STROKE AND MULTIPLE SCLEROSIS

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Stroke and Multiple Sclerosis

**Stroke or Brain Attack**
- 5th Leading cause of Death for men
- 4th leading cause of Death for women
- 3rd leading cause of death for Blacks
- Acute brain injury due to a vascular etiology
- Sudden onset
- Persist at least 24 hours
- Associated neurological deficit/deficits

**TIA**
- Neurological deficits lasting less than 24 hours
Stroke Imaging

(a) CT scan showing acute right MCA infarction.
(b) Diagram of brain anatomy, including normal gray-white matter junction, normal basal ganglia (putamen), and normal fissures and sulci.
(c) Additional CT scans for comparison.
(d) Further CT scans for detailed analysis.
Stroke Imaging - diffusion/perfusion
STROKE

- 795,000 Strokes Occur each year
- 87 percent of those strokes are ischemic
- Stroke kills 130,000 Americans/year
- Stroke costs the US an estimated 34 billion/yr
- Leading cause of serious long-term disability
STROKE

- Race/Sex/Geography
  - Black risk of death is 1.49X Whites
  - Males greater risk than females
  - Hispanics higher risk for lacunar infarcts
  - Southeastern US has higher risk

- Age
  - Stroke occurs in all ages
  - Stroke increases with age
  - Age >64 is where 75% of occurrence
STROKE RISK FACTORS

• Non-modifiable Risk Factors
  • Age
  • Race
  • Sex
  • Ethnicity
  • History of Migraine
  • Sickle Cell Disease
  • Fibromuscular Dysplasia
  • Heredity
STROKE RISK FACTORS

- Laboratory Monitoring Risk
  - Glucose and Electrolytes
  - CBC with Platelets
  - Prothrombin Time/ Partial Thromboplastin Time
  - Cholesterol/LDL/HDL
  - ANA/RF/Homocysteine/ESR
  - Protein C/ Protein S/ Antithrombin III/ Leiden
  - Anticardiolipin Antibody
  - Lupus Inhibitor/ Antiphospholipid Antibodies
VASCULAR RISK FACTORS

- Modifiable conditions and lifestyle characteristics identified as a risk factors for stroke:

  High blood pressure
  Atrial fibrillation
  Diabetes mellitus
  Carotid artery disease
  Myocardial infarction

  High Cholesterol
  Hyperhomocysteinemia
  Smoking
  Heavy alcohol use
  Physical inactivity
  Obesity
Background

- Independent risk factor for ischemic stroke in men and women
- 2-3 fold increased risk compared to non-smokers\(^1\)
- Spousal cigarette smoking may be associated with an increased stroke risk\(^2\)
- 50% risk reduction by 2 years after stopping smoking\(^3\)

Background

- Increased risk for both ischemic (RR 1.69) and hemorrhagic stroke (RR 2.18) with heavy alcohol consumption (>60g/day)\(^1\)

- BP elevation might be a reasonable explanation\(^3\)

- Light alcohol consumption (<12g/day) associated with reduced ischemic (RR 0.80) and hemorrhagic stroke\(^1\)

- Red wine consumption carries the lowest risk\(^2\)

PHYSICAL ACTIVITY

**Background**

- Regular exercise (at least 3x30min/week) is associated with a decreased risk of stroke.
- Physically active individuals have a lower risk of stroke or death than those with low activity (RR 0.73)<sup>1</sup>
- This is mediated, in part, through beneficial effects on body weight, blood pressure, serum cholesterol, and glucose tolerance<sup>2</sup>

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BODY WEIGHT, DIET, NUTRITION

• Background
  • High body mass index (BMI ≥25) increases risk of stroke in men and women¹
  • Abdominal adiposity is a risk factor for stroke in men but not women²
  • A randomized trial in women found no effect of dietary interventions to reduce the incidence of stroke³
  • Tocopherol and beta carotene supplementation do not reduce the risk of stroke. Vitamin E might increase mortality when used at high-dose (≥400 IU)

