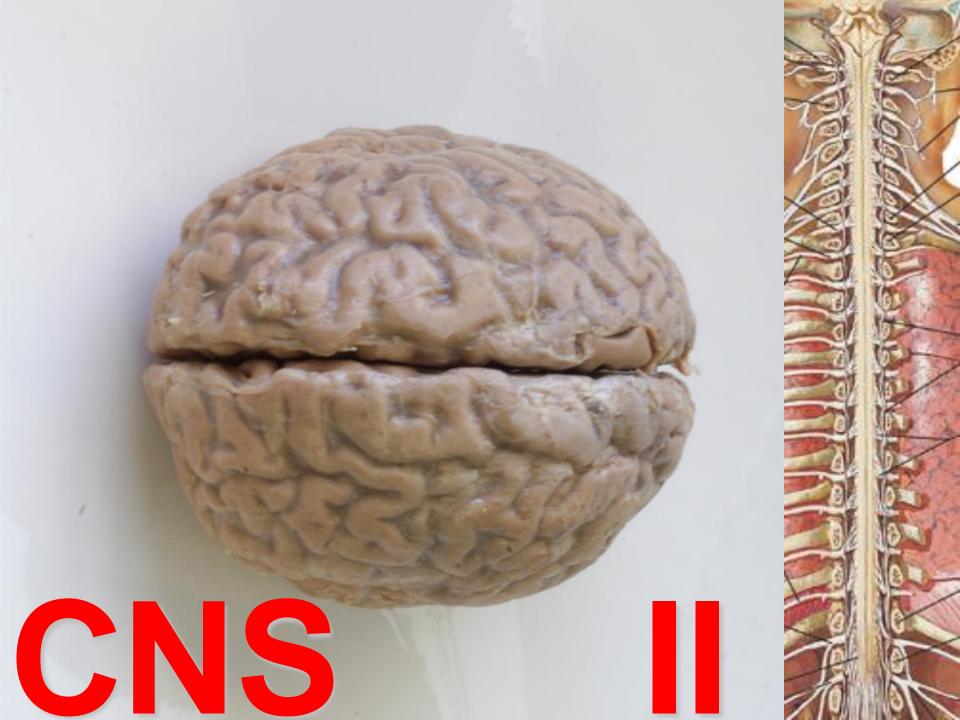




### CRYPTOCOCCUS MICROABSCESSES

### OTHERS

- MALARIA
- TOXOPLASMOSIS (in HIV)
- AMEBIASIS
- TRYPANOSOMES
- RICKETTSIAE
- ECHINOCOCCUS



- 1) What are general patterns of CNS cell pathology?
- 2) What are the consequences of ↓↑ CSF pressure?
- 3) What are common patterns of CNS malformations?
- 4) What are common perinatal CNS injuries?
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- 13) What are the CNS tumors?

### PRION DISEASES

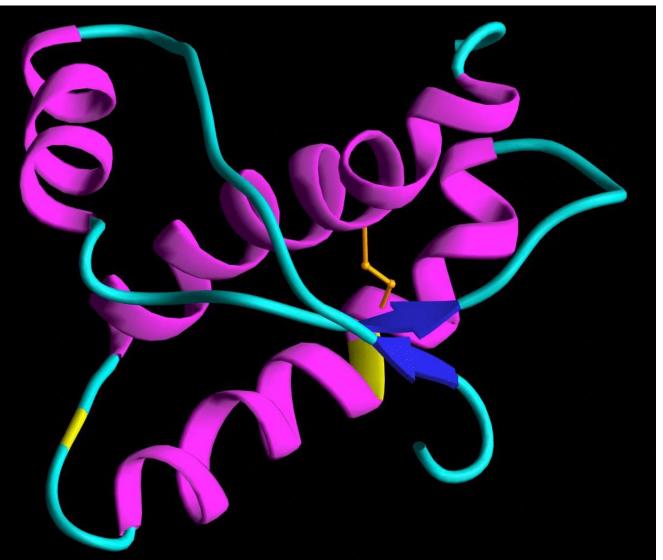
- Creutzfeldt-Jakob Disease (CJD)
- Gerstmann-Straussler-Scheinker syn. (GSS)
- Fatal familial insomnia
- Kuru, human variety
- Scrapie (sheep and goats)
- Mink transmissible encephalopathy
- Chronic wasting disease (deer and elk)
- Bovine Spongiform Encephalopathy (BSE)

### PRION DISEASES:

#### common features

- Infectious agents with apparently no DNA
- DEMENTIA
- Prion Protein (PrP) accumulation
- "SPONGIFORM" changes in neurons and glia
- TRANSMISSIBLE, FATAL, NO Rx

### PRION PROTEIN

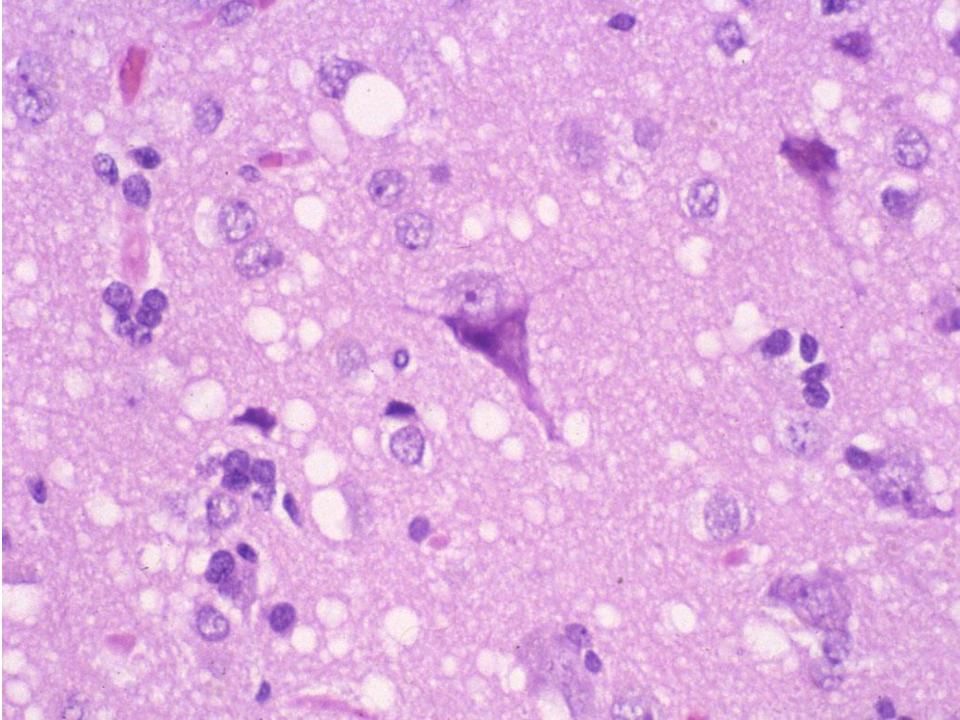


Normally found in humans

Exact structure known, 208 amino acids

Specific chromosome, #20, specific genes also known

Requires a conformational change to accumulate and do damage



#### CJD (Creutzfeldt-Jakob)

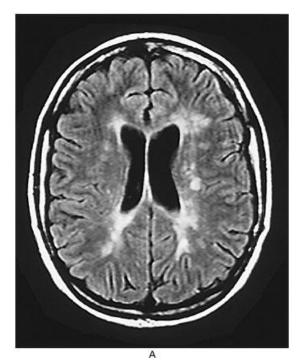
- 1 per million incidence, 7th decade
- Sporadic cases, NOt epidemic
- Transmitted!
- Familial cases well documented
- Rapidly progressive dementia
- Grey Matter
- Cerebellar ataxia also, usually
- FATAL, no treatment known, like ALL prion diseases

# DEMYELINATING DISEASES • MS (MULTIPLE SCLEROSIS)

- MS variants
- ACUTE DISSEMINATED ENCEPHALOMYELITIS (ADEM)
- ACUTE NECROTIZING HEMORRHAGIC ENCEPHALOMYELITIS (ANHE)
- Many, many, many others. Remember:
   DEMYELINATION is a NON-SPECIFIC
   reaction to MANY types of CNS injury, and demyelination also causes edema



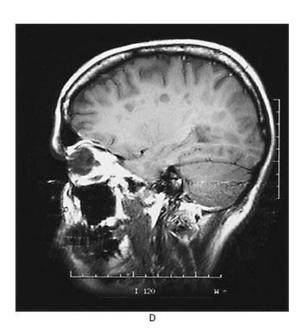
- · Cause: ?
- USA prevalence: 1:1000
- F>>M, Ages: 30's, 40's
- Immune response primarily against CNS myelin (white matter)
- Regional area of white matter demyelination is called "PLAQUE"
- Increased CSF gamma globulin, i.e., oligoclonal bands
- Often presents with VISUAL problems
- EXACERBATIONS/REMISSIONS

