INTRODUCTION

• Brain and spinal cord blood supply:
  – Anterior flow (~70% of CBF) – internal carotid artery
  – Posterior flow (~30% of CBF) – vertebral arteries

INTRODUCTION

• Clinical and pathologic findings depend on:
  ▪ Collateral circulation
  ▪ Duration of ischemia
  ▪ Degree and rapidity of reduction of blood flow

• Selective neuronal necrosis:
  neurons > oligodendrocytes > endothelial cells > astrocytes.

• Variable neuronal susceptibility to ischemia:
  ▪ Cortical pyramidal neurons
  ▪ Pyramidal neurons in CA1 region of hippocampus
  ▪ Purkinje cells of cerebellum
**Stroke:**

“Abrupt onset of focal or global neurological symptoms caused by ischemia or hemorrhage”

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**Cerebrovascular disease**

- **ISCHEMIC STROKE** (lack of blood flow to brain = 85%):  
  - Damage depends on **location and time**  
  - **TIA <24h**  
  - **Global** cerebral ischemia  
  - **Focal** cerebral ischemia

- **HEMORRHAGIC STROKE** (bleeding into the brain = 15%):  
  - **Intraparenchymal** hemorrhage (HTN, amyloid)  
  - **Subarachnoid** hemorrhage (saccular aneurysms, AVM)

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**STROKE**

- Common causes: atherosclerosis, hypertension, coagulation disorders, cardiac disease  
- Clinical symptoms are similar for both ischemic and hemorrhagic stroke (except for SAH)  
- Diagnosis:  
  - Neurological exam  
  - Non-contrast head CT  
  - Angiography
CEREBRAL ISCHEMIA

- Pan-necrosis: all cell types
- Selective vulnerability
  - Mechanism: transient ischemia (e.g., resuscitation following cardiac arrest)
  - Cell-specific sensitivity to ischemic injury:
    - Pyramidal neurons in cerebral cortex (layers 3 and 5) – leads to LAMINAR NECROSIS (if the patient survives longer than 3 days)
    - Pyramidal neurons of hippocampus (long term memory)
    - Purkinje cells of cerebellum

Selective neuronal vulnerability

<table>
<thead>
<tr>
<th>Adults</th>
<th>Infants</th>
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<tbody>
<tr>
<td>“Big neurons”</td>
<td>Subiculum</td>
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<tr>
<td>Cortical layers 3&amp;5</td>
<td>Thalamus</td>
</tr>
<tr>
<td>CA1 of hippocampus</td>
<td>Pontine nuclei</td>
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<tr>
<td>Purkinje cells</td>
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</table>

Normal neurons:
- Normal cortex
- Acute infarct

Red neurons:
- Cytoplasmic eosinophilia
- Loss of Nissl substance
- Nuclear pyknosis
LAMINAR CORTICAL NECROSIS

Preserved superficial cortex

Selective necrosis of cerebral cortex

Selective vulnerability – hippocampal CA1 (Sommer’s sector)

WATERSHED INFARCT

• Stroke in the region between two major arterial territories
  – ACA/MCA: frontal and paramedian cortex
  – MCA/PCA: occipital cortex
• Due to systemic hypoperfusion
WATERSHED INFARCT

FOCAL ISCHEMIA (ISCHEMIC INFARCT)

- Regional ischemia resulting in focal neurologic deficits lasting >24 h (<24 h – TIA)
- Mechanisms
  - Thrombotic stroke
    - Atherosclerotic plaque (75%) – at bifurcation of internal carotid and MCA
    - In situ thrombosis
  - Embolic stroke (10%)
    - Cardiac emboli (A fib, myocardial aneurysm) - MCA
    - Atheroemboli (internal carotid, vertebral sources)
    - Infectious emboli: bacterial endocarditis
  - Small vessel disease
    - Penetrating arteries that originate directly from large vessels (MCA, ACA)
    - Lacunar stroke (cystic infarct <1.5 cm) – lenticulostriate vessels

Severe atherosclerosis of circle of Willis
Atherosclerotic plaque in the internal carotid artery
1 – common carotid
2 – external carotid
3 – internal carotid

Atherosclerosis

Fibrous atherosclerotic plaques in a small leptomeningeal artery

Necrotic core with cholesterol crystals and foam cells and fibrosis of the media with loss of smooth muscle cells

MRI brain:
- Ischemic hemispheric infarct
- MCA territory
- Midline shift

Symptoms:
- Contralateral hemiparesis affecting the lower face and upper extremity more than the leg
- Similar distribution contralateral hemisensory loss
- Contralateral visual field deficits
- Dominant hemisphere infarct is often associated with expressive aphasia where as non-dominant infarct is associated with neglect syndrome.
PATHOLOGY OF ISCHEMIC INFARCT

