Physiology of cerebral blood flow

Brain makes up only 2% of body weight

Percentage of cardiac output: 15-20%
Percentage of O₂ consumption (resting): 15%

Distribution of circulation:
- anterior circulation > posterior circulation
  (70%)  (30%)
- gray matter > white matter
Blood flow is a fraction of:

- perfusion pressure
- resistance of vascular bed as modified by:
  - arterial pressure
  - pCO\(_2\), pH, and oxygen
  - intracranial pressure
  - blood viscosity
  - neurotransmitters???

Relatively constant blood flow primarily governed by autoregulatory mechanism

Effects of cerebral perfusion pressure on cerebral blood flow

Striatum: Lenticulostriate arteries from MCA (mostly) & ACA
Globus Pallidus: Ant. choroidal arteries from ICA
Thalamus & Hippocampus: PCA

Boundary zone (watershed) most distal part of arterial irrigation
Epidemiology of stroke

- Almost 750,000 new or recurrent strokes per year in the U.S.

- Third leading cause of death in the U.S.; second worldwide

- Almost 4 million Americans are living with neurologic deficits due to stroke

- Prevention, prevention, and prevention (Only 1-2% of ischemic stroke patients nationally are treated with Tissue Plasminogen Activator.)
**Stroke**
Classical definitions (WHO 1980):
“Rapidly developing clinical signs of focal (at times global) disturbance of cerebral function, lasting more than 24 hours or leading to death with no apparent cause other than that of vascular origin.”

If symptoms resolve within 24 hours the episode is called a transient ischemic attack – **TIA**.

* Total risk 25% for stroke in 90 days

**Types of stroke**
- thromboembolism
- hemorrhage

- Ischemic stroke (infarction) 85%
- Hemorrhagic stroke 15%
  - intracranial 67%
  - SAH 33%
Types of stroke vary in the world.

Determinants of stroke

**Nonmodifiable risk factors**
- Age
- Gender
- Ethnicity
- Heredity

**Modifiable risk factors**
- Hypertension
- Diabetes
- Cardiac disease (atrial fibrillation)
- Hypercholesterolemia
- Cigarette smoking
- Alcohol abuse
- Physical inactivity
Cerebral infarction

Morphologic Evolution

Sequence of microscopic changes in brain infarcts

> 1 hour  
Microvacuoles within neurons  
(swollen mitochondria)  
Perineuronal vacuolation  
(swollen astrocytic processes)
### Sequence of microscopic changes in brain infarcts

<table>
<thead>
<tr>
<th>Time Frame</th>
<th>Changes</th>
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<tbody>
<tr>
<td>&gt; 1 hour</td>
<td>Microvacuoles within neurons (swollen mitochondria)</td>
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<tr>
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<td>Perineuronal vacuolation (swollen astrocytic processes)</td>
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<td>4-12 hours</td>
<td>Neuronal cytoplasmic eosinophilia</td>
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<td>Disappearance of Nissl bodies</td>
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<td>Pyknotic nuclei</td>
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<td>Leakage of blood-brain barrier</td>
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<td>15-24 hours</td>
<td>Neutrophil infiltration begins</td>
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- Neutrophil infiltration begins

2-3 days
- Macrophages (foam cells) appear

5 days
- Neutrophilic infiltration ceases

~ 1 week
- Proliferation of astrocytes around core infarct

4-12 hours
- Neuronal cytoplasmic eosinophilia
- Disappearance of Nissl bodies
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- Neutrophil infiltration begins

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Topographic features – size & extent of infarct

Site of occlusion

Presence/absence of anastomosis
- Ophthalmic artery (EC-IC)
- The circle of Willis
- Leptomeningial anastomosis
Underlying conditions of infarction

I. Atherosclerosis
Underlying conditions of infarction

II. Arteriolar sclerosis (small vessel disease)

- aging
- sustained systemic hypertension
- diabetes mellitus
Underlying conditions of infarction

III. Cerebral embolism

Some causes of cerebral embolism

Large or small emboli:
- atrial fibrillation
- myocardial infarction
- bacterial endocarditis
- rheumatic endocarditis
- nonbacterial endocarditis
- cardiac surgery
- arterial thrombosis

Small emboli:
- ulcerated atheroma
- trauma (fat emboli)
IV. Vasculitis/vasculitides

Underlying conditions of infarction

Inflammatory CNS vascular diseases

Non-infectious vasculitides
  Primary cranial and/or cerebral inflammations
    - Takayasu’s arteritis
    - giant cell or temporal arteritis
    - primary angitis of the CNS
      (granulomatous angiitis)

Manifestations of systemic diseases
  - systemic lupus erythematosus
  - polyarteritis nodosa
  - Wegener’s granulomatosis
  - Churg-Strauss syndrome
  - Behcet’s syndrome
  - malignancy related

Drug induced vasculitis

Infectious vasculitis
I. Intracerebral hemorrhage

Incidence:
Asians > African Americans > Caucasians

Causes of non-traumatic ICH:
- Hypertension: 50%
- Cerebral amyloid angiopathy: 12%
- Anticoagulants: 10%
- Tumors: 8%
- Illicit and licit drugs: 6%
- Arteriovenous malformations and aneurysms: 5%
- Miscellaneous: 9%
Hypertensive hemorrhage

Frequent sites of involvement
Cerebral hemorrhage

II. SAH subarachnoidal hemorrhage

Frequency: Approx. 5% of all strokes
Reported annual incidence: 10-11 / 100,000

• Non-traumatic conditions
  - rupture of aneurysm* 80%
  - arteriovenous malformations** 5-10%
  - unidentified cause 10-15%

• Traumatic
## Underlying conditions of SAH

### a. Saccular (berry) aneurysms

<table>
<thead>
<tr>
<th></th>
<th>1 to 6%</th>
<th>30 - 70 yrs</th>
<th>F:M = 3:2</th>
<th>50%</th>
<th>Rare</th>
<th>Anterior circulation &gt; 80%</th>
<th>Posterior circulation &lt; 20%</th>
<th>20%</th>
<th>Size &gt; 0.5 cm</th>
<th>60%</th>
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<tbody>
<tr>
<td>Frequency at autopsy</td>
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<td>Age at autopsy</td>
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<td>Ruptured aneurysms</td>
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<td>Mortality</td>
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</tbody>
</table>
2. Arteriovenous malformation

IPH / SAH
# Arteriovenous malformations

<table>
<thead>
<tr>
<th>Clinical onset:</th>
<th>Age 10 to 40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex ratio:</td>
<td>M:F = 2:1</td>
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<tr>
<td>Location:</td>
<td>Usually supratentorial</td>
</tr>
<tr>
<td>Clinical presentation:</td>
<td>Headache, seizures, focal neurologic deficit, hemorrhage</td>
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<tr>
<td>Angiography:</td>
<td>Evidence of arteriovenous shunt and abnormal blood vessels</td>
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<tr>
<td>Mortality after hemorrhage:</td>
<td>20%</td>
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</tbody>
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Genetics and Stroke

**Genetic cardiovascular disorders** leading to thromboemboli in CNS
- Arterial dissection, Cardiomyopathies, Neuromuscular diseases, Metabolic conditions (e.g. Homocysteinuria, Coagulopathies, Dyslipidaemia)

**Genetic metabolic disorders** prone to obstruct CNS vessels (e.g. Fabry’s disease)
- CADASIL (AD arteriopathy with subcortical infarcts and leukoencephalopathy)
  - notch 3
- MELAS (Mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes)
  - mitochondrial DNA mutations

The End

ENJOY small group study!