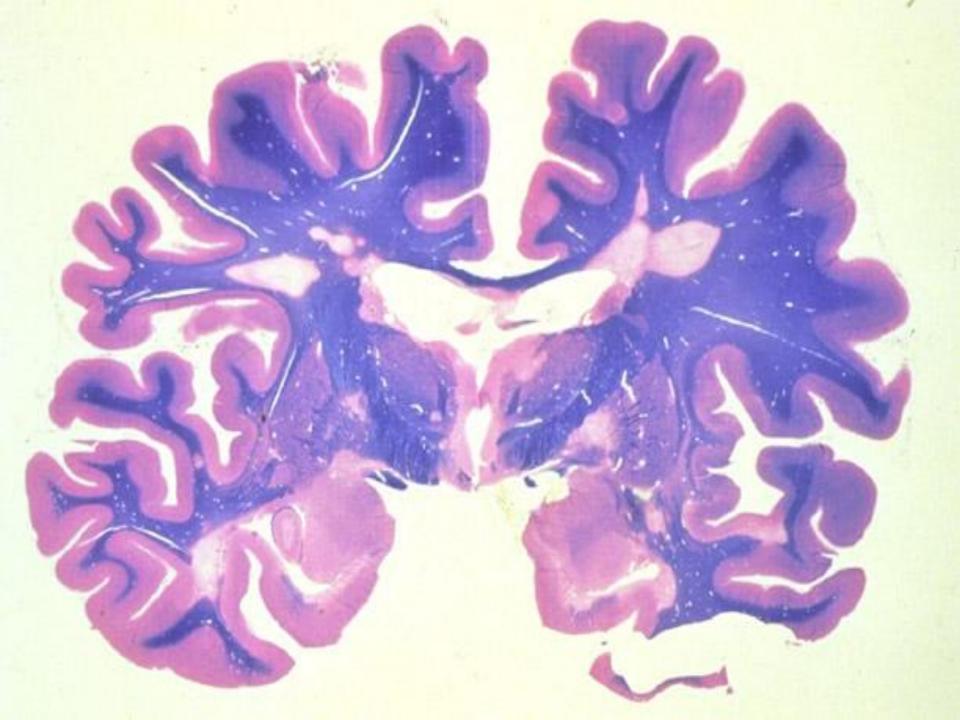




В

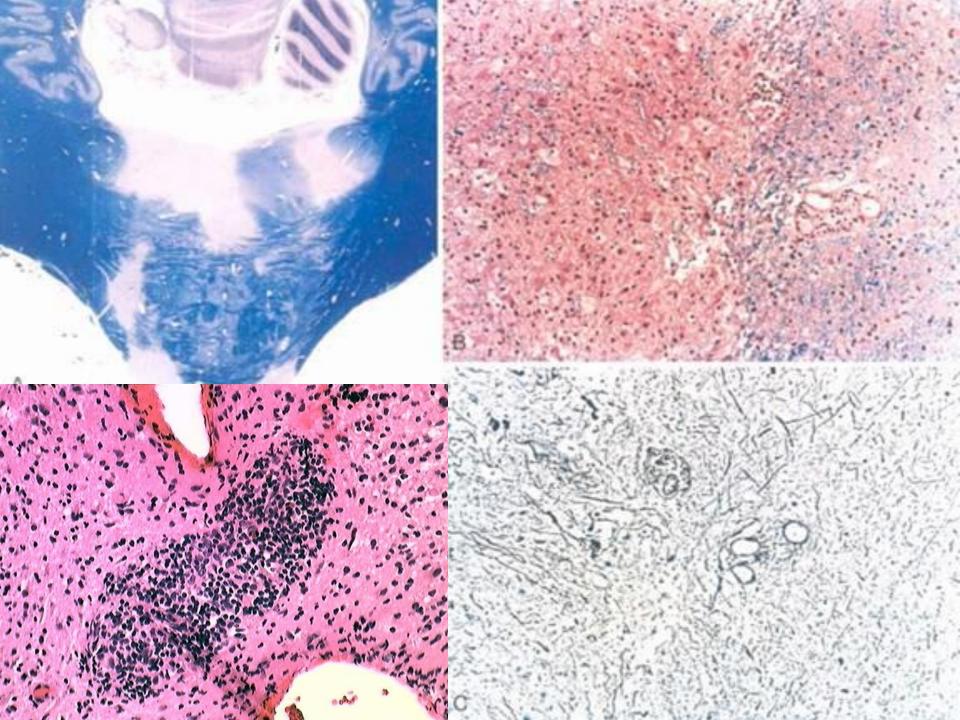








## PLAQUES, MS



- CORTEX (dementias)
- BASAL GANGLIA and BRAIN STEM (parkinsonian)
- SPINOCEREBELLAR (ataxias)
- MOTOR NEURONS (muscle atrophy)

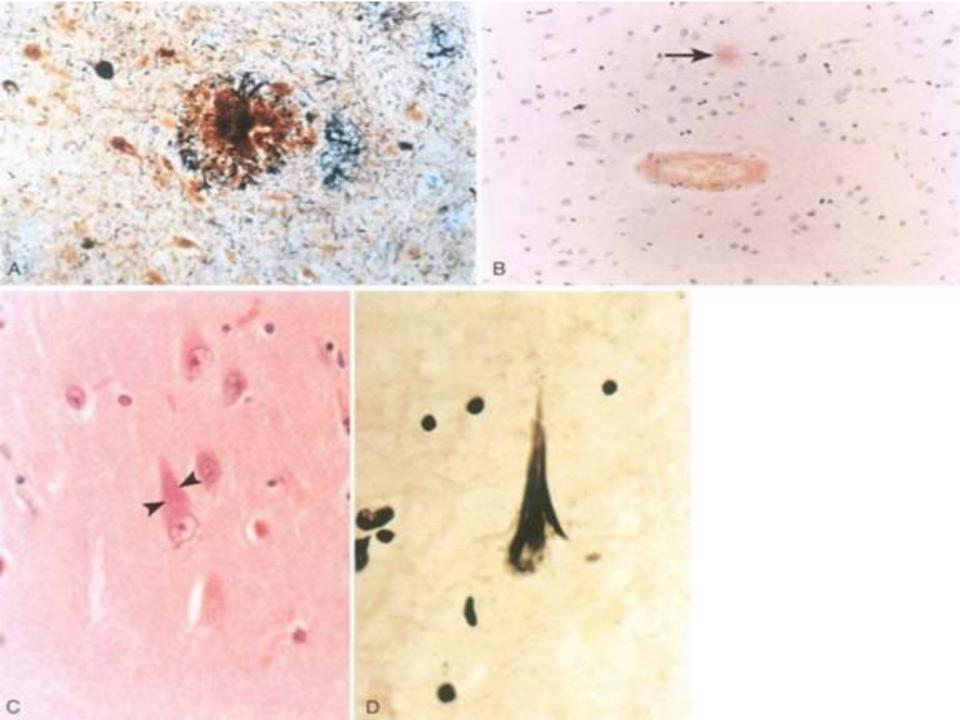
- CORTEX (dementias)
  - -ALZHEIMER DISEASE
  - Frontotemporal
  - -Pick Disease (also primarily frontal)
  - -Progressive Supranuclear Palsy (PSP)
  - -CorticoBasal Degeneration (CBD)
  - -Vascular Dementias (MID)

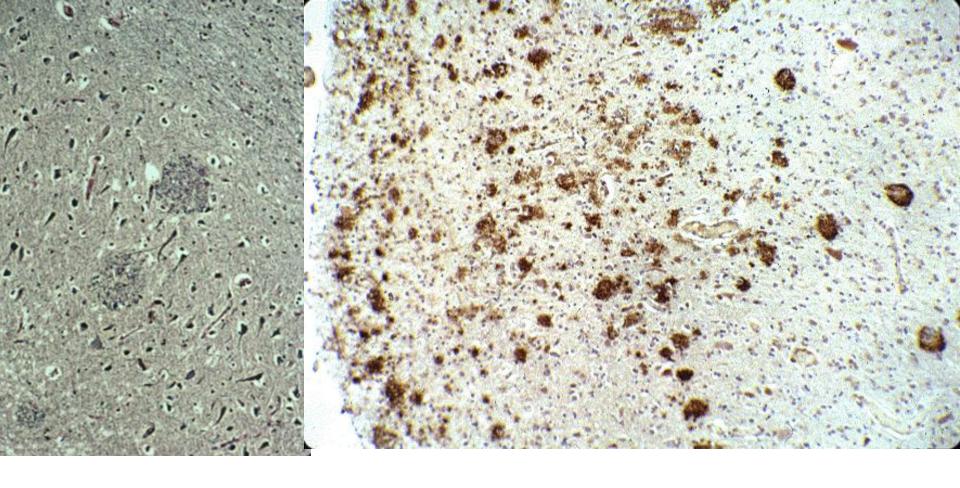
## **ALZHEIMER DISEASE**

- Commonest cause of dementias (majority)
- Sporadic, 5-10% familial
- CORTICAL (grey matter) ATROPHY
- NEURITIC PLAQUES (extraneuronal)
- NEUROFIBRILLARY TANGLES (intraneuronal)
- AMYLOID!!!