Background

- Stroke rates rise rapidly in women after the menopause
- Hormone replacement therapy in postmenopausal women is associated with an 44% increased risk of stroke\(^1\)

1: Gabriel S et al.: Cochrane Review (2005) CD002229
Background

- In low risk persons low dose aspirin reduced coronary events, but not stroke\(^1\)
- In women over 45 years aspirin reduces the risk of ischemic stroke (OR 0.76; 95%CI 0.63-0.93) \(^2\)
- Aspirin reduces MI in patients with asymptomatic carotid artery disease\(^3\)

VITAMINS

- Background
  - Beta carotene increased the risk (RR 1.10) of cardiovascular death\(^1\)
  - Antioxidant supplements may increase mortality\(^2\)
  - Folate, B12, B6 vitamins given to lower homocysteine levels may not reduce stroke recurrence and may increase vascular events\(^3\)

• Background

• Sleep-disordered breathing (SDB) is both a risk factor and a consequence of stroke
• More than 50% of stroke patients have SDB, mostly in the form of obstructive sleep apnoea (OSA).
• SDB is linked with poorer long-term outcome and increased long-term stroke mortality\(^1\)
• Continuous positive airway pressure is the treatment of choice for OSA.

MANAGEMENT OF COMPLICATIONS

- Falls
  - Are common in every stage of stroke treatment
  - Risk factors include cognitive impairment, depression, polypharmacy and sensory impairment\(^1\)
  - A multidisciplinary package focusing on personal and environmental factors might be preventive\(^2\)
  - Exercise, calcium supplements and bisphosphonates improve bone strength and decrease fracture rates in stroke patients\(^3,4\)

MANAGEMENT OF COMPLICATIONS

- Dysphagia and feeding

  - Dysphagia occurs in up to 50% of patients with unilateral hemiplegic stroke and is an independent risk-factor for poor outcome\(^1\)

  - For patients with continuing dysphagia, options for enteral nutrition include NG or PEG feeding

  - PEG does not provide better nutritional status or improved clinical outcome, compared to NG\(^2,3\)

REHABILITATION

- Early rehabilitation
  - More than 40% of stroke patients need active rehabilitation

- Active rehabilitation should start early, providing the patient is clinically stable

- Passive rehabilitation should be given if the patient is unconscious or paralyzed

- Rehabilitation should be continued as long as perceptable recovery is taking place
Multidisciplinary stroke team for rehabilitation

- Stroke physician
- Nurses experienced in stroke management
- Physiotherapist trained in stroke rehabilitation
- Occupational therapist skilled in stroke
- Speech therapist familiar with speech problems in stroke patients
- Neuropsychologist accustomed to stroke rehabilitation
- Social worker familiar with the problems of stroke patients
Calculating Risk

**ABCD2**

To identify individuals at high early risk of stroke after transient ischemic attack.

**A** (Age); 1 point for age ≥60 years,

**B** (Blood pressure ≥ 140/90 mmHg); 1 point for hypertension at the acute evaluation,

**C** (Clinical features); 2 points for unilateral weakness, 1 for speech disturbance without weakness,

**D** (Symptom Duration); 1 point for 10–59 minutes, 2 points for ≥60 minutes.

**D** (Diabetes); 1 point Total scores ranged from 0 (lowest risk) to 7 (highest risk).

**Scale:**
Stroke risk at 2 days, 7 days, and 90 days:
Scores 0-3: low risk
Scores 4-5: moderate risk
Scores 6-7: high risk
Stroke and Multiple Sclerosis

Types of Stroke

**Ischemic** - most common >70%
- Thrombotic
  - Atherosclerosis
- Embolic
  - Emboli form the Heart or Vessels

**Hemorrhagic**
- Intracerebral
  - Hypertension or Amyloid Angiopathy
- Subarachnoid
- Berry Aneurysms
Stroke and Multiple Sclerosis

