Brain Tumors

Dr. John F. Shea
Loyola University Chicago

Tumor

- an uncontrolled, unregulated growth of a body tissue
- may retain function
- may resume a more primitive state (undifferentiated)

Brain Tumors Types

- infratentorial *children*
- supratentorial *adult*

Introduction

- in infants and children, brain tumors are the 2nd most common form of cancer
- in adolescents and young adults, brain tumors are the 5th - 8th most common form of cancer
- primary brain tumors have a pre-valence of 14.7 per 100,000 in the US
- 80,000 - 100,000 new tumors diagnosed each year
- 50% of primary brain tumors are relatively benign tumors that can be treated successfully

Brain Tumors

primary:

- arising from within the CNS
- glia, neurons, meninges

secondary:

- spreading from non-CNS
- locally or distantly

Benign Tumors

- grow slower
- more differentiated
- encapsulated or segregated from normal tissue
- meningiomas, pituitary adenomas, neurinomas

Malignant Tumors

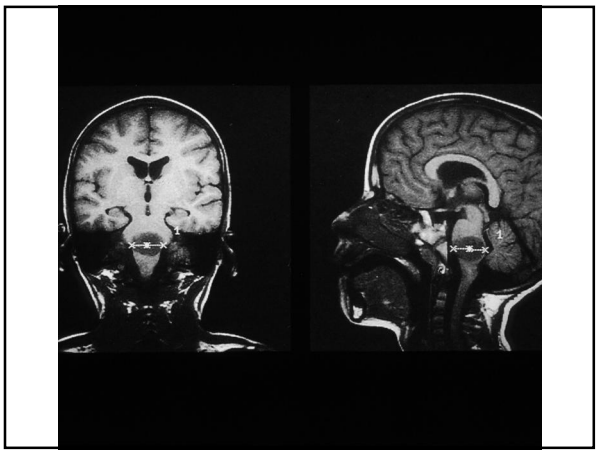
- grow faster and spread more rapidly
- less differentiated
- invade normal surrounding tissues
- gliomas, metastases

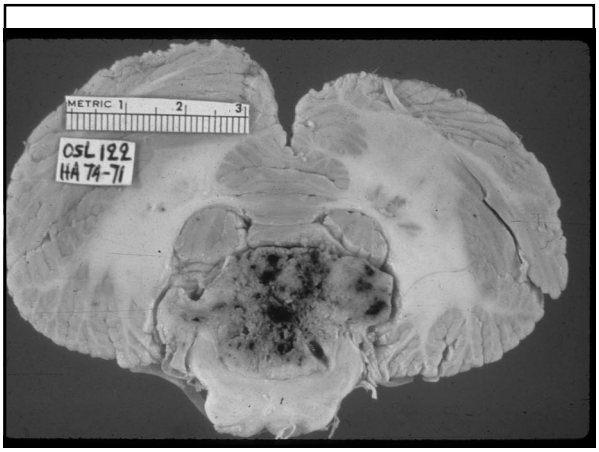
Blood Brain Barrier

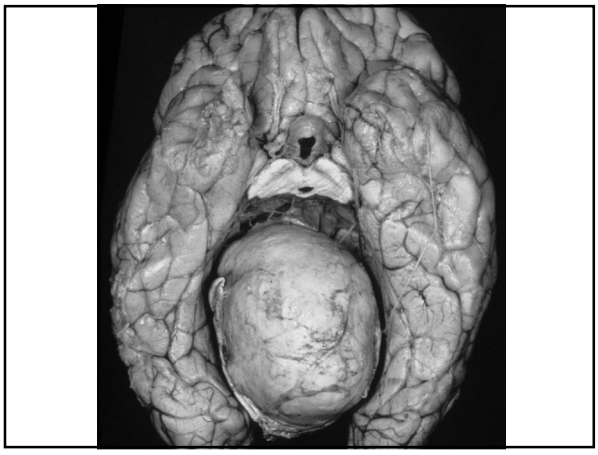
- spread of primary brain tumors to other organs virtually never occurs

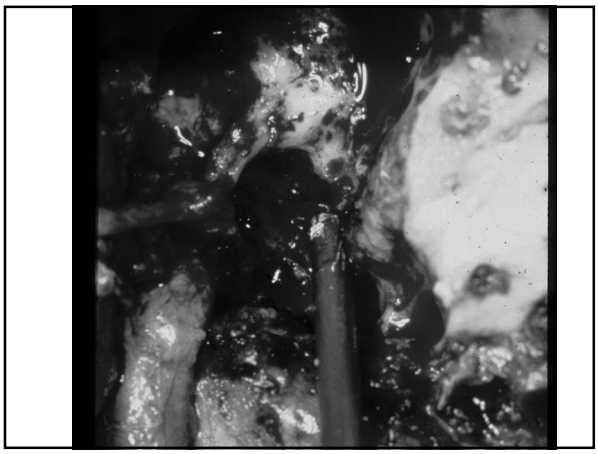
TUMORS AFFECT BRAIN

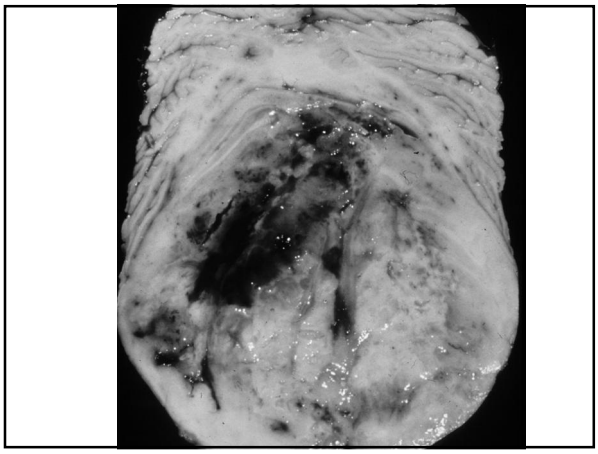
- COMPRESSION
- INVASION
- INFILTRATION

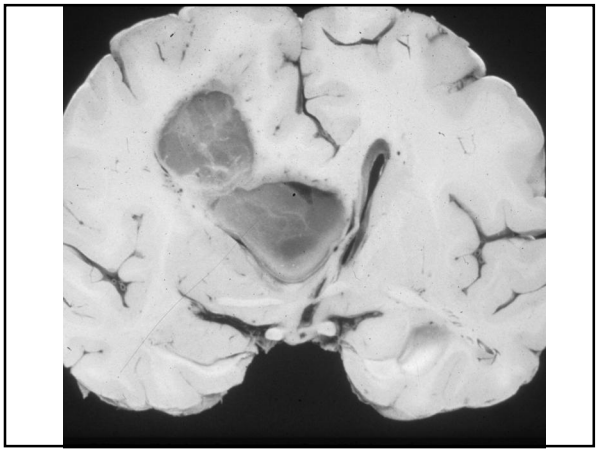


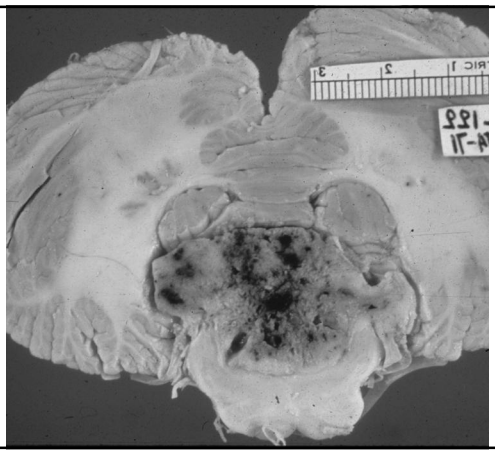

METRIC 1 2 3
OSL 122
HA 74-71





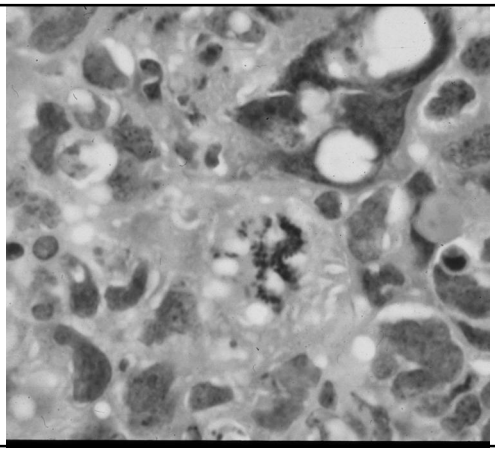






THE MOST PRIMITIVE TUMORS EMBRYOLOGICALLY

ARE THE MOST MALIGNANT



Brain Tumors Types

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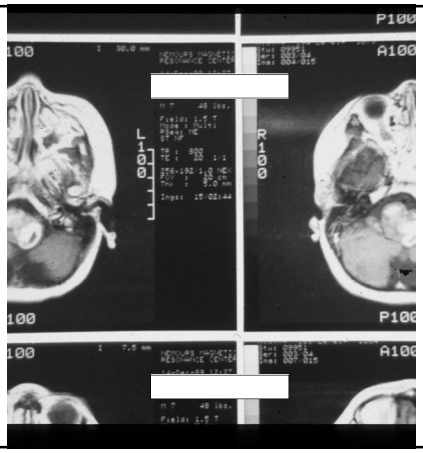
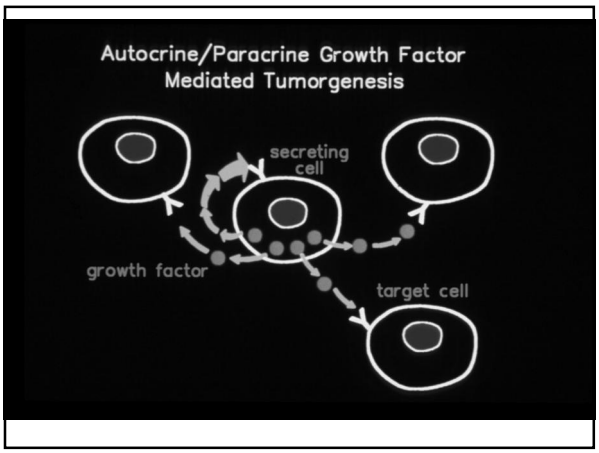
- supratentorial *adult*

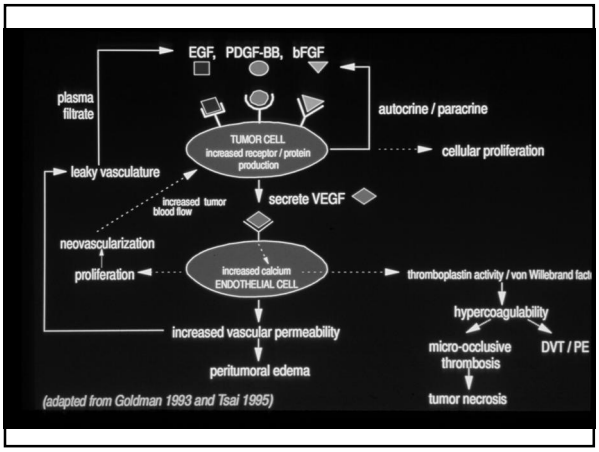


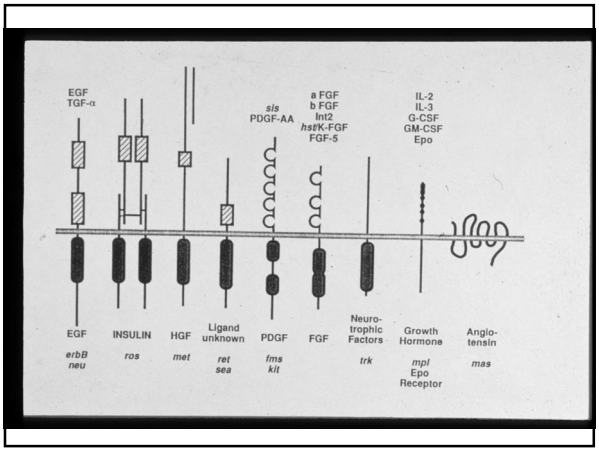
Tumor Growth

causative hypotheses:

- loss of suppressor gene
- inappropriate expression of oncogenes


Autocrine/Paracrine Growth Factor
Mediated Tumorgenesis
secreting
cell
growth factor
target cell


EGF, PDGF-BB, bFGF
plasma
filtrate
autocrine / paracrine
TUMOR CELL
increased receptor / protein
production
cellular proliferation
leaky vasculature
increased tumor
blood flow
secrete VEGF
neovascularization
proliferation
increased calcium
ENDOTHELIAL CELL
thromboplastin activity / von Willebrand fact
hypercoagulability
increased vascular permeability
micro-occlusive
thrombosis
DVT / PE
peritumoral edema
tumor necrosis
(adapted from Goldman 1993 and Tsai 1995)


EGF
TGF-α
sis
PDGF-AA
a FGF
b FGF
Int2
hstK-FGF
FGF-5
IL-2
IL-3
G-CSF
GM-CSF
Epo
EGF
erbB
neu
INSULIN
ros
HGF
met
Ligand
unknown
ret
sea
PDGF
fms
kit
FGF
Neuro-
trophic
Factors
trk
Growth
Hormone
mpl
Epo
Receptor
Angio-
tensin
mas

Symptoms of Brain Tumors

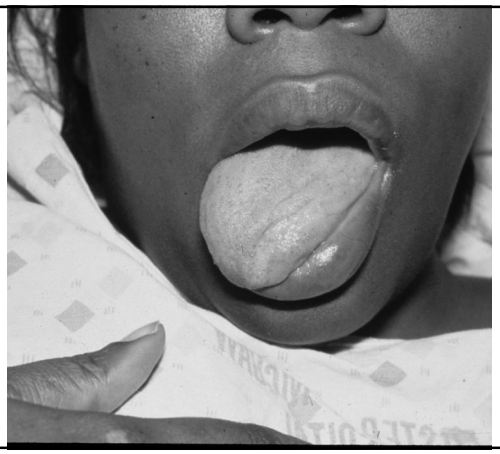
- slower than stroke
- specific localizable syndromes
- seizures
- increased ICP
- impairment of mental function

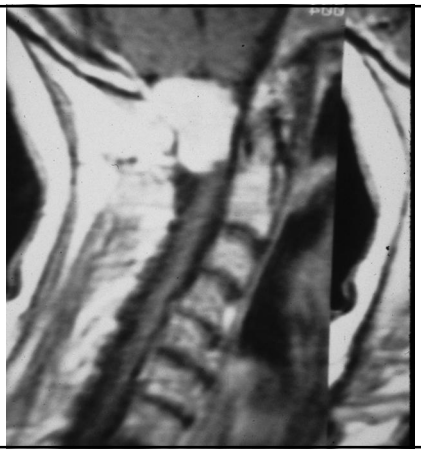
PATHOPHYSIOLOGIC FINDINGS

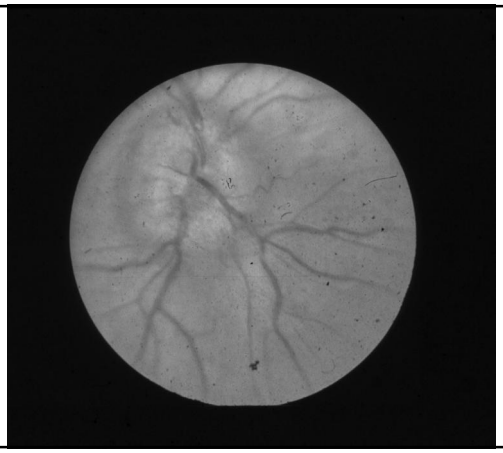
- CEREBRAL EDEMA
- INCREASED ICP
- FOCAL NEUROLOGICAL DEFICITS
- SEIZURE ACTIVITY
- ALTERATIONS IN HYPOPHYSEAL FUNCTION
- OBSTRUCTION OF CSF

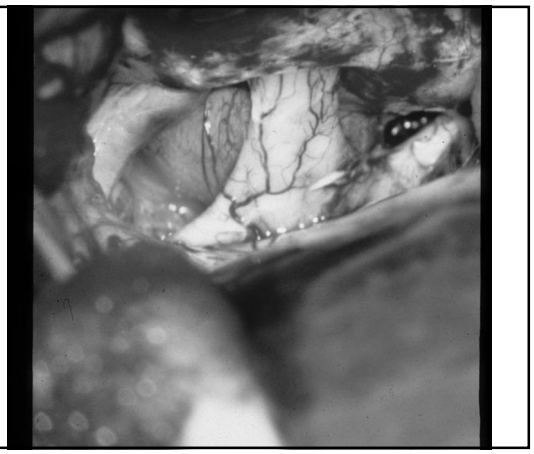
SIGNS AND SYMPTOMS

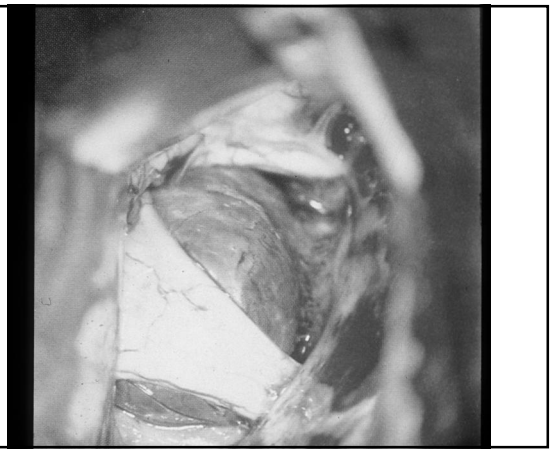
- HEADACHE 60 - 70%
- SEIZURES ◦ FOCAL ◦ 30%
- PERSONALITY CHANGES
- HEMIPLEGIA
- VISUAL SYMPTOMS
- MEMORY LOSS
- VOMITING AM ± MEALS
- GAIT DISTURBANCES
- PAPILLEDEMA 70%
- CRANIAL NERVES - 3, 4, 6, 8

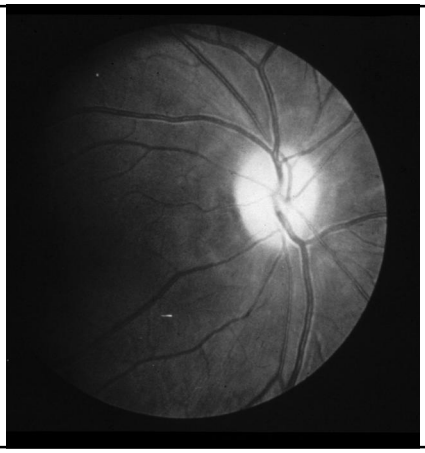


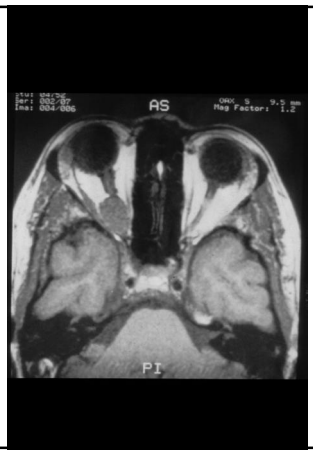








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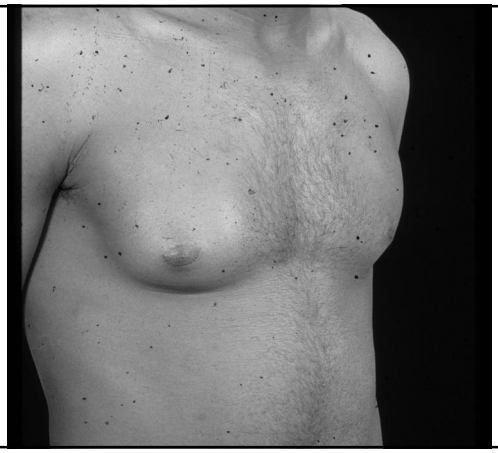

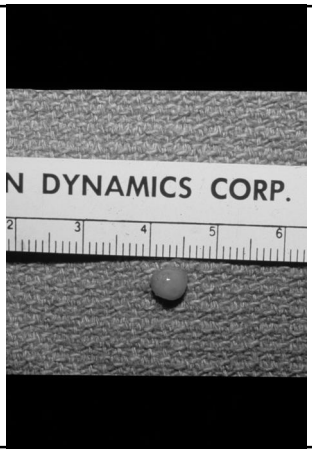
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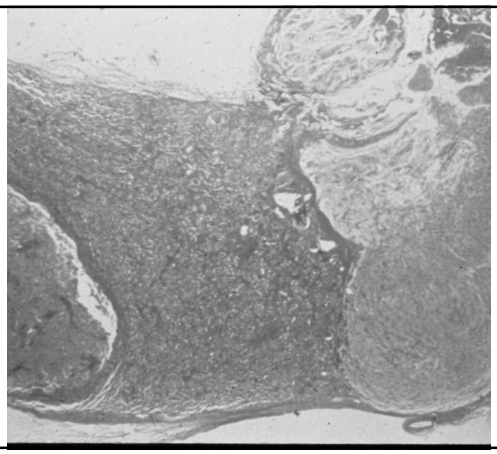
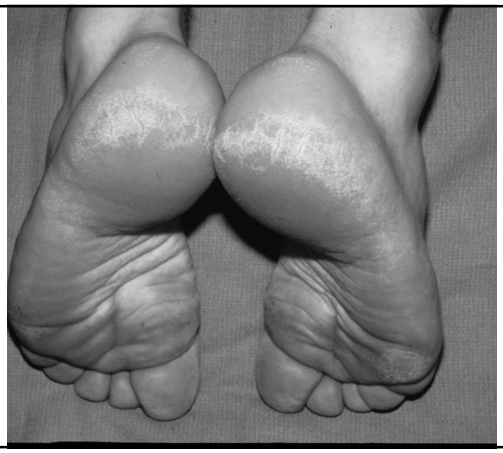
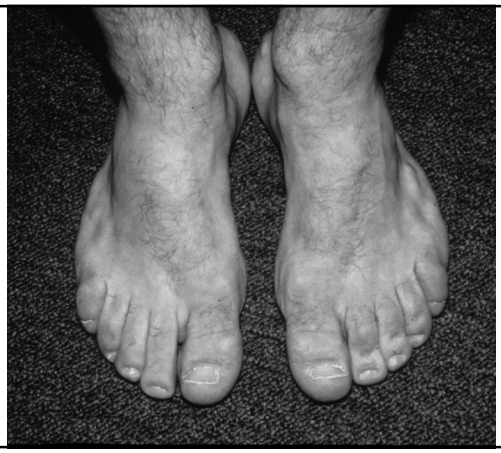
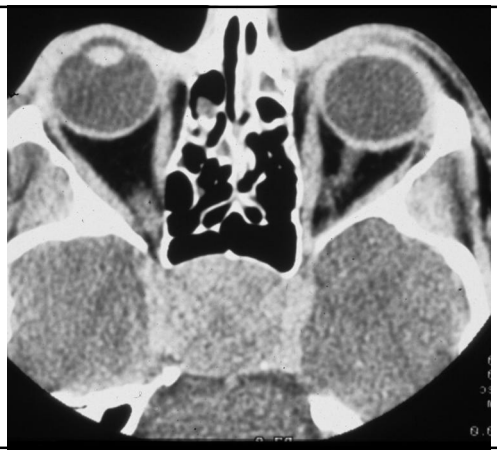
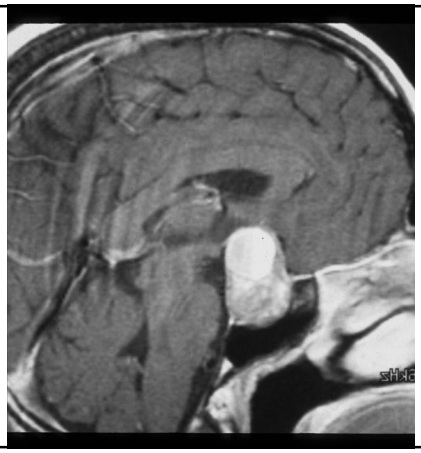
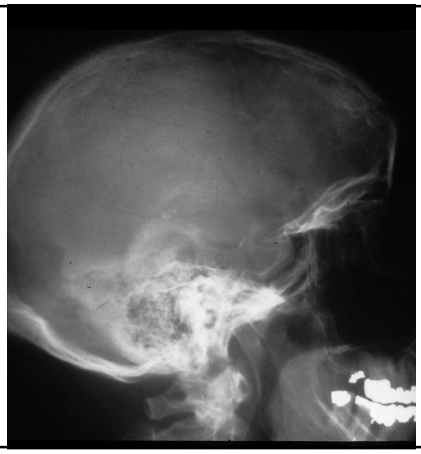


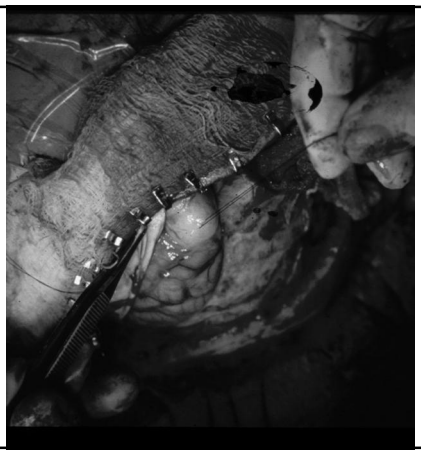


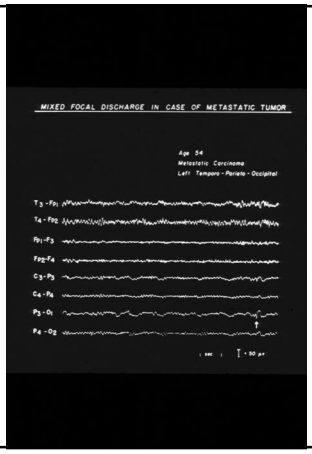


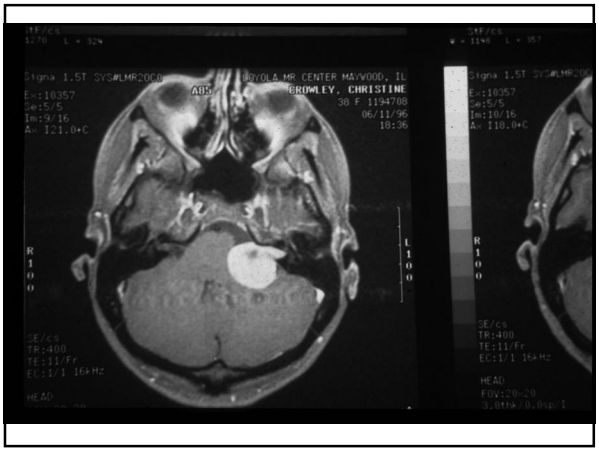


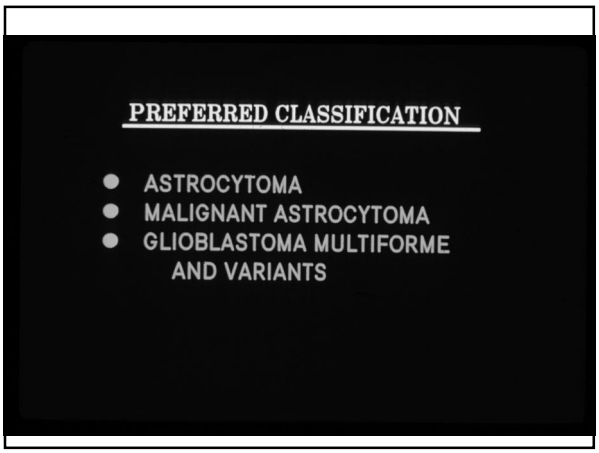


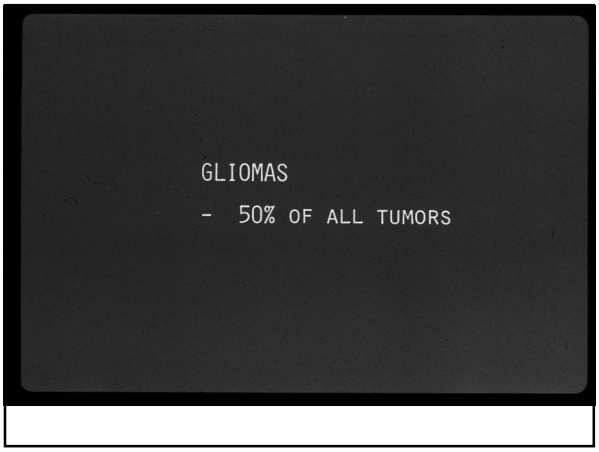


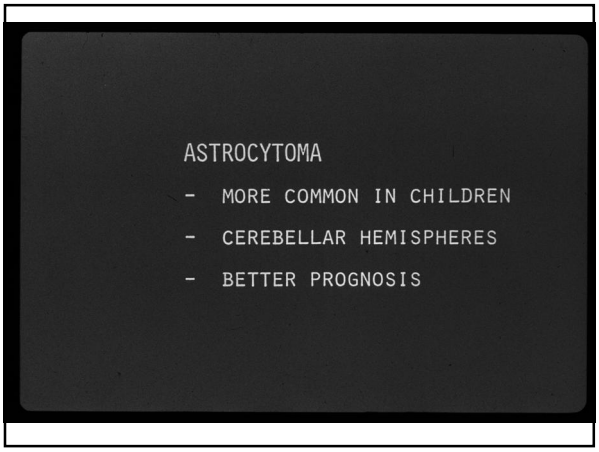


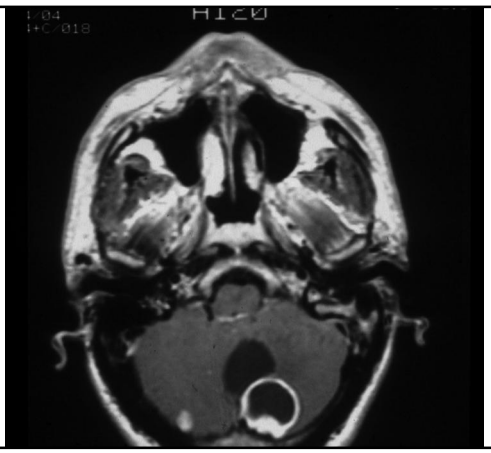

MIXED FOCAL DISCHARGE IN CASE OF METASTATIC TUMOR
Age: 54
Metastatic Carcinoma
Left Tempora - Parieto - Occipital
T3 - Fp1
T4 - Fp2
Fp1 - F3
Fp2 - F4
C3 - P3
C4 - P6
P3 - O1
P4 - O2

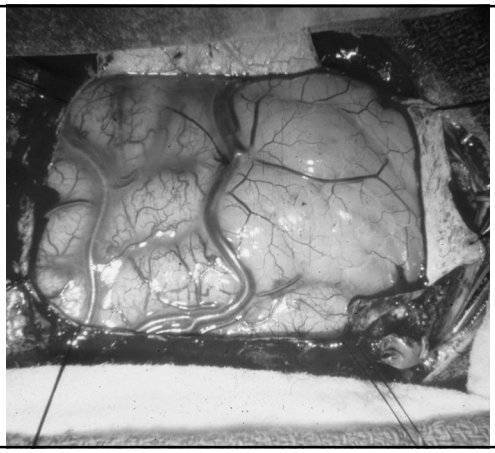

LOYOLA MR CENTER MAYWOOD, IL
BROWLEY, CHRISTINE
38 F 1194708
06/11/96
18:36
Signa 1.5T SYS#LMR20C0
Ex:10357
Se:5/5
Im:9/16
A: I21.0+C
SE/cs
TR:400
TE:11/Fr
EC:1/1 16kHz
HEAD
R
L