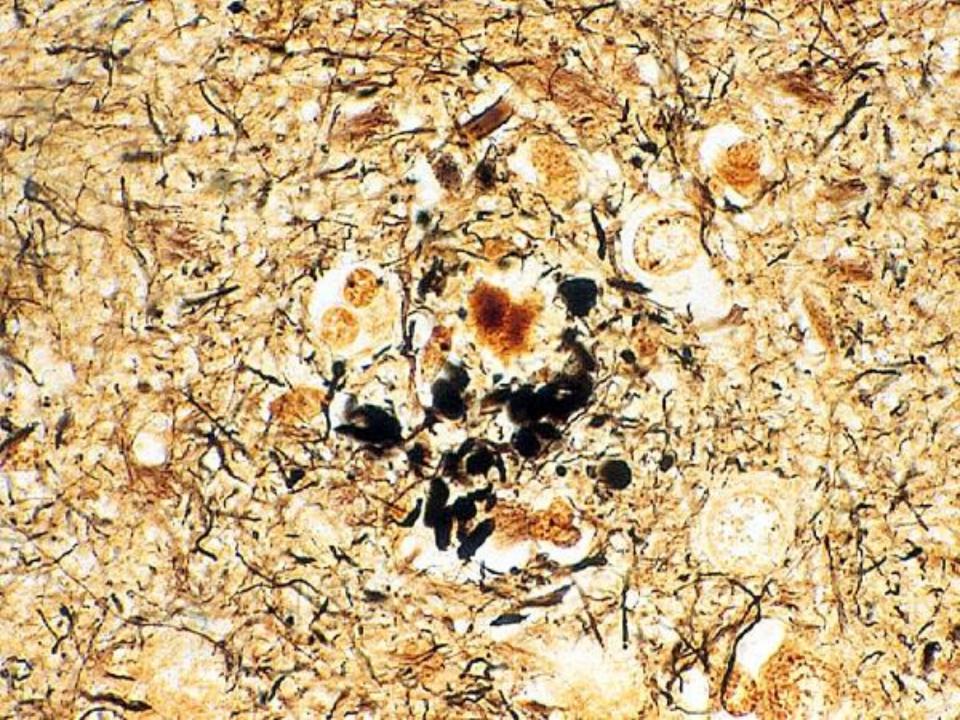


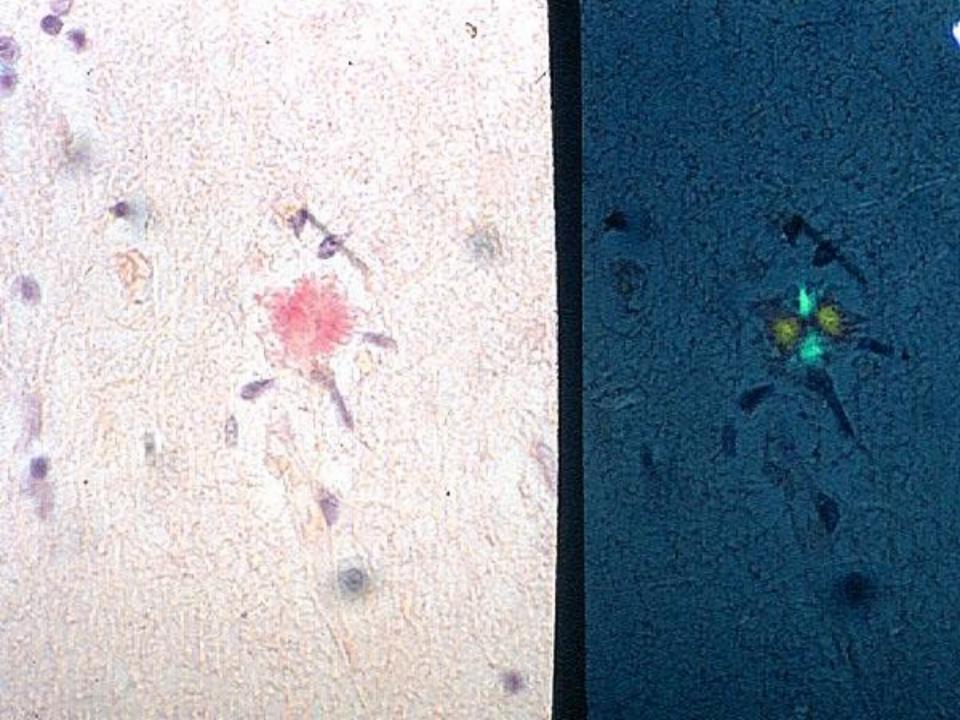


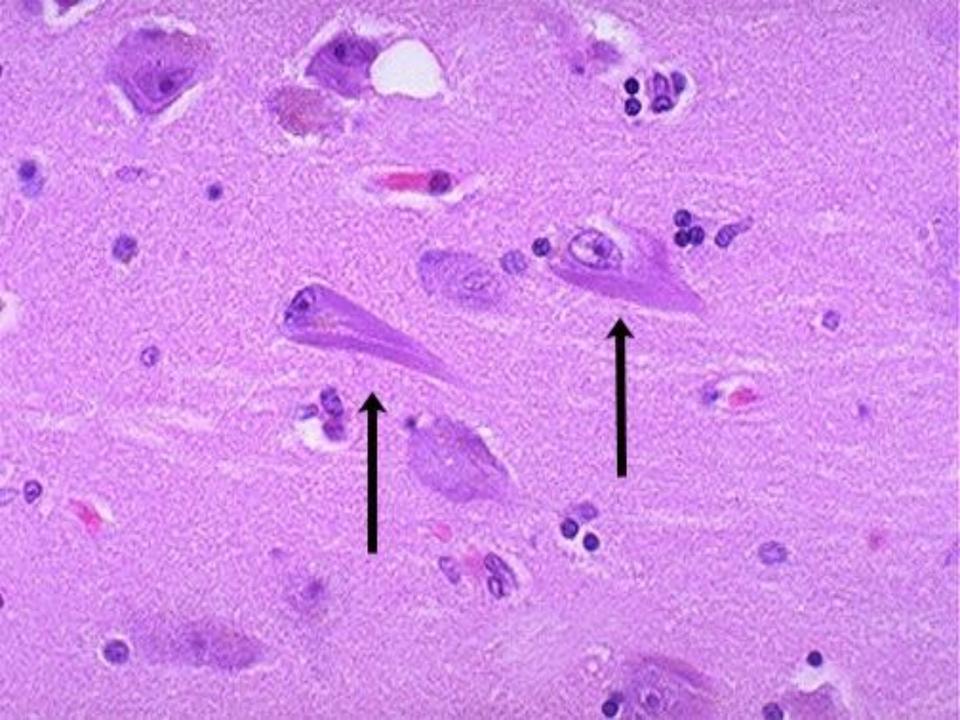


**Neuritic plaques** 

Neuritic plaques, stained with anti- beta amyloid immunostain









Tangle
Nucleus

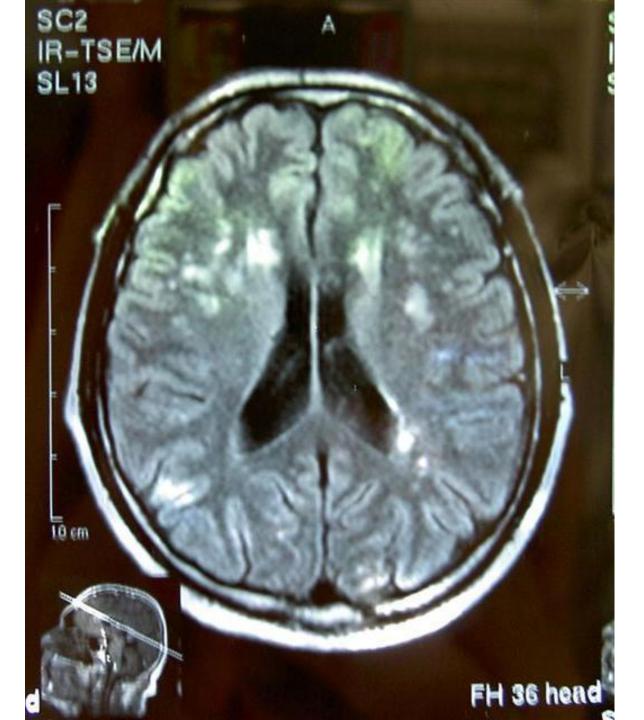
## OTHER CORTICAL DEMENTIAS (tau gene/protein, tau-opathies)

- FRONTOTEMPORAL
- PICK DISEASE (LOBAR ATROPHY)
- PROGRESSIVE SUPRANUCLEAR PALSY (PSP)
- CORTICOBASAL DEGENERATION (CBD)

VASCULAR DEMENTIA (MID)

## VASCULAR DEMENTIA

- Associated with multiple infarcts, hence the name MID (Multiple Infarct Dementia)
  - Lacunar infarcts
  - -Cortical microinfarcts
  - Multiple embolic infarcts
- SECOND commonest form of dementia after Alzheimer



 BASAL GANGLIA and BRAIN STEM

## -Parkinsonism

- -Parkinson Disease
- -Multiple System Atrophy
- -Huntington Disease

#### **Parkinsonism**

- Is a clinical "syndrome", NOT a disease
  - Diminished facial expression
  - Stooped posture
  - Slowness of voluntary movement
  - "Festinating" gate (short, fast)
  - Rigidity (cogwheel)
  - "Pillrolling" tremor
- The above clinical findings involve pathology of the SUBSTANTIA NIGRA, and include:
  - -PARKINSON DISEASE
  - MULTIPLE SYSTEM ATROPHY
  - POSTENCEPHALIC PARKINSONISM
  - Progr. Supranuc. Palsy, Cort. Basal Degen. (cortical disorders)

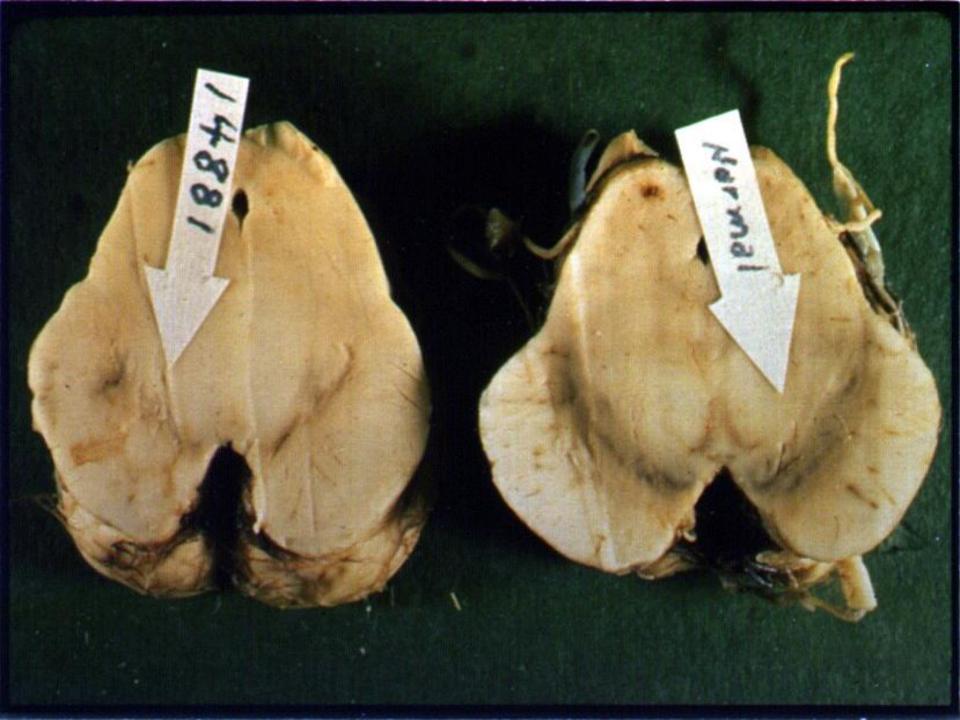
## PARKINSON DISEASE

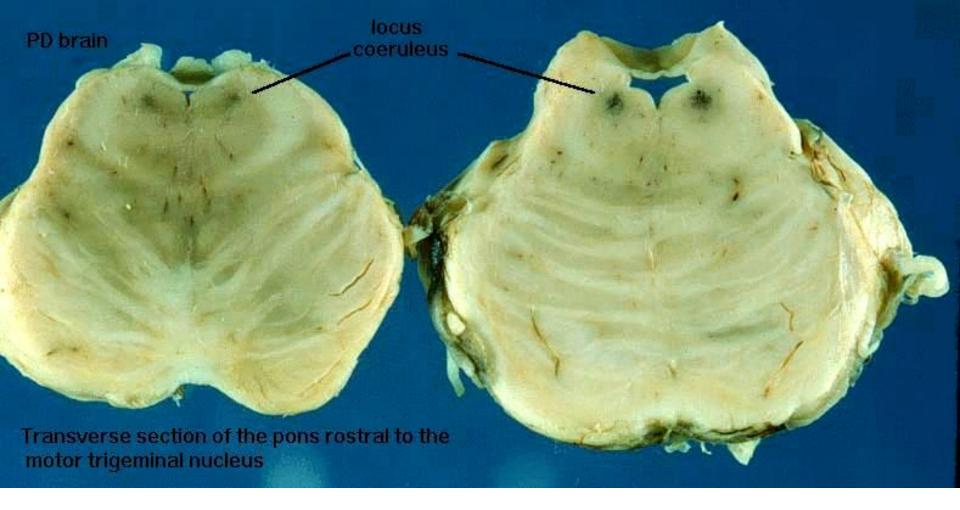
 PALLOR of the SUBSTANTIA NIGRA

(and LOCUS COERULEUS)

LEWY BODIES (alpha-synuclein protein)