Thrombotic Strokes

Atherosclerosis
  Internal Carotid
  Middle Cerebral
  Vertebrobasilar

Symptoms
  Slow stepwise progression of symptoms
  Usually preceded by TIA’s

Other Causes
  Lupus anticoagulant
  Polycythemia
  Syphilis
  Thrombocytosis
  Dissecting Aortic Aneurysm
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**Embolic Stroke**

Not usually preceded by TIA

Emboli

Heart

Large Blood vessel

Usually effects middle > posterior > anterior cerebral

Symptoms

Neurodeficits worst at onset

Weakness is greater in distal extremities
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Stroke Symptoms By Region

Middle cerebral
Anterior cerebral
Posterior cerebral
Single Hemisphere
Vertebrobasilar
Lateral Medullary syndrome
Lacunar-small vessel
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Middle Cerebral Artery Occlusion

Contralateral hemiplegia
Contralateral hemianesthesia
Homonymous hemianopsia
Impaired conjugate gaze in opposite direction
Impaired spatial- nondominant
Impaired language-dominant
If lesion high- >loss face/upper ext
If it is in the main trunk- same throughout
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Anterior Cerebral Artery Occlusion
Most affected in distal contralateral leg
Urinary incontinence
Gait abnormalities
If includes corpus callosum the patient will have tactile anomia (cannot name what they touch)
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Posterior Cerebral Artery Occlusion

Contralateral homonymous hemianopsia
Usually upper quadrantanopsia
Mild contralateral hemiplegia/anesthesia
Color anomia = corpus callosum damage
Memory loss
If occlusion bilateral memory will be severe/persistent
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Single Hemisphere injury

Does not affect paraspinal muscles
Does not affect pharynx
Does not affect jaw
Does not affect the forehead
If any or all of the above are affected think:
   Bilateral hemispheric infarct
   Brainstem infarct
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Vertebrobasilar Artery Occlusion

Associated with brain stem strokes
Bilateral extremity motor/sensory dysfunction
Quadraplegia in severe cases
Crossed motor and sensory deficits
Horner syndrome
Cerebellar signs/stupor/coma
Cranial nerve dysfunction
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Lateral Medullary Syndrome
Also called *Wallenberg Syndrome*
Nausea
Vomiting
Nystagmus
Ipsilateral Horner Syndrome
Ipsilateral palate and vocal cord weakness
Ipsilateral face hemianesthesia
Contralateral body hemianesthesia
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Lacunar Strokes

Due to hypertension
Occlusion of very small arterioles
Over time they form cysts in the brain
Pure hemiplegia
Pure hemisensory
Multiple bilateral frontal lobe “lacunes” can cause pseudobulbar palsy
Stroke and Multiple Sclerosis

**Work up:**
- History
- Computerized Tomography Brain
- CBC with platelets
- Troponin
- Electrolytes, Glucose, Bun, Cr, Coagulation profiles
- EKG
- Trans-thoracic Echocardiogram
- Carotid Ultrasound/Trans-cranial Doppler
- MRI/MRI Diffusion/Angiography
Stroke and Multiple Sclerosis

Ischemic Stroke Treatment

- Thrombolysis-Alteplase
  - >18 yrs old with an ischemic stroke Dx
  - Onset time – 3 hours (3-4.5 with caveats)

- Oxygen

- Treat BP-gradually

- Aspirin/Antiplatelets

- Surgical Intervention
  - intra-arterial therapy
  - mechanical thrombectomy
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- **CONTRAINDICATIONS TO ALTEPLASE (tPA)**

  **Absolute** -
  - Intracranial hemorrhage on CT
  - Clinical Presentation suggests subarachnoid hemorrhage
  - Neurological surgery, serious head trauma, or previous stroke past 3 months
  - Uncontrolled hypertension (>185 mmHg SBP or >110 mm Hg DBP)
  - History of intracranial hemorrhage
  - Seizure at stroke onset
  - Known AVM, neoplasm, or aneurysm
  - Active internal bleeding
  - Suspected/confirmed endocarditis
  - Known bleeding diathesis: plts <100,000, heparin with elevated PTT, oral anticoagulants and INR >1.7, thrombin inhibitors
  - Abnormal blood glucose (<50 or >400 mg/dl)

