Stroke II: Diagnosis, Evaluation, and Prevention

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Definition of Stroke/Brain Attack
• A syndrome caused by disruption in the flow of blood to part of the brain due to either:
  - occlusion of a blood vessel
    • ischemic stroke
  - rupture of a blood vessel
    • hemorrhagic stroke
• The interruption in blood flow deprives the brain of nutrients and oxygen resulting in injury to cells in the affected vascular territory of the brain

Stroke: The Problem
• Third leading cause of death in US
  – after heart disease and cancer
• 740,000 new strokes each year
• 4.5 million stroke survivors
• Leading cause of disability in adults in US
• $45.5 billion per year in the USA
• 1 of 6 Americans will be affected

Stroke: The Problem
• Among 6 month or longer survivors:
  – 48% have a hemiparesis
  – 22% cannot walk
  – 24-53% report complete or partial dependence for activities
  – 12-18% are aphasic
  – 32% are clinically depressed
  – only 10% fully recover

Symptoms of Brain Attack: Teach your patients!
• Sudden weakness, paralysis, or numbness of:
  – face
  – arm and the leg on one or both sides of the body
• Sudden loss of speech, or difficulty speaking or understanding speech
• Sudden dimness or loss of vision
  – particularly in only one eye

Symptoms of Brain Attack: Teach your patients!
• Sudden unexplained dizziness
  – especially when associated with other neurologic symptoms
  – unsteadiness
  – sudden falls
• Sudden severe headache and/or loss of consciousness
Ischemic Stroke

• Most common stroke type
  – 85% of all strokes
• 65% of 1st time strokes

Ischemic Stroke Risk Factors: Nonmodifiable

• Older age
• Male sex
• Race
• Genetic factors

Ischemic Stroke Risk Factors: Modifiable

• Hypertension
  – increases risk 6-8 times above baseline population
  – even “borderline” HTN is associated with increased risk of stroke
• Controlling HTN is the single most important measure to be taken in decreasing the risk of stroke

Ischemic Stroke Risk Factors: Modifiable

• Cigarette smoking
  – RR =1.5
• Asymptomatic carotid artery stenosis
• Physical inactivity
• Diabetes mellitus
  – RR+1.5 - 3
• Elevated cholesterol
• Prior TIA
• Cardiac risk factors
  – Afib, etc.

Ischemic Stroke Risk Factors: Modifiable/Putative

• Elevated homocysteine
• Migraine
• Oral contraceptives
• Obesity
• Alcohol abuse
• Stress
• Sleep apnea
• Illegal drug use
• Infection
  – chlamydia
  – pneumonia
• Hypercoagulable states
• Systemic inflammation/
  connective tissue disorders
• Sympathomimetic medications

Is it a stroke?
NINDS Classification: Ischemic Strokes

- **Clinical**
  - atherothrombotic
  - cardioembolic
  - lacunar

- **Mechanism**
  - thrombotic
  - embolic
  - hemodynamic

- **Arterial territory**
  - internal carotid
  - middle cerebral
  - anterior cerebral
  - vertebral
  - basilar
  - posterior cerebral

Stroke Syndromes by Location: Middle Cerebral Artery (MCA)

- Contralateral face=arm>leg paralysis
- Contralateral cortical and primary sensory impairment
  - face
  - arm
  - leg

Stroke Syndromes by Vascular Territory: MCA

- Complete
- Superior division
- Inferior division
- Gerstman Syndrome
  - agraphia - inability to write
  - acalculia - inability to calculate
  - right-left confusion
  - finger agnosia - inability to recognize fingers
    - ideomotor apraxia may be associated
- Ataxic hemiparesis

Stroke Syndromes by Location: MCA

- Language disorders:
  - aphasia
  - alexia
  - agraphia
    - cortical signs c/w dominant hemisphere involvement