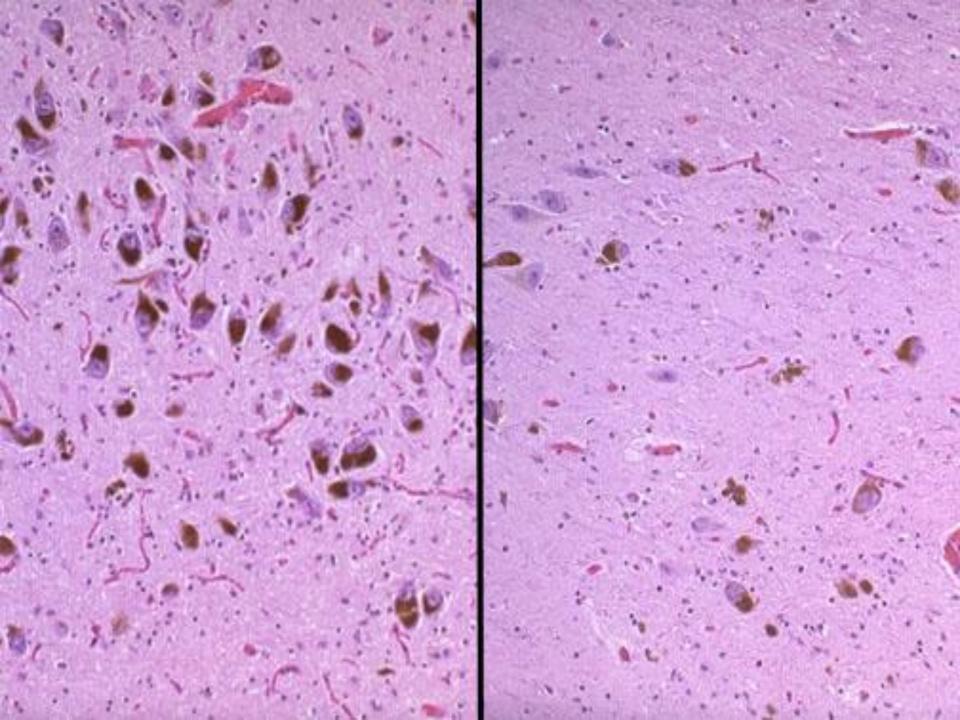


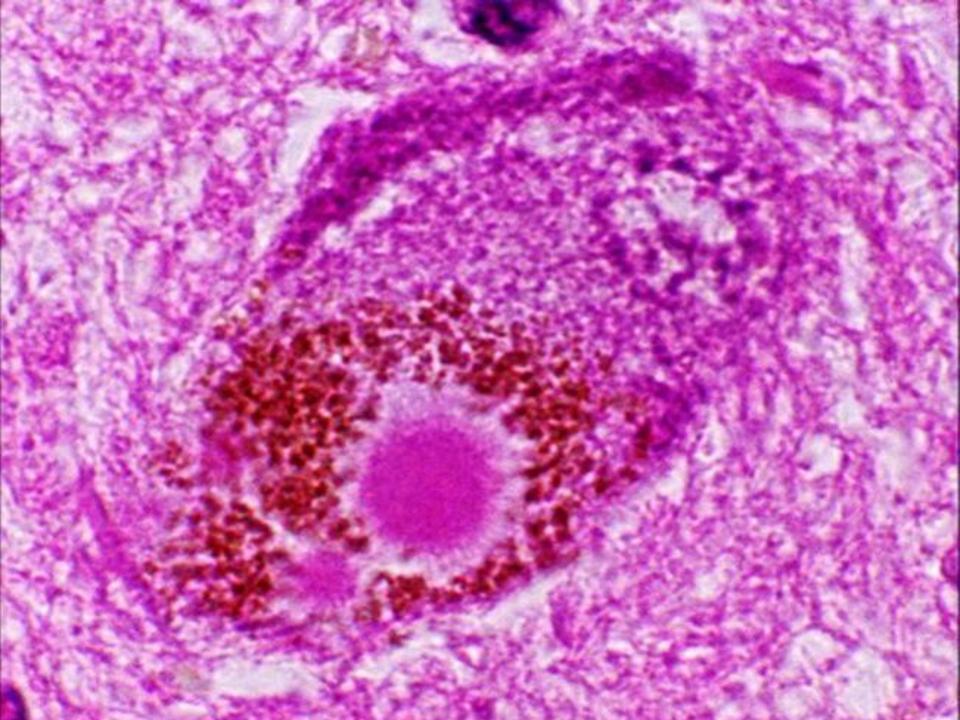


### **LOCUS COERULEUS\* in PONS**

(CERULEUS\*\*)

\* **254,000** \*\* **76,000** 



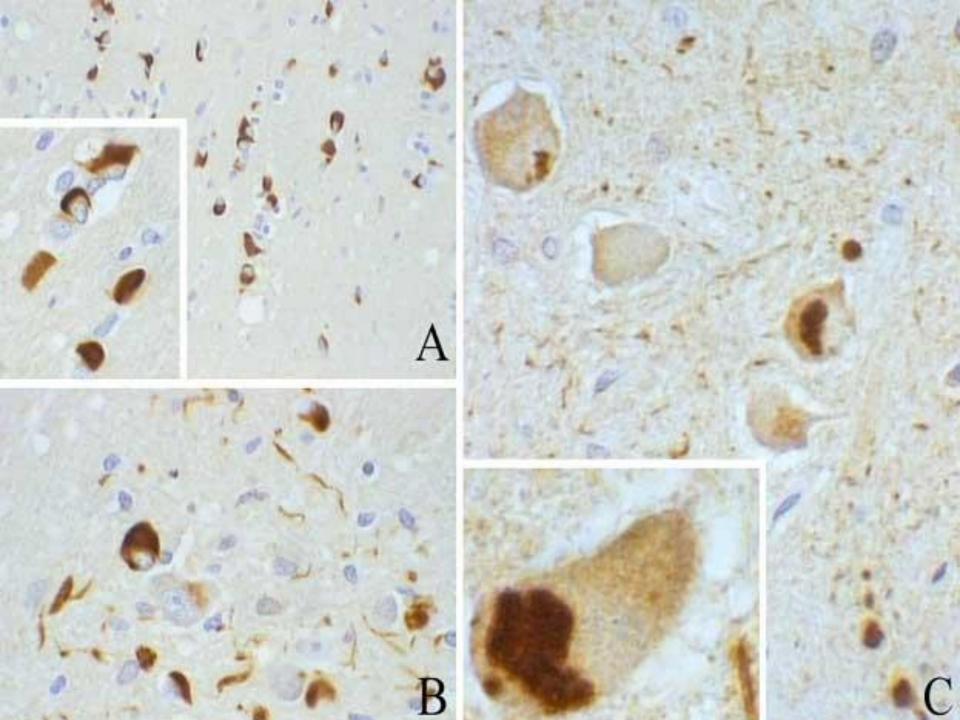


## PARKINSON DISEASE

- Parkinsonism symptoms, i.e.,
  - cogwheel rigidity
  - intention tremor
- Progressive
- Hallucinations
- Dementia
- Symptomatic response to L-DOPA

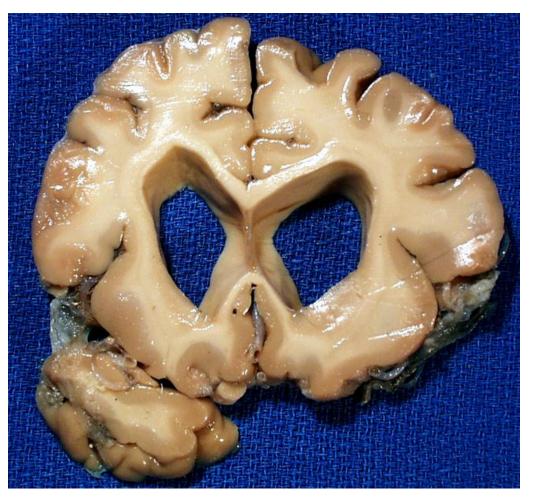
#### **MULTIPLE SYSTEM ATROPHY**

- MSA
- WIDE SPECTRUM of diseases
- GLIAL CYTOPLASMIC INCLUSIONS (GCIs) in oligodendrocytes (alpha synuclein)
- Clinically,
  - parkinsonism symptoms
  - autonomic dysfunction



## **HUNTINGTON DISEASE**

- Classical familial, genetic disease
- Progressive motor loss and dementia
- "chorea", i.e."jerky" movements
- Progressive, fatal
- Atrophy of basal ganglia, i.e., corpus striatum



**Cortical (basal ganglia) atrophy** 

Ventricular enlargement

- SPINOCEREBELLAR
   DEGENERATIONS (ATAXIAS)
  - -Spinocerebellar ataxias
  - -Friedrich Ataxia
  - -Ataxia-Telangiectasia

#### SPINOCEREBELLAR DEGENERATIONS

- Cerebellar cortex
- Spinal cord
- Peripheral nerves
- FEATURES:
  - -ATAXIA (loss of extremity muscle coordination)
  - SPASTICITY
  - **NEUROPATHIES**

#### MOTOR NEURONS

- -ALS (Amyotrophic Lateral Sclerosis, i.e., Lou Gehrig's disease)
- BulboSpinal Atrophy (Kennedy Syndrome)
- -Spinal Muscular Atrophy

#### **Amyotrophic Lateral Sclerosis**

- Unknown etiology
- Progressive muscle atrophy due to motor neuron loss (lower, upper)
- 5-10% familial
- Lou Gehrig had it, so does Steven Hawking
- Hand weakness 

  diaphragm
- Anterior horn cells reduced and gliotic

### A BRIEF HISTORY OF TIME

From the Big Bang to Black Holes

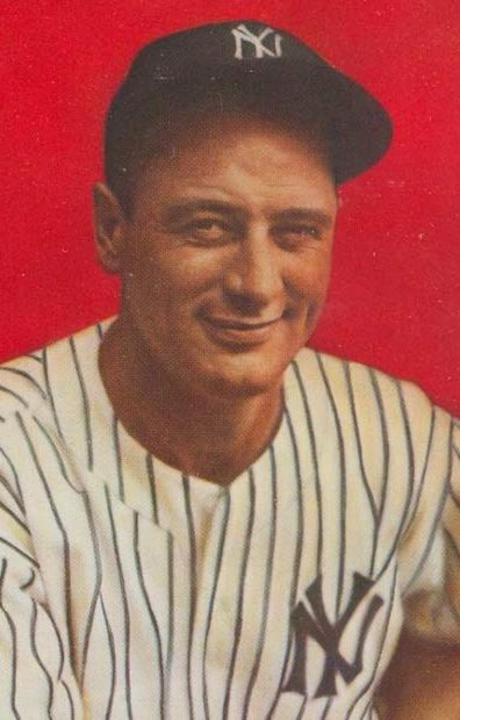
'This book marries a child's wonder to a genius's intellect. We journey into Hawking's universe, while marvelling at his mind'