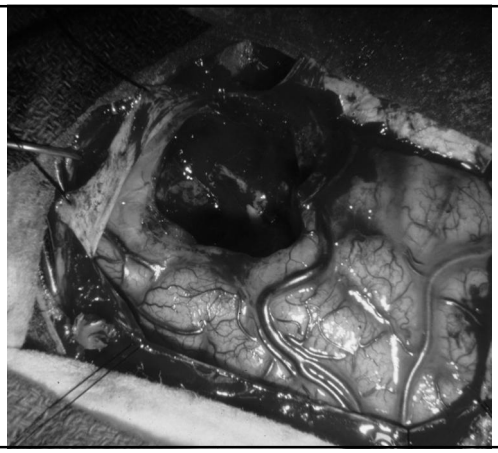

PREFERRED CLASSIFICATION
ASTROCYTOMA
MALIGNANT ASTROCYTOMA
GLIOBLASTOMA MULTIFORME
AND VARIANTS

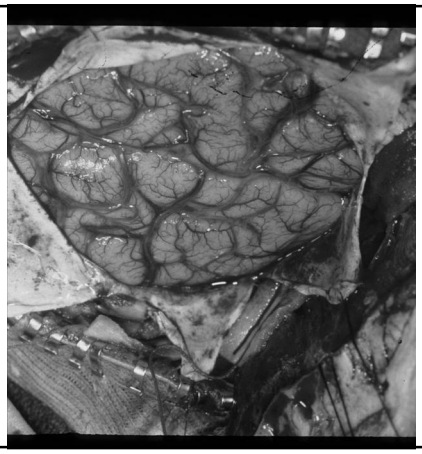

GLIOMAS
- 50% OF ALL TUMORS

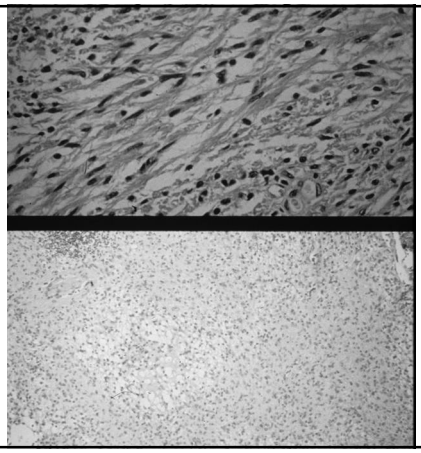

ASTROCYTOMA
- MORE COMMON IN CHILDREN
- CEREBELLAR HEMISPHERES
- BETTER PROGNOSIS





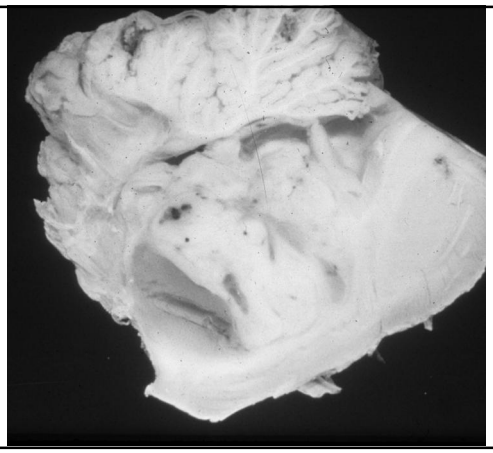


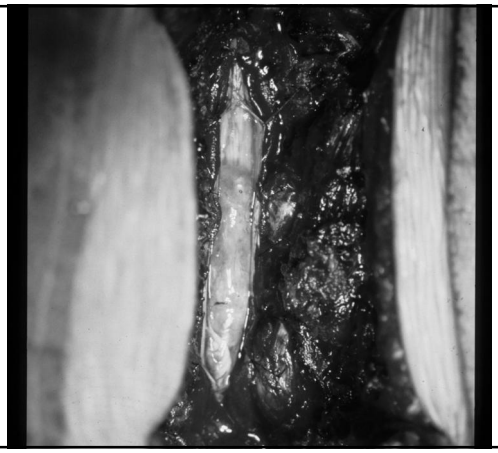


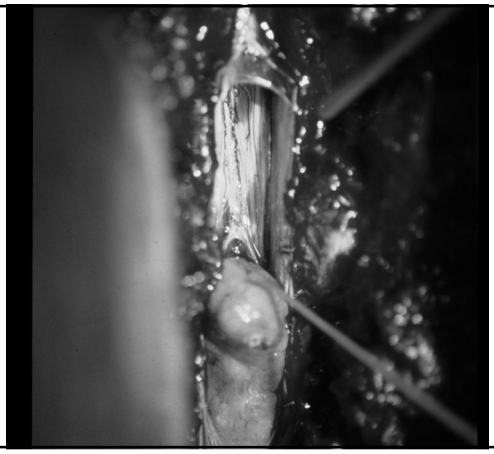


EPENDYMOMA

- EPENDYMAL GLIA
- VENTRICLES
- SPINAL CORD

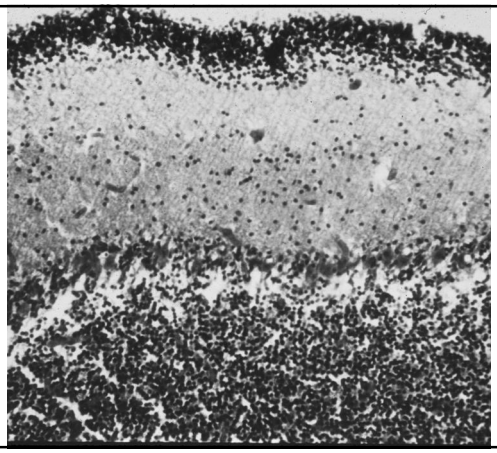


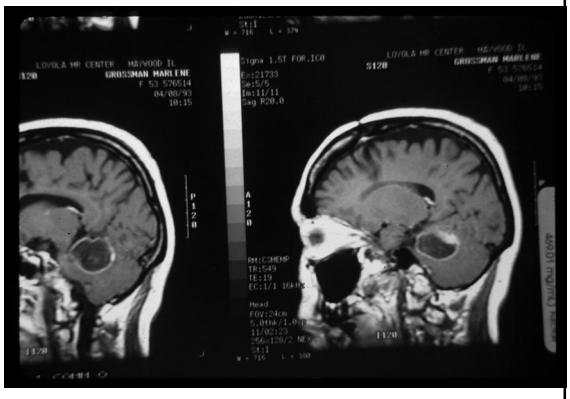




MEDULLOBLASTOMA

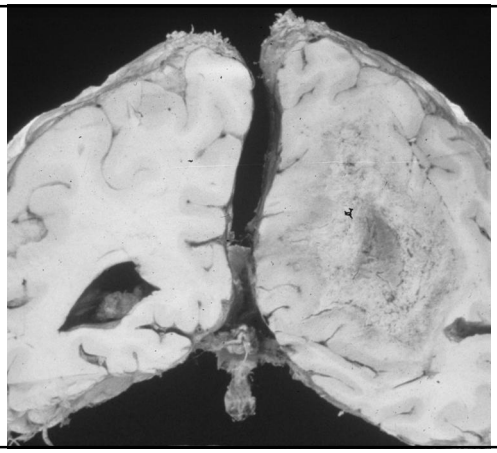
- POST FOSSA
- EXTERNAL GRANULAR LAYER
- TRIAD
  - HEADACHE
  - NAUSEA - VOMITING
  - PAPILLEDEMA

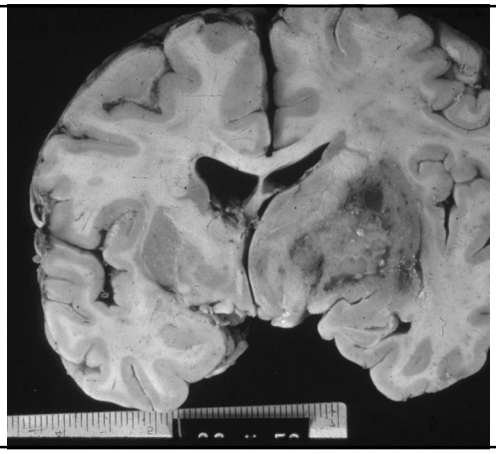


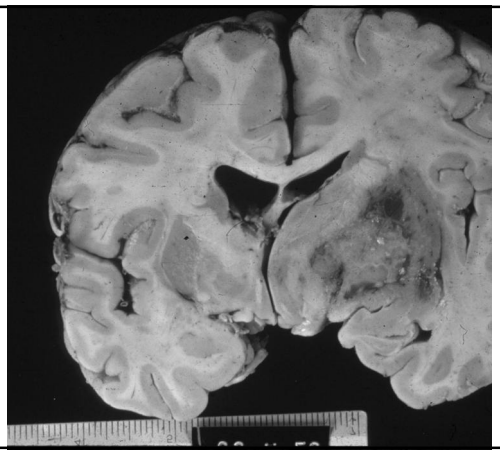


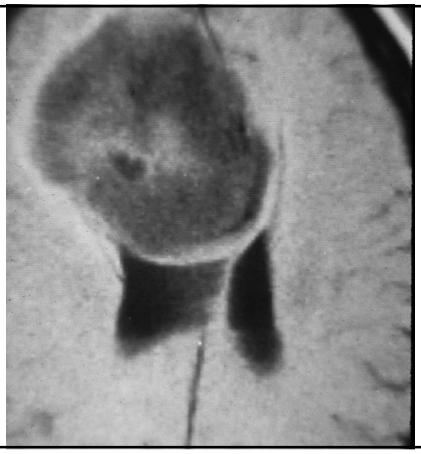
GLIOBLASTOMA MULTIFORME

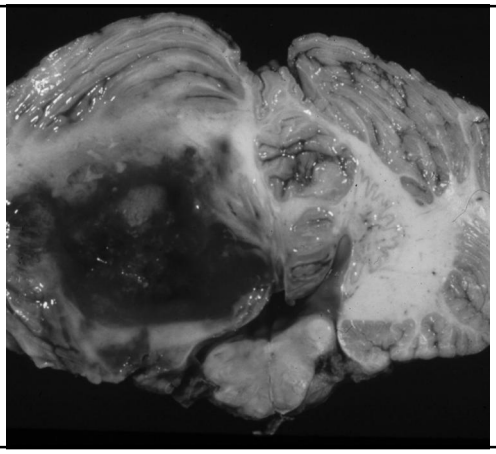
- 33% OF ALL GLIOMAS
- HIGHLY MALIGNANT
- SILENT





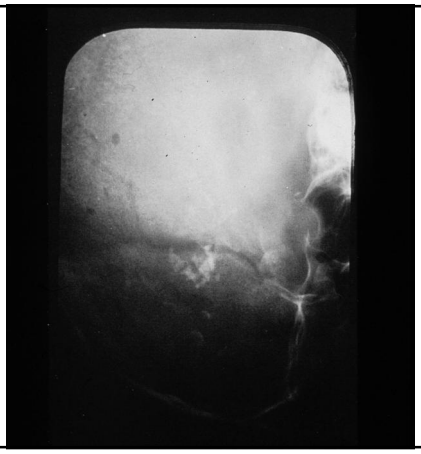


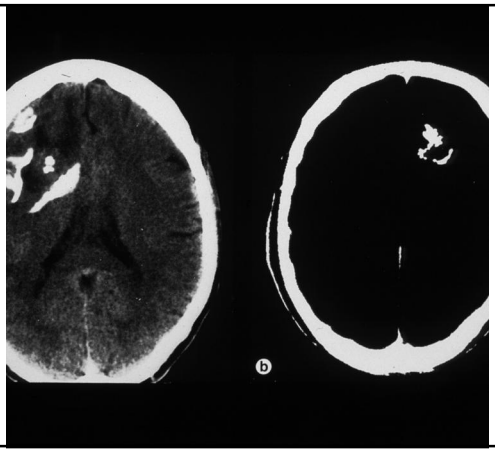


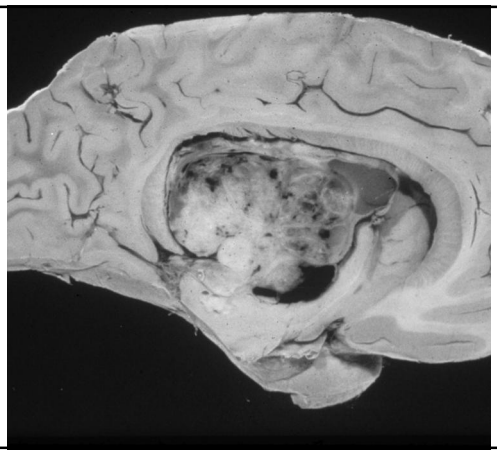


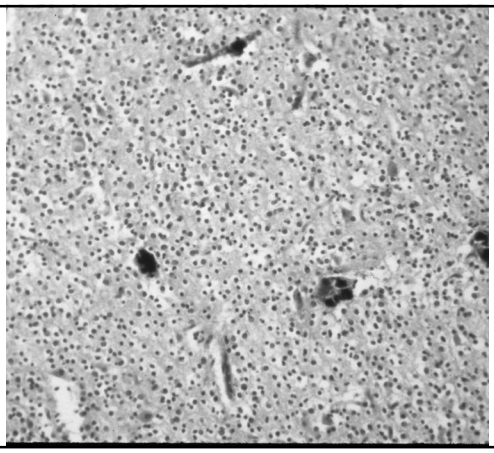
OLIGODENDROGLIA

- 5% OF GLIOMAS
- SLOW GROWING
- CALCIFIED
- SEIZURES



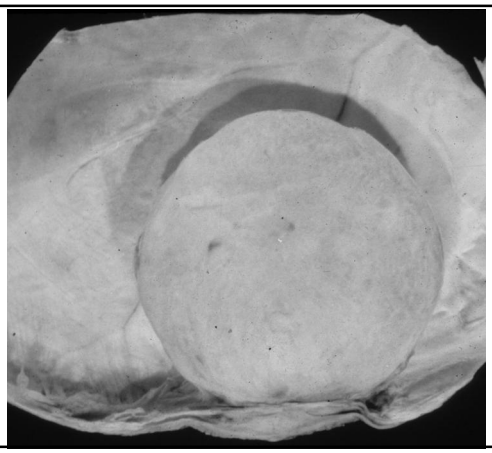


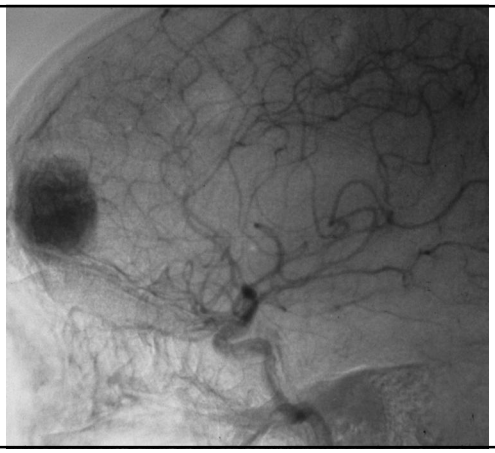


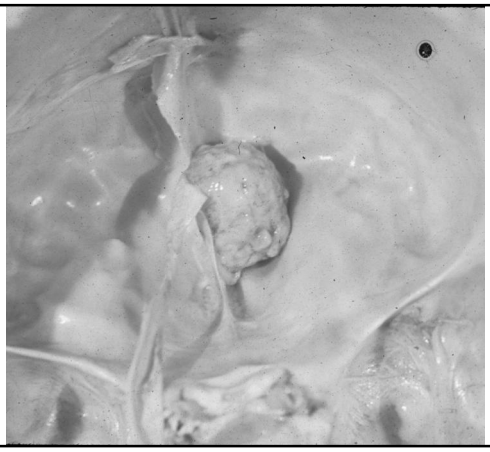


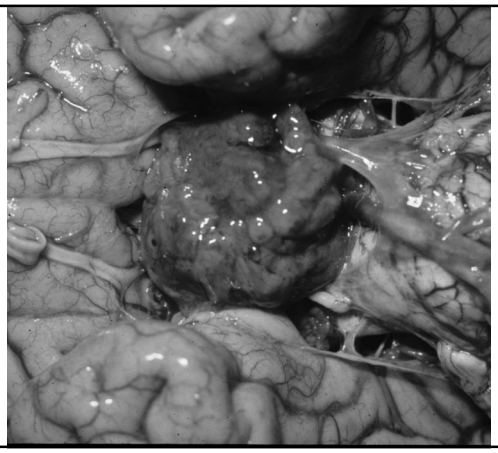
MENINGIOMA - 10 - 15% ALL TUMORS

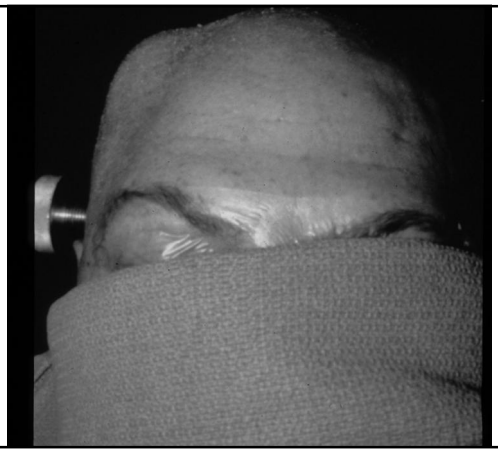
1. Location: over the reflection of the meninges = parasagittal (21%), convexities (17%), sphenoid ridge (17%), floor of anterior fossa (18%).
2. Sex ratio: M:F = 2:3.
3. Clinical presentation: very slow-growing. Mild focal findings such as focal seizures are common.
4. Syndrome of the olfactory groove meningioma (Foster - Kennedy).

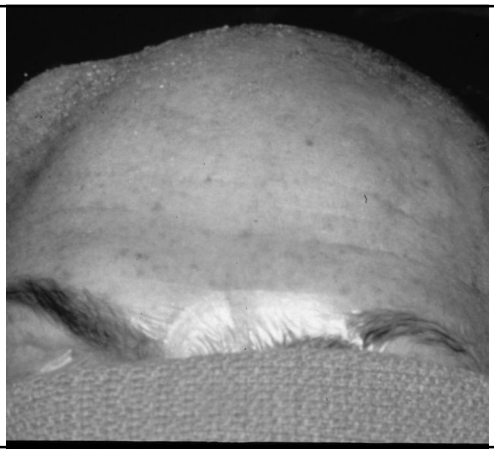


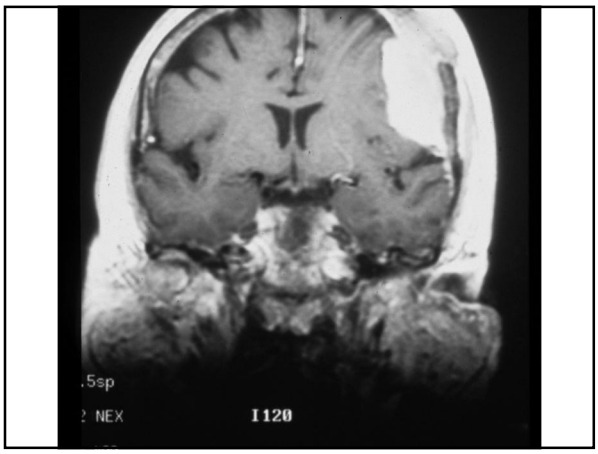








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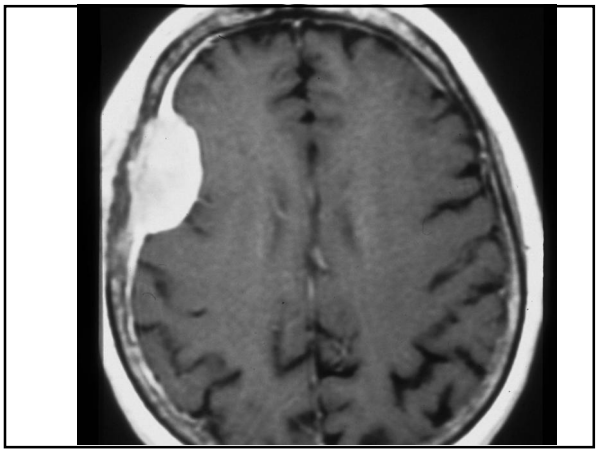
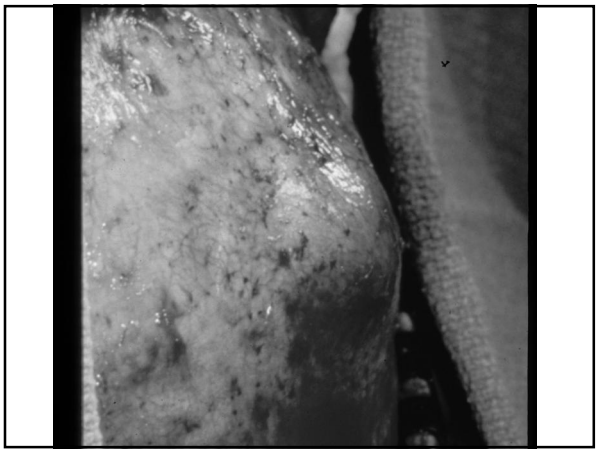
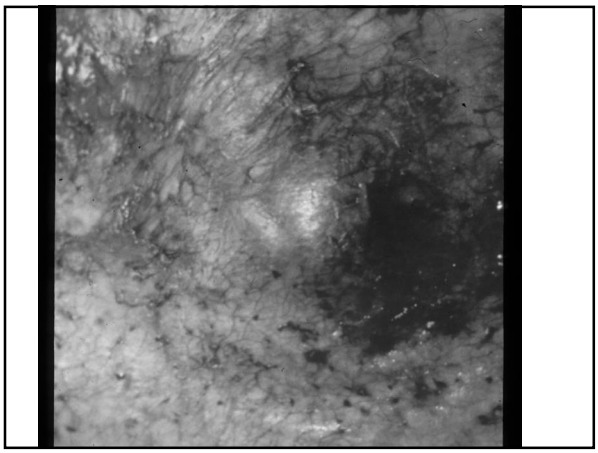
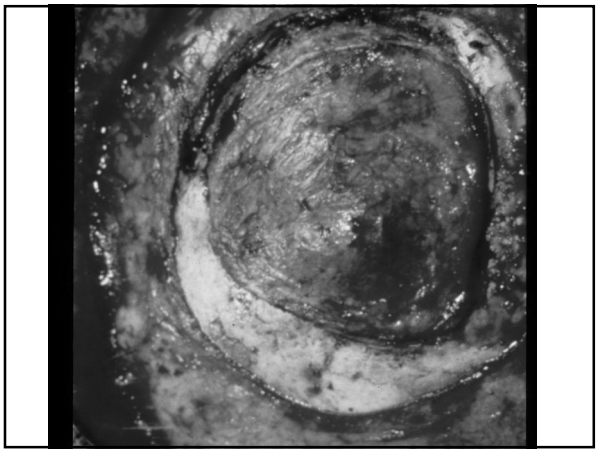
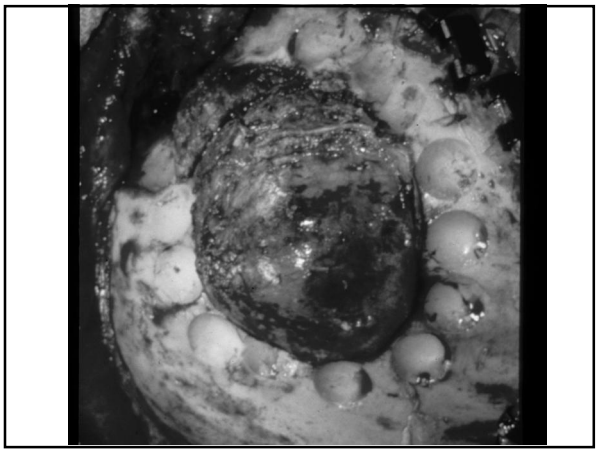
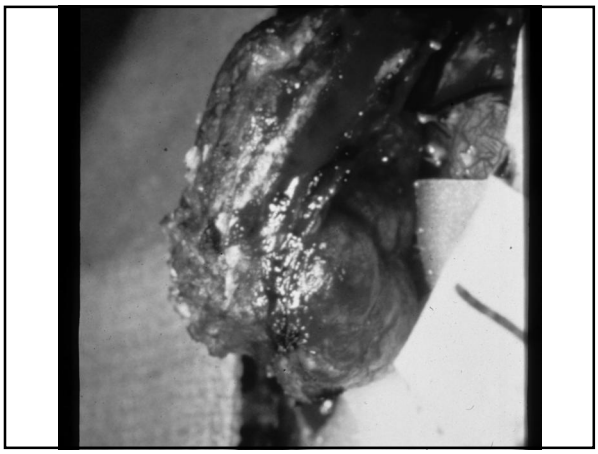


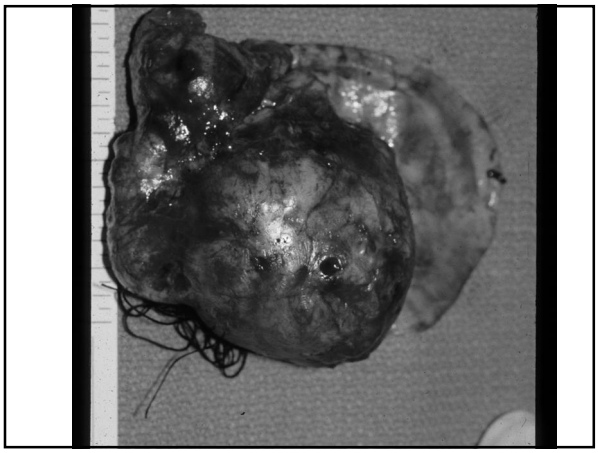


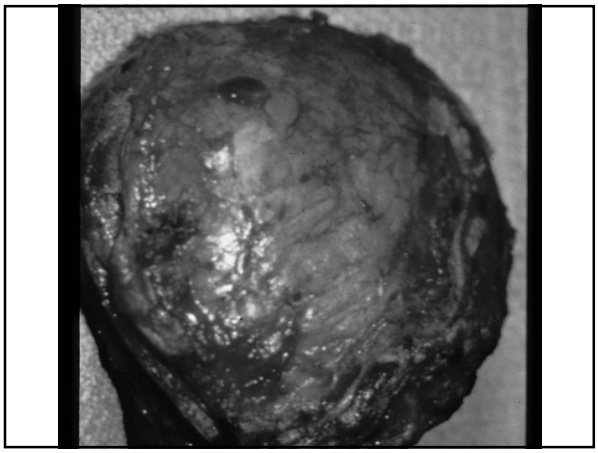


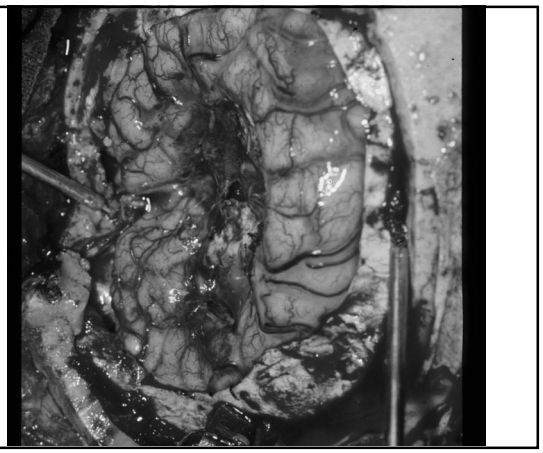


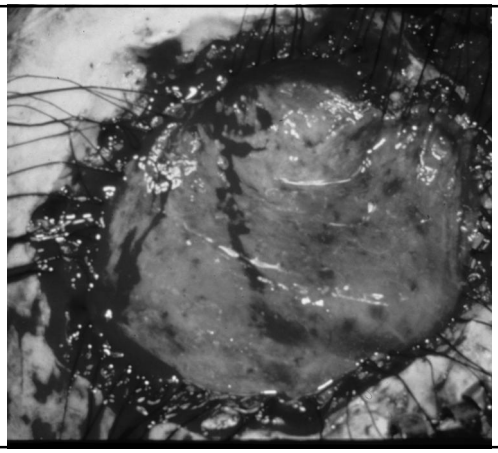


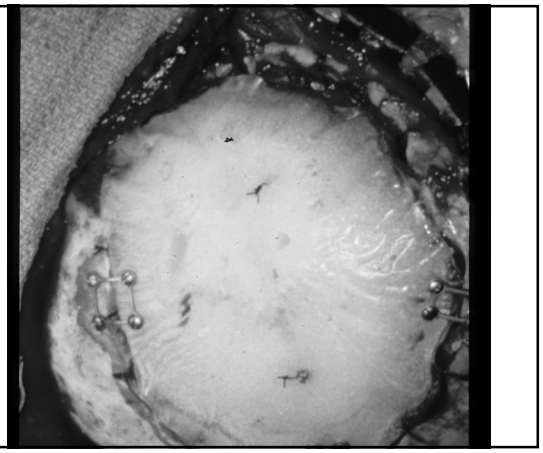


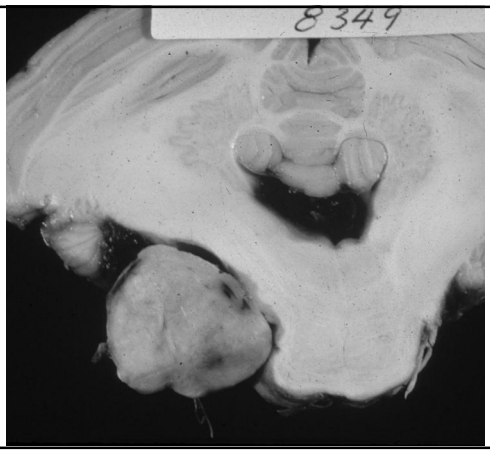


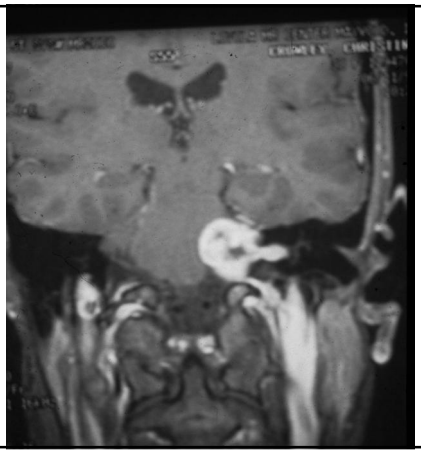










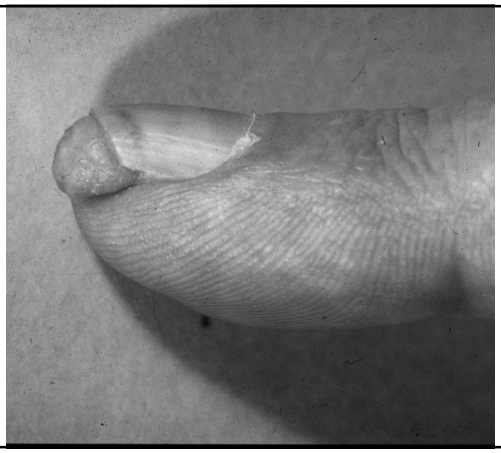


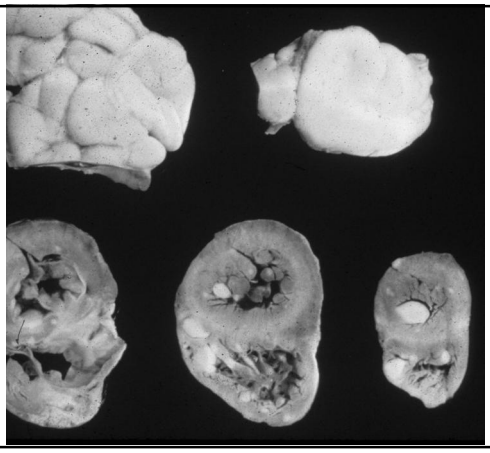
ACOUSTIC NEURINOMA - 10% ALL TUMORS

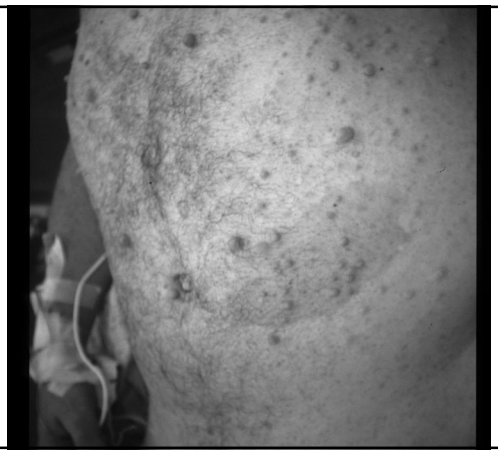
1. Location: the cerebellopontine angle.
2. Age: 53% between 30 and 60.
3. Clinical presentation: a slow-growing tumor.
4. Signs: deafness, nystagmus, absence of caloric response, loss of facial sensation, VII nerve palsy.
5. Diagnosis: enlargement of the internal auditory canal on tomogram, CT scan

