III. Neuropathology of Cerebrovascular Disease

Physiology of cerebral blood flow

Brain makes up only 2% of body weight

Percentage of cardiac output: 15-20%
Percentage of $O_2$ consumption (resting): 15%

Distribution of circulation:
- anterior circulation > posterior circulation (70%) (30%)
- gray matter > white matter
Blood flow is a function 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
- Striatum: Lenticulostriate arteries from MCA (mostly) & ACA
- Globus Pallidus: Ant. choroidal arteries from ICA
- Thalamus & Hippocampus: PCA
Epidemiology of stroke

American Heart Association:
USA - almost 4 million stroke survivors
- almost 730,000 new strokes occur per year

Overall age adjusted incidence rates: 100 to 300 / 100,000

Overall, stroke accounts for about 10% of all deaths in most industrialized countries.

Most of these deaths are among persons over the age of 65.

Average age-adjusted stroke mortality in US: 50 to 100/100,000

Stroke
Cerebrovascular accident
"Brain attack"

Defined as an abrupt onset of focal or global neurological symptoms caused by ischemia or hemorrhage.

By convention, symptoms must continue for >24 hours and is usually associated with permanent damage to brain tissue.

If symptoms resolve within 24 hours the episode is called a transient ischemic attack - TIA.
Frequencies of stroke subtypes

- Cerebral infarction: 60-80%
- Intracerebral hemorrhage: 10-30%
- Subarachnoid hemorrhage: 5-10%
- Other (unspecified): 3-25%

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
Annual risk of stroke (all subtypes combined)

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Approximate population risk</th>
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<tbody>
<tr>
<td>0-14</td>
<td>1 in 100,000</td>
</tr>
<tr>
<td>15-24</td>
<td>1 in 20,000</td>
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<tr>
<td>25-34</td>
<td>1 in 10,000</td>
</tr>
<tr>
<td>35-44</td>
<td>1 in 5,000</td>
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<tr>
<td>45-54</td>
<td>1 in 1,000</td>
</tr>
<tr>
<td>55-64</td>
<td>1 in 300</td>
</tr>
<tr>
<td>65-74</td>
<td>1 in 100</td>
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<tr>
<td>75-85</td>
<td>1 in 50</td>
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<tr>
<td>&gt;85</td>
<td>1 in 33</td>
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Cerebral infarction

Morphologic Evolution
Sequence of microscopic changes in brain infarcts

> 1 hour
- Microvacuoles within neurons (swollen mitochondria)
- Perineuronal vacuolation (swollen astrocytic processes)

4-12 hours
- Neuronal cytoplasmic eosinophilia
- Disappearance of Nissl bodies
- Pyknotic nuclei
- Leakage of blood-brain barrier
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15-24 hours  
Neutrophil infiltration begins

2-3 days  
Macrophages (foam cells) appear

5 days  
Neutrophilic infiltration ceases

~ 1 week  
Proliferation of astrocytes around core infarct
**Sequence of microscopic changes in brain infarcts**

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<th>Time</th>
<th>Changes</th>
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<td>&gt; 1 hour</td>
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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
II. Arteriolar sclerosis
(small artery disease)

- aging
- sustained systemic hypertension
- diabetes mellitus
III. Cerebral embolism

Underlying conditions of infarction
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)
Underlying conditions of infarction

IV. Vasculitis/vasculitides
Inflammatory CNS vascular diseases

Non-infectious vasculitides

Primary cranial and/or cerebral inflammations
- Takayasu’s arteritis
- giant cell or temporal arteritis
- primary angiitis 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

Cerebral hemorrhage

- intracerebral
- subarachnoid

- epidural /subdural (trauma)
Intracerebral hemorrhage

Incidence:
Caucasian populations - 16-32 / 100,000
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%

Cerebral hemorrhage

I. Hypertensive hemorrhage
Cerebral hemorrhage

II. SAH subarachnoidal hemorrhage

Frequency: 5-9% 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%

• Secondary
  ♦ intracerebral hemorrhage
  ♦ intraventricular hemorrhage

• Traumatic
Underlying conditions of SAH

1. Intracranial (saccular) aneurysms

- Frequency at autopsy: 1 to 6%
- Age at autopsy: 30 - 70 yrs
- Sex ratio: F:M = 3:2
- Associated hypertension: 50%
- Familial: Rare
- Location: Anterior circulation > 80%
  Posterior circulation < 20%
- Multiple: 20%
- Ruptured aneurysms: Size > 0.5 cm
- Mortality: 60%
Underlying conditions of SAH/IPH

2. Vascular malformations
Arteriovenous malformations

<table>
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<th>Clinical onset:</th>
<th>Age 10 to 40</th>
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<tbody>
<tr>
<td>Sex ratio:</td>
<td>M:F = 2:1</td>
</tr>
<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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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