- **Gross and microscopic findings** differ with:
  - **Time**
    - Acute vs. subacute vs. remote
  - **Mechanism**
    - Embolic (red) versus thrombotic (pale) insult
  - **Central (ischemic) core**: dead zone
  - **Penumbra**: surrounding tissue with capacity to recover if perfusion is restored

AGE OF INFARCT

- **Acute**
  - 6-48 h
  - Gross: pale, soft, swollen, indistinct border, blurred grey-white junction
  - Micro:
    - 6-12 h: Neuronal ischemia ("red dead" neurons), pallor (edema)
    - 1-3 days: Neutrophils (liquefactive necrosis)

- **Subacute**
  - 4d-3wks
  - Gross: gelatinous, friable, distinct border, tissue liquefaction
  - Micro: Neutrophils (early), Macrophages (4-7 days), Vascular proliferation (2-3 weeks)

- **Chronic**
  - >3wks
  - Gross: cystic, +/- hemosiderin staining, secondary degeneration
  - Micro: Astrocytic Gliosis, residual macrophages

ACUTE ISCHEMIC INFARCT

Indistinct border
Blurring of cortex/white matter differentiation
Swelling, softening and pallor of brain parenchyma

6-12 h: pallor (edema) and neuronal ischemia ("red dead" neurons)
1-3 days: Neutrophils
SUBACUTE ISCHEMIC INFARCT

- Distinct borders
- Tissue liquefaction
- Macrophages and vascular proliferation

CHRONIC INFARCT = CYSTIC SPACE

- Cystic space
- Gliosis
EMBOLIC INFARCT

- Usually smaller, centered at gray-white jxn
- Single or multiple
- May involve more than one vascular territory
- MCA most common

LACUNAR INFARCT

- Lacuna (pl. lacunae) – Latin: gap, cavity, pool
- Causes
  – Hypertensive small vessel disease: lipohyalinosis
  – Diabetes
  – Vasculitis
- Small, up to 1.5 cm
- Location:
  – Internal capsule – pure motor stroke
  – Thalamus – pure sensory stroke
  – Base of pons – dysarthria, “clumsy hand”
  – Subthalamic nucleus - hemiballismus

Arteriolesclerosis

- Affects small vessels (arterioles) in longstanding hypertension
- Lipohyalinosis – old term
- There is disruption of the blood brain barrier and the vessels are prone to rupture
- Fibrinoid material is eventually replaced by collagen (“hyalinosis”)
LACUNAR INFARCTS

INTRACRANIAL HEMORRHAGE

– Above the arachnoid
  • Traumatic in nature
    – Epidural and subdural hematomas

– Below the arachnoid
  • Underlying cerebrovascular disease
    – Subarachnoid hemorrhages (SAH)
      » Aneurysms
    – Parenchymal
      » Hypertension

ARACHNOID

DURA

BRAIN

INTRAPARENCHYMAL HEMORRHAGE (IPH)

• Hypertension (most common cause of spontaneous IPH)
• Cerebral amyloid angiopathy, CAA (most common cause of spontaneous IPH in elderly)
• Arteriovenous malformation (most common cause of spontaneous IPH in children)
• Secondary hemorrhagic
  – Hemorrhagic conversion of ischemic stroke
INTRAPARENCHYMAL HEMORRHAGE

• HYPERTENSIVE HEMORRHAGES
  – Common locations:
    • PUTAMEN
    • THALAMUS
    • PONS
    • CEREBELLUM
  – Secondary to rupture of pseudaneurysms (Charcot-Bouchard)
    • Chronic HTN
    • Lenticulostriate arteries, paramedial pontine vessels and short circumferential vessels of the cerebellum and in the central white matter (similar distribution as lacunar infarcts)
  – Other causes:
    • CAA
    • Vasculitis
    • Neoplasms

HYPERTENSIVE HEMORRHAGE
- Circumscribed hematoma surrounded by brain tissue
- Hemorrhage may extend into the subarachnoid space or to the ventricles

THALAMUS
PONS

INTRAPARENCHYMAL HEMORRHAGE
INTRAVENTRICULAR HEMORRHAGE

- Primary
  - Very rare in adults
  - Common in premature infants
- Site of hemorrhage is in germinal matrix located beneath the ependyma which easily ruptures into the ventricles
- Massive intraventricular hemorrhages are instantaneously fatal
SUBARACHNOID HEMORRHAGE

- Bleeding into subarachnoid space
  - "Berry" aneurysm
    - 80% of non-traumatic subarachnoid hemorrhage
  - AVM
  - Anticoagulated state

- CSF shows xanthochromia (yellow hue due to bilirubin)

PATHOLOGY:

- Gross - "berry-like" thin-walled (no media) outpouchings from arterial branching points
- Site of rupture is at the dome
- Associated vascular spasm produces global cerebral ischemia

SACCULAR (BERRY) ANEURYSMS

- Etiology unclear
  - Congenital defect in media hypothesized
  - Genetic component
    - Associated with: autosomal dominant polycystic kidney disease, Ehlers-Danlos IV, NF I, Marfan’s
  - Female predominance (2:1)
- Most are asymptomatic until rupture
- Fatal in 50% of patients in first 24 hours
- Most in anterior circle of Willis (anterior communicating artery)
**EPIDURAL HEMATOMA**

- Due to head trauma
- Mechanism: rupture of *middle meningeal artery* due to fracture of temporal bone
- Blood accumulates between dura and the skull
- Non-contrast CT: lens-shaped hyperdense lesion
- Lucid interval may precede neurologic signs
- Herniation is lethal complication

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**SUBDURAL HEMATOMA**

- Usually due to head trauma (may be trivial)
- Blood between the dura and the arachnoid
- Mechanisms: tearing of bridging veins between dura and arachnoid – low pressure venous bleed
- Non-contrast CT: crescent – shaped lesion
- Progressive neurologic signs
- ↑ in elderly due to age-related cerebral atrophy, which stretches bridging veins
- Herniation is lethal complication
SUBDURAL HEMATOMA

CEREBRAL VENOUS THROMBOSIS (CVT)
• Thrombotic obstruction of cerebral veins or dural sinuses
• All age groups affected (from neonates to elderly)
  – Predisposing conditions: pregnancy, oral contraceptives, malignancy, infections
• Symptoms may be non-specific and mild
  – Headaches and clinical picture of benign intracranial hypertension should prompt imaging

CEREBRAL VENOUS THROMBOSIS (CVT)
• Noninfectious
  – Coagulation disorders (factor V Leiden, antiphospholipid syndrome etc.)
  – Hematologic diseases (polycythemia, sickle cell disease)
  – Pregnancy
  – Malignancy
  – Malnutrition
  – Association with certain systemic conditions (inflammatory bowel disease, collagen disorders)
• INFECTIONS
  – Cavernous sinus – Staph aureus: spread from facial, sphenoid or ethmoid sinus infection
  – Lateral sinus – from otitis media or mastoiditis
CEREBRAL VENOUS THROMBOSIS (CVT)

- Most common sites: superior sagittal sinus and lateral sinus
- Superior sagittal sinus thrombosis:
  - Hemorrhagic infarction
  - Parasagittal hemorrhages extending to the white matter
  - Edema

CEREBRAL VENOUS THROMBOSIS (CVT)

Thrombosis of the anterior part of the superior sagittal sinus. T1-weighted post contrast image

a) Hemorrhagic necrosis of parasagittal brain parenchyma in the superior sagittal sinus thrombosis. b) thrombus occluding the sinus

BRAIN HERNIATION

- Displacement of the brain due to mass effect or increased intracranial pressure
Tonsillar herniation

- Downward displacement of the cerebellar tonsils through foramen magnum
- An expansile mass in the posterior cranial fossa or supratentorial
- Hemorrhagic necrosis of the cerebellar tonsils and a groove on the ventral surface of the medulla
- Results in compression of brain stem and cardiopulmonary arrest

Uncal herniation

- Any supratentorial hemispheric mass may cause herniation of ipsilateral uncus (medial temporal lobe) through the tentorium
- Central transtentorial herniation
- Effects:
  - Compression of CN III (oculomotor) – eye "down and out" + dilated pupil
  - Compression of PCA – occipital lobe infarct (contralateral homonymous hemianopia)
  - Rupture of paramedian artery – Duret hemorrhages

DURET HEMORRHAGES

Wide left uncal grooving from patient with large inoperable brain tumor in the left temporal and parietal lobes.
Quiz. See last slide for answers.

Questions?

"Mr. Osborn, may I be excused? My brain is full."

ISCHEMIC INFARCT – HISTOLOGIC CHANGES

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<th>24-72 HOURS</th>
<th>3-7 DAYS</th>
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ANSWERS

• A – INFARCT IN THE MIDDLE CEREBRAL ARTERY TERRITORY
• B1 – SUBFALCINE HERNIATION
• B2 – UNCAL HERNIATION
• C – DURET HEMORRHAGE