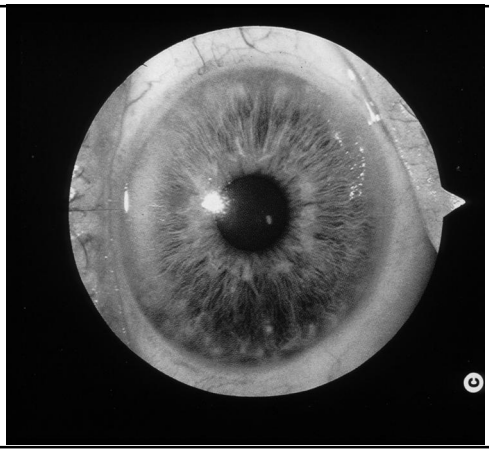
HEREDITARY TUMORS

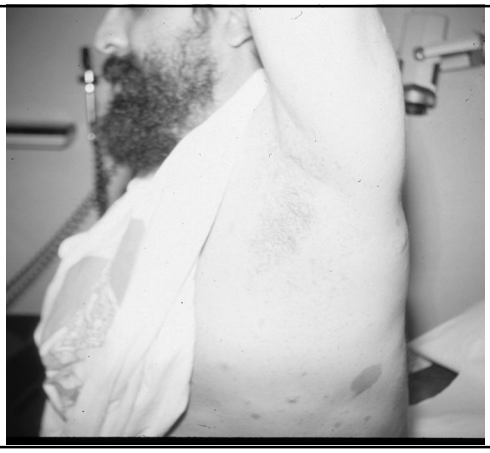
- TUBEROUS SCLEROSIS
- VON RECKLINGHAUSEN
- VON HIPPEL - LINDAY

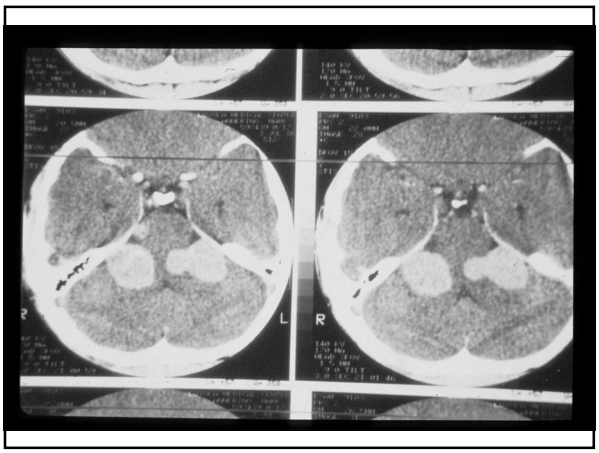






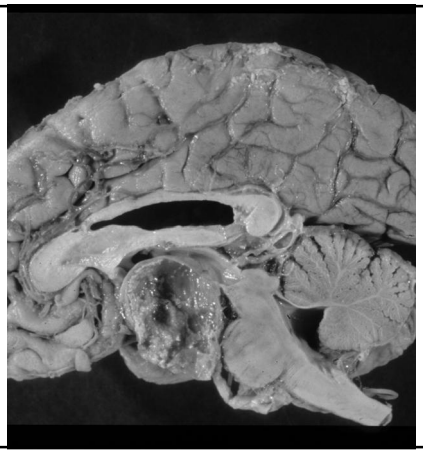


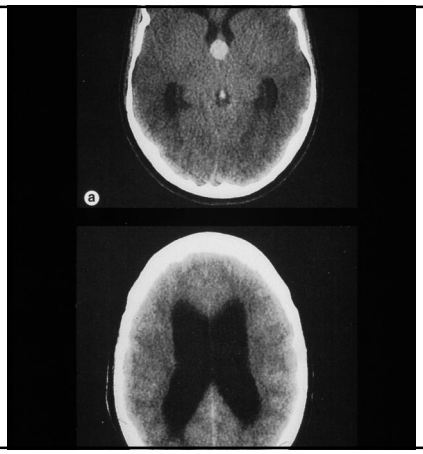


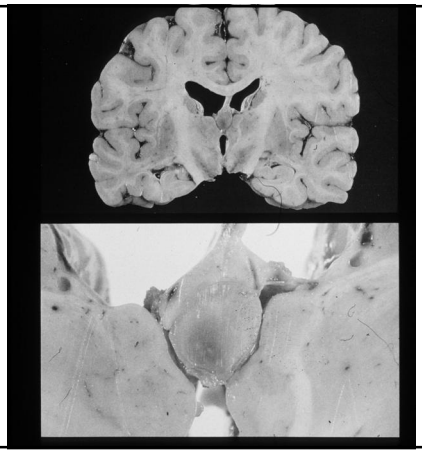


CONGENITAL TUMORS

- 4 - 5%
- CRANIOPHARGNGIOMA
- HEMANGIOBLASTOMA







INTRACRANIAL METASTASES

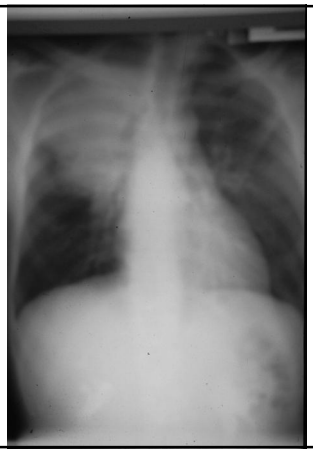
- 10%
- HEMATOGENOUS (LUNG & BREAST)
- MELANOMA
- HYPERNEPHROMA
- RARE
  - A) PROSTATIC
  - B) CERVIX
  - C) OVARY
  - D) GASTROINTESTINAL
- NO LYMPHATICS

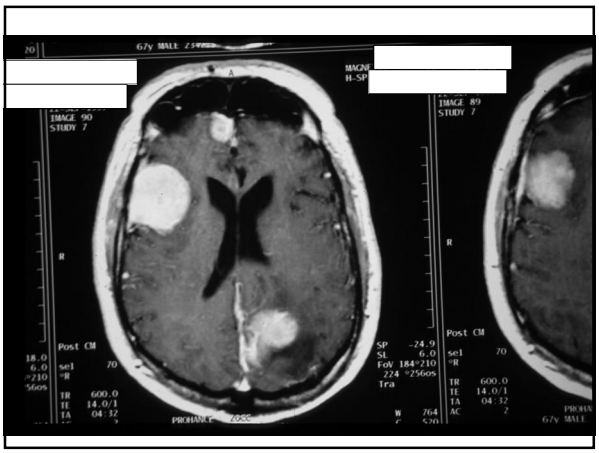
Metastatic Tumors

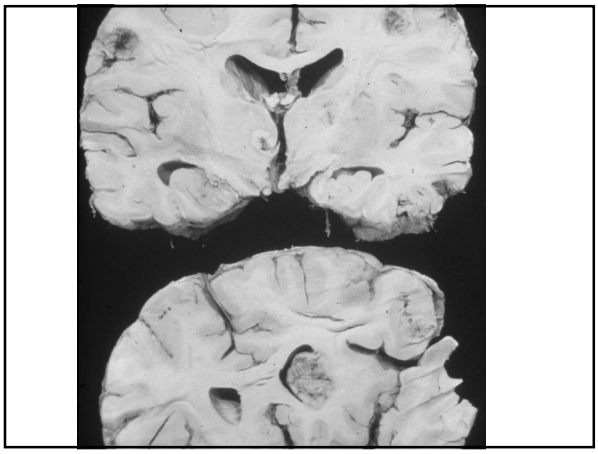
- 20% of blood flow from the heart
- 30% of brain tumors in general

WHEN METASTASIZE

- 2 YEARS OF DISCOVERING THE PRIMARY LESION
- 1 YEAR FOLLOWING A NEUROLOGICAL SYMPTOM





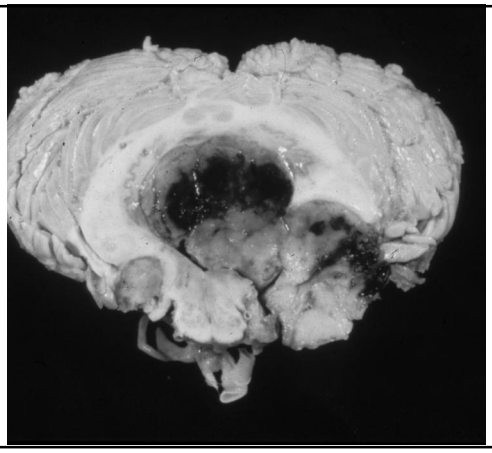


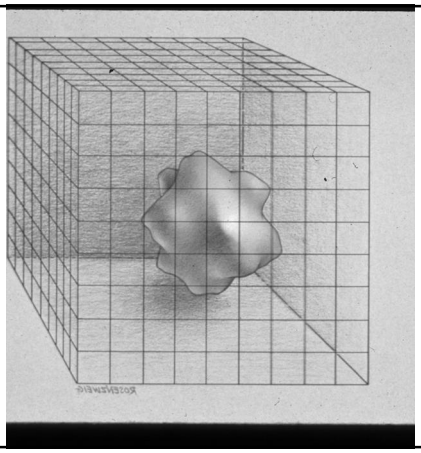
TREATMENT OF BRAIN TUMOR

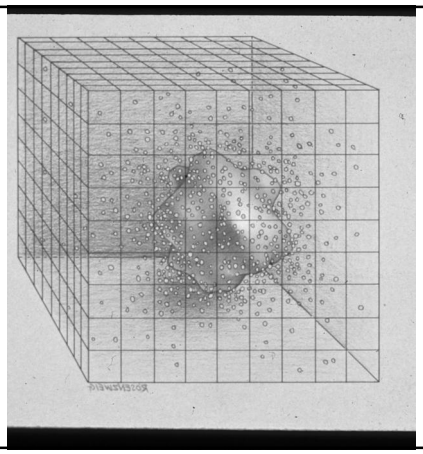
- REDUCE TUMOR SIZE
- MINIMIZE SIDE EFFECTS
- RECOVER FUNCTION

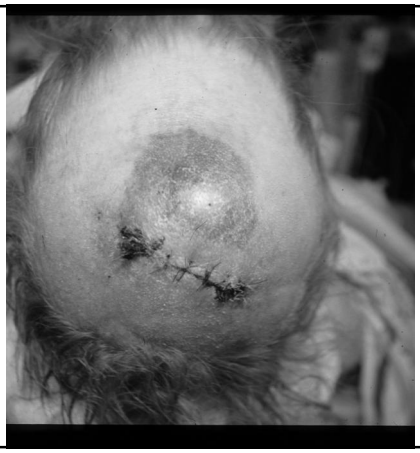
INDICATIONS FOR SURGERY

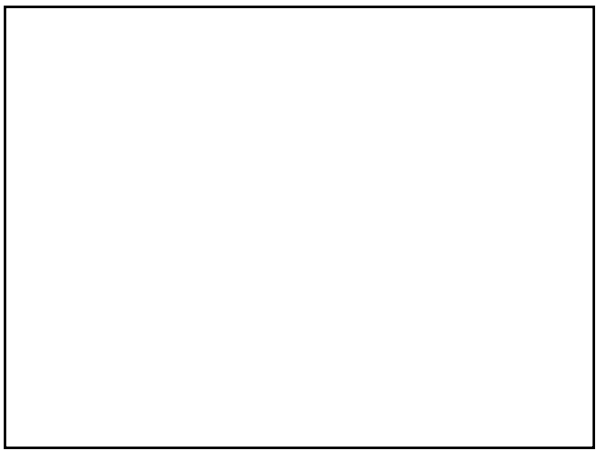
- TOTAL REMOVAL
- BUY TIME
- DECREASE ICP
- TISSUE DIAGNOSIS
- CONVENT INACTIVE CELLS TO ACTIVE CELLS





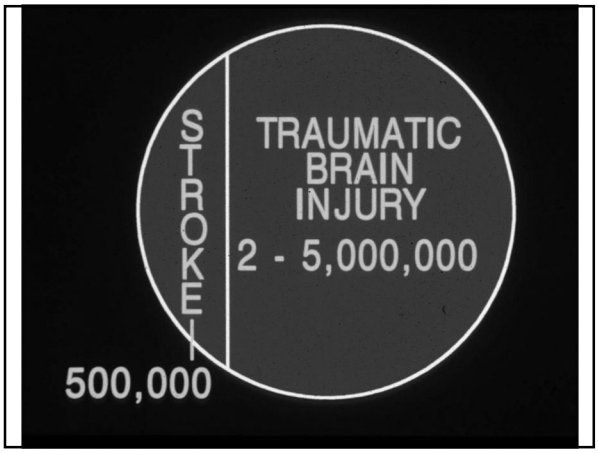






Clinical Neurology: Trauma

Dr. John F. Shea



Traumatic Brain Injury

- Common
- Often Lethal or Severely Disabling
  - "High Stakes"
- Management is often Complex
- Management is often Non Uniform

Primary Brain Injury

- lacerations and contusions
- DAI
- moment of impact
- axon shearing
- GSW
- difficult to change

Secondary Brain Injury

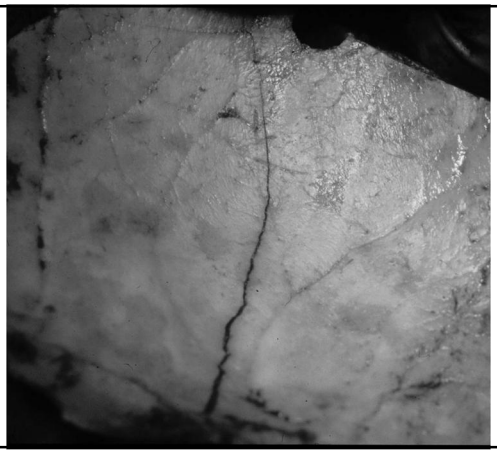
- mass lesions
- ischemia
- free radicals
- hypoxia
- hypertension

CLASSIFICATION OF HI

- SKULL
- FOCAL
- DIFFUSE

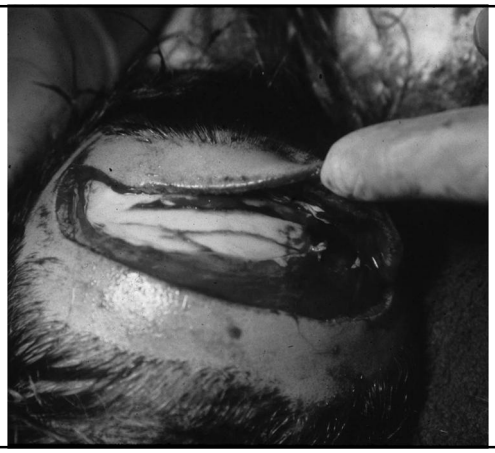
SKULL FRACTURES

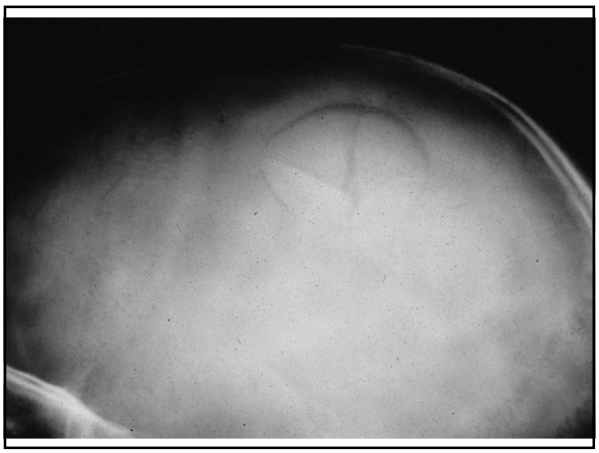
- open or closed
- linear
- depressed
- basilar skull signs
  - a) raccoon sign
  - b) battle sign
  - c) CSF leak
  - d) telechantus

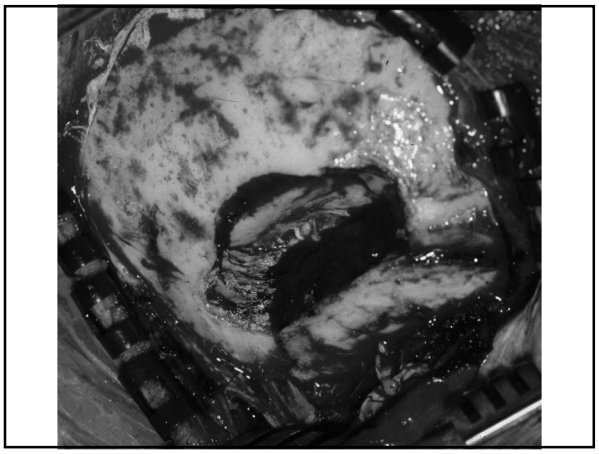


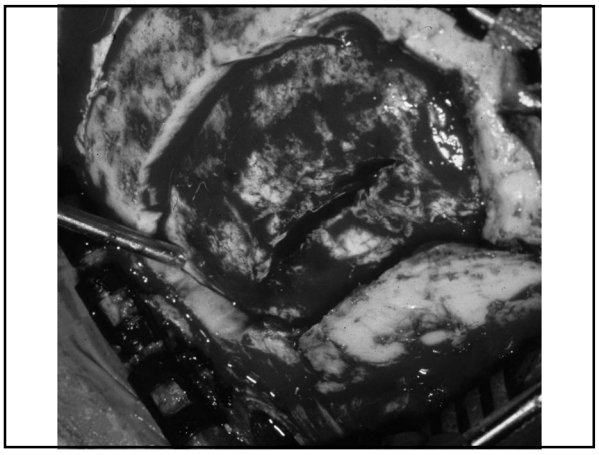
SKULL FRACTURES IMPORTANT

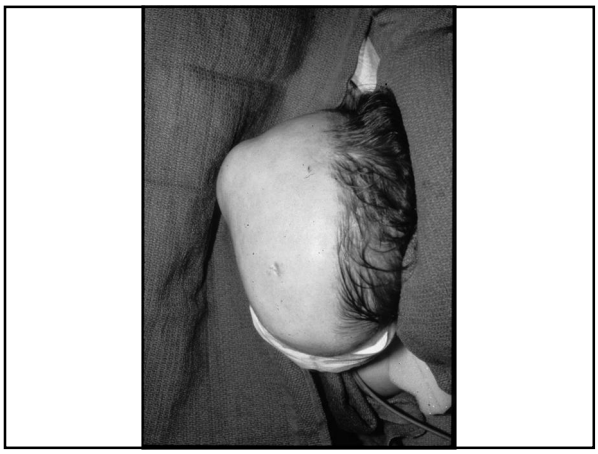
- 1/50 will require surgical procedure
- 1/5000 without skull fracture

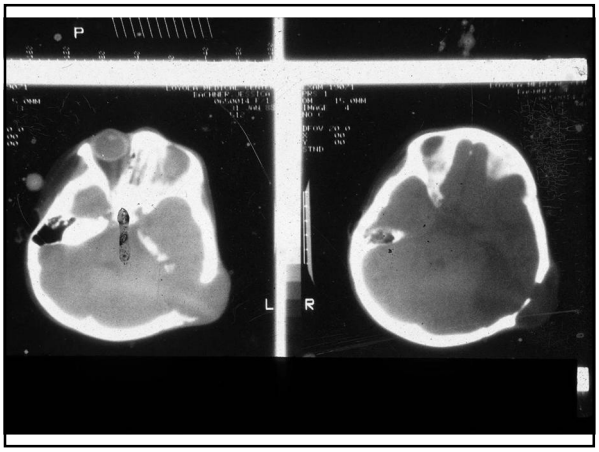








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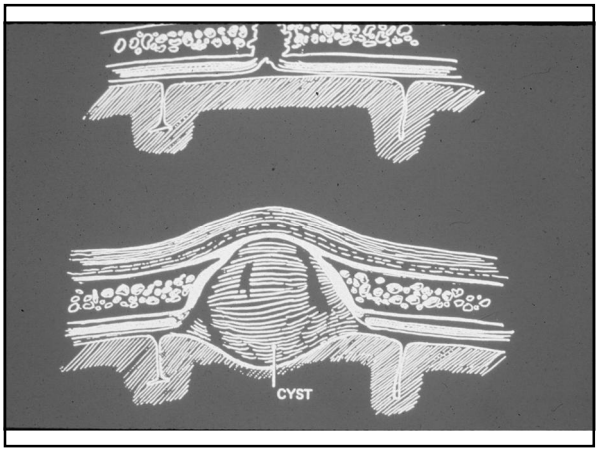
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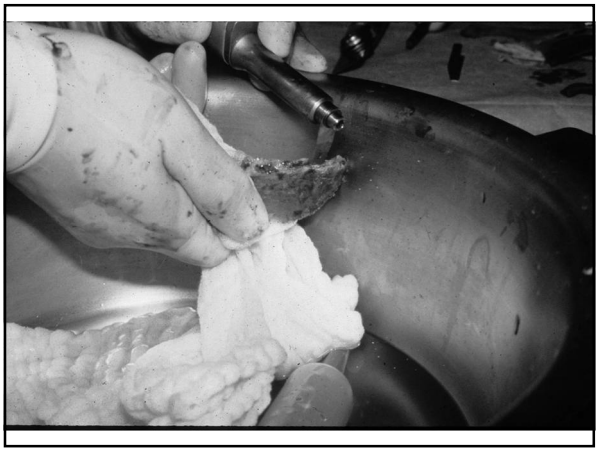
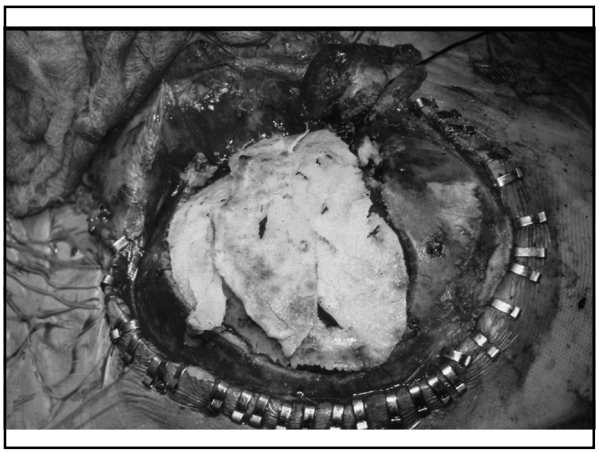
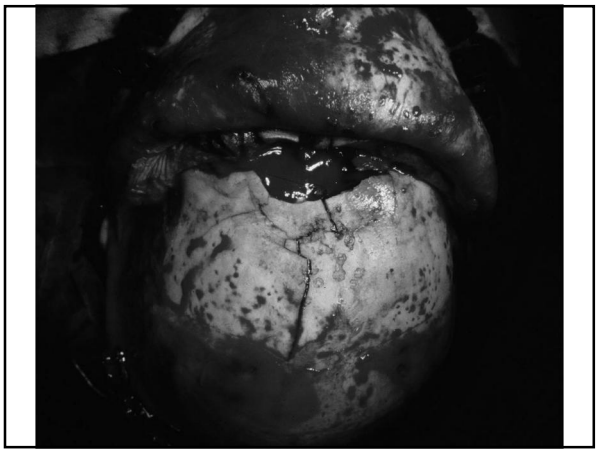
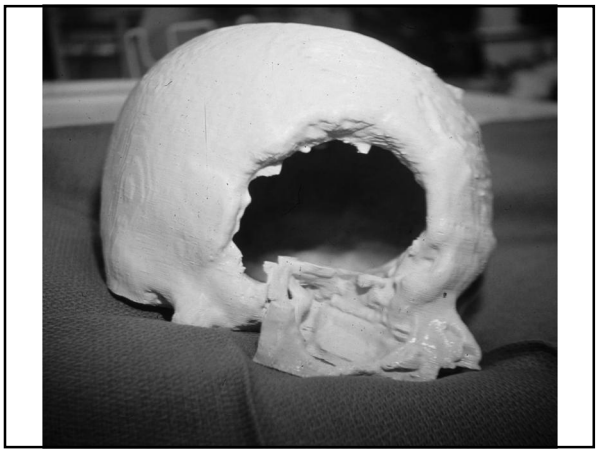
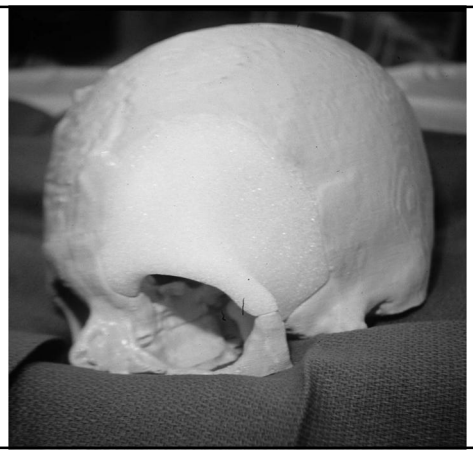


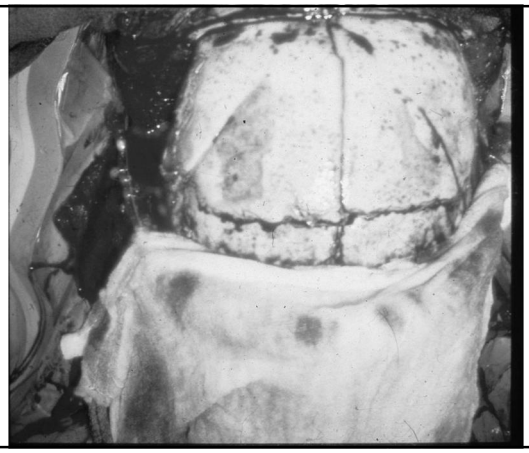


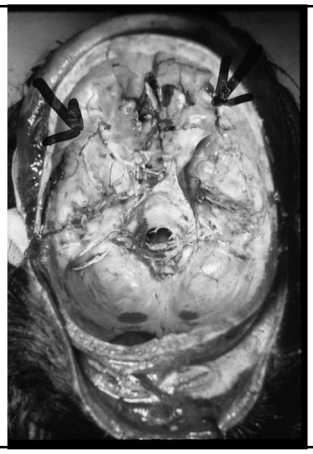






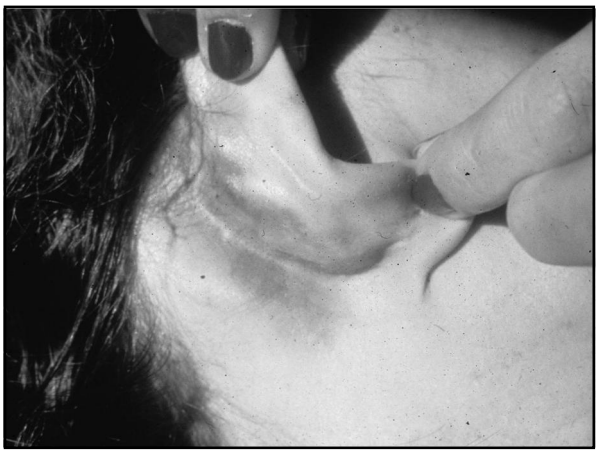
diastatic sagittal suture fracture

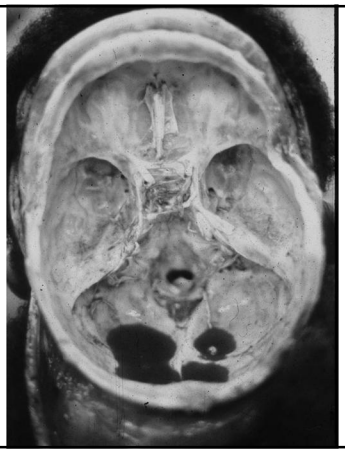


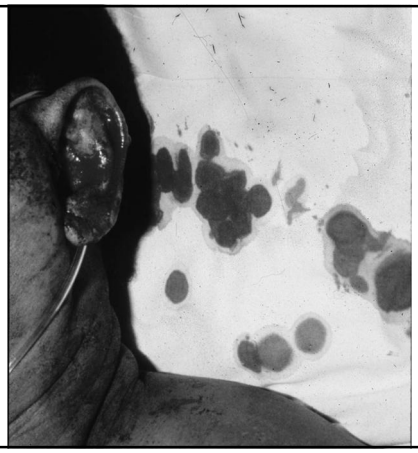


Battle Sign

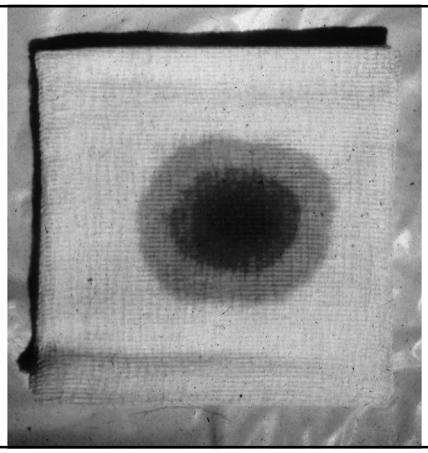
- post auricular ecchymosis

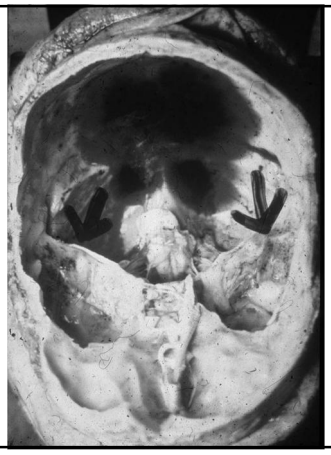


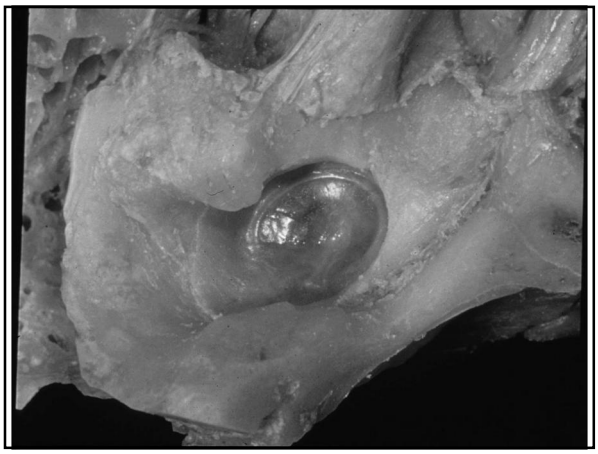




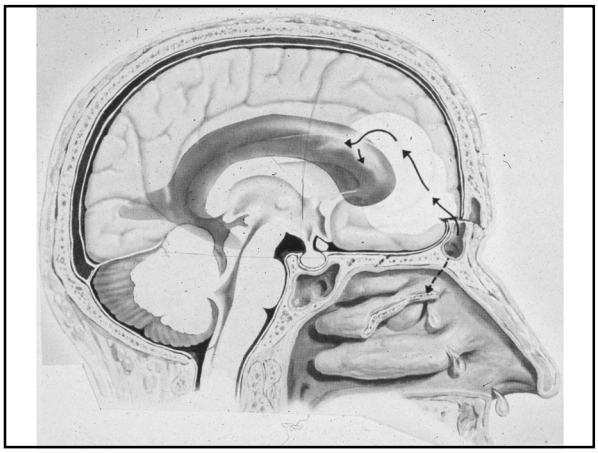
Bulls Eye








Telechanthus



Diagnosis

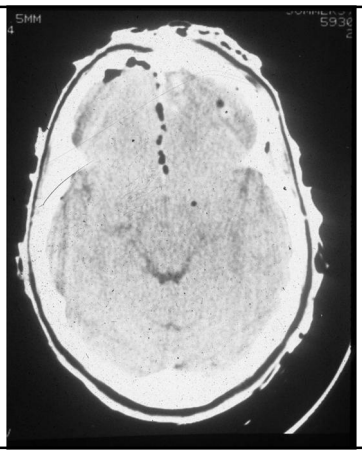
- glucose
  - > 50% - serum
  - 10% - nasal
- reservoir sign
- target sign
- headache (high and low)
- taste (159 meq Na^+)