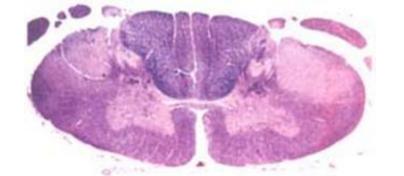
Sunday Times

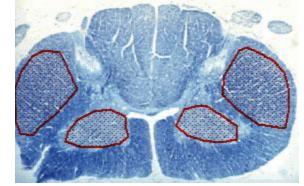


Introduction by Carl Sagan

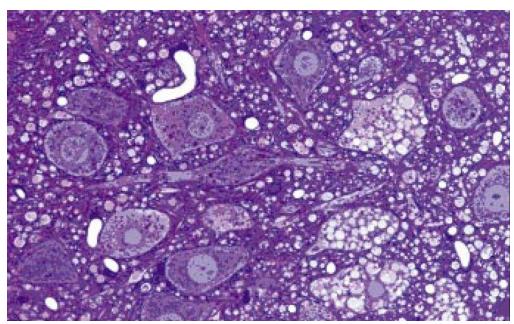
#### STEPHEN HAWKING







# A.L.S., DEMYELINATION IN CORTICOSPINAL TRACTS



ALS, pathologic changes in anterior horn cells

#### **GENETIC METABOLIC DISEASES**

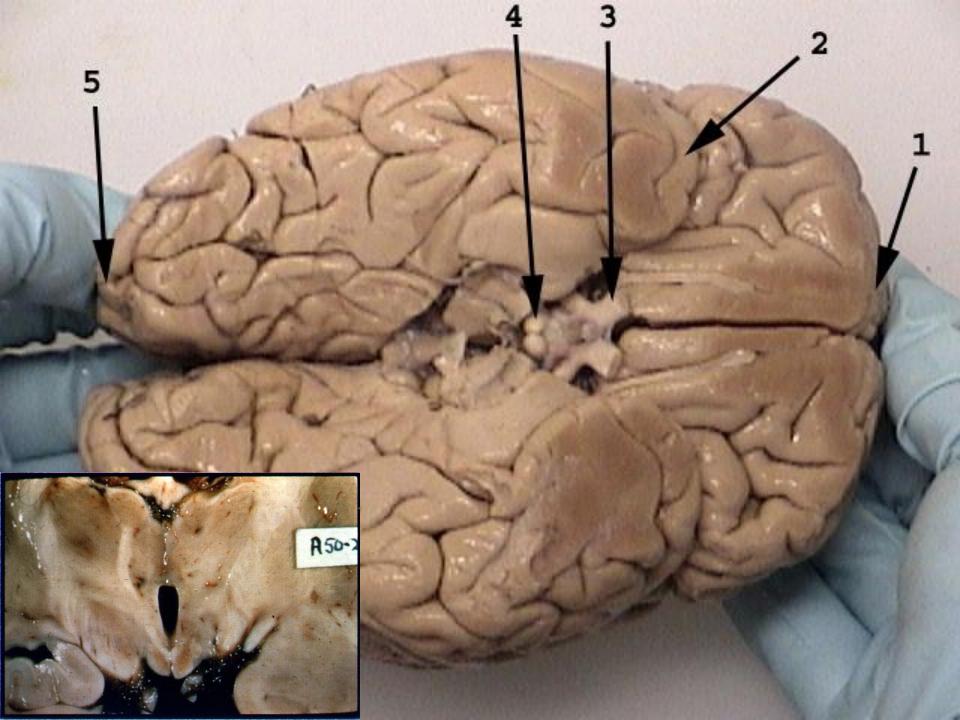
- NEURONAL STORAGE DISEASES
  - (classical autosomal recessive enzyme deficiencies)
- "LEUKO"-DYSTROPHIES
  - (abnormal "myelin" synthesis)
- MITOCHONDRIAL ENCEPHALOPATHIES
  - (mitochondrial gene mutations)

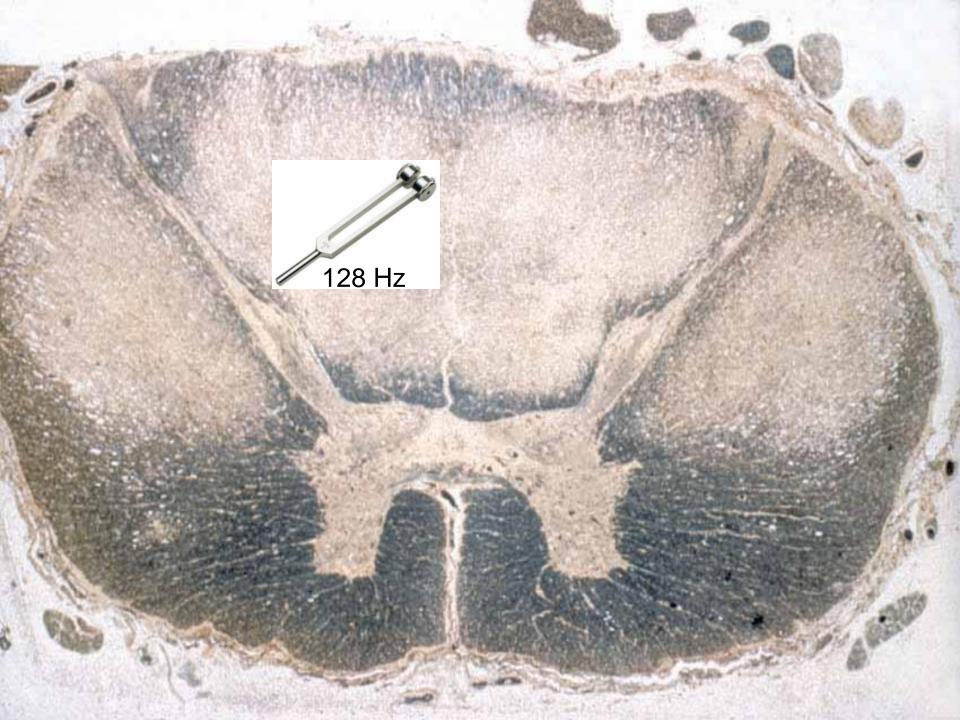
#### **LEUKODYSTROPHIES**

- Krabbe
- Metachromatic-
- Adreno-
- Pelizaeus-Merzbacher
- Canavan

# ACQUIRED TOXIC/METABOLIC CNS DISEASES

- Vitamin B1 deficiency (Wernicke-Korsakoff)
- Vitamin B12 deficiency (vibratory sense)
- Diabetes Increased/Decreased GLUCOSE
- Hepatic Failure (NH4+)
- CO (Cortex, hippocampus, Purkinje cells)
- CH3-OH, Methanol (Retinal ganglion cells)
- CH3-CH2-OH (acute/chronic, direct/nutrit'l)
- Radiation (Brain MOST resistant to Rad. Rx.)
- Chemo (Methotrexate + Radiation)





- GLIOMAS (do not metastasize out of the CNS)
  - Astrocytes (I, II, III, IV)
  - Oligodendroglioma
  - Ependymoma
- NEURONAL (neuroblastoma)
- POORLY DIFFERENTIATED (medulloblastoma)
- MENINGIOMAS
- LYMPHOMAS
- METASTATIC

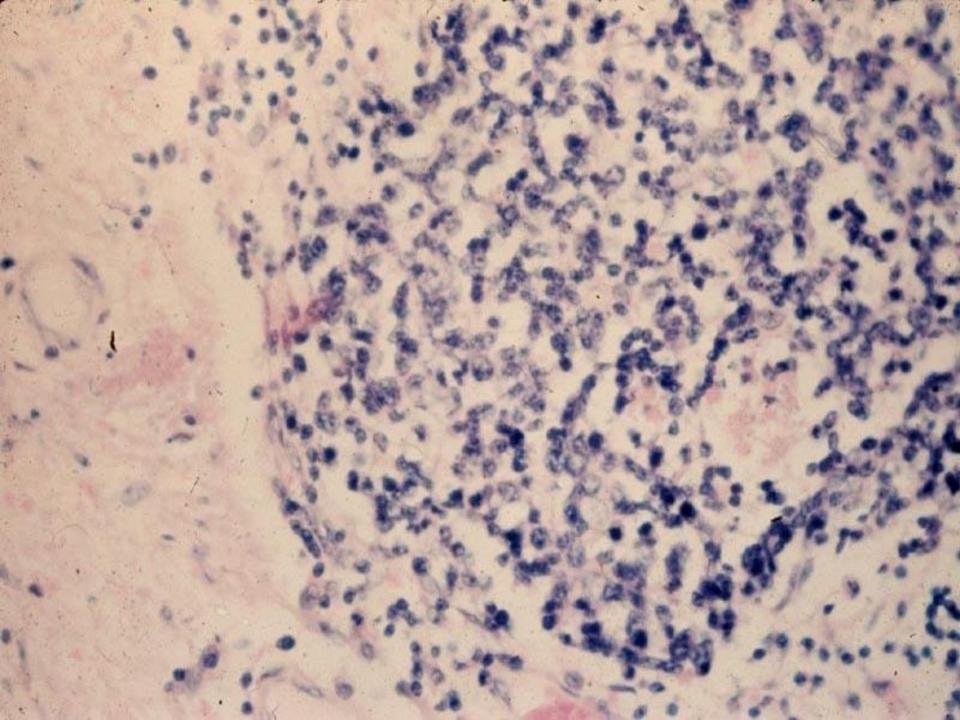
- SYMPTOMS?
  - -Headache
  - Vomiting
  - Mental Changes
  - Motor Problems
  - -Seizures
  - -Increased Intracranial Pressure
  - -ANY localizing CNS abnormality

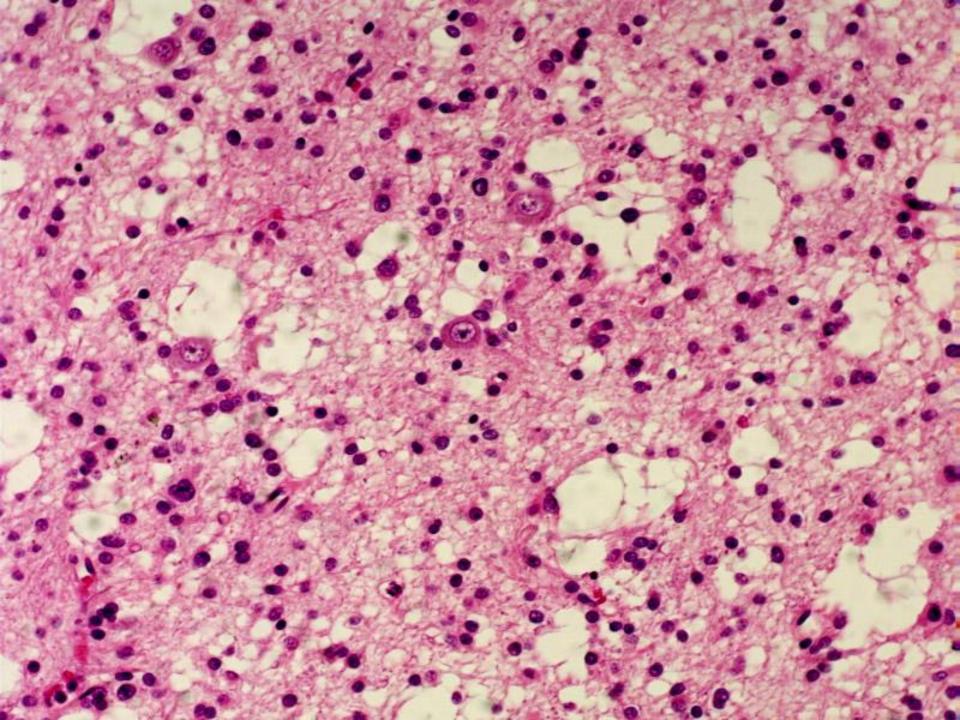
- History
- Physical
- Neurologic exam
- LP (including cytology)
- CT
- MRI
- Brain angiography
- Biopsy