Stroke Syndromes by Location: MCA

- Anosognosia - ignorance of deficit
  - unilateral neglect
  - constructional apraxia
  - abnormal spatial localization
    - cortical signs c/w nondominant hemisphere involvement
Large Vessel Ischemic Stroke

- MCA territory distribution stroke due to critical stenosis of the right internal carotid artery

Stroke Syndromes by Vascular Territory: Anterior Cerebral Artery (ACA)

Stroke Syndromes by Location: ACA

- Contralateral foot and leg paralysis
- Contralateral “cortical sensory” impairment of the lower extremity
- Extreme apathy (abulia) especially in bilateral lesions
- Gait apraxia or “cerebral paraplegia” in bilateral lesions with injury to the corpus callosum

Stroke Syndromes by Location: Posterior Circulation

Stroke Syndromes by Location: Posterior Cerebral Artery (PCA)

- Homonymous hemianopsia
  - due to ischemia of the calcarine cortex
  - usually with macular or the optic radiation
- Cortical blindness
  - bilateral homonymous hemianopsia
  - may see Anton’s syndrome: visual confabulation
- Thalamic syndromes
  - sensory loss or spontaneous pain/dysaesthesias or movement disorders
    - chorea/tremor

Stroke Syndromes by Vascular Territory: PCA

- Balint Syndrome
  - loss of voluntary but not reflex eye movements
  - optic ataxia
  - asimultagnosia
    - unable to understand visual objects as a whole
- Alexia without agraphia
- Weber Syndrome (Midbrain)
  - weakness contralateral upper and lower extremity
  - ipsilateral gaze palsy (CN3)
Stroke Syndromes by Vascular Territory: PCA

Patient with alexia w/o agraphia

Stroke Syndromes by Location: Posterior Circulation

Stroke Syndromes by Vascular Territory: Posterior Circulation

- Hallmarks of brainstem/cerebellum involvement:
  - diplopia
  - vertigo
  - ataxia
  - nystagmus

Stroke Syndromes by Vascular Territory: Basilar Branch

- Anterior Inferior Cerebellar Artery
- Lateral pontine syndrome - Marie-Foix Syndrome
  - Ipsilateral cerebellar ataxia due to involvement of cerebellar tracts (middle cerebellar peduncle)
  - Contralateral hemiparesis due to corticospinal tract involvement
  - Variable contralateral hemihypesthesia for pain and temperature due to spinothalamic tract involvement
- Posterior inferior cerebellar artery
- Lateral medullary syndrome - of Wallenberg
  - Ipsilateral limb ataxia, vertigo, nystagmus, dysphagia, Homer syndrome

Stroke Syndromes by Vascular Territory: Basilar Branch/Penetrators

- Locked-in Syndrome
- Lateral pontine syndrome - Marie-Foix Syndrome
- Ventral pontine syndrome - Raymond Syndrome
- Ventral pontine syndrome - Millard-Gubler Syndrome
- Inferior medial pontine syndrome - Foville Syndrome
- Ataxic Hemiparesis
- Cortical blindness - Anton Syndrome
- Medial medullary syndrome
- See www.strokecenter.org for details

Stroke Syndromes by Vascular Territory: Vertebral Artery

- Lateral Medullary syndrome - of Wallenburg
- Medial medullary syndrome - Dejerine Syndrome
- May also be seen with anterior spinal artery involvement
  - rare stroke syndrome (<1% of vertebrobasilar strokes, Bassetti et al., 1994)
  - Medial medullary infarct is associated with clinical triad of ipsilateral hypoglossal palsy, contralateral hemiparesis, and contralateral lemniscal sensory loss
  - variable manifestations may include isolated hemiparesis, tetraparesis, ipsilateral hemiparesis, I or C facial palsy, ataxia, vertigo, nystagmus, dysphagia
  - palatal and pharyngeal weakness rare in pure MMI, common in lateral medullary infarct
NINDS Classification: Ischemic Strokes

- **Clinical**
  - atherothrombotic/
large vessel ischemia
  - cardioembolic
  - lacunar