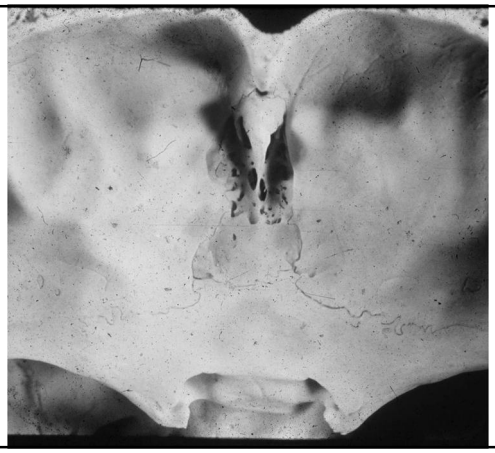
Immunofixation Method

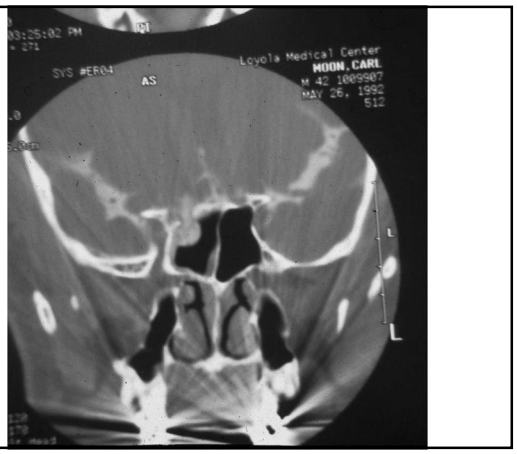
- B_2 transferrin

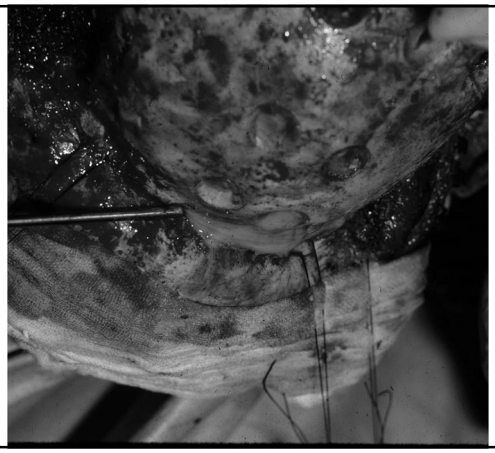
Anterior Cranial Fossa Basilar Fracture

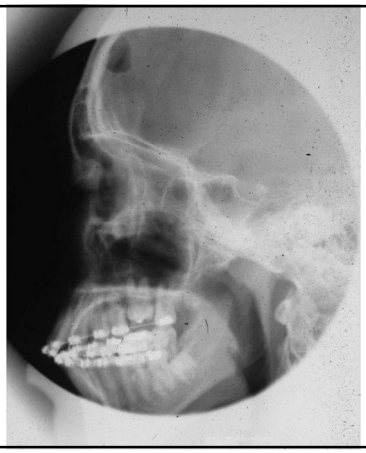
1) Periorbital ecchymosis (Racoon's eyes)
2) CSF Rhinorrhea (25%)
3) Associated with facial fractures and bleeding into the orbit

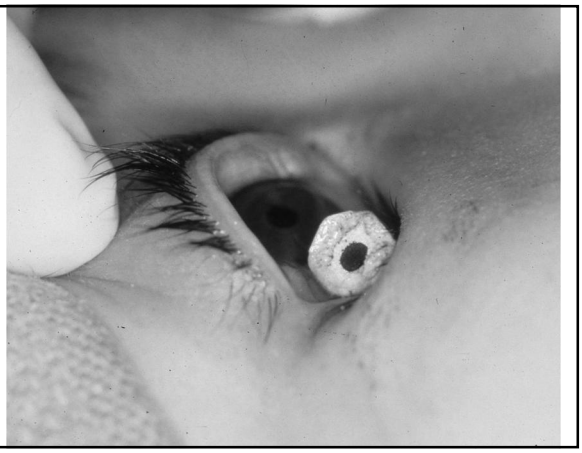

5MM

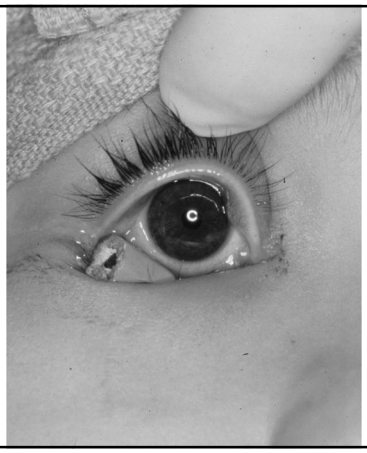


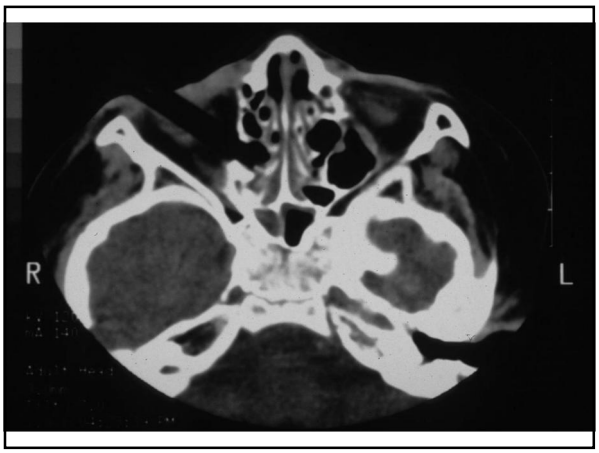

Loyola Medical Center
MOON, CARL
AS
L

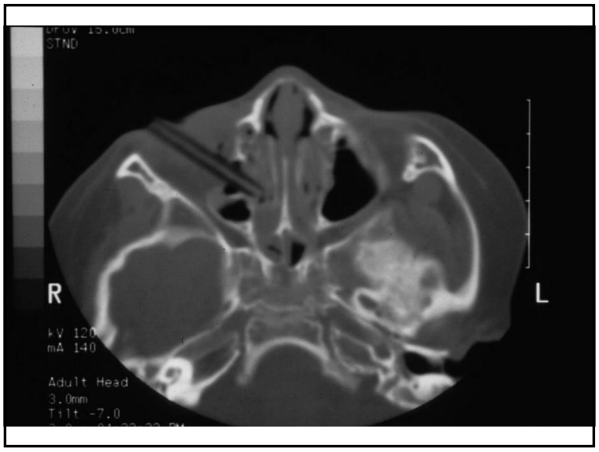


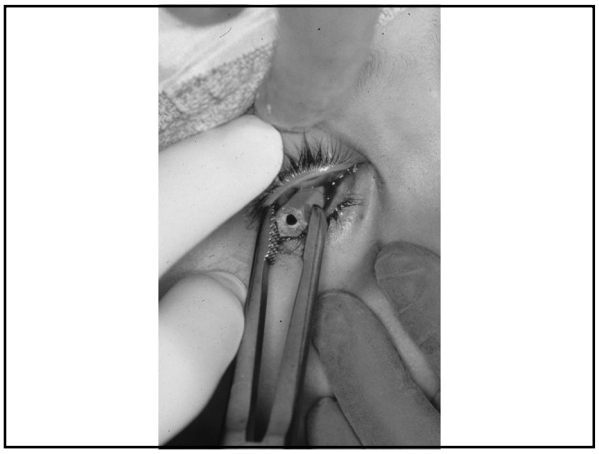


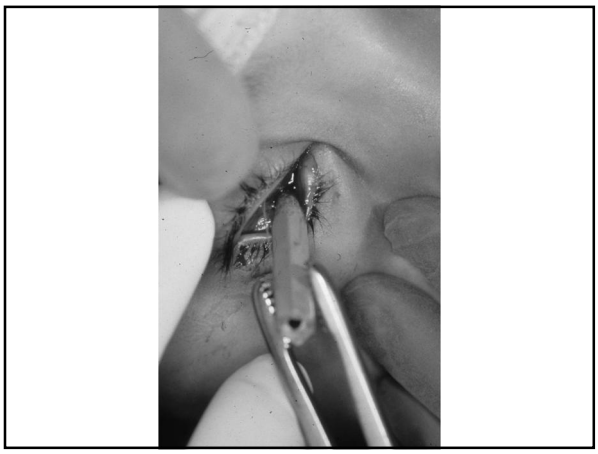


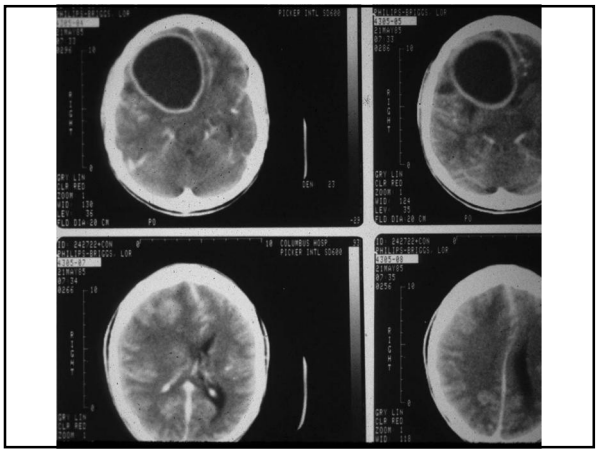


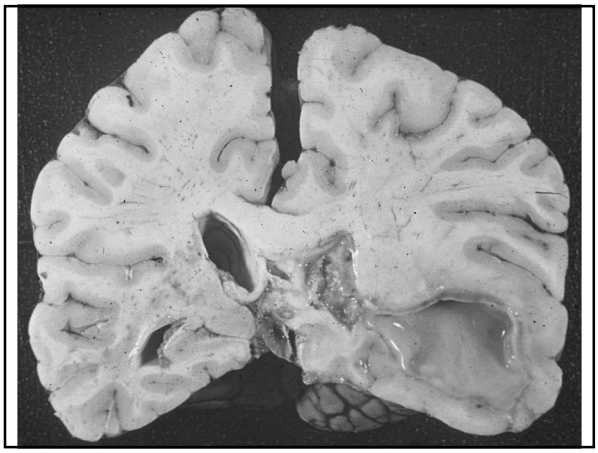

R
L

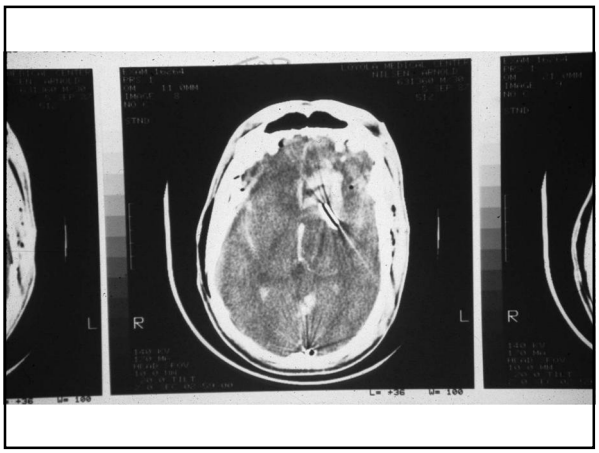

STND
R
L
kV 120
mA 140
Adult Head
3.0mm
Tilt -7.0

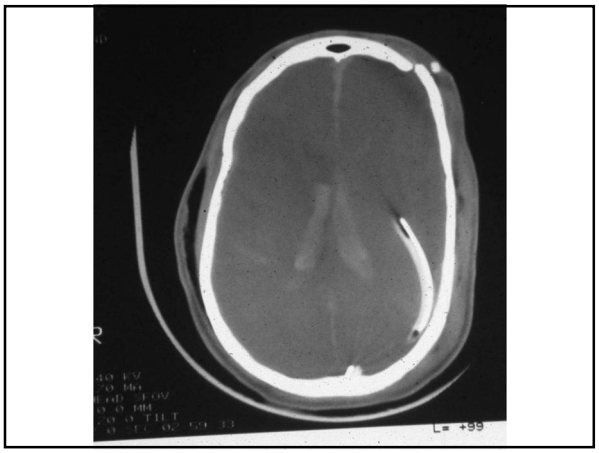


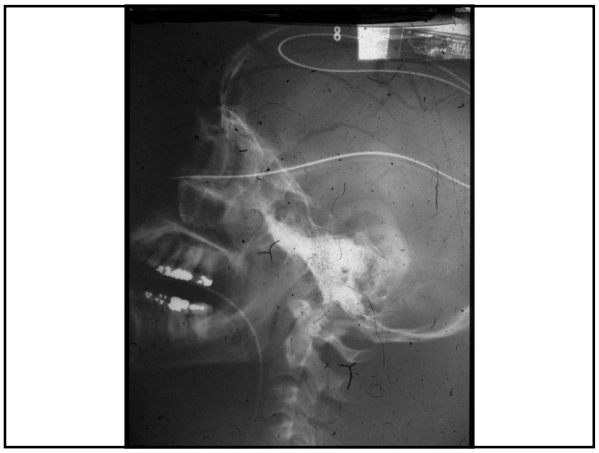






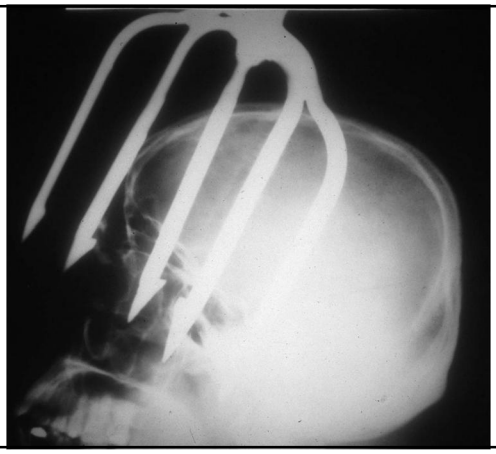

L
R
L
R





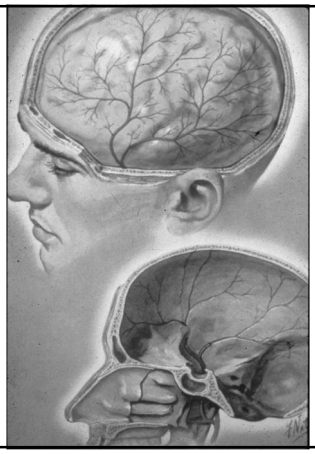
FOCAL INJURIES

- Large enough to be seen with naked eye
- Local brain damage
- Masses within cranium to cause shift
- Coma due to brain stem compression
- 50% of head injuries
- 66% of all deaths



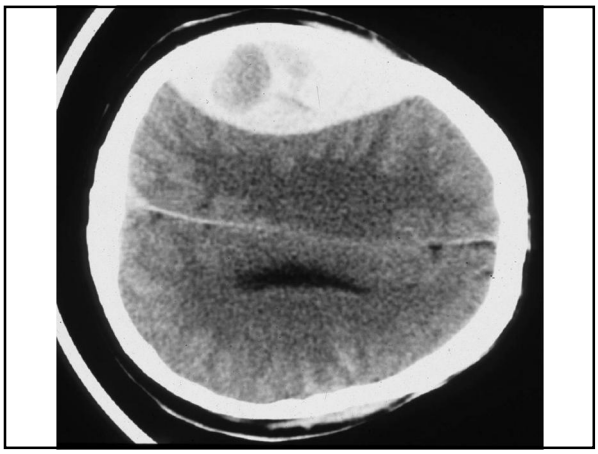
FOCAL INJURY

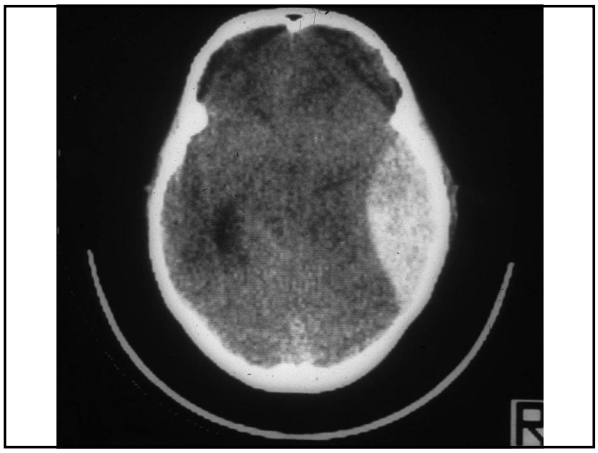
- epidural hematoma
- subdural hematoma
- intracerebral hematoma
- cerebral contusion
- subarachnoid hemorrhage
- brain laceration

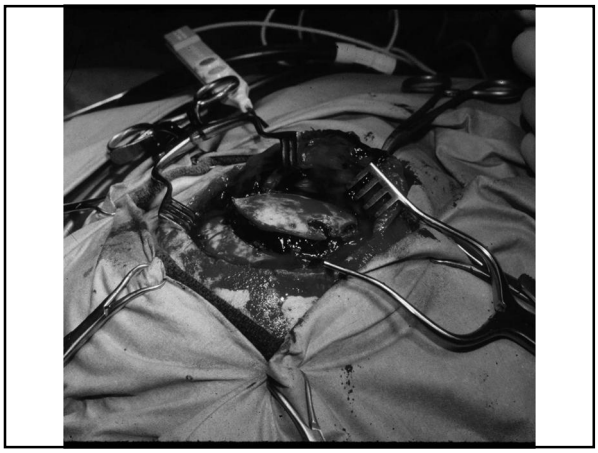


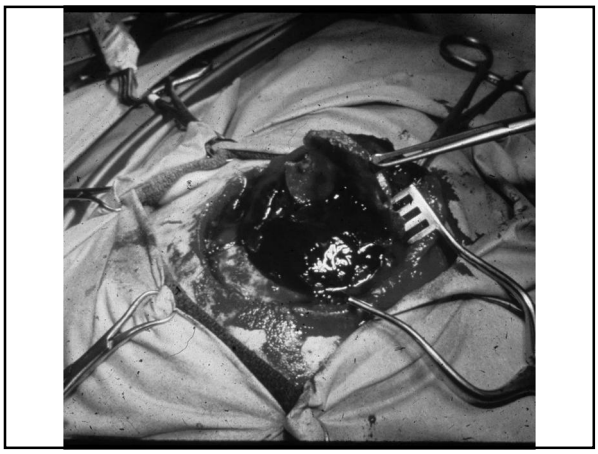
EPIDURAL HEMATOMA

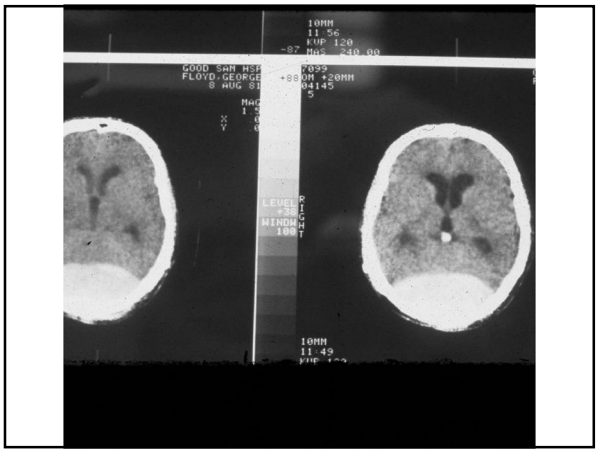
- 0.2 ⟶ 6%
- Second decade
- Skull fractures majority
- Middle meningeal 50%
- Lucid interval 33%










10MM
11:56
KVP 120
-87 MAS 240.00
GOOD SAM HSP
FLOYD,GEORGE
8 AUG 81
+88
7099
0M +20MM
04145
5
LEVEL
+36
WINDOW
100
RIGHT
10MM
11:49

PEDIATRIC PITFALLS

- BLOOD LOSS IS LETHAL
- TACHYCARDIA IS OMINOUS
- < 1 YEAR OF AGE
- HYPERTHERMIA IS LETHAL

FOCAL INJURY

epidural hematoma

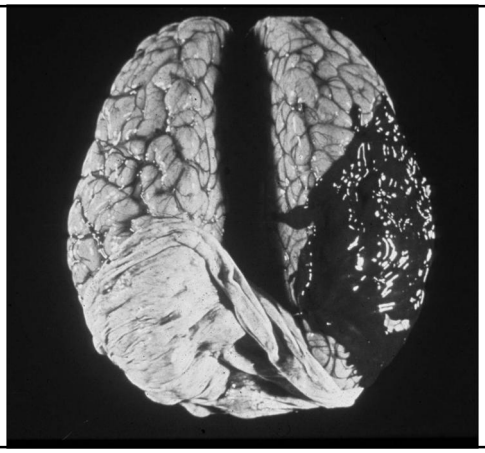
subdural hematoma

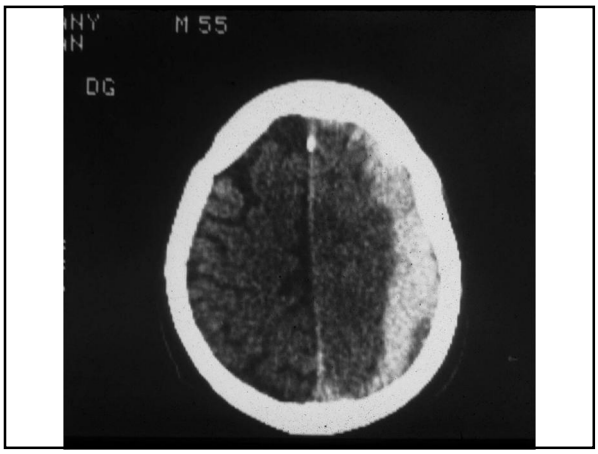
intracerebral hematoma

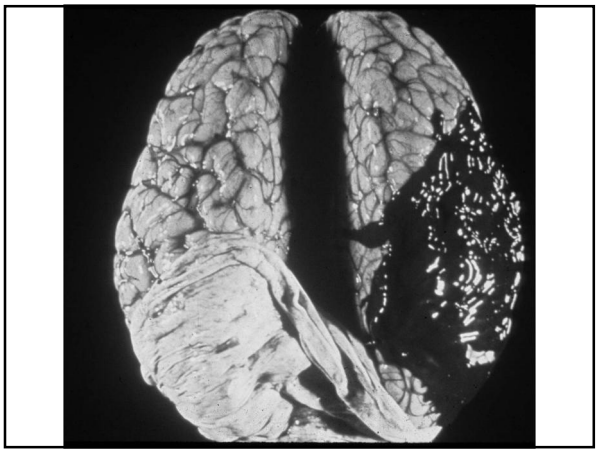
cerebral contusion

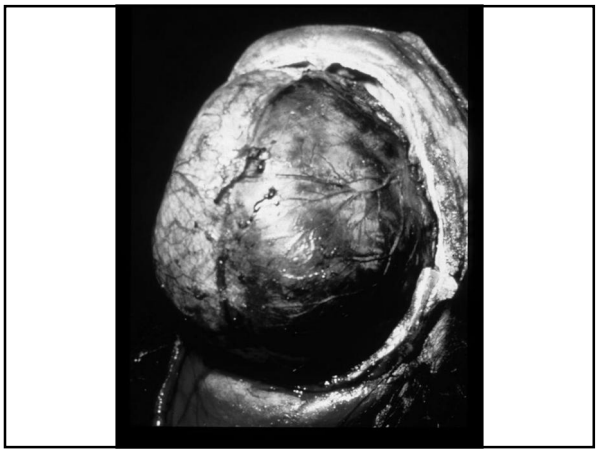
subarachnoid hemorrhage

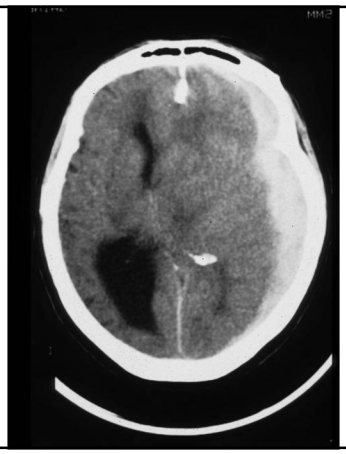
brain laceration

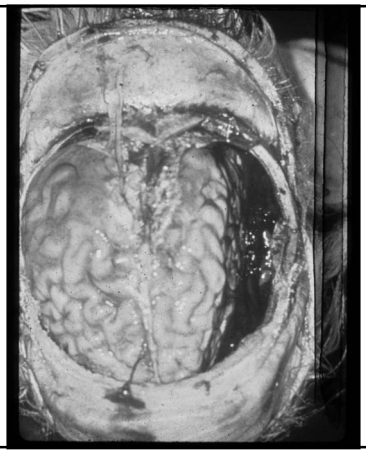


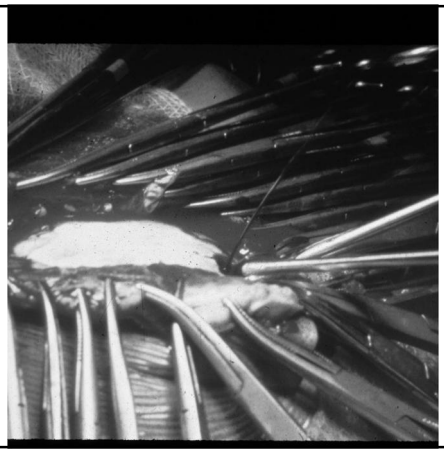

M 55
DG

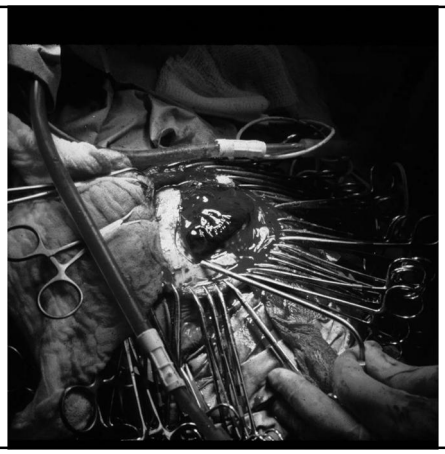


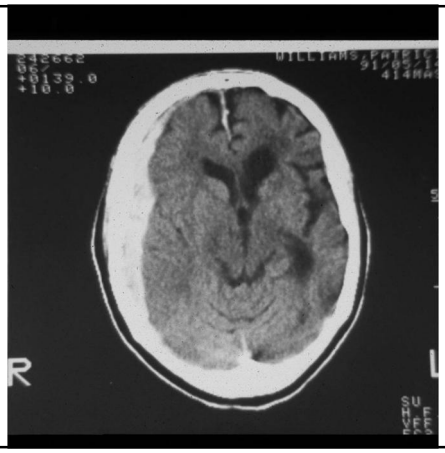






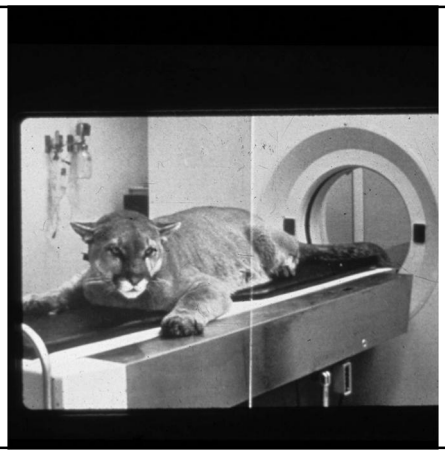


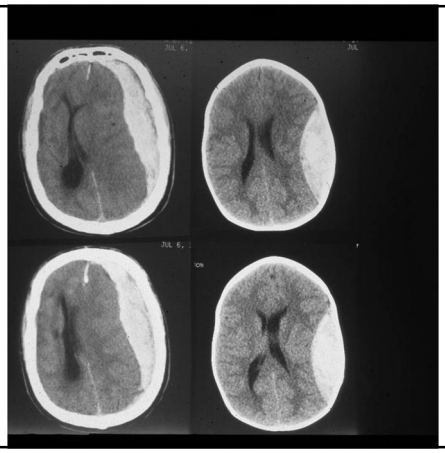




Cerebral Perfusion

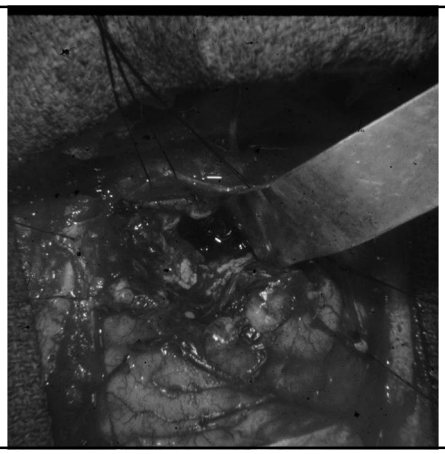
CPP = MAP - ICP

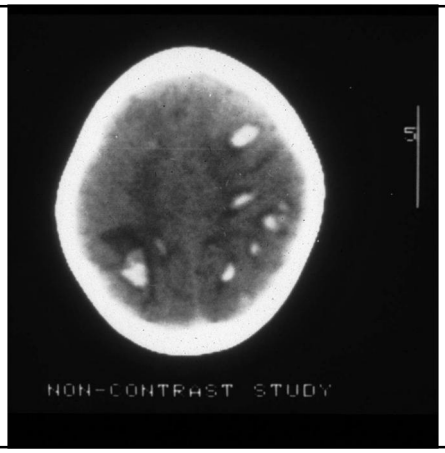




FOCAL INJURY

- epidural hematoma
- subdural hematoma
- intracerebral hematoma
- cerebral contusion
- subarachnoid hemorrhage
- brain laceration





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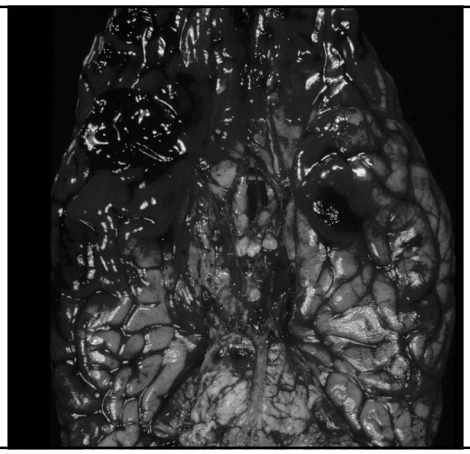
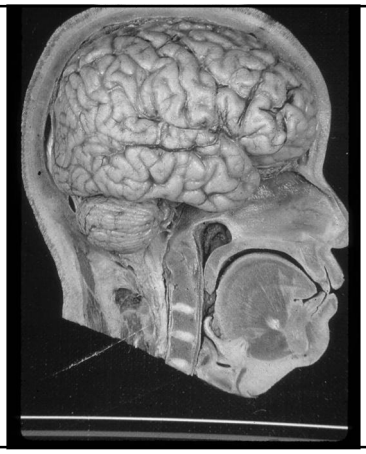
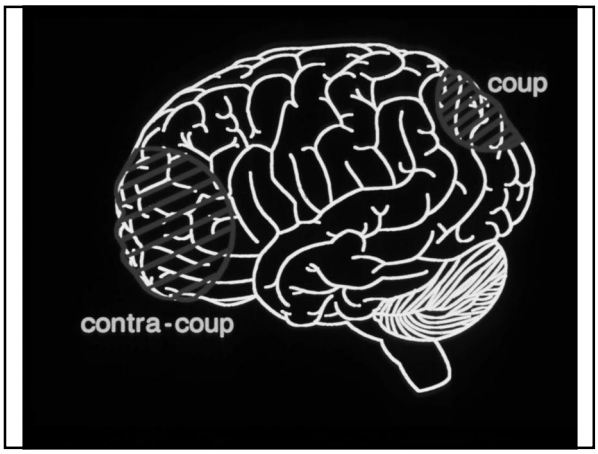
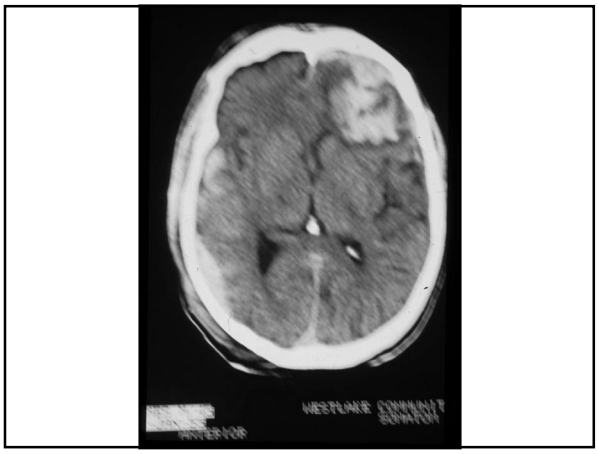


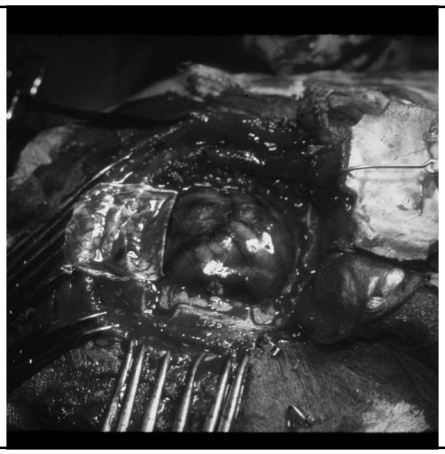
TEMPORAL LOBE
- boxing glove thumb
- contusion