  **Relative** –
  - Only minor or rapidly improving stroke symptoms
  - Patient has had major surgery or serious trauma excluding head trauma in previous 14 days
  - History of GI/Urinary hemorrhage in last 21 days
  - Recent arterial puncture at a noncompressible site
  - Recent lumbar puncture
  - Post myocardial infarction pericarditis
  - Pregnancy

  **Additional WARNINGS to tPA > 3 hr onset** -
  - Age >80
  - History of prior stroke and diabetes
  - Any active anticoagulant use (even with INR <1.7)
  - NIHSS >25
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• Post Acute Care Therapy

Antiplatelets

ASA (60-300 mg)/Aggrenox/Ticlodipine
Clopidogrel
Coumadin
Dabigatran, Apixaban, Rivaroxaben- (non valvular Atrial Fibrillation)

Manage underlying causes

Cardiac- per ACC
HTN- JNC guidelines- >120/80
Diabetes- HbA1C <6.5-7.0
Tobacco abuse management
Hyperlipidemia- LDL <70
If >70% carotid stenosis- surgery in 48 hrs-7 days
Stroke and Multiple Sclerosis

- **CHADS2**

Score for Atrial Fibrillation Stroke Risk

- Congestive Heart Failure: 1pt
- Hypertension: 1pt
- Age > 75: 1pt
- Diabetes Mellitus: 1pt
- Stroke or TIA Symptoms: 2pt

<table>
<thead>
<tr>
<th>Score</th>
<th>Risk Level</th>
<th>Treatment</th>
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<tbody>
<tr>
<td>&gt;2</td>
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<tr>
<td>&gt;1 &lt;2</td>
<td>Moderate</td>
<td>oral anticoagulant or ASA</td>
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<tr>
<td>0</td>
<td>Low</td>
<td>ASA 75-325mg</td>
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Stroke and Multiple Sclerosis

Intracerebral Hemorrhage

Amyloid Angiopathy
- Commonly causes recurrent bleeds
- >65 yrs old
- Subcortical, rarely affects deep structures
- Can cause multi-infarctional dementia
- Also found in Alzheimer's patients—unclear association
- Occasionally can be associated with subarachnoid
Intracerebral Hemorrhage

Hypertension
Gradual and smooth onset of symptoms
Putamen > Thalamus > Pons > Cerebellum

Putamen
- Contralateral hemiparesis/sensory loss/hemianopsia
- Acts just like a middle cerebral infarct

Thalamus
- Contra hemiplegia/hemianesthesia/sensory > motor

Pons
- Coma/pinpoint pupils/complete paralysis
- Can have decerebrate posturing bilaterally

Cerebellum
- Acute dizziness/ataxia/vomiting
- No mentation change or loss of consciousness
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Subarachnoid Hemorrhage

Cerebral saccular aneurysm bleed
   Usually Circle of Willis
   IC=40%/AC=35%/MC=20%
Hypertensive hemorrhages with ventricular rupture
A-V Malformations
Symptoms
   Acute/Severe headache (thunderclap)-unresponsive to meds
   May be alert/confused /comatose
   No focal neurological signs
   Neck stiffness is classic- but not always present
Stroke and Multiple Sclerosis

• Hemorrhagic Stroke Work Up

- Computerized Tomography (CT misses 10% of Bleeds)
- Lumbar Puncture
- Xanthochromic supernatent is diagnostic
- If LP (-) can be hours before blood gets in CSF
- Cerebral Angiography
- Can rebleed in 24 hours/Vasospasm

Treatment

- Neurosurgery consult/Intervention
- ABC’S/ Intracranial Pressure monitoring
- Hemodynamic and edema management/Nimodipine/Mannitol/Glycerol/Saline
- Seizure management
Stroke and Multiple Sclerosis

**Multiple Sclerosis**
Myelin deterioration
- Brain-
- Spinal Cord-
- Optic Nerve -

**Pathophysiology**
10x more common in northern latitudes
May be viral in origin— Female 2:1 Males
Autoimmune but does have genetic components
Onset 20-50 yrs of age