- **Mechanism**
  - thrombotic
  - embolic
  - hemodynamic

Large Vessel Ischemic Stroke

- **Arterial territory**
  - internal carotid
  - middle cerebral
  - anterior cerebral
  - vertebral
  - basilar
  - posterior cerebral

Large Vessel Ischemic Stroke

- The large extracranial and intracranial arteries are predisposed to atherosclerotic narrowing/occlusion
- Bifurcations are common sites:
  - internal carotid artery at the bulb
  - vertebral and basilar arteries
  - middle cerebral arteries

Large Vessel Ischemic Stroke: Mechanisms

- Artery to artery embolism
  - plaque/thrombus from a proximal artery becomes dislodged, travels distally, and obstructs a smaller segment or branch of the artery
- Thrombosis
  - propagation of thrombus along arterial wall until the vessel is occluded or critically stenosed
- Hypoperfusion
  - through a critical arteriosclerotic stenosis affecting the territory of that artery

Large Vessel Ischemic Stroke

- Normal carotid bifurcation
- Stenosis of the ICA will usually produce stroke syndromes referable to the middle cerebral artery territory

Large Vessel Ischemic Stroke

- MCA territory distribution stroke due to critical stenosis of the right internal carotid artery

Large Vessel Ischemic Stroke

Doppler study of the right internal carotid artery showing 80% stenosis near the origin (in the bulb)
Cardiac Embolism

- Among the most devastating of the stroke types
- Least likely to present with prior transient ischemic attacks
- Most likely to recur if patient is not adequately prophylaxed for subsequent events
- Cortical, rather than deep white matter, strokes predominate

Atrial Fibrillation (AF)

- Most common cardiac arrhythmia and affecting 1% of the population
- Prevalence increases with increasing age
- Relatively infrequent in those under 40 years old
- Occurs in upwards of 5% of those over 80 years of age

Incidence of Stroke

- Incidence of stroke associated with AF increases with age

<table>
<thead>
<tr>
<th>Stroke Rate (percent per year)</th>
<th>Age Group (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.3</td>
<td>50-59</td>
</tr>
<tr>
<td>2.2</td>
<td>60-69</td>
</tr>
<tr>
<td>4.2</td>
<td>70-79</td>
</tr>
<tr>
<td>5.1</td>
<td>80-89</td>
</tr>
</tbody>
</table>

Cardiogenic Embolism

- Atrial Fibrillation
- Acute Myocardial Infarction
- Valvular disease
  - mitral and aortic valves
- Dilated cardiomyopathy
- Intracardiac tumors
  - atrial myxoma
- Intracardiac defects

Risk of Stroke in AF: Other Studies

- Once you have had a cardioembolic stroke, the risk of recurrence in the first 2-3 years may be as high as 12% per year if untreated
- International Stroke Trial
  - Lancet 1997;349:1569
- Oxfordshire community stroke project
  - BMJ1992;305:1460

Cardiogenic Embolism

- "Hyperdense MCA sign" – due to embolic occlusion of the right middle cerebral artery with distal clot propagation
Small Vessel Ischemic Stroke
Lacunar Infarctions

• Occlusion of one of the lenticulostriate vessels with resultant lacunar stroke
• Typically <1.5 cm in diameter
• Stuttering clinical course

Lacunar Syndromes

<table>
<thead>
<tr>
<th>Anatomical Site</th>
<th>Stroke Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genu of the internal capsule</td>
<td>Dysarthria-Clumsy Hand Syndrome</td>
</tr>
<tr>
<td>Ventral posterior thalamus</td>
<td>Pure sensory loss without weakness</td>
</tr>
<tr>
<td>Posterior of the internal capsule</td>
<td>Pure motor weakness without sensory loss</td>
</tr>
<tr>
<td>3rd nerve and cerebral peduncle</td>
<td>Weber’s syndrome: 3rd n. palsy + contralateral weakness</td>
</tr>
</tbody>
</table>