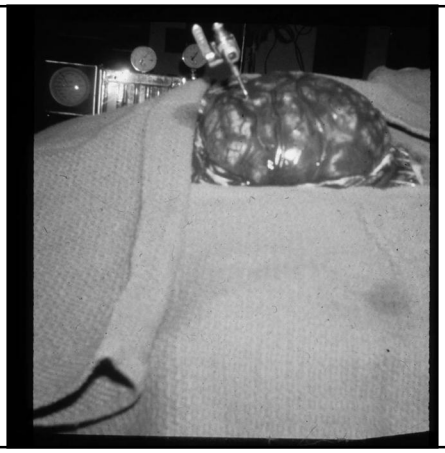


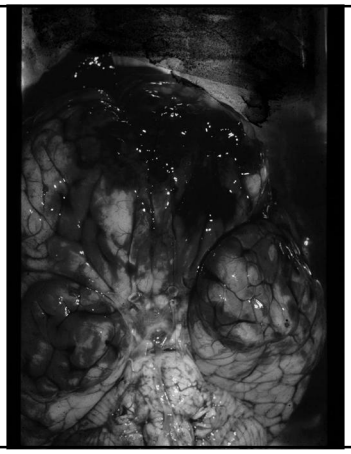


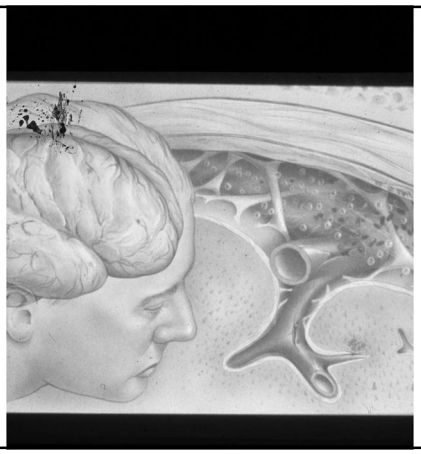


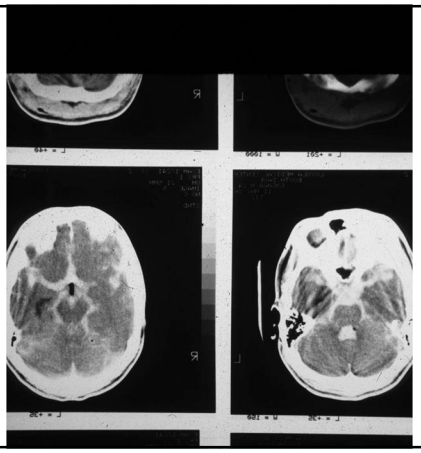
Cerebral Contusion
red angry swollen brain

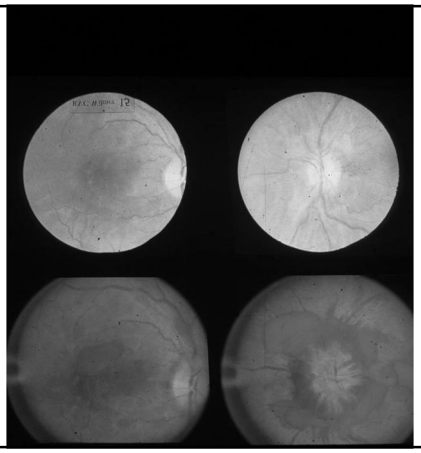


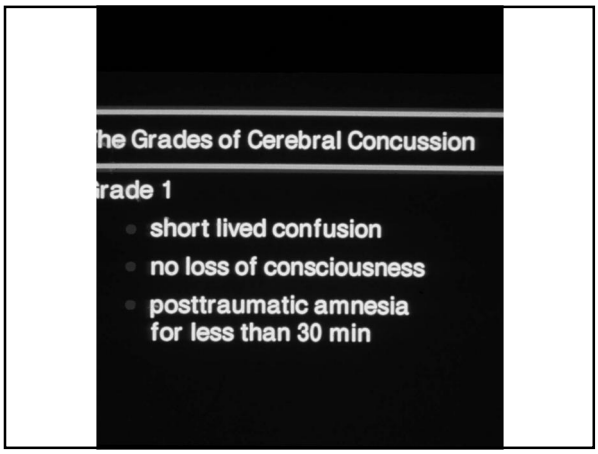


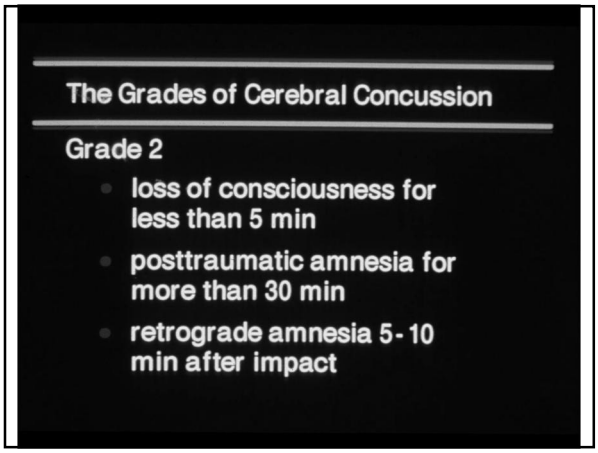


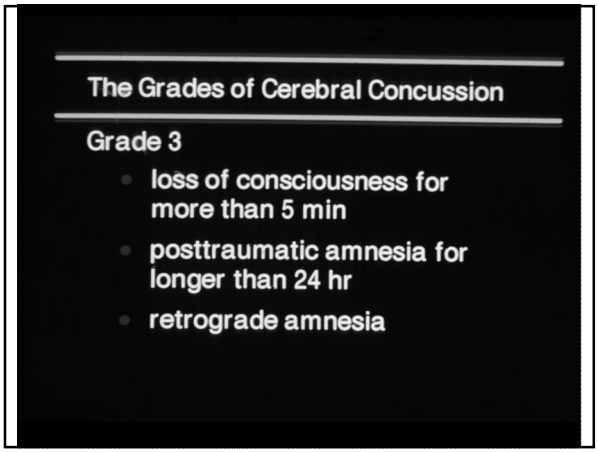




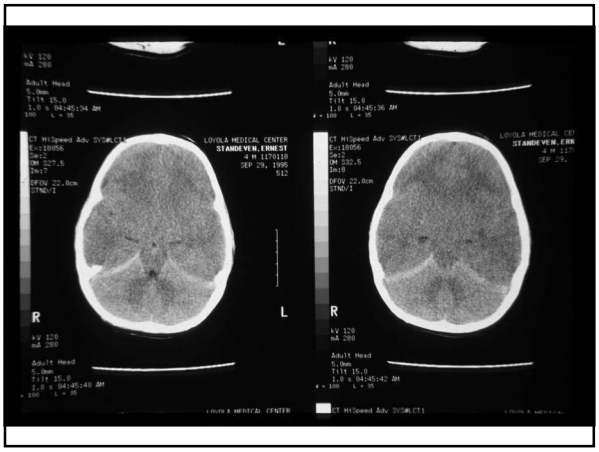



he Grades of Cerebral Concussion
rade 1
short lived confusion
no loss of consciousness
posttraumatic amnesia for less than 30 min


The Grades of Cerebral Concussion
Grade 2
loss of consciousness for less than 5 min
posttraumatic amnesia for more than 30 min
retrograde amnesia 5-10 min after impact


The Grades of Cerebral Concussion
Grade 3
loss of consciousness for more than 5 min
posttraumatic amnesia for longer than 24 hr
retrograde amnesia

DIFFUSE AXONAL INJURY



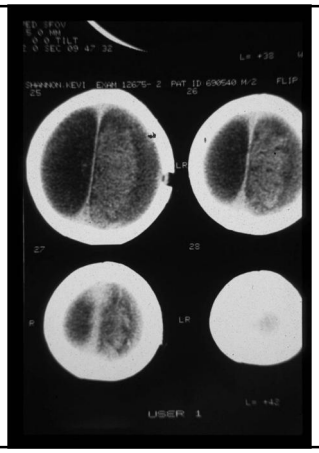
CLASSIFICATION

- MILD DAI
  - COMA 6 - 24 HRS
- MODERATE DAI
  - COMA > 24 HRS
  - NO BRAIN STEM SIGNS
  - 20% MORTALITY
- SEVERE DAI
  - COMA > 24 HRS
  - ⊕ BRAIN STEM SIGNS
  - 60% MORTALITY

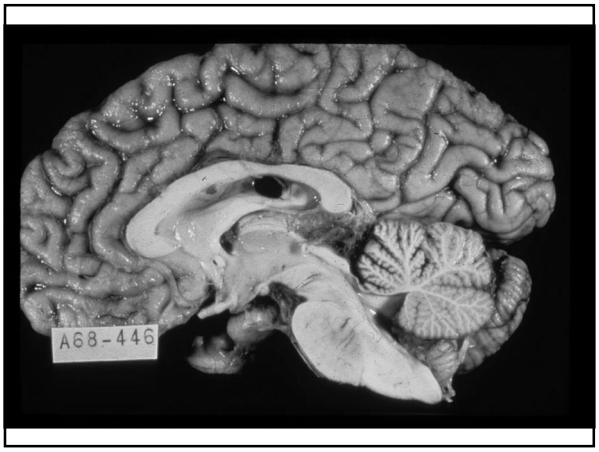
DIFFUSE BRAIN INJURY

- twice as common in children
- 53% mortality vs. 16%

BLACK BRAIN



CAT Scan
NEURONS not AXONS



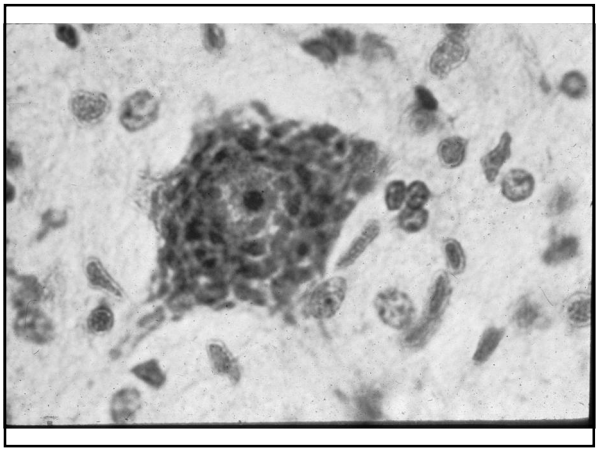
Pieces of the Discussion

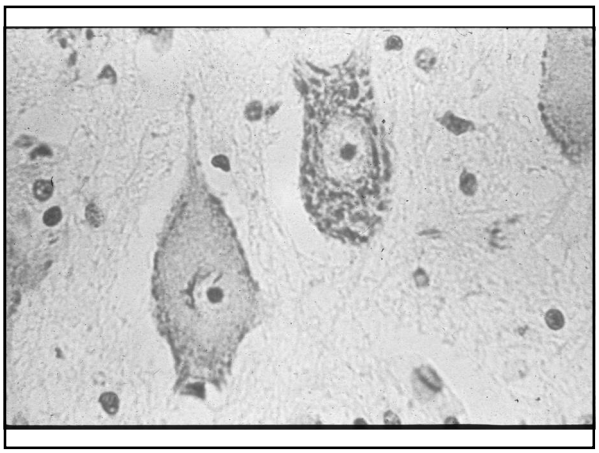
- Traumatic Brain Injury
  - AANS Guidelines
- Prehospital Management of Traumatic Brain Injury
- Aeromedical Management of Traumatic Brain Injury

Hypoxia

- 30%-60% of severely head injured patients are hypoxic
  - Becker DP, Miller JD, Ward JD, et al: J Neurosurg 47:491-502, 1977
  - Miller JD, Sweet RC, Narayan RK et al, JAMA 240:439-442
  - Chestnut RM, Marshall LF, Klauber MR, et al: J Trauma 34:216-22, 1993

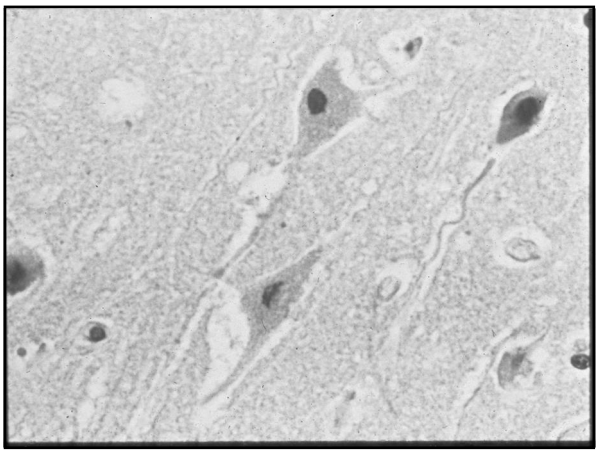
Oxygen is GOOD
Hypoxia is BAD





BETTER DEAD THAN RED

NOT NEURONS



Hypoxia

- temporal lobe most susceptible
- oculomotor nucleus most resistant

Pupils are extremely resistant to hypoxia.

Hypoxia

- Commonly Accepted as Deleterious to the Head Injured Patient
- Documented Evidence that Many Head Injured Patients present with Hypoxic
- Class II Evidence that PaO2<60 is associated with worse outcomes
- No studies tell absolute values

Summary

- Hypoxia is a major contributor to poor outcome in head injured patients
- 30-60% of Head Injured Patients are Hypoxic at some time in their management
- Less than aggressive Airway Management and ventilation leads to hypoxia in 20% of Head Injured patients
- Arterial pO_2>100mm Hg may be needed to assure protection against secondary injury.(Not part of AANS guidelines)

AIRWAY MANAGEMENT IN THE TRANSFER OF UNCONSCIOUS PATIENTS

Annals of the
Royal College of Surgeons
of England

November, 1983 Robinson, et al

INTUBATION

- ☑ Gold Standard
- ☑ Oral vs Nasal
- ☑ Not children

Oral Intubation

vs.

Nasal Intubation

Children have airways.

96% OF SPINAL INJURIES
ORAL ENDOTRACHEAL
INTUBATION

HYPERVENTILATION

- Mainstay
- Immediate
- Pressure refractory to hypocarbia poor prognosis
- $PaCO_2$ 25-30 torr

Outcome Studies

- Muizelaar 1991
  - Prospective,randomized clinical trial
  - 77 patients
  - Hyperventilation(pCO_2 25) vs.. Normocapnia (pCO_2 35)
  - At 3 and 6 months patients with GCS 4-5 in the hyperventilated group had a significantly worse outcome.
    - Muizelaar JP, Marmarou A, Ward JD, et al:J Neurosurg 75:731-739, 1991

Hyperventilation

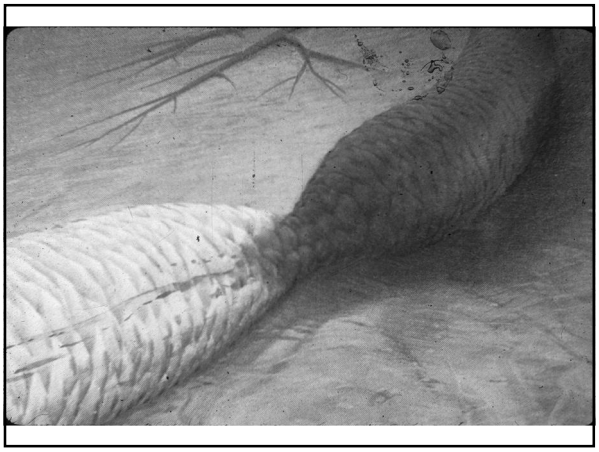
- CBF the first day after injury is less than half that of normal individuals
  - Typically 30cc/100g/min during first 8 hours after injury
  - May be less than 20cc/100g/min in first four hours in patients with the worst injuries
    - Bouma GJ, Muizelaar JP, Choi SC, et al: J Neurosurg 75:685-693, 1991
    - Bouma GJ, Muizelaar JP, Stringer WA, et al: J Neurosurg 77:360-368, 1992
    - Cruz J:J Neurosurg 80:143-147, 1994
    - Fieschi C, Battistini N, Beduschi A, et al: J Neurol Neurosurg Psyciatry 37:1378-1388, 1974

Hyperventilation

- Histologic evidence of cerebral ischemia is found in most patients who die of TBI

ischemic brain death

Cerebral ischemia dominates traumatic brain injury as the single most important event determining outcome.



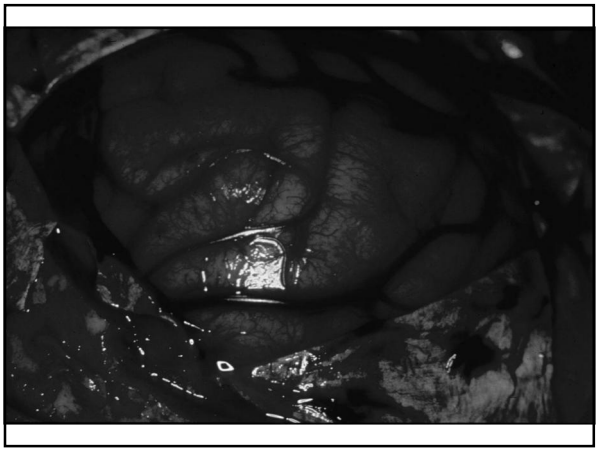
Hyperventilation acts by reducing CBF via vasoconstriction

- Evidence that Hyperventilation may lead to significant ischemia and further cellular injury.

Hyperventilation

- AANS Guidelines
  - In the presence of clinical signs of herniation, hyperventilation should be used
    - » unilateral of bilateral pupillary dilatation
    - » Asymmetric pupillary reactivity
    - » motor posturing
    - » deterioration of neurologic exam
  - There is evidence that short periods of hyperventilation may not lead to metabolic damage
    - Letarte PB, Puccio A, Brown D, Marion DW: In Press

Which is the larger effect from Hyperventilation, the benefit of ICP reduction or the threat of cerebral ischemia?



Hyperemia

- ✓ global CBF >55
- ✓ 1/3 of TBI
- ✓ increased ICP
- ✓ 1-5 days post-trauma
- ✓ better outcome

Hypotension

- Patients with a single episode of SBP<90 have a statistically significant worse outcome
  - Chestnut RM, Marshall LF, Klauber MR, et al: J Trauma 34:216-22, 1993
- Patients whose hypotension is not corrected in the field have a worse outcome
  - Chestnut RM, Marshall LF, Klauber MR, et al: J Trauma 34:216-22, 1993
  - Fearnside MR, Cook RJ, McDougall P, et al:Br J Neurosurgery 7:267-279, 1993

Hypotension

- Long Acknowledged as a Major cause of morbidity and Mortality in Head Injury
  - MillerJD, Sweet RC, Narayan R, et al, JAMA240:439-442, 1978
- Multiple studies have shown the disastrous consequences of hypotension in the field.
  - Chestnut RM, Marshall LF, Klauber MR, et al: J Trauma 34:216-22, 1993
  - Fearnside MR, Cook RJ, McDougall P, et al:Br J Neurosurgery 7:267-279, 1993
  - Gentleman D: Int Surg 77:297-302, 1992
  - Kohi YM, Mendelow AD, Teasdale GM et al: Injury 16:25-29, 1984

Hypertonic Saline

- 7.5% saline
- 250cc = 2500cc
- rob Peter to pay Paul
- cellular robbery

INJURED BRAIN

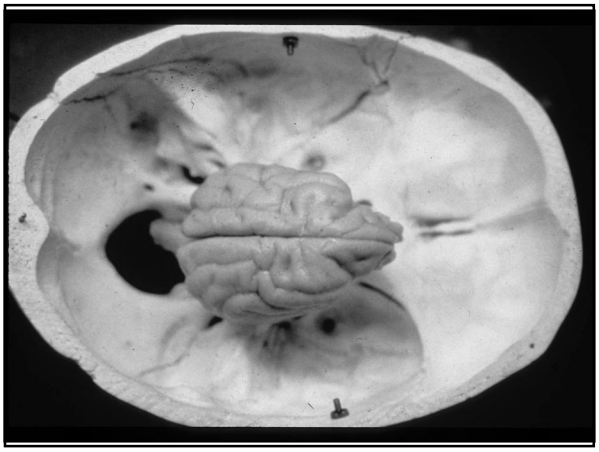
- 15 min hypotension
- CBF ≠ SAP
- CBF → C.O. ↓ hyperventilation
- Hypertonic saline
- Neosynephrine at scene?

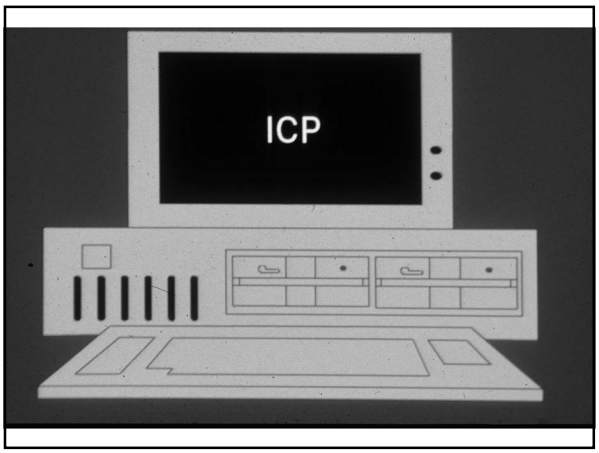
Summary

- True desirable level for Blood Pressure in the field is unknown
- Current level of SBP>90 is arbitrary
- Patients with one episode of SBP<90 have worse outcomes
- Even with attention to blood pressure, hypotensive episodes are common

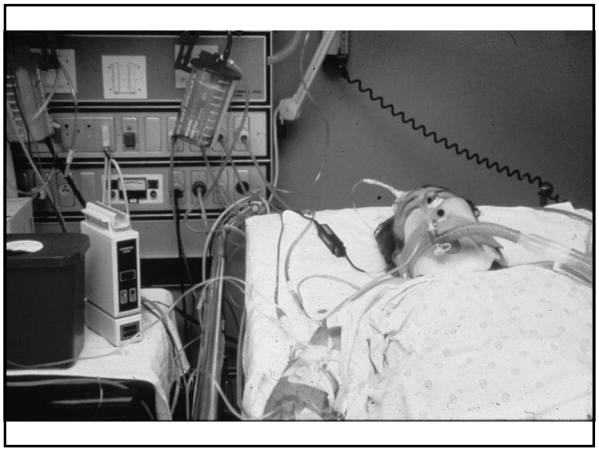
Do IV Fluids Help?

DO NOT DEHYDRATE
THE BRAIN



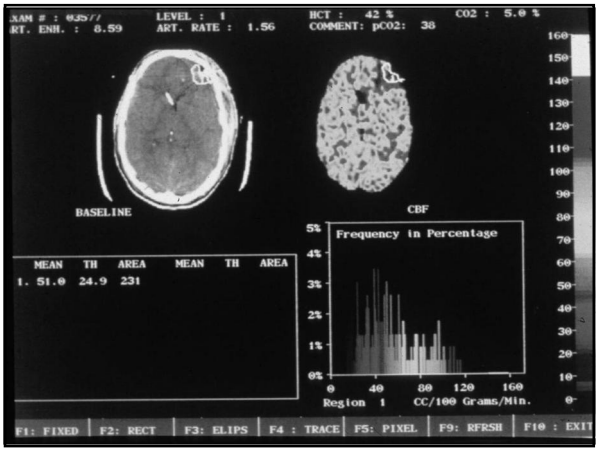


INTRACRANIAL HYPERTENSION IS THE MOST COMMON CAUSE OF DEATH FOLLOWING A CATASTROPHIC NEUROLOGICAL EVENT



Hypothermia Study

- temperature decrease 32° C for 48 hours
- watch potassium with rewarming
- brain one degree higher

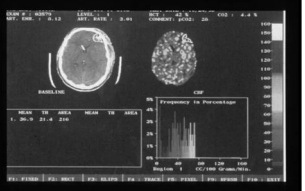


ICP

- ✓ maximum medical treatment
- ✓ sedation
- ✓ CSF drainage
- ✓ paralysis
- ✓ osmotic therapy
- ✓ hyperventilation
- ✓ hypothermia
- ✓ surgical

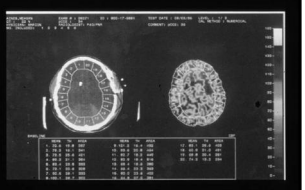
XeCT

- Ischemia or Normal Blood Flow
  - Hypothermia
  - Decompressive Craniectomy



XeCT

- Hyperemia
  - Escalate Hyperventilation
  - Hypothermia
  - Decompressive Craniectomy



When Do We Hyperventilate ???

- ✓ GCS drops 3 points
- ✓ unilateral extremity weakness
- ✓ unilateral pupil change

BLOOD GLUCOSE IN SBI

- Intracranial hemorrhage ↑
- Secondary ischemia versus physiological response
- Neurological outcome ↓

Barbiturate Coma

- Must be clear on endpoints
  - ICP Control
  - Burst Suppression
    - EEG Monitoring
  - Drug Levels

Cerebyx: fosphenytoin sodium

- ✓ better at IV site
- ✓ infused 3X faster
- ✓ water soluble - pH 9
- ✓ IM injection

Brain Resuscitation

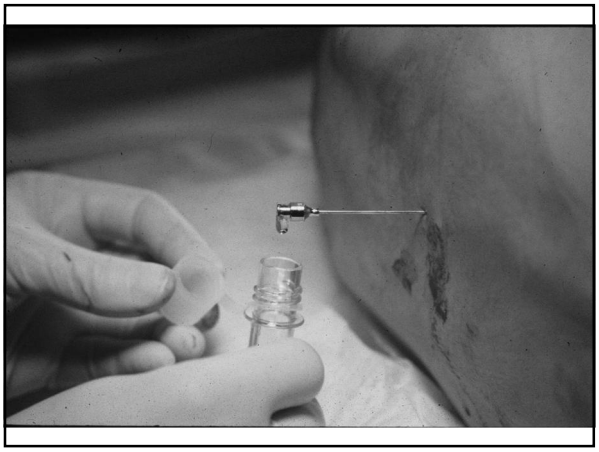
- hypermetabolic
- glucose intolerance
- hypercatabolic

POOR OUTCOME

- High glucose on admission
- Abnormal magnesium level
  < 1.8 or > 2.4

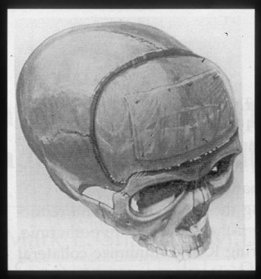
ARE STEROIDS BENEFICIAL FOR TRAUMATIC BRAIN INJURY ? ? ?

DO PROPHYLACTIC ANTICONVULSANTS PREVENT SEIZURES ? ?



Decompressive Craniectomy

- Best results seem to be in children
- No data exists
- Use highly dependent on local experience



P.V.S.

- eyes open spontaneously
- awake but unaware
- no comprehensive words
- no obey commands
- normal temp - BP - respiration

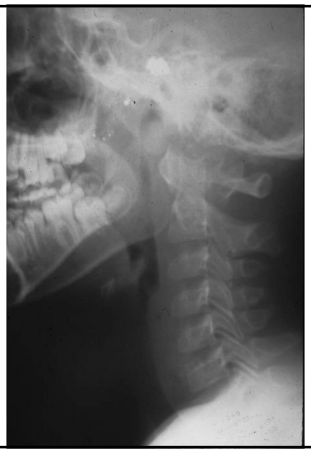
PERSISTENT VEGETATIVE STATE

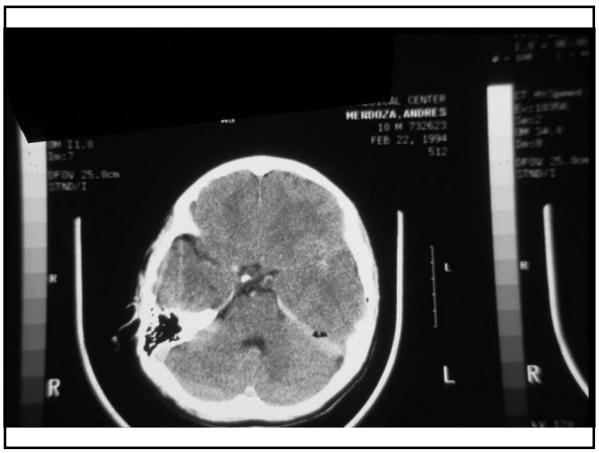
- 20 years approx $2.8 million
- Feed themselves $900,000
- Bowel and bladder continent $250,000

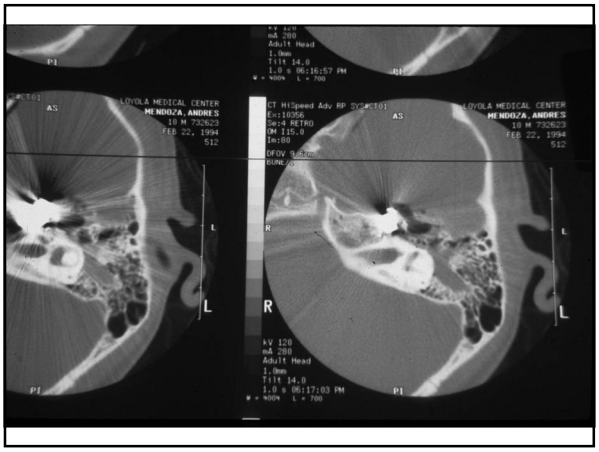
PERSISTENT VEGETATIVE STATE

- 650 patients - 14% P.V.S.
- worse GCS
- diffuse injury
- midline shift
- consciousness
  - 41% - 6 months
  - 52% - 1 year
  - 58% - 3 years

Traumatic Data Coma Bank
Arch Neurol, 1991




MENDOZA, ANDRES
10 M 732623
FEB 22, 1994
512
R
L
R
L
R


LOYOLA MEDICAL CENTER
MENDOZA, ANDRES
10 M 732623
FEB 22, 1994
512
Adult Head
1.0mm
Tilt 14.0
L
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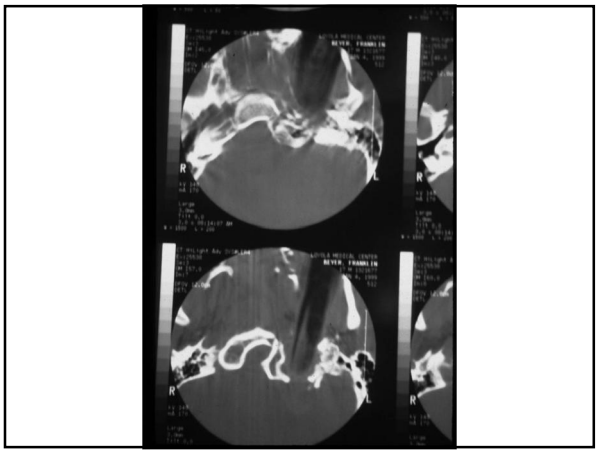
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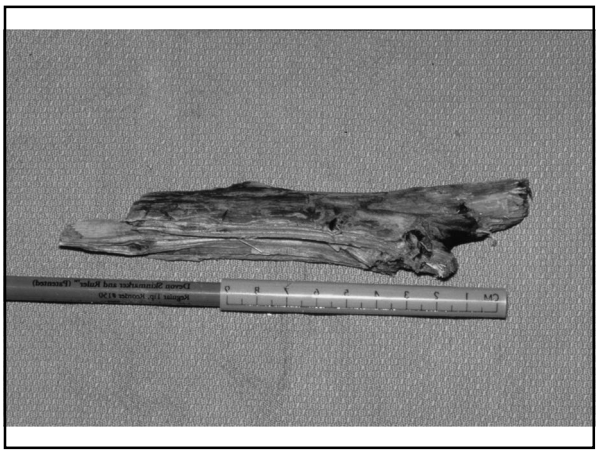
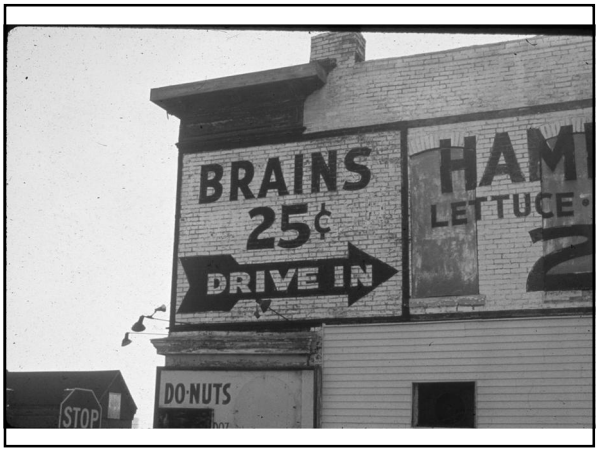



BRAINS
25¢
DRIVE IN
LETTUCE
DO-NUTS
STOP

NEURODEGENERATIVE DISEASES

John M. Lee, M.D., Ph.D.

Read:*Robbins Pathologic Basis of Disease* (Cotran, Kumar, Robbins) 7th Ed. Chapter 28, pp. 1385-1397. Castro, Neuroscience text, pp. 261-264; 345-349.