**Plaques**
- Cause a mononuclear inflammation
- Demyelination with axonal sparing
- Oligodendrogial cell loss and astrocyte proliferation
- Long standing lesion Astrogliosis
Stroke and Multiple Sclerosis

Symptoms

Mononeuropathy +/- multiplex
Optic neuritis
Ophthalmoplegia/Ophthalmoparalysis-
Intermittent Diplopia
Extremity weakness
Tremors
Lhermitte sign-
(Paresthesias radiating down the spine into extremities on neck flexion)
Multiple Sclerosis - H&E STAIN
Stroke and Multiple Sclerosis

• Types of Multiple Sclerosis

Clinically Isolated Syndrome (CIS)
  No occurrence after initial

Relapsing-remitting
  Most common
  Has attacks followed by none then reoccurs

Primary-Progressive
  Men
  Gradual decline few plateaus

Secondary-progressive
  Stage II relapsing-remitting. No periods of remission

Progressive-relapsing
  Rare. Progressive form until the end

Malignant (Marburg Variant)
  Very rare. Decline to death in few months
Stroke and Multiple Sclerosis

- McDonald Criteria: (attack must last 24 hours and 30 day interval)

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<tr>
<th>Attacks</th>
<th>Lesions</th>
<th>Additional Information</th>
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<td>Dissemination in space or further attack</td>
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<td>1</td>
<td>Dissemination space/time or further attack</td>
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<tr>
<td>0</td>
<td></td>
<td>1 yr of disease progression and 2 of below:</td>
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<tr>
<td></td>
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<td>Positive MRI Brain</td>
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<tr>
<td></td>
<td></td>
<td>Positive MRI Spinal Cord</td>
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<tr>
<td></td>
<td></td>
<td>Positive CSF</td>
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</tbody>
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Stroke and Multiple Sclerosis

- Diagnostic Tests
  - MRI – TEST OF CHOICE - Brain/Spinal Cord
    - White plaques lesions
  - Evoked Action Potentials
    - Silent lesions
  - Lumbar Puncture
    - Increased IgG / Oligoclonal IgG bands in CSF
    - Elevated protein
Stroke and Multiple Sclerosis
Stroke and Multiple Sclerosis
Stroke and Multiple Sclerosis

Treatment*

Acute Phase/Initial
- Steroids  500mg daily x 5 days
- Plasma exchange for severe deficits with poor response to steroids

Oral Immunomodulator-
- Fingolimod (Gilenya), Ampyra,Aubagio, Tecfidera

Relapsing-Remitting- most common
- Beta-interferons (1-a,1-b)-
  -Avonex/Rebif/Betaseron/Extavia/Plegridy
- Monoclonal Antibodies-
  -Tysarbi
  -Alemtuzumab (Lemtrada)- HIV negative

Copolymer-
- Copaxone/Glatoba

Primary Progressive
- Ocrevus (ocrelizumab)

Chronic/Advanced
- Novantrone (mitoxantrone)- IV

*Ambulation difficulties treatment is Ambyra (helps with MS ambulation only)
Stroke and Multiple Sclerosis

- 34 yr old with history of ataxia, ophthalmoplegia and paresthesia of the legs intermittently with a massive weight loss over the past few months.
- His history is significant for HIV and has been on gancyclovir and protease inhibitors and T-cell counts have remained <200.
- His mentation is going quickly and he has no memory and has stopped eating.

- **What is your diagnosis?**
Stroke and Multiple Sclerosis

Answer

PML

Progressive Multifocal Leukencephalopathy

PML is caused by the JC Virus but there are some drugs that can create a reversible leukencephalopathy.
Stroke and Multiple Sclerosis

Central Pontine Myelinolysis

- Occurs in patients with severe hyponatremia
- Their sodium is corrected too aggressively
- Quadraparesis
- Mutism
- Pseudobulbar palsy
- Swallowing dysfunction

Treatment

Correct Na slowly and treat underlying cause