Transitory Ischemic Attack (TIA)

• Occur in over half of patients who subsequently develop a stroke
• Not a stroke
  – “warning” event that eventual stroke is likely
• Deficits may be as profound as that of major stroke—but transient
• Symptoms last less than 24 hours with full return to baseline by definition
  – typically, less than 30 minutes

TIA

• Transient monocular visual loss
  – amaurosis fugax
  – suggests lesion of the ipsilateral carotid artery
• Episodic/Transient aphasia
• Episodic/Transient hemiparesis
• Episodic/Transient vertigo
  – brain stem TIA
• Episodic/Transient diplopia
  – double vision
  – brain stem TIA
**TIA: Implications**
- 10.5% of patients with a TIA will go on to have a stroke in the next 90 days
- Half (5.2%) of these strokes will occur within 2 days of TIA presentation
- 20% of patients with a TIA will have a stroke within the 2 years following the event
- Patients should be evaluated just as fully as if they have had a completed stroke

**The “Stroke Work-up”**
- Avoid the “Million-Dollar-Shot-Gun” work-up
  - tailor testing to the relevant clinical picture and feasible treatment options

**The “Stroke Work-up”**
- Basics (*for everybody*):
  - chest X-ray
  - EKG
  - CBC
  - electrolytes
  - renal function
  - basis coagulation studies
  - glucose, urinalysis
  - stool hemoccult
  - liver panel
  - Initial CT scan
    - in just about every acute presentation of stroke

**The “Stroke Work-up”: Other Studies**
- Cardiac monitoring
  - ICU, floor monitoring, Holter monitoring in selected patients
- Hypercoagulable state work-up
- Immune mediated/vasculitic serological studies
- Modifiable risk factor screens
- Cerebrospinal fluid evaluation
- Toxin, pregnancy, myocardial infarction screens

**The “Stroke Work-up”: Imaging Studies**
- Consider:
  - Carotid Duplex Ultrasound
    - dopplers
  - MRI of the brain with diffusion/ perfusion sequences
  - MR-angiography
    - MRA
  - Conventional angiography
  - Cardiac imaging in suspected cardiac embolism
    - echocardiography

**Intracerebral Hemorrhage**
- 15-20% of all strokes
- Poorer prognosis than ischemic stroke
- 40-50% mortality in 30 days
  - rate is higher if 2nd bleed in 2 weeks
- Large decline in this stroke type primarily due to control of HTN over the past 30+ years
Intracerebral Hemorrhage: Mechanisms/Subtypes

- Hypertensive intracerebral hemorrhage
  - usually involves deep structures such as
    - the basal ganglia
      - putamen, globus pallidus, caudate
    - thalamus, pons, and deep layers of the cerebellum.
  - on presentation, BP is usually extremely elevated, but not always.
  - occurs as a result of chronic uncontrolled (severe) hypertension

- Amyloid Angiopathy
  - usually involves the cerebral lobes
    - temporal/frontal/parietal/occipital
    - with extension to the cortex or subcortex
  - often will see cortical syndromes
    - aphasia
    - neglect

- Subarachnoid Hemorrhage Due to Ruptured Berry Aneurysm
  - sudden “Thunderclap”, worst headache of one’s life
  - posterior communicating and anterior communicating arteries are most common sites

ICH: Hypertensive Hemorrhage

- high mortality
- patients present with
  - severe headache + meningismus
  - subhyaloid (retinal) hemorrhages
  - nausea and vomiting
  - +/- deficit/coma
Intracerebral Hemorrhage: Mechanisms/Subtypes

- **Subarachnoid Hemorrhage Due to Arteriovenous Malformation (AVM) Bleed**
  - may present like ruptured berry aneurysm
  - sudden “thunderclap” headache
  - more often, patients have prior symptoms
  - frequent episodic, very stereotyped
  - headaches
  - seizures