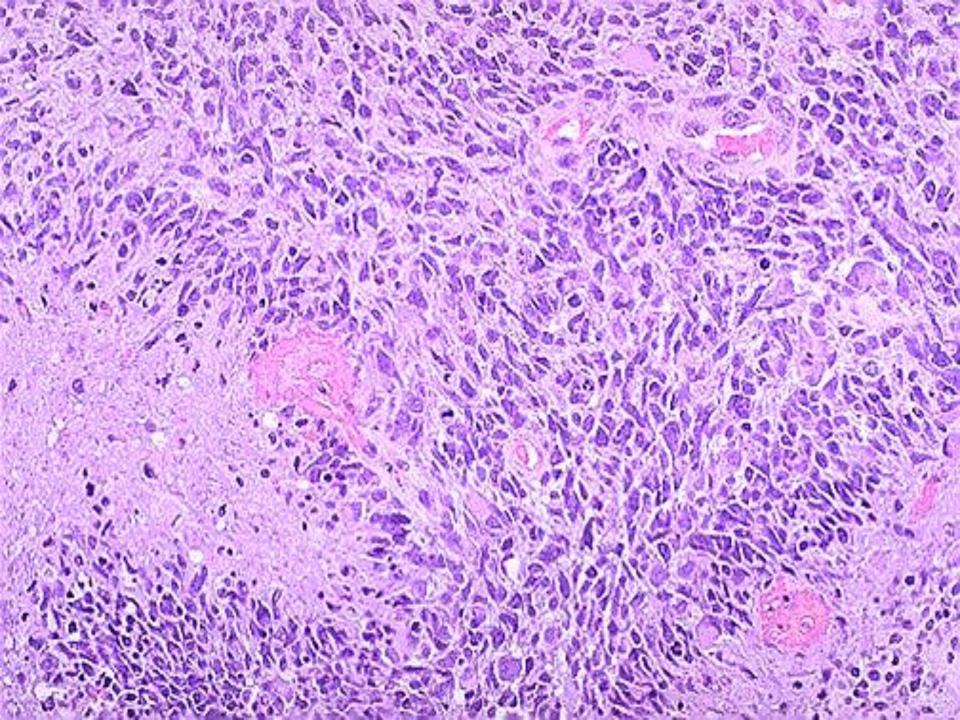
- Benign? Malignant?, Primary vs. met?
- Location?
- Age?
- X-ray Density? MRI signals?
- Calcifications?
- Vascularity?
- Necrosis?
- Liquefaction?
- Edema?
- Compression of neighbors?

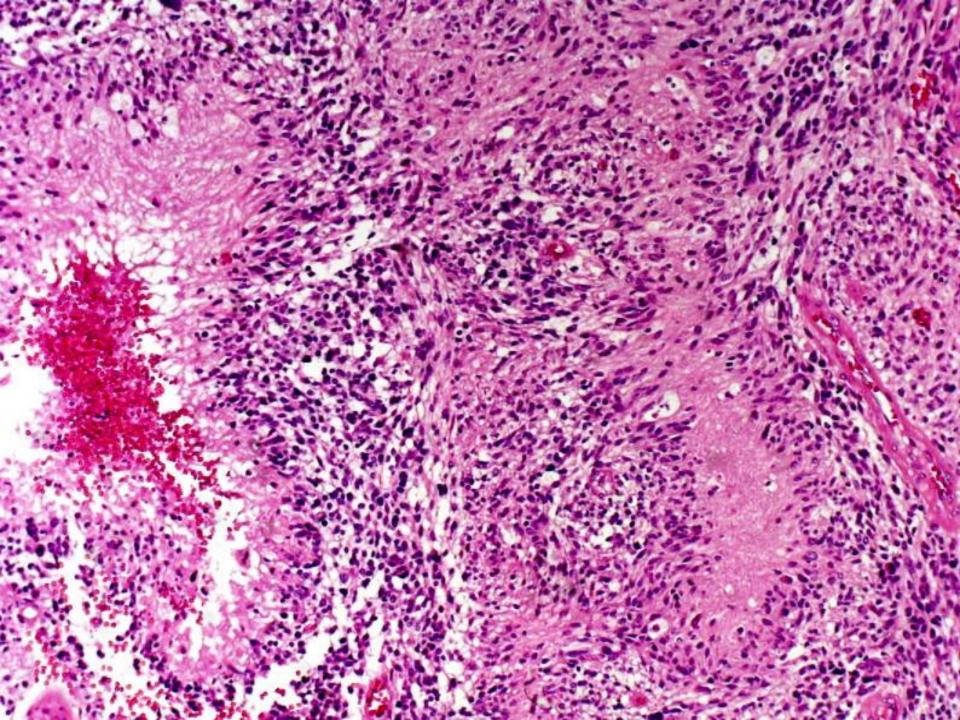
### GLIOSIS vs. GLIOMA

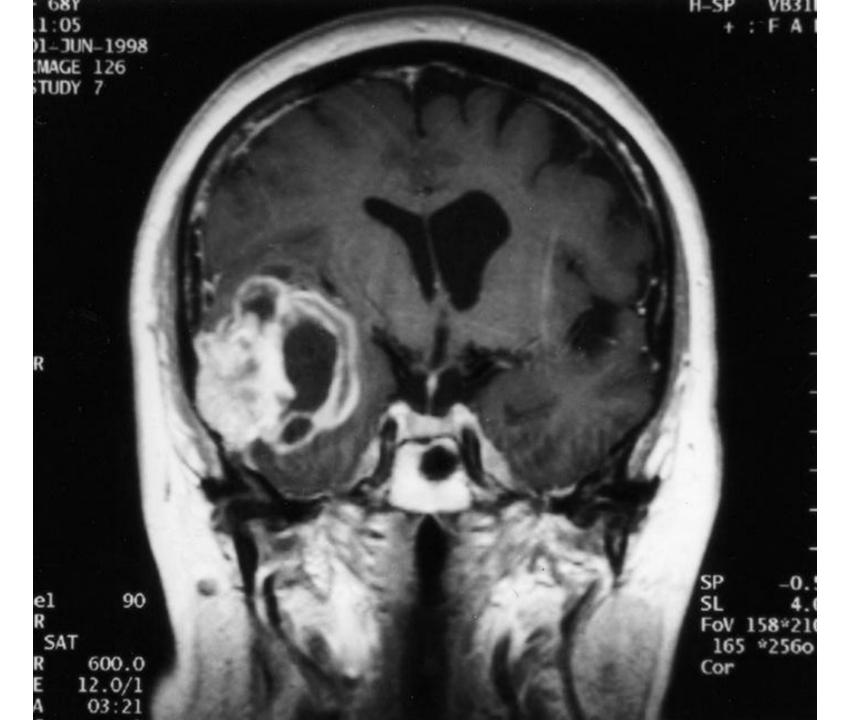
- Age?
- White vs. Grey Matter?
- Gross texture?
- Vascularity?
- Mitoses?
- (N/C, Pleomorphism, Hyperchromasia)
- Calcifications?
- Cysts?
- Satellitosis?
- Delineation?

