CEREBRAL BLOOD FLOW AND METABOLISM

Part 1
Basilar A.

- ant-inf. Cerebellar A.
- int. Auditory A.
- Pontine Aa.
- sup. Cerebellar A.
- POSTERIOR CEREBRAL A.

Carotidian system ~ ICA

- Hypophyseal A.
- Ophthalmic A.
- post. Communicating A.
- MIDDLE CEREBRAL A.
- ANTERIOR CEREBRAL A.
Capillaries in the brain

Blood vessels are responsible for 25-30% of total brain volume.

Capillaries:
- diameter 6-7μm
- at a distance of 40 μm
- total length ~ 650 km

Capillaries in the brain

The endothelium is the thin layer of cells that lines the interior surface of blood vessels. In the brain there are highly differentiated endothelial cells to perform specialized functions:

- Protection (blood-brain barrier)
- Selective permeability
- Regulation of transport

Total cross sectional area $\sim 12 \, m^2$
Brain blood supply features

Oxygen requirement

2% of body weight (1400-1500g)
15% of cardiac output (700-750ml)
20% of total body oxygen

Continuous oxygen requirement:

Neurons are predominantly aerobic

Few minutes of ischemia causes irreversible injury

Oxygen extraction = 35%
Oxygen supply is 3 times bigger than demand

Sensitive areas

**Adults:**
- Hippocampus,
- 3,5th & 6th layer of cortex,
- Purkinje cells
- Border zone (watershed areas)

**Infants:**
- Brain stem nuclei in infants.
Clinical Categories of Inadequacy

1. **Global Ischemia**
   - Hypotension, hypoxemia, anemia
   - Hypoxemic encephalopathy

2. **Focal Ischemia**
   - Obstruction to blood supply to focal area
   - Thrombosis, embolism or hemorrhage
1. Global Ischemia

**Etiology:**
- Impaired blood supply - Lung & Heart disorders
- Impaired O$_2$ carrying - Anemia/ Blood disorders

**Morphology:**
- Laminar necrosis, damage in: Hippocampus, Purkinje cells
- Border zone infarcts - “Watershed”
- Sickle shaped band of necrosis on cortex.

**Clinical Features:**
- Mild transient confusion state
- Severe irreversible brain death; flat EEG, vegetative state, coma
2. Focal Ischemia

Cessation of blood circulation, oxygen and nutrients in a particular region of brain

~ Stroke
Definition of Stroke

Cerebro-vascular disorder caused by insufficient cerebral circulation, and resulting in sudden neurological deficits.

- Infarction (~Ischemia)
- Haemorrhage (~Bleeding)

Outcome depending on the location and the extent of the vasculature involved.
**Common causes and incidence**

**Infarction:** tissue death (necrosis) due to a local lack of oxygen caused by obstruction of the tissue's blood supply.

- **Incidence 80% - mortality 40%**
  - 50% - Thrombotic – atherosclerosis
    - Large-vessel 30% (carotid, middle cerebral)
    - Small vessel 20% (lacunar stroke)
  - 30% Embolic (heart disease/atherosclerosis)
    - Young, rapid, extensive

**Hemorrhage:** bleeding, within the skull

- **Incidence 20% - mortality 80%**
  - Intracerebral or subarachnoid.
  - Aneurysm (hypertension/congenital), arteriovenous malformation
Infarction ~ Ischemia

Emboli formation

Cell death in **6min**

**Umbra** = central infarct area

surrounded by: **Penumbra** = ischemic tissue that may recover
Correlation of Cerebral Blood Flow with Tissue Oxygenation

- Anaerobic Metabolism
- ATP Depletion
- Membrane Failure

Graph showing the correlation between CBF (mLs/100 gms/min) and Tissue PO$_2$ (mmHg).
Collateral circulation helps to maintain some CBF to post obstruction area

- **Core** ~ CBF < 10 ml/100gm/min
  Early irreversible membrane rupture & cell death

- **Periphery** ~ CBF < 20 ml/100gm/min
  Rapid energy depletion & loss of neuronal activity (electrically silent)
  Manifets as neuro deficit bigger than infarct
  Neuronal membrane & cellular functions remain intact ~ neurons remain viable
Infarct Pathogenesis

- Reduced blood supply – hypoxia/anoxia
- Altered metabolism ‡ Na/K pump block
- Glutamate receptor act. ‡ Ca influx

1-6 min – ischemic injury ‡ vacuolation
>6 min – cell death
Animal models & human studies (MRI, PET) of acute ischemia shows:

- < 2 hrs → reversible neuro deficit
- > 6 hrs → irreversible neuro deficit

Clinical studies & current therapies aim for reperfusion within 2 to 6 hrs (therapeutic window)
Infarct Stages

- **Immediate – 6 hours**
  - No change (both macro & micro)

- **Acute stage – 2 days**
  - Oedema, loss of grey/white matter border
  - Inflammation, Red neurons, neutrophils

- **Intermediate stage – 2 weeks**
  - Demarcation, soft friable tissue, cysts
  - Macrophages, liquifactive necrosis

- **Late stage – After 4 weeks**
  - Fluid filled cysts with dark grey margin (gliosis)
  - Removal of tissue by macrophages
  - Gliosis – proliferation of glia, loss of architecture
Investigations

- CT of the brain without contrast – location/extension
- Electrocardiogram - heart
- Chest x-ray - heart
- complete blood count, platelet count – hematology
- PT, aPTT – coagulation
- Serum electrolytes – complications
- Blood glucose - DM
- Renal and hepatic chemical analyses – status
- National Institutes of Health Scale (NIHSS) score – clinical/prognosis?

Brott et al, NEJM 2000
Diagnosis of Thrombotic Stroke

CT scan

Cerebral Hemorrhage

Cerebral Infarct

Further Investigation

Atrial fibrillation

Anticouagulation

Carotid artery stenosis

Surgery at 70% stenosis

Antiplatelet therapy
Ischemic penumbra
Risk Factors of Stroke

Non modifiable
- Age
- Male sex
- Race
- Heredity

Modifiable
- Hypertension
- Diabetes
- Smoking
- Hyperlipidemia
- Excess Alcohol*
- Heart disease (AF)
- Oral contraceptives
- Hypercoagulability
National Stroke Association’s Stroke Prevention Guidelines

1. Know your **blood pressure**. Have it checked at least annually. If it is elevated, work with your doctor to control it.
2. Find out if you have **atrial fibrillation**.
3. If you **smoke**, stop.
4. If you drink **alcohol**, do so in moderation.
5. If you have high **cholesterol**, work with your doctor to control it.
National Stroke Association’s Stroke Prevention Guidelines

6. If you are diabetic, follow your doctor’s recommendations carefully to control your diabetes.

7. Include exercise in the activities you enjoy in your daily routine.

8. Enjoy a lower sodium (salt), lower fat diet.

9. Work with your doctor if you have circulation problems.

10. If you experience any stroke symptoms, seek immediate medical attention.
## The Perceptions of Stroke

<table>
<thead>
<tr>
<th>Myth</th>
<th>Reality</th>
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<tbody>
<tr>
<td>Stroke is not preventable</td>
<td>Up to 80% percent of strokes are preventable</td>
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<tr>
<td>Stroke cannot be treated</td>
<td>Stroke requires emergency treatment</td>
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<tr>
<td>Stroke only strikes the elderly</td>
<td>Anyone can have a stroke</td>
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<td>Stroke happens in the heart</td>
<td>Stroke is a “Brain Attack”</td>
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<tr>
<td>Stroke recovery ends after 6 months</td>
<td>Stroke recovery can last a lifetime</td>
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Be Stroke Smart!

The “3 R’s” of Stroke:

**Reduce** Stroke Risk

**Recognize** Stroke Symptoms

**Respond**: At the first sign of stroke, Call emergency or Get to the Hospital Fast!

80% of all Strokes are **Preventable**!
Stroke Symptoms

Severe headache
Trouble seeing in one or both eyes
Sudden: dizziness
confusion
numbness

Get to the hospital or call emergency
FAST! Time is brain!
Stroke Management

- Acute care
  1. General measures
  2. Drug therapy
  3. Other therapies

- Chronic care
  1. Nutritional
  2. Stroke unit care
General Treatment

- Maintenance of appropriate BP
- Maintenance of euglycemia
- Fever control
- Nutrition + prevention of aspiration
- Deep Vein Thrombosis (DVT)-prophylaxis
- Rehabilitation
- Early mobilization
BP Control in Acute Stroke

Intervention is needed in

1. Marked hypertension
   § SBP > 220 mmHg
   § DBP > 120 mmHg
   § MAP > 130 mmHg

2. Thrombolysis
   § BP > 185/110
   § Two attempts at correction

Specific medical indication
   § AMI / aortic dissection / CHF / hypertensive encephalopathy (rare)
CPP = cerebral Perfusion Pressure
MAP = Mean Arterial Pressure
ICP = Intracranial Pressure
Cerebral Autoregulation

![Graph showing cerebral blood flow and cerebral perfusion pressure relationship with intact and lost autoregulation](image-url)
Types of Stroke Rehabilitation

1. Physical Therapy (PT)
   Walking, range of movement
2. Occupational Therapy (OT)
   Taking care of one’s self
3. Speech Language Therapy
   Communication skill, swallowing, cognition
4. Recreational Therapy
   Cooking, gardening, etc.
Stroke Recovery

10% recover almost completely

25% recover with minor impairments

40% experience moderate to severe impairments requiring special care

10% require care within either a skilled-care or other long-term care facility

15% die shortly after the stroke
Causes of Hypotension

- Myocardial infarction
- Septic shock
- Internal hemorrhage
  - Massive GI bleed (e.g. ruptured varices, bleeding ulcer, carcinoma)
- Ruptured aortic aneurysm
- Others