I. INTRODUCTION

A. IN ALL NEURODEGENERATIVE DISEASES, THERE IS A "SELECTIVE" VULNERABILITY OF BOTH:

1. specific neurons in any one brain area as well as
2. specific neuronal systems within the brain as a whole.

B. ALL NEURODEGENERATIVE DISEASES ARE PROGRESSIVE AND IRREVERSIBLE.

C. NEURODEGENERATIVE DISEASES THAT AFFECT SIMILAR BRAIN REGIONS GENERALLY WILL HAVE SIMILAR CLINICAL SYMPTOMS.

D. NEURODEGENERATIVE DISEASES CAN DIFFER, HOWEVER, IN PATTERNS OF HERITABILITY, MICROSCOPIC FEATURES AND TIME COURSES.

II. DISEASES PRIMARILY AFFECTING THE CEREBRAL CORTEX

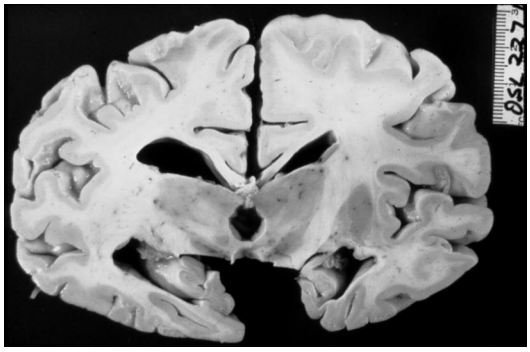
A. ALZHEIMER'S DISEASE (AD)

1. Most common cause of senile dementia in patients over the age of 65 years, the prevalence rate is approximately 2.5 % of the population over 65 years of age.
2. There is a slight female predominance for the development of AD.
3. Approximately 10% of the cases are familial and inherited in an autosomal dominant fashion.

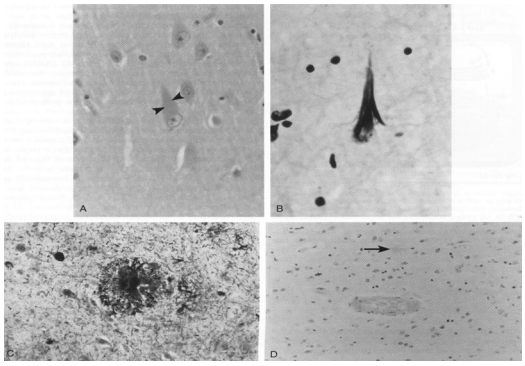
4. The major pathological features are:

   On gross examination, there is decreased brain weight, generalized cerebral atrophy, hydrocephalus ex vacuo, and atrophy of the hippocampus and amygdala.

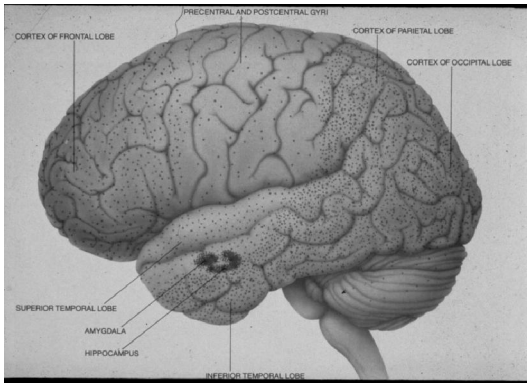
ALZHEIMER'S DISEASE
HIPPOCAMPAL ATROPHY



ALZHEIMER'S DISEASE PATHOLOGY



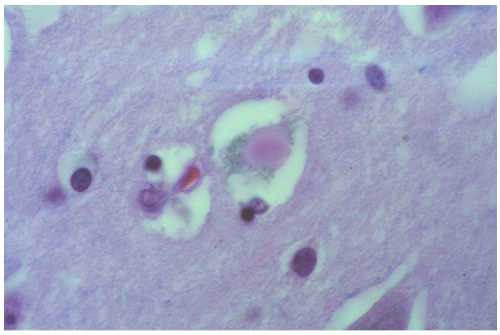
ANATOMICAL DISTRIBUTION



- The major pathological features microscopically, there is loss of cortical neurons, variable reactive gliosis, intraneuronal neurofibrillary tangles (NFT's) composed of paired helical filaments, dystrophic neurites, and neuropil deposition of senile or amyloid plaques.

- In some 20% of cases rather than NFT's cortical neurons contain predominately Lewy bodies. These cases are called the Lewy Body Variant of Alzheimer's Disease.

CORTICAL LEWY BODY



•The amyloid plaques and NFTs are most numerous in the association areas of the neo-cortex as well as in the limbic system. In the neocortex, it is the large neurons in layers 3 and 5 that are selectively vulnerable to NFT formation. There is relative sparing of the primary sensory areas in all but the most severe cases

- Cerebral amyloid angiopathy of subarachnoid and cortical vessels is found to a variable extent in patients with AD. The amyloid that is deposited in the vessel walls is the same amyloid that is found in the senile plaques.

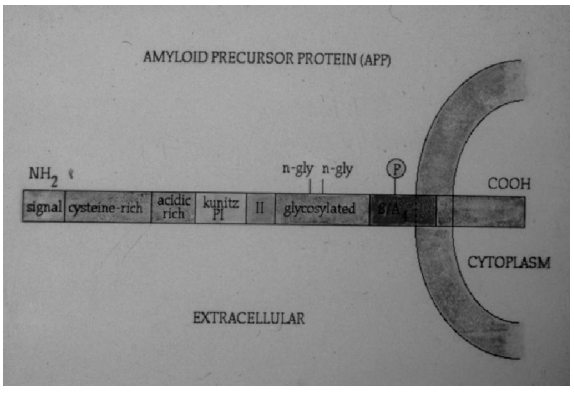
A. ALZHEIMER'S DISEASE (AD)

5. A major component of senile plaques is an unique molecule called ßeta-amyloid. It is a fragment of a larger transmembrane protein called Beta amyloid precursor protein (β-APP) coded for on chromosome 21. The normal function of this precursor protein and the role of β-amyloid has not been elucidated.

A. ALZHEIMER'S DISEASE (AD)

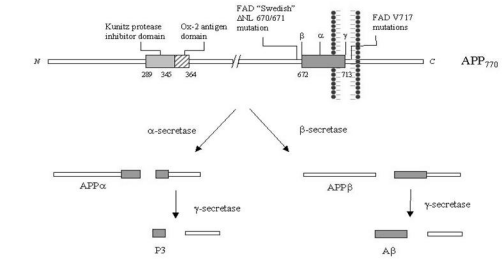
6. The number of plaques and tangles is only roughly correlated with the severity of dementia. However, the amount of synaptic loss and deposition of dystrophic neurities (abnormal axonal and dendritic elements) is better correlated with the severity of the dementia.

7. It is important to remember that subcortical nuclei that project to the neocortex are also degenerate In AD. These systems include the cholinergic nucleus basalis of Meynert in the basal forebrain and the pontine noradrenergic locus cereuleus and serotonergic raphe nuclei.



Amyloid Precursor Protein

Figure 1



(Wilson, Doms and Lee, 2000))

B-APP PROCESSING

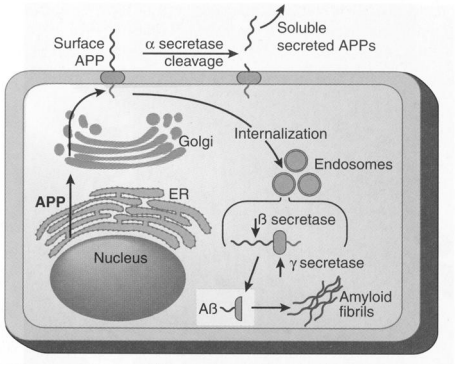


TABLE 28-2 GENETICS OF ALZHEIMER DISEASE

Chromosome	Gene	Mutations/Alleles	Consequences
21	Amyloid precursor protein (*APP*)	• Single missense mutations Double missense mutation Trisomy 21 (gene dosage effect)	• Early-onset FAD Increased Aβ production
14	Presenilin-1 (*PS1*)	• Missense mutations Splice site mutations	• Early-onset FAD Increased Aβ production
1	Presenilin-2 (*PS2*)	• Missense mutations	• Early-onset FAD Increased Aβ production
19	Apolipoprotein E (*APOE*)	• Allele ε4	• Increased *risk* of development of AD Decreased age at onset of AD

AD, Alzheimer disease; FAD, familial Alzheimer disease.

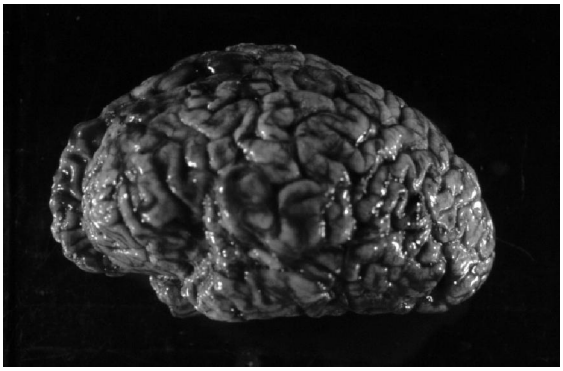
A. ALZHEIMER'S DISEASE (AD)

8. Current research is now focused on the role of β-APP and its fragment β-amyloid in the etiology of the disease. This is based on the discovery of mutations in the gene coding for β-APP in familial cases of AD and the fact that people with Down's syndrome (Trisomy 21) if they live into their 40's and 50's will usually develop the clinical and microscopic features of AD
9. Recently, mutations on chromosomes 14 & 1 have also been implicated in the familiar forms of AD. These code for Presenilin 1 and Presenilin 2 proteins, respectively. They have been implicated in abnormal β-APP processing.

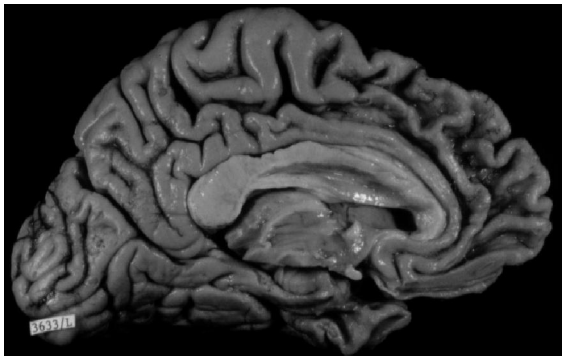
B. PICK'S DISEASE

1. Rare form of dementia (only 1 % of all dementia cases over 65 years of age) where patients present with aphasia rather than memory loss but who go on to have dementia late in the course of the disease.
2. Major pathological features include primarily frontal lobe atrophy with neuronal loss, extensive gliosis with or without ballooned neurons and intraneuronal accumulations call "Pick bodies." Amyloid plaques and neurofibrillary tanbles are not present.

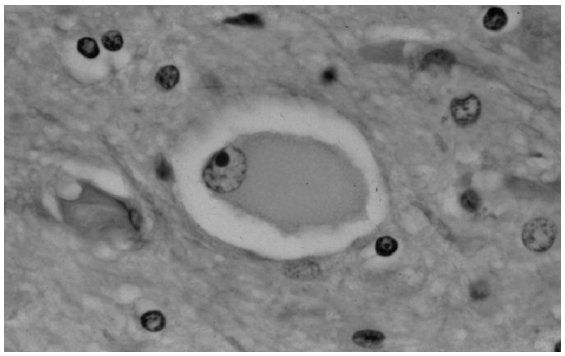
PICK'S DISEASE:LOBAR ATROPHY



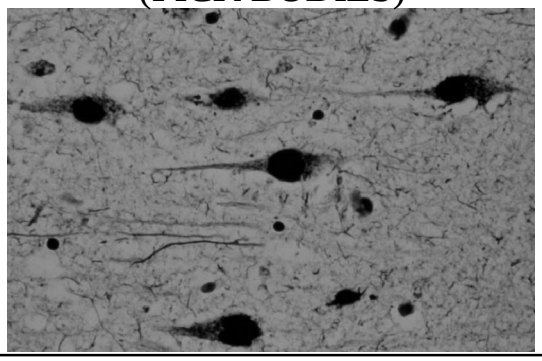
PICK'S DISEASE:LOBAR ATROPHY



PICK'S DISEASE
BALLOON NEURON



PICK'S DISEASE
(PICK BODIES)



C. FRONTOTEMPORAL DEMENTIAS

1. 1. Majority are linked to mutations in the tau protein located on chromosome 17.

2. They present with similar symptoms as those with Pick's Disease; in fact some of the cases with tau mutations can have similar pathology to Pick's disease including Pick bodies. However the majority of the cases have abnormal tau/NFT's in the grey and white matter of the frontal and temporal lobes. Some cases have Parkinson's symptoms as well with abnormal tau accumulations in the substanita nigra

III. DISEASES OF THE BASAL GANGLIA

A. HUNTINGTON'S DISEASE (HD)

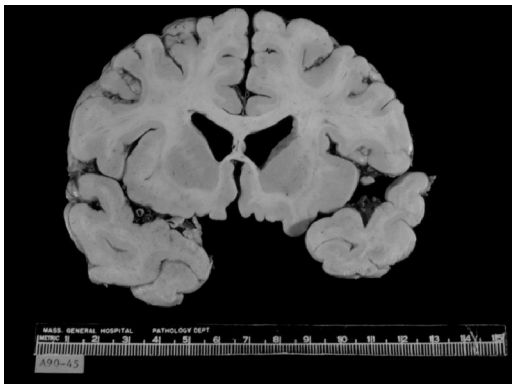
1. Affects both males and females between the ages of 20 to 50 years of age and is transmitted in an autosomal dominant mode of inheritance. The gene responsible has been isolated on chromosome 4.

HUNTINGTON'S DISEASE (HD)

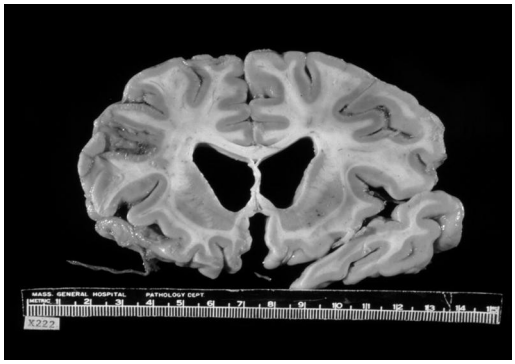
2. Grossly, brains are small with marked atrophy of the caudate and putamen. The classic neuropathologic feature is a "concave" caudate nucleus in severe cases. The atrophy of the caudate and putamen is far greater than the cortical atrophy.

3. Microscopically, there is marked gliosis and loss of small and medium sized neurons with relative sparing of the large neurons in the caudate and putamen.

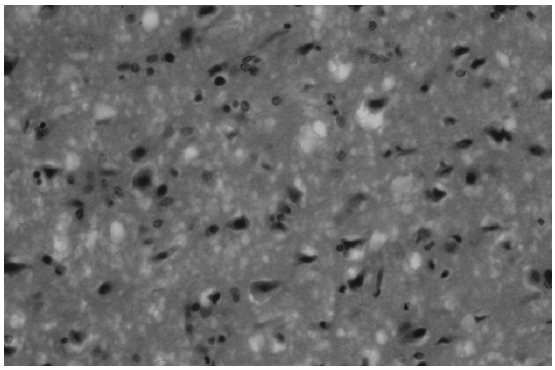
HUNTINGTON'S GRADE I



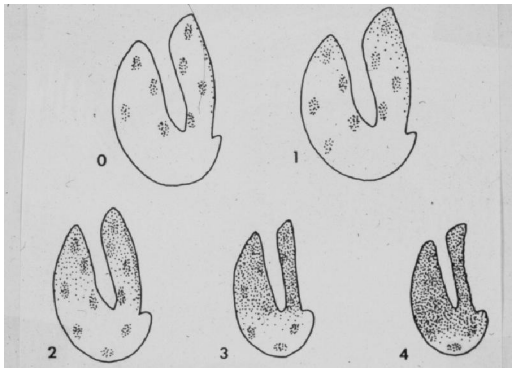
HUNTINGTON'S GRADE III-IV



HUNTINGTON'S GRADE III



HUNTINGTON'S DISEASE GRADES



HUNTINGTON'S DISEASE (HD)

4. The disease is manifested by abnormal extrapyramidal and choreiform motor movements with progressive dementia. The average time course of the disease from onset to death is approximately 15 years.

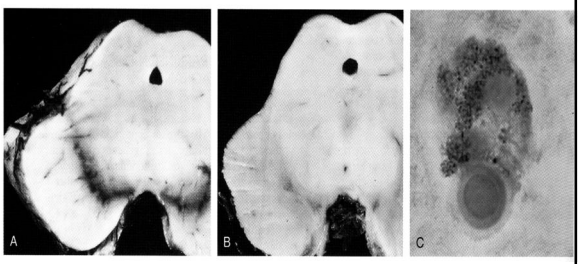
5. The abnormality is a CAG repeat in the gene encoding a protein called huntingtin. It has an expanded polyglutamine tail on the protein leading to abnormal intranuclear aggregates. The number of CAG repeats (>35abnormal) is inversely correlated with the age of onset.

B. IDIOPATHIC PARKINSON'S DISEASE (PD)

1. Largely a sporadic disease with onset between the ages of 50 and 80 years of age. Major symptoms include resting tremor, bradykinesia, stooped posture, masked facies and shuffling gait. Rare families with familial PD (α–synuclein and parkin protein mutations).

2. Symptoms are correlated with loss of the nigrostriatal dopamine system.

IDIOPATHIC PARKISON'S DISEASE:CELL LOSS AND LEWY BODIES



IDIOPATHIC PARKINSON'S DISEASE

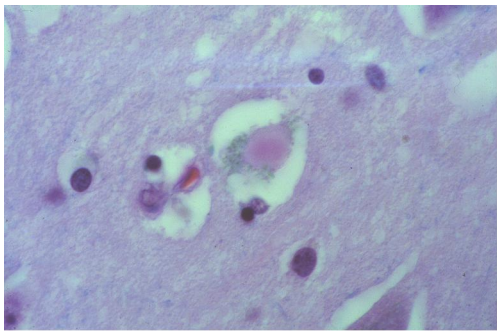
3. Grossly, there is pallor of the midbrain substantia nigra with microscopic loss of neuromelanin containing cells, gliosis, extraneuronal pigment deposition and intraneuronal cytoplasmic inclusions called Lewy bodies in the remaining neurons.

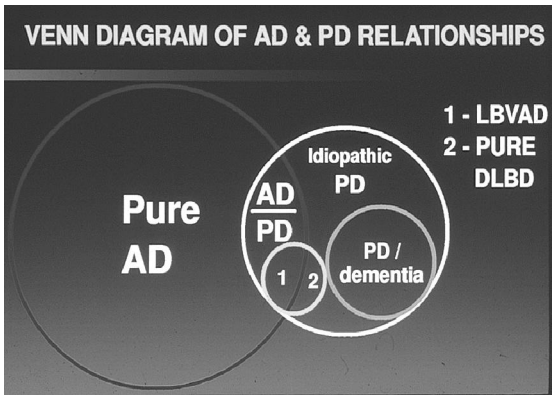
IDIOPATHIC PARKINSON'S DISEASE

4. Severity of PD symptoms is proportional to neuronal loss but can be treated with replacement therapies such as L-Dopa (the precursor for dopamine), and dopamine agonists such as bromocriptine, pergolide and pramipexole and ropinirole.

5. Recent studies have shown that L-Dopa along with monamine oxidase (MAO) inhibitors such as Deprenyl can slow the progression of the disease. The reason that MAO inhibitors may be effective is based on the hypothesis that are endogenous and/or exogenous toxins(s) present in the CNS that are oxidized by MAO to cause specific damage to dopamine containing cells.

CORTICAL LEWY BODY





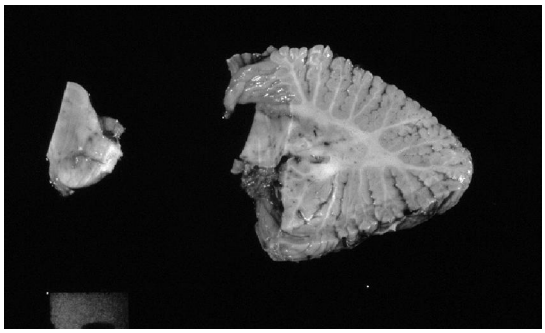
C. PROGRESSIVE SUPRANUCLEAR PALSY (PSP)

1. Relatively rare disease that usually affects males between the ages of 50 and 70 years. Symptoms included Parkinsonism, neck rigidly, gait disturbances, ophthalmoplegia and mild dementia. The Parkinsonian symptoms in contrast to idiopathic Parkinson's disease, are not benefited by treatment with L-Dopa or other dopamine agonists.

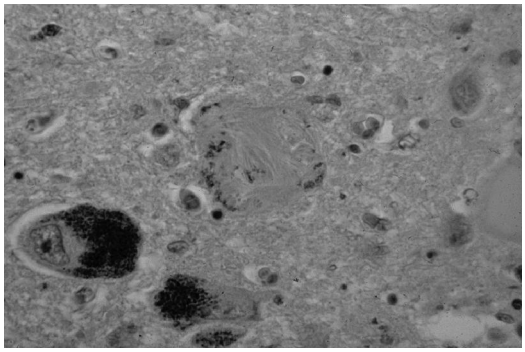
PROGRESSIVE SUPRANUCLEAR PALSY (PSP) - continued

2. On gross examination, the cerebral cortex is unremarkable, however, there is marked pallor of the substantia nigra in the midbrain and atrophy of the globus pallidus, subthalamic nuclei and the dentate nuclei of the cerebellum. Microscopically, there is cell loss and numerous "globose" neurofibrillary tangles in the areas described above as well as in the 3rd and 4th cranial nerve nuclei and many pontine and medullary nuclei as well.

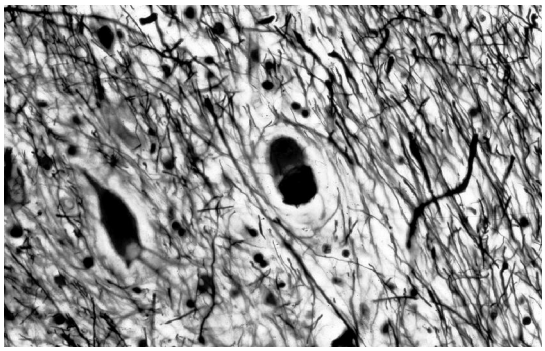
PROGRESSIVE SUPRANUCLEAR PALSY (PSP)



PROGRESSIVE SUPRANUCLEAR PALSY (PSP): TANGLE



PROGRESSIVE SUPRANUCLEAR PALSY (PSP): TANGLE (SILVER STAIN)



IV. DISEASES OF THE CEREBELLUM AND THE SPINAL CORD

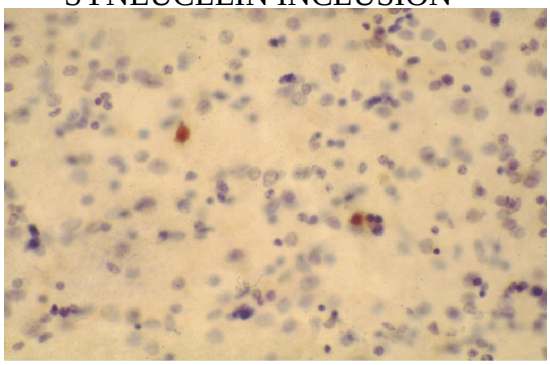
A. MULTIPLE SYSTEM ATROPHY

1. 1. Sporadic disorder with features of Parkinsonian symptoms, cerebellar ataxia and Shy-Drager syndrome (Parkinsonism with orthostatic hypotension).

2. 2. Major symptoms include gait disturbances which progress to the point where the patient becomes totally bedridden at the end-stage.

3. 3. Gross exam: the cerebral cortex and spinal cord are normal but the putamen (posterior/lateral), substania nigra, cerebellum, pons and olivary nuclei are atrophied with microscopic evidence of marked neuronal loss and gliosis and glial cytoplasmic inclusions in

PONTINE OLIOGDENDROCYTE SYNEUCLEIN INCLUSION



B. FRIEDREICH'S ATAXIA

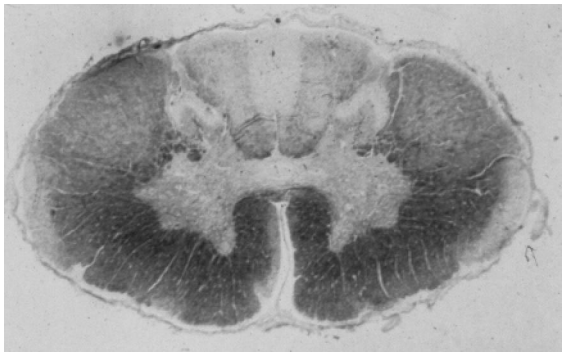
1. It is the most common form of hereditary ataxia and is usually inherited in an autosomal recessive manner. Caused by a trinucleotide repeat GAA (glutamic acid) in the frataxin protein coded on chromosome 9.

FRIEDREICH'S ATAXIA - continued

2. Major pathological findings include degeneration of spinal cord posterior columns, spinocerebellar and to a lesser extent the corticospinal tracts.

3. Most patients have associated electrical conduction and structural anomalies of the heart which results in over 50 % of the deaths due to a cardiac cause.

FRIEDREICH'S ATAXIA



V. MOTOR NEURON DISEASES

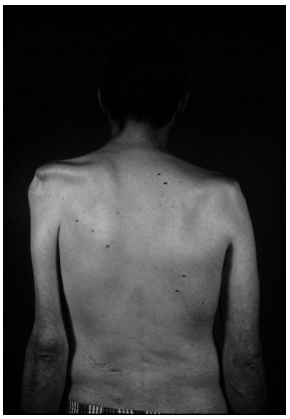
A. A**MYOTROPHIC LATERAL SCLEROSIS (ALS)**

1. ALS affects males more than females in a (2:1 ratio) and begins in the middle to late age. Patients present with both upper motor neuron symptoms including spasticity and hyperreflexia and lower motor neuron symptoms including muscle weakness and atrophy. It may also be associated with bulbar signs such as slurred speech.

AMYOTROPHIC LATERAL SCLEROSIS (ALS) - continued

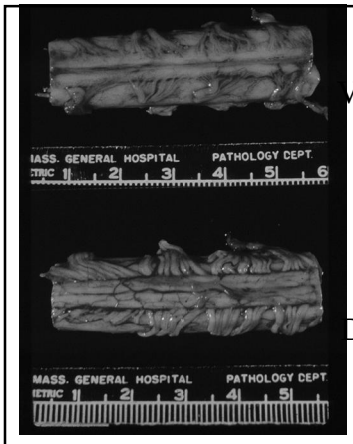
2. Grossly, the cerebral cortex may appear normal, but in severe cases there can be symmetrical atrophy of the motor cortex (Brodmann area 4). Generally, there is discoloration of the corticospinal tract, atrophy of the ventral roots of the spinal cord, and muscular atrophy. Microscopically, there is neurogenic atrophy of the muscle, loss of axons and myelin in the ventral roots, loss of motor neurons and gliosis in anterior horns (particularly at the cervical levels), and axonal loss and myelin loss in the anterior and lateral corticospinal tracts. There is variable involvement of the lower cranial nerve nuclei and the motor cortex.

- Patients generally die from pneumonia due to weakness of pulmonary musculature.
- Five to 10% of cases are familial with a subset having mutations in the superoxide dismutase gene (SOD1) located on chromosome 21.



ALS

MUSCLE ATROPHY

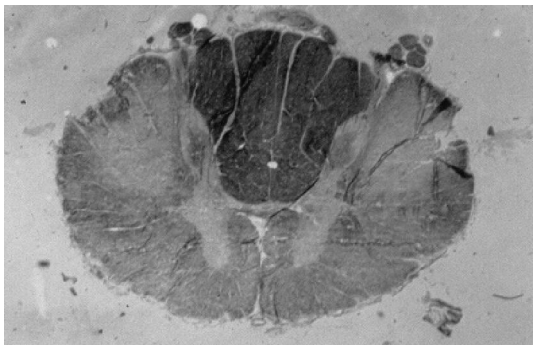


VENTRAL CORD

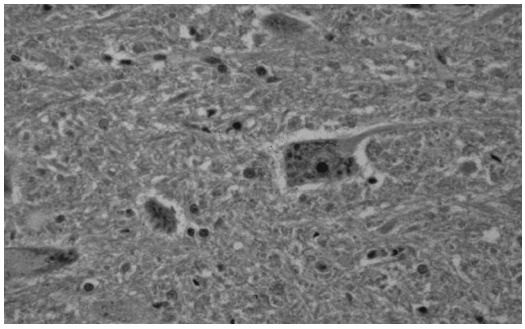
ALS

DORSAL CORD

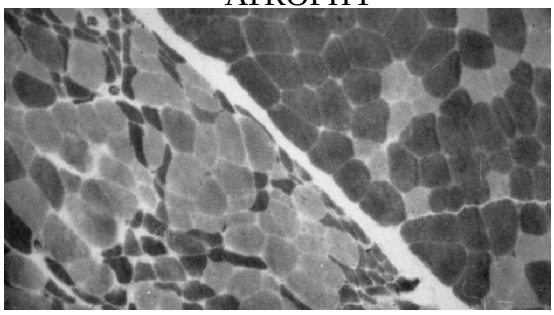
ALS:CORTICOSPINAL TRACT DEGENERATION



ALS: ANTERIOR HORN CELL LOSS AND DEGENERATION



ALS:MUSCLE BIOPSY WITH FIBER TYPE GROUPING AND ATROPHY



B. SPINAL MUSCULAR ATROPHIES

1. Werdnig-Hoffmann Disease (SMA 1): An autosomal recessive disease affecting fetus and newborns which presents classically as a "floppy" infant. Main pathological features include degeneration confined solely to the lower motor neurons resulting in a neurogenic atrophy of the distal musculature.

2. Kugelberg-Walander Disease (SMA II): Similar to Werdnig-Hoffmann disease but presents after 3 months of age or later. The course is progressive but slower. It is compatible with a normal life span.

3. SMA Type III (Rare): Onset in infancy to early adolescence; AR or sporadic

4. All are caused by mutations in the survivial of motor neuron (SMN) genes, SMN1 and SMN2 located on chromosome 5.

EDUCATIONAL OBJECTIVES
NEURODEGENERATIVE DISEASES

John M. Lee, M.D., Ph.D.

1. Understand what is meant by the concept of "selective vulnerability" with regard to neurodegenerative diseases.
2. Know the modes of inheritance, if any, of the major neurodegenerative diseases.
3. Know the gross as well as major micropcopic findings of the classical neurodegenerative diseases.

CENTRAL NERVOUS SYSTEM DISEASES
CEREBROVASCULAR DISEASE

John M. Lee, M.D., Ph.D.

Read: ***Robbins Pathologic Basis of Disease*** **(Cotran, Kumar, Robbins) 7th Ed., Chapter 28, pp. 1361-1369.**

I. INTRODUCTION:

A. The brain and spinal cord are supplied by two arterial systems:

1. Anterior: supplied through the branches of the internal carotid artery.
2. Posterior system: the vertebral arteries and their branches.

There is an abundant anastomosis at the base of the brain through the Circle of Willis between these two systems. The posterior system is connected to the anterior spinal artery -single vessel running through the central fissure and numerous collaterals from the thoracic and abnormal aorta through the radicular branches.

B. Cerebrovascular disease (CVA) is the third leading cause of death in the U.S. and is a major cause of morbidity particularly in the elderly population.

C. Brain depends on aerobic metabolism for the energy source, and is particularly dependant on the 02 supply, and accounts for 20% of total body 02 consumption. Since there is no reserve 02 in the brain, normal cerebral function can continue only for 8-10 seconds after cerebral ischemia and irreversible damage follows after 6-8 minutes of ischemia.

D. Cessation of blood flow can occur as a result of reduction in the perfusion pressure as in hypotension or secondary to small or large vessel occlusion.

E. The clinical and pathological finding will depend on a number of factors namely collateral circulation and the duration of ischemia, the degree and the rapidity of the reduction of blood flow.

F. The cells most sensitive to ischemia are the neurons, followed by oligodendrocytes, endothelial cells and astrocytes

There is a great variability in neuronal susceptibility to ischemia from one area to another. (eg. Pyramidal cells of the hippocampus and Purkinje cells of the cerebellum are the most sensitive).

G. In ischemia there are two extremes: In transient ischemia (TIA) there is complete recovery. In prolonged ischemia- widespread damage leads to coma and eventually "respirator brain".