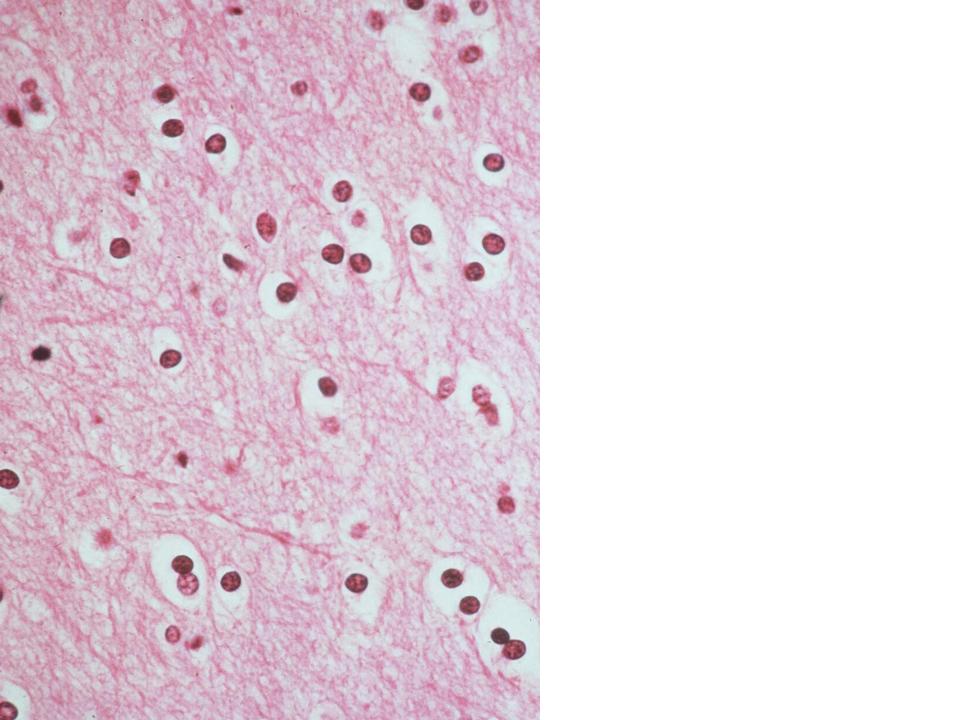


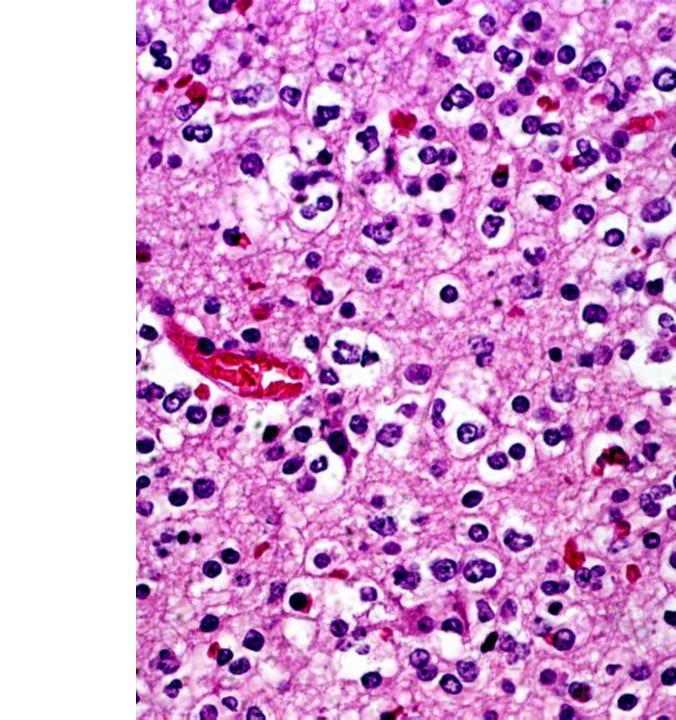


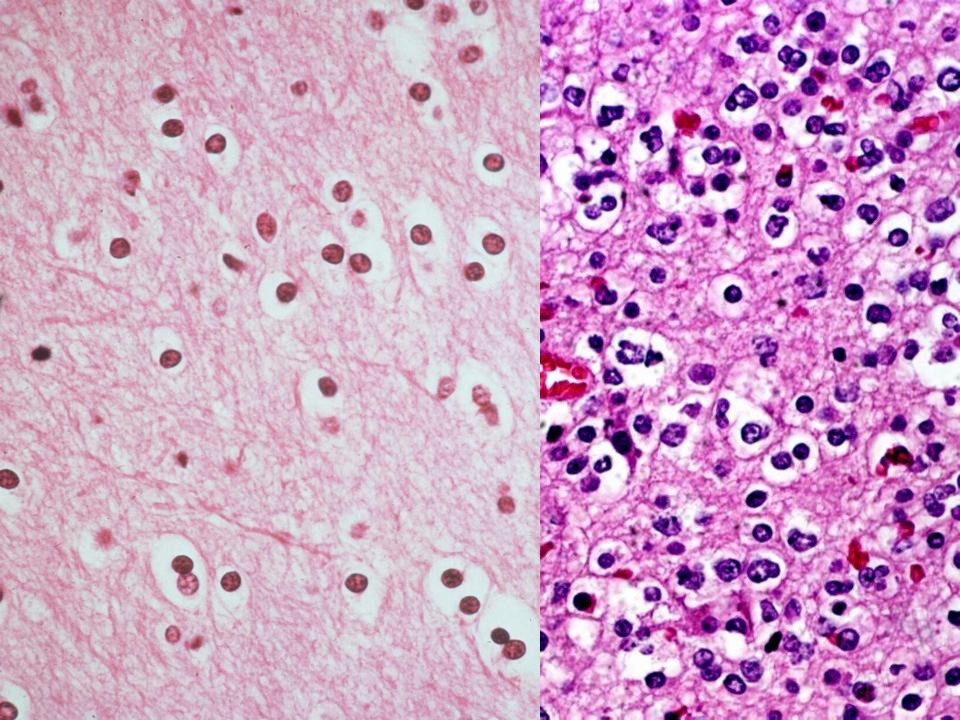


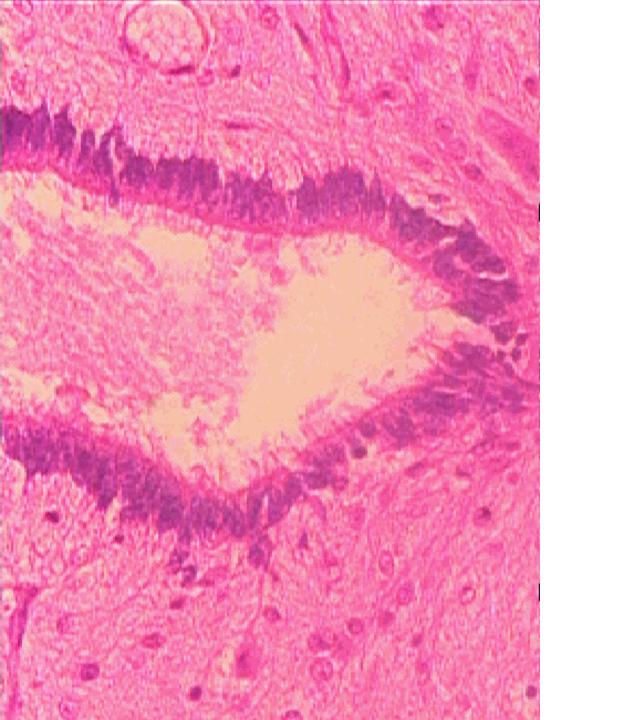


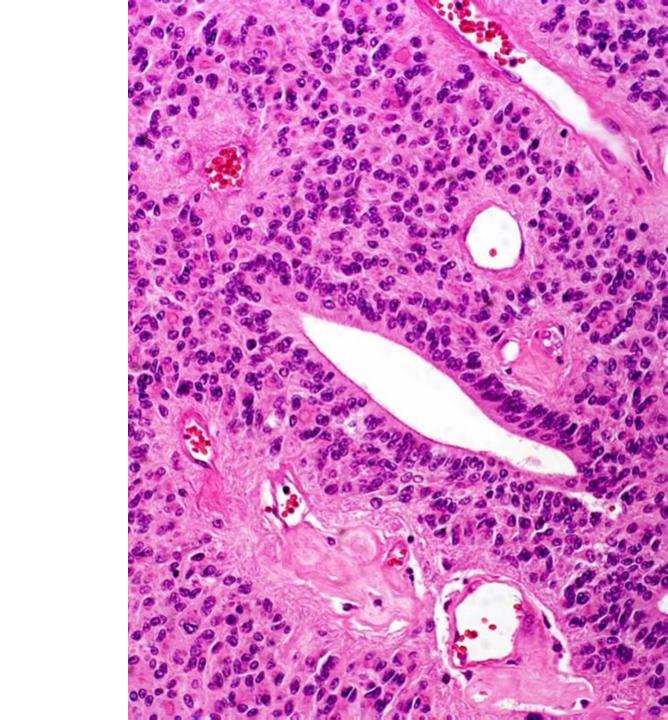


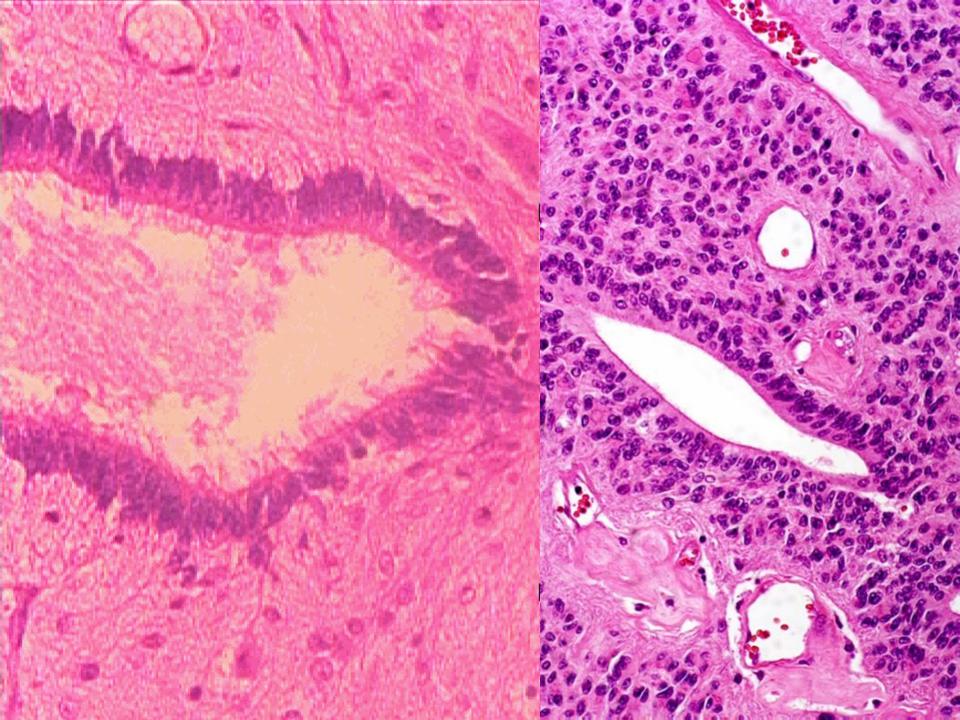


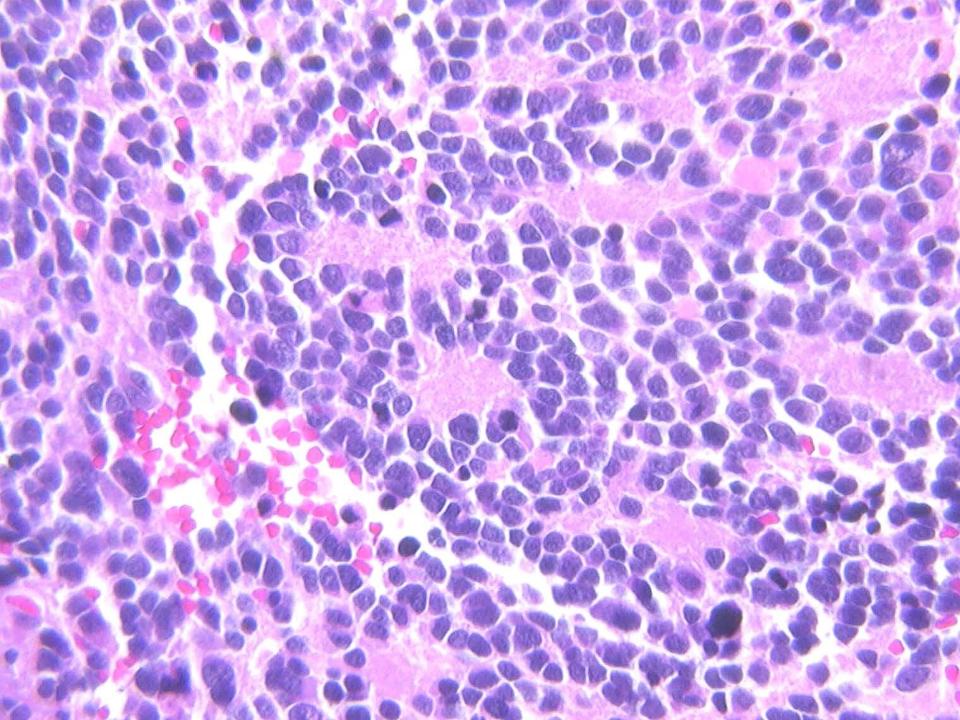


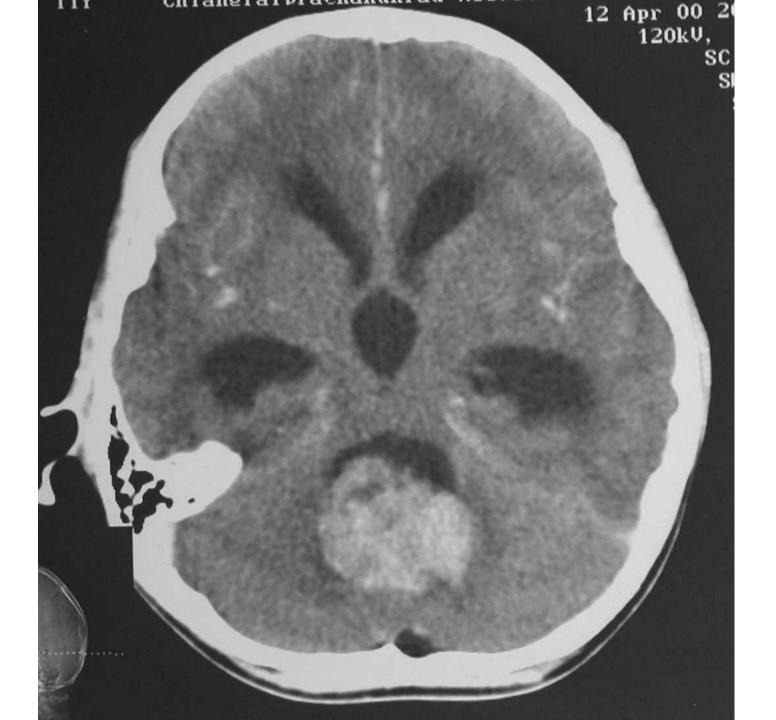


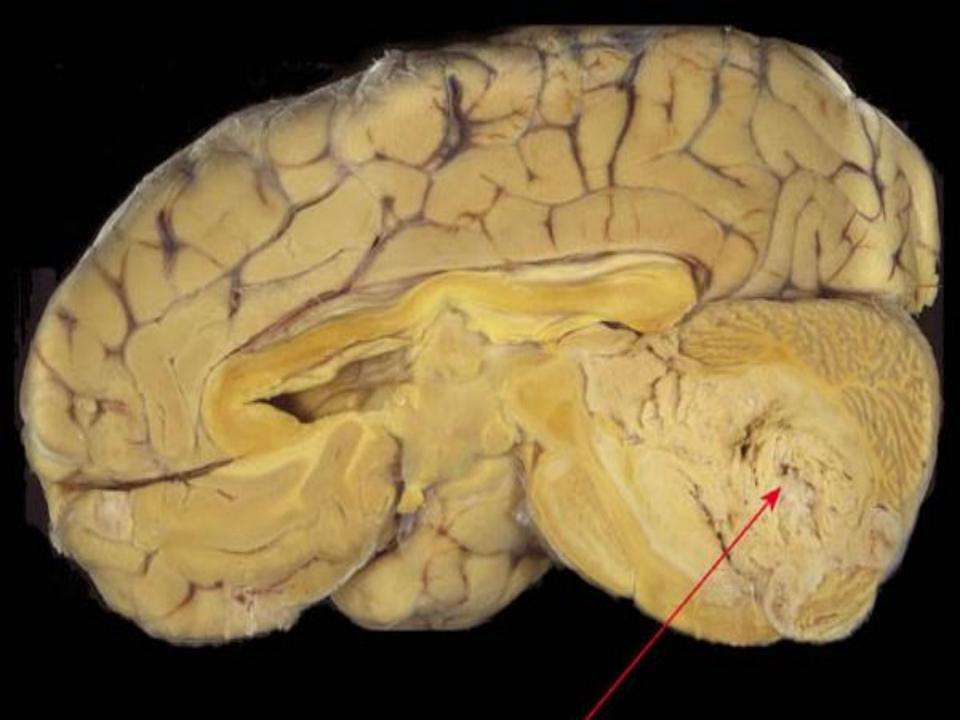






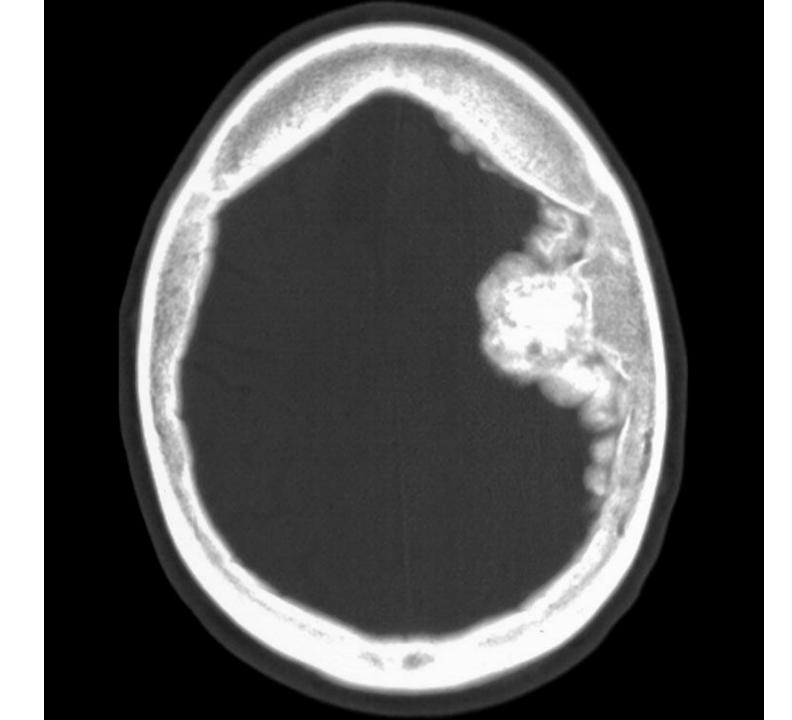




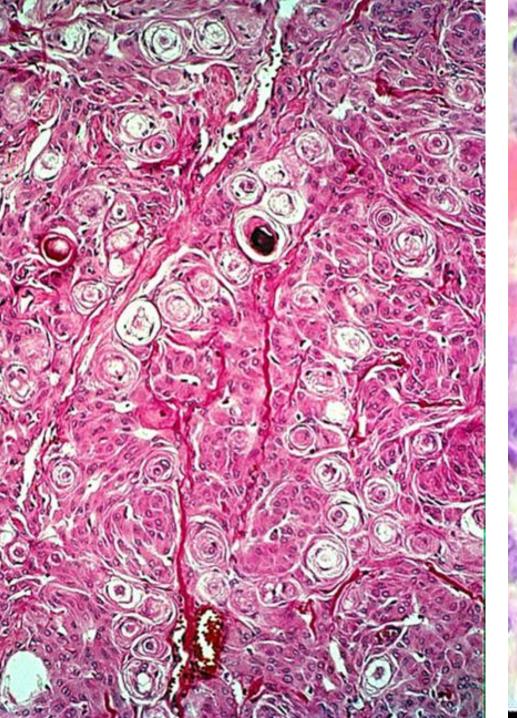


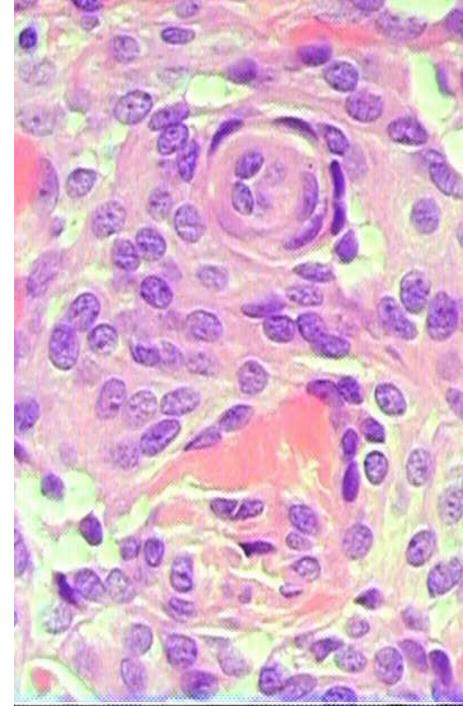
## MENINGIOMAS

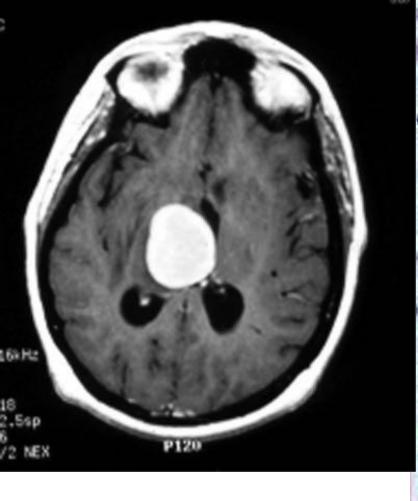
- Occur where dura is
- Very vascular
- BENIGN, but.....(can be damned invasive)
- Can invade skull, etc.