ICH: Subarachnoid Hemorrhage

ICH: Berry Aneurysm on Contrast CT

ICH: Artero-Venous Malformation on Contrast CT

Symptomatic Carotid Artery Stenosis

Doppler study of the right internal carotid artery showing 80% stenosis near the origin (in the bulb)

NASCET I: Stroke Rate at 18 Months after First Symptoms (70 to 99% ICA stenosis)

<table>
<thead>
<tr>
<th>Stenosis</th>
<th>Medical</th>
<th>Surgical</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>90-99%</td>
<td>33%</td>
<td>6%</td>
<td>27%</td>
</tr>
<tr>
<td>80-89%</td>
<td>28%</td>
<td>8%</td>
<td>20%</td>
</tr>
<tr>
<td>70-79%</td>
<td>19%</td>
<td>7%</td>
<td>12%</td>
</tr>
<tr>
<td>Total</td>
<td>25%</td>
<td>7%</td>
<td>18%</td>
</tr>
</tbody>
</table>
NASCET II: Stroke Rate at 18 Months after First Symptoms (50 - 69% ICA stenosis)

- Selective benefit for:
  - men
  - non/mild hypertensives
  - non-diabetics
  - unilateral lesion only
  - hemispheric symptoms
- ACAS (American Carotid Atherosclerosis Study) benefit in asymptomatic men with >60% unilateral stenosis if surgeon with <3% complication rate

Carotid Stenting

- Non surgical candidates
- Fibromuscular dysplasia
- Carotid dissection
- Radiation angiitis
- Inaccessible lesions
- Carotid Revascularization Endarterectomy vs. Stent Trial (CREST) now on-going
  - As of March, 2004:
    - 840 patients enrolled
    - 186 randomized at 55 centers
    - recruitment of patients and centers is ongoing

Medications used in the secondary prevention of stroke

Anti-platelet Agents: Aspirin

- Often first line therapy after first non-cardiac source ischemic stroke
- Approximately 20 – 25% stroke recurrence reduction
- Low cost
- FDA recommends 50-325 mg Qday
- GI side effects most common

Anti-platelet Agents: Ticlopidine

- More effective in reducing recurrence (21% RRR) compared to ASA
- Also effectively maintains coronary stent patency in combination with ASA
- 250 mg BID
- Risk of Leukopenia, Thrombocytopenia, Hepatic dysfunction
- GI symptoms, diarrhea (in 10%)
- May be more effective, with less side effects in African Americans

Anti-platelet Agents: Clopidogrel

- More effective than ASA in reducing recurrence (8% RRR)
- Best maintains coronary stent patency in combination with ASA
- Good ASA substitute when there is an allergy to ASA
- 75 mg per day
- Less GI side effects than ASA
- Strong benefit in peripheral vascular disease
Anti-platelet Agents: ASA + Extended Release Dipyridamole (ERDP)

- More effective in reducing recurrence (23% RRR) compared to ASA alone
- Good safety profile
- Can’t use in the ASA allergic
- May not contain enough ASA for those with coronary artery disease
- 200(ERDP)/25(ASA) BID
- Headache in upwards of a third of patients

Antiplatelet Therapy

<table>
<thead>
<tr>
<th>Relative risk reduction (above ASA alone)</th>
<th>Stroke or Stroke/MI/Death</th>
<th>Cost per month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clopidogrel (Plavix) 75 mg QD</td>
<td>8%</td>
<td>$75</td>
</tr>
<tr>
<td>Ticlopidine (Ticlid) 250 mg BID</td>
<td>21%</td>
<td>$120 or $78</td>
</tr>
<tr>
<td>Aspirin + Extended Release Dipyridamole (Aggrenox) 25/200 BID</td>
<td>23%</td>
<td>$81</td>
</tr>
<tr>
<td>Clopidogrel and ASA</td>
<td>16% not SS MATCH</td>
<td>$75 + $3</td>
</tr>
</tbody>
</table>