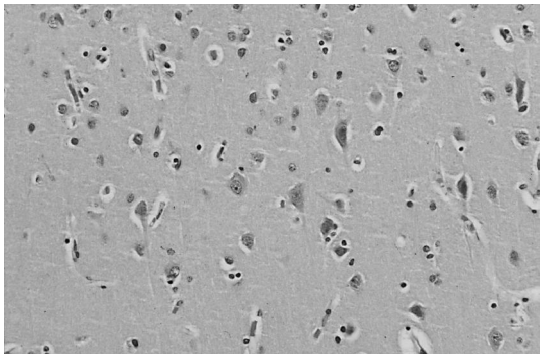
II. CEREBRAL ISCHEMIA AND INFARCTION

A. GENERALIZED ISCHEMIA:

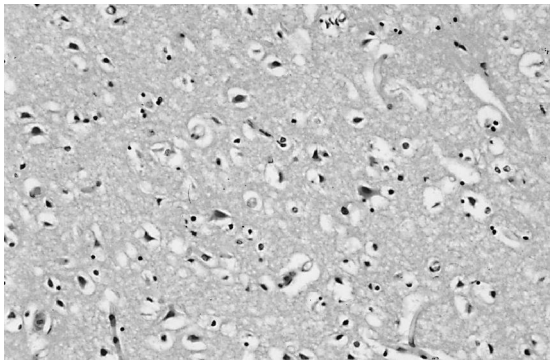
1. **Global Ischemia** (ischemic encephalopathy, anoxic encephalopathy). There is a selective vulnerability of certain neurons to global hypoxic insults namely the pyramidal cells of the hippocampus, Purkinje cells of the cerebellum and deep cortical neurons. The neurons show eosinophilia of the cytoplasm, loss of Nissl granules and dark pyknotic nuclei; these neurons are known as "pink" neurons. Changes are not seen if the patient dies within 6 hours.

Laminar Necrosis diffuse necrosis of the entire cerebral cortex if the patient survives for longer than 3 days.

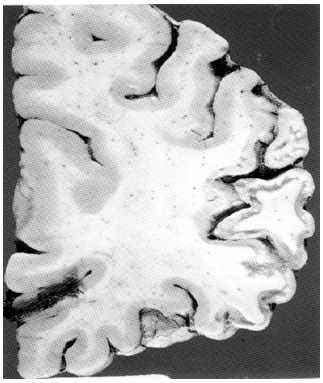
NORMAL CORTEX



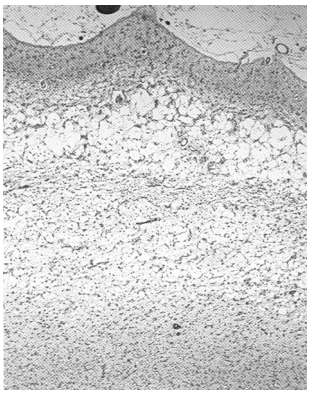
ACUTE INFARCT



LAMINAR NECROSIS



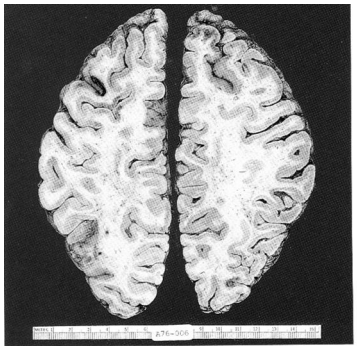
LAMINAR NECROSIS

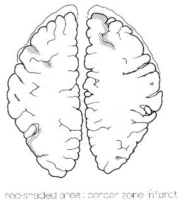


2. **Watershed or Border Zone Infarcts -**

The areas between the arterial territories undergoing necrosis with low perfusion pressures.

WATERSHED INFARCTS





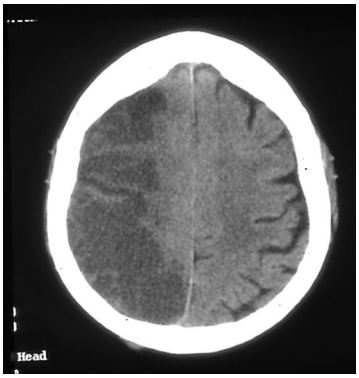
B. **FOCAL ISCHEMIA**

1. **ISCHEMIC INFARCTION**

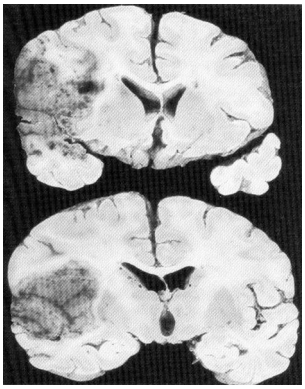
75% of cases are due to atherosclerosis and thrombosis, 10% are due to embolic obstruction. Infarcts are more common in the territory of the middle cerebral arteries. This is a large vessel disease.

GROSS PATHOLOGY: Softening and discoloration of the infarcted area in about 48-72 hours. Later the area undergoes liquefaction necrosis leaving behind a partly collapsed cavity in about 1-2 months time.

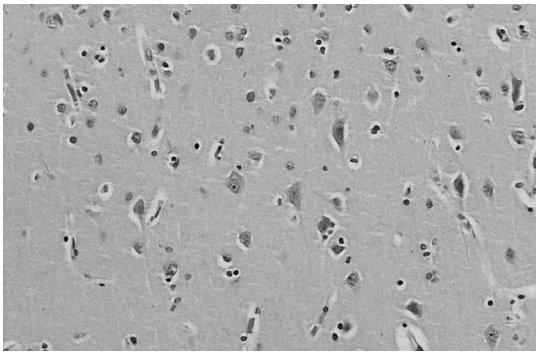
ACUTE INFARCT



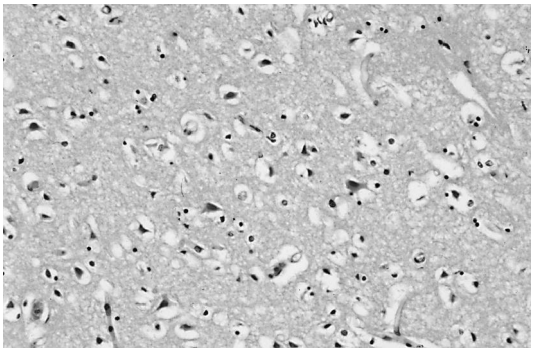
ISCHEMIC INFARCTION



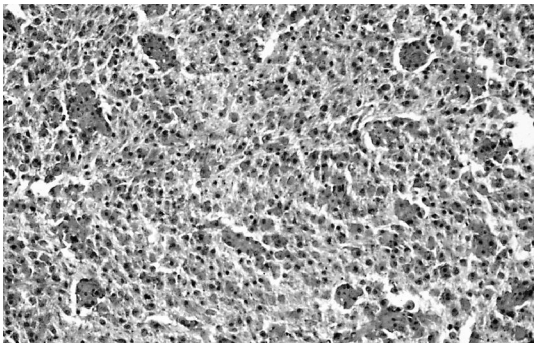
NORMAL CORTEX



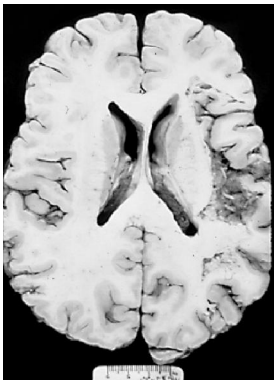
ACUTE CORTICAL INFARCT

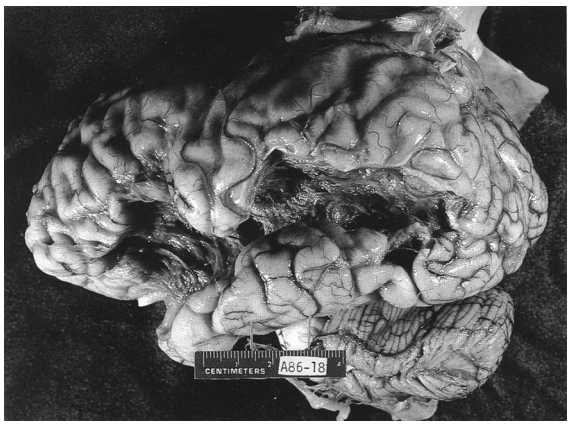


SUBACUTE CORTICAL INFARCT



OLD CORTICAL INFARCT





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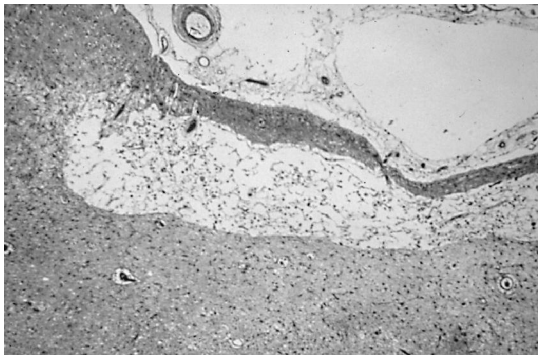
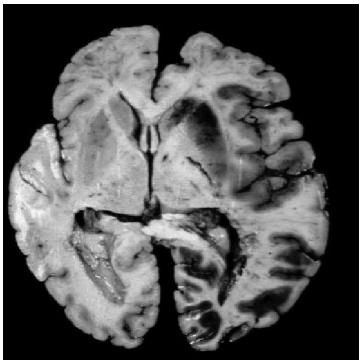


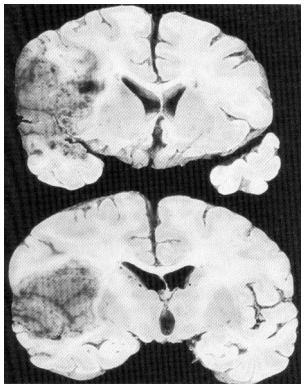
2. **HEMORRHAGIC INFARCTION**

Usually embolic in nature. The reperfusion of the already damaged area secondary to opening up of the anastomotic channels and/or disintegration of the embolus. The infarcted area is grossly hemorrhagic

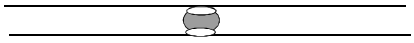
HEMORRHAGIC INFARCTIONS



ISCHEMIC INFARCTION

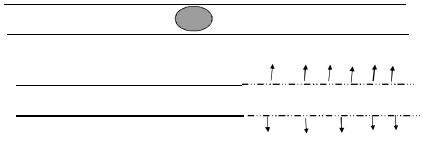


A. ISCHEMIC(BLAND)INFARCTION



PALE
COLOR

B. HEMORRHAGIC INFARCTION

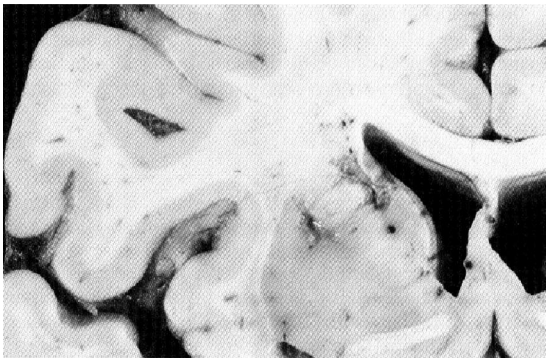


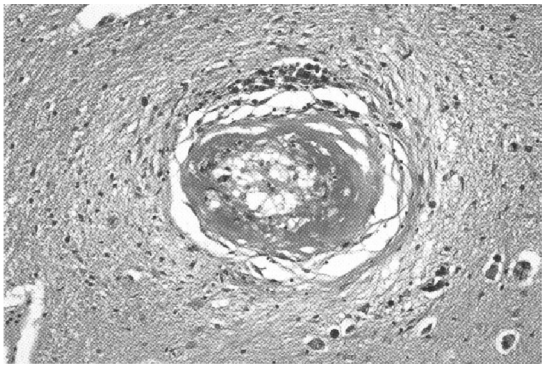
BLOODY
COLOR

3. **LACUNAR INFARCTION**

Small infarcts, usually cystic, measuring up to 1.5 cm. in diameter. Most frequently seen in basal ganglia, thalamus, pons and subcortical white matter. Almost always associated with hypertension. This is primarily due to small vessel disease.

LACUNAR INFARCTIONS (BASAL GANGLIA)





III. CEREBRAL HEMORRHAGE

A. **SUBARACHNOID HEMORRHAGE** - the common cause of non-traumatic spontaneous subarachnoid hemorrhage is rupture of a "Berry" aneurysm.

PATHOLOGY: Gross - "Berry" like outpouchings from the arterial branching points. The site of rupture is at the dome. The associated vascular spasm produces global cerebral ischemia and usually is fatal, in 50% of patients in the first 24 hours.

BERRY ANEURYSMS ANATOMY

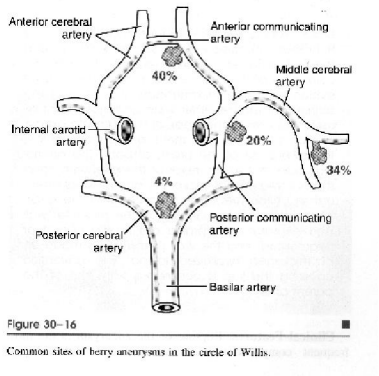
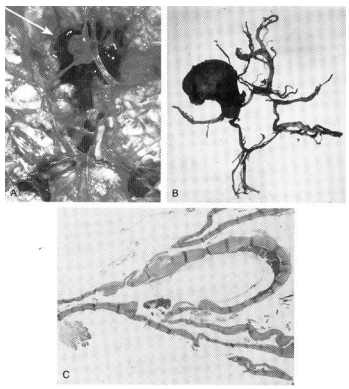


Figure 30–16

Common sites of berry aneurysms in the circle of Willis.



B. **INTRAPARENCHYMAL HEMORRHAGE**

The most common etiological factor is hypertension. Other causes include vascular malformation vasculitis, mycotic aneurysms and coagulopathies. Hemorrhage in tumors sometimes mimic stroke.

Hemorrhages in hypertension are secondary to rupture of pseudoaneurysms, (Charcot-Bouchard). These occur most frequently in the lenticulostriate arteries, paramedia pontine vessels and short circumferential vessels of the cerebellum and in the central white matter. The clinical outcome depends on the site and size of the hemorrhage. Similar distribution as lacunar infarcts.

GROSS PATHOLOGY: Circumscribed hematoma surrounded by brain tissue. The hemorrhage may extend into the subarachnoid space or to the ventricles.

MICROSCOPICALLY: Recent hemorrhage, surrounded by edematous lesion. Minimal tissue necrosis. Resolution of hematoma leaves behind a slit like space usually containing hemosiderin containing macrophages.

HYPERTENSIVE HEMORRHAGES

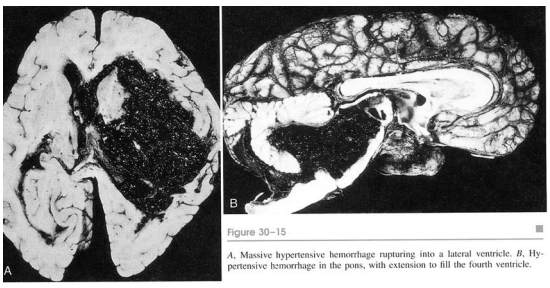
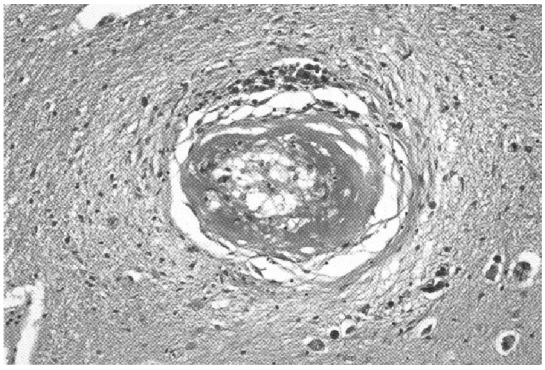


Figure 30–15

A, Massive hypertensive hemorrhage rupturing into a lateral ventricle. *B*, Hypertensive hemorrhage in the pons, with extension to fill the fourth ventricle.

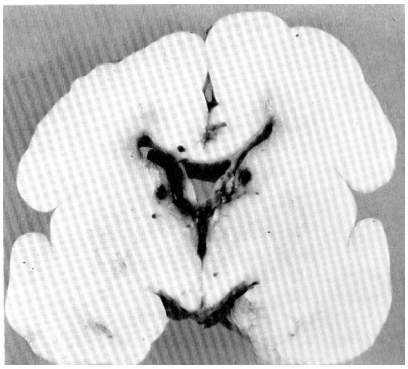
THALAMUS PONS



C. **INTRAVENTRICULAR HEMORRHAGE**

Primary intraventricular hemorrhage is very rare in adults, but very common in premature infants. The site of hemorrhage is in the germinal matrix, located beneath the ependyma, which easily ruptures into the ventricles. Massive intraventricular hemorrhages are fatal instantaneously.

GERMINAL MATRIX HEMORRHAGE



IV. CLINICOPATHOLOGICAL CORRELATION:

Cerebrovascular disorders are a major cause of morbidity and mortality in the U.S. and accounts for 10% of all deaths, and is the third most common cause of death. Those who survive, about 50% are severely disabled and only 10% return to normal activity.

CLINICOPATHOLOGICAL CORRELATION: Continued.

Incidence of stroke increased rapidly with age and 80% occur past the age of 65. The etiology of stroke in young people are different from those occurring in older people. Cerebral infarcts are secondary to either thrombosis or embolism, the former being more common. The premonitory symptoms called transient ischemic attacks (TIA's) often point to a significant atherosclerotic vascular disease.

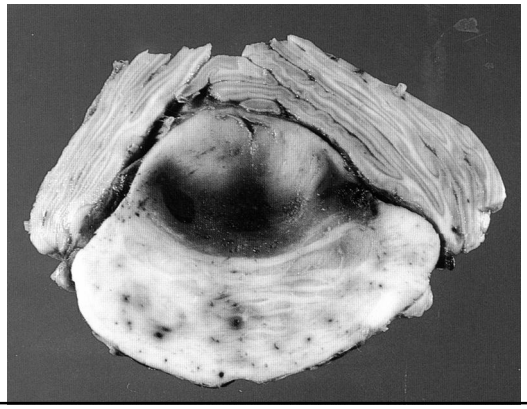
CLINICOPATHOLOGICAL CORRELATION: Continued

Acute subarachnoid hemorrhage very often present with severe headache and rapid loss of consciousness. Thrombotic stroke may have a few hours to develop, "step-wise progression" before losing consciousness. The development of focal signs as hemiplegia cranial nerve paralysis, depends on the size and location of the infarction. For example, infarction in the middle cerebral territory produces arm and leg paralysis as opposed to the anterior cerebral, occlusion which produces the lower limb paralysis. Posterior cerebral infarcts on the other hand produce only partial visual loss.

CLINICOPATHOLOGICAL CORRELATION: Continued.

Supratentorial hemorrhages tend to present with progressive hemiplegia in which the maximum deficit is early on. Cerebellar hemorrhage may produce intractable vomiting. Any massive hemorrhage will lead to death in less than 24 hours secondary to herniation.

DURET HEMORRHAGES



TONSILLAR HERNIATION

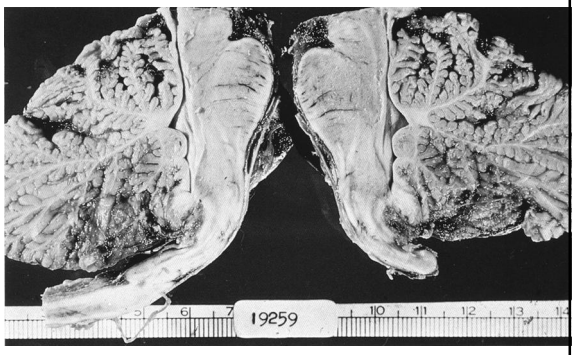


Table IV. Risk-factor management to prevent stroke.

Risk Factor	Potential Management Strategies
Hypertension	Weight reduction; Na^+ and K^+ intake regulation; antihypertensive drugs
Heart disease	Aspirin; warfarin; antiarrhythmic drugs
Prior CVA, TIA	Aspirin; ticlopidine
Carotid bruit	Aspirin; omega-3 fatty acids?; pentoxifylline?; surgery
Diabetes	Glucose control
Tobacco smoking	Cessation
High-dosage estrogen therapy	Low-dosage estrogen therapy
Lipids	Diet; lipid-lowering drugs
Obesity	Weight control
Blood abnormality	Treatment of underlying disorder
Alcohol abuse	Moderate use or cessation

CVA=cerebrovascular accident; TIA=transient ischemic attack.
Adapted from *National Stroke Assoc.*, 1991.[1]

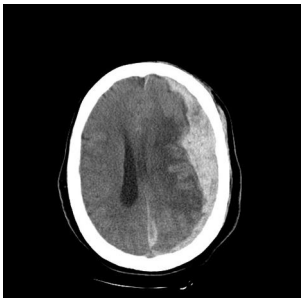
Cerebral Spinal Fluid, Cerebral Vasculature and the Blood Brain Barrier

Peter B. Letarte M.D., FACS
Loyola University Medical School
Maywood, IL

"Localization" of Coma

- Focal
  - Localizable Lesion
    - Bleed
    - Tumor
    - Seizure Focus
    - Vascular Lesion
      - AVM
- Non Focal – Diffuse
  - Metabolic

Anatomic (Focal) Causes of Coma



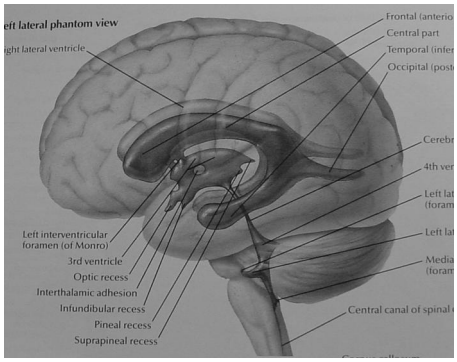
Focal Causes of Coma

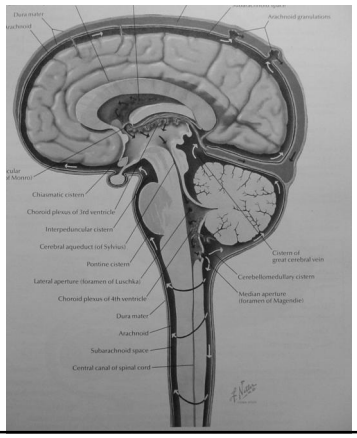
- Mass Effect/Herniation Syndromes
  - Mechanical Damage to the Brain
  - Elevated Intracranial Pressure
    - Ischemic Injury to the Brain
      - Low Blood Flow
    - Hypoxic Injury to the Brain

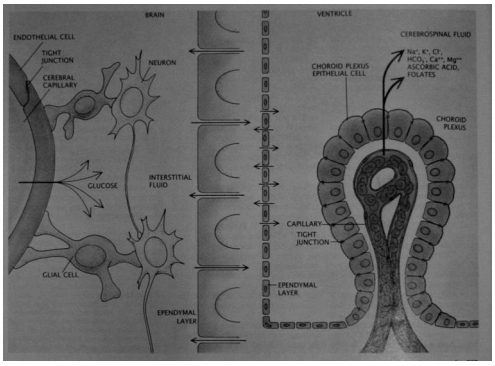
Elevated Intracranial Pressure

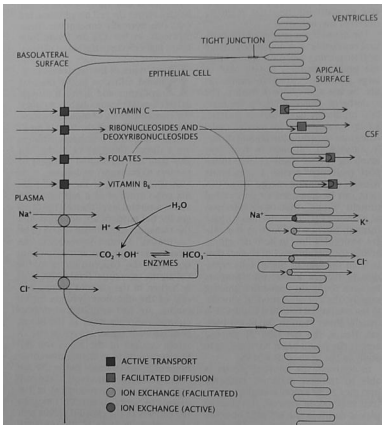
- Focal Lesion
  - Bleed
  - Tumor
  - Seizure Focus
  - Vascular Lesion
    - AVM
- Generalized Process
  - Hydrocephalous

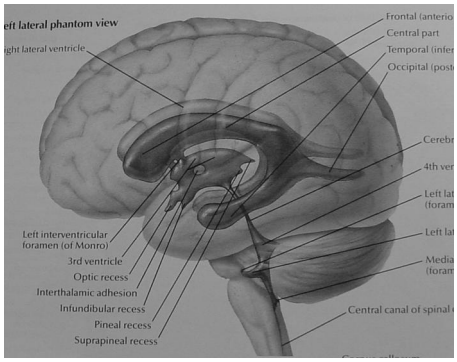
CSF & Hydrocephalous

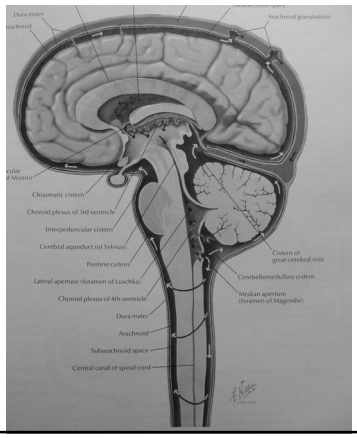

eft lateral phantom view
ight lateral ventricle
Frontal (anterio
Central part
Temporal (infer
Occipital (post
Cerebr
4th ver
Left lat
(foram
Left lat
Media
(foram
Left interventricular
foramen (of Monro)
3rd ventricle
Optic recess
Interthalamic adhesion
Infundibular recess
Pineal recess
Suprapineal recess
Central canal of spinal

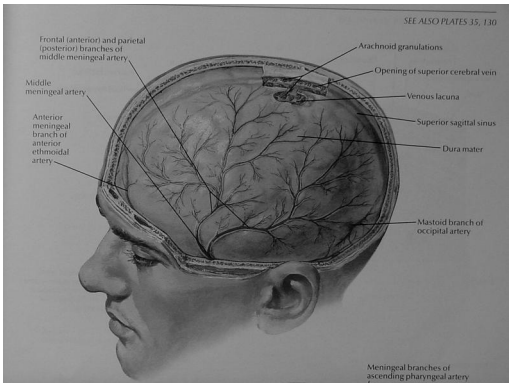

Dura mater
Arachnoid granulations
Chiasmatic cistern
Choroid plexus of 3rd ventricle
Interpeduncular cistern
Cerebral aqueduct (of Sylvius)
Pontine cistern
Lateral aperture (foramen of Luschka)
Choroid plexus of 4th ventricle
Dura mater
Arachnoid
Subarachnoid space
Central canal of spinal cord
Cistern of great cerebral vein
Cerebellomedullary cistern
Median aperture (foramen of Magendie)

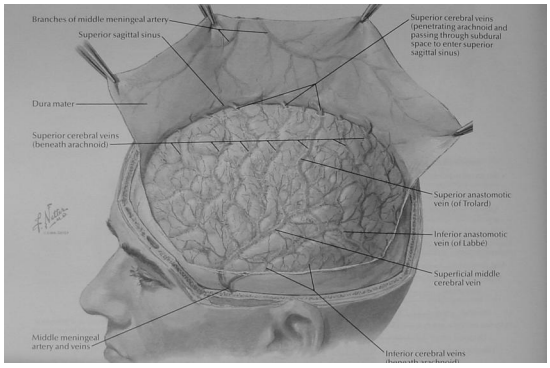

BRAIN
VENTRICLE
ENDOTHELIAL CELL
TIGHT JUNCTION
CEREBRAL CAPILLARY
NEURON
GLUCOSE
INTERSTITIAL FLUID
GLIAL CELL
EPENDYMAL LAYER
CEREBROSPINAL FLUID
CHOROID PLEXUS EPITHELIAL CELL
CHOROID PLEXUS
CAPILLARY
TIGHT JUNCTION
EPENDYMAL LAYER

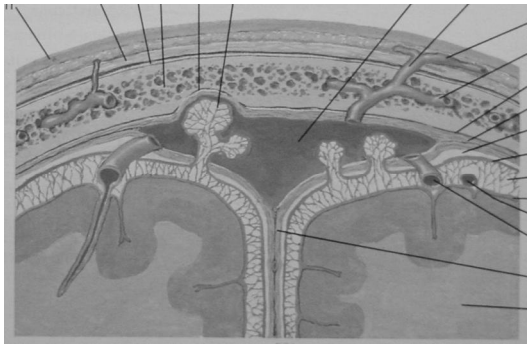

VENTRICLES
TIGHT JUNCTION
BASOLATERAL SURFACE
EPITHELIAL CELL
APICAL SURFACE
VITAMIN C
RIBONUCLEOSIDES AND DEOXYRIBONUCLEOSIDES
CSF
FOLATES
VITAMIN B12
PLASMA
Na+
H+
H2O
Na+
K+
CO2 + OH-
HCO3-
ENZYMES
Cl-
Cl-
ACTIVE TRANSPORT
FACILITATED DIFFUSION
ION EXCHANGE (FACILITATED)
ION EXCHANGE (ACTIVE)


eft lateral phantom view
ght lateral ventricle
Frontal (anterio
Central part
Temporal (infer
Occipital (poste
Cerebr
4th ven
Left lat
(foram
Left lat
Media
(foram
Left interventricular foramen (of Monro)
3rd ventricle
Optic recess
Interthalamic adhesion
Infundibular recess
Pineal recess
Suprapineal recess
Central canal of spinal


Dura mater
Arachnoid granulations
Chiasmatic cistern
Choroid plexus of 3rd ventricle
Interpeduncular cistern
Cerebral aqueduct (of Sylvius)
Pontine cistern
Lateral aperture (foramen of Luschka)
Choroid plexus of 4th ventricle
Dura mater
Arachnoid
Subarachnoid space
Central canal of spinal cord
Cistern of great cerebral vein
Cerebellomedullary cistern
Median aperture (foramen of Magendie)


SEE ALSO PLATES 35, 130
Frontal (anterior) and parietal (posterior) branches of middle meningeal artery
Middle meningeal artery
Anterior meningeal branch of anterior ethmoidal artery
Arachnoid granulations
Opening of superior cerebral vein
Venous lacuna
Superior sagittal sinus
Dura mater
Mastoid branch of occipital artery
Meningeal branches of ascending pharyngeal artery

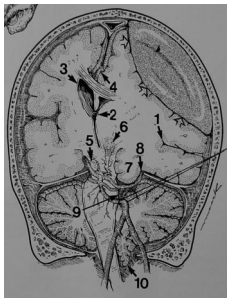

Branches of middle meningeal artery
Superior sagittal sinus
Dura mater
Superior cerebral veins (beneath arachnoid)
Middle meningeal artery and veins
Superior cerebral veins (penetrating arachnoid and passing through subdural space to enter superior sagittal sinus)
Superior anastomotic vein (of Trolard)
Inferior anastomotic vein (of Labbé)
Superficial middle cerebral vein
Interior cerebral veins



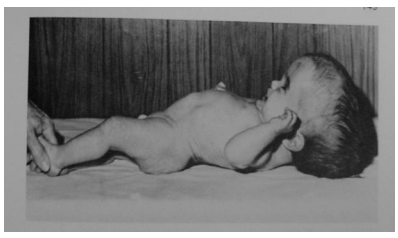
Hydrocephalous

- Communicating
  - Failure of Absorption and Arachnoid Villa
- Non Communicating
  - Obstruction of Flow at Cerebral Aqueduct

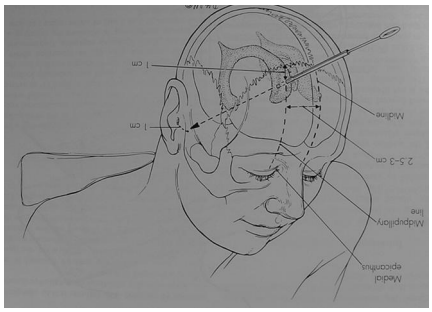
Herniation

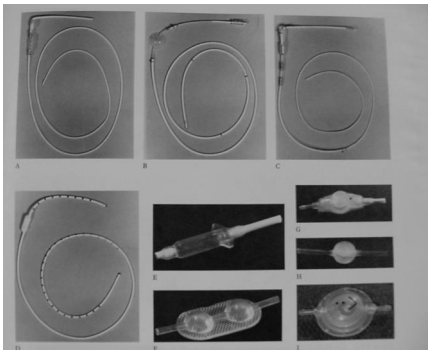


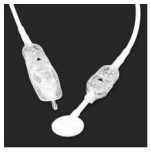
History

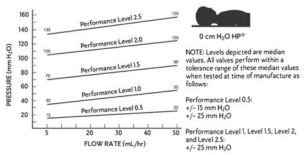


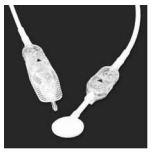
Ventriculostomy





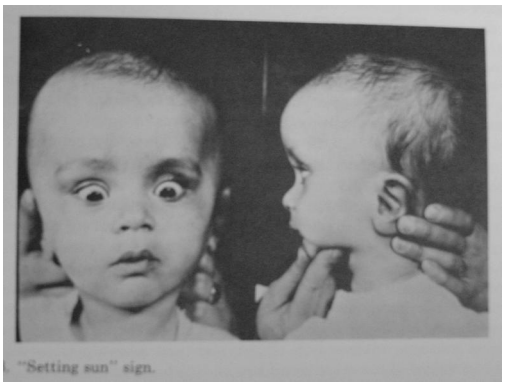



160
140
120
100
80
60
40
20
PRESSURE (mm H_2O)
Performance Level 2.5
Performance Level 2.0
Performance Level 1.5
Performance Level 1.0
Performance Level 0.5
5
20
30
40
50
FLOW RATE (mL/hr)
0 cm H_2O HP*
NOTE: Levels depicted are median values. All valves perform within a tolerance range of these median values when tested at time of manufacture as follows:
Performance Level 0.5:
+/- 15 mm H_2O
+/- 25 mm H_2O
Performance Level 1, Level 1.5, Level 2, and Level 2.5:
+/- 25 mm H_2O



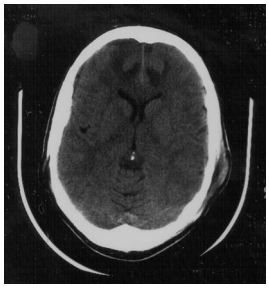
Hydrocephalous

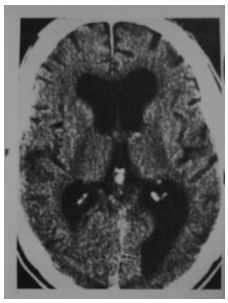
- Clinical Presentation
  - Headache
  - Lethargy
    - Hard to Arouse
  - Loss of Appetite/Vomiting



"Setting sun" sign.