- Only invade (displace) brain in areas adjacent to dura, i.e., parasagittal, falx, tentorium, venous sinuses
- Small, firm, and well defined like a SUPERBALL
- Often (usually?) have PSAMMOMA bodies



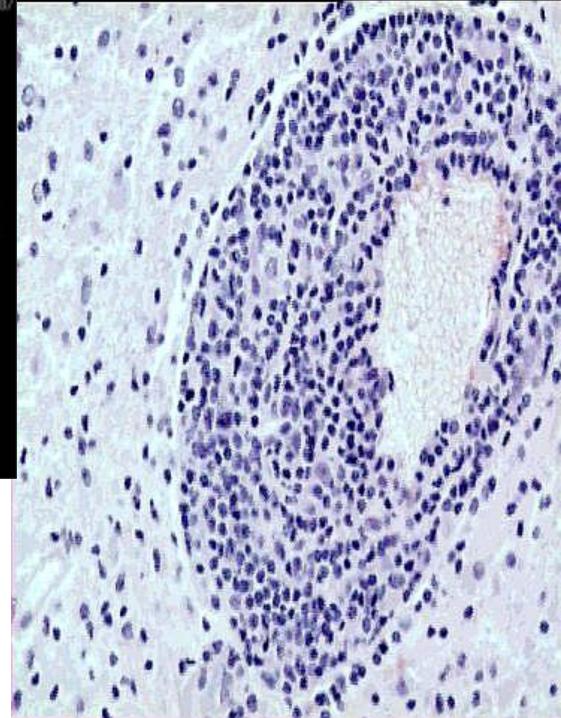








## HIV



# METASTATIC CNS TUMORS

### LUNG

- BREAST
- MELANOMA
- KIDNEY
- GI

#### "PARA" NEOPLASTIC SYNDROMES

- SMALL CELL, LUNG
- LYMPHOMAS
- BREAST CA

- Purkinje Cell Degeneration
- Encephalitis, Limbic System
- Sensory Neuron
   Degeneration, DRG
- Eye Movement Disorders

#### **FAMILIAL TUMOR SYNDROMES**

- NF1
  - Neurofibromas
  - -Gliomas
- NF2
  - -Schwannomas
  - Meningiomas
- Tuberous Sclerosis, i.e., CNS and somatic "hamartomas"
- Von-Hippel-Lindau, CNS hemangioblastomas, chiefly cerebellar