Hydrocephalous

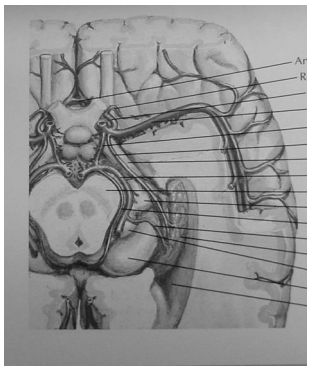


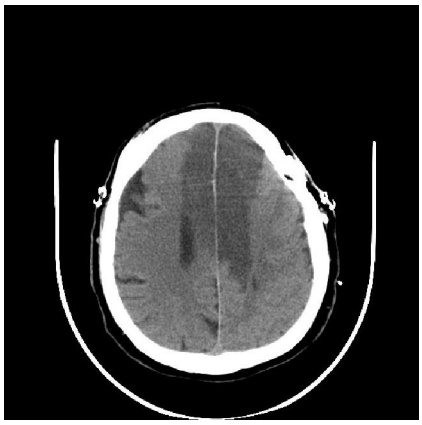


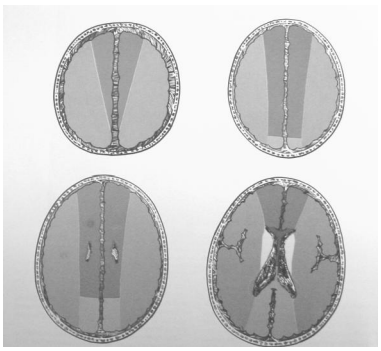
Hydrocephalous

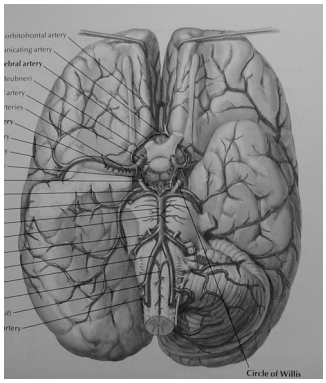
- Other Contexts for Presentation
  - After Bleeding into the Brain
    - Non communicating Hydrocephalous
      - Obstruction of Cerebral Aqueduct
    - Examples
      - After Subarachnoid Hemorrhage
      - After Trauma
      - After Intraparenchymal Bleed
  - After Meningitis
    - Communicating Hydrocephalous
      - Scarring of Arachnoid Villa
  - With Meningeal Tumor
    - Communicating Hydrocephalous
      - Occlusion of Arachnoid Villa

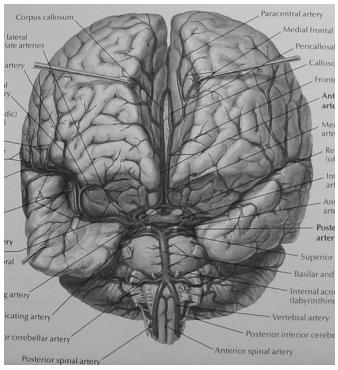
Cerebral Vasculature

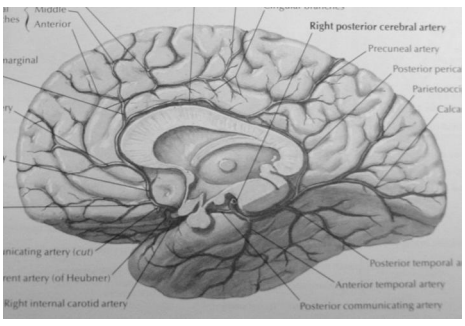


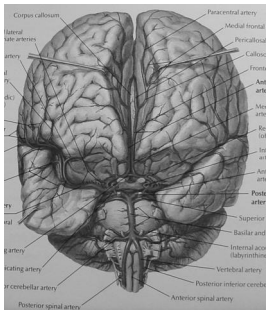





Circle of Willis


Corpus callosum
Paracentral artery
Superior
Basilar and
Vertebral artery
Anterior spinal artery
Posterior spinal artery


Anterior
Right posterior cerebral artery
Precuneal artery
Posterior temporal a
Anterior temporal artery
Posterior communicating artery


Corpus callosum
Paracentral artery
Medial frontal
Pericallosal
Callosc
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arter
Superior
Basilar and
Internal acou
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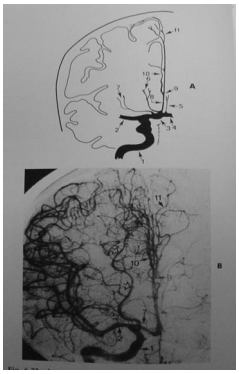
Vertebral artery
Posterior inferior cerebe
Anterior spinal artery
Posterior spinal artery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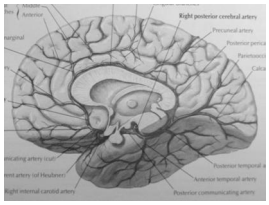
Right posterior cerebral artery
Precuneal artery
Posterior pericall
Parietooccip
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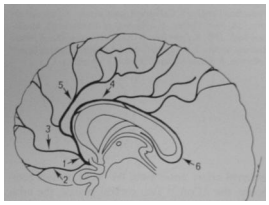
Posterior temporal a
Anterior temporal artery
Posterior communicating artery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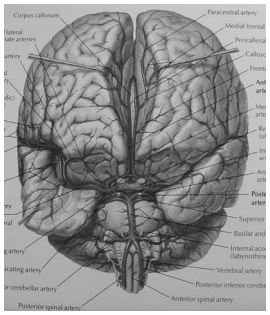
Corpus callosum
Paracentral artery
Medial frontal
Pericallosal
Callosc
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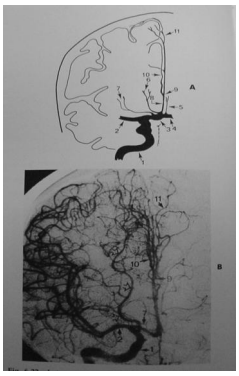
Vertebral artery
Posterior inferior cerebe
Anterior spinal artery
Posterior spinal artery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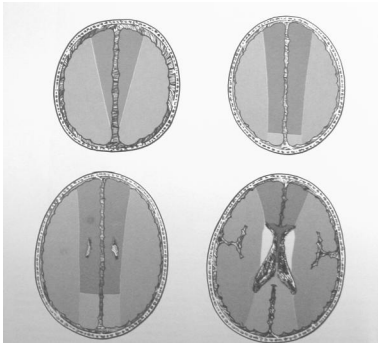
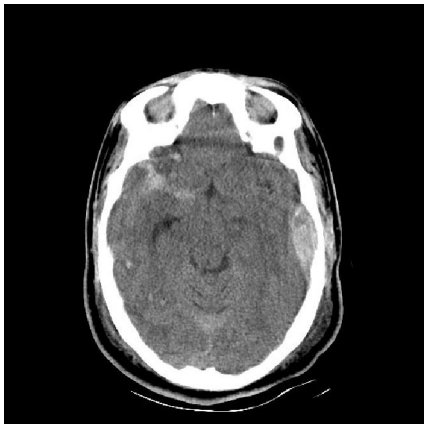
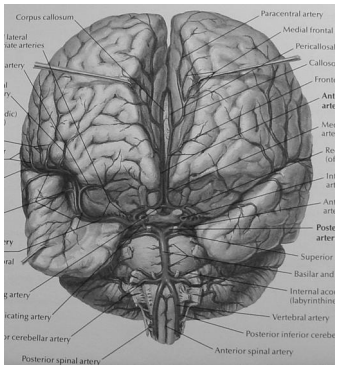
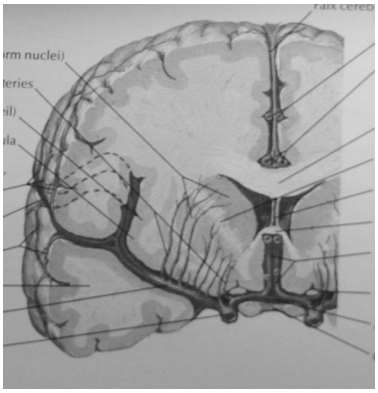
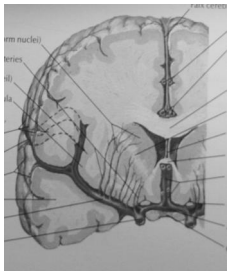
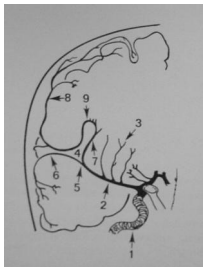





Corpus callosum
Paracentral artery
Medial frontal
Pericallosal
Superior
Basilar and
Vertebral artery
Posterior inferior cerebe
Anterior spinal artery
Posterior spinal artery



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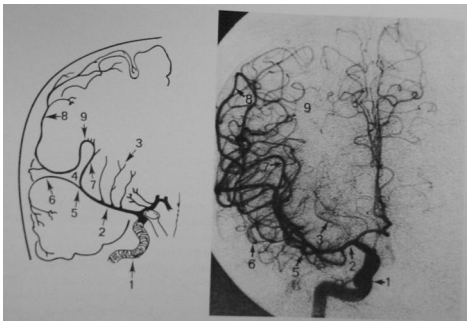
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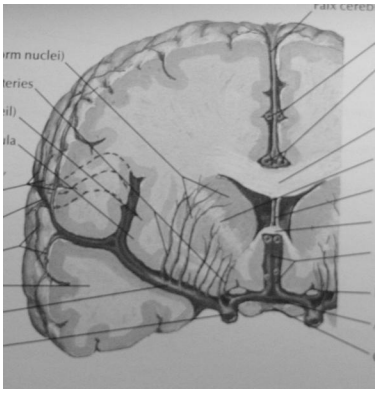
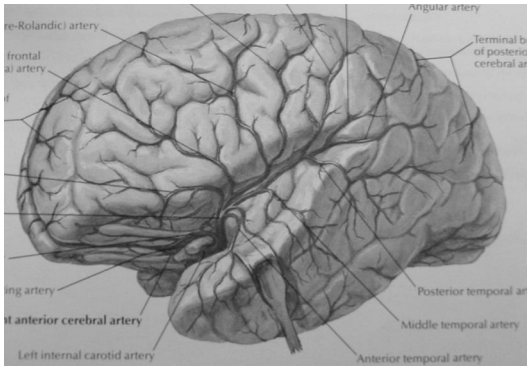
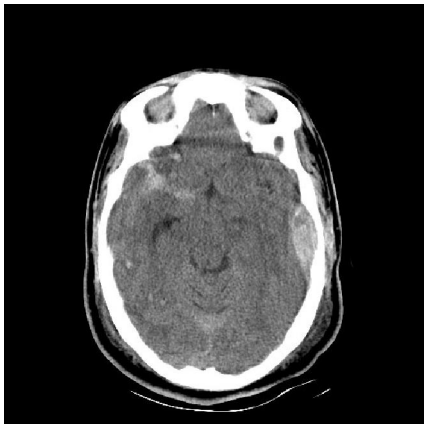
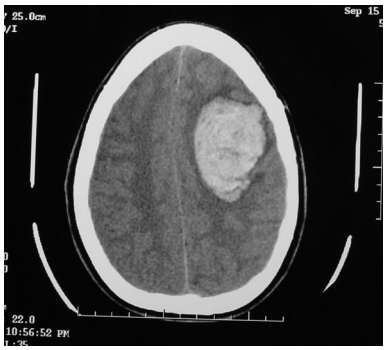



Angular artery
Posterior temporal ar
Middle temporal artery
Anterior temporal artery
Left internal carotid artery

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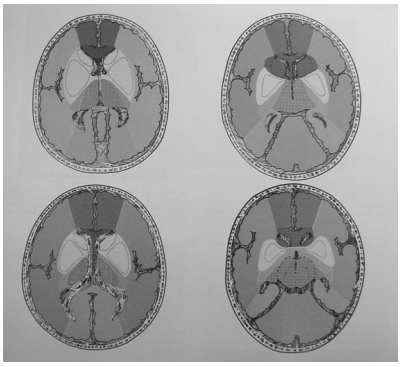
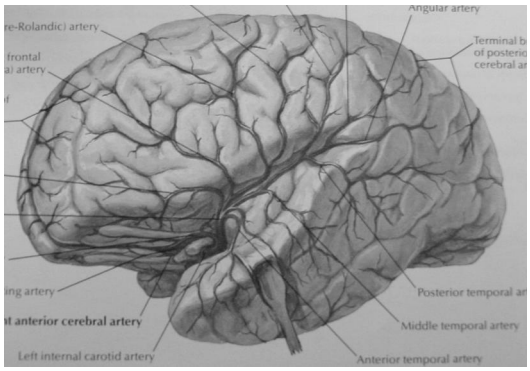
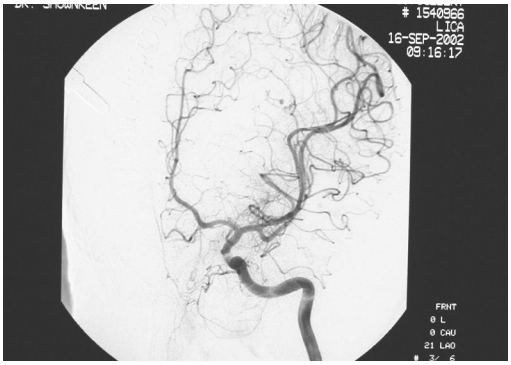
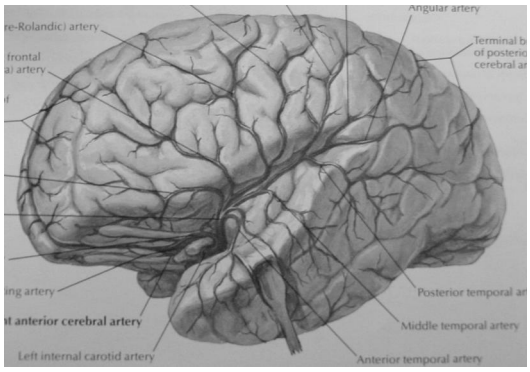



Angular artery
Posterior temporal ar
Middle temporal artery
Anterior temporal artery
Left internal carotid artery





Intraop photos BS 6

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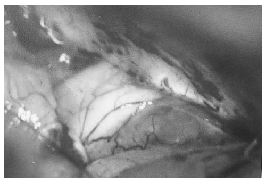

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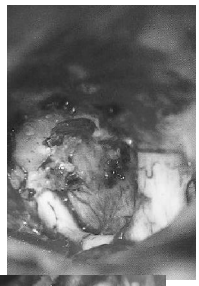

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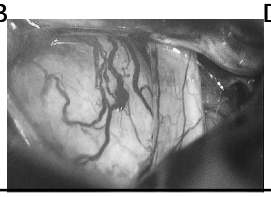

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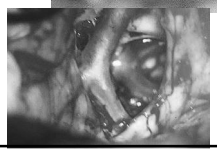
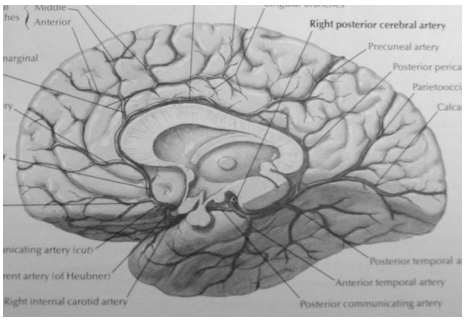
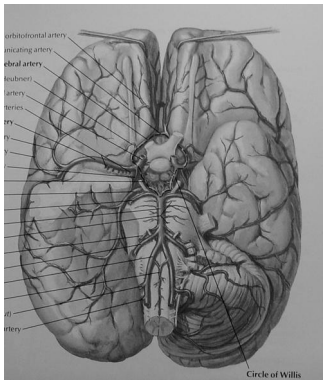
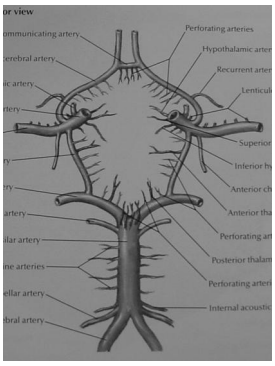
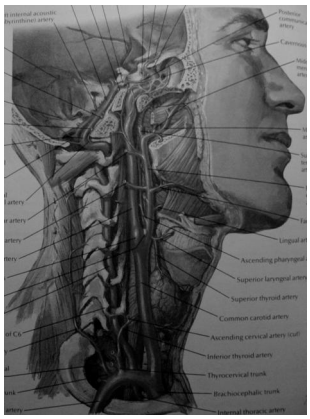
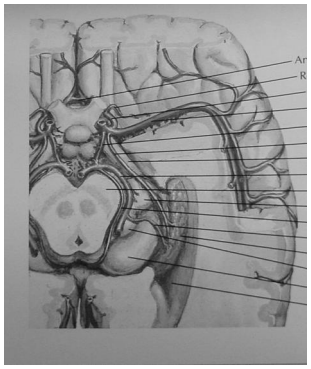


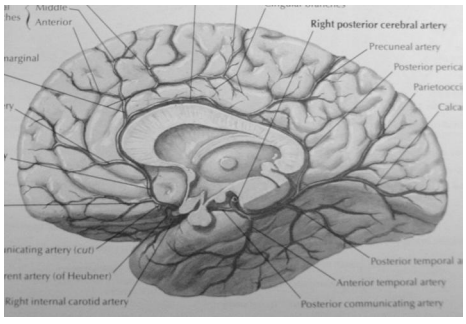

Anterior
Right posterior cerebral artery
Precuneal artery
Posterior temporal a
Anterior temporal artery
Posterior communicating artery


Circle of Willis


Perforating arteries
Hypothalamic arter
Recurrent arter
Superior
Anterior ch
Anterior tha
Perforating art
Posterior thalam
Perforating arteri
Internal acoustic


Lingual ar
Ascending pharyngeal
Superior laryngeal artery
Superior thyroid artery
Common carotid artery
Ascending cervical artery (cut)
Inferior thyroid artery
Thyrocervical trunk
Brachiocephalic trunk




Middle
Anterior
Right posterior cerebral artery
Precuneal artery
Posterior perica
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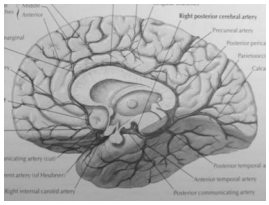
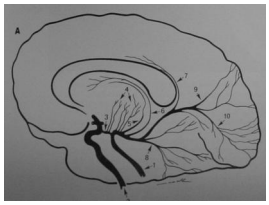
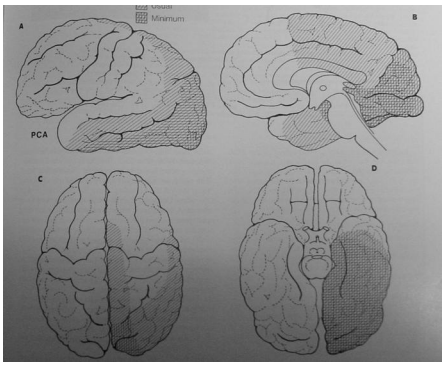
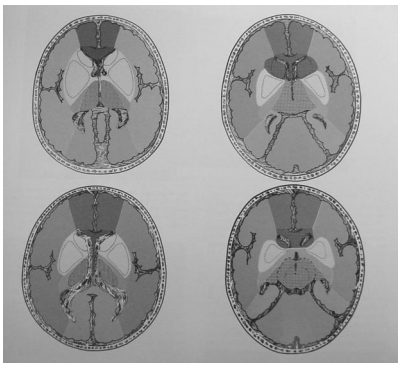
Calca
Posterior temporal a
Anterior temporal artery
Posterior communicating artery
Right internal carotid artery

Posterior Cerebral Artery

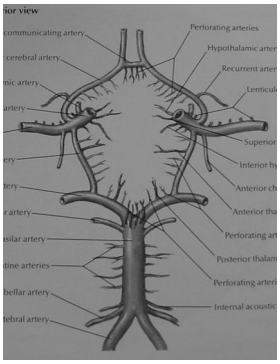


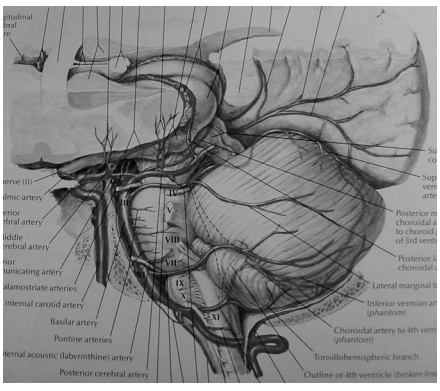


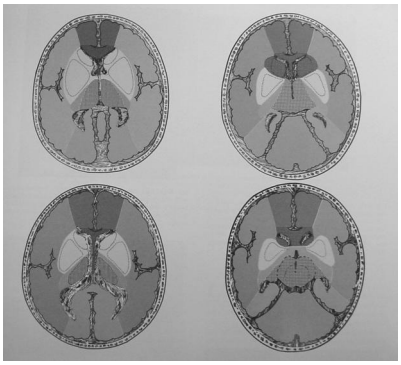




Subcortical Strokes



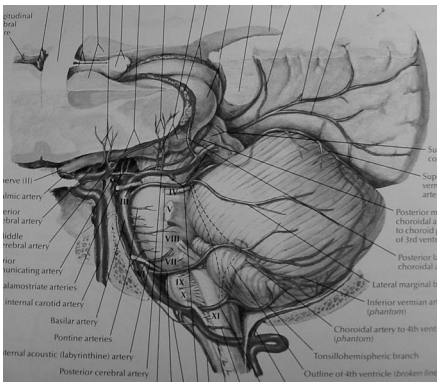


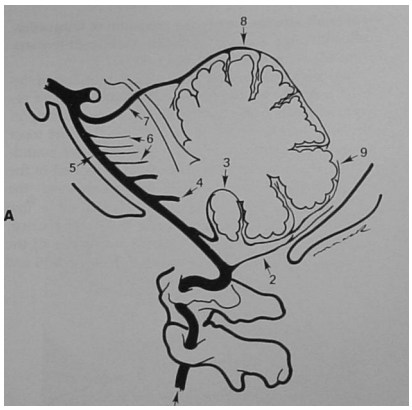


Strokes

- Cortical
  - Attack Cortical Function
    - Speech
    - Strength
    - Sensation
- Subcortical
  - More Subtle
  - Harder to Localize

Posterior Fossa Circulation


Basilar artery
Pontine arteries
Posterior cerebral artery
Tonsillohemispheric branch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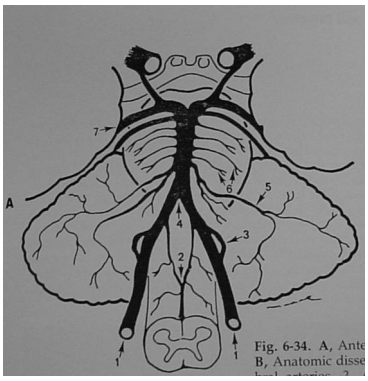
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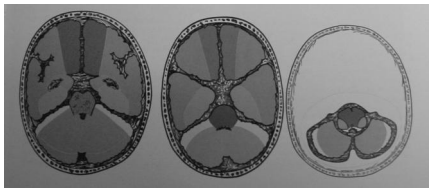
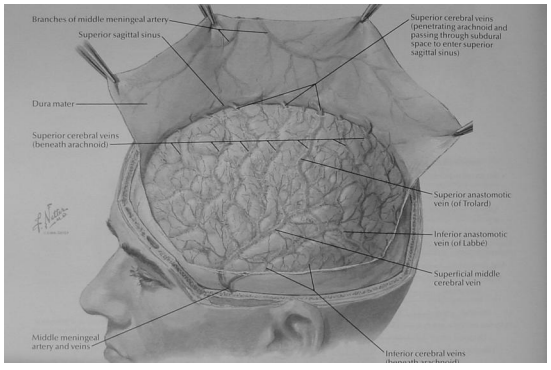
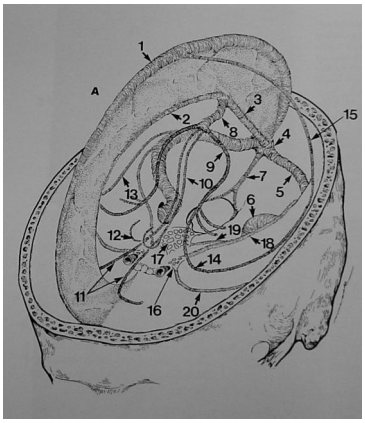
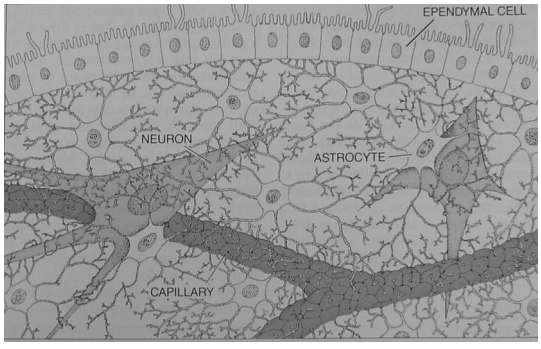


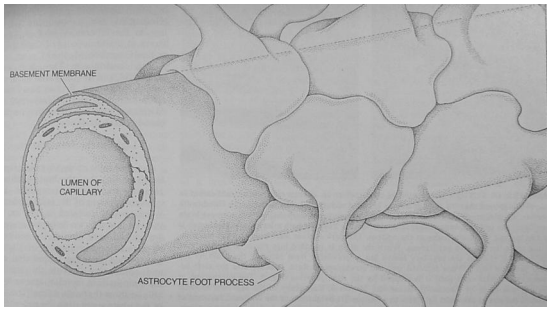
Cerebral Venous System

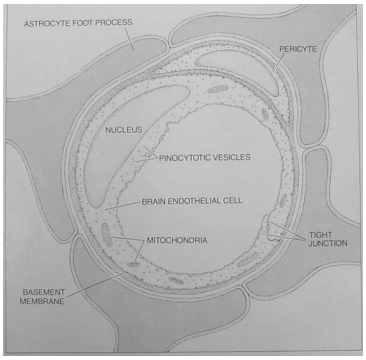


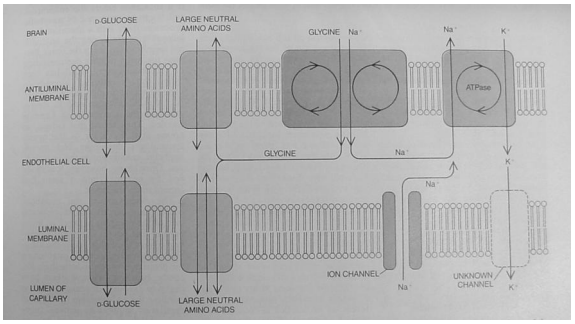


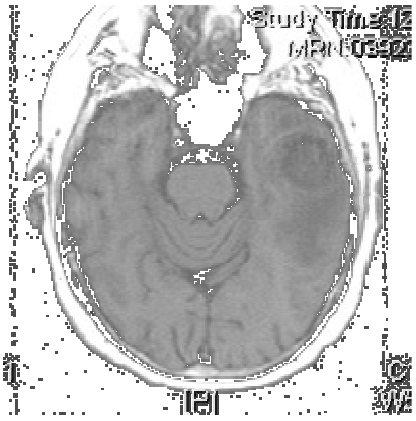
Blood Brain Barrier

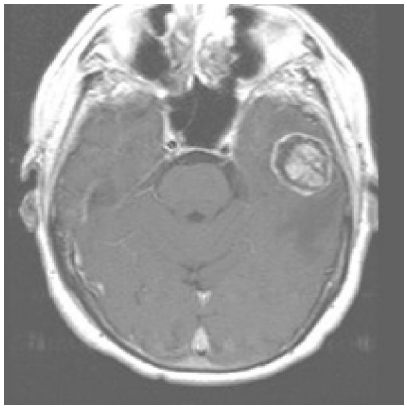



BASEMENT MEMBRANE
LUMEN OF CAPILLARY
ASTROCYTE FOOT PROCESS

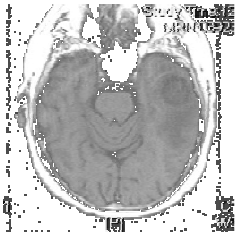

ASTROCYTE FOOT PROCESS
PERICYTE
NUCLEUS
PINOCYTOTIC VESICLES
BRAIN ENDOTHELIAL CELL
MITOCHONDRIA
TIGHT JUNCTION
BASEMENT MEMBRANE

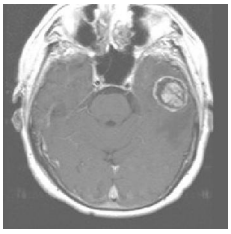

BRAIN
D-GLUCOSE
LARGE NEUTRAL AMINO ACIDS
GLYCINE
Na+
Na+
K+
ANTILUMINAL MEMBRANE
ATPase
ENDOTHELIAL CELL
GLYCINE
Na+
K+
Na+
LUMINAL MEMBRANE
ION CHANNEL
Na+
UNKNOWN CHANNEL
K+
LUMEN OF CAPILLARY
D-GLUCOSE
LARGE NEUTRAL AMINO ACIDS





Enhancing Lesions





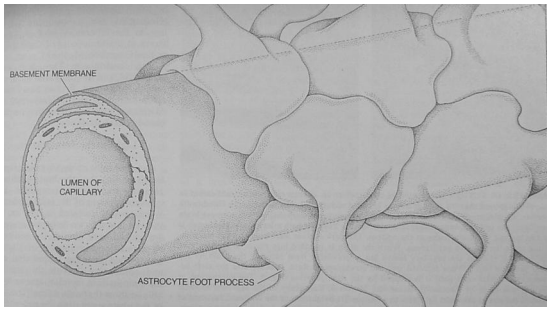
Ring Enhancing Lesions

- ø M- Meningeoma
- ø A-Abscess
- ø G-Glioma
- ø I-Resolving Infarction
- ø C-Resolving Contusion

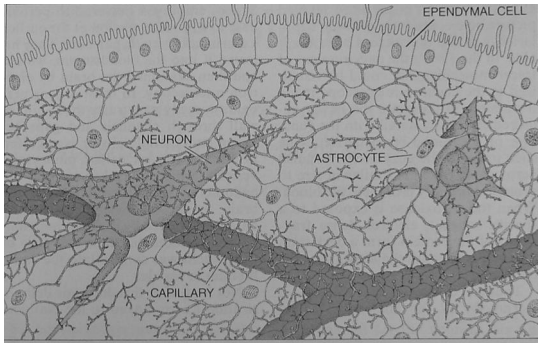
- ø D- Demylinating Disease
- ø R- Resolving Hematoma

- ø L-Lymphoma

Antibiotic Penatrance



Detection of CNS Infections



Delivery of